日本骨髄腫学会誌
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第46回 The 46th Annual Meeting of the Japanese Society of Myeloma
日本骨髄腫学会学術集会

プログラム・抄録集

温故知新

会 期 2021年5月29日(土)～30日(日)

会 場 ザ・セレクトン福島

会 長 坂井　晃 (福島県立医科大学医学部　放射線生命科学講座　教授)

運営準備室　日本コンベンションサービス株式会社
コンベンション事業部 メディカル部
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TEL: 03-3508-1214　FAX: 03-3508-1302　Email:46jsm@convention.co.jp

命を明日につなぐ。希望は世界中にある。

課題と国境を越えて、人々の明日をひらく製薬会社、ヤンセンファーマ。

世界のすべてが、私たちの研究室。
病と懸命に闘う患者さんのために、
高い科学技術、独創的な知性、
世界中の力を合わせ、新しい可能性を切り拓く。

すべては、私たちの解決策を待つ、ひとつの命のために。
複雑な課題にこそ挑んでいく。
新しい薬を創るだけではなく、それを最適な方法で提供する。

革新的な薬や治療法を、届ける。
世界中に、私たちを待つ人がいる限り。

誰もが健やかに、いきいきと暮らす社会。
そんな「当たり前」の願いのために、
自ら変化し、努力を続けます。

Janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson

ヤンセンファーマ株式会社
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第46回 日本骨髄腫学会学術集会

プログラム・抄録集

目　次

会長挨拶…… 3
プログラム編成と一般演題(プレナリー・ポスター)の
査読・評価の方法について…… 4
アクセスマップ…… 5
会場案内図…… 6
参加者へのご案内…… 8
発表者へのご案内……11
日程表（Schedule）……16
プログラム（Programs）……21
会長講演（Presidential Lecture）……41
特別講演（Special Lecture）……45
シンポジウム温故知新
(Symposium -Discover new truths by studying the past-)……49
2020年日本多発性骨髄腫学会奨励賞受賞講演
(JSM Research Award Lecture)……65
2020年骨髄腫患者会助成金受賞講演
(Multiple Myeloma Research Grant from Myeloma
Patients and Families, Japan Award Lecture)……69
プレナリー（Plenary）……73
ポスター発表（Poster Presentation）……81
共催セミナー（Co-sponsored Seminars）…… 127
次回学術集会のご案内…… 139
過去の学術集会一覧…… 140
協賛企業一覧…… 141

第 46 回日本骨髄腫学会学術集会 事務局

福島県立医科大学医学部　放射線生命科学講座
〒 960-1295 福島県福島市光が丘 1 番地

会長挨拶

第 46 回日本骨髄腫学会学術集会　会長
（福島県立医科大学医学部　放射線生命科学講座）

坂井　晃

この度、第 46 回日本骨髄腫学会学術集会会長を拝命いたしました、福島県立医科大学放射線生命科学講座の坂井　晃です。本学術集会は、2021 年 5 月 29 日（土）、30 日（日）に福島市で開催いたします。2011 年の東日本大震災と東京電力（株）福島第一原子力発電所の事故による甚大な被害から復興中の福島で、震災後 10 年の節目に開催できることを大変嬉しく存じます。

さて多発性骨髄腫の治療は、プロテアソーム阻害薬、免疫調節薬、ヒストン脱アセチル化酵素阻害薬、抗体薬といった多様な薬剤選択が可能となり、明らかに骨髄腫患者の生存期間が延長してきておりますが、それら薬剤の組合せ方や治療開始時期、維持療法のあり方など多くの課題があるのも事実です。

第 46 回の学術集会では、これらの新規治療薬の情報だけでなく、もう一度多発性骨髄腫という疾病がどういうものか見つめ直すため、学術集会のテーマを「温故知新」としました。骨髄腫の治療開始時期は、現状では基本的に CRAB（高 Ca 血症、腎機能障害、貧血、骨病変）のいずれかを認める症候性骨髄腫からということになっておりますが、骨髄腫においてこれら CRAB が生じる機序と意義を見直し理解を深めることで、骨髄腫の治療が今後さらに発展することを期待します。実際、骨髄腫における貧血の機序は十分に解明されておりません。また骨髄腫で正常免疫グロブリンが抑制される機序も不明です。

骨髄腫に興味をお持ちの若い方には治療方法だけではなく、骨髄腫の基礎研究や斬新な診療方法をご紹介いただき、活発な議論を交わしていただきたいと思います。また第 46 回の学術集会では、2020 年度の日本骨髄腫学会奨励賞及び骨髄腫患者会助成金を受賞された計 4 人の方に研究内容をご講演いただく予定です。

なお、過日よりご案内の通り、本学術集会は新型コロナウイルスの感染拡大を鑑み、感染対策を徹底した上で、現地開催とウェブを併用したハイブリッド開催といたします。（会場はザ・セレクトン福島のみといたします。）感染状況が好転しているとは言い切れないものの、医療従事者を中心としたワクチン接種も開始し、2 年ぶりの学術集会にてより多くの皆様に福島の地でお目にかかれることを楽しみにしています。

福島県は豊かな温泉に恵まれ、また日本一の日本酒の産地です。5 月末の新緑の福島を堪能していただければ幸いです。一人でも多くの方の来福をお待ちしております。

プログラム編成と一般演題（プレナリー・ポスター）の査読・評価の方法について

本学術集会のプログラム編成および一般演題の査読・評価方法について、以下のように進めましたので、会員の皆様にご報告いたします。

1）プログラム委員は、27 名で構成されました。

2）以下の 4 項目でプログラム委員に採点をしていただき、その採点結果に基づき会長・プログラム委員長がプログラム案を作成いたしました。

①倫理構成 / 記述の正確性　②方法･結果の妥当性　③重要性 / 貢献度　④新規性 / オリジナリティ

3）一般演題は、以下の 8 つのカテゴリで募集をさせていただきました。

①病因・基礎、病態解析　②検査・診断関連　③移植適応患者の治療関連
④移植非適応患者の治療関連　⑤合併症、支持療法、メディカルスタッフ関連
⑥アミロイドーシス・POEMS 症候群・その他
⑦臨床試験・臨床研究および治療に関する基礎研究　⑧症例報告

その結果、国内外で計 61 演題のご応募をいただきました。

4）一般演題の査読は、プログラム委員 27 名によって行われました。各演題につき 3 名が独立して査読を行い、判定基準に従って 1 ～ 5 点の 5 段階で評価しました。

ご協力いただきましたプログラム委員を掲載させていただき、この場を借りて深謝いたします。

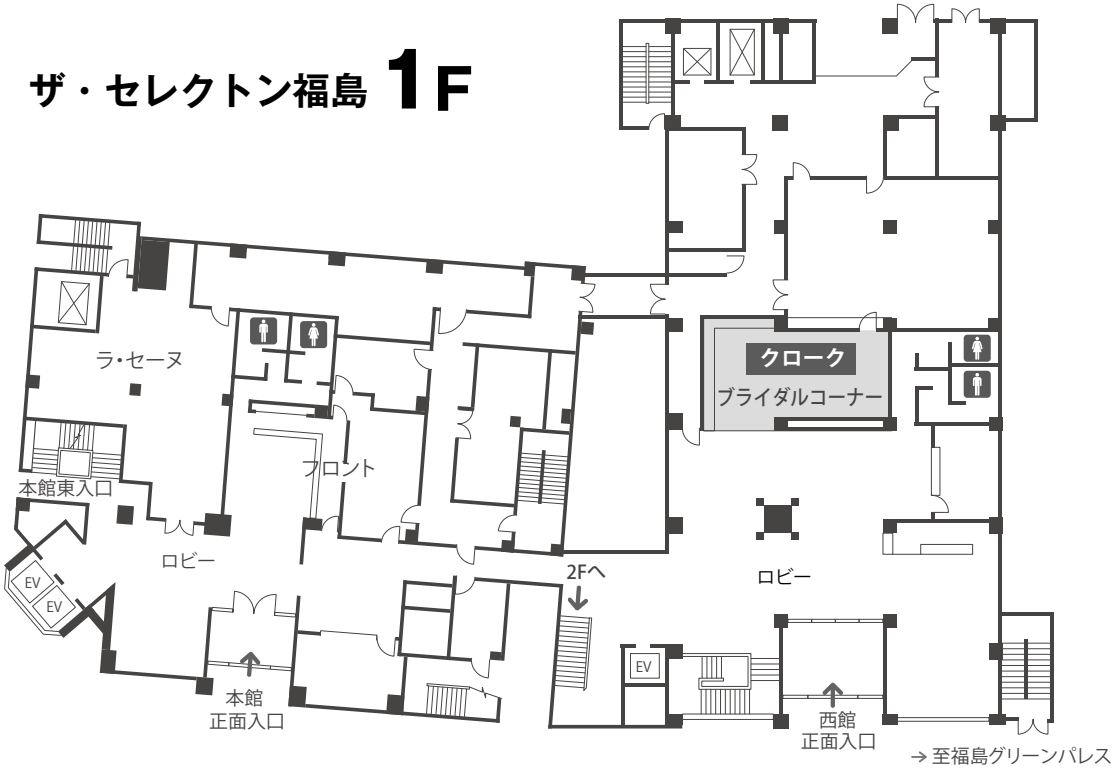
第 46 回日本骨髄腫学会学術集会　プログラム委員　※敬称略、50 音順

石橋真理子（日本医科大学微生物学・免疫学）
一井　倫子（大阪大学大学院医学系研究科　血液・腫瘍内科学講座）
伊藤　薫樹（岩手医科大学　血液腫瘍内科）
今井　陽一（東京大学医科学研究所附属病院血液腫瘍内科）
上田　真寿（自治医科大学　内科学講座　血液学部門）
尾崎　修治（徳島県立中央病院血液内科）
河野　　和（熊本大学病院　血液内科）
菊池　次郎（自治医科大学分子病態治療研究センター幹細胞制御研究部）
黒田　純也（京都府立医科大学大学院医学系研究科血液内科学）
黒田　芳明（国立病院機構　広島西医療センター）
小杉　浩史（大垣市民病院血液内科）
堺田惠美子（千葉大学医学部附属病院　血液内科）
柴山　浩彦（国立病院機構　大阪医療センター　血液内科）
角南　一貴（国立病院機構岡山医療センター）
高松　博幸（金沢大学）
竹迫　直樹（災害医療センター）
田村　秀人（獨協医科大学埼玉医療センター）
塚田　信弘（日本赤十字社医療センター）
得平　道英（埼玉メディカルセンター）
花村　一朗（愛知医科大学血液内科）
原田　武志（徳島大学大学院　医歯薬学研究部血液・内分泌代謝内科学分野）
半田　　寛（群馬大学大学院医学系研究科・内科学講座血液内科学分野）
三木　浩和（徳島大学病院　輸血・細胞治療部）
三村　尚也（千葉大学医学部附属病院　輸血・細胞療法部）
安井　　寛（東京大学医科学研究所）
横山　明弘（国立病院機構　東京医療センター　血液内科）
李　　政樹（名古屋市立大学病院　輸血・細胞療法部）

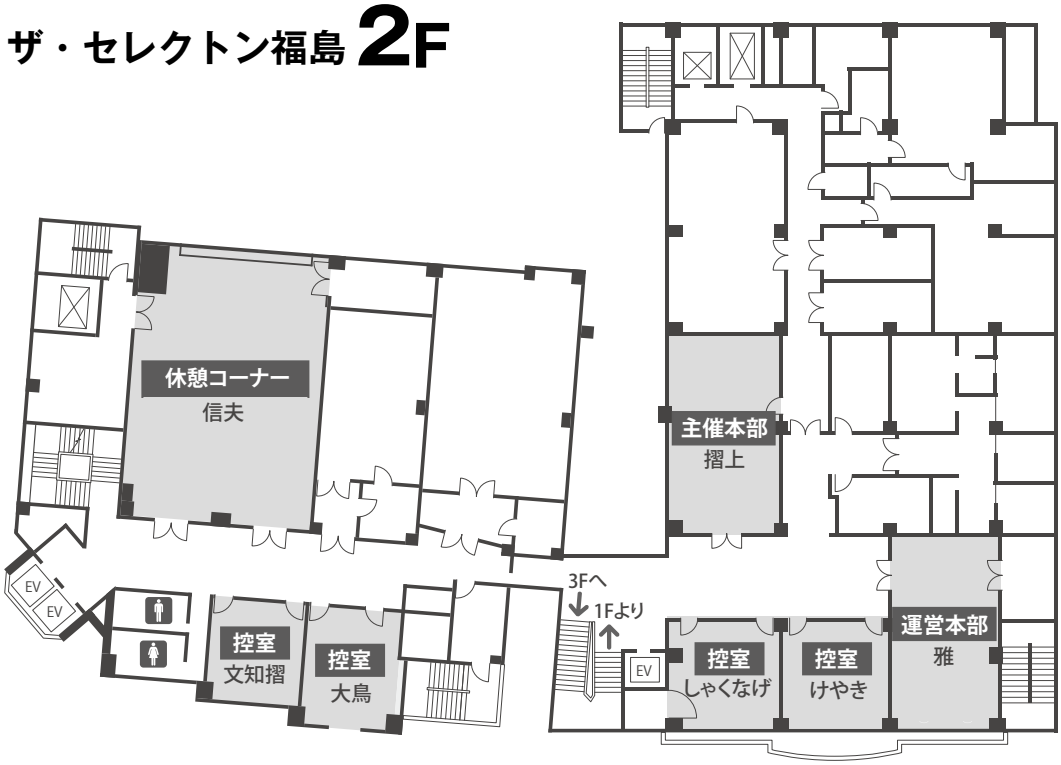
アクセスマップ


東　口
至仙台
JR 福島駅
至東京
西　口
あづま陸橋
●バス
ターミナル
●タクシー
のりば
●一般車
乗降場
●駐輪場
東邦銀行
高湯街道
イトーヨーカ堂
ザ・セレクトン福島
福島民報社
支払
基金
入口
指定駐車場
至福島西 I.C

ザ・セレクトン福島 1F



ザ・セレクトン福島 2F



ザ・セレクトン福島 3F

参加者へのご案内

第 46 回日本骨髄腫学会学術集会は新型コロナウイルス感染症の拡大に伴い、従来の現地開催とウェブ配信を併用したハイブリッド開催といたしました。

【開催期間】
ライブ配信（主題セッション）：5/29（土）・30（日）
オンデマンド配信（ポスター発表）：5/29（土）～ 6/30（水）
※音声付スライドデータ掲載のみ
オンデマンド配信（主題セッション）：6/15（火）～ 6/30（水）
※ライブ配信した映像をオンデマンド配信いたします。

1. 参加登録方法

本学術集会はハイブリッド開催に際し、参加者全員にオンライン参加登録をお願いしております。
詳細は本学術集会ホームページをご確認ください。

2. 参加登録期間

2021 年 5 月 12 日（水）～ 6 月 30 日（水）

3. 参加費

※以下の参加費でライブ配信・オンデマンド配信ともに視聴可能です。
※現地参加・ウェブ参加問わず参加費は一律で以下の通りです。

医師	10,000 円
メディカルスタッフ	5,000 円
企業	10,000 円
患者	2,000 円
新研修制度における初期研修医	無料[*1]
非 M.D. の大学院生・学部生・留学生	無料[*2]

[*1]「参加費免除申請書」をご提出ください。
[*2]「参加費免除申請書」とともに「学生証のコピー」をご提出ください。
参加費免除申請書は本学術集会のホームページからダウンロード可能です。
参加費免除申請書や学生証のコピーの提出方法は本学術集会ホームページの「オンライン参加登録」ページに記載いたします。

4. ネームカード発券

場所：総合案内（ザ・セレクトン福島　3 階　吾妻Ⅱ）
時間：5 月 29 日（土）8：00 ～ 16：40
　　5 月 30 日（日）7：30 ～ 15：30
オンライン参加登録をお済ませの上、総合案内にてネームカードをお受け取りください。
※ネームカードを着用されていない方の講演会場等への入場はできません。

5. 抄録集販売

総合案内にて 1 冊 1,000 円にて抄録集を販売いたします。

6. ランチョンセミナー整理券

【現地参加の場合】

1） オンライン参加登録時に聴講予定のランチョンセミナーをご選択ください。

2） 会期当日に総合案内にてネームカードをお渡しする際に、整理券をお渡しいたします。再発行は行いませんので、大切に保管してください。

3） ランチョンセミナーの開始前に各会場前で整理券を回収いたします。

【ウェブ参加の場合】

ウェブ参加での聴講者数の制限はございません。開始時間になりましたら、聴講を開始してください。

7. モーニングセミナー・スポンサードシンポジウム整理券

【現地参加の場合】

整理券の配布はございませんので、直接会場へお越しください。

【ウェブ参加の場合】

ウェブ参加での聴講者数の制限はございません。開始時間になりましたら、聴講を開始してください。

8. 事務局受付

事務局受付は設置いたしません。

本年度の会費納入や新入会については、以下の日本骨髄腫学会事務局へお問い合わせください。

日本骨髄腫学会事務局

〒 371-8511　群馬県前橋市昭和町 3 丁目 39-22

国立大学法人群馬大学　大学院医学系研究科　血液内科学講座内

FAX：027-220-8173　Email: jsm-info@jsmm.or.jp

事務局責任者：半田　寛

担当：青山　明日香

※事務局あてのご連絡は E メールにてお願い申し上げます。

9. クローク

場所：ザ・セレクトン福島　西館 1 階　ロビー前（ブライダルコーナー）

※貴重品、パソコン、傘はお預かりできませんので、予めご了承ください。

10. 休憩スペース

場所：ザ・セレクトン福島　2 階　信夫

会期中、上記に休憩スペースを設けております。

11. ホスピタリティスペース

場所：ザ・セレクトン福島　3 階　吾妻Ⅱ

時間：5 月 29 日（土）8：00 ～ 16：40

5 月 30 日（日）7：30 ～ 15：30

共催：ヤンセンファーマ株式会社

12.Free Wi-Fi のご案内について

場所	SSID	パスワード
「第 1 会場」内	Adatara3011-g	0245311111
	Adatara3011-a	
「総合案内・第 2 会場」内	AzumaH3021-g	
	AzumaH3021-a	
「信夫」内	Shinobu2001-gw	
	Shinobu2201-ga	
本館・西館 3 階全般	AzumaWH3022-a	
	AzumaWH3022-g	
本館 2 階	ShinobuWH2021-a	
	ShinobuWH2021-g	
西館 2 階	SurikamiH2011-g	
	SurikamiH2011-a	

発表者へのご案内

1. 発表方法

会場での発表、ウェブからの発表を選択可能です。

2. セッションごとの発表形式

セッション種別	講演動画（音声付スライドデータ）作成	発表方法	
		現地登壇	ウェブ登壇
特別講演	×	PowerPoint にて発表データを作成し、講演会場で登壇	PowerPoint にて発表データを作成し、Zoom にて画面共有で登壇
会長講演	×		
シンポジウム温故知新	×		
2020 年日本多発性骨髄腫学会奨励賞受賞講演	×		
2020 年骨髄腫患者会助成金受賞講演	×		
プレナリー	○	事前提出された講演動画をオペレーターが放映し、質疑のみライブで行う	事前提出された講演動画をオペレーターが放映し、質疑のみ Zoom にてライブで行う
ポスター発表（オンデマンド配信）	○	なし（オンデマンド配信のため）	なし（オンデマンド配信のため）

3. 発表時間および討論・質疑時間

セッション種別	発表時間	討論・質疑時間
特別講演	45 分	5 分（質疑）
会長講演	30 分	なし
シンポジウム温故知新	セッションごとに設定	
2020 年日本多発性骨髄腫学会奨励賞受賞講演	12 分	3 分（質疑）
2020 年骨髄腫患者会助成金受賞講演		
プレナリー	7 分	3 分（質疑）
ポスター発表（オンデマンド配信）	5 分	なし

4. セッションごとの実施方法

1）特別講演、会長講演、シンポジウム温故知新、2020 年日本多発性骨髄腫学会奨励賞受賞講演、2020 年骨髄腫患者会助成金受賞講演：

（現地参加の場合）

当日、会場にてご発表ください。

※事前の発表データのご提出はございません。当日 PC 受付にて確認・試写をお願いいたします。

（ウェブ参加の場合）

事前に Zoom の URL をお送りいたします。

当日は Zoom にご入室の上、「画面共有」にてご発表ください。

※事前の発表データのご提出はございません。Zoom の操作方法等は別途個別にご案内いたします。

2）プレナリー：

（現地参加の場合）

事前に音声付スライドデータを作成し、運営準備室へご提出ください。

当日は、発表を音声付スライドデータの放映（運営準備室にて対応）、質疑をライブにてお願いいたします。

※音声付スライドデータの作成方法等は別途個別にご案内いたします。

（ウェブ参加の場合）

事前に Zoom の URL をお送りいたしますので、Zoom にご入室ください。

事前に音声付スライドデータを作成し、運営準備室へご提出ください。

当日は、発表を音声付スライドデータの放映（運営準備室にて対応）、質疑をライブ（Zoom より）にてお願いいたします。

※ Zoom の URL や音声付スライドデータの作成方法等は別途個別にご案内いたします。

3）ポスター発表（オンデマンド配信）：

オンデマンド配信のため、会期当日の発表・質疑はございません。

事前に音声付スライドデータを作成し、運営準備室へご提出ください。

オンデマンド配信期間（5/29（土）～ 6/30（水））にウェブ上で閲覧が可能です。

5. 発表データの作成について

本学術集会では、すべてのセッションにおいて以下の通りといたします。

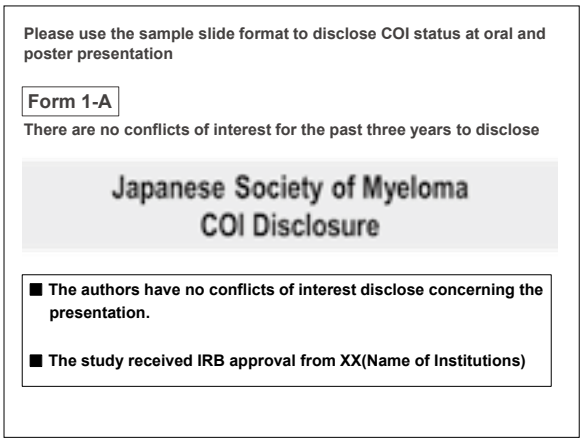
スライド：英語のみ

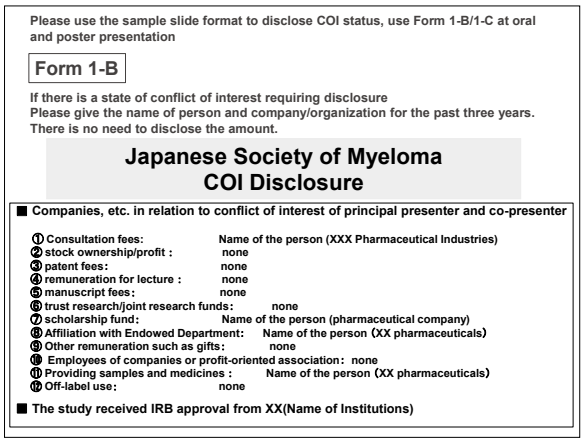
発表言語：日本語、英語どちらでも可

6. 利益相反の開示について

発表スライドの最初または、演題・発表者などを紹介するスライドの次に利益相反（COI）状態を開示してください。

【掲示ポスターサンプル】





7. 発表データの受付（現地参加の場合のみ）

※ウェブ上で登壇の場合は、別途個別にご案内済みです。

ご発表の 30 分前までにザ・セレクトン福島 3 階の PC 受付にお越しいただき、データの確認、試写を行ってください。

受付時間：

5 月 29 日（土）8：15 ～ 16：40

5 月 30 日（日）8：15 ～ 15：30

8. 当日の流れについて（現地参加の場合のみ）

※ウェブ上で登壇の場合は、別途個別にご案内済みです。

ご自身の発表の 10 分前にはスクリーンに向かって左前方の次演者席にお越しください。
セッションの進行は、座長の指示に従い、時間厳守でお願いいたします。

9. 発表機材（現地参加の場合のみ）

	Windows	Mac
PC 本体の持込	○	○
メディアの持込 （USB メモリー）	○	×
アプリケーション	PowerPoint 2010，2013，2016，2019	PowerPoint、Keynote
動画ソフト	Windows Media Player	—

※ Mac でプレゼンテーションデータを作成された場合はご自身のパソコンをご持参ください。
※本学会は、PC プレゼンテーションのみの発表といたします。
※動画ファイルがある場合は、パソコン本体のお持込みをお奨めいたします。
【データのみ持ち込まれる方へ】

1．当日は発表予定時間の 30 分前までに「PC 受付」にて試写用パソコンで発表データの確認を行ってください。
（データのお持込みは、発表日以外でも受付けます。）
2．お持込みいただけるメディアは以下の通りです。
・USB フラッシュメモリー
※ メディアは、ウイルス定義データを最新のものに更新された状態のセキュリティーソフトで、メディアにウイルスが感染していないことをご確認いただいた上でお持込みください。
3．OS とアプリケーションは以下のものをご用意します。
・OS：Windows 10
・アプリケーション：Windows 版 PowerPoint 2010、2013、2016、2019
4．フォントは OS（Windows）に標準のもののみ、ご用意いたします。
5．発表に使用する PC は全てフル HD（1980 × 1080）に統一してあります。
6．動画や音声をご使用になる場合は、データ登録の際に必ずお知らせください。
7．動画などの参照ファイルがある場合は、全てのデータを同じフォルダに入れてください。
※動画ファイルの注意点
Windows の場合 Windows10（OS）及び WindowsMediaPlayer12 の初期状態に含まれるコーデックで再生できる動画ファイルをお持ちください。（動画ファイルは WMV 形式を推奨します。）
8. 発表データ作成後、作成したパソコン以外のパソコンで正常に動作するかチェックしてください。
9. 発表会場ではデータの修正はできませんので、予めご了承ください。
10. 試写が終了しましたらデータはご発表会場まで転送されます。
11. 発表時には、ご発表データの 1 枚目をスライドショー状態でスクリーンに映写しますので、演台上のマウス、キーパッドで、ご自身でデータの送りの操作を行ってください。
12. ご発表データは、「PC 受付」のサーバと会場のパソコンにご発表データを一時保存いたしますが、これらのデータは本学会終了後、責任を持って廃棄します。

発表者へのご案内

【ノートパソコンを持ち込まれる方へ】

1．発表予定時間の 30 分前までに「PC 受付」へお越しください。
2．「PC 受付」の試写用モニターにてケーブルの接続を確認してください。
3．「PC 受付」では HDMI のケーブルをご用意いたします。
4．一部のノートパソコンでは本体附属（別売り）のコネクターが必要な場合がありますので、必ずお持ちください。

D-sub15 ピン（ミニ）	付属外部出力ケーブル　例
	

5．ノートパソコンから外部モニターに正しく出力されるか確認してください。
6．個々のパソコンや OS により設定方法が異なりますので、事前にご確認ください。
7．デスクトップ上の分かりやすい場所に発表データのショートカット（エイリアスを「演題番号 _ 演者名」として作成してください。（例：O-1_ 骨髄腫太郎）
8．画面の解像度はフル HD（1980 × 1080）です。
9．動画や音声をご使用になる場合は、発表データ確認の際に必ずお知らせください。
10. 予め、スクリーンセーバー、省電力設定を解除してください。
11. 起動時にパスワード等を設定している場合は、必ず解除しておいてください。
12. 会場にて電源をご用意しておりますので､AC アダプターを必ずお持ちください。ご発表予定時間の 30 分前位（講演中でもかまいません）に会場内左手前方演台付近の PC デスクまでお越しのうえ、スタッフに、PC をお渡しください。スタッフが、ケーブルを接続し、外部出力の確認を行います。
13. ご発表時には、演台にセットされているモニター、マウス、キーパッドをご使用ください。発表者ツールのご使用はできません。
14. 念のため、バックアップデータを必ずお持ちください。
15. 発表会場ではデータの修正はできませんので、予めご了承ください。
16. 先に PC を預けた会場内左手前方演台付近の PC デスクで、パソコンをご返却いたします。講演終了後 PC デスクのスペースの問題がありますので、出来るだけ速やかに PC のお引取りをお願いします。

会議のご案内

理事会
日時：別途学会事務局よりご案内
会場：ウェブ開催（別途学会事務局よりご案内）

代議員会
日時：別途学会事務局よりご案内
会場：ウェブ開催（別途学会事務局よりご案内）

日程表

5月29日（土）

会場名	第1会場	第2会場
部屋名	安達太良Ⅰ＋Ⅱ （3F）	吾妻Ⅰ （3F）
8:00		
9:00	**開会式**　8:50－9:00	
	シンポジウム温故知新 1 9:00－10:30 **骨病変・貧血** **座長**：李　政樹、堺田　惠美子 **演者**：安倍　正博、高須　深雪、三輪　哲義、 原田　武志、磯田　淳、三木　浩和	
10:00		
	特別講演 1 10:40－11:30 **多発性骨髄腫における免疫調節薬：我々はどこまで識りえたか？** **座長**：安井　寛　　**演者**：秀島　輝	
11:00		
12:00	**ランチョンセミナー 1**　12:00－12:50 **新たな再発難治性多発性骨髄腫の治療戦略 -IsaPd療法を基礎と臨床から考える-** **座長**：角南　一貴　　**演者**：古川　雄祐、石田　禎夫 **サノフィ株式会社**	**ランチョンセミナー 2**　12:00－12:50 **多発性骨髄腫におけるT細胞免疫不全と免疫治療戦略** **座長**：黒田　純也　　**演者**：田村　秀人 **セルジーン株式会社 / ブリストル・マイヤーズ スクイブ株式会社**
13:00	**総会** 13:00－13:30	
14:00	**会長講演**　13:50－14:20 **正常Bリンパ球由来iPS細胞を用いた骨髄腫起源細胞の探索** **座長**：麻奥　英毅　　**演者**：坂井　晃	
15:00	**シンポジウム温故知新 2** 14:40－15:40 **腎障害・染色体異常** **座長**：高松　博幸、石橋　真理子 **演者**：風間　順一郎、花村　一朗、北山　智草、北舘　明宏	
16:00	**スポンサードシンポジウム1**　15:50－16:40 **多発性骨髄腫の治療戦略** **座長**：半田　寛　　**演者**：鈴木　一史、塚田　信弘 **武田薬品工業株式会社**	
17:00		
18:00		
19:00		
20:00		

※ポスター発表はオンデマンド配信いたします。

5月30日（日）

会場名	第1会場	第2会場
部屋名	安達太良Ⅰ＋Ⅱ （3F）	吾妻Ⅰ （3F）
8:00	**モーニングセミナー 1**　8:00－8:40 **地域医療における高齢者/Frailの骨髄腫治療** **座長：**竹迫　直樹　　**演者：**花本　仁 **武田薬品工業株式会社**	**モーニングセミナー 2**　8:00－8:40 **診療に役立つ全身性ALアミロイドーシスの診断と評価のコツ** **座長：**鈴木　憲史　　**演者：**加藤　修明 **ヤンセンファーマ株式会社 メディカルアフェアーズ本部**
9:00	**シンポジウム温故知新 3** 8:50－9:50 **AL型アミロイドーシス** **座長：**三村　尚也、上田　真寿 **演者：**田崎　雅義、塚田　信弘、淵田　真一、甲田　素子	
10:00	**2020年日本多発性骨髄腫学会奨励賞受賞講演**　10:00－10:30 **座長：**菊池　次郎 **演者：**池田　翔、石橋　真理子	
	2020年骨髄腫患者会助成金受賞講演　10:30－11:00 **座長：**今井　陽一 **演者：**山本　雄介、一井　倫子	
11:00		
12:00	**ランチョンセミナー 3**　11:20－12:10 **再発難治骨髄腫に対するカルフィルゾミブ含有治療戦略のエビデンスと実際** **座長：**安倍　正博　　**演者：**黒田　純也 **小野薬品工業株式会社**	**ランチョンセミナー 4**　11:20－12:10 **免疫調節薬に焦点を当てた多発性骨髄腫における至適な初回および継続的治療戦略** **座長：**石田　禎夫　　**演者：**田中　宏和 **セルジーン株式会社 / ブリストル・マイヤーズ スクイブ株式会社**
13:00	**特別講演 2**　12:30－13:00 **分子細胞遺伝学によるt(11;14)(q13;q32)を持つ骨髄腫の生物学** **座長：**服部　豊　　**演者：**三浦　偉久男	
	スポンサードシンポジウム2　13:10－14:00 **Daratumumabと未治療移植非適応多発性骨髄腫の新しい世界-基礎・臨床から-** **座長：**池田　宇次　　**演者：**北舘　明宏、石田　禎夫 **ヤンセンファーマ株式会社**	
14:00		
15:00	**プレナリー** 14:10－15:20 **座長：**伊藤　薫樹、得平　道英	
	閉会式　15:20－15:35	
16:00		
17:00		
18:00		
19:00		
20:00		

※ポスター発表はオンデマンド配信いたします。

Schedule

Day 1: May 29, 2021

会場名	Room 1	Room 2
部屋名	Adatara I + II (3F)	Azuma I (3F)
8:00		
9:00	**Opening Ceremony** 8:50 - 9:00	
	Symposium -Discover new truths by studying the past- 1 9:00 - 10:30 **Bone lesion・Anemia** **Chairpersons:** Masaki Ri, Emiko Sakaida **Speakers:** Masahiro Abe, Miyuki Takasu, Akiyoshi Miwa, Takeshi Harada, Atsushi Isoda, Hirokazu Miki	
10:00		
11:00	**Speacial Lecture 1** 10:40 - 11:30 **Immunomodulatory drugs in multiple myeloma: How far have we come?** **Chairperson:** Hiroshi Yasui **Speaker:** Teru Hideshima	
12:00	**Luncheon Seminar 1** 12:00 - 12:50 **New treatment strategy for relapsed and refractory multiple myeloma -Understand IsaPd regimen based on basic and clinical-** **Chairperson:** Kazutaka Sunami **Speakers:** Yusuke Furukawa, Tadao Ishida **【Sanofi K.K.】**	**Luncheon Seminar 2** 12:00 - 12:50 **Mechanisms of T cell immune dysfunction and immunotherapeutic strategies in multiple myeloma** **Chairperson:** Junya Kuroda **Speaker:** Hideto Tamura **【Celgene K.K. / Bristol-Myers Squibb K.K.】**
13:00	**General Assembly** 13:00 - 13:30	
14:00	**Presidential Lecture** 13:50 - 14:20 **Study for exploring myeloma-initiating cell using normal B cell-derived induced pluripotent stem cells** **Chairperson:** Hideki Asaoku **Speaker:** Akira Sakai	
15:00	**Symposium -Discover new truths by studying the past- 2** 14:40 - 15:40 **Renal insufficiency・Choromosomal abnormality** **Chairpersons:** Hiroyuki Takamatsu, Mariko Ishibashi **Speakers:** Junichiro James Kazama, Ichiro Hanamura, Chigusa Kitayama, Akihiro Kitadate	
16:00	**Sponsored Symposium 1** 15:50 - 16:40 **Treatment Strategies for Multiple Myeloma** **Chairperson:** Hiroshi Handa **Speakers:** Kazuhito Suzuki, Nobuhiro Tsukada **【Takeda Pharmaceutical Company Limited】**	
17:00		
18:00		
19:00		
20:00		

＊ Poster Presentation is available on-demand streaming.

Day 2: May 30, 2021

会場名	Room 1	Room 2
部屋名	Adatara I + II (3F)	Azuma I (3F)
8:00	**Morning Seminar 1** 8:00 - 8:40 **Multiple myeloma treatment for Elderly / Frail in community medicine** **Chairperson:** Naoki Takezako **Speaker:** Hitoshi Hanamoto **【Takeda Pharmaceutical Company Limited】**	**Morning Seminar 2** 8:00 - 8:40 **Tips of how to detect and assess systemic AL amyloidosis smartly for good clinical practice** **Chairperson:** Kenshi Suzuki **Speaker:** Nagaaki Katoh **【Janssen Pharmaceutical K.K. Medical Affairs Division】**
9:00	**Symposium -Discover new truths by studying the past- 3** 8:50 - 9:50 **AL amyloidosis** **Chairpersons:** Naoya Mimura, Masuzu Ueda **Speakers:** Masayoshi Tasaki, Nobuhiro Tsukada, Shin-ichi Fuchida, Motoko Kohda	
10:00	**JSM Research Award Lecture** 10:00 - 10:30 **Chairperson:** Jiro Kikuchi **Speakers:** Sho Ikeda, Mariko Ishibashi	
	Multiple Myeloma Research Grant from Myeloma Patients and Families, Japan Award Lecture 10:30 - 11:00 **Chairperson:** Yoichi Imai **Speakers:** Yusuke Yamamoto, Michiko Ichii	
11:00		
12:00	**Luncheon Seminar 3** 11:20 - 12:10 **Evidence and practice with carfilzomib-containing strategy for relapsed/refractory myeloma** **Chairperson:** Masahiro Abe **Speaker:** Junya Kuroda **【ONO PHARMACEUTICAL CO., LTD.】**	**Luncheon Seminar 4** 11:20 - 12:10 **The optimal first line and sequential treatment strategies in multiple myeloma with focus on immunomodulatory drugs** **Chairperson:** Tadao Ishida **Speaker:** Hirokazu Tanaka **【Celgene K.K. / Bristol-Myers Squibb K.K.】**
	Speacial Lecture 2 12:30 - 13:00 **Biology of multiple myeloma with t(11;14)(q13;q32) based on molecular cytogenetics** **Chairperson:** Yutaka Hattori **Speaker:** Ikuo Miura	
13:00	**Sponsored Symposium 2** 13:10 - 14:00 **Daratumumab and the New World of Transplant Ineligible Untreated Multiple myeloma patients - From a Academic and Clinical Standpoint** **Chairperson:** Takashi Ikeda **Speakers:** Akihiro Kitadate, Tadao Ishida **【Janssen Pharmaceutical K.K.】**	
14:00	**Plenary** 14:10 - 15:20 **Chairpersons:** Shigeki Ito, Michihide Tokuhira	
15:00	**Closing Ceremony** 15:20 - 15:35	
16:00		
17:00		
18:00		
19:00		
20:00		

＊ Poster Presentation is available on-demand streaming.

プログラム（Program）

会長講演

5月29日(土)　13:50－14:20　第1会場

座長：麻奥　英毅（Hideki Asaoku）（日本赤十字社広島県赤十字血液センター）

PL-1　正常 B リンパ球由来 iPS 細胞を用いた骨髄腫起源細胞の探索
Study for exploring myeloma-initiating cell using normal B cell-derived induced pluripotent stem cells

坂井　晃（Akira Sakai）
福島県立医科大学医学部 放射線生命科学講座

特別講演 1

5月29日(土)　10:40－11:30　第1会場

座長：安井　寛（Hiroshi Yasui）（東京大学医科学研究所附属病院 血液腫瘍内科）

SL-1　多発性骨髄腫における免疫調節薬：我々はどこまで識りえたか？
Immunomodulatory drugs in multiple myeloma: How far have we come?

秀島　輝（Teru Hideshima）
ハーバード大学医学部 ダナ・ファーバー癌研究所

特別講演 2

5月30日(日)　12:30－13:00　第1会場

座長：服部　豊（Yutaka Hattori）（慶應義塾大学大学院薬学研究科）

SL-2　分子細胞遺伝学による t(11;14)(q13;q32) を持つ骨髄腫の生物学
Biology of multiple myeloma with t(11;14)(q13;q32) based on molecular cytogenetics

三浦　偉久男（Ikuo Miura）
株式会社エスアールエル 遺伝子・染色体解析センター

シンポジウム温故知新 1

5月29日(土)　9:00－10:30　第1会場

骨病変・貧血
Bone lesion・Anemia

座長：李　政樹（Masaki Ri）（名古屋市立大学病院 輸血・細胞療法部）
　　堺田　惠美子（Emiko Sakaida）（千葉大学医学部附属病院 血液内科）

SY1-1　骨髄腫骨病変の病態解明と治療の進歩と展望
A new insight into the biology and treatment for bone disease in multiple myeloma

安倍　正博（Masahiro Abe）
徳島大学大学院医歯薬学研究部 血液・内分泌代謝内科学分野

SY1-2　多発性骨髄腫の画像診断
Role of imaging in multiple myeloma patients

高須　深雪（Miyuki Takasu）
広島市民病院 放射線診断科

SY1-3　骨髄腫における貧血 －こんなにも多様な機序が！－
Anemia in myeloma -diversity and spectrum of pathogenesis-

三輪　哲義（Akiyoshi Miwa）
国際骨髄腫先端治療研究センター、東京北医療センター

SY1-4　骨髄腫細胞と破骨細胞を標的とするTh1様γδT細胞とエロツズマブの併用療法の開発
Development of combinatory treatment of Th1-like γδ T cells with elotuzumab against osteoclasts as well as myeloma cells

原田　武志（Takeshi Harada）[1]、井上　雄介[1]、天眞　寛文[2]、小田　明日香[1]、住谷　龍平[1]、大浦　正博[1]、曽我部　公子[1]、藤井　志朗[3]、中村　信元[4]、三木　浩和[5]、賀川　久美子[3]、日浅　雅博[2]、寺町　順平[6]、安倍　正博[1]
[1] 徳島大学大学院医歯薬学研究部 血液・内分泌代謝内科学分野、
[2] 徳島大学大学院医歯薬学研究部 口腔顎顔面矯正学分野、[3] 徳島大学病院 血液内科、
[4] 徳島大学大学院医歯薬学研究部 実践地域診療・医科学分野、[5] 徳島大学病院 輸血・細胞治療部、
[6] 岡山大学大学院医歯薬学総合研究科 口腔機能解剖学分野

SY1-5　日本人多発性骨髄腫患者における血中ビタミンD濃度の検討
The prevalence and clinical outcomes of vitamin D deficiency in Japanese multiple myeloma patients: A single-center observational study

磯田　淳（Atsushi Isoda）[1,2]、宮澤　悠里[2]、石川　哲也[2]、中山　敬太[2]、金谷　秀平[2]、入内島　裕乃[2]、斉藤　明生[2]、松本　守生[2]、澤村　守夫[2]
[1] 医療法人星医院 血液内科、[2] 渋川医療センター 血液内科

SY1-6　骨髄腫骨関連事象の発生予防における身体機能維持の重要性
The importance of retaining physical functions to prevent SRE in multiple myeloma

三木　浩和（Hirokazu Miki）[1]、中村　信元[2]、中村　昌史[3]、水口　槙子[3]、住谷　龍平[3]、大浦　雅博[3]、曽我部　公子[3]、高橋　真美子[3]、丸橋　朋子[3]、原田　武志[3]、藤井　志朗[3]、賀川　久美子[3]、濱野　裕章[4]、近藤　正輝[4]、岡田　直人[4]、坂東　良美[5]、遠藤　逸朗[3]、安倍　正博[3]
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[3] 徳島大学大学院医歯薬学研究部 血液・内分泌代謝内科学、[4] 徳島大学病院 薬剤部、[5] 徳島大学病院 病理部

シンポジウム温故知新 2

5月29日(土)　14:40－15:40　第1会場

腎障害・染色体異常

Renal insufficiency・Choromosomal abnormality

座長：高松　博幸（Hiroyuki Takamatsu）（金沢大学医薬保健研究域医学系血液内科）
　　石橋　真理子（Mariko Ishibashi）（日本医科大学 微生物学・免疫学）

SY2-1　多発性骨髄腫とその周辺疾患の腎病変
Kidney lesions in multiple myeloma and related diseases

風間　順一郎(Junichiro James Kazama)、藤原　もも子
福島県立医科大学 腎臓高血圧内科学講座

SY2-2　骨髄腫における染色体１ｑ２１増多と１ｐ欠失
Gain/amplification of chromosome arm 1q21 and deletion of chromosome 1p in multiple myeloma

花村　一朗(Ichiro Hanamura)
愛知医科大学 医学部 内科学講座 血液内科

SY2-3　透析を要する多発性骨髄腫症例におけるダラツムマブの有効性と安全性の検討
Efficacy and Tolerability of Daratumumab-based regimens in dialysis-dependent Japanese patients with myeloma

北山　智草(Chigusa Kitayama)、水野　真一
地域医療機能推進機構 仙台病院 腎センター内科

SY2-4　t(11;14) 転座に関連する未熟型骨髄腫では CD38 低発現、BCL2/BCL2L1 比高値を呈する
Multiple myeloma with t(11;14)-associated immature phenotype has lower CD38 expression and higher BCL2/BCL2L1 ratio

北舘　明宏(Akihiro Kitadate)[1,2]、成田　健太郎[2]、寺尾　俊紀[2]、池田　翔[1]、津島　隆史[2]、三浦　大典[2]、竹内　正美[2]、高橋　直人[1]、末永　孝生[2]
[1] 秋田大学医学部 血液腎臓膠原病内科、[2] 亀田総合病院 血液腫瘍内科

シンポジウム温故知新 3

5月30日(日)　8:50－9:50　第1会場

AL型アミロイドーシス

AL amyloidosis

座長：三村　尚也（Naoya Mimura）（千葉大学医学部附属病院 輸血・細胞療法部（血液内科兼任））
　　上田　真寿（Masuzu Ueda）（自治医科大学内科学講座 血液学部門）

SY3-1　AL アミロイドーシスにおけるアミロイド線維形成機構の Up to date
Mechanism of amyloid fibril formation in AL amyloidosis: an up-to-date overview

田崎　雅義(Masayoshi Tasaki)[1]、植田　光晴[2]
[1] 熊本大学大学院 生命科学研究部構造機能解析学講座、[2] 熊本大学大学院生命科学研究部脳神経内科学

SY3-2　ALアミロイドーシス診療の最前線
Recent advances in diagnosis and treatment of AL amyloidosis

塚田　信弘(Nobuhiro Tsukada)
日本赤十字社医療センター 血液内科

SY3-3　アミロイドーシス調査研究班によるIgM型ALアミロイドーシス21例の後方視的解析
A retrospective analysis of 21 patients with IgM-related AL amyloidosis in Japan: A Study by the amyloidosis-research-committee

淵田　真一(Shin-ichi Fuchida)[1]、**小倉　瑞生**[2]、**石田　禎夫**[2]、**畑　裕之**[3]、**半田　寛**[4]、**加藤　修明**[5]、**中世古　知昭**[6]、**角南　一貴**[7]、**片山　雄太**[8]、**野畑　宏信**[9]、**大城　一郁**[10]、**飯田　真介**[11]、**関島　良樹**[5]、**内木　宏延**[12]、**島崎　千尋**[1]
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[3] 熊本大学生命科学研究部 生体情報解析学、[4] 群馬大学大学院医学系研究科 血液内科学分野、
[5] 信州大学医学部 脳神経内科，リウマチ・膠原病内科、[6] 国際医療福祉大学医学部 血液内科、
[7] 国立病院機構岡山医療センター 血液内科、[8] 広島赤十字・原爆病院 血液内科部、
[9] 愛知医科大学 腎臓・リウマチ膠原病内科、[10] 沖縄県立南部医療センター・こども医療センター 血液腫瘍科、
[11] 名古屋市立大学大学院医学研究科 血液・腫瘍内科学分野、[12] 福井大学医学部 分子病理学 (病理学 2)

SY3-4　ALアミロイドーシスに対するVCD治療中に心不全を合併し、ダラツムマブを導入した一例
Introduction of daratumumab in a patient with AL amyloidosis who developed acute heart failure during VCD

甲田　素子(Motoko Kohda)、**吉原　享子**、**吉原　哲**、**佐守　真実**、**宇都宮　惟人**、**日笠　聡**
兵庫医科大学病院 血液内科

2020年日本多発性骨髄腫学会奨励賞受賞講演

5月30日(日)　10:00－10:30　第1会場

座長：菊池　次郎（Jiro Kikuchi）（自治医科大学 分子病態治療研究センター 幹細胞制御研究部）

JRAL-1　多発性骨髄腫の分子病態と治療抵抗性における低酸素誘導性遺伝子の意義
Significance of hypoxia-inducible genes in molecular pathogenesis and therapy resistance of multiple myeloma

池田　翔(Sho Ikeda)
秋田大学大学院医学系研究科 血液・腎臓・膠原病内科学講座

JRAL-2　多発性骨髄腫における新規免疫チェックポイントSiglecファミリー分子
Novel immune checkpoint sialic acid-binding Ig-like lectin (Siglec) family molecules in multiple myeloma

石橋　真理子(Mariko Ishibashi)[1]、**田村　秀人**[2]、**森田　林平**[1]
[1] 日本医科大学 微生物学・免疫学、[2] 獨協医科大学埼玉医療センター 糖尿病内分泌・血液内科

2020年骨髄腫患者会助成金受賞講演

5月30日(日)　10:30－11:00　第1会場

座長：今井　陽一（Yoichi Imai）（東京大学医科学研究所附属病院血液腫瘍内科）

MRGAL-1 多発性骨髄腫の進行における細胞外小胞の新たな役割
The Emerging Roles of Extracellular Vesicles in Multiple Myeloma Progression

山本　雄介(Yusuke Yamamoto)[1]、山元　智史[2]、服部　豊[2]、落谷　孝広[3]
[1] 国立がん研究センター研究所 細胞情報学、[2] 慶應義塾大学 薬学部 病態生理学講座、
[3] 東京医科大学 医学総合研究所 分子細胞治療研究部門

MRGAL-2 多発性骨髄腫における Signal transducing adaptor protein ファミリーの役割
The role of Signal-transducing adaptor protein family in multiple myeloma

一井　倫子(Michiko Ichii)、保仙　直毅
大阪大学大学院医学系研究科 血液・腫瘍内科学講座

プレナリー

5月30日(日)　14:10－15:20　第1会場

座長：伊藤　薫樹（Shigeki Ito）（岩手医科大学 内科学講座 血液腫瘍内科分野）
　　得平　道英（Michihide Tokuhira）（地域医療機能推進機構埼玉メディカルセンター血液内科）

PS-1 髄外病変はヒアルロン酸を介した骨髄腫細胞同士の凝集から発症する
Extramedullary diseases originate from hyaluronan-induced homophilic cell-cell interaction of myeloma cells

菊池　次郎(Jiro Kikuchi)[1]、小玉　信之[2,3]、竹下　昌孝[2,3]、比島　智子[2,3]、池田　翔[4]、小林　敬宏[4]、黒田　芳明[5]、内山　倫宏[6]、長田　直希[1]、小山　大輔[1]、ボーゲン　ビヤーネ[7]、安井　寛[8]、高橋　直人[4]、三輪　哲義[2,3]、古川　雄祐[1]
[1] 自治医科大学分子病態治療研究センター幹細胞制御研究部、[2] 国際骨髄腫先端治療研究センター、
[3] 東京北医療センター、[4] 秋田大学医学部血液・腎臓・膠原病内科、[5] 広島西医療センター、[6] 諏訪赤十字病院、
[7] オスロ大学、[8] 東京大学医科学研究所

PS-2 TAK-1 が誘導する内因性 PP2A 阻害因子 CIP2A の骨髄腫細胞の生存・増殖に及ぼす重要な役割
Critical role of TAK1-mediated upregulation of the endogenous PP2A inhibitor CIP2A in myeloma cell growth and survival

清水　宗(So Shimizu)[1,2]、寺町　順平[3]、原田　武志[2]、天真　寛文[1,2]、小田　明日香[2]、日浅　雅博[1,2]、大浦　雅博[2]、曽我部　公子[2]、遠藤　逸朗[4]、松本　俊夫[5]、田中　栄二[1]、安倍　正博[2]
[1] 徳島大学大学院医歯薬学研究部 口腔顎顔面矯正学分野、
[2] 徳島大学大学院医歯薬学研究部 血液・内分泌代謝内科学、
[3] 岡山大学大学院医歯薬学総合研究科 口腔機能解剖学分野、
[4] 徳島大学大学院医歯薬学研究部生体情報内科学分野、[5] 徳島大学 藤井節郎記念医科学センター

PS-3 Carfilzomib 含有救援療法後に 2 回目の自家末梢血幹細胞移植を実施した再発多発性骨髄腫の検討

Efficacy of salvage treatment with carfilzomib based rescue chemotherapy followed by HDT/2nd ASCT in relapsed/refractory multiple myeloma patients

水谷　信介(Shinsuke Mizutani)[1]、太田　沙絵子[1]、金山　悠加[1]、村松　彩子[1]、岡本　明也[1]、大西　朗生[1]、水原　健太郎[1]、民西　葉子[1]、山口　純子[1]、伊佐　怜子[1]、藤野　貴大[1]、西山　大地[1]、木元　弥生[1]、塚本　拓[1]、志村　勇司[1]、古林　勉[1]、志村　和穂[2]、高橋　良一[3]、兼子　裕人[2]、黒田　純也[1]

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PS-4 SUBCUTANEOUS DARATUMUMAB COMBINATION THERAPIES FOR MULTIPLE MYELOMA: INITIAL RESULTS FOR D-KD AND UPDATED RESULTS FOR D-VMP AND D-RD FROM PLEIADES

Shinsuke Iida[1]、Philippe Moreau[2]、Ajai Chari[3]、Mathias Haenel[4]、Albert Oriol[5]、Paula Rodriguez-Otero[6]、Helen McCarthy[7]、Kenshi Suzuki[8]、Vania Hungria[9]、Anna Sureda Balari[10]、Lauriane Clement-Filliatre[10]、Cyrille Hulin[10]、Hila Magen[10]、Vladimir Maisnar[10]、Lionel Karlin[10]、Ludek Pour[10]、Cyrille Touzeau[10]、Shiyi Yang[10]、Michele Kosh[10]、Maria Delioukina[10]、Christoph Heuck[10]

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PS-5 SUBCUTANEOUS DARATUMUMAB + BORTEZOMIB/CYCLOPHOSPHAMIDE/ DEXAMETHASONE (D-VCD) IN NEWLY DIAGNOSED AL AMYLOIDOSIS: ASIAN SUBGROUP ANALYSIS FROM ANDROMEDA

Kenshi Suzuki[1]、Ashutosh D. Wechalekar[2]、Kihyun Kim[3]、Chihiro Shimazaki[4]、Jin Seok Kim[5]、Takayuki Ikezoe[6]、Chang-Ki Min[7]、Fude Zhou[8]、Shinsuke Iida[9]、Nagaaki Katoh[10]、Tomoaki Fujisaki[10]、Ho-Jin Shin[10]、NamPhuong Tran[10]、Xiang Qin[10]、Sandra Y. Vasey[10]、Brenda Tromp[10]、Brendan M. Weiss[10]、Jessica Vermeulen[10]、Raymond L. Comenzo[10]、Efstathios Kastritis[10]、Jin Lu[10]

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PS-6 新規改変型二重特異性抗体の作製と骨髄腫に対する革新的免疫療法の開発

Development of innovative antitumor antibodies armed with Bridging-BiTE to advance anti-myeloma immunotherapy

小西　達矢(Tatsuya Konishi)[1]、越智　俊元[1,2]、丸田　雅樹[1]、谷本　一史[1]、齋藤　卓[3]、今村　健志[3]、安川　正貴[2,4]、竹中　克斗[1]

[1] 愛媛大学大学院医学系研究科 血液・免疫・感染症内科学講座、
[2] 愛媛大学プロテオサイエンスセンター 免疫制御学部門、[3] 愛媛大学大学院医学系研究科 分子病態医学講座、
[4] 愛媛県立医療技術大学

PS-7 CARTITUDE-1: PHASE 1B/2 STUDY OF CILTACABTAGENE AUTOLEUCEL IN RELAPSED/ REFRACTORY MULTIPLE MYELOMA (RRMM)

Deepu Madduri[1]、Jesus G Berdeja[2]、Saad Z Usmani[3]、Andrzej Jakubowiak[4]、Mounzer Agha[5]、Adam D Cohen[6]、A.Keith Stewart[7]、Parameswaran Hari[8]、Myo Htut[9]、Elizabeth O'Donnell[10]、Nikhil C Munshi[11]、David Avigan[12]、Abhinav Deol[13]、Alexander Lesokhin[14]、Indrajeet Singh[15]、Enrique Zudaire[15]、Tzu-Min Yeh[16]、Alicia J Allred[15]、Yunsi Olyslager[17]、Arnob Banerjee[15]、Jenna D Goldberg[16]、Jordan M Schecter[16]、Carolyn C Jackson[16]、William Deraedt[17]、SenHong Zhuang[16]、Jeffrey Infante[16]、Dong Geng[18]、Xiaoling Wu[18]、Marlene J Carrasco-Alfonso[18]、Muhammad Akram[18]、Farah Hossain[18]、Syed Rizvi[18]、Frank Fan[19]、Sundar Jagannath[1]、Yi Lin[20]、Thomas Martin[21]

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[7]UHN and the Princess Margaret Cancer Centre, Toronto, ON, Canada、
[8]Medical College of Wisconsin, Milwaukee, WI, USA、
[9]City of Hope Comprehensive Cancer Center, Duarte, CA, USA、
[10]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA、
[11]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA、
[12]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA、
[13]Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA、
[14]Memorial Sloan Kettering Cancer Center, New York, NY, USA、[15]Janssen R&D, Spring House, PA, USA、
[16]Janssen R&D, Raritan, NJ, USA、[17]Janssen R&D, Beerse, Belgium、
[18]Legend Biotech USA, Inc., Piscataway, NJ, USA、[19]Nanjing Legend Biotechnology Co., Ltd., Nanjing, China、
[20]Mayo Clinic, Rochester, MN, USA、
[21]UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

ポスター発表（オンデマンド配信）

病因・基礎、病態解析
Cause / basic, pathological analysis

P-1 EZH2 と G9a の共阻害はインターフェロンシグナルと IRF4-MYC axis を制御し多発性骨髄腫の増殖を抑制する

Dual EZH2 and G9a inhibition suppresses multiple myeloma cell proliferation by regulating the interferon signal and IRF4-MYC axis

石黒　一也(Kazuya Ishiguro)[1,2]、北嶋　洋志[1]、新沼　猛[1]、丸山　玲緒[3]、五十嵐　哲祥[2]、仲瀬　裕志[4]、鈴木　拓[1]

[1]札幌医科大学医学部分子生物学講座、[2]天使病院血液内科、[3]がん研究所がんエピゲノムプロジェクト、
[4]札幌医科大学医学部消化器内科学講座

P-2 SORT1 と LAMP2 を介したエクソソーム分泌と細胞接着によるレナリドミド耐性獲得機構

SORT1/LAMP2-mediated Exosome Secretion and Cell Adhesion Are Associated with Lenalidomide Resistance in Multiple Myeloma

山元　智史(Tomofumi Yamamoto)[1,2,3]、中山　淳[3]、山本　雄介[3]、落谷　孝広[1]、服部　豊[2]

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P-3 KDM5A は多発性骨髄腫において MYC 標的遺伝子の維持に必須な因子である
KDM5A is a vulnerability of MYC target genes essential to multiple myeloma

大口　裕人(Hiroto Ohguchi)[1]、扇屋　大輔[2]、ワン　チンジャン[3]、グライダー　バークレイ[4]、パーク　ポール[3]、倉田　啓史[2]、デヤオ　リー[3]、増田　豪[5]、日野　信次朗[6]、臼杵　慎吾[7]、河野　和[8]、タイ　ユーツー[2]、ムンシ　ニキール[2]、松岡　雅雄[8]、大槻　純男[5]、中尾　光善[6]、南　敬[9]、ダービン　アダム[10]、アンダーソン　ケネス[2]、秀島　輝[2]、キ　ジュン[3]

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P-4 骨髄腫細胞のプロテアソーム阻害薬の耐性機序における PIM2 と Akt 活性および NRF2 蓄積の役割
Mechanisms for the resistance to proteasome inhibitors in myeloma cells: the role of PIM2 and Akt kinase activation and NRF2 accumulation

曽我部　公子(Kimiko Sogabe)[1]、原田　武志[1]、中村　信元[2]、三木　浩和[3]、小田　明日香[1]、井上　雄介[1]、住谷　龍平[1]、大浦　雅博[1]、藤井　志朗[4]、賀川　久美子[4]、天眞　寛文[5]、日浅　雅博[5]、寺町　順平[6]、李　政樹[7]、飯田　真介[7]、安倍　正博[1]

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P-5 HDAC 阻害薬と IMiDs の骨髄腫細胞の CD38 と SLAMF7 発現に及ぼす影響
Effects of HDAC inhibitors and IMiDs on CD38 and SLAMF7 expresssion in MM cells

井上　雄介(Yusuke Inoue)[1]、原田　武志[1]、小田　明日香[1]、住谷　龍平[1]、大浦　雅博[1]、曽我部　公子[1]、藤井　志朗[2]、中村　信元[3]、三木　浩和[4]、賀川　久美子[2]、天眞　寛文[5]、日浅　雅博[5]、寺町　順平[6]、安倍　正博[1]

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P-6 t(4;14) 陽性骨髄腫患者における FGFR3 過剰発現は予後不良に関与しない
FGFR3 overexpression was not associated with poor survival in t(4;14)$^{+}$ multiple myeloma patients

木下　量介(Ryosuke Kinoshita)[1]、石橋　真理子[2]、半田　寛[3]、佐々木　純[4]、小松　則夫[4]、今井　陽一[5]、伊藤　薫樹[6]、田中　紀奈[7]、田中　淳司[7]、磯田　淳[8]、松本　守生[8]、田野崎　栄[9]、砂川　実香[1]、朝山　敏夫[1]、猪口　孝一[1]、田村　秀人[1,10]

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P-7　骨髄腫細胞生存における CD38 の意義
The role of CD38 in myeloma cell survival

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P-8　多発性骨髄腫に対する Venetoclax 至適併用薬の同定
Identification of suitable drugs to be combined with venetoclax for the treatment of multiple myeloma

長田　直希(Naoki Osada)[1]、菊池　次郎[1]、小山　大輔[1]、黒田　芳明[2]、安井　寛[3]、古川　雄祐[1]
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[3] 東京大学医科学研究所

P-9　多発性骨髄腫患者における末梢血幹細胞採取効率についての後方視的解析
Retrospective study of peripheral blood stem cell harvest (PBSCH) in patients with multiple myeloma

竹下　昌孝(Masataka Takeshita)[1,2]、小玉　信之[1,2]、比島　智子[1,2]、平井　理泉[1]、谷村　聡[1]、
岡崎　幸治[1]、奥田　優子[1]、工藤　大輔[1]、三輪　哲義[1,2]
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検査・診断関連
Examination / diagnosis-related

P-10　セル・フリー DNA による多発性骨髄腫の早期再発診断
Circulating cell-free DNA in the peripheral blood plasma of patients is an informative biomarker for multiple myeloma relapse

安井　寛(Hiroshi Yasui)[1,2]、小林　真之[2,3]、佐藤　広太[4]、近藤　幹也[2]、石田　禎夫[4]、海渡　裕太[5]、
田村　秀人[5,6]、半田　寛[7]、築根　豊[8]、佐々木　純[8]、小松　則夫[8]、田中　紀奈[9]、田中　淳司[9]、
木崎　昌弘[10]、川俣　豊隆[1]、牧山　純也[1]、横山　和明[1]、井元　清哉[2]、東條　有伸[1,2]、今井　陽一[1]
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P-11　ダラツムマブ治療時代における CD319 を用いた骨髄腫細胞表面抗原検査の有用性
Use of CD319 in detection of myeloma cells in daratumumab era

黒田　芳明(Yoshiaki Kuroda)、角野　萌、宗正　昌三、下村　壮司
国立病院機構広島西医療センター 血液内科

P-12　骨髄腫における微小残存病変の臨床的な意義：単施設後方視的研究
Clinical significance of minimal residual disease in myeloma; single center retrospective analysis

鈴木　一史(Kazuhito Suzuki)[1,2]、西脇　嘉一[1,2]、長尾　陸[1,2]、香取　美津治[1,2]、田上　晋[1,2]、
服部　大樹[1,2]、増岡　秀一[1,2]、矢野　真吾[2]
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P-13 BJP-MGUS を呈する Fanconi 症候群症例における MYD88 L265P 変異の検出
Serial detection of MYD88 L265P mutation in BJP-MGUS patient with Fanconi syndrome

小玉　信之(Nobuyuki Kodama)[1,2]、竹下　昌孝[1,2]、比島　智子[1,2]、工藤　大輔[1]、岡崎　幸治[1]、奥田　優子[1]、平井　理泉[1]、谷村　聡[1]、三輪　哲義[1,2]
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P-14 多発性骨髄腫患者における腎障害マーカーとしての尿中 L 型脂肪酸結合蛋白の有用性
Urinary liver-type fatty acid binding protein (L-FABP) as a new biomarker of renal impairment in patients with multiple myeloma

藤岡　洋成(Yosei Fujioka)[1]、遠山　和博[1]、中原　史雄[1]、黒川　峰夫[1,2]
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臨床試験・臨床研究および治療に関する基礎研究
Clinical trials・Basic research on clinical research and treatment

P-15 多発性骨髄腫の継続・維持療法の有効性に関する傾向スコアマッチング解析
Propensity-score matched analysis of the efficacy of maintenance or continuous therapy on multiple myeloma

尾崎　修治(Shuji Ozaki)[1]、半田　寛[2]、小磯　博美[3]、齋藤　貴之[4]、角南　一貴[5]、石田　禎夫[6]、鈴木　憲史[6]、成田　朋子[7]、飯田　真介[7]、中村　裕一[8]、鈴木　一史[9]、西村　倫子[10]、村上　博和[11]、清水　一之[12]
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P-16 多発性骨髄腫における免疫原性細胞死に寄与する小胞体ストレス応答の検討
The study of ER stress signaling pathways contributing to immunogenic cell death in multiple myeloma

清水　湧太(Yuta Shimizu)
慶應義塾大学院薬学研究科 薬科学専攻病態生理学講座

P-17 再発難治性骨髄腫に対するカルフィルゾミブ療法の有効性と安全性：京都血液臨床研究グループ (KOTOSG) 前方視的観察研究
Efficacy and safety of carfilzomib-containing therapy for relapsed/refractory myeloma: Kyoto Clinical Hematology Study Group prospective observation

金山　悠加(Yuka Kawaji-Kanayama)[1]、古林　勉[1]、村松　彩子[1]、内山　人二[2]、佐々木　奈々[3]、魚嶋　伸彦[3]、中尾　光成[4]、高橋　良一[5]、志村　和穂[6]、兼子　裕人[6]、清田　実希[7]、和田　勝也[7]、知念　良顕[8]、平川　浩一[8]、淵田　真一[9]、島崎　千尋[9]、志村　勇司[1]、堀池　重夫[1]、谷脇　雅史[6,10]、黒田　純也[1]
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P-18 カルフィルゾミブによる高血圧合併における血清 TGFb と IL-6 のバイオマーカーとしての意義

Predictive value of serum TGFb and serum IL-6 for hypertension by carfilzomib in patients with relapsed/refractory multiple myeloma

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P-19 リプログラミング因子の高発現による多発性骨髄腫細胞の悪性形質獲得

Overexpression of reprogramming genes leads to acquisition of malignant phenotype in multiple myeloma

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P-20 ベネトクラクスは BCL2 高発現の多発性骨髄腫細胞株に対するダラツムマブの抗体依存性細胞傷害活性を増強させる

Venetoclax enhances NK-cell-mediated ADCC with daratumumab in myeloma cells expressing BCL2

中村　文乃(Ayano Nakamura)[1]、鈴木　進[2,3]、瀬戸　加大[1]、高杉　壮一[1]、金杉　丈[1]、花村　一朗[1]、上田　龍三[2]、高見　昭良[1]

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P-21 移植適応多発性骨髄腫患者における初回採取レジメンによる自家末梢血幹細胞採取不良例の多施設共同後方視的研究

The multicenter retrospective study of poor PBSC mobilization in patients with multiple myeloma

長井　友莉恵(Yurie Nagai)[1]、三村　尚也[1,2]、塚田　信弘[3]、青墳　信之[4]、李　政樹[5]、勝岡　優奈[6]、若山　聡雄[7]、鈴木　利貴央[8]、原崎　頼子[9]、松本　守生[10]、熊谷　匡也[11]、三宅　隆明[12]、尾崎　修治[13]、鐘野　勝洋[14]、田中　宏明[15]、志村　有香[16]、黒田　芳明[17]、角南　一貴[18]、鈴木　一史[19]、山下　剛史[20]、清水　一之[21]、村上　博和[22]、安倍　正博[23]、中世古　知昭[24]、堺田　惠美子[1]

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P-22 MDV レセプトデータベースを用いた国内の多発性骨髄腫患者における実臨床下での治療パターンおよび臨床転帰の検討

Real world treatment patterns and clinical outcomes in multiple myeloma patients from the MDV claims database in Japan

半田　寛(Hiroshi Handa)[1]、石田　禎夫[2]、尾崎　修治[3]、森　明日香[4]、加藤　賢一[5]、飯田　真介[6]
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[6] 名古屋市立大学大学院医学研究科 血液・腫瘍内科学分野

P-23 当院における多発性骨髄腫患者に対するダラツムマブの使用経験

Daratumumab containing regimen for multiple myeloma patients; a single center experience

高橋　寛行(Hiroyuki Takahashi)[1]、酒井　リカ[1]、貫井　淳[1]、徳永　真由美[1]、鈴木　泰生[1]、
中島　秀明[2]
[1] 神奈川県立がんセンター 血液・腫瘍内科、[2] 横浜市立大学医学部 血液・免疫・感染症内科学

移植適応患者の治療関連

Treatment-related for transplant-adapted patients

P-24 移植適応多発性骨髄腫に対する ixazomib による維持療法の後方視的解析

Retrospective analysis of maintenance therapy with ixazomib for patients with multiple myeloma undergoing autologous stem-cell transplantation

塚田　信弘(Nobuhiro Tsukada)、野村　萌、入田　博史、佐藤　広太、小倉　瑞生、阿部　有、
石田　禎夫、鈴木　憲史
日本赤十字社医療センター 血液内科

P-25 自家末梢血幹細胞採取におけるボルテゾミブ併用シクロフォスファミド大量療法の有用性の解析

Usefulness of bortezomib and high-dose cyclophosphamide therapy as a conditioning regimen for autologous peripheral blood stem cell harvest

大野　沙耶香(Sayaka Ohno)[1]、林　清人[1]、清水　亮[1]、石井　昭広[2]、田中　宏明[1]
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P-26 多発性骨髄腫に対する新規治療薬の移植後再発に関する影響

Effects of new agents on multiple myeloma recurrence after autoPBSCT

小倉　瑞生(Mizuki Ogura)、石田　禎夫、野村　萌、入田　博文、梨本　淳一郎、佐藤　広太、阿部　有、
塚田　信弘、鈴木　憲史
日本赤十字社医療センター 血液内科

P-27　新規薬剤時代における原発性形質細胞白血病の治療成績：8 例の後方視的検討

Clinical outcome of primary plasma cell leukemia in the novel agent era: a retrospective study of eight cases

佐分利　益穂(Masuho Saburi)[1]、坂田　真規[1]、高田　寛之[1]、宮崎　泰彦[1]、佐々木　人大[2]、井谷　和人[2]、安部　美由紀[2]、幸野　和洋[2]、曽我　泰裕[3]、河野　克也[4]、中山　俊之[2]、大塚　英一[1]

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移植非適応患者の治療関連

Treatment-related for transplant-non-adapted patients

P-28　自家移植歴のない初発の多発性骨髄腫患者を対象とした一次治療後のイキサゾミブ維持療法の多施設共同国際臨床第 3 相試験

TOURMALINE-MM4: Ixazomib vs placebo maintenance in newly diagnosed multiple myeloma patients not undergoing autologous stem cell transplant

飯田　真介(Shinsuke Iida)[1]、Meletios A. Dimopoulos[2]、Ivan Špička[3]、Hang Quach[4]、Albert Oriol[5]、Roman Hájek[6]、Mamta Garg[7]、Meral Beksac[8]、Sara Bringhen[9]、Eirini Katodritou[10]、Wee Joo Chng[11]、María-Victoria Mateos[13]、Xavier Leleu[12]、Gareth Morgan[14]、Alexander Vorog[15]、Richard Labotka[15]、Bingxia Wang[15]、Sagar Lonial[16]

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P-29 DARATUMUMAB PLUS LENALIDOMIDE/DEXAMETHASONE (D-RD) IN PTS WITH TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): UPDATED ANALYSIS OF MAIA

Katja Weisel[1]、Shaji K. Kumar[2]、Thierry Facon[3]、Saad Z. Usmani[4]、Torben Plesner[5]、Robert Z. Orlowski[6]、Cyrille Touzeau[7]、Supratik Basu[8]、Nizar J. Bahlis[9]、Hartmut Goldschmidt[10]、Michael O'Dwyer[10]、Christopher P. Venner[10]、Cyrille Hulin[10]、Lionel Karlin[10]、Meir Preis[10]、Annemiek Broyl[10]、William Renwick[10]、Markus Hansson[10]、Maria Krevvata[10]、Jianping Wang[10]、Rian Van Rampelbergh[10]

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P-30 LONG-TERM OUTCOMES AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) BY RESPONSE FOR BORTEZOMIB/MELPHALAN/PREDNISONE (VMP) ± DARATUMUMAB (DARA) IN ALCYONE

Hiroyuki Takamatsu[1]、Paula Rodriguez-Otero[2]、Mario Boccadoro[3]、Roman Hajek[4]、Tomoaki Fujisaki[5]、Jae Hoon Lee[6]、Joaquin Martinez-Lopez[7]、Paulo Lucio[8]、Zsolt Nagy[9]、Ganna Usenko[10]、Anna Marina Liberati[10]、Mihaela Lazaroiu[10]、Dariusz Woszczyk[10]、Joanna Romejko-Jarosinska[10]、Stefan Tobias Knop[10]、Astrid Pavlovsky[10]、Cecily Forsyth[10]、Takayuki Ishikawa[10]、Katharine Gries[10]、Huiling Pei[10]、Anupa Kudva[10]

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P-31 CR で治療を終了した MM 患者の予後解析

Prognostic analysis of MM patients who discontinued treatment with CR status

麻奥　英毅(Hideki Asaoku)[1]、板垣　充弘[1]、片山　充弘[1]、岡谷　健史[1]、今中　亮太[1]、許　鴻平[1]、陳之内　文昭[1]、布村　拓也[1]、川野　玄太郎[1]、牟田　毅[2]、勝谷　慎也[3]、岩戸　康治[3]

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P-32 当院における再発難治性多発性骨髄腫患者に対する Daratumumab 投与による治療効果とその特徴

The therapeutic effects in Relapsed and/or Refractory multiple myeloma patients treated with Daratumumab

長尾　陸(Riku Nagao)、鈴木　一史、香取　美津治、田上　晋、服部　大樹、増岡　秀一、西脇　嘉一、矢野　真吾

東京慈恵会医科大学 腫瘍・血液内科

P-33 再発・難治性多発性骨髄腫に対する Carfilzomib/dexamethasone 療法
Carfilzomib/dexamethasone therapy for relapsed and refractory multiple myeloma

植田　裕子(Hiroko Ueda)、守山　喬史、石川　立則、吉岡　尚徳、牧田　雅典、角南　一貴
独立行政法人国立病院機構岡山医療センター 血液内科

P-34 当院における移植非適応再発・難治多発性骨髄腫の患者に対する daratumumab の有効性の検討
Daratumumab with bortezomib, or lenalidomide and dexamethasone was efficacy for relapse or refractory multiple myeloma in our hospital

外山　孝典(Takanori Toyama)
宮崎県立延岡病院 内科

P-35 当院における再発・難治多発性骨髄腫に対するダラツムマブの使用経験
Experience of using Daratumumab for relapse and refractory multiple myeloma in our hospital

内原　潤之介(Jun-nosuke Uchihara)
那覇市立病院 血液内科

合併症、支持療法、メディカルスタッフ関連
Complications, supportive therapy, medical staff-related

P-36 新規薬剤時代のプロテアソーム阻害薬治療を受けた多発性骨髄腫患者における帯状疱疹ウイルス再活性化に関する 10 年間の調査
A 10-year survey of varicella-zoster virus reactivation in multiple myeloma patients treated with proteasome inhibitors in the novel agent era

大橋　養賢(Yasukata Ohashi)[1,2]、矢田部　恵[1]、新島　大輔[1]、今村　有那[1]、長山　佳之[1]、
大塚　健太郎[1]、谷地　豊[1]、上野　博則[3]、矢野　尊啓[3]、桧貝　孝慈[2]、横山　明弘[3,4]
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P-37 重症かつ可逆性の Carfilzomib による薬剤性肺障害の一例
A Case of Life-threatening but Reversible Carfilzomib-induced Pulmonary Toxicity

宮島　徹(Toru Miyajima)、小笠原　励起、横山　絵美、泉山　康、盛　暁生、齋藤　誠、森岡　正信、
近藤　健
愛育病院 血液病センター

アミロイドーシス・POEMS症候群・その他
Amyloidosis / POEMS syndrome・Others

P-38 シングルセル RNA 解析によって明らかとなる POEMS 症候群特異的な形質細胞クローン
Single cell RNA analysis successfully identifies plasma cell clones with specific features in POEMS syndrome

三村　尚也(Naoya Mimura)[1,2]、一色　佑介[1]、大島　基彦[3]、栢森　健介[1]、長井　友莉恵[1]、関　真秀[4]、中島　やえ子[3]、武藤　朋也[1]、塚本　祥吉[1]、竹田　勇輔[1]、大和田　千佳子[1,5]、三澤　園子[6]、池田　純一郎[7]、真田　昌[8]、桑原　聡[6]、鈴木　穣[4]、堺田　惠美子[1]、中世古　知昭[5]、岩間　厚志[3]
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P-39 POEMS 症候群における骨病変の臨床的意義
Clinical impact of the bone lesion in POEMS syndrome; a single-center experience of 119 patients

三科　達三(Tatsuzo Mishina)[1]、大和田　千桂子[1,4]、水地　智基[2]、大島　渚[1]、武藤　朋也[1]、塚本　祥吉[1]、三川　紫緒[1,3]、竹田　勇輔[1]、三村　尚也[1,3]、井関　徹[1,3]、中世古　知昭[4]、三澤　園子[2]、桑原　聡[2]、堺田　惠美子[1]
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症例報告
Case reports

P-40 多発性骨髄腫の患者における COVID-19：単一施設での経験
COVID-19 in patients with multiple myeloma: A single center experience

高木　雄介(Yusuke Takagi)、川口　拓哉、久納　俊祐、新美　圭子、小杉　浩史
大垣市民病院 血液内科

P-41 ITP 合併多発性骨髄腫に対する化学療法により骨髄腫と ITP の改善を認めた一例
A case of symptomatic multiple myeloma developing in a patient with immune thrombocytopenia

久納　俊祐(Shunsuke Kunou)、川口　拓哉、高木　雄介、新美　圭子、小杉　浩史
大垣市民病院 血液内科

P-42 CD19 陽性クローンを有する t(11;14) 転座陽性多発性骨髄腫の一例
A case of newly diagnosed t(11;14) multiple myeloma with CD19-positive clone

清原　千貴(Kazuki Kiyohara)、佐藤　剛、前田　峻大、宮島　真理、高野　幹、西谷　真来、菅原　教史、佐々木　了政、岡野　良昭、上原　さつき、古和田　周吾、小宅　達郎、伊藤　薫樹
岩手医科大学医学部 血液腫瘍内科

P-43 Carifilzomib により TMA を発症した治療抵抗性多発性骨髄腫

Carfilzomib-induced thrombotic microangiopathy in a patient with refractory multiple myeloma

山本　聡(Satoshi Yamamoto)、齋藤　祐美花、笠原　郁美、山口　圭介
市立札幌病院 血液内科

P-44 多発腫瘤形成を伴う未治療移植非適応骨髄腫に対し Daratumumab-VMP 療法が早期かつ深い奏効を示した一例

A case of Daratumumab with VMP therapy achieved a rapid and deep response for transplant-ineligible multiple myeloma with multiple plasmacytomas

郡司　匡弘(Tadahiro Gunji)、勝部　敦史、齋藤　健、横山　洋紀、福島　僚子、石井　敬人、仲野　彩、石井　彰子、桃木　真美子、望月　泰孝、島田　貴、矢野　真吾
東京慈恵会医科大学付属病院 腫瘍・血液内科

ランチョンセミナー 1

5月29日(土)　12:00－12:50　第1会場

新たな再発難治性多発性骨髄腫の治療戦略 -IsaPd療法を基礎と臨床から考える-

New treatment strategy for relapsed and refractory multiple myeloma -Understand IsaPd regimen based on basic and clinical-

座長：角南　一貴（Kazutaka Sunami）（独立行政法人国立病院機構岡山医療センター 血液内科）

LS1-1 **古川　雄祐(Yusuke Furukawa)**
自治医科大学 分子病態治療研究センター 幹細胞制御研究部

LS1-2 **石田　禎夫(Tadao Ishida)**
日本赤十字社医療センター 血液内科

〈共催：サノフィ株式会社〉

ランチョンセミナー 2

5月29日(土)　12:00－12:50　第2会場

座長：黒田　純也（Junya Kuroda）（京都府立医科大学大学院医学研究科 血液内科学）

LS2 多発性骨髄腫における T 細胞免疫不全と免疫治療戦略

Mechanisms of T cell immune dysfunction and immunotherapeutic strategies in multiple myeloma

田村　秀人(Hideto Tamura)
獨協医科大学 埼玉医療センター 糖尿病内分泌・血液内科

〈共催：セルジーン株式会社 / ブリストル・マイヤーズ スクイブ株式会社〉

ランチョンセミナー 3

5月30日(日)　11:20–12:10　第1会場

座長：安倍　正博（Masahiro Abe）（徳島大学大学院医歯薬学研究部 血液・内分泌代謝内科学）

LS3　再発難治骨髄腫に対するカルフィルゾミブ含有治療戦略のエビデンスと実際
Evidence and practice with carfilzomib-containing strategy for relapsed/refractory myeloma

黒田　純也(Junya Kuroda)
京都府立医科大学 血液内科学

〈共催：小野薬品工業株式会社〉

ランチョンセミナー 4

5月30日(日)　11:20–12:10　第2会場

座長：石田　禎夫（Tadao Ishida）（日本赤十字社医療センター 血液内科）

LS4　免疫調節薬に焦点を当てた多発性骨髄腫における至適な初回および継続的治療戦略
The optimal first line and sequential treatment strategies in multiple myeloma with focus on immunomodulatory drugs

田中　宏和(Hirokazu Tanaka)
近畿大学医学部 血液・膠原病内科

〈共催：セルジーン株式会社 / ブリストル・マイヤーズ スクイブ株式会社〉

モーニングセミナー 1

5月30日(日)　8:00–8:40　第1会場

座長：竹迫　直樹（Naoki Takezako）（独立行政法人国立病院機構災害医療センター 血液内科）

MS1　地域医療における高齢者 /Frail の骨髄腫治療
Multiple myeloma treatment for Elderly / Frail in community medicine

花本　仁(Hitoshi Hanamoto)
近畿大学奈良病院 血液内科

〈共催：武田薬品工業株式会社〉

モーニングセミナー 2

5月30日(日)　8:00–8:40　第2会場

座長：鈴木　憲史（Kenshi Suzuki）（日本赤十字社医療センター 骨髄腫・アミロイドーシスセンター）

MS2　診療に役立つ全身性 AL アミロイドーシスの診断と評価のコツ
Tips of how to detect and assess systemic AL amyloidosis smartly for good clinical practice

加藤　修明(Nagaaki Katoh)
信州大学医学部附属病院 脳神経内科 リウマチ・膠原病内科

〈共催：ヤンセンファーマ株式会社 メディカルアフェアーズ本部〉

スポンサードシンポジウム1

5月29日(土)　15:50－16:40　第1会場

多発性骨髄腫の治療戦略

Treatment Strategies for Multiple Myeloma

座長：半田　寛（Hiroshi Handa）（群馬大学大学院医学系研究科 血液内科学分野）

SS1-1　移植非適応多発性骨髄腫治療の現状と課題

Current status and issues of treatment for transplant-ineligible multiple myeloma

鈴木　一史（Kazuhito Suzuki）
東京慈恵会医科大学附属柏病院 腫瘍・血液内科

SS1-2　移植適応多発性骨髄腫治療の現状と課題

Current status and issues of treatment for transplant-eligible multiple myeloma

塚田　信弘（Nobuhiro Tsukada）
日本赤十字社医療センター 血液内科

〈共催：武田薬品工業株式会社〉

スポンサードシンポジウム2

5月30日(日)　13:10－14:00　第1会場

Daratumumabと未治療移植非適応多発性骨髄腫の新しい世界 -基礎・臨床から-

Daratumumab and the New World of Transplant Ineligible Untreated Multiple myeloma patients – From a Academic and Clinical Standpoint

座長：池田　宇次（Takashi Ikeda）（静岡県立静岡がんセンター 血液・幹細胞移植科）

SS2-1　CD38 発現から考える初期治療としての DLd 療法の意義

Significance of DLd therapy as initial treatment considering CD38 expression status

北舘　明宏（Akihiro Kitadate）
秋田大学大学院医学系研究科・医学部 血液・腎臓・膠原病内科学講座

SS2-2　移植非適応新規多発性骨髄腫患者に対する新規治療戦略～ Daratumumab をいかに使用するか～

New treatment strategy for patients with newly diagnosed multiple myeloma who are ineligible for ASCT ～ How to use Daratumumab ～

石田　禎夫（Tadao Ishida）
日本赤十字社医療センター 血液内科 骨髄腫アミロイドーシスセンター

〈共催：ヤンセンファーマ株式会社〉

会長講演（Presidential Lecture）

PL-1 正常 B リンパ球由来 iPS 細胞を用いた骨髄腫起源細胞の探索

Study for exploring myeloma-initiating cell using normal B cell-derived induced pluripotent stem cells

坂井　晃
Akira Sakai

福島県立医科大学医学部 放射線生命科学講座
Radiation Life Sciences, Fukushima Medical University School of Medicine

Multiple myeloma (MM) cells are derived from mature B cells based on immunoglobulin heavy chain (*IgH*) gene analysis. The onset of MM is often caused by a reciprocal chromosomal translocation (cTr) between chr 14 with *IgH* and chr 11 with *CCND1*. We propose that mature B cells gain potential to transform by reprograming, and then chromosomal aberrations cause the development of abnormal B cells as a myeloma-initiating cell during B cell redifferentiation. To study myeloma-initiating cells, we have already established normal B cell-derived induced pluripotent stem cells (BiPSCs). We established two BiPSCs with reciprocal cTr t(11;14) using the CRISPR/Cas9 system; the cleavage site were located in the *IgH* Eμ region of either the VDJ rearranged allele or non-rearranged allele of *IgH* and the 5′-upsteam region of the *CCND1* (two types of BiPSC13 with t(11;14) and MIB2-6 with t(11;14)). Furthermore, *p53* was deleted using the CRISPR/Cas9 system in BiPSC13 with t(11;14). These BiPSCs differentiated into hematopoietic progenitor cells (HPCs). However, unlike cord blood, those HPCs did not differentiated into B lymphocytes by co-culture with BM stromal cell. Therefore, further ingenuity is required to differentiate those BiPSCs-derived HPCs into B lymphocytes.

学歴・職歴

1986 年　愛媛大学医学部卒業
1986 年　広島大学医学部附属病院内科医員（研修医）
1987 年　県立広島病院臨床研修医
1988 年　広島市立安佐市民病院内科医師
1993 年　広島大学大学院医学系研究科修了
1993 年　国立大竹病院内科医師
1996 年　広島大学原爆放射線医学研究所（血液内科）助手
1997-1998 年　米国国立衛生研究所 / 国立癌研究所（NIH/NCI), Lab. of Pathology, Visiting Fellow
2003 年　広島大学医学部附属病院血液内科講師
2011 年　福島県立医科大学医学部放射線生命科学講座主任教授

資格

1990 年　日本内科学会認定内科医
1992 年　日本血液学会認定医（2003 年から専門医に改変）
1992 年　日本内科学会認定内科専門医（2008 年から総合内科専門医に改変）
1995 年　日本血液学会指導医
2008 年　日本がん治療認定機構認定医
2011 年　日本臨床腫瘍学会　がん薬物療法専門医
2014 年　第 1 種放射線取扱主任者
2018 年　日本臨床腫瘍学会指導医

役職

2000 年　日本血液学会評議員　（2002 年より代議員へ改変）
2002 年　日本骨髄腫研究会幹事　（2004 年から日本骨髄腫学会）
2013 年　日本臨床腫瘍学会協議員
2014 年　日本リンパ網内系学会評議員
2019 年　Int J Hematol 編集委員

受賞

2006 年　堀之内朗記念研究助成（骨髄腫患者会助成金）
2007 年　広島大学病院長賞
2018 年　公益信託　日本白血病研究基金助成金（一般研究賞）

趣味

東京マラソン 9 回出場（2010, 2012-2019）：ベストタイム 3 時間 47 分（2019 年）
広島カープ優勝祈願

特別講演（Speacial Lecture）

SL-1 多発性骨髄腫における免疫調節薬：我々はどこまで識りえたか？

Immunomodulatory drugs in multiple myeloma: How far have we come?

秀島　輝
Teru Hideshima

ハーバード大学医学部 ダナ・ファーバー癌研究所
Jerome Lipper Myeloma Center, Dana-Farber Cancer Institute, Harvard Medical School

An important treatment advances in multiple myeloma (MM) is the development of immunomodulatory drugs (IMiDs) thalidomide (Thal), lenalidomide (Len), and pomalidomide (Pom). IMiDs directly induce growth arrest and apoptosis in MM cells, as well as downregulation of adhesion molecules. Moreover, IMiDs indirectly inhibit MM growth by suppressing neovascularization and downregulating production of tumor supportive cytokines from accessory cells in the bone marrow microenvironment. Importantly, IMiDs also modulates anti-MM immune effects, associated with enhanced T cell, NK cell, and NK-T cell activity, along with decreased regulatory T cell activity. Molecular mechanism of IMiDs-induced anti-MM activities has been extensively delineated during the last decade. IMiDs directly bind cereblon (CRBN), a substrate adaptor of Cullin4 Ring Ligase (CRL4) and activate $CRL4^{CRBN}$ ligase to ubiquitinate IKZK1/3 and other substrates for proteasomal degradation, thereby inducing direct anti-MM activities. However, development of resistance to IMiDs commonly underlies relapse of the disease. Importantly, previous preclinical studies have shown that the level of the proteins (ie, CRBN, CD147, CD44, TRAF2) is associated with IMiDs sensitivity. In MM patients with relapsed/ refractory to IMiD, mutations in *KRAS*, *NRAS*, *BRAF*, and *CRBN* have been reported. Recently, IMiDs have also been utilized to generate bifunctional proteolysis-targeting chimera (PROTAC) molecules consisting of a ligand to the protein of interest (POI) and a covalent linkage to CRBN, thereby allowing for its ubiquitination and proteasomal degradation. PROTACs therefore have great potential to treat cancer including MM, as well as autoimmune, neurologic and infectious diseases.

Education

1981	MD	Medicine	Fukuoka University School of Medicine, Fukuoka, Japan
1990	PhD	Immunology	Fukuoka University, Fukuoka, Japan

Postdoctoral Training

04/1981-03/1983	Intern & Resident	2nd Department of Surgery	Fukuoka University Hospital, Fukuoka, Japan
04/1983-03/1984	Resident	2nd Department of Surgery	National Fukuoka Central Hospital, Fukuoka, Japan
08/1989-09/1990	Research Fellow	Department of Medicine, Monoclonal Antibody Laboratory (Marshall Posner Lab)	Roger Williams Cancer Center, Brown University, Providence, RI
04/1998-03/2001	Research Fellow	Department of Medical Oncology (Ken Anderson Lab)	Dana-Farber Cancer Institute, Boston, MA

Faculty Academic Appointments

10/1990-03/1998	Assistant Professor	2nd Department of Surgery (Chief, Breast and Thyroid Cancer Division)	School of Medicine, Fukuoka University, Fukuoka, Japan
2002-	Principal Associate	Dept. of Medicine	Harvard Medical School, Boston, MA
2014-		Institute Scientist Medical Oncology	Dana-Farber Cancer Institute, Boston, MA

Editorial Activities

Ad hoc Reviewer

Blood, Blood Advances, Blood Cancer Journal, Cancer Cell, Cancer Research, Cancer Science, Clinical Cancer Research, Haematologica, International Journal of Hematology, Leukemia, Nature Medicine, Oncogene, Oncotarget, PNAS

Current Editorial Roles

2010-present	Editorial Board	Blood Cancer Journal

Recognition

2014	World's Most Influential Scientific Minds (Thomson Reuters)

SL-2 分子細胞遺伝学による t(11;14)(q13;q32) を持つ骨髄腫の生物学

Biology of multiple myeloma with t(11;14)(q13;q32) based on molecular cytogenetics

三浦　偉久男
Ikuo Miura

株式会社エスアールエル 遺伝子・染色体解析センター
Center for Genetic and Chromosomal Analysis, SRL, Inc.

More than 40% of plasma cell myeloma (PCM) cases present the 14q32 abnormality, which corresponds with the locus of the immunoglobulin heavy chain gene (IGH). During B cell development, the IGH gene undergoes VDJ recombination in the bone marrow (BM) and class switch (CS) recombination in the germinal center (GC). Among the 14q32/IGH translocations that occur in PCM, t(11;14)(q13;q32)/IGH-CCND1 is the most common (15%–20%). It was once considered that the t(11;14) generated through VDJ recombination t(11;14)/VDJ leads to mantle cell lymphoma (MCL) (IgM/D, κ < λ, CD5+, CD20+, SOX11+), while the t(11;14) generated through CS recombination t(11;14)/CS leads to PCM. However, it has been reported that approximately 20% of PCM cases with t(11;14) are t(11;14)/VDJ (IgG/A, κ < λ, CD5−, CD20+/−, SOX11−). It follows that, as double-hit lymphoma (DHL) of both t(14;18)/IGH-BCL2/VDJ and t(8;14)/IGH-MYC/CS, myeloma cells with t(11;14)/VDJ can differentiate into the GC and there acquire t(8;14)(q24;q32)/IGH-MYC, resulting in double-hit myeloma (DHM). Cytogenetically, there are two types of DHM: simple translocation type, t(11;14) + t(8;14), and complex translocation type, t(8;14;11)(q24;q32;q13). Although the remaining normal allele of myeloma cells with t(8;14;11) is productive and these cells can further differentiate into IgG/A myeloma, those with t(11;14) + t(8;14) are not productive and become either IgM/D or light-chain-only myeloma, because of the allelic exclusion at VDJ recombination. The other 14q32/IGH translocations also need to be biologically characterized through a multicenter study that includes a representative number of patients for each translocation.

学歴・職歴

1980 年 3 月　秋田大学医学部卒業
　　4 月　秋田大学医学部付属病院医員（研修医）（第三内科）
1981 年 4 月　秋田大学大学院医学研究科医学第三系入学
1985 年 3 月　秋田大学大学院医学研究科医学第三系卒業
　　4 月　秋田大学医学部第三内科助手
　　5 月　山本組合総合病院内科勤務
1986 年 5 月　秋田大学医学部付属病院第三内科
1988 年 8 月　University of Maryland Cancer Center (Research Associate)
1989 年10 月　Fox Chase Cancer Center (Postdoctoral Associate)
1990 年 8 月　男鹿市立総合病院内科勤務
1991 年 3 月　秋田大学医学部第三内科
　　5 月　秋田大学医学部第三内科 助手
1994 年10 月　秋田大学医学部附属病院第三内科 講師
2003 年 2 月　秋田大学医学部第三内科 助教授
2005 年 9 月　聖マリアンナ医科大学血液・腫瘍内科 教授
2019 年 4 月　株式会社エスアールエル 遺伝子・染色体解析センター 顧問
2020 年 4 月　東海大学医学部医学科 客員教授

所属学会

日本内科学会（認定医）
日本血液学会（専門医、指導医、功労会員）
日本リンパ網内系学会（名誉会員）
日本人類遺伝学会（臨床細胞遺伝学認定士・指導士）

シンポジウム温故知新
(Symposium -Discover new truths by studying the past-)

SY1-1 骨髄腫骨病変の病態解明と治療の進歩と展望

A new insight into the biology and treatment for bone disease in multiple myeloma

安倍　正博
Masahiro Abe

徳島大学大学院医歯薬学研究部 血液・内分泌代謝内科学分野
Department of Hematology, Endocrinology and Metabolism, Tokushima University Graduate School

Bone destruction still remains a leading cause for deterioration in quality of life (QoL) in patients with multiple myeloma (MM), despite recent great strides achieved in MM treatment owing to the implementation of new anti-MM agents. Importantly, aggressive bone destruction and thereby deterioration of physical functions with immobilization and muscle weakness further negatively impact the prognosis of patients with MM in terms of survival even in the era of new agents. The interaction between myeloma cells and the bone microenvironment causes the uncoupling of the bone-remodeling process with the activation of osteoclasts and suppression of osteoblastogenesis. We have demonstrated the critical roles of the TAK1-PIM2 pathway in such close interplay between MM cells and the bone marrow microenvironment in MM, posing this pathway as an efficacious therapeutic target. In addition to cellular components in the bone marrow, osteocytes embedded in bone have emerged as key regulators of bone loss in MM through interactions with cells in the bone marrow milieu, including MM cells, osteoclasts, and osteoblasts. Osteocytes secrete various cytokines, including RANKL, sclerostin and FGF23, to modulate bone cell function. Besides the mechanisms triggered by these well reported factors, acidic conditions and mechanical loading also affect pathological processes in MM tumor expansion and dissemination along with bone destruction. A new insight into the underlying pathogenesis of bone disease and tumor expansion and possible directions for future treatment will be presented.

【学歴・職歴】
昭和59年 3月　徳島大学医学部卒業
昭和59年 4月　徳島大学医学部附属病院 医員（第一内科）
昭和60年 2月　佐川町立高北国民健康保険病院 内科医員
昭和62年 4月　健康保険鳴門病院 内科医員
昭和63年11月　徳島大学医学部附属病院 医員（第一内科）
平成元年10月　米国テネシー州立大学メディカルセンターへ留学（2 年 7 ヶ月）
平成 4年 5月　徳島大学医学部附属病院 医員（第一内科）
平成 5年 9月　修誠会吉野川病院 内科医員
平成 6年 4月　徳島大学医学部附属病院　助手
平成11年 6月　徳島大学医学部附属病院　講師
平成18年10月　徳島大学大学院ヘルスバイオサイエンス研究部　生体情報内科学　助教授
平成19年 4月　同　准教授
平成21年 2月　徳島大学病院　病院教授
平成27年 1月　徳島大学大学院ヘルスバイオサイエンス研究部　生体情報内科学　教授
平成27年 4月　徳島大学大学院医歯薬学研究部　血液・内分泌代謝内科学（名称変更）教授
現在に至る

【所属学会】
日本骨髄腫学会（令和２年５月より理事長）、日本血液学会（代議員、プログラム企画委員、造血器腫瘍ガイドライン委員、MM 研究実行委員）、日本骨代謝学会（理事、プログラム選定委員）、日本内科学会（評議員）、日本造血細胞移植学会、日本臨床免疫学会、日本癌学会、日本癌転移学会、日本輸血細胞治療学会、日本老年学会、Cancer and Bone Society (Board Member)、ASH、ASBMR など
International Journal of Myeloma (Associate Editor), Journal of Bone Mineral and Metabolism (Editorial board), Journal of Medical Investigation (Editorial board), International Journal of Hematology (Editorial board)

【受賞】
平成13年10月　Award in Aki's Memory (International Myeloma Foundation)
平成14年12月24日　徳島大学医学部研究奨励賞
平成16年　平成 16 年度 康楽賞（徳島大学）
平成17年12月21日　第 4 回徳島新聞医学研究賞
平成20年10月30日　第 26 回日本骨代謝学会学術集会 学術賞
平成21年10月　平成 21 年度 公益信託 日本白血病研究基金　一般研究賞
平成28年7月22日　第 34 回日本骨代謝学会学術集会　尾形賞
平成29年10月　平成 29 年度 公益信託 日本白血病研究基金　一般研究賞

SY1-2 多発性骨髄腫の画像診断

Role of imaging in multiple myeloma patients

高須　深雪

Miyuki Takasu

広島市民病院 放射線診断科

Department of Diagnostic Radiology, Hiroshima City Hiroshima Citizens Hospital

Overview

This course will introduce technical and clinical aspects of conventional and advanced topics in imaging multiple myeloma, including computed tomography (CT), positron emission tomography (PET) using the radiotracer [18F]FDG (2‐[18F]‐fluoro‐2‐deoxy‐D‐glucose), and whole-body MRI. The course emphasis will be on incorporating advanced imaging techniques for these applications in relevant clinical settings.

Target Audience

The target audience is hematologists and radiologists with specialty expertise in hematology and musculoskeletal imaging who are interested in diagnostic medical imaging into clinical practice and research.

Educational Objectives

As a result of attending this course, participants should be able to:

- Summarize the current standard imaging techniques for patients with multiple myeloma;
- Describe advanced and quantitative imaging for MRI and FDG-PET/CT for improved value and diagnostic accuracy in multiple myeloma;
- Identify clinical applications and opportunities for the use of diagnostic medical imaging;
- Identify the current unmet imaging needs for multiple myeloma; and
- Discuss potential solutions based on conventional/advanced imaging techniques.

＝参加学会・資格＝

日本医学放射線学会（専門医）
日本磁気共鳴医学会（正会員）
International Society for Magnetic Resonance in Medicine（正会員）
Radiological Society for North America（正会員）
日本骨髄腫学会（正会員）
日本血液学会（正会員）
日本神経放射線学会（正会員）
日本脳神経 CI 学会（正会員）
日本骨代謝学会（正会員）
日本核医学会（正会員）

＝学歴　・　資格＝

1993　広島大学医学部卒業
1993　日本医師国家試験合格（医籍第 356975 号）
1998　放射線科専門医認定
2000　学位取得
2006　マンモグラフィー読影認定医
2007　磁気共鳴専門技術者認定
2011　PET 核医学認定医
2011　磁気共鳴上級専門技術者認定
2013　日本医学放射線学会放射線診断指導医認定
2017　核医学専門医認定
2017　日本ディープラーニング協会 G 検定

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1993 ～ 1994　広島大学医学部附属病院・放射線科　研修医
1994 ～ 1997　広島市立安佐市民病院・放射線科　研修医
1997 ～ 1999　呉市医師会病院・放射線科　医師
1999 ～ 2000　広島大学医学部附属病院・放射線科
2000 ～ 2001　マツダ株式会社マツダ病院・放射線科
2001 ～ 2002　中国電力株式会社中電病院・放射線科
2002 ～ 2009　広島赤十字・原爆病院・放射線科　医師
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2021 ～　広島市民病院・放射線診断科部長，広島大学病院・放射線診断科　客員准教授

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2000　文部科学省科学研究費・奨励研究 B
2009　加納基金研究助成
2009　財団法人土谷記念医学振興基金助成金
2011　科学研究費補助金（基盤 C）
2012　日本多発性骨髄腫患者の会堀之内朗記念多発性骨髄腫研究助成
2014　科学研究費補助金（基盤 C）
2017　科学研究費補助金（基盤 C）

SY1-3 骨髄腫における貧血 －こんなにも多様な機序が！－
Anemia in myeloma -diversity and spectrum of pathogenesis-

三輪　哲義
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Anemia is commonly observed among symptomatic myeloma patients. Beside, CRAB has been thought to be a representative finding. However, in some cases, anemia is the only manifestation without C, R or B. Why anemia is frequently seen in myeloma has been apparently thought to be solved by two mechanisms. One is the 'crowding-out' or 'space-occupying' effect by marrow myeloma cell growth. Another is decreased erythropoietin production by myeloma-related renal damage through overlapping causes, including cast-nephropathy, amyloidosis, renal invasion of myeloma cells (especially at advanced stage) and others. In addition to these two pathway, recent reports have shown the diversity and spectrum of pathogenesis of anemia in myeloma. Receznt publication can be classified as follows. 1. factors secreted from myeloma cells can cause apoptosis of marrow eryrhroblasts (eg. Fas-L, TRAIL) 2. myeloma marrow stroma alteration supressing erythropoiesis (eg. CCL3/CCR1/p38 activation causing GATA1 suppressin). 3. associated clonal erythropoiesis (eg. PNH clone). 4. immune related or M-component mediated hemolysis 5. altered iron and transferrin kinetics including including hepcidin (inducible by BMP-2) and IL-6 alteration and binding between transferrin and M-component. 6. bleeding-related anemia through thrombocytopenia, coagulopathy, enhanced fibrinolysis, local amyloid deposition and direct invation of myeloma cells including gastrointestinal plasmacytoma formation 7. prior autoimmune disease-related anemia 8. plasma cell dyscrasia developing in Gaucher's disease. 9. prior anemic diseases preceding myeloma in cases (aplastic anemia, megaloblastic anemi, PRCA, HS, hemoglobinopathy, sideroblastic anemia, G6PD deficiency) 10. co-incidence between myeloma and non-malignant hematological disorders (myelofibrosis, bone marrow necrosis, hemophagocytic syndrome) 11. myeloma with pre-malignant condition (MDS) 12. myeloma with other hematological malignancy 13. therapy-related (carfilzomib-induced hemolysis, IMID-related aplasia, daratumumab-associated transfusion problems) 14. other causes

In this session, etiology of anemia in myeloma will be discussed intensively and extensively.

SY1-4 骨髄腫細胞と破骨細胞を標的とするTh1様γδT細胞とエロツズマブの併用療法の開発

Development of combinatory treatment of Th1-like γδ T cells with elotuzumab against osteoclasts as well as myeloma cells

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Takeshi Harada[1], Yusuke Inoue[1], Hirofumi Tenshin[2], Asuka Oda[1], Ryohei Sumitani[1], Masahiro Oura[1], Kimiko Sogabe[1], Shiro Fujii[3], Shingen Nakamura[4], Hirokazu Miki[5], Kumiko Kagawa[3], Masahiro Hiasa[2], Jumpei Teramachi[6], Masahiro Abe[1]

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We have reported that Th1-like γδ T cells, which can be expanded *ex vivo* using aminobisphosphonates and immunomodulatory drugs of lenalidomide or pomalidomide, target myeloma (MM) cells and osteoclasts (OCs). More recent, Anti-MM mAbs have been attractive therapeutic modalities against MM. The present study is aimed to develop the treatment of Th1-like γδ T cells in combination with anti-MM mAbs against MM and OCs. Because expanded Th1-like γδ T cells highly expressed CD16, FcγRIIIa, we first examined whether anti-MM mAbs, elotuzumab (ELO), daratumumab (DARA), and isatuximab (ISA), induced ADCC in the presence of the γδ T cells. DARA and ISA did not induce cytotoxicity against CD38-expressing MM cells in the presence of the γδ T cells; however, addition of ELO further increased cytotoxicity of the γδ T cells against SLAMF7-expressing MM.1S and OPM-2 cells but not RPMI 8226 cells with marginal SLAMF7 expression, suggesting induction of ELO's ADCC with the γδ T cells. To elucidate the effect of ELO on OCs, we next examined SLAMF7 expression in osteoclastogenesis of monocytes-OC differentiation. Monocytes did not express SLAMF7; however, OCs robustly increased its expression along with osteoclastogenesis under stimulation of M-CSF and RNAKL. Of note, the combinatory treatment of γδ T cells with ELO significantly induced cytotoxicity against OCs. Furthermore, the combination eradicated MM cells and OCs in their coculture. Taken together, our findings provide the rationale for targeting vicious cycle between MM progression and osteoclastogenesis.

SY1-5 日本人多発性骨髄腫患者における血中ビタミンD濃度の検討

The prevalence and clinical outcomes of vitamin D deficiency in Japanese multiple myeloma patients: A single-center observational study

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Atsushi Isoda[1,2], Yuri Miyazawa[2], Tetsuya Ishikawa[2], Keita Nakayama[2], Shuhei Kanaya[2], Hirono Iriuchijima[2], Akio Saito[2], Morio Matsumoto[2], Morio Sawamura[2]

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Purpose: Vitamin D is the basic mediator of skeletal metabolism and also plays a significant role in the pathophysiology of multiple myeloma (MM). Recent studies have shown an association between vitamin D deficiency and racial outcomes in MM patients. The aim of this study was to assess the prevalence of vitamin D deficiency in Japanese MM patients and the association of the vitamin D status with their clinical outcomes.

Methods: The serum 25 (OH) D levels of 68 unselected Japanese MM patients were tested from December 2015 to March 2016 (winter season).

Results: The median serum 25 (OH) D level was 22 ng/mL (7-60 ng/mL); 32% and 51% of patients showed vitamin D deficiency (<20 ng/mL) and insufficiency (20-29 ng/mL), respectively. The 25(OH)D levels were not associated with sex, age, ISS stage, disease duration, or skeletal morbidity. Patients with vitamin D deficiency tended to show lower QOL scores. We subsequently recommended a dietary vitamin D supplement (cholecalciferol, 1000 IU/day) to 15 patients with suboptimal 25 (OH) D levels. After 3 months, all patients showed significantly increased 25 (OH) D levels ($p < 0.001$) and decreased PTH levels ($p<0.001$). However, their bone turnover markers, total P1NP and TRACP-5b, did not significantly change after vitamin D replacement. After a median follow-up period of 4.7 years, patients with vitamin D deficiency had significantly worse overall survival in comparison to patients with insufficient or sufficient levels (logrank, $p=0.03$).

Conclusion: Vitamin D deficiency predicted poor overall survival in Japanese MM patients.

SY1-6 骨髄腫骨関連事象の発生予防における身体機能維持の重要性

The importance of retaining physical functions to prevent SRE in multiple myeloma

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Bone destruction is a debilitating clinical event in patients with multiple myeloma (MM). Denosumab and zoledronic acid are widely used for the prevention of skeletal-related events (SRE) in MM. Although MM tumor progression is accepted to be major causative factor for SRE occurrence, the baseline risk factors of SRE in MM are not well established. Here, we retrospectively analyzed to identify baseline conditions and triggering factors for SRE in patients with MM on denosumab. Denosumab was given to 75 MM patients with a bone disease (38 males and 37 females) with a median age of 69 years old (range 44-88). The severity of bone disease at baseline was as follows: 13, 45 and 17 patients were scored to be bone scale1, 2 and 3, respectively. During the median follow-up of 17 months, SRE occurred in 6 out of 52 newly diagnosed patients, 5 out of 23 relapsed/refractory patients. The cumulative incidence of SRE was 33.2 % at 5 years. Univariate logistic regression analysis revealed that combination with AL amyloidosis (p=0.009) and PS with ECOG 3 or 4 (p=0.037) were significant risk factors for SRE. In multivariate logistic regression analysis, combination with AL amyloidosis remain as independent risk factor for SRE (p=0.035). Bone fractures occurred by falling down due to orthostatic hypotension and/or muscle weakness in 3 out of 4 cases with AL amyloidosis. These results suggest that balance loss and falling down appear to be triggering factors for SRE especially in MM patients with AL amyloidosis, indicating the importance of retaining physical functions to prevent SRE.

SY2-1 多発性骨髄腫とその周辺疾患の腎病変

Kidney lesions in multiple myeloma and related diseases

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Multiple myeloma and its related diseases are often associated with kidney impairment, which leads to a poor life prognosis. Although most of those kidney lesions share paraproteinemia as a common pathogenesis, the phenotype is quite heterogeneous. When the paraprotein takes microfibrillar or microgranular forms, they tend to deposit on glomerular subendothelial space, displaying a mesangial proliferative glomerulonephritis (MPGN) in classical glomerular histological categorization. They generally present nephrotic syndrome without evident hematuria, which is characteristic for MPGN. Some of those paraproteinemia related glomerulopathies are associated with other organ impairment such as neuropathy, that makes treatment even mor difficult. The paraprotein is metabolized in proximal convoluted tubular epithelia through megalin dependent manner after glomerular filtration. When the amount of paraprotein exceeds the level manageable by proximal convoluted tubular epithelia, tubular damage appears along with paraproteinuria. However, since usual dipstick method overlooks parapriteinuria, ratio of serum kappa/lambda chain is often applied as a screen tool instead. Although so cold cast nephropathy used to be considered as a major form of myeloma related nephropathy, different views are sometimes shown today. Cast nephropathy is not a sort of myeloma kidney form, but rather the terminal form of paraproteinuria related tubular damage in general. Therefore, aggressive renoprotective therapy may reduce the prevalence of cast nephropathy even in the autopsy cases. In Fukushima Medical University, we encountered 5 cases of cast nephropathy in 2000's. However, only 1 case in 2010's and no cases after 2015 were documented so far.

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1979（昭和 54）年　米国オハイオ州ベイ・ハイスクール卒業
1981（昭和 56）年　石善学園新潟第一高校卒業
1987（昭和 62）年　新潟大学医学部医学科卒業
1990（平成　2）年　同　歯学部口腔解剖第一講座（小澤英浩教授主宰）研究生
1995（平成　7）年　同　大学院医学研究科博士課程修了・医学博士
1996（平成　8）年　豪州聖ヴィンセント医学研究所（TJ Martin 教授主宰）研究員

【職歴】
1987（昭和 62）年　新潟大学医学部附属病院内科研修医
1989（平成 元）年　同　内科学第二講座（荒川正昭教授主宰・現腎膠原病内科学講座）医員
2002（平成 14）年　同　附属病院講師・集中治療部副部長
2009（平成 21）年　同　医歯学総合病院准教授・高次救命災害治療センター副センター長
2010（平成 22）年　同　医歯学総合病院准教授・血液浄化療法部副部長
2016（平成 28）年　福島県立医科大学腎臓高血圧内科学講座主任教授
2018（平成 30）年　同　生活習慣病慢性腎臓病病態治療学講座教授併任
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【主な所属学会】
日本内科学会（評議員／総合内科専門医・指導医）、日本腎臓学会（評議員／専門医・指導医）、日本透析医学会（評議員／専門医・指導医）、日本骨粗鬆症学会（評議員／専門医）、日本骨代謝学会（評議員）、日本骨形態計測学会（評議員）、日本サルコペニア・フレイル学会、日本転倒予防学会、日本遠隔医療学会、アメリカ内科学会、アメリカ腎臓学会、アメリカ骨ミネラル代謝学会、国際腎臓学会、国際骨ミネラル代謝学会、など

【専門領域】
内科学、腎臓学、骨ミネラル代謝学、血液浄化療法、遠隔医療、集団災害医療、救急・集中治療

【受賞歴】
1982-83（昭和 59-60）年　東日本医学生体育大会剣道部門団体優勝（連覇）
1992（平成 4）年　弥彦音楽祭声楽部門第一席
2011（平成 23）年　新潟県医師会学術奨励賞
2014（平成 26）年　日本骨代謝学会学術賞

【趣味・特技】
クラシック声楽・合唱指導・アニメ制作・奥さんと JR 福島駅東口周辺でデート♡

SY2-2 骨髄腫における染色体１ｑ２１増多と１ｐ欠失

Gain/amplification of chromosome arm 1q21 and deletion of chromosome 1p in multiple myeloma

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Multiple myeloma (MM) is a plasma cell malignancy characterized by a complex genetic heterogeneity. Gain or amplification of chromosome band 1q21 (1q21+) and deletion of chromosome 1p (del(1p)) are frequent adverse cytogenetics in MM. 1q21+ is the most common adverse chromosomal aberration that occurs in 40% of patients with newly diagnosed MM (NDMM). 1q21+ is mostly caused as a result of trisomy of chromosome 1, jumping whole-arm translocations of chromosome arm 1q (JT1q), and segmental duplications of 1q21. JT1q can introduce loss of multiple chromosome arm resulting in chromosomal instability, which may cause progressive complex chromosomal changes. This may be a mechanism accounting for the aggressive phenotype of MM cells with 1q21+. In MM cells with 1q21+, along with the chromosomal instability, increased expression of genes in the 1q21 amplicon are also likely to contribute to the development of the aggressive phenotype of MM (*CKS1B*, *PSMD4*, *MCL1,* and others). The simultaneous enhancement of the function of various genes in the 1q21 amplicon might, in part, account for the resistance to different drugs in MM with 1q21+. Del(1p) is also common and found in around 20% of NDMM patients. Among the genes located on chromosome 1p, *CDKN2C* (1p32), *FAF1* (1p32), and *FAM46C* (1p12) are suggested as candidate tumor suppressor genes. We have reported that bi-allelic loss of *FAM46C* activated the PI3K-Akt signaling and inhibitors of AKT and/or PI3K suppressed cell growth in FAM46C-KO cells compared with that in FAM46C-WT cells in MM. The inhibition of PI3K-Akt might be a therapeutic option for MM with del(1p). In this session, we will present the current knowledge about the pathology of 1q21+ and del(1p) in MM. This can provide clues for the effective therapeutic approach to patients with those abnormalities, leading to one more improvement of patient outcomes in MM.

1994 年 3 月　名古屋市立大学医学部 医学科 卒業、4 月　医師免許取得
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1996 年 4 月　静岡済生会総合病院 血液内科 医員
1998 年 4 月　名古屋市立大学 大学院 入学
2002 年 3 月　名古屋市立大学 大学院 修了、博士（医学）取得
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2003 年 6 月　University of Arkansas for Medical Sciences （米国アーカンソー州立大学）, Myeloma Institute for Research and Therapy, ポスドク (Drs Barlogie & Shaughnessy)
2006 年 4 月　愛知医科大学　血液内科　助教
2007 年 4 月　愛知医科大学　血液内科　講師
2011 年 4 月　愛知医科大学　血液内科　准教授（特任）
2013 年 1 月　愛知医科大学　血液内科　准教授
2015 年 4 月　愛知医科大学　血液内科　教授（特任）

国内留学
1999 年 6 月～ 7 月　京都府立医科大学 第 3 内科 血液研究室（谷脇 雅史 先生）
1999 年 4 月～ 2001 年 3 月 愛知県心障者コロニー 発達障害研究所 遺伝学部（孫田 信一 先生）

専門医・認定医
日本内科学会 総合内科専門医、日本血液学会 認定専門医、日本造血細胞移植学会 造血細胞移植認定医 など

所属学会代議員、評議員、委員
日本血液学会 評議員、日本骨髄腫学会 代議員、日本血液疾患免疫療法学会 評議員 など

SY2-3 透析を要する多発性骨髄腫症例におけるダラツムマブの有効性と安全性の検討

Efficacy and Tolerability of Daratumumab-based regimens in dialysis-dependent Japanese patients with myeloma

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Background: Daratumumab (DARA)-based regimens for multiple myeloma are highly regarded for their effectiveness and tolerability today, but there are few reports in dialysis patients. In this case series, we show a positive response and safety profile from our experience of four cases.
Cases: All patients were over 65 years old at diagnosis, and the oldest was 81. Of four cases, two were newly diagnosed and two were relapsed/refractory cases. The former received DARA-lenalidomide-dexamethasone (DRd) and the latter received DARA-bortezomib-dexamethasone. All patients were on hemodialysis at the start of DARA treatment. The causes of renal impairment were presumed to be myeloma cast nephropathy, expect for one patient with diabetic nephropathy who had initiated dialysis 9 months prior to the diagnosis of myeloma. DARA was administered in a standard dose (16 mg/kg), but in the reduced infusion rate. The observation period was 2-12 months. Every patient achieved VGPR or better within two cycles on DARA-based regimens. Two of the three patients with cast nephropathy were able to achieve dialysis-independence. No severe infusion related reactions was observed. DRd patients experienced grade 3 neutropenia and one of them developed febrile neutropenia. Both recovered with temporally withdrawal of treatment.
Conclusion: DARA-based treatments can be safely administered and have favorable effect for dialysis-dependent Japanese patients.

SY2-4 t(11;14) 転座に関連する未熟型骨髄腫では CD38 低発現、BCL2/BCL2L1 比高値を呈する

Multiple myeloma with t(11;14)-associated immature phenotype has lower CD38 expression and higher BCL2/BCL2L1 ratio

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Akihiro Kitadate[1,2], Kentaro Narita[2], Toshiki Terao[2], Sho Ikeda[1], Takafumi Tsushima[2], Daisuke Miura[2], Masami Takeuchi[2], Naoto Takahashi[1], Kosei Matsue[2]

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CD38 expression on myeloma cells is a critical factor affecting the early response to the anti-CD38 antibody daratumumab. It has been shown that IMiDs can enhance CD38 expression, thus, prior exposure to IMiDs may cause heterogeneous CD38 expression in previously treated myeloma patients. However, the factors affecting CD38 expression in untreated myeloma are not yet fully elucidated. In this study, we found that CD38 expression was significantly lower in myeloma patients with translocation t(11;14)-associated immature plasma cell phenotype, and especially in those expressing B-cell-associated genes such as PAX5 and CD79A. Furthermore, the BCL2/BCL2L1 ratio, the response marker of the BCL2 inhibitor venetoclax, was significantly higher in patients with the immature phenotype expressing B-cell-associated genes. BCL2/BCL2L1 ratio and CD38 expression were significantly negatively correlated. Moreover, all-trans-retinoic acid (ATRA), which is known to enhance CD38 expression and induce cell differentiation in myeloma cells, reduced B-cell marker expression and the BCL2/BCL2L1 ratio in myeloma cell lines, leading to reduced efficacy of venetoclax. Venetoclax is known to specifically induce cell death in myeloma harboring t(11;14), although it is unclear why the t(11;14) cases show BCL2 dependence. These results suggested that BCL2 dependence, as well as CD38 expression, may be deeply associated with the differentiation and maturation stages of myeloma cells. This study highlights the importance of examining t(11;14) and considering cell maturity in myeloma treatment strategies.

SY3-1 AL アミロイドーシスにおけるアミロイド線維形成機構の Up to date

Mechanism of amyloid fibril formation in AL amyloidosis: an up-to-date overview

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AL amyloidosis is a disorder caused by deposition of amyloid fibrils derived from monoclonal immunoglobulin light chain lambda or kappa type in various organs, such as heart, kidneys, gastrointestinal tract and peripheral nerves. An amyloidogenic precursor protein is produced by a malignant plasma cell clone. AL amyloidosis is classified into two types according to the pattern of amyloid deposition: systemic type and localized type. The systemic form is the most prevalent type of systemic amyloidosis in the Western countries. Due to the diverse amino acid sequences of the amyloid precursor proteins, experimental approach had been limited and the mechanism of amyloid formation remains unknown. However, recently, the development of research techniques, such as mass spectrometry, cryo-electron microscopy, and genome wide association study known as GWAS, help us for understanding of amyloid fibril structure, fibrogenesis and genetic risk. In addition, the pathogenesis, in particular cellular toxicity induced by precursor protein, is being clarified by recent studies based on established animal models, such as Caenorhabditis elegans and zebrafish. In this lecture, we will review the mechanism of amyloid formation in AL amyloidosis on up-to-date knowledge.

学　　位	博士（医学）（2015 年 3 月　熊本大学）	
所属学会	日本検査医学会（11 年間、2019 年より評議員） 日本臨床化学会（11 年間、2013 年より評議員） 日本アミロイドーシス学会（7 年間） 日本医用マススペクトル学会（7 年間） 世界アミロイドーシス学会（6 年間） 九州遺伝子診断研究会（10 年間、2013 年より世話人）	
学　　歴	2005 年 3 月 31 日	長崎県立佐世保南高等学校　卒業
	2005 年 4 月 1 日	熊本大学医学部保健学科検査技術科学専攻　入学
	2009 年 3 月 31 日	同　卒業
	2009 年 4 月 1 日	熊本大学大学院医学教育部修士課程　入学 （医科学専攻）
	2011 年 3 月 31 日	同　修了（医科学修士）
	2011 年 4 月 1 日	熊本大学大学院医学教育部博士課程　入学
	2015 年 3 月 31 日	同　修了　博士（医学）
職　　歴	2011 年 4 月 1 日	熊本大学大学院生命科学研究部
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	～現在	構造機能解析学講座・助教
	2013 年 4 月 1 日	熊本大学附属病院中央検査部
	～ 2020 年 3 月 31 日	非常勤臨床検査技師（兼任）
	2017 年 3 月 15 日	University of Pavia（イタリア）
	～ 2018 年 9 月 14 日	Visiting researcher
	2019 年 11 月 1 日	熊本大学病院アミロイドーシス診療センター
	～現在	質量分析解析主任（兼任）
社会貢献	日本検査医学会（全国評議員、九州支部評議員）、 日本臨床化学会（全国評議員、九州支部評議員）	
賞　　罰	2020 年	日本臨床化学会 2020 年度奨励賞
	2019 年	日本臨床検査医学会 2019 年度検査・技術賞
	2019 年	日本アミロイドーシス学会若手優秀ポスター賞
	2018 年	“Graziella Bonacchi”Awards. Italian Society of Amyloidosis
	2018 年	Junior Researcher Travel Awards, Amyloidosis Foundation
	2016 年	日本アミロイドーシス研究会 2016 年度研究奨励賞
	2014 年	日本臨床検査医学会 2014 年度国際学会奨励賞
	2014 年	Junior Researcher Travel Awards, Amyloidosis Foundation
	2014 年	日本臨床化学会 2014 年度 Young Investigator Award
	2014 年	熊本大学医療活動表彰
	2013 年	日本医用マススペクトル学会若手優秀ポスター賞
	2013 年	日本臨床検査医学会学会若手研究者優秀発表賞
	2011 年	病態情報解析学賞
免許・資格	2009 年	臨床検査技師免許（登録第 168143 号）
	2018 年	D 合（熊本大学大学院保健学教育部）
	2016 年	認定臨床化学者（日本臨床化学会）
	2010 年	遺伝子分析科学認定士（初級）（日本臨床検査同学院）

SY3-2 AL アミロイドーシス診療の最前線
Recent advances in diagnosis and treatment of AL amyloidosis

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Amyloidosis is protein conformational disease caused by the misfolding and aggregation of autologous proteins, which are deposited in tissues in the form of amyloid fibrils. Recently, TTR tetramer stabilizer (tafamidis) was reported to be effective in treatment of ATTR amyloidosis. Differential diagnosis between AL and ATTR amyloidosis is increasingly focused for adequate treatment for patients with cardiac amyloidosis.
AL amyloidosis is caused by abnormally produced monoclonal light chains that aggregate and deposit in various tissues, including the heart, kidneys, liver, gastrointestinal tract, peripheral nerves, skin, and other tissues. The outcome of AL amyloidosis varies among individuals and it depends on the dominant organ system involved. Diagnosis of AL amyloidosis is made by pathological assessment, measurement of serum FLC, and detection of clonal plasma cells in bone marrow. Treatment strategy is based on reduction of FLC by chemotherapy and melphalan plus dexamethasone is one of standard of care for AL amyloidosis. Bortezomib-based chemotherapy may increase treatment response, although it has not officially approved for primary AL amyloidosis in Japan. High-dose melphalan and autologous stem cell transplantation has been introduced as a treatment option for eligible patients and was reported to induce a higher response rate compared to conventional chemotherapy. Anti-CD38 monoclonal antibody which acts on clonal plasma cells is reported to be highly effective for patients with AL amyloidosis with rapid hematological response.

昭和 42（1967）年　　新潟市生まれ

昭和 61 年 3 月	新潟県立新潟高校卒業
平成 5 年 3 月	新潟大学医学部卒業
平成 5 年 5 月	新潟大学医学部附属病院　内科　臨床研修医
平成 7 年 4 月	新潟大学大学院医学研究科　入学
平成 8 年 5 月～ 10 年 10 月	順天堂大学医学部免疫学教室に国内留学（奥村康教授）
平成 11 年 3 月	新潟大学大学院医学研究科　卒業
平成 11 年 7 月～ 13 年 3 月	米国　カリフォルニア大学サンディエゴ校　留学 ポストドクトラルフェロー（Prof. Thomas J. Kipps）
平成 13 年 4 月	日本学術振興会　特別研究員 PD
平成 16 年 5 月	長岡赤十字病院　血液内科
平成 17 年 8 月	東京大学医科学研究所附属病院　血液腫瘍内科　助手
平成 19 年 4 月	同　助教
平成 22 年 8 月	順天堂大学医学部内科学血液学講座　准教授
平成 23 年 10 月	日本赤十字社医療センター　血液内科
平成 24 年 6 月	日本赤十字社医療センター　血液内科　副部長

賞罰
平成 12 年　上原記念生命科学財団ポストドクトラルフェローシップ海外留学助成
平成 20 年　日本造血細胞移植学会　学会奨励賞

所属学会
日本内科学会、日本血液学会、日本造血細胞移植学会、日本骨髄腫学会、日本癌学会、日本免疫学会、日本臨床腫瘍学会、日本輸血細胞療法学会、ASH、ASBMT

学会活動
日本血液学会　評議員（2015 年 10 月～）、専門医・指導医
日本造血細胞移植学会　評議員（2009 年 4 月～）、認定医
日本骨髄腫学会　代議員（2017 年 5 月～）
日本内科学会　総合内科専門医・指導医
がん治療認定医（2010 年 4 月～）

SY3-3 アミロイドーシス調査研究班による IgM 型 AL アミロイドーシス 21 例の後方視的解析

A retrospective analysis of 21 patients with IgM-related AL amyloidosis in Japan: A Study by the amyloidosis-research-committee

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Immunoglobulin M (IgM)-related light chain (AL) amyloidosis is a rare and poorly studied clinical entity.
We retrospectively analyzed data of 21 patients diagnosed with IgM AL amyloidosis from 10 centers in Japan.
They were 13 men and 8 women, with a median age of 65 years old (44-81). Light chain types were kappa in 5 and lambda in16 cases. Cardiac involvement was observed in 7 (33%), and renal involvement in 15 (71%) cases. Other involved organs were digestive tract (11), liver (6), nerves (4), and lymph nodes (5 cases). Median IgM and dFLC at diagnosis were 1215mg/dl (34-3008mg/dl) and 34.3mg/l (12.7-290.8mg/l), respectively. In IgM-related AL amyloidosis, the M protein value was high and the dFLC value was low compared with non-IgM AL amyloidosis.
The initial treatments were MEL/DEX in 7, BOR/CPM/DEX in 3, auto-SCT in 3, rituximab/bendamustine in 1, and others in 3 cases.
Hematological responses were 3 CR (20%), 1 VGPR (7%), and 4 PR (13%) out of 15 assessable cases, with overall response rate of 40%.
Median OS was 14.0 months (3.1-206.2) and 1-year OS was 71.4%. The prognosis was significantly poorer in patients with cardiac involvement than no-cardiac involvement group (1-year OS 27.8% vs. 85.7%, p=0.0468).
IgM-related AL amyloidosis was relatively common in the elderly, with a high frequency of renal involvement and low frequency of cardiac involvement. There were many cases with low dFLC value, therefore therapeutic response was difficult to assess. Further accumulation of cases is necessary to determine the most suitable treatment regimen for IgM AL amyloidosis.

SY3-4 AL アミロイドーシスに対する VCD 治療中に心不全を合併し、ダラツムマブを導入した一例

Introduction of daratumumab in a patient with AL amyloidosis who developed acute heart failure during VCD

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Motoko Kohda, Kyoko Yoshihara, Satoshi Yoshihara, Mami Samori, Nobuto Utsunomiya, Satoshi Higasa

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Although novel drug-based regimens for myeloma are effective for AL amyloidosis, patients with cardiac amyloidosis often develop cardiac events during treatment that could result in treatment discontinuation. Here, we report a patient who developed acute heart failure (AHF) during VCD, and was rescued with an introduction of daratumumab in combination with reduced doses of bortezomib (Bor) and dexamethasone (Dex).

A 62-year-old woman recurrently developed gastrointestinal bleeding, and was diagnosed with AL amyloidosis (κ-type) after repeated biopsies from colon ulcers. Blood tests showed the presence of BJP-κ M-protein with an elevated level of free κ light-chain (κ 442 mg/L, λ 19 mg/L, κ/λ 23, and dFLC 423 mg/L). Bone marrow examination revealed phenotypically abnormal plasma cells (5.8%). Findings of electrocardiography and echocardiography were compatible with cardiac amyloidosis. VCD (Bor 1.3mg/m2/week, cyclophosphamide 300mg/m2/week, and Dex 40mg/week) was started. On day 26, she was admitted to the hospital with AHF. A chest X-ray showed pulmonary edema, and blood test showed a remarkable elevation of NT-proBNP (24458 pg/mL). Because of the concerns about an involvement of Bor in the development of AHF, daratumumab was introduced in combination with significantly reduced doses of Bor (0.5mg/m2/week) and Dex (10mg/week) after recovery from AHF. She achieved hematologic VGPR and dFLC <10 mg/dL after 1 and 3 courses of DVd, respectively. An introduction of daratumumab may enables less cardiotoxic treatment by allowing to reduce potentially cardiotoxic drugs.

2020年日本多発性骨髄腫学会奨励賞受賞講演
(JSM Research Award Lecture)

JRAL-1 多発性骨髄腫の分子病態と治療抵抗性における低酸素誘導性遺伝子の意義

Significance of hypoxia-inducible genes in molecular pathogenesis and therapy resistance of multiple myeloma

池田　翔
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Hypoxic response helps maintain cellular homeostasis in response to environmental changes. Accumulation of hypoxia-inducible factor (HIF) and its transcriptional activity regulate the expression of various essential genes. Furthermore, changes in gene expression in response to hypoxia play important roles in not only normal cells but also various cancers, which may lead to treatment resistance and poor prognosis. We performed comprehensive gene and microRNA expression analysis on samples from multiple myeloma (MM) patients and cell lines cultured under hypoxia. We identified histone demethylase KDM3A, glycolytic enzyme HK2, and microRNA-210 as factors that play important roles in hypoxia. KDM3A upregulates the long noncoding RNA (lncRNA) MALAT1 and consequently activates the HIF-glycolytic system. HK2 not only controls important steps in glycolysis, but also contributes to autophagy by manipulating mTOR signaling, leading to proteasome inhibitor resistance. microRNA-210 represses IRF4 via regulation of a ribosomal RNA methyltransferase and promotes hypoxic adaptation. Currently, we are analyzing the expression and function of hypoxia-inducible lncRNAs to further elucidate the molecular pathogenesis of MM under hypoxia. Overall, our studies suggest that the regulatory factors that induce drug resistance and anti-apoptotic potential in myeloma cells are constantly change depending on the partial pressure of environmental oxygen. Therefore, identifying hypoxia-specific anti-apoptotic factors will be important in the search for a cure for MM.

学歴
2003 年 4 月　秋田大学医学部医学科入学
2009 年 3 月　同卒業
2012 年 4 月　秋田大学大学院博士課程医学専攻
2016 年 3 月　同卒業（医学博士）

職歴
2009 年 4 月から 2011 年 3 月　市立秋田総合病院　初期研修医
2011 年 4 月から 2012 年 3 月　秋田大学医学部附属病院　血液・腎臓・膠原病内科　医員
2012 年 4 月から 2012 年 9 月　JA 秋田厚生連　能代厚生医療センター　血液腎臓内科　医員
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JRAL-2 多発性骨髄腫における新規免疫チェックポイント Siglec ファミリー分子

Novel immune checkpoint sialic acid-binding Ig-like lectin (Siglec) family molecules in multiple myeloma

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The B7 family checkpoint molecules expressed on tumor cells from multiple myeloma (MM) patients, such as PD-L1, PD-L2, and CD86 (B7-2), have previously been shown to be associated with not only suppression of antitumor immune responses but also aggressive myeloma behaviors including cell proliferation and drug resistance. Sialic acid-binding Ig-like lectin (Siglec) family molecules are similar to B7 family members and screened out as a new therapeutic target for cancers. This study investigated the expression and biological functions of the Siglec family molecules in MM. Of the human Siglec family 15 molecules, the mRNA of Siglec-10 and Siglec-15 were detected in almost all MM cell lines and CD138+ plasma cells from MM patients. In particular, MM patients in the group with high Siglec-15 mRNA expression (n=13) had significantly shorter progression-free survival (PFS) times compared with those in the low group (n=32; P= 0.001). On multivariate analysis, the Siglec-15 mRNA levels were independent prognostic factors for PFS. Moreover, the Siglec-15 expression was increased by the granulocyte-macrophage colony-stimulating factor produced from the stoma cell lines HS-5 and IFN-γ, resulting in its expression that may be upregulated in the bone marrow MM microenvironment. These results suggest that Siglec-15 expression levels may reflect MM disease progression and be a promising therapeutic target for immunotherapy. Further studies are in progress to clarify the biological functions of Siglec-15 in myeloma and immune cells.

学歴
2001 年 4 月　東邦大学理学部生物分子科学科　入学
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2005 年 4 月　東邦大学大学院理学研究科生物分子科学専攻修士課程 入学
2007 年 3 月　東邦大学大学院理学研究科生物分子科学専攻修士課程 修了
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受賞歴
2020 年　日本骨髄腫学会 日本骨髄腫学会奨励賞
2019 年　第 44 回日本骨髄腫学会学術集会優秀演題賞
2019 年　日本骨髄腫患者の会 多発性骨髄腫研究助成
2016 年　日本医科大学度丸山記念研究助成金

2020 年骨髄腫患者会助成金受賞講演
(Multiple Myeloma Research Grant from Myeloma Patients and Families, Japan Award Lecture)

MRGAL-1 多発性骨髄腫の進行における細胞外小胞の新たな役割

The Emerging Roles of Extracellular Vesicles in Multiple Myeloma Progression

山本　雄介[1]、山元　智史[2]、服部　豊[2]、落谷　孝広[3]

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Extracellular vesicles (EVs) are lipid membranous vesicles, secreted from almost all types of cells. In general, EVs work as an intracellular communication tool by transferring cellular cargoes such as microRNAs, proteins and metabolites to adjacent or distant cells. Accumulating evidence demonstrated that secretion of EVs are tightly related to a series of physiological and pathological phenomena, including cancer progression. One of the difficulties in cancer therapeutics is due to drug resistance. Here we show a novel molecular mechanism on drug resistance via EVs secretion in multiple myeloma. Comparative analysis based on whole transcriptome profiling between drug resistant and sensitive cell lines revealed key genes responsible for EVs secretion in multiple myeloma. The inhibition of the genes decreased the amount of EVs secretion and re-sensitized the drug response in multiple myeloma. Unexpectedly, the attenuation of the genes also influenced cellular adhesion in multiple myeloma cells. Because the relationship between cell adhesion and drug resistance has been well studied in multiple myeloma, this finding indicates that EV secretion linked both drug resistance and cell adhesion. Thus, the genes and the pathways we identified in this study might be a good therapeutic target for drug-resistant multiple myeloma.

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MRGAL-2 多発性骨髄腫における Signal transducing adaptor protein ファミリーの役割

The role of Signal-transducing adaptor protein family in multiple myeloma

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The activation of inflammatory signaling pathways is known to be one of the important mechanisms for the progression of multiple myeloma (MM). Recently, preclinical studies showed the inhibition of JAK signaling is effective in suppressing MM cell proliferation. Interestingly, these studies revealed that the targets of the inhibitors are not only tumor cells, also the cellular components of MM microenvironment, such as macrophages and mesenchymal stromal cells. In 2003, we cloned signal-transducing adaptor protein (STAP) -2 as a C-FMS/M-CSFR interacting protein and subsequently found to function as an adaptor of signaling or transcription factors. These include STAT5, p38 MAPK, MyD88 and IκB kinase in immune and malignant cells. Based on previous findings, we hypothesized that STAP family members might contribute to the pathogenesis of MM.

To study the role of STAPs in MM microenvironment, we performed RNA-sequence experiments using mesenchymal stromal cells freshly isolated from healthy donor and patient bone marrow. The bioinformative analyses with GO and KEGG libraries generated using Enrichr showed that various pathways associated with inflammation and cytokines, including type I IFN, insulin-like growth factor, MAPK and JAK/STAT signaling, are activated in MM patient stromal cells. Among them, transcription factor enrichment analysis with ENCODE library indicated that the target genes of STAT2 and STAT1 are significantly upregulated (p=9.68E-12, FDR=4.25E-09 and p=1.04E-11, FDR=4.25E-09, respectively). We also confirmed the expression of STAP-2 is upregulated in MM stromal cells. Our findings indicated that STAP-2 related signaling pathways might affect MM pathogenesis via the microenvironment. Further studies with gene modification could be clarified the details about the effects of STAP-2 on MM cells.

＜略歴＞
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プレナリー（Plenary）

㊧ PS-1 髄外病変はヒアルロン酸を介した骨髄腫細胞同士の凝集から発症する

Extramedullary diseases originate from hyaluronan-induced homophilic cell-cell interaction of myeloma cells

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Extra-medullary disease (EMD) in multiple myeloma (MM) is associated with poor prognosis and resistance to chemotherapy. However, the mechanisms by which EMD occurs and whether it can be therapeutically targeted to improve the survival of patients with EMD remain poorly explored.

We found that MM cells interacted with each other and generated cell clusters under co-culture with stroma cells or their conditioned medium. Hyaluronan induced cell cluster formation in CD44-positive MM cell lines but not in CD44-negative MM cell lines. MM cell clusters rendered the resistance to bortezomib and carfilzomib via the activation of intracellular domains of CD44 and Notch2.

The concentrations of hyaluronan were higher in the serum of MM patients with EMD than those without EMD. The administration of hyaluronan could generate EMD in the liver, skin, and soft tissue, and shortened the survival in mice transplanted with the MM cell line MOPC315BM.

The administration of anti-CD44 antibody could inhibit the generation of EMD and prolonged the survival in combined with bortezomib, whereas single administration of bortezomib could not. In addition, γ-secretase inhibitor (GSI) overcame bortezomib resistance and inhibited the growth of MM cells in mice.

We show here that hyaluronan could generate MM cell clusters and recapitulate EMD in a mouse model. These results suggest that EMD originates from hyaluronan-induced homophilic cell-cell interaction. Anti-CD44 antibody and GSI may increase the therapeutic index in clinical settings via counteracting MM cell homophilic interaction.

㊧ PS-2 TAK-1 が誘導する内因性 PP2A 阻害因子 CIP2A の骨髄腫細胞の生存・増殖に及ぼす重要な役割

Critical role of TAK1-mediated upregulation of the endogenous PP2A inhibitor CIP2A in myeloma cell growth and survival

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Cancer cells are generally accepted to repress the activity of protein phosphatase 2A (PP2A) to facilitate their growth and survival signaling. Recently, cancerous inhibitor of PP2A (CIP2A), an endogenous PP2A inhibitor, has been demonstrated as a prognostic factor for multiple myeloma (MM). We recently reported that TGF-b-activated kinase-1 (TAK1) is constitutively over-expressed and phosphorylated in MM cells to mediate their growth and survival. Here, we explored the mechanism of CIP2A upregulation and the therapeutic role of targeting CIP2A in MM cells. MM cells highly expressed CIP2A, while normal peripheral blood cells did not. CIP2A expression as well as TAK1 phosphorylation were further upregulated in MM cells by IL-6 or when co-cultured with bone marrow stromal cells. The upregulation of CIP2A expression was abolished by TAK1 inhibition with shRNA as well as TAK1 kinase inhibitors, indicating TAK1-mediated upregulation of CIP2A. Importantly, *CIP2A* knockdown suppressed TAK1 phosphorylation, suggesting feedforward amplification of the TAK1-CIP2A-PP2A axis. Furthermore, although IGF1 did not phosphorylated TAK1 in MM cells, TAK1 inhibition enhanced phosphorylation or activation of the IGF1-PI3K-Akt survival pathway through CIP2A downregulation. These results collectively suggest that TAK1 mediates CIP2A upregulation to inhibit PP2A activity to enhance phosphorylation of a wide variety of serine/threonine kinases, including TAK1 and PI3K-Akt kinases, thereby orchestrating the activation of multiple survival signaling pathways in MM cells in an auto-amplified manner.

㊧ PS-3 Carfilzomib 含有救援療法後に 2 回目の自家末梢血幹細胞移植を実施した再発多発性骨髄腫の検討

Efficacy of salvage treatment with carfilzomib based rescue chemotherapy followed by HDT/2nd ASCT in relapsed/refractory multiple myeloma patients

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[Introduction] With the advent of proteasome inhibitors (PIs) and immunomodulatory drugs (IMiDs), the treatment results and prognosis of multiple myeloma (MM) have improved significantly, but complete cure for patients with relapsed/refractory MM (RRMM) is still difficult. We investigated the clinical course of 9 cases of RRMM who underwent a second high-dose chemotherapy with autologous peripheral blood stem cell transplantation (HDT / ASCT) after carfilzomib (CFZ), a second-generation PI, based rescue chemotherapy, i.e., with lenalidomide (LEN) plus dexamethasone (DEX) (KRD) and with DEX (KD) in Kyoto Clinical Hematology Study Group.

[Results] All patients had a history of bortezomib (BTZ) treatment. The median period from the first to the second HDT / ASCT was 1958 days, and the age at the second HDT / ASCT was 63.2 years. The best therapeutic effect of KD therapy (4 cases) and KRd therapy (5 cases) were stringent complete response (sCR) in 2 cases, very good partial response (VGPR) in 2 cases, and PR in 5 cases. Pre-transplant treatment were melphalan (MEL) alone in 3 cases and BTZ / MEL in 6 cases. The best treatment effects after transplantation were sCR in 6 cases, VGPR in 2 cases, and PR in 1 case. No serious adverse events were observed in any cvases.

[Conclusion] These cases suggested that the salvage chemotherapy with CFZ based treatment followed by second HDT / ASCT might be promising treatment strategy for young RRMM patients.

㊫ PS-4 SUBCUTANEOUS DARATUMUMAB COMBINATION THERAPIES FOR MULTIPLE MYELOMA: INITIAL RESULTS FOR D-KD AND UPDATED RESULTS FOR D-VMP AND D-RD FROM PLEIADES

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Daratumumab 1,800 mg for subcutaneous administration (DARA SC) has a short administration time and low rates of IRRs. We present the primary analysis of DARA SC + carfilzomib/dexamethasone (D-Kd) and updated data for DARA SC + lenalidomide/dexamethasone (D-Rd) and DARA SC + bortezomib/melphalan/prednisone (D-VMP) in the phase 2 PLEIADES study. RRMM pts with 1 prior line of therapy (1PL) received 28-day cycles of Kd (K 20 mg/m^2 Cycle [C] 1 D1; K 70 mg/m^2 C1 D8, D15; K 70 mg/m^2 C2+ D1, D8, D15; d 40 mg IV or PO QW). RRMM pts with ≥1PL received 28-day cycles of Rd (R 25 mg PO D1-21; d 40 mg IV/PO QW each cycle). Both cohorts with RRMM pts also received DARA SC (C1-2 QW, C3-6 Q2W, C7+ Q4W). Transplant-ineligible NDMM pts received 9, 6-week cycles of VMP (V 1.3 mg/m^2 SC twice weekly in C1, C2-9 QW; M [9 mg/m^2] and P [60 mg/m^2] PO C1-9 D1-4) + DARA SC (C1 QW, C2-9 Q3W in 42-day cycles, C10+ Q4W). The primary endpoint was overall response rate (ORR). In the D-Kd cohort (n=66), ORR was 84.8%. For the updated analysis of D-Rd (n=65) and D-VMP (n=67), ORRs were 93.8% and 89.6% respectively. The response rates of all cohorts were consistent with corresponding DARA IV studies. The median duration of DARA SC administration was 5 minutes for all D-Kd injections. D-Kd showed a comparable safety profile with DARA IV regimens and reduced rates of IRRs and administration time. Additional data will be presented. The primary analysis of D-Kd and extended follow-up of D-Rd and D-VMP cohorts continue to support the use of DARA SC across lines of therapy for multiple myeloma.

㊧ PS-5 SUBCUTANEOUS DARATUMUMAB + BORTEZOMIB/CYCLOPHOSPHAMIDE/ DEXAMETHASONE (D-VCD) IN NEWLY DIAGNOSED AL AMYLOIDOSIS: ASIAN SUBGROUP ANALYSIS FROM ANDROMEDA

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Subcutaneous daratumumab (DARA SC) with bortezomib, cyclophosphamide, and dexamethasone (D-VCd) vs VCd improved outcomes for newly diagnosed light chain (AL) amyloidosis in the phase 3 ANDROMEDA study. Here, we report a subgroup analysis of Asian pts (China, Japan, and Korea) from ANDROMEDA. Pts were randomized to receive six 28-day cycles of VCd (V: 1.3 mg/m^2 SC QW; C: 300 mg/m^2 PO or IV QW; d: 40 mg PO or IV QW) ± DARA SC (QW Cycles 1-2, Q2W Cycles 3-6; DARA monotherapy Cycle 6+ up to 24 cycles). The primary endpoint was overall hematologic complete response (CR) rate. Among 388 randomized pts (D-VCd, n=195; VCd, n=193), 60 were Asian (D-VCd, n=29; VCd, n=31). The median duration of treatment was 9.2 months for D-VCd and 5.3 months for VCd. The CR rate was 59% for D-VCd and 10% for VCd (odds ratio, 13.2; 95% CI, 3.3-53.7; P<0.0001). With 9.4 months median follow-up, major organ deterioration-PFS favored D-VCd (HR, 0.21; 95% CI, 0.06-0.75, P=0.0079), and 12 total deaths occurred (D-VCd, n=3; VCd, n=9). The most common (≥10%) grade 3/4 TEAEs were lymphopenia (D-VCd, 35%; VCd, 32%), neutropenia (10%; 3%), diarrhea (10%; 7%), pneumonia (7%; 10%), cardiac failure (7%; 10%), hypokalemia (7%; 10%), anemia (3%; 10%), thrombocytopenia (3%; 10%), hypoalbuminemia (3%; 10%), and syncope (3%; 10%). One patient in each arm discontinued treatment due to TEAEs. D-VCd was superior to VCd in Asian patients with a safety profile consistent with the overall study population supporting the use of D-VCd in Asian patients with newly diagnosed AL amyloidosis.

㊧ PS-6 新規改変型二重特異性抗体の作製と骨髄腫に対する革新的免疫療法の開発

Development of innovative antitumor antibodies armed with Bridging-BiTE to advance anti-myeloma immunotherapy

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Relapsed/refractory multiple myeloma (RRMM) can be heterogeneous, and is still an incurable disorder. Bispecific T-cell engager (BiTE) has shown promise in patients with RRMM. To improve the treatment efficacy, we have developed a novel BiTE-based modality, Bridging-BiTE (B-BiTE), which endows a series of clinically available monoclonal antibodies (mAbs) with both NK-cell and T-cell activation capacity. B-BiTE possesses two single chain fragment variables (scFvs) specific for an Fc domain of a mAb and the CD3ε, respectively. Using Rituximab as a model, B-BiTE/Rituximab complex bound to both $CD20^+$ tumor cells and human T cells, and activated T cells/NK cells against tumor cells. Then, we applied B-BiTE to Daratumumab (Dar) and Elotuzumab (Elo) for targeting myeloma cells. Human T cells proliferated, and produced multiple cytokines against both $CD38^+SLAMF7^-$ and $CD38^-SLAMF7^+$ heterogeneous myeloma cells in the presence of B-BiTE/Dar and B-BiTE/Elo without increasing the frequency of regulatory T cells. Their antitumor cytotoxicity induced by B-BiTE/Dar and B-BiTE/Elo was enhanced when compared with that mediated by Dar/Elo alone *in vitro and in vivo*. Importantly, T cells/NK cells obtained from patients cooperatively responded to their own myeloma cells in the presence of B-BiTE/mAb. In contrast, B-BiTE/mAb with polyclonal immunoglobulin did not induce any reactivity to normal cells. Therefore, B-BiTE can be a new modality to easily and broadly generate stable, safe, and effective next-generation bispecific antibodies, resulting in further advancement of immunotherapy for RRMM.

㊧ PS-7 CARTITUDE-1: PHASE 1B/2 STUDY OF CILTACABTAGENE AUTOLEUCEL IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

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CARTITUDE-1 is a phase (ph) 1b/2 study of ciltacabtagene autoleucel (cilta-cel), a CAR-T cell therapy with 2 BCMA-targeting single-domain antibodies designed to confer avidity (NCT03548207).

Patients (pts) had measurable disease, ≥3 prior regimens (or double refractory to PI and IMiD), and received an anti-CD38. After Cy/Flu lymphodepletion, a targeted dose of 0.75×10^6 ($0.5–1.0\times10^6$) CAR+ viable T cells/kg was infused. Primary objectives were to assess safety and establish the recommended phase 2 dose of cilta-cel (ph 1b) and to evaluate efficacy (ph 2). Response was assessed per IMWG criteria. Cytokine release syndrome (CRS) was graded by Lee et al (*Blood* 2014) and neurotoxicity by CTCAE in ph 1b and ASTCT criteria in ph 2. In this report, Lee et al and CTCAE grading were mapped to ASTCT criteria for CRS and ICANS, respectively.

As of 20 May 2020, 97 pts received cilta-cel (29, ph1b; 68, ph2). Median follow-up was 8.8 mo (1.5–20.4), median prior lines of therapy (LoT) was 6 (3–18), 87.6%/41.2% triple/penta-refractory, and 97.9% refractory to last LoT. ORR was 94.8% (95% CI, 88.4–98.3): 55.7% sCR, 32.0% VGPR, and 7.2% PR. Median time to first response was 1.0 mo (0.9–5.8) and median time to ≥CR was 1.8 mo (0.9–12.5). Of 52 evaluable pts, 94.2% were MRD-negative at 10^{-5}. 6-mo PFS and OS rates (95% CI) were 87.4% (78.9–92.7) and 93.8% (86.7–97.2), respectively. Ten deaths occurred: 6 related and 2 unrelated AEs and 2 from progressive disease. AEs included CRS (94.8%; 4.1% grade [gr] 3/4), neutropenia (90.7%; 90.7% gr 3/4), and anemia (81.4%; 68.0% gr 3/4). 20.6% had CAR-T cell-related neurotoxicity (10.3% gr 3/4). Peak peripheral expansion of CAR+ T cells occurred at 14 d (9–43). Among pts with 6-mo follow-up, 67% had CAR+ T cells <2 cells/μL in peripheral blood.

A single low-dose of cilta-cel leads to early, deep, and durable responses in heavily pretreated pts with RRMM.

ポスター発表（Poster Presentation）

P-1 EZH2 と G9a の共阻害はインターフェロンシグナルと IRF4-MYC axis を制御し多発性骨髄腫の増殖を抑制する

Dual EZH2 and G9a inhibition suppresses multiple myeloma cell proliferation by regulating the interferon signal and IRF4-MYC axis

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Epigenetic mechanisms such as histone modification play key roles in the pathogenesis of multiple myeloma (MM). We previously showed that EZH2, a histone H3 lysine 27 (H3K27) methyltransferase, and G9, a H3K9 methyltransferase, are potential therapeutic targets in MM. Moreover, recent studies suggest EZH2 and G9a cooperate to regulate gene expression. We therefore evaluated the antitumor effect of dual EZH2 and G9a inhibition in MM. A combination of an EZH2 inhibitor and a G9a inhibitor strongly suppressed MM cell proliferation in vitro by inducing cell cycle arrest and apoptosis. Dual EZH2/G9a inhibition also suppressed xenograft formation by MM cells in vivo. In datasets from the Gene Expression Omnibus, higher *EZH2* and *EHMT2* (encoding G9a) expression was significantly associated with poorer prognoses in MM patients. Microarray analysis revealed that EZH2/G9a inhibition significantly upregulated interferon (IFN)-stimulated genes and suppressed IRF4-MYC axis genes in MM cells. Notably, dual EZH2/G9a inhibition reduced H3K27/H3K9 methylation levels in MM cells and increased expression of endogenous retrovirus (ERV) genes, which suggests that activation of ERV genes may induce the IFN response. These results suggest that dual targeting of EZH2 and G9a may be an effective therapeutic strategy for MM.

P-2 SORT1 と LAMP2 を介したエクソソーム分泌と細胞接着によるレナリドミド耐性獲得機構

SORT1/LAMP2-mediated Exosome Secretion and Cell Adhesion Are Associated with Lenalidomide Resistance in Multiple Myeloma

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Multiple myeloma (MM) is a hematological tumor. For MM therapy, immunomodulatory drugs (IMiDs) were commonlyused; however, the long-term exposure of these drugs frequently caused drug resistance. Although MM cell adhesion onto bone marrow stromal cells was considered to be important for acquiring drug resistance, the molecular mechanism is still elusive. Recently, exosomes have attracted significant attention as an intercellular communication system. In this study, we examined a relationship between exosome secretion, cell adhesion and drug resistance in MM. As a first step, lenalidomide (Len) resistant cell lines were established by the long-term exposure of Len. Comparative analysis betweenresistant and sensitive cell lines revealed that the resistant cells secreted a greater number of exosomes and enhanced cell adhesion ability. Coculture system showed that the Len resistant cell-derived exosomes influenced drug susceptibility in the Len sensitive cells. Interestingly, Len resistant cell-derived exosomes also affected the state of cell adhesion in the sensitive cells. Whole transcriptome analysis identified SORT1 and LAMP2, which increased exosome secretion and cell adhesion ability in Len resistant cells. Notably, silencing of SORT1 or LAMP2 ameliorated the Len sensitivity in the resistant cells. Furthermore, our finding regarding the SORT1 and LAMP2 was confirmed with clinical samples. In conclusion, our results showed that exosome secretion via SORT1 or LAMP2 could induce cell adhesion, leading to theacquisition of Len resistance in MM.

P-3 KDM5A は多発性骨髄腫において MYC 標的遺伝子の維持に必須な因子である

KDM5A is a vulnerability of MYC target genes essential to multiple myeloma

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Dysregulation of MYC is implicated in the pathogenesis of multiple myeloma (MM). However, little is currently known about the crucial factors involved in the aberrant MYC transcriptional program in MM. KDM5A is the histone H3 lysine 4 (H3K4) demethylases, and is involved in tumorigenesis; however, the biological roles of KDM5A in MM have not been elucidated. Here we characterized the biological and molecular functions of KDM5A in MM. KDM5A was highly expressed in MM cells, and higher KDM5A expression was associated with poor prognosis in MM. Knockdown of KDM5A or novel KDM5 inhibitor JQKD82 reduced growth of MM cells. Importantly, JQKD82 decreased expression of MYC target genes. Expression of MYC target genes was significantly downregulated by KDM5A knockdown, but little altered by KDM5B or KDM5C knockdown, indicating that KDM5A regulates MYC target genes. ChIP-seq analysis revealed that KDM5A coexisted with MYC across the genome. We further showed that KDM5A and MYC coordinately increased the CDK4 promoter activity which is one of the representative MYC targets. Interestingly, the baseline H3K4me3 level at the TSS of MYC target genes was higher than that in other genes, and this level was further increased after JQKD82 treatment, coincident with RNA pol2 pausing. These results suggest that proximal TSS hyper-H3K4me3 induced by JQKD82 inhibits RNA pol2 pause-release and reduces MYC target gene transcription. Our results delineate KDM5A function that enables MYC target gene expression by reducing H3K4me3 level, and identify KDM5A as a potential therapeutic target in MM.

P-4 骨髄腫細胞のプロテアソーム阻害薬の耐性機序における PIM2 と Akt 活性および NRF2 蓄積の役割

Mechanisms for the resistance to proteasome inhibitors in myeloma cells: the role of PIM2 and Akt kinase activation and NRF2 accumulation

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Resistance to proteasome inhibitors (PIs) emerges as a clinical issue. We reported the accumulation of anti-apoptotic mediator PIM2 by blockade of its proteasomal degradation. The present study was aimed to develop a maneuver to overcome MM cell resistance to PIs. Along with PIM2 protein accumulation, phosphorylation of Akt was prolonged in MM cells after pulsatile treatment with bortezomib at 100 and 400 nM and carfilzomib at 250 and 500 nM for 1 hour, which mimicked the PK/PD profile of PIs in patients. At 24 hours after pulse PIs, β5 proteasome subunit activity restored with translational puromycin incorporation more in PI-resistant KMS-11 cells than PI-sensitive MM.1S cells even with carfilzomib, suggesting recovery from the suppression of global translation by ER stress. The PIM inhibitor SMI-16a and the Akt inhibitor MK-2206 added in sequence after the pulsatile PI treatment cooperatively suppressed mTORC1-induced translation output as determined with puromycin incorporation and thereby induced MM cell death. We also found substantial accumulation of NRF2, a critical transcription factor for anti-oxidant genes, by pulse PI. Knockdown of *NFE2L2*, an NRF2 gene, restored and its overexpression further compromised PI's cytotoxicity against MM cells, which was abolished by the simultaneous addition of SMI-16a and MK-2206. These results collectively suggest that pulsatile PIs rather enhance PIM and Akt kinase-mediated survival signaling in parallel with accumulation of NRF2 in MM cells and that simultaneous PIM and Akt inhibition effectively restores PIs' anti-MM effects.

P-5 HDAC 阻害薬と IMiDs の骨髄腫細胞の CD38 と SLAMF7 発現に及ぼす影響

Effects of HDAC inhibitors and IMiDs on CD38 and SLAMF7 expresssion in MM cells

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CD38, SLAMF7, and BCMA have been drawn attention as therapeutic targets because of their high expression on multiple myeloma (MM) cells. However, we previously demonstrated that anti-MM agents, proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and histone deacetylase (HDAC) inhibitors, all downregulated IRF4-mediated BCMA upregulation in MM cells. The present study was aimed to further elucidate the effect of these anti-MM agents on CD38 and SLAMF7 expression in MM cells. Class 1 HDAC inhibitors and panobinostat dose-dependently and IMiDs, pomalidomide and lenalidomide, time-dependently upregulated CD38 expression in MM cells though to the levels far lower than type I and II interferons and ATRA. In contrast, the HDAC inhibitors and these IMiDs reduced SLAMF7 expression in MM cells, while the interferons and ATRA marginally affected it. IRF4 gene knockdown downregulated SLAMF7 expression in MM cells. The HDAC inhibitors and these IMiDs alone were able to reduce IRF4 and thereby SLAMF7 expression; and the combination of the HDAC inhibitors with these IMiDs cooperatively suppressed IRF4 and SLAMF7 expression in MM cells, which may reduce membrane bound SLAMF7-mediated MM cell growth by ambient soluble SLAMF7 and help neutralizing efficiency by elotuzumab. Given formation of immunosuppressive adenosin by CD38, ambient immune effector function should also be taken into account in patients on these anti-MM agents. Further study is warranted on the combination of these anti-MM agents to make the best use of therapeutic antibodies against CD38, SLAMF7, and BCMA.

P-6 t(4;14) 陽性骨髄腫患者における FGFR3 過剰発現は予後不良に関与しない

FGFR3 overexpression was not associated with poor survival in t(4;14)$^{+}$ multiple myeloma patients

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Introduction: Multiple myeloma (MM) patients with the t(4;14) translocation have a poor prognosis and that translocation leads to overexpression of FGFR3 and MMSET, which both have potential oncogenic activity. In this study, we investigated the characteristics and prognosis of MM patients with FGFR3 overexpression.

Materials and Methods: Clinical and laboratory data were obtained from 243 newly diagnosed MM patients in KT-MM institutions. FGFR3 mRNA and protein expression was analyzed by real-time PCR and flow cytometry, respectively. We analyzed the prognostic significance of FGFR3 expression in those patients.

Results: 1) The t(4;14) translocation was found in 13% of newly diagnosed MM patients and associated with worse overall survival (OS) [median OS 37 months]. FGFR3 mRNA was detected in 78% in MM patients with t(4;14). In t(4;14)$^{+}$ MM patients, overexpression of FGFR3 protein on CD38^{high} MM cells was detected in 82% with a median OS of 35 months. Higher FGFR3 mRNA level was significantly associated with higher cell-surface expression of FGFR3. In a limited number of patients (N = 4), MM patients with no FGFR3 overexpression had extremely short OS. 2) Twenty-five percent of MM patients without t(4;14) had FGFR3 overexpression, although their prognosis did not differ with that overexpression.

Conclusions: FGFR3 overexpression was not associated with poor prognosis in t(4;14)$^{+}$ MM patients. We are now analyzing the function of FGFR3 signaling in t(4;14)$^{+}$ MM. The results may point to a new treatment strategy for those patients.

P-7 骨髄腫細胞生存における CD38 の意義
The role of CD38 in myeloma cell survival

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Introduction. Anti-CD38 monoclonal antibodies have shown high efficacy in multiple myeloma (MM) clinical practice. However, the role of CD38 in MM cell survival is not well understood. In the present study, we analyzed differences in metabolic profile and cell proliferation between CD38 positive and negative MM cells. Additionally, CD38 enzyme activity was inhibited using 78c, a CD38 NADase inhibitor, to study the role of CD38 NADase activity in MM cell survival.
Materials and methods. MM cell lines were sorted according to CD38 expression using CD38 Micro-Beads. Intracellular NAD+ and NADH concentrations were analyzed using NAD/NADH Assay kit. Cell metabolites were determined by GC-MS analysis. MM cell lines and patient derived bone marrow cells were treated with 78c in vitro. Cell viability and cell cycle were determined by flow cytometry.
Results. We observed significant increase of NAD+/NADH ratio and higher glycolytic activity in CD38 negative fraction of MM cell lines compared to their CD38 positive counterparts. CD38 negative MM cells were less proliferative compared to CD38 positive MM cells. 78c induced cell cycle arrest and cell death to MM cells accompanying marked increase of NAD+/NADH ratio. CD38 expression in MM cells were associated with 78c induced cell death.
Conclusions. CD38 is responsible for intracellular NAD+ concentration and cell metabolism in MM cells. CD38 NADase activity is associated with MM cell proliferation and survival, indicating that modulation of cell metabolism by CD38 NADase inhibition could provide a novel therapeutic strategy for MM.

P-8 多発性骨髄腫に対する Venetoclax 至適併用薬の同定

Identification of suitable drugs to be combined with venetoclax for the treatment of multiple myeloma

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Bcl-2 was cloned as a molecule located at the breakpoint of t(14;18)(q32;q21), a chromosomal translocation specific for follicular lymphoma, and was found to be an apoptosis inhibitor by subsequent functional analysis. Therefore, the Bcl-2 family is considered an important therapeutic target. Venetoclax is a physicochemically designed selective inhibitor of Bcl-2, and its efficacy has been validated in several clinical trials for lymphoid tumors. A phase I trial revealed that venetoclax is especially effective for multiple myeloma (MM) with t(11;14) because of a high expression of Bcl-2. Subsequently, a phase III trial has been conducted to test the efficacy of venetoclax in combination with bortezomib and dexamethasone (BD). An interim analysis revealed that the combination of venetoclax and BD significantly prolonged progression-free survival of MM patients compared with placebo plus BD, but failed to prolong overall survival because of higher incidence of severe adverse events (Lancet Oncol. 20: 601, 2019). This result points to the urgent need of identification of more suitable drugs to be combined with venetoclax for future clinical testing. With this background, we investigated the combined effects of venetoclax and several anti-cancer drugs using an isobologram method. We found that IMiDs and mTOR inhibitors showed synergistic cytotoxicity with venetoclax by increasing the expression of Bcl-2 mRNA and protein. This finding may provide basic information for the establishment of venetoclax-based treatment strategies for MM patients.

P-9 多発性骨髄腫患者における末梢血幹細胞採取効率についての後方視的解析

Retrospective study of peripheral blood stem cell harvest (PBSCH) in patients with multiple myeloma

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Background

To overcome poor mobilization in PBSCH, we are analyzing clinical samples from our TKMC MM biobank. We have identified a genetic polymorphism of CXCR4 which leads to over-mobilization or poor mobilization. (JSH2020, PS-33-10)

Purpose

To retrospectively analyze our clinical data, we extracted factors that affect stem cell mobilization, and examined the predictability of mobilization efficiency using these factors.

Method

CBC, peripheral CD34, usage of Plerixafor, number of collected stem cells were extracted from 67 patients who underwent PBSCH.

We omitted cases with known factor of poor mobilization, which is, irradiation, multiple regimens, thrombocytopenia, or treatment of other cancers.

Result

Because of the mechanism of G-CSF and Plerixafor, in which stem cells anchored to BM niche or vascular niche are released, peripheral CD34 count of the 1st day of PBSCH (defined as "V_0") is considered to be important.

Focusing on successful harvests (CD34 $\geq 5\times10^6$/kg in single PBSCH), V_0 of all cases were ≥50/μl (55-105).

Interestingly, we found 2 cases who needed multiple PBSCH sessions even their V_0 were exceedingly high.

#1: 50F. IgG(κ)-MM, Tx: VRd×4, V_0=95, Plerixafor: no, total CD34: 5.27 /3 sessions

#2: 64F, IgG(λ)-MM, Tx: VRd×3, V_0=102, Plerixafor: yes, total CD34: 5.29 /2 sessions

Discussion

Since platelets have G-CSF receptors, G-CSF may interfere in platelet function that leads poor mobilization, but it didn't match our cases.

This result implies hidden factor(s) which affects mobilization or homing.

We are planning to add genetic analyzation of these specimens.

P-10 セル・フリー DNA による多発性骨髄腫の早期再発診断

Circulating cell-free DNA in the peripheral blood plasma of patients is an informative biomarker for multiple myeloma relapse

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Multiple myeloma (MM) is an incurable hematological malignancy. Despite the introduction of several novel drugs, most patients relapse. Biomarkers to identify the early signs of relapse will make it possible to adjust the therapeutic strategy before the disease worsens. Although understanding genetic changes is important for the treatment of MM, currently known biomarkers of relapse, including serum free-light chains and monoclonal paraproteins, are not associated with genetic changes. Therefore, we performed a multicenter study to examine the usefulness of circulating cell-free DNA (cfDNA) present in the peripheral blood (PB) plasma of patients as a biomarker for MM relapse. We identified several driver mutations by combined analysis of next generation sequencing and existing databases of candidate oncogenes. Furthermore, relapse was detected more sensitively by monitoring the circulating cfDNA with these driver mutations than by conventional serum free-light chain examination. These results suggest the potential utility of cfDNA in the PB plasma of patients as a relevant early biomarker for MM relapse.

P-11 ダラツムマブ治療時代における CD319 を用いた骨髄腫細胞表面抗原検査の有用性
Use of CD319 in detection of myeloma cells in daratumumab era

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Advanced 8-color or 10-color flow cytometry assays (next-generation flow) have now been used for MRD detection and showed a strong correlation with both PFS and OS in multiple myeloma(MM) patients. Treatment with CD38 antibodies such as daratumumab and isatuximab can alter the antigen expression in MM cells and sometimes down-regulate the expression. This sets a limit for the use of CD38 and maybe multi-epitope CD38 antibody as a marker for the detection of plasma cells during MRD assessments at follow-up. The aim of our study is identifying new surface MM cell marker alternative to the backbone markers such as CD38 and CD138 during daratumumab era. We picked up two SLAMF molecules, CD48 (SLAMF2) and CD319 (SLAMF7), due to their high and stable expression in MM cells. Our FCM analysis was done prospectively in patients diagnosed with symptomatic MM from Jan 2020 until Jan 2021 in Hiroshimanishi Medical Center. Total number of patients were 21 and six patients were tested before and after treatment with CD38 antibodies. All samples were acquired in a Navios Flow Cytometer (Beckman Coulter) and data analysis was performed on the Kaluza Analysis Software. By using anti-CD319 antibody we can distinguish MM cells from other normal blood cells clearly in almost all patients and CD319 expression was little-affected by anti-CD38 treatment, while in half of the patients we cannot detect MM cells by using anti-CD48 antibody as initial gating. CD319 is a useful surface MM cell marker for FCM analysis in daratumumab era.

P-12 骨髄腫における微小残存病変の臨床的な意義：単施設後方視的研究

Clinical significance of minimal residual disease in myeloma; single center retrospective analysis

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Minimal residual disease (MRD) is one of surrogate markers for survival in multiple myeloma (MM). The purpose of this retrospective analysis is to evaluate association between MRD and clinical outcome. We reviewed the medical records of newly diagnosed (NDMM) and relapse and/or refractory MM (RRMM) patients at the Jikei Kashiwa Hospital. We classified the patients into three groups; autologous stem cell transplantation (ASCT), daratumumab containing treatment (DARA), and the others. MRD was analyzed using multicolor flow cytometry by SRL. The cutoff of MRD negativity was $1x10^{-5}$. Sixty-one patients included in this study. Median age was 70-year. The numbers of NDMM and RRMM were 35 and 26, respectively. All the patients achieved complete response when MRD was tested. The numbers of patients received with ASCT, DARA, and the other group were 28, 13, and 20. The ratio of MRD negativity in the all the patients, ASCT, DARA, and the other groups were 67.2%, 75.0%, 76.9%, and 50.0%, respectively (P=0.207). MRD negativity was not associated with high-risk cytogenetic abnormality, age, and the number of prior chemotherapy (P=0.746, 0.410, and 0.999). In median follow-up time 11.0 months, 1-year PFS rates in MRD negative and positive groups were 87.2% and 73.1% (P=0.123). Asymptomatic relapse was pointed out in six patients including 2 patients who stopped treatment due to adverse events, and symptomatic relapse was not pointed out after MRD status was checked. In conclusion, MRD negativity tended to predict long PFS independently from treatment groups, cytogenetic risk, and age.

P-13 BJP-MGUS を呈する Fanconi 症候群症例における MYD88 L265P 変異の検出

Serial detection of MYD88 L265P mutation in BJP-MGUS patient with Fanconi syndrome

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[Case]

A 20-year female consulted our hospital because of mild renal impairment associated to BJP-MGUS. She was diagnosed as Fanconi syndrome when she was 15 years old. Renal biopsy revealed light chain proximal tubulopathy with crystals.
At our hospital, serial bone marrow surveys were performed in 6 months, since disease progression was suspected from immunofixation electrophoresis.
We assumed that some kind of indolent lymphoid proliferative disease may preclinically exist in her background, so we added deeper analysis to her specimen and compared with other patients in our biobank.

[Method]

Genomic DNA was extracted from bone marrow mononuclear cells. MYD88 L265P mutation status were analyzed by PCR-RLFP and confirmed with Sanger sequencing. Sample from a patient who was clinically diagnosed as WM was used as positive control of L265P mutation. We also checked CXCR4 WHIM-like mutations in similar method.

[Results]

At first sample, MYD88 L265P mutation was not detected, but it turned into positive at later sample. CXCR4 WHIM-like mutation was negative for both time points.

[Discussion]

MYD88 L265P mutation is essential at diagnosis of WM, and treatment outcome of BTK inhibitor (e.g. Iburutinib) depends on CXCR4 WHIM status (Treon et al, ASH 2017), but these detection system is not yet standardized.
Most cases of WM present IgM type monoclonal protein. This case implies a sub category of BJP-WM or disease progression pathway to IgM-WM.

Early detection of these mutation may provide a treatment path with developing novel agents, so we need to refine and standardize these methods.

P-14 多発性骨髄腫患者における腎障害マーカーとしての尿中Ｌ型脂肪酸結合蛋白の有用性

Urinary liver-type fatty acid binding protein (L-FABP) as a new biomarker of renal impairment in patients with multiple myeloma

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【Backgrounds】

Renal impairment (RI) is a common complication of multiple myeloma (MM) and is associated with an unfavorable prognosis. While several new markers of kidney damage have been introduced in recent years, urinary liver-type fatty acid binding (L-FABP) has been developed as a sensitive biomarker in acute renal injury. We aimed to measure the value of L-FABP for the early diagnosis of renal injury in MM patients and assess whether L-FABP can be used as a biomarker of RI in patients with MM.

【Material and Methods】

We studied 14 patients with newly diagnosed MM. Urinary L-FABP, serum creatinine (sCr), cystatin C (Cys-C), serum free light chain (sFLC), myeloma protein (M protein) and proportion of plasma cells in bone marrow (pBM) were assessed, and estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease formula.

【Results】

Urinary L-FABP strongly correlated with sFLC, M protein and pBM in untreated MM patients.

【Conclusion】

In spite of small samples, this study suggested that the value of L-FABP reflects tumor progression. L-FABP is not only a sensitive biomarker of renal function but may also be a useful marker that reflects tumor burden in patients with MM. However, further large-scale studies are necessary to validate our findings.

P-15 多発性骨髄腫の継続・維持療法の有効性に関する傾向スコアマッチング解析

Propensity-score matched analysis of the efficacy of maintenance or continuous therapy on multiple myeloma

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Maintenance or continuous therapy is considered a standard of care for both transplant-eligible and -ineligible patients with MM. However, the long-term benefits of such therapy have not yet been clarified in the context of routine practice. We conducted a retrospective study of patients between 2013 and 2016 at 32 hospitals of the Japanese Society of Myeloma. Patients were divided into two groups composed of those who received maintenance and others who did not receive such therapy to be evaluated by propensity-score matching based on age, gender, R-ISS stage, and implementation of ASCT by using EZR software adjusted for confounding factors between the two groups. Among 720 patients, 161 in each group were evaluated. Maintenance regimens included IMiDs (n=83), PI (n=48), combination of both (n=29), and DEX alone (n=1). PFS was significantly prolonged in the maintenance group compared with the no maintenance group (median, 37.7 and 21.9 months, respectively, p=0.0002). Prolongation of PFS was observed in both transplant and non-transplant patients (p=0.017 and p=0.0008, respectively), patients without reaching CR (p=0.0018), as well as in those with R-ISS stage I and II (p=0.037 and 0.00094, respectively). In contrast, there was no significant benefit of maintenance therapy on OS (p=0.19). Thus, maintenance therapy was associated with a reduced risk of progression in patients with standard risk and/or suboptimal response. Novel treatment strategies besides maintenance are needed to further improve outcome specifically in high-risk patients in routine clinical practice.

P-16 多発性骨髄腫における免疫原性細胞死に寄与する小胞体ストレス応答の検討

The study of ER stress signaling pathways contributing to immunogenic cell death in multiple myeloma

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Background Protease inhibitors (PIs) are highly effective in treatment of multiple myeloma (MM), which can inhibit the proliferation of myeloma cells by causing the accumulation of unfolded or misfolded proteins, leading to endoplasmic reticulum (ER) stress. In addition to these mechanisms, we have shown that PIs strongly induce immunogenic cell death (ICD), sensitizing cancer cells to immune cells such as dendritic cells, compared to other myeloma drugs. It has been reported that unfolded protein response (UPR) plays an important role to induce ICD in several cancers, however, the precise mechanism of ICD in MM is still unknown. In this study, we attempted to identify UPR signaling pathways involved in ICD of MM cells.

Methods Myeloma cell lines were treated with anti-myeloma drugs, including bortezomib (BTZ) and carfilzomib (CFZ) with or without PERK inhibitors or IRE1 inhibitors. Subsequently, the phosphorylation of eIf2α and the splicing of XBP1 were detected using Western blotting in high- risk myeloma cell line, MUM24. Expression of cell surface Calreticulin (CRT), which is reported as a biomarker of ICD, was also detected using flow cytometry.

Results / Discussion Cell surface expression of CRT induced by CFZ treatment was diminished by coculture with STF083010, an inhibitor of IRE1 pathway, but not by GSK2606414, an inhibitor of PERK pathway which is involved in ICD of solid tumor. These results suggested that PIs induced ICD in MM via distinct mechanisms from those observed in solid tumor. Further clarification of MM-specific signaling pathway in ICDs is required.

P-17 再発難治性骨髄腫に対するカルフィルゾミブ療法の有効性と安全性：京都血液臨床研究グループ (KOTOSG) 前方視的観察研究

Efficacy and safety of carfilzomib-containing therapy for relapsed/refractory myeloma: Kyoto Clinical Hematology Study Group prospective observation

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We performed prospective observational study for the efficacy and safety of carfilzomib (CFZ) with lenalidomide plus dexamethasone (KRd) or with dexamethasone (Kd) in 50 patients with relapsed and/or refractory multiple myeloma (RRMM) treated between 2017 and 2019 in Kyoto Clinical Hematology Study Group (KOTOSG). KRd and Kd were administered to 31 and 19 patients, respectively. Overall response rates of KRd and of Kd were 80.0 % and 76.5 %, respectively. One-year progression-free survival (PFS) and overall survival (OS) of KRd were 53.3 % and 84.8 %, and those of Kd were 44.0 % and 72.6 %. Multivariate analysis identified the refractoriness to bortezomib (BTZ) and/or lenalidomide (LEN) as independent risks for both PFS and OS. The common grade 3/4 adverse events (AEs) included lymphopenia (42.0 %), thrombocytopenia (26.0 %), neutropenia (24.0 %), anemia (20.0 %), hypertension (6.0 %), infection (6.0 %), hypoxia (6.0%), and AST/ALT increased (6.0%). No incidence of ischemic heart disease or cardiomyopathy was observed. Frailty was associated with hematologic toxicity and infections, and more than two previous treatment lines were associated with hematologic toxicity; the incidence of hypoxemia was higher in patients with high β2-microglobulin levels and decreased renal function. Our data also suggested the need of careful observation for AEs especially in early cycle after initiation of treatment. This study collectively suggested the impacts of patients' background, including treatment history and fitness, on the success with CFZ-containing treatment in RRMM.

P-18 カルフィルゾミブによる高血圧合併における血清 TGFb と IL-6 のバイオマーカーとしての意義

Predictive value of serum TGFb and serum IL-6 for hypertension by carfilzomib in patients with relapsed/refractory multiple myeloma

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Carfilzomib (CFZ) has demonstrated efficacy for relapsed/refractory multiple myeloma (RRMM), while the safe management of cardiovascular adverse events (CVAEs) is essential with the use of CFZ. To investigate the incidence and risk factor for CVAEs in CFZ-containing treatment, we conducted a multi-institutional prospective observational study in Kyoto Clinical Hematology Study Group. Fifty patients with RRMM were registered, and were subjected to preplanned follow-up of symptoms, electrocardiogram findings, echocardiogram findings, and serum/plasma levels of 18 biomarker candidates, including 2 myocardial injury markers, 4 inflammation markers, 4 endothelial damage markers and 8 neurohormones. Common CVAEs were hypertension (HT) (42%), arrhythmia (14%), and thrombosis (12%). Although decrease in ejection fraction (EF) more than 10% occurred in 7 of 43 evaluable patients, only one experienced EF reduction below 50%. Abnormal QTc interval prolongation was observed in 10% of patients. No ischemic heart disease, cardiomyopathy or symptomatic cardiac failure was detected. Baseline blood levels of cTnT, BNP, TGFb (<4.96ng/mL), IL-6 (>2.5pg/mL) and hsCRP were shown to associate with HT by univariate analysis, while low serum TGFb and high serum IL-6 values were identified as independent risk factors for HT by multivariate analysis. Biomarkers associated with other CVAEs were not evaluable due to their infrequent incidences. In conclusion, HT is the most frequent CVAEs with CFZ-containing therapy, which might be associated with baseline low serum TGFb and high serum IL-6 values.

P-19 リプログラミング因子の高発現による多発性骨髄腫細胞の悪性形質獲得

Overexpression of reprogramming genes leads to acquisition of malignant phenotype in multiple myeloma

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Background and Purpose We previously discovered ectopic expression of epithelial or mesenchymal genes in multiple myeloma (MM) cells. Moreover, our preliminary observation showed overexpression of OCT4, SOX2 or NANOG in almost all MM cell lines, suggesting that reprogramming of MM cells may induce differentiation into the cells with epithelial or mesenchymal phenotype. The purpose of this study is to clarify the biological significance of expression and function of these reprogramming genes in MM cells.

Results 1) Overexpression of OCT4 decreased sensitivity to lenalidomide, pomalidomide and bortezomib in MM cells. We also demonstrated that MRP1 overexpressed in OCT4/KMS21 cells, and MRP1 inhibitor, MK-571, restored their sensitivity to bortezomib. These results indicated that OCT4 overexpression induced drug resistance via increased expression of MRP1. 2) OCT4/KMS21 cells formed “pseudopodia” which is characteristic feature of mesenchymal cells and is reported to be associated with metastasis of solid tumor cells. 3) Overexpression of OCT4 enhanced Cyclin D2 expression and conversely decreased Cyclin D1 expression. In addition, OCT4/KMS21 cells exhibited high clonal proliferation. 4) Database analysis showed shorter survival of the patients with OCT4 overexpression in their MM cells.

Conclusion Overexpression of reprogramming genes, OCT4, differentiated MM cells into the cells having mesenchymal phenotype. These transdifferentiation may lead to the acquisition of malignant phenotype of MM cells.

P-20 ベネトクラクスは BCL2 高発現の多発性骨髄腫細胞株に対するダラツムマブの抗体依存性細胞傷害活性を増強させる

Venetoclax enhances NK-cell-mediated ADCC with daratumumab in myeloma cells expressing BCL2

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Despite recent advances in treatment outcomes of patients with multiple myeloma (MM) by the introduction of new drugs, MM is incurable and new treatments need to be developed. Venetoclax, a selective inhibitor of BCL2, is a potent new drug for MM. In this study, we investigated the synergistic cytotoxic effects of venetoclax and daratumumab *in vitro* using human myeloma cell lines (KMS12PE and SKMM1). The WST1 assay was used to assess the cytotoxicity of venetoclax. Flow cytometric analysis of Annexin V was used to determine NK cell-mediated antibody-dependent cellular cytotoxicity (ADCC) with daratumumab. Western blotting was used to evaluate the expression levels of the BCL2 protein. Flow cytometry showed that KMS12PE and SKMM1 cells were positive for CD38, 100% and 75%, respectively. Western blotting showed that BCL2 was strongly expressed in KMS12PE cells but not in SKMM1 cells. KMS12PE cells were sensitive at 100 nM of venetoclax, while SKMM1 cells were not sensitive even at the concentration of 10 uM of venetoclax, which corresponded to the expression level of BCL2 in each cell line. Furthermore, in KMS12PE cells, NK-cell-mediated ADCC with daratumumab in the presence of venetoclax was significantly higher than that with daratumumab alone. Our findings suggest that venetoclax enhances NK-cell-mediated ADCC with daratumumab in myeloma cells expressing BCL2. These findings may provide a rationale for the benefits of the combination of venetoclax and daratumumab in MM patients with BCL2 expression.

P-21 移植適応多発性骨髄腫患者における初回採取レジメンによる自家末梢血幹細胞採取不良例の多施設共同後方視的研究

The multicenter retrospective study of poor PBSC mobilization in patients with multiple myeloma

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Background: Autologous stem cell transplantation (ASCT) is an important therapeutic strategy for fit patients with multiple myeloma even in the era of novel agents. However, a proportion of patients fail to mobilize enough peripheral blood stem cells (PBSCs) to proceed to ASCT. In this study, we aimed to clarify the characteristics and outcomes of poor mobilizers. **Methods**: This is a retrospective study conducted through the Japanese Society of Myeloma (JSM). Clinical data of the poorly mobilized patients who underwent PBSC harvest at 44 institutions between 2008/4 and 2018/9 were collected. Poor mobilizers were defined as patients with less than 2×10^6/kg of CD34+cells harvested at the first mobilization. The number of good mobilizers in the same period was also examined. A nationwide JSM database was used for the reference. **Results:** The proportion of poor mobilization was 15.1% (259/1714). 92 out of 258 poor mobilizers (35.7%) did not receive subsequent ASCT, mainly due to insufficient PBSCs. The median OS from apheresis of poor mobilizers who received ASCT was longer than those who did not receive it (86.0 vs. 61.9 mon., p=0.02). The outcome of 228 poor mobilizers was analyzed to refer to the JSM database in the same condition. The OS from diagnosis of poor mobilizers who received ASCT in our cohort was similar to those who received ASCT in the JSM database (3yOS 86.8%, 85.9%). **Conclusion:** In this cohort, one-third of poor mobilizers did not receive ASCT associated with relatively poor survival. In contrast, the OS of poor mobilizers who received ASCT might be rescued.

P-22 MDV レセプトデータベースを用いた国内の多発性骨髄腫患者における実臨床下での治療パターンおよび臨床転帰の検討

Real world treatment patterns and clinical outcomes in multiple myeloma patients from the MDV claims database in Japan

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Background and Purpose: Since few studies have reviewed recent MM treatments in Japan in a real-world setting, this study evaluated treatment patterns and outcomes in patients with MM receiving routine clinical care in Japan.

Methods: This is a retrospective longitudinal observational cohort study in patients with MM using the Japanese Medical Data Vision (MDV) database covering over 24 million patients. A total of 4,029 patients with MM patients with a diagnosis of MM between 2003 and 2018.

Results: Within eligible patients of whom 1,558 (38.7%) were >75 years, the line of treatment (LOT) was countable for 1,861 patients (1st line SCT-conducted (FL TE): n=774, 1st line SCT not-conducted (FL TIE): n=1,017, 2L: n=1,121, 3L: n=658).
Study population was separated into two groups as first diagnosis was 2003-2015 and 2016-2018. The most commonly used regimens in early lines are, FL TIE: Vd (38.9%) and MP (20.2%) in 2003-2015 and Vd (34.0%) and Rd (31.2%) in 2016-2018, 2L: Rd (51.6%) and VTd (7.9%) in 2003-2015 and Rd (33.2%) and KRd(13.1%) in 2016-2018, 3L: Rd (20.5%) and Pd (19.9%) in 2003-2015 and Pd (16.8%) and Rd (15.0%) in 2016-2018.

Conclusions: MDV claims database analysis well captured the real world MM treatment regimens in Japan. Novel agents were administered for later therapy lines until 2015, however these were gradually shift to earlier lines in these years.

P-23 当院における多発性骨髄腫患者に対するダラツムマブの使用経験

Daratumumab containing regimen for multiple myeloma patients; a single center experience

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We performed a retrospective survey of MM patients treated with DARA-containing regimen at our institute between Dec. 2017 and Oct. 2020. Median age of 24 patients at DARA induction was 68 years (range, 58-83 years) and 13 were male. At diagnosis, ISS risk score was 1/2/3 for 8/8/8 patients, and 12 patients received transplantation after induction treatment. Previous treatment line(s) at DARA induction was 1 for 11, 2 for 4, 3 or later for 4 patients and other five patients have received DARA regimen as first line treatment. Median time from diagnosis to DARA induction was 25 months (0.1-96.9). Drugs combined with DARA were lenalidomide plus dexamethasone (DEX) for 10, bortezomib (BOR) plus DEX for 9, BOR plus melphalan plus prednisolone for 5 patients, and two patients required treatment change among DARA regimen due to intolerance for partner drug. Among median observation period of 10.1 months (0.9-35.2) for surviving patients, median cycles of DARA regimen were 4 (1-38). Eight patients discontinued treatment due to disease progression, one by patient' s will, and three by intolerance. Seven patients progressed within a year and all but one of them have introduced DARA about three years or later from the diagnosis as at least third line treatment. On the other hand, five out of six patients who could continue on DARA regimen over a year was receiving the treatment as a second line treatment. Although short observation with limited patients, our result suggests that DARA treatment may better applied in earlier line.

P-24 移植適応多発性骨髄腫に対する ixazomib による維持療法の後方視的解析

Retrospective analysis of maintenance therapy with ixazomib for patients with multiple myeloma undergoing autologous stem-cell transplantation

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Background: High-dose melphalan and autologous stem-cell transplantation (HDM/ASCT) is recognized as a standard of care for newly diagnosed eligible patients with multiple myeloma (MM). Lenalidomide (LEN) is reported to prolong progression free survival (PFS) as maintenance therapy. Ixazomib (IXA) is recently reported to prolong PFS in a randomized phase 3 trial and has been approved for maintenance therapy after HDM/ASCT in Japan.

Methods: We conducted a retrospective analysis on 94 patients with MM who received HDM/ASCT in Japanese Red Cross Medical Center between Dec. 2016 and Apr. 2020. High-risk chromosome (HR) was defined as having at least one of t(4;14), t(14;16), or del(17p).

Results: Median age was 58 (36-70) and M:F was 57:37. HR was detected in 20 patients (21%). 4-year PFS of all cases was 67%. 4-year PFS of patients with HR was 29% and was significantly worse than that of patients without HR (79%, P<0.01). Twenty-four patients received treatments containing IXA and 17 patients received IXA as maintenance therapy (median 13 months (2-42)). In a subgroup analysis on patients with HR, 2-year PFS of patients received IXA-maintenance was 100% and that of remained patients was 37%. Grade 3 adverse events with IXA-maintenance was observed in one patient (pneumonia).

Conclusions: This retrospective analysis has two major limitations. The number of patients is small and selection of patients for IXA-maintenance was conducted by each physician’s choice. However, IXA-maintenance may overcome HR and further analysis is warranted.

P-25 自家末梢血幹細胞採取におけるボルテゾミブ併用シクロフォスファミド大量療法の有用性の解析

Usefulness of bortezomib and high-dose cyclophosphamide therapy as a conditioning regimen for autologous peripheral blood stem cell harvest

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Peripheral blood stem cell harvest (PBSCH) is a crucial procedure for autologous stem cell transplantation in patients with multiple myeloma (MM). We herein report a retrospective study to verify the usefulness of bortezomib and HD-CY therapy (Bor-HDCY) as a conditioning regimen for PBSCH. Thirty-five patients, three of whom underwent PBSCH twice, were evaluated. In two patients who were unable to receive apheresis because of poor mobilization, the PBSC count was 0. The median age at the first apheresis was 61 (range, 42-69) years old, and 19 (54.3%) patients were male. There were 33 patients with MM, 1 with primary AL amyloidosis, and 1 with POEMs syndrome. Bor-HDCY therapies were performed in 15 patients, and HDCY therapies were performed in 20. Plerixafor was used in seven patients. The median number of treatment regimens until PBSCH was 1 (range, 1-8). Before PBSCH, 16 patients achieved very good partial remission (VGPR) or better. The median number of CD34+ cells/kg in the PBSC yields collected via apheresis on the day 1 was 2.4 (range, 0-17.9) × 10 6 /kg. According to a univariate analysis, Bor-HDCY therapy ($P<0.01$), PBSCH performed after January 2016 ($P<0.05$), and VGPR or better before PBSCH ($P<0.05$) were significant factors associated with more PBSCs. In a ultivariate analysis, Bor-HDCY therapy was the only independently significant factor associated with more PBSCs ($P<0.05$). Our study suggests that Bor-HDCY therapy is a useful conditioning regimen for increasing the number of PBSCs collected.

P-26 多発性骨髄腫に対する新規治療薬の移植後再発に関する影響

Effects of new agents on multiple myeloma recurrence after autoPBSCT

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New drugs for multiple myeloma, such as proteasome inhibitors, immunomodulatory drugs, and antibody drugs, improved the prognosis of myeloma patients.
A retrospective observational analysis was performed on patients who received initial autologous transplant at our hospital and post-transplant treatment effect was PR or better, between Mar 2008 and May 2018. In this analysis, the cases of scheduled tandem transplantation were excluded. The purpose of our study is to examine the effect of new agents for multiple myeloma on the prognosis and recurrence rate.
The subjects analyzed totaled 122 transplant-eligible patients. Median age at diagnosis was 58 (range 30-70) and M:F=1.3:1. 98 patients received maintenance therapy after transplantation. 63 had relapses, with a median time to relapse of 30 months. The median OS and PFS from diagnosis in all cases were 168(7-200) and 50 months (6-140).
The initial regimen before ASCT is mainly VAD for patients diagnosed before 2011(20 cases), mainly VCD for patients diagnosed from 2012 to 2016 (56 cases), and mainly VRD based regimen for patients diagnosed after 2016 (46 cases). In these three groups, post-transplant PFS was significantly different from 36 months, 45 months, and NR, respectively (P=0.01). Recurrence rate was also significantly different from 85%, 63%, 26% respectively (P <0.01).
Prognosis and recurrence rate after transplantation is thought to be improving with the new drugs.

P-27 新規薬剤時代における原発性形質細胞白血病の治療成績：8 例の後方視的検討

Clinical outcome of primary plasma cell leukemia in the novel agent era: a retrospective study of eight cases

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[Background] Few studies have been reported on prognosis of primary plasma cell leukemia (pPCL) in the novel agent era. [Methods] We retrospectively analyzed clinical outcome of eight patients with pPCL treated with novel agents (PIs, IMids, or monoclonal antibodies), extracted from 246 patients with newly diagnosed MM at Oita Prefectural Hospital or Oita Kouseiren Tsurumi Hospital from 2010 to 2020. [Results] Median age was 76 years (range: 53-84) and two patients were male (25%). Median absolute counts and ratio of plasma cells in the peripheral blood were 1771 /μL (range: 806-16891) and 27% (range: 22-70), respectively. Median serum LDH levels were 282 U/L (range: 135-1929), and the type of M-protein was as follows (IgG, n=4; BJP, n=3; non-secretory, n=1). Four patients had complex chromosomal karyotypes. Seven patients were classified into stage III in ISS. Bortezomib-containing regimen was six (BD, n=4; VCD, n=1; iPAD, n=1), lenalidomide-containing regimen (Rd) was one, and both agents-containing regimen (VRD) was one in first line. Carfilzomib-containing regimen was three (Kd, n=2; KRd, n=1) and daratumumab-containing regimen was two (DVd, n=1; DLd, n=1) in second or later line for refractory pPCL. ORR after second or later line was 25%. No patient underwent auto-PBSCT and one patient received rBMT with having a relapse of pPCL two months after BMT. Median follow-up period is 270 days (21-598) with seven patients died of pPCL. Median PFS and OS was 215 and 306.5 days, respectively. [Conclusion] Even in the novel agent era, prognosis of pPCL is still extremely poor.

P-28 自家移植歴のない初発の多発性骨髄腫患者を対象とした一次治療後のイキサゾミブ維持療法の多施設共同国際臨床第３相試験

TOURMALINE-MM4: Ixazomib vs placebo maintenance in newly diagnosed multiple myeloma patients not undergoing autologous stem cell transplant

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We report results from the phase 3, double-blind, placebo-controlled TOURMALINE-MM4 study (NCT02312258; Dimopoulos JCO 2020). Non-autologous stem cell transplant (ASCT) newly diagnosed multiple myeloma (NDMM) patients (pts) who achieved ≥partial response after 6-12 months (m) of standard-of-care induction therapy were randomized (3:2) to the oral proteasome inhibitor (PI) ixazomib (n=425; 3mg then, if tolerated, 4mg from cycle 5 onwards) or placebo (n=281) on days 1, 8, & 15 of 28-day cycles as maintenance for ≤24 m. TOURMALINE-MM4 met its primary endpoint; with a median follow-up of 21.1 m, there was a clinically meaningful 34.1% reduction in risk of progression or death with ixazomib vs placebo (median progression-free survival [PFS] since randomization, 17.4 vs 9.4 m; hazard ratio [HR] 0.659; 95% CI 0.542-0.801; p<0.001). A significant PFS benefit was seen with ixazomib vs placebo in pts who had a complete or very good partial response post induction (median 25.6 vs 12.9 m; HR 0.586; p<0.001). Treatment-emergent adverse events (TEAEs) were mostly grade 1-2; 36.6% vs 23.2% of pts had grade ≥3 TEAEs with ixazomib vs placebo, 12.9% vs 8.0% discontinued treatment due to TEAEs. Common any-grade TEAEs included nausea (26.8% vs 8.0%), vomiting (24.2% vs 4.3%), & diarrhea (23.2% vs 12.3%). There was no increase in new primary malignancies (5.2% vs 6.2%); 2.6% vs 2.2% of pts died on study. Ixazomib prolonged PFS vs placebo as post-induction maintenance in non-ASCT NDMM pts with a well-tolerated safety profile; it is the first oral PI maintenance option in this setting.

P-29 DARATUMUMAB PLUS LENALIDOMIDE/DEXAMETHASONE (D-RD) IN PTS WITH TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): UPDATED ANALYSIS OF MAIA

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In the phase 3 MAIA study, D-Rd vs Rd significantly improved progression-free survival (PFS) in transplant-ineligible NDMM. We report updated efficacy and safety from MAIA after approximately 4 years of follow-up. Pts with transplant-ineligible NDMM were randomized to 28-day cycles of Rd (R 25 mg PO on Days 1-21; d 40 mg PO QW) ± DARA (16 mg/kg IV QW Cycles [C] 1-2, Q2W C3-6, Q4W C7+). The primary endpoint was PFS. 737 pts were randomized (D-Rd, n=368; Rd, n=369). After 47.9 months median follow-up, PFS remained significantly improved for D-Rd vs Rd (median, not reached [NR] vs 34 mo; HR, 0.54; 95% CI, 0.43-0.67; $P<0.0001$). The estimated 48-month PFS rate was 60% with D-Rd vs 38% with Rd. The PFS benefit of D-Rd in prespecified subgroups, including high cytogenetic risk, was generally consistent with overall results. D-Rd continued to result in deeper responses with higher rates of ≥CR and ≥VGPR. Median duration of response was NR with D-Rd vs 44 months with Rd. The most common (≥10%) grade 3/4 TEAEs (D-Rd/Rd) were neutropenia (53%/37%), pneumonia (18%/11%), anemia (16%/21%), lymphopenia (16%/11%), hypokalemia (12%/10%), leukopenia (11%/6%), and cataract (11%/10%); grade 3/4 infection rates were 40%/29%. The most common serious TEAE was pneumonia (17%/11%). 11% in the D-Rd arm and 22% in the Rd arm discontinued treatment due to TEAEs. The complete updated data set will be presented. D-Rd vs Rd continues to demonstrate superior efficacy with no new safety concerns after longer follow-up. These results support D-Rd as first line treatment for transplant-ineligible NDMM.

P-30 LONG-TERM OUTCOMES AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) BY RESPONSE FOR BORTEZOMIB/MELPHALAN/PREDNISONE (VMP) ± DARATUMUMAB (DARA) IN ALCYONE

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In the phase 3 ALCYONE study, DARA + VMP (D-VMP) vs VMP reduced the risk of disease progression/death by 58% and the risk of death by 40% for transplant-ineligible newly diagnosed multiple myeloma (TIE NDMM). We report a subgroup analysis by response on efficacy and HRQoL. Pts received up to nine 6-week cycles of VMP (V 1.3 mg/m^2 SC twice weekly in Cycle [C] 1, C2-9 QW; M [9 mg/m^2] and P [60 mg/m^2] PO C1-9 Days 1-4) ± DARA (16 mg/kg IV C1 QW, C2-9 Q3W). The D-VMP group received DARA Q4W for C10+ until disease progression. The primary endpoint was PFS. 706 pts were randomized (D-VMP, n=350; VMP, n=356). D-VMP vs VMP improved PFS in pts with a best response of PR, VGPR, or ≥CR. All pts who achieved ≥CR with MRD negativity demonstrated prolonged PFS, regardless of treatment. Clinically meaningful improvements in HRQoL occurred in both groups across response categories. In the pooled population, global health status improved with deepening responses at month 12 (mean change from baseline: ≥PR, 11.11; ≥VGPR, 13.19; ≥CR, 14.48; ≥CR with MRD-negativity, 15.81). More D-VMP pts had clinically meaningful improvements in pain and fatigue as responses deepened. In the D-VMP group at C10+, ≥CR rates improved from 44% at the beginning of maintenance to 64% and 68% at 1 and 2 years, respectively. PFS, overall survival, and time to subsequent anticancer therapy also improved with deepening responses. The findings that D-VMP induced and maintained deep responses, which led to improvements in efficacy and HRQoL, continue to support the use of D-VMP in TIE NDMM.

P-31 CR で治療を終了した MM 患者の予後解析

Prognostic analysis of MM patients who discontinued treatment with CR status

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We retrospectively analyzed the prognosis of patients with MM who were treated at our hospital from 2001 to 2017 and whose treatment was interrupted with CR status. 47 patients were extracted. 28 females and 19 males. The ages of the patients ranged from 45 to 88 years (mean 67 years). Stage ISS I19 (40.5%), II19 (40.5%), and III9 (19%), with 31 cases of IgG type, 8 cases of IgA type, 1 case of IgD type, 6 cases of BJP type, and 1 case of non-secretory type. The duration of treatment ranged from 8 to 98 months (mean 26 months), and autologous transplantation was performed in 21 cases (45%).[Results] The overall survival rate of all patients was 86.3% at 10 years. (Median follow- up: 108M) The 5-year PFS after completion of treatment was 55.7%, and the 5-year overall survival rate was 87.8%. (Median follow-up: 69M) There was no significant difference in PFS between patients with and without autologous HSCT. There was no significant difference in PFS between patients who discontinued treatment within 2 years and those who remained on treatment for more than 2 years. In a small number of cases, MRD was examined, and several patients remained in remission for a long time despite MRD positivity at the 10^{-4} level.[Discussion and Conclusion] More than half of the patients with CR remained treatment-free for more than 5 years. There was no difference in PFS between patients who discontinued treatment within 2 years and those who discontinued after long-term treatment, suggesting that long-term maintenance therapy may not be necessary when the goal is to complete treatment.

P-32 当院における再発難治性多発性骨髄腫患者に対する Daratumumab 投与による治療効果とその特徴

The therapeutic effects in Relapsed and/or Refractory multiple myeloma patients treated with Daratumumab

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Daratumumab, an anti-CD38 monoclonal antibody, is effective in combination with lenalidomide or bortezomib in patients with newly diagnosed and relapsed and/or refractory multiple myeloma (RRMM). We analyzed the therapeutic effects of forty-one RRMM patients treated with daratumumab, lenalidomide plus dexamethasone (DRd) retrospectively. The median age was 73 years. The median number of prior treatments was 1. Fourteen patients had high-risk cytogenetic abnormality (HRCA). Twenty-five patients had administered lenalidomide, and 18 patients had refractoriness for lenalidomide. We defined elderly age equal to 75 years or more. There were no patient characteristics associated with elderly age by Fisher's exact test.

In median follow-up time was 13.5 months, the median time to next treatment (TTNT) was 11.9 months. The median TTNT in the patients without HRCA was significantly longer than those with HRCA (14.3 vs 7.2 months, $P = 0.008$), and the median TTNT in the patients over 75 years was significantly longer than those 75 years or younger (14.9 vs 9.5 months, $P = 0.042$). The 1year overall survival (OS) rate was 86.1%. The 1year-OS rate in the patients without HRCA tended to be high compared with those with HRCA (91.1% vs 75.0%, $P = 0.062$) while the 1year-OS rate was similar classified with the other prognostic factors.

In conclusion, we demonstrated that DRd might be more effective for the patients without HRCA than in those with HRCA, and be effective for the elderly patients.

P-33 再発・難治性多発性骨髄腫に対する Carfilzomib/dexamethasone 療法

Carfilzomib/dexamethasone therapy for relapsed and refractory multiple myeloma

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Background and purpose: The efficacy of carfilzomib (CFZ) and dexamethasone therapy (Cd) for relapsed and refractory multiple myeloma (RRMM) has been reported. We investigated the efficacy and safety of Cd. **Patients and methods**: Twenty-eight patients received Cd between 2017/5 and 2020/7. The response was evaluated according to the IMWG criteria. Adverse events (AEs) were assessed using CTCAE ver. 4.0. **Results**: Nineteen and 9 received twice-weekly Cd and once-weekly Cd, respectively. The median age was 70.5 years, and the median number of prior regimens was 5.5. Twenty-two patients were refractory to proteasome inhibitors (PIs) and immunomodulatory drugs (IMiDs), and 18 were refractory to PIs, IMIDs and antibody drugs. The overall response rate (ORR), median progression-free survival (PFS) and median overall survival (OS) were 42.9%, 5.8 months and 13.5 months, respectively. ≧ Grade 3 hematological AEs included thrombocytopenia in 16 patients, neutropenia in 7, anemia in 18 and lymphopenia in 21. ≧ Grade 3 non-hematological AEs included acute renal failure in 6 patients, gastrointestinal toxicity in 3, cryptococcus pneumonia in 1 and tumor lysis syndrome in 1. Two patients had to discontinue treatment due to drug toxicity. **Discussion**: The outcome of Cd in this study was poorer than that in clinical trials regarding ORR, PFS and OS, and the toxicities were higher. The reason for this was that most patients were heavily treated. However, Cd was effective in some double and triple refractory patients, suggesting it to be an effective agent for the treatment of RRMM.

P-34 当院における移植非適応再発・難治多発性骨髄腫の患者に対する daratumumab の有効性の検討

Daratumumab with bortezomib, or lenalidomide and dexamethasone was efficacy for relapse or refractory multiple myeloma in our hospital

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<Introduction> Daratumumab showed promising efficacy with bortezomib or lenalidomide and dexamethasone with relapse or refractory multiple myeloma. We studied whether our regimen “DBd therapy followed by DLd therapy” was effective with relapse or refractory transplantation ineligible patients or not.
<Regimen> All patients received 1 to 3 cycles daratumumab 16mg/kg days 1, 8, and 15, bortezomib 1.3mg/m2 days 1, 8, and 15, and dexamethasone (DBd), followed by 4 to 8 cycles daratumumab 16mg/kg days 1, 15, lenalidomide 25mg days 1 to 21, and dexamethasone (DLd), thereafter daratumumab 16mg/kg day 1, lenalidomide 25mg days 1 to 21, and dexamethasone until PD.
<Results> A total of 16 patients were enrolled, but we excluded 4 patients, because they did not accomplish DBd therapy. The median age of the 12 patients was 74.5 years (range, 61 to 90). The median time since the initial diagnosis of multiple myeloma was 39.5 months (range, 7 to 180). Patients had received a median of 3.5 (range, 1 to 7) previous lines of therapy. The overall response rate was 75.0 %, and complete response or better was 75.0 %. They were maintaining deep response up to now.
<Conclusions> Our regimen “DBd therapy followed by DLd therapy” resulted deep response and longer progression free survival among patients with relapse or refractory transplantation ineligible multiple myeloma.

P-35 当院における再発・難治多発性骨髄腫に対するダラツムマブの使用経験

Experience of using Daratumumab for relapse and refractory multiple myeloma in our hospital

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The cases of relapse or refractory multiple myeloma (RRMM) treated by the combination of Daratumumab, a humanized IgG1 monoclonal antibody against CD38, with lenalidomide and dexamethasone (Dld) are increasing in our hospital. We retrospectively analyzed 12 cases of RRMM treated with Dld therapy in our hospital.8 men and 5 women, median age of cases was 68 years (range : 64-80). The median number of prior regimens of cases was 4 (range : 1-8). The best response was CR in 6, VGPR in 1, PR in 1, SD in 5. Overall response rate (≧ PR) was 61.5%. The outcome was survival in 9 and death in 4. There were no adverse infusion reactions. Grade3 non-hematological adverse events were bacterial pneumonia in 4, bronchitis in 1, enteritis in 1, sinusitis in 1. Overall survival (OS) and progression free survival (PFS) were not seen in the significant difference in the condition of a patient at the time of the number of the previous regimens and the start of therapy.

P-36 新規薬剤時代のプロテアソーム阻害薬治療を受けた多発性骨髄腫患者における帯状疱疹ウイルス再活性化に関する 10 年間の調査

A 10-year survey of varicella-zoster virus reactivation in multiple myeloma patients treated with proteasome inhibitors in the novel agent era

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Many reports of varicella-zoster virus reactivation (VZVr) in patients with hematologic malignancies, including multiple myeloma (MM), have been received. However, few of them include novel agents that have become available in recent years. We retrospectively studied the clinical characteristics and outcomes of 118 consecutive patients with MM at a high risk of VZVr who had been treated with proteasome inhibitors between July 2009 and June 2019 at the National Hospital Organization Tokyo Medical Center. The risk factors were also analyzed by dividing the patients into two groups: those who developed VZVr and those who did not (non-VZVr). Thirty-nine episodes of VZVr were observed in 37 patients. The cumulative incidence was 16.5% after one year and 36.5% during the observation period. The proportion of prophylactic antiviral prescriptions and compliance with antiviral prophylaxis in the National Cancer Center Network Clinical Practice Guidelines (NCCN GL) was 76% and 30% in the VZVr group, and 88% and 74% in the non-VZVr group. Multivariate analysis showed that compliance with NCCN GL was the only independent risk factor for VZVr ($P = 0.0017$). In the 16, 18, 3, and 13 patients who received the novel agents represented by carfilzomib, ixazomib, elotuzumab, and daratumumab, prophylactic antivirals were prescribed to all patients throughout the treatment period, and there was no VZVr. Our study suggests that in the treatment of MM, prophylactic antivirals are prescribed in many cases, but it is important to take them according to the guidelines for the prescribed period.

P-37 重症かつ可逆性の Carfilzomib による薬剤性肺障害の一例

A Case of Life-threatening but Reversible Carfilzomib-induced Pulmonary Toxicity

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Background: Several studies have reported that bortezomib has a potential adverse effect of lung toxicity, but there is scarce information that carfilzomib (CFZ) does.

Case presentation: A 72-year-old woman with a history of lung cancer after lobectomy, was diagnosed with multiple myeloma. She started treatment with once-weekly CFZ and dexamethasone (Kd) after two years of treatment with three prior lines which had become refractory. She achieved VGPR after three cycles of Kd. She presented with fever, dry cough and worsening dyspnea that started within one day after receiving her first dose of the fifth course of Kd. Echocardiography was normal, but a computed tomography of the chest revealed diffuse bilateral ground-glass opacities. She was diagnosed with pneumonia of unknown etiology because cultures were all negative, but immediately recovered with antibiotics. However, she developed again severe pneumonia after the next administration of CFZ and required intubation and mechanical ventilation. She recovered very quickly only with single-dose steroids. She was diagnosed with CFZ-induced lung injury based on the temporal relationship between the exposure to the drug and the onset of symptoms.

Discussion: It was previously reported that CFZ-induced lung toxicity occurred after the first or second administration. It should be noted that it could occur during the late cycle like this case.

P-38 シングルセル RNA 解析によって明らかとなる POEMS 症候群特異的な形質細胞クローン

Single cell RNA analysis successfully identifies plasma cell clones with specific features in POEMS syndrome

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The pathogenic significance of clonal plasma cells in POEMS syndrome remains undetermined despite our analyses of purified plasma cells (Nagao et al. Leukemia 2019). In the current study, we performed single cell RNA sequencing (scRNA-seq) of bone marrow (BM) plasma cells from 10 patients with POEMS syndrome, 2 with MM, 2 with MGUS, and 2 normal controls. Sorted CD138+ plasma cells were subjected to scRNA-seq using Fluidigm C1. In 6 out of 10 cases, we could detect POEMS clones with specific *IGL* sequences derived from *IGLV1-36*, *40*, *44*, and *47* with *IGLJ3*02* associated with disease-specific amino acid changes. The size of POEMS clones in total BM plasma cells (median: 12.9%, range: 1.7–32.5%) was much smaller than MM (96-100%) and MGUS (57-81%) cases. Transcriptome analyses revealed the hyper-production of proteins, down-regulation of proliferative genes such as *MYC*, and down-regulation of MHC-II genes in POEMS clones. POEMS clones had higher expression in several specific genes than MM and MGUS, including *SERPING1*, *CFI*, *C2*, *MSLN*, *MUC1* and *SPP1*. Especially, the serum levels of osteopontin, encoded by *SPP1*, were significantly higher in POEMS patients than those in healthy donors, and were correlated with disease activity. Importantly, *VEGF* mRNA levels were not upregulated in either POEMS clones or POEMS non-clones. Finally, POEMS clones were successfully purified by FACS sorting in CD138+CD19-HLA-DR-/low fraction, evidenced by POEMS-specific *IGLV* expression analyzed by RNA-seq. These results enhance our understanding of the disease pathogenesis.

P-39 POEMS 症候群における骨病変の臨床的意義

Clinical impact of the bone lesion in POEMS syndrome;
a single-center experience of 119 patients

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Background: POEMS syndrome is a multisystemic disease related to monoclonal plasma cell disorder. Although bone lesions are familiar, their precise manifestations and prognostic impact are still unknown. Here, we retrospectively analyzed the bone lesion in POEMS syndrome and evaluated its clinical features and prognostic significance.

Patients and methods: We obtained clinical data and bone lesion information at diagnosis in 114 POEMS syndrome patients diagnosed at Chiba University Hospital between 1995 and 2019.

Results: Among 84 patients (73%) with at least one bone lesion, 67 (59%) patients had osteosclerotic lesions alone (SC group), and 17 (15%) patients had osteolytic lesions with or without osteosclerosis (LY group). The median maximum diameter of bone lesions and frequency of solitary lesion was significantly higher in the LY group than those in the SC group (50 vs. 14 mm, $p < 0.001$; 41% vs. 15%, $p = 0.012$). One patient presented pathological fracture, and 4 patients received local radiation therapy in the LY group. With the median follow-up of 64 months, there were no significant differences in OS between SC and LY group (5-year OS: 92% vs. 74%, $p = 0.11$). Bone lesion improvement was observed in 28% of the SC group and 41% of the LY group.

Conclusion: Most of the bone lesions in POEMS syndrome were osteosclerotic, and the type of bone lesion did not affect prognosis. Radiotherapy and systemic chemotherapy are expected to prevent pathological fractures by improving osteolytic lesions. Further investigation will be needed to evaluate its long-term outcome.

P-40 多発性骨髄腫の患者における COVID-19：単一施設での経験
COVID-19 in patients with multiple myeloma: A single center experience

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Introduction: COVID-19 has been rapidly emerged as a pandemic around the world. We report two cases of COVID-19 in patients with multiple myeloma.
Case 1: A male in his 60s with multiple myeloma and diabetes mellitus was treated with ixazomib + lenaridomide + dexamethasone (IRd). At cycle 27 day 14, he admitted to our hospital because of shortness of breath and loss of appetite. Chest CT revealed bilateral and peripheral predominant ground-glass opacities. Rapid antigen test for SARS-CoV2 proved negative, but the next day PCR test proved positive. Ceftriaxone and favipiravir were administered. On the 27th hospital day, he recovered and was discharged from hospital.
Case 2: A male in his 70s was diagnosed as multiple myeloma 2 years ago. He was treated with thalidomide, carfilzomib + dexamethasone (Kd), and lenalidomide + dexamethasone (Ld). Chemotherapy was stopped after achieving sCR. Six months later, he presented with fatigue, taste disorder, and loss of appetite. He was hospitalized with positive PCR result. He was followed closely without therapy, and was discharged from hospital on the eleventh hospital day.
Discussion: We treated two cases of COVID-19 with myeloma, and this resulted in 1.1% of patients with COVID-19 hospitalized in our single institute. Fortunately, these two cases diagnosed as mild symptom and recovered within a few weeks. This may be partly due to their status of myeloma and initial manifestation manner without pneumonia. We need to perform epidemiologic analysis with larger multi-institutional cohort to clarify myeloma with COVID-19 issues.

P-41 ITP 合併多発性骨髄腫に対する化学療法により骨髄腫と ITP の改善を認めた一例

A case of symptomatic multiple myeloma developing in a patient with immune thrombocytopenia

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Background
It has been reported multiple myeloma (MM) is sometimes accompanied with immune thrombocytopenia (ITP). But there are few reports that ITP accompanied with MM was treated with novel agents for MM.
Case report
A 75-year-old man had asymptomatic MM at the time of diagnosis of ITP. ITP was treated with IVIG, prednisolone, dexamethasone (Dex), rituximab, and TPO receptor agonists, but was resistant to those treatment. Since the patient progressed to symptomatic MM during the course of treatment, treatment with carfilzomib and Dex (Car+Dex) introduced, and resulted in PR for MM and platelets(Plt) recovered to normal. After 3 courses of Car+Dex treatment, the Plt decreased again with the recurrence of myeloma, and the treatment was changed to lenalidomide and Dex therapy (Len+Dex). After 2 courses of Len+Dex treatment, the myeloma had a therapeutic effect on CR and the Plt count was normalized.
Discussions
ITP is rare in MM and there are only a limited number of case reports. In our case, the amount of M protein and the Plt count showed a correlation, and the Plt count was recovered by the treatment of MM. This suggests the condition of MM and the condition of ITP are closely related. It has been reported the M protein of MM has antibody activity against Plt (G.Merlini Blood 2006), and also has been reported in cases of MM complicated with ITP, treatment of MM restored Plt (T.Itoh Jpn J Clin Hemato 2016). These suggest the M protein of MM has antibody activity against Plt and destroys Plt, but detailed elucidation of the pathophysiology is expected in the future.

P-42 CD19 陽性クローンを有する t(11;14) 転座陽性多発性骨髄腫の一例

A case of newly diagnosed t(11;14) multiple myeloma with CD19-positive clone

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【Introduction】It is essential for predicting prognosis and decision-making of treatment strategies in multiple myeloma (MM) to evaluate surface markers and karyotype of myeloma cells. Here, we show the patient with newly diagnosed t(11;14) MM with CD19-positive clone resistant to initial therapy.【Case presentation】A 54-year-old male was diagnosed as having MM (IgG-k, R-ISS: II) with multiple compression fractures, renal dysfunction and hypercalcemia. Bone marrow examination showed that plasma cells with both immature and mature morphology occupied 74.6%. Flow cytometric analysis revealed CD38 and CD20 positivity. Interestingly, both positive and negative populations of CD19, CD138 and MPC-1 were detected. FISH analysis showed t(11;14) translocation without del(17p) and 1q gain. Although he treated with bortezomib and dexamethasone as an initial therapy, no response was obtained. He next treated with daratumumab plus lenalidomide and dexamethasone. However, no response was obtained. After administration of carfilzomib plus lenalidomide and dexamethasone, a very good partial response was obtained. He then received autologous stem cell transplantation.【Discussion】Myeloma cells are usually CD19-negative and CD19 expression is associate with a poor prognosis. In general, t(11;14) MM has a better prognosis. Our case suggested that t(11;14)MM with CD19 positivity may be associated with resistance to bortezomib and poor prognosis. More intensified induction therapy such as carfilzomib-containing triplet regimen might be necessary for this myeloma population.

P-43 Carifilzomib により TMA を発症した治療抵抗性多発性骨髄腫

Carfilzomib-induced thrombotic microangiopathy in a patient with refractory multiple myeloma

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Introduction: Carfilzomib is an irreversible proteasome inhibitor that has been approved for relapse and refractory multiple myeloma. It has been implicated as a cause of thrombotic microangiopathy (TMA) in several cases.
Case: A 60-year-old male was diagnosed with symptomatic myeloma, ISS 3 with multiple bone disease. He was treated with four cycles of bortezomib+ lenalidomide+ dexamethasone (VRD) and subsequently underwent peripheral blood stem cell harvest. He achieved a partial response (PR). He was then started on once-weekly carfilzomib + dexamethasone (Kd) at 20/70 mg/m^2. On day 9 of Cycle 1, he presented with high fever and general fatigue and was transferred to our hospital with weakness and anorexia on day 13. At admission, his laboratory data showed thrombocytopenia (8000/μl), hemolysis (I-bil, 1.6mg/dL; LDH, 2808 U/L; haptoglobin, 4.5 mg/dL) and renal dysfunction (BUN, 95.4mg/dL; Cr, 6.57 mg/dL). A peripheral smear confirmed the presence of schistocytes . ADMATS-13 level was normal (58%) and inhibitor of ADAMTS-13 was negative. A diagnosis of carfilzomib-induced TMA was made and administration of Kd was stopped . He was started on hemodialysis and received 6 sessions of plasma exchange. At 11 days after admission, his platelet count has recovered with decreased serum creatinine level and and increased urine output, eventually allowing withdrawal of dialysis therapy.
Conclusion: Although the occurrence of TMA is infrequent, once TMA occurs, it can become a serious event. Physicians should be aware of possibility of occurrence of TMA during carfilzomib treatment.

P-44 多発腫瘤形成を伴う未治療移植非適応骨髄腫に対し Daratumumab-VMP 療法が早期かつ深い奏効を示した一例

A case of Daratumumab with VMP therapy achieved a rapid and deep response for transplant-ineligible multiple myeloma with multiple plasmacytomas

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<Introduction>

It is generally difficult to obtain a good response for multiple myeloma with plasmacytoma, although many novel agents contribute to improve prognosis of myeloma patients. We report Daratumumab with VMP therapy (D-VMP) was effective for transplant-ineligible NDMM with multiple plasmacytomas.

<Case>

A 78 year-old male was introduced to our hospital for a suspicious of advanced-stage lung cell carcinoma because of solid masses in left upper lobe of lung and at adjacent to thoracic vertebrae with multiple osteolytic lesion detected by CT scan. However, any tumor markers were normal and solid masses were spread from rib and vertebrae. In addition, immunofixation electrophoresis test revealed IgG-λ type M protein and clonal plasma cells were detected by bone marrow specimen. We diagnosed symptomatic MM with hypercalcemia, anemia, multiple osteolytic lesions and multiple plasmacytomas. He was immediately treated with radiotherapy (RT 30Gy) to mass on thoracic vertebrae combined with one cycle of BD due to weakness of lower limb caused by spinal nerve compressed by tumor. After initial treatment, weakness has been completely improved and we started D-VMP. The other plasmacytoma from rib remarkably regressed after only one cycle of D-VMP without RT. He could finally reach stringent CR with no accumulation of FDG on plasmacytomas by FDG-PET after the 9th cycle of D-VMP.

<Conclusion>

Our case indicates that this quadruple regimen has a possibility of a suitable combination and an effective therapy for NDMM with plasmacytoma.

共催セミナー（Co-sponsored Seminars）

LS1-1 新たな再発難治性多発性骨髄腫の治療戦略 -IsaPd 療法を基礎と臨床から考える -

New treatment strategy for relapsed and refractory multiple myeloma -Understand IsaPd regimen based on basic and clinical-

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Isatuximab is a novel anti-CD38 antibody approved for the treatment of double-refractory multiple myeloma (MM) in combination with pomalidomide and dexamethasone (Pd). Isatuximab exerts anti-myeloma action via immunological mechanisms, including CDC, ADCC, ADCP and NK/CTL activation, the inhibition of CD38 ectoenzyme activity, and direct induction of cell death. Among them, the latter two mechanisms are unique to isatuximab and provide a rationale for distinct usage of isatuximab from the first-in-class anti-CD38 antibody daratumumab. It has been demonstrated that isatuximab induces non-apoptotic cell death via cathepsin B release from the lysosome and subsequent generation of ROS in MM cells (Jiang et al. Leukemia 30: 399, 2016). The generation of ROS may contribute to synergistic effects of isatuximab and pomalidomide because the anti-myeloma action of IMiDs is at least partly mediated via ROS production (Sebastian et al. Blood 129: 991, 2017). In addition, pomalidomide enhances immunostimulatory effects of isatuximab via activation of effector cells and up-regulation of CD38 expression on MM cells. The mechanistic synergism of the two agents explains the results of the ICARIA-MM trial, in which the combination of isatuximab with Pd achieved significantly longer progression-free survival in MM patients refractory to both bortezomib and lenalidomide than Pd alone (Attal et al. Lancet 394: 2096, 2019). Furthermore, the ICARIA-MM study revealed that the Isa-Pd combination was beneficial to patients with 1q gain chromosome abnormalities or extramedullary diseases. In this seminar, we will discuss the mechanisms by which isatuximab is effective for MM cells with high-risk features from a standpoint of basic research.

LS1-2 新たな再発難治性多発性骨髄腫の治療戦略 -IsaPd 療法を基礎と臨床から考える -

New treatment strategy for relapsed and refractory multiple myeloma -Understand IsaPd regimen based on basic and clinical-

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Multiple myeloma (MM) is an incurable disease of mature B cell. However, the long-term outcome has markedly improved in the last decade due to the development of new treatment armamentaria. However, many patients experience disease relapse or become refractory to conventional therapies, including immunomodulatory drugs (eg lenalidomide and pomalidomide) and proteasome inhibitors (PI, eg bortezomib, ixazomib and carfilzomib). In particular, the prognosis of lenalidomide refractory or lenalidomide and bortezomib refractory patients is poor, and new treatment is required for such patients.

Isatuximab is an IgG1κ monoclonal antibody (mAb) that binds to a specific epitope on human CD38 and targets cells that strongly express CD38, including malignant plasma cells. In June 2020, isatuximab was approved for use in combination with pomalidomide and dexamethasone (IsaPd) in patients who relapsed/refractory MM (RRMM) who have received at least two prior therapies including lenalidomide and a PI. ICARIA trial is the first positive randomised, phase 3 study adding an anti-CD38 antibody, isatuximab, to a pomalidomide and dexamethasone for RRMM. In this study, median progression-free survival was significantly longer in the IsaPd group compared with the pomalidomide–dexamethasone (Pd) group (11.5 months *vs* 6.5 months; HR 0.596, p=0.001) at a median follow-up of 11.6 months. The most frequent treatment-emergent adverse events (any grade; IsaPd *vs* Pd) were upper respiratory tract infections (28% *vs* 17%). In this session, I would like to talk about efficacy, safety and best timing of use of IsaPd.

LS2 多発性骨髄腫における T 細胞免疫不全と免疫治療戦略

Mechanisms of T cell immune dysfunction and immunotherapeutic strategies in multiple myeloma

田村　秀人
Hideto Tamura

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Multiple myeloma (MM) represents impaired immune surveillance characterized by impaired antibody production, deregulation of the T and natural killer cell compartment, disruption of antigen presentation machinery, and increased numbers of immunosuppressive cells such as regulatory T and B cells, myeloid-derived suppressor T cells. Immune modulatory drugs (IMiDs) such as lenalidomide and pomalidomide have the dual effects with direct tumoricidal and immune enhancing effects. The CD38-targeting antibodies, which have classic Fc-dependent immune effector mechanisms including ADCC, ADCP and CDC, improve host-anti-tumor immune response by eliminating CD38-positive immune suppressor cells. Furthermore, the monoclonal antibody treatments combined with IMiD have synergic effects, resulting in long-term disease control with high rates of sustained minimal residual disease (MRD)-negativity. Excellent clinical efficacy of immunomodulatory drug-intensified monoclonal antibody treatment has been reported in advanced-stage MM patients. The elucidation of the mechanisms underlying T cell immune dysfunction is therefore very important and new treatment strategies will improve prognosis and possibly point toward a cure for myeloma.

LS3 再発難治骨髄腫に対するカルフィルゾミブ含有治療戦略のエビデンスと実際

Evidence and practice with carfilzomib-containing strategy for relapsed/refractory myeloma

黒田　純也
Junya Kuroda

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The appropriate selection of effective and safe salvage treatment strategy is critically important for prolonging the survival period of patients with relapsed/refractory multiple myeloma (RRMM). Carfilzomib (CFZ), a second generation epoxyketone-derived proteasome inhibitor, is one of the potent therapeutic components for RRMM. Indeed, several pivotal clinical trials have shown promising clinical efficacies of CFZ-containing strategies for RRMM in combination with dexamethasone (DEX) in Kd regimen, anti-CD38 monoclonal antibody daratumumab and DEX in KDd regimen, or immunomodulatory drug lenalidomide (LEN) and DEX in KRd regimen for RRMM. Achievement of deeper response by CFZ-containing treatment contributes to the longer survival, even in patients with high-risk cytogenetics, and also contributes to the faster and better renal response. Despite these advantages shown in clinical trials, there also exist clinical data gaps regarding the efficacy and safety of CFZ-containing strategies, for instance, the efficacies of Kd in bortezomib-refractory patients, of KRd in LEN-refractory patients, and of KDd in patients those were previously exposed to daratumumab. Information for toxicity profiles and risk factors for major adverse events, such as cardiovascular adverse event (CVAEs) have been insufficient in real world setting, especially in Asian cohort. In this seminar, we discuss the clinical benefits, safety, risk and possible biomarker of adverse events with CFZ-containing strategy based on data obtained by clinical trials and our won real-world experience.

LS4 免疫調節薬に焦点を当てた多発性骨髄腫における至適な初回および継続的治療戦略

The optimal first line and sequential treatment strategies in multiple myeloma with focus on immunomodulatory drugs

田中　宏和
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Current therapeutic strategies, including combination and sequential treatments with proteasomal inhibitors, immunomodulatory drugs (IMiDs), and monoclonal antibodies has resulted in considerably improved survival in patients with multiple myeloma (MM). Furthermore, innovative therapeutics are being developed with immunotherapy, such as chimeric antigen receptor T-cells. Among wide range of approval first-line treatments, lenalidomide has been firmly established as a key drug of therapy in both transplant-eligible and transplant-ineligible until disease progression. However, the number of patients treated with lenalidomide that will progress while on therapy is likely to increase, and it remains unclear how to best manage these patients. In this setting, understanding the precise mechanisms underlying IMiDs response and resistance is becoming important for development of specific strategies that could prevent the acquisition of resistance or overcome it.

In this seminar, I would like to provide an overview of strategies to improve first line and sequential therapies for MM with particular focus on IMiDs and especially discuss the role of measurable residual disease (MRD)-driven strategies which will have an important role for designing the best treatment options tailored to each MM patient.

MS1 地域医療における高齢者 /Frail の骨髄腫治療

Multiple myeloma treatment for Elderly / Frail in community medicine

花本　仁
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Japan has become a super aging society, and the number of elderly people is increasing more and more. It is estimated that the elderly population aged 65 years or older will reach about 36 million people (35% of the total population) in 2025. According to the estimated number of patients with multiple myeloma based on the community cancer registry, the annual incidence rate has been increasing year by year, and the incidence rate in patients younger than 50 years is almost constant. Therefore, it is suggested that the number of elderly patients with multiple myeloma will rise in Japan with the increase in the elderly population. In the treatment of multiple myeloma in the elderly, different from that in the young, treatment strategies should be considered for each frailty such as less intensive treatment strategies for unfit or frail patients. In addition, even for fit patients, if it is difficult for elderly patients to go to the hospital by myself, they must be accompanied by their families, and in such patients, physical and geographical barrier in the region where they live make treatment difficult. Currently, many new drugs have been developed, and the survival rate of multiple myeloma has been improving. In this situation, we are faced with difficult to determine how elderly patients with multiple myeloma should be treated at community medicine. In this lecture, I would like to outline the current data on multiple myeloma which is ineligible for transplantation, as well as discuss the issues in the treatment of multiple myeloma in daily clinical practice and the efforts at my facility.

MS2 診療に役立つ全身性 AL アミロイドーシスの診断と評価のコツ

Tips of how to detect and assess systemic AL amyloidosis smartly for good clinical practice

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To diagnose AL amyloidosis accurately at the early stage of the disease is essential to provide better outcome. Because the first step of diagnosis is to suspect the possibility of amyloidosis, it is important to know “clue” symptoms and how to exam the patients. (1) uTP/Cre > 0.5g/gCre, (2) mean wall thickness > 1.2cm on echocardiogram and/or NTproBNP > 332pg/mL and/or troponin T > 0.025~0.035ng/mL, (3) serum ALP > 1.5 times institutional upper limit of normal, and (4) asking neuropathic symptoms are critical exams to find (1) proteinuria due to renal amyloidosis, (2) heart failure due to cardiac amyloidosis, (3) liver dysfunction due to hepatic amyloidosis, and (4) neuropathy due to nerve involvement, respectively. After suspecting the amyloidosis, the next step to confirm amyloid deposition is biopsy. Less invasive, more sensitive, and less often biopsy should be perused. Renal biopsy for those with proteinuria, or gastroduodenal mucosa biopsy or skin biopsy for those without proteinuria is recommended. To inspect biopsy specimens properly, standard Congo red staining investigation and accurate immunohistochemical staining with high quality antibodies are required. In this step, to utilize amyloidosis diagnosis service at the experienced institutions is good option. Finally, to know about some clinical subtypes with adverse outcome is important to provide highly effective treatment as soon as possible. NTproBNP > 8500pg/mL, T-bil > 2mg/dL, and eGFR <50 with proteinuria > 5g/day are signs of cardiac, hepatic, and renal AL amyloidosis with unfavorable prognosis, respectively.

SS1-1 移植非適応多発性骨髄腫治療の現状と課題
Current status and issues of treatment for transplant-ineligible multiple myeloma

鈴木　一史
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Aging is a evidently heterogeneous phenomenon. The incidence of MM increases steadily with advanced age. Elderly patients for multiple myeloma have renal failure due to age, with larger proportion of patients with higher ISS stages, classified as high or ultra-high risk. Furthermore, there is an increased frequency of gain in chromosomes(1q) for patients over 80 years of age.
The achievement in deep response is an predictor of long-term outcome regardless of age, including elderly patients. On the other hand, grade 3-4 AEs have a significant negative impact on survival outcomes for elderly patients.
From the above, treatment strategies for older patients highly require consideration for individual patient factors and characteristics.

SS1-2 移植適応多発性骨髄腫治療の現状と課題
Current status and issues of treatment for transplant-eligible multiple myeloma

塚田　信弘
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More than 20 years after its introduction, autologous stem cell transplantation (ASCT) remains the standard of care for young patients with newly diagnosed multiple myeloma. Not only did the arrival of novel agents such as immunomodulatory drugs (IMiDs) and proteasome inhibition (PI) not replace ASCT, instead they solidified its central role as standard of care. Novel agent use is now inarguably essential in induction, maintenance, and possibly consolidation.
Recently, TOURMALINE-MM3 study was conducted to investigate its efficacy as a maintenance therapy in transplant-eligible newly diagnosed MM patients. In this double-blind, placebo-controlled randomized phase 3 trial, ixazomib maintenance was shown to prolong PFS.
From the results of this study, there will be a change treatment strategies for transplant eligible patients in the maintenance setting.

SS2-1 CD38 発現から考える初期治療としての DLd 療法の意義

Significance of DLd therapy as initial treatment considering CD38 expression status

北舘　明宏
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Daratumumab, a fully humanized monoclonal antibody against CD38, has shown substantial clinical activity for multiple myeloma (MM) in several clinical trials, especially in combination with immunomodulatory drugs (IMiDs). Recently, promising results have been reported in untreated patients with newly diagnosed MM who were ineligible for autologous stem cell transplantation. Accordingly, daratumumab has recently been approved for the treatment of newly diagnosed MM patients. CD38 expression on myeloma cells is a critical factor that affects the response to daratumumab. Indeed, we have shown that CD38 expression levels on myeloma cells are associated with an early response to daratumumab, reflecting direct cytotoxicity. CD38 expression was shown to be significantly decreased at relapse, suggesting the significance of daratumumab treatment as an initial therapy. Moreover, we have also recently reported that CD38 expression is heterogeneous in newly diagnosed MM and is associated with the differentiation and maturation stages of MM cells. Considering lower CD38 expression at diagnosis in some cases, the combination of daratumumab and IMiDs may be recommended for patients with newly diagnosed MM, because IMiDs enhance CD38 expression on myeloma cells and the immunomodulatory effect of daratumumab. This presentation highlights the significance of DLd therapy as an initial treatment from the perspective of CD38 expression on myeloma cells and the mode of action of daratumumab.

SS2-2 移植非適応新規多発性骨髄腫患者に対する新規治療戦略 〜Daratumumab をいかに使用するか〜

New treatment strategy for patients with newly diagnosed multiple myeloma who are ineligible for ASCT 〜 How to use Daratumumab 〜

石田　禎夫
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Multiple myeloma (MM) is an incurable disease of mature B cell, emphasizing the need for more effective therapies. However, the long-term outcome has markedly improved in the last decade due to the development of new treatment armamentaria. The combination of melphalan, prednisone and bortezomib and (MPB) and lenalidomide plus dexamethasone (Ld) were standard treatments for patients with newly diagnosed multiple myeloma (NDMM) who were ineligible for autologous stem-cell transplantation (ASCT). Daratumumab is a human IgG-κ monoclonal antibody that targets CD38 having direct antitumor and immunomodulatory activity. Supported by preclinical data, efficacy of daratumumab was synergistically enhanced in combination with immunomodulatory drugs and proteasome inhibitors. Among patients with NDMM who were ineligible for ASCT, daratumumab combined with MPB (DMPB) resulted in significantly longer progression-free survival (PFS) than MPB and was associated with a 50% lower risk of disease progression or death in the phase 3 trial, ALCYONE. Furthermore, among patients with NDMM who were ineligible for ASCT, treatment with daratumumab plus Ld (DLd) resulted in significantly longer PFS than Ld and was associated with 44% lower risk of disease progression or death in the phase 3 trial, MAIA. From the updated MAIA data in ASH 2020, the estimated percentage of patients who were alive without disease progression at 48 months was 60% in the DLd group and 38% in the Ld group. In Japan in 2019, daratumumab in combination with MPB (DMPB) or Rd (DLd) received approval for the treatment of transplant-ineligible patients with NDMM. In this session, I would like talk about the importance for use of first-line daratumumab combination therapy among patients with ASCT-ineligible NDMM.

会長
小杉　浩史（大垣市民病院　血液内科）

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会期
2022 年 5 月 21 日（土）～ 22 日（日）

会場
岐阜グランドホテル
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会長からの一言
日本骨髄腫学会学会員の皆様、COVID19 パンデミック下にあっても、日々の弛まぬ日常診療と学術活動に取り組まれていることと思います。
さて、私儀、本学会理事として二期目在任中ですが、2022 年度の第 47 回学術集会長に、昨年春に指名いただき、準備を進めております。ここに謹んでご挨拶申し上げます。
2020 年度の第 45 回（服部先生）は中止の決定となり、第 46 回（坂井先生）の学術集会で 2 年ぶりに開催の運びとなり、関係者のご努力に敬服いたします。当学会に限りませんが、COVID19 パンデミックの社会状況の中、本学会員の皆様の学術情報の交流をいかに Society として実現するか、準備組織委員会の皆様と腐心しているところです。
この間、当学会も、安倍理事長・中世古副理事長・半田事務局担当理事の執行部体制のもと、村上前理事長および学会員の皆様の悲願であった一般社団法人となり、ますます社会的な責務を担う形に発展してきました。これ以前には、高月清前前々理事長時代に多くの学会員が薫陶を受け、前々理事長の清水一之先生の国際骨髄腫学会（IMS）による IMW 2013 Kyoto を日本骨髄腫学会が一丸となって実現し、村上前理事長時代に研究会から学会組織へと転換した大いなる歩みがあります。
COVID19 パンデミックについては、ワクチン接種がようやく始まり、新たな段階へと向かおうとしています。第 47 回学術集会では、様々な意味での分断を乗り越え、骨髄腫および類縁疾患の患者さんたちへ、学術的なインフラを使って、希望を提供するために必要な「創造と共生」をテーマにさせていただきました。学術集会プログラムや開催形式については、これから準備が本格化する段階ですが、現地開催が成立するのであれば、2022 年 5 月 21 日（土）～ 22 日（日）にはじめての岐阜の地での開催で、岐阜グランドホテルでの開催を準備しております。一方、アフター・コロナ元年ともいうべき、今年、ウェビナー形式の参加も、若手研究者、遠方の方々にも、参加いただくツールとしての重要性は今後も変わらない位置づけを得つつあるようにも考えており、開催収支等が見合えば、実現したいところです。
運営委託会社の公募、準備組織委員会による開催準備など、一般社団法人化を見越して、学会法人事業としての学術集会として、新しい体制で準備を進めつつあるところです。
研究会時代から幾度かの大きな変遷を経て発展して、新たなフェーズに入った、日本骨髄腫学会のミッションは変わりません。本学術集会で、新しい時代の新たな希望を参加の皆様に感じていただけるよう精一杯、準備を進めて参る所存です。
最後になりますが、本学術集会の準備組織委員の先生方を列挙させていただき、会長として謝辞を申し上げるとともに、それを支えていただく学会員の皆様、代議員の先生方、執行部をはじめ理事の同僚先生方におかれましても、引き続き、ご支援のほど、よろしくお願い申し上げるとともに、皆様の益々のご健勝を祈念申し上げてご挨拶とさせていただきます。

日本骨髄腫学会第 47 回学術集会準備組織委員会（敬称略・順不同）
小杉　浩史（大垣市民病院）（委員長）
石田　禎夫（日本赤十字社医療センター）（副委員長）
永井　宏和（名古屋医療センター）
鶴見　　寿（松波総合病院）
中世古知昭（国際医療福祉大学）
半田　　寛（群馬大学）
黒田　純也（京都府立医科大学）
神谷　悦功（中東遠総合医療センター）

令和 3 年 4 月吉日

過去の学術集会一覧

第 45 回(中止)　2020.5.16-17 浜松町コンベンションホール（東京都港区）　服部　豊「骨髄腫治療の限界の打破 新たな視点から病態を見つめて」
第 44 回　2019. 5. 11-12 ウインクあいち（愛知県名古屋市）飯田真介「個性に基づく骨髄腫治療時代の幕開け」
第 43 回　2018. 5. 12-13 東京ベイ幕張ホール（千葉県千葉市）中世古知昭「さらなる新しい時代の幕開け」
第 42 回　2017. 5. 27-28 日本赤十字看護大学　広尾キャンパス（東京都渋谷区）　石田禎夫「治療を目指した骨髄腫研究の発展と治療の進歩」
第 41 回　2016. 5. 28-29 あわぎんホール（徳島県徳島市）安倍正博「骨髄腫研究の深化とさらなる治療の展開」
第 40 回　2015. 5. 16-17 くまもと森都心プラザ（熊本県熊本市）畑　裕之「内科学から見た骨髄腫」
第 39 回　2014. 5. 17-18 掛川グランドホテル(静岡県掛川市)名倉英一「骨髄腫治療の the State of the Art を考える」
第 38 回　2013. 7. 27 名古屋ルーセントタワー（愛知県名古屋市）清水一之
IMW2013 Kyoto 2013. 4. 3-7 国立京都国際会館（京都府京都市）清水一之
第 37 回　2012. 7. 7-8 京都テルサ（京都府民総合交流プラザ内）（京都府京都市）島崎千尋「骨髄腫診療の原点を見つめ、未来を拓く」
第 36 回　2011. 11. 12-13 東京コンファレンスセンター（東京都港区）三輪哲義
第 35 回　2010. 11. 20-21 富山国際会議場（富山県富山市）吉田　喬
第 34 回　2009. 11. 21-22 新潟コンベンションセンター、朱鷺メッセ　スノーホール（新潟県新潟市）張　高明
第 33 回　2008. 11. 15 広島大学医学部 広仁会館（広島県広島市）麻奥英毅
第 32 回　2007. 11. 10 日本赤十字看護大学 広尾ホール（東京都渋谷区）鈴木憲史
第 31 回　2006. 11. 11 伊香保温泉 ホテル天坊（群馬県渋川市）村上博和
第 30 回　2005. 11. 12 京都府立医科大学付属図書館ホール（京都府京都市）谷脇雅史
第 29 回　2004. 11. 13 名古屋市中小企業振興会館（愛知県名古屋市）清水一之
第 28 回　2003. 10. 04 ロイトン札幌（北海道札幌市）今井浩三
第 27 回　2002. 11. 16 セミナーハウスクロス・ウェーブ（千葉県船橋市）高木敏之
第 26 回　2001. 10. 27 山口大学医学部霜仁会（山口県宇部市）河野道生
第 25 回　2000. 11. 18 国立国際医療センター（東京都新宿区）戸川　敦
第 24 回　1999. 11. 20 京都パークホテル（京都府京都市）加納　正
第 23 回　1998. 10. 17 札幌プリンスホテル北海道札幌市）三國主税
第 22 回　1997. 11. 29 虎ノ門パストラル（東京都港区）川戸正文
第 21 回　1996. 11. 30 徳島東急イン（徳島県徳島市）小阪昌明
第 20 回　1995. 11. 25 マーキュリーホール（群馬県前橋市）土屋　純
第 19 回　1994. 12. 03 岡山プラザホテル（岡山県岡山市）瀬崎達雄
第 18 回　1993. 12. 03 東京ガーデンパレスホテル（東京都文京区）高月　清
第 17 回　1992. 12. 04 東京ガーデンパレスホテル（東京都文京区）今村幸雄
第 16 回　1992. 01. 10 東京ガーデンパレスホテル（東京都文京区）今村幸雄
第 15 回　1990. 12. 14 東京ガーデンパレスホテル（東京都文京区）今村幸雄
第 14 回　1989. 12. 15 東京ガーデンパレスホテル（東京都文京区）今村幸雄
第 13 回　1989. 06. 23 新神戸オリエンタルホテル（兵庫県神戸市）磯部　敬
第 12 回　1988. 11. 18 東京ガーデンパレスホテル（東京都文京区）今村幸雄
第 11 回　1987. 12. 04 銀座東急ホテル（東京都中央区）今村幸雄
第 10 回　1987. 07. 24 ホテルギンモンド東京（東京都中央区）今村幸雄
第 9 回　1986. 12. 05 全共連ビル（東京都千代田区）今村幸雄
第 8 回　1985. 11. 29 キャピトル東急ホテル（東京都千代田区）今村幸雄
第 7 回　1984. 11. 29 パレスホテル（東京都千代田区）今村幸雄
第 6 回　1984. 06. 27 キャピトル東急ホテル（東京都千代田区）今村幸雄
第 5 回　1984. 01. 20 住友三角ビル・住友クラブ（東京都新宿区）今村幸雄
第 4 回　1983. 06. 24 住友三角ビル・住友クラブ（東京都新宿区）今村幸雄
第 3 回　1981. 11. 19 住友三角ビル・住友クラブ（東京都新宿区）今村幸雄
第 2 回　1981. 11. 18 住友三角ビル・住友クラブ（東京都新宿区）今村幸雄
第 1 回　1980. 06. 04 パレスホテル（東京都千代田区）今村幸雄

協賛企業一覧

第 46 回日本骨髄腫学会学術集会の開催にあたり、以下の企業・団体様のご協賛、ご協力をいただきました。
ここに深甚なる感謝の意を表します。

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■企業展示
ヤンセンファーマ株式会社

■広告
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サノフィ株式会社
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50 音順
2021 年 3 月 30 日現在

MEMO

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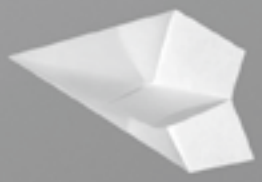

「病気と苦痛に対する人間の闘いのために」

わたしたちは、新薬の開発に挑み続けます。
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新発売

抗CD38モノクローナル抗体

サークリサ® 点滴静注 100mg 500mg

SARCLISA®

イサツキシマブ(遺伝子組換え)製剤

生物由来製品、劇薬、処方箋医薬品　薬価基準収載

：注意－医師等の処方箋により使用すること

1. 警告

本剤の投与は、緊急時に十分対応できる医療施設において、造血器悪性腫瘍の治療に対して十分な知識・経験を持つ医師のもとで、本剤の投与が適切と判断される症例のみに行うこと。また、治療開始に先立ち、患者又はその家族に有効性及び危険性を十分に説明し、同意を得てから投与を開始すること。

2. 禁忌(次の患者には投与しないこと)

本剤の成分に対し過敏症の既往歴のある患者

4. 効能又は効果

再発又は難治性の多発性骨髄腫

5. 効能又は効果に関連する注意

5.1 本剤による治療は、少なくとも2つの標準的な治療が無効又は治療後に再発した患者を対象とすること。

5.2 臨床試験に組み入れられた患者の前治療歴等について、「17. 臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。

6. 用法及び用量

ポマリドミド及びデキサメタゾンとの併用において、通常、成人にはイサツキシマブ(遺伝子組換え)として1回10mg/kgを点滴静注する。28日間を1サイクルとし、最初のサイクルは1週間間隔で4回(1、8、15、22日目)、2サイクル以降は2週間間隔で2回(1、15日目)点滴静注する。

7. 用法及び用量に関連する注意

7.1 本剤を単独投与した場合の有効性及び安全性は確立していない。

7.2 本剤と併用する抗悪性腫瘍剤の投与に際しては、「17. 臨床成績」の項の内容を熟知し、投与すること。

7.3 ポマリドミド及びデキサメタゾン以外の抗悪性腫瘍剤との併用による有効性及び安全性は確立していない。

7.4 本剤投与によるInfusion reactionを軽減させるために、本剤投与開始15～60分前に、本剤と併用するデキサメタゾン、抗ヒスタミン剤、H_2受容体拮抗剤及び解熱鎮痛剤を投与すること。[11.1.1 参照]

7.5 本剤は生理食塩液又は5%ブドウ糖液を用いて総量を250mLとし、175mg/時の投与速度で点滴静注を開始する。Infusion reactionが認められなかった場合には、患者の状態を観察しながら、投与速度を以下のように段階的に上げることができる。ただし、投与速度は400mg/時を超えないこと。

本剤の投与速度

投与時期	投与速度(mg/時)	
	初回投与	2回目投与以降
投与開始　0～60分	175	175
投与開始　60～90分	225	275
投与開始　90～120分	275	375
投与開始　120～150分	325	400
投与開始　150～180分	375	400
投与開始　180分以降	400	400

7.6 Infusion reactionが発現した場合、以下のように、本剤の休薬、投与速度の変更等、適切な処置を行うこと。[11.1.1 参照]

・Grade 2[注]：
Grade 1[注]以下に回復するまで休薬すること。回復後、87.5mg/時の投与速度で投与を再開することができる。Infusion reactionの再発が認められなかった場合には、30分ごとに50mg/時ずつ最大400mg/時まで投与速度を上げることができる。

・Grade 3[注]以上：
本剤の投与を中止し、本剤を再投与しないこと。

7.7 Grade 3又は4[注]の好中球減少が発現した場合、好中球数が1,000/mm³以上に回復するまで休薬すること。[11.1.2 参照]

注)GradeはNCI-CTCAE v4.03に準じる。

8. 重要な基本的注意

8.1 骨髄抑制があらわれることがあるので、本剤の投与前及び投与中は定期的に血液検査等を行い、患者の状態を十分に観察すること。[11.1.2 参照]

8.2 本剤は、赤血球上に発現しているCD38と結合し、間接クームス試験の結果が偽陽性となる可能性がある。このため、本剤投与前に不規則抗体のスクリーニングを含めた一般的な輸血前検査を実施すること。輸血が予定されている場合は、本剤を介した間接クームス試験への干渉について関係者に周知すること。[12.1 参照]

11. 副作用

次の副作用があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止するなど適切な処置を行うこと。

11.1 重大な副作用

11.1.1 Infusion reaction
アナフィラキシー、呼吸困難、咳嗽、悪寒、悪心等のInfusion reaction(37.5%)があらわれることがあり、多くの場合は、初回投与時に発現が認められたが、2回目以降の投与時にも認められている。異常が認められた場合は、本剤の投与を中断又は中止し適切な処置を行うとともに、症状が回復するまで患者の状態を十分に観察すること。[7.4、7.6 参照]

11.1.2 骨髄抑制
好中球減少(43.4%)、血小板減少(11.2%)、発熱性好中球減少(10.5%)、貧血(3.3%)等の骨髄抑制があらわれることがある。[7.7、8.1 参照]

11.1.3 感染症(38.2%)
肺炎(15.1%)、敗血症(1.3%)等の重篤な感染症があらわれることがある。

11.2 その他の副作用

	10%以上	10%未満5%以上	5%未満
呼吸器、胸郭及び縦隔障害		呼吸困難	
胃腸障害	下痢	悪心、嘔吐	
代謝および栄養障害			食欲減退
心臓障害			心房細動
その他			体重減少

21. 承認条件

21.1 医薬品リスク管理計画を策定の上、適切に実施すること。

21.2 国内での治験症例が極めて限られていることから、製造販売後、一定数の症例に係るデータが集積されるまでの間は、全症例を対象に使用成績調査を実施することにより、本剤使用患者の背景情報を把握するとともに、本剤の安全性及び有効性に関するデータを早期に収集し、本剤の適正使用に必要な措置を講じること。

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※その他の使用上の注意については製品添付文書をご覧ください。

文献請求先：くすり相談室(フリーダイヤル)
0120-109-905
月～金 9:00～17:00(祝日・会社休日を除く)
ホームページ：https://www.sanofi.co.jp/ja

製造販売元：サノフィ株式会社
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SANOFI GENZYME