Highlights from IMS 20th meeting 2023

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Strategie terapeutiche nel paziente difficile da trattare

- malattia extramidollare

30-31 gennaio 2024
BOLOGNA, Royal Hotel Carlton

Silvia Mangiacavalli MD
COI Disclosure

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
AMGEN					x	x	
BMS					x	x	
GSK					x	x	
JANSSEN					x	x	
SANOFI					x	x	
TAKEDA					x	x	

Extramedullary myeloma definition and incidence

- Paraskeletal (Local growth):
  - Soft-tissue masses arising from focal bone involvement
- Extramedullary plasmacytomas (hematogenous spread):
  - Subcutaneous tumors
  - Multiple nodules (skin, liver, breast, kidney)
  - Lymph nodes
  - Central nervous system

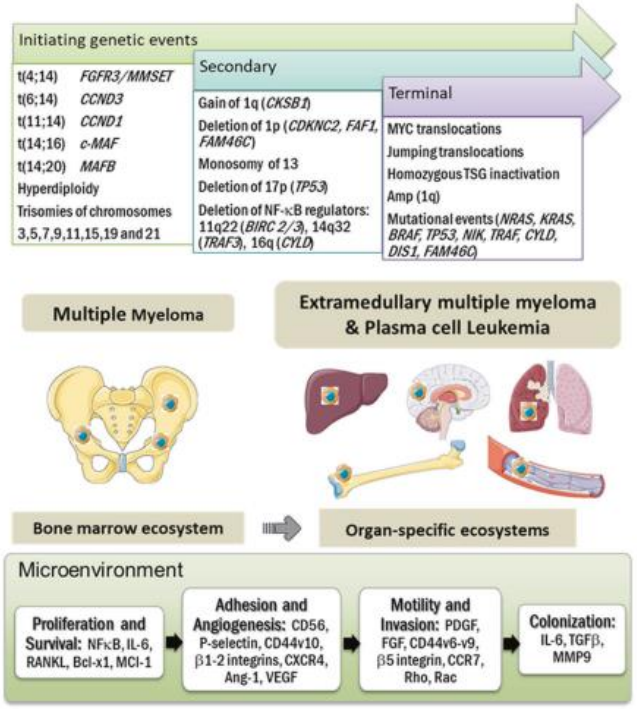
Table I. Plasmacytomas in multiple myeloma: incidence at diagnosis and at relapse.

	Paraskeletal (PS), %*	Extramedullary (EMD), %†
At diagnosis	7–34·4	1·75–4·5
At relapse‡	6–34·2	3·4–10

*PS: soft-tissue masses arising from vertebrae, ribs, sternum, skull.
†EMD: skin (single or multiple subcutaneous tumours), liver, pleura, breast, lymph nodes and central nervous system (CNS).
‡At relapse >liver, pleura, CNS.

Rosinõl et al. Br Journal of Hematol 2021

Game of bones, how MM manipulates microenvironment



Bhutani et al. Leukemia 2020

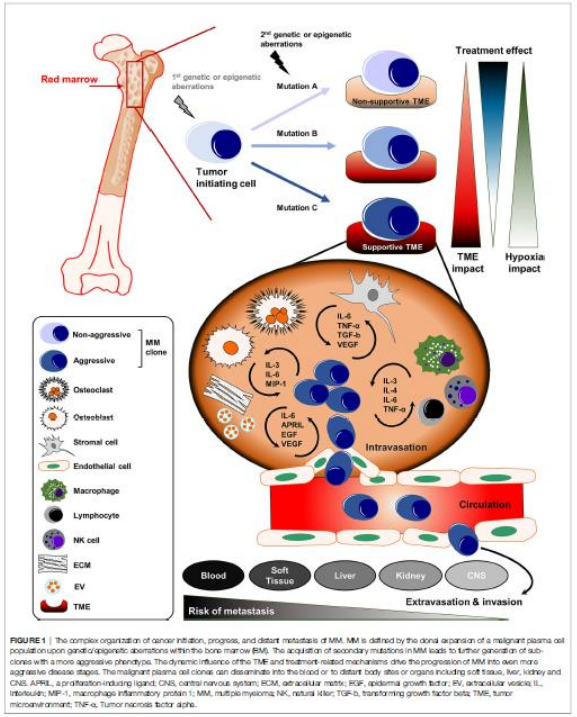


FIGURE 1 | The complex organization of cancer initiation, progress, and distant metastasis of MM. MM is defined by the clonal expansion of a malignant plasma cell population upon genetic/epigenetic aberrations within the bone marrow (BM). The acquisition of secondary mutations in MM leads to further generation of subclones with a more aggressive phenotype. The dynamic influence of the TME and treatment-related mechanisms drive the progression of MM into even more aggressive disease stages. The malignant plasma cell clones can disseminate into the blood or to distant body sites or organs including soft tissue, liver, kidney and CNS. APRIL, a proliferation-inducing ligand; CNS, central nervous system; ECM, extracellular matrix; EGF, epidermal growth factor; EV, extracellular vesicle; IL, interleukin; MIP-1, macrophage inflammatory protein 1; MM, multiple myeloma; NK, natural killer; TGF-b, transforming growth factor beta; TME, tumor microenvironment; TNF-α, Tumor necrosis factor alpha.

Moser-Katz et al. Front Oncol 2021
Forster et al. Front Oncol 2022

Extramedullary myeloma definition and incidence

Table 1. Baseline characteristics of the patients.

	Overall series $N = 1304$	Pts without Ps $N = 1048$	Pts with Ps $N = 256$	*P*-value
Gender (male), *n* (%)	674 (51.6%)	526 (50.15)	148 (57.8%)	0.03
Age (years), median (range)	64 (21-92)	65 (21-92)	61 (24-87)	
ISS, *n* (%)*				
• I	266 (30.8%)	174 (25.7%)	92 (49.7%)	<0.0001
• II	282 (32.7%)	232 (34.3%)	50 (27%)	0.06
• III	313 (36.3%)	270 (39.9%)	43 (23.2%)	<0.0001
Heavy chain type, *n* (%)				
• IgG	703 (53.9%)	579 (55.2%)	124 (48.4%)	
• IgA	360 (27.6%)	295 (28.1%)	65 (25.3%)	
• Ligh chain	180 (13.8%)	130 (12.4%)	50 (19.5%)	0.004
• IgD	21 (1.6%)	17 (1.6%)	4 (1.5%)	NS
• IgM	8 (0.6%)	6 (0.5%)	2 (0.7%)	NS
• Oligosecretory	13 (0.9%)	5 (0.4%)	8 (3.1%)	0.0005
• Biclonal	12 (0.9%)	10 (0.9%9)	2 (0.7%)	NS
• Unknown	7 (0.5%9)	6 (0.5%)	1 (0.3%)	NS
Ligh chain type, *n* (%)				
• Kappa	722 (55.3%)	582 (55.5%)	140 (54.6%)	NS
• Lambda	530 (40.6%)	427 (40.7%9)	103 (40.2%)	
• Non-secretory	14 (1.07%)	6 (0.5%)	8 (3.1%)	0.001
• Biclonal	9 (0.69%)	7 (0.6%)	2 (0.7%)	NS
• Unknown	39 (3.2%)	36 (3.4%)	3 (1.1%)	
Serum M-protein (g/L)(mean ± SD)	33.2 ± 21.9	35.3 ± 21.6	24.5 ± 21.08	0.0001
Bone marrow plasma cells (%)(mean ± SD)	46 ± 28.9	50 ± 27.8	31 ± 28.8	0.0001

Available in 861 patients.

Jiménez-Segura et al, Blood Cancer J 2022

Extramedullary myeloma definition and incidence

Table 2. Incidence of plasmacytomas overtime at diagnosis and at first relapse.

Plasmacytomas	Overall	Period 1	Period 2
At diagnosis	*N* = 1304	*N* = 577	*N* = 727
No	1048 (80.3%)	488 (84.5%)	560 (77%)
Yes	256 (19.6%)	89 (15.4%)	167 (22.9%)
• EMPs	26 (1.9%)	9 (1.5%)	17 (2.3%)
• PPs	230 (17.6%)	80 (13.8%)	150 (20.6%)
Relapsed patients (with data available)	*N* = 967	*N* = 415	*N* = 552
No	775 (80.1%)	330 (79.5%)	445 (79.6%)
Yes	192 (19.8%)	85 (20.4%)	107 (19.3%)
• EMPs	50 (5.1%)	19 (4.5%)	31 (5.6%)
• PPs	142 (14.6%)	66 (15.9%)	76 (13.7%)

Table 3. Location of plasmacytomas at diagnosis and at first relapse.

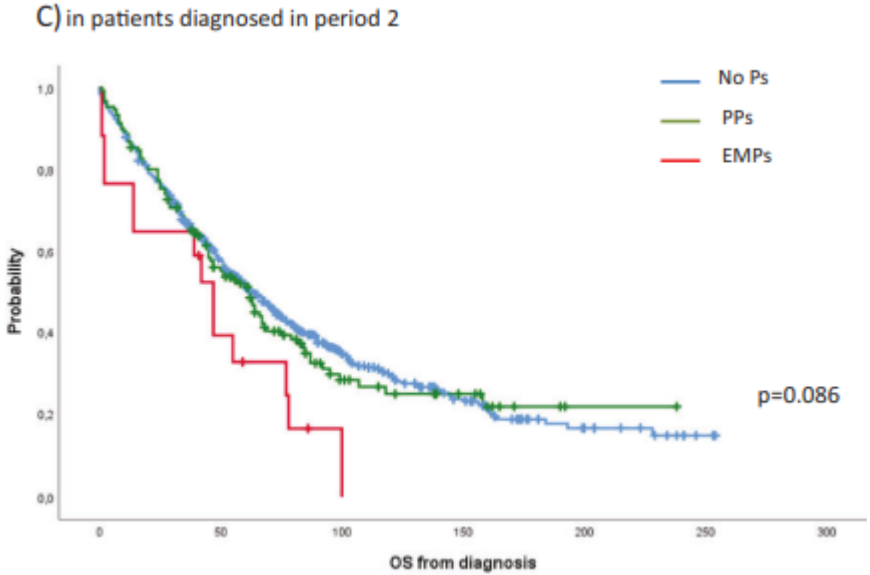
Location*	At diagnosis	At first relapse
Paraskeletal	*N* = 230	*N* = 142
• Chest	92 (40%)	65 (45.7%)
• Paravertebral	90 (39.1%)	71 (50%)
• Skull	30 (13%)	24 (16.9%)
• Pelvis	26 (11.3%)	16 (11.2%)
• Long bones	3 (1.3%)	9 (6.3%)
Extramedullary	*N* = 26	*N* = 50
• Pleura, lung	6 (23%)	13 (26%)
• Skin, subcutaneous cell tissue, muscle	5 (19.2%)	20 (40%)
• Liver	4 (15.3%)	8 (16%)
• Other locations (EMPs: kidney, peritoneum)	15 (57.6%)	13 (26%)
• Central Nervous System	1 (3.8%)	4 (8%)

*34% and 56% of patients had more than one location at diagnosis and first relapse, respetively.

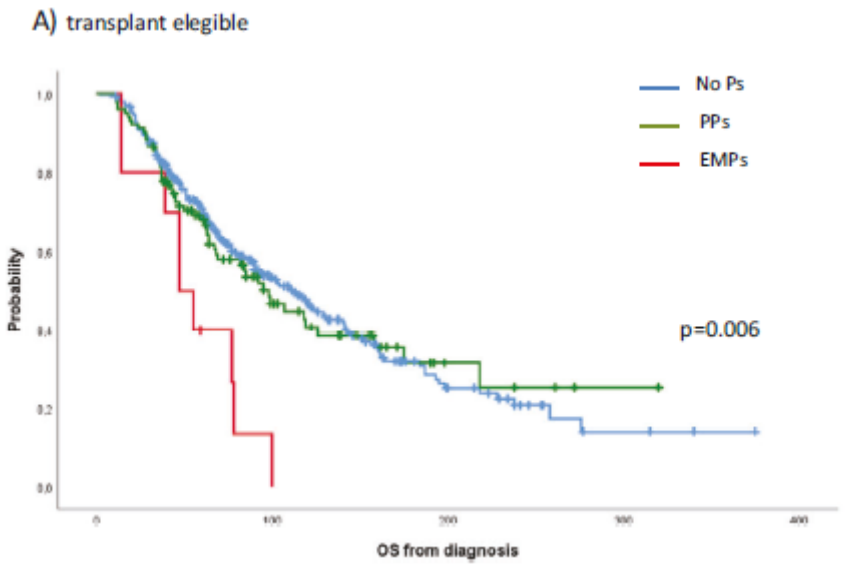
Jiménez-Segura et al, Blood Cancer J 2022

Extramedullary myeloma prognostic impact and outcome

OS for all cohort after 2000



OS for TE after 2000



Jiménez-Segura et al, Blood Cancer J 2022

Extramedullary myeloma definition and risk factor

Table 2 Sites of first extramedullary escape in 93 patients of the study cohort developing extramedullary relapse*

	N°	% (out of 93 patients)
EMR-B	49	52.7
EMR-S	69	74.2
Head and neck	10	10.7
Lymph nodes	5	5.4
Chest		
pleura	6	6.5
lung	5	5.4
Liver	2	2.2
Skin and soft tissue	15	17.2
Plasmacell leukemia	26	28
Unique EMR site	6	6.4
In association with other EMR sites	20	21.5

*Different localizations can occur simultaneously in each single patient

EMR-B extramedullary relapse arising from adjacent bone, *EMR-S* extramedullary relapse located in extraosseous organs

		HR	95%CI	*p* value
Baseline clinical risk factor	ISS = 1	–	–	–
	ISS ≥ 2	1.4	0.6–2.9	0.443
	Bone marrow infiltration (%)	1.0	0.99–1.02	0.374
	sMC (g/dL)	1.1	0.9–1.2	0.328
	Lytic bone lesions	1.2	0.7–2.3	0.480
	Hemoglobin ≥10 g/dl	–	–	–
	Hemoglobin <10 g/dl	1.0	0.5–2.1	0.965
	Serum calcium ≤ 11.5 mg/dl	–	–	–
	Serum calcium >11.5 mg/dl	1.4	0.7–2.8	0.283
	Serum creatinine ≤2 mg/dl	–	–	–
	Serum creatinine >2 mg/dl	1.7	0.6–4.6	0.289
Treatment-related risk factors	0 risk factor	–	–	–
	1 risk factor[a]	4.5	2.2–9.0	<0.001
	2 risk factors[b]	9.0	4.3–19.1	<0.001

sMC serum monoclonal component

[a] (N° of subsequent treatments > 2 and treatment duration < 6 months) or (N° of subsequent treatments ≤ 2 and treatment duration ≥ 6 months)

[b] N° of subsequent treatments > 2 and treatment duration ≥ 6 months

Mangiacavalli S et al, Ann of Hematol 2017

Extramedullary myeloma: clonal evolution

TABLE 1 Baseline characteristics at diagnosis of multiple myeloma in patients with de novo and secondary extramedullary disease.

Parameter at diagnosis of MM	Entire cohort N – 299	De novo EMM N – 95	Secondary EMM n – 204	p-value
Median age (range) at MM diagnosis	59.7(18–89.3)	61	58.7	.09
Median age (range) at EMM	62.1(18–92.1)	61	62.4	.12
ISS (n – 231)				.22
Stage I	45%	46%	45%	
Stage II	27%	33%	23%	
Stage III	28%	21%	32%	
Revised ISS (n – 211)				.57
Stage I	29%	33%	28%	
Stage II	35%	33%	35%	
Stage III	36%	34%	37%	
Cytogenetics at diagnosis of MM (n – 236)				
High-risk cytogenetics[a], %	54%	53%	54%	.89
17p deletion	16%	18%	16%	.7
1q duplication	30%	26%	31%	.44
t(4;14)	16%	15%	16%	.84
MAF translocation				
t(14;16)	8%	9%	7%	.78
t(14;20)	2%	6%	1%	.06
t(11;14)	13%	7%	15%	.13
Hyperdiploid without other HR	24%	21%	26%	.42
Deletion 13q	29%	31%	29%	.75
Deletion 1p	3%	4%	3%	.69
MYC disruption	7%	7%	7%	.78
Involved/Uninvolved FLC ratio, median (IQR)	79 (15–329)	48.8	106	.17
Involved FLC value, median (IQR)	34 (8–124)	26.8	39	.7
Heavy and light Chain				.42
IgG	51%	45%	53%	
IgA	24%	29%	22%	
IgD	1%	0%	2%	
Light Chain only	23.1%	26%	22%	
Non-secretory	0.4%	0%	0.4%	
Light chain type				.99
Kappa	61%	61%	61%	
Lambda	39%	39%	39%	
LDH > ULN at MM diagnosis	31%	33%	30%	.7
Marrow plasma cell infiltrate at diagnosis, median (IQR)	40% (20–70)	30%	50%	**0.005**

Note: Bold values indicate a statistically significant difference.
Abbreviations: EMM, extramedullary multiple myeloma; FLC, free light chain; HR, high risk; ISS, international staging system; IQR, interquartile range; LDH, lactate dehydrogenase.
[a]High-risk cytogenetic features were defined using the mSMART 3.0 criteria [deletion 17p, *TP53* mutation, t(4;14), t(14;16), t(14;20), 1q duplication].

122/204 patients with secondary EMM with FISH at EMM

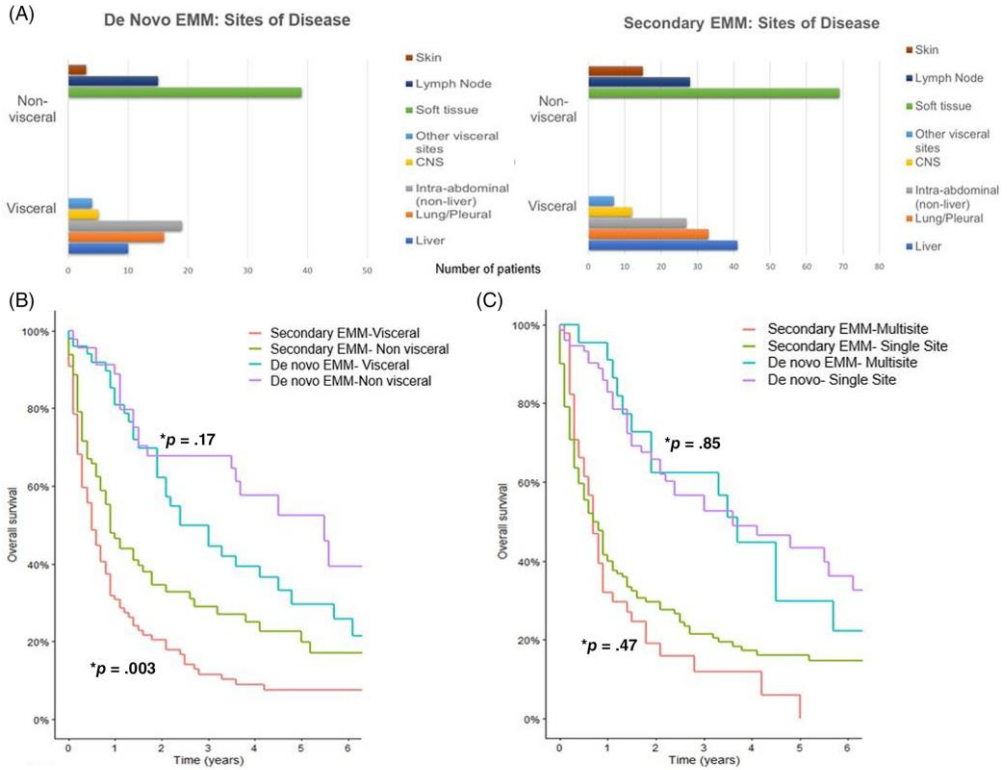
- 49 (40%) had a new structural variant vs FISH at diagnosis
- 1q duplication in 23% (28/122) patients
- deletion 17p in 16% (20/122) patients
- MYC disruption in 8% (10/122)patients
- 1q duplication plus del 17p were 8% (10/122)

median OS from EMM with clonal evolution on FISH

- 4.8 vs 9.6 months

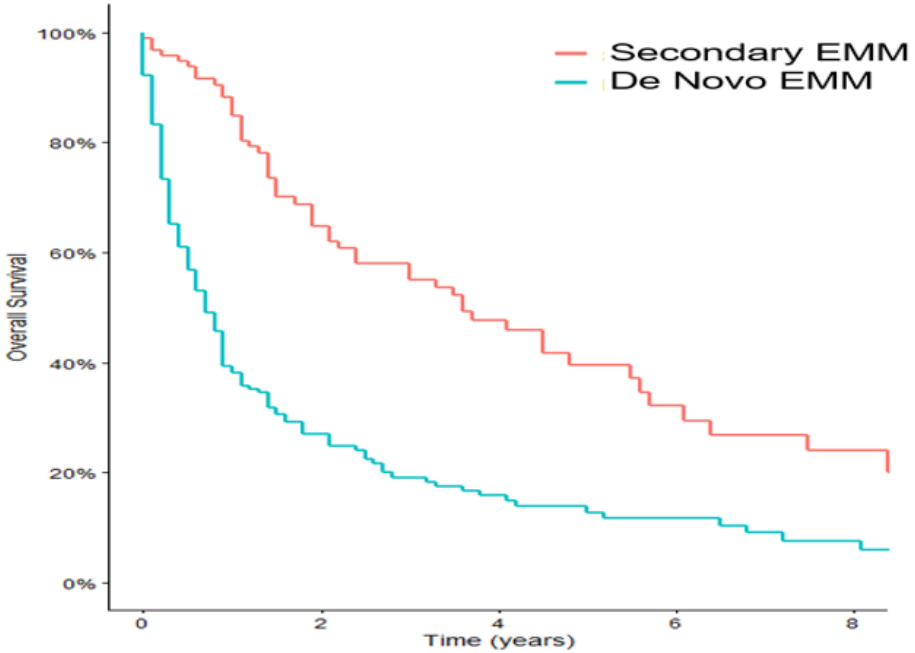
Zanwar et al, Am J Hematol 2023

Extramedullary myeloma prognostic impact and outcome



Zanwar et al, Am J Hematol 2023

prognostic impact of EMM at relapse



median OS from **secondary EMM**

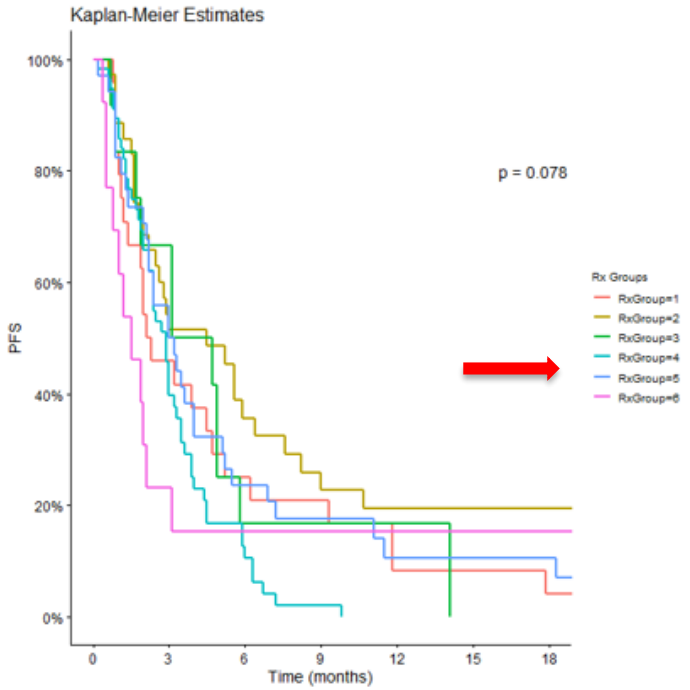
- 0.7 years (95% CI: 0.6-0.9 years)
- iFLC >100 worst outcome

Median OS with **de novo EMM**

- 3.6 years (95%CI: 2.4-5.6)
- No impact of HR FISH

Zanwar et al, Am J Hematol 2023

EMM Therapy in the last decade (CAR-T and BiAb available)

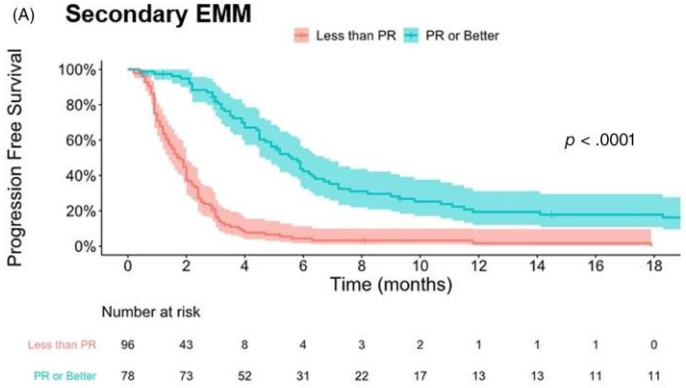


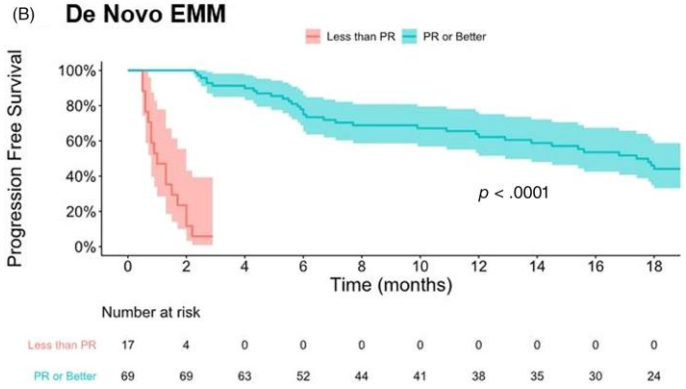
Supplementary Table 3. Progression Free Survival (PFS) with initial treatment for secondary EMM

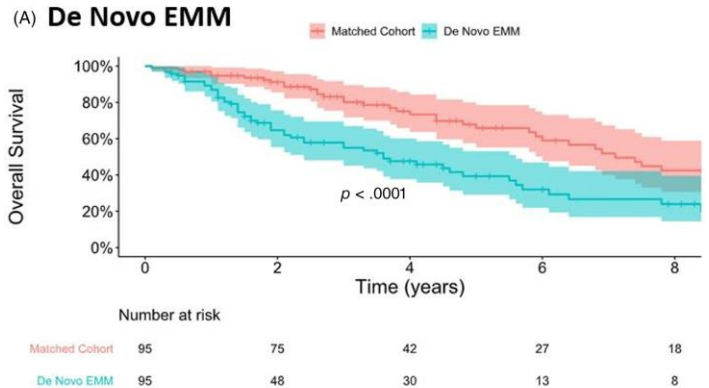
Groups	n	Median PFS (95%CI), months	P value
Proteasome Inhibitor (PI) plus IMiD based combination without CD38 antibody (group 1)	24	2.2 (1.9-5.2)	0.078
CD38 antibody-based combination (including in combination with PI or ImiD (group 2)	36	4.5 (2.5-7.6)	
Immune effector therapies (CAR-T or Bispecific T-cell redirecting	12	3.9 (1.9-NA)	
VDT-PACE like chemotherapy and other alkylator-based combinations (group 4)	59	2.9 (2.4-3.5)	
Either PI or IMiD-based combination without CD38 antibody (group 5)	34	3.1 (2.2-5.1)	
(group 6)			

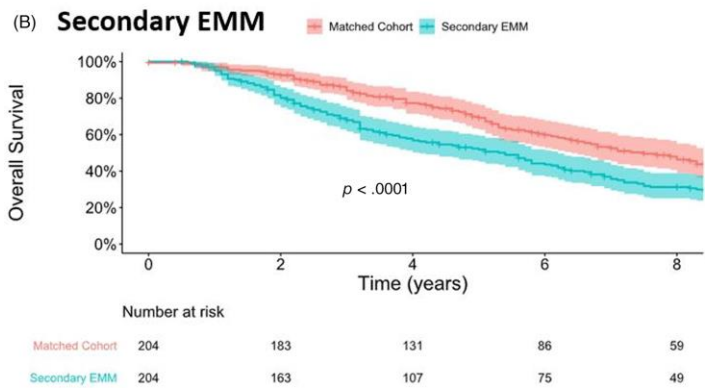
*4 patients received radiation therapy alone, 2 patients were treated with belantamab PT-112 (clinical trial), 1 patient each received selinexor-dexamethasone, venetoclax-dexamethasone, high dose methylprednisone, allogenic stem cell transplantation, TAK-981.

Zanwar et al, Am J Hematol 2023









Zanwar et al, Am J Hematol 2023

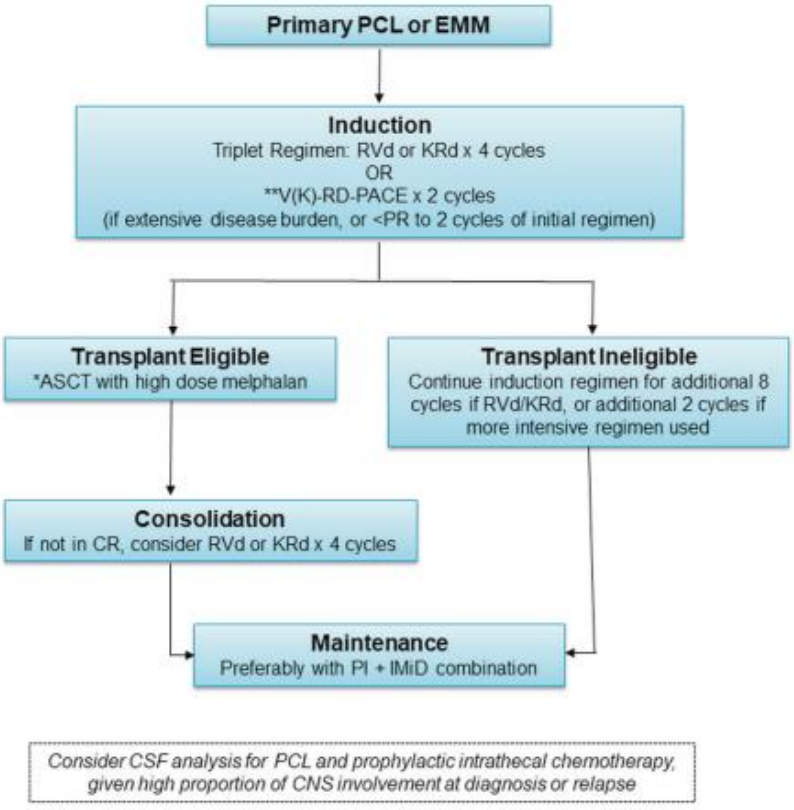
EMM Therapy in the last decade (CAR-T and BiAb available)

Supplementary Table 4. Immune effector therapies in Extramedullary Multiple Myeloma

Parameter	CAR-T	Bispecific antibodies
N	20 (%)	12 (%)
Median Prior Lines of therapy (range)	5 (4-8)	5 (4-8)
Type	idecabtagene vicleucel: 11 ciltacabtagene autoleucel: 4 CC-98633: 3 CT053: 1 ALLO715: 1	TNB383B: 7 REGN5459: 3 GPRC5DxCD3:1 FcRH5xCD3: 1
Response (PR or better)	15/20 (75%)	4/12 (33%)
MRD negative CR	8 (53%)	1 (8%)
CR with MRD positivity	2 (13%)	0
VGPR	2 (13%)	0
PR	3 (20%)	3 (25%)
SD	1 (7%)	2 (17%)
PD	4 (27%)	6 (50%)
Median PFS (95%CI)	4.9 months (3.1- NR)	2.9 months (2.2-NR)
Site of Progression	Progressed=15	Progressed=10
Systemic + Extramedullary	7 (46%)	8 (80%)
Extramedullary alone	4 (27%)	1 (10%)
Systemic Alone	4 (27%)	1 (10%)

CAR-T: chimeric antigen receptor-t cell therapy; CR: complete response; MRD: minimal residual disease; PD: progressive disease; PFS: progression free survival; PR: partial response; SD stable disease; VGPR: very good partial response
*two patients received both a CAR-T and Bispecific antibody

Zanwar et al, Am J Hematol 2023



Bhutani et al. Leukemia 2020

LEUKEMIA & LYMPHOMA
2021, VOL. 62, NO. 9, 2235–2241
https://doi.org/10.1080/10428194.2021.1907373

Taylor & Francis

ORIGINAL ARTICLE

Role of D(T)PACE-based regimens as treatment of multiple myeloma with extramedullary relapse or refractory disease

Tony Huynh[a], Elise Corre[a], Marie-Paule Lemonnier[a], Rémy Duléry[a], Zora Marjanovic[a], Nabaz Jaff[a], Simona Lapusan[a], Mohamad Mohty[a,b,c], Laurent Garderet[a,b] and Paul Coppo[a,b,d,e]

- **ORR 58%**
- **CR 14%**
- **PFS 5 months**

Original Study

KD-PACE Salvage Therapy for Aggressive Relapsed Refractory Multiple Myeloma, Plasma Cell Leukemia and Extramedullary Myeloma

Aseel Alsouqi,[1] Muhammad Khan,[2] Binod Dhakal,[2] Liping Du,[3] Shelton Harrell,[4] Parameswaran Hari,[2] Robert F. Cornell[4]

- **ORR 77%**
- **CR12%**
- **PFS 8,3 months (bridging to TX)**

Byun et al. Journal of Hematology & Oncology (2022) 15:150
https://doi.org/10.1186/s13045-022-01374-5

Journal of Hematology & Oncology

RESEARCH Open Access

Phase II trial of daratumumab with DCEP in relapsed/refractory multiple myeloma patients with extramedullary disease

Ja Min Byun[1], Chang-Ki Min[2], Kihyun Kim[3], Soo-Mee Bang[4], Je-Jung Lee[5], Jin Seok Kim[6], Sung-Soo Yoon[1] and Youngil Koh[1*]

- **ORR 67,7%**
- **CR 35,5%;**
- **PFS 5 months**

EMN 19 phase II trial for ND-EMM and RR-EMM

Key Eligibility Criteria

1. Newly Diagnosed or 1st relapse MM patients with EMD (paraskeletal plasmacytomas ONLY are not eligible)
2. ECOG PS ≤ 2. Note: for subjects with CNS involvement, an ECOG PS >2 is also acceptable
3. Measurable Disease (Serum, Urine or sFLC MM)
4. Non refractory to Bortezomib based regimens
5. No prior treatment with anti-CD38 or anti-CS1 MoAB
6. Adequate Bone Marrow function (minimum laboratory requirements)
7. No ASCT within 12 weeks of C1D1
8. No prior allo-SCT (regardless of timing)

Sponsor Approval

D-VCd (n=40)
Until PD or unacceptable toxicity (max. 36 months)*

Daratumumab (D) 16 mg/kg IV
- QW in Cycles 1-2, Q2W in Cycles 3-6, Q4W in Cycles 7+

Bortezomib (V) 1.5 mg/m² SC
- QW in every cycle

Cyclophosphamide (C) 300 mg/m² IV or PO
- QW in every cycle

Dexamethasone (d) 20 mg PO or IV
- Days 1, 2, 8, 9, 15, 16, 22, 23 of every cycle

Objectives

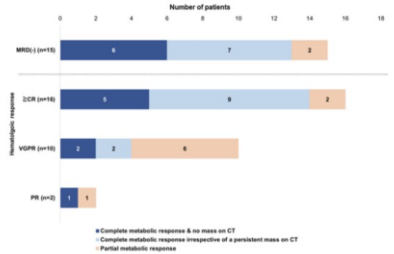
Primary
- CR rate

Secondary
- DoR
- PFS
- ORR
- TnT
- OS
- Safety (Adverse Events)

Exploratory
- GEP in BM and EMD site(s)
- Circulating Tumor Cell characterization
- Clinical and biological biomarker characterization
- Immune Profiling of BM and EMD site(s)

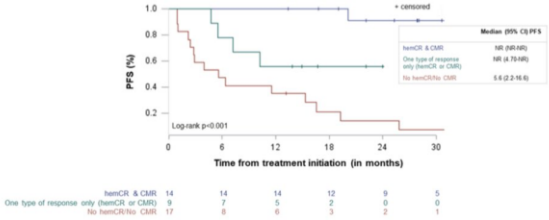
*Patients who have not demonstrated at least a confirmed PR by the end of Cycle 3 will discontinue study treatment

Figure 1. Combinations of best hematologic and EMD metabolic responses, among patients with at least partial response in and outside the marrow (n=28)



CR, complete response; VGPR, very good partial response; MRD, minimal residual disease; PR, partial response

Figure 2. PFS by best hematologic and EMD response status



CMR, complete metabolic response; hemCR, hematologic complete response; NR, not reached; PFS, progression-free survival

median FU 19 months
- mOS =NR
- mPFS 20 months
- NDEMM= NR
- RREMM=15 months

Beksac et al, poster 1956, ASH 2023

OA-31

Efficacy of bispecific antibodies in the treatment of extramedullary disease and high risk cytogenetics in relapsed multiple myeloma: a systematic review

Charan Vegivinti[1,2], Jaison Lawrence Alexander Santhi[3], Lawrence Liu[4], M Bakri Hammami[1,2], Rahul Thakur[1], Ananta Ghimire[5], Nagarathna Poojary[5], Murali Mohan Reddy Gopireddy[5], Anusha Manoj Kallamvalappil[6], Sahas Reddy Jitta[7], Nikita Chintapally[8], Nishi Shah[9,2], Murali Janakiram[4]

[1]Jacobi Medical Center; [2]Albert Einstein College of Medicine; [3]Government Sivagangai Medical College; [4]City of Hope National Comprehensive Cancer Center; [5]coGuide Academy; [6]Phoenix Hospital; [7]Mercy Hospital St louis Missouri; [8]MedStar Washington Hospital Center; [9]Montefiore Medical Center and Albert Einstein College of Medicine

Methods

- **Meta-analysis of clinical trial using BiAb**
- 14 studies were included in this analysis (787 patients)
- 3 studies (n = 78) reported ORRs in cohorts of patients with EMM
- 5 studies (n = 111) reported ORRs in cohorts of patients with HR-CA
- 3 studies reported ORRs with combination therapies (176 patients)

Results in the entire cohort

- the ORR was 0.59 (95% CI, 0.54-0.65)
- After stratified by bispecific antibody:
  - 0.70 with talquetamab
  - 0.63 with teclistamab
  - 0.62 with elranatamab

Results in the cohort with EMM

- The ORR was 0.38
- After stratified by bispecific antibody:
  - 0,45 with talquetamab
  - 0.36 with teclistamab
  - 0. 38 with elranatamab

ORR with BiAb COMBO: 0.85 (95% CI, 0.80-0.90)
ORR with BiAb COMBO in EMM (only The RedirecTT-1 trial with Tec+Tal): 0.71 (95% CI, 0.51-0.87).

Conclusions:

- only 4 trials reported EMD responses
- clinical trials should report EMD responses distinctly as it directly informs clinical decisions
- EMD responses are significantly lower than the full cohort ORR

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 28, 2023

Efficacy of Bispecific Antibodies Vs CAR-T in the Treatment of Extramedullary Disease and High-Risk Cytogenetics in Relapsed Multiple Myeloma: A Systematic Review and Meta-Analysis

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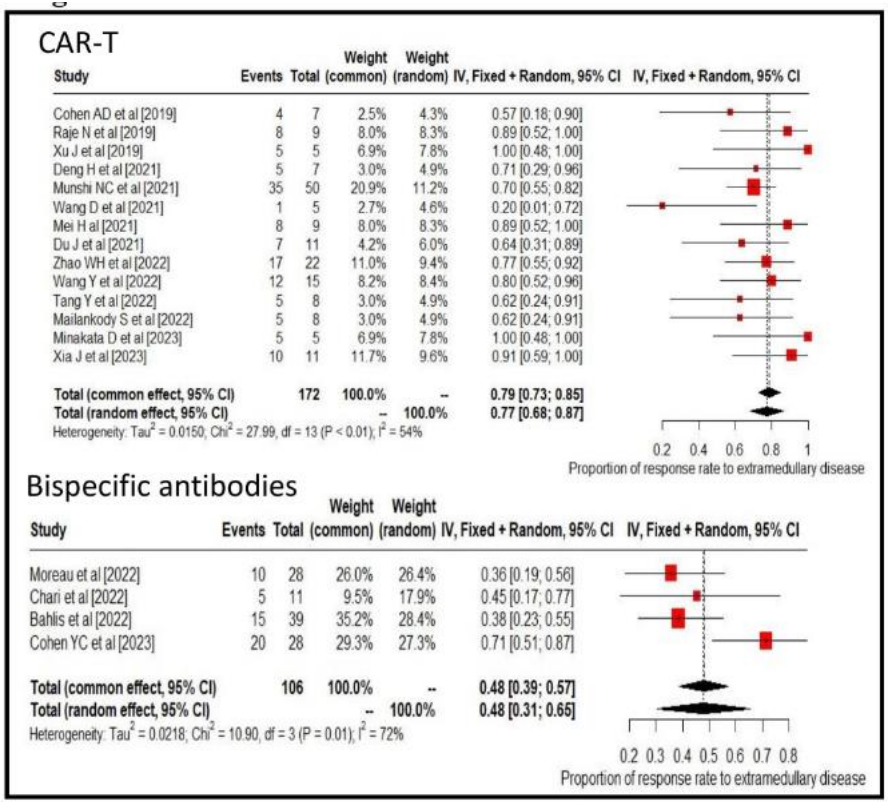
CAR-T

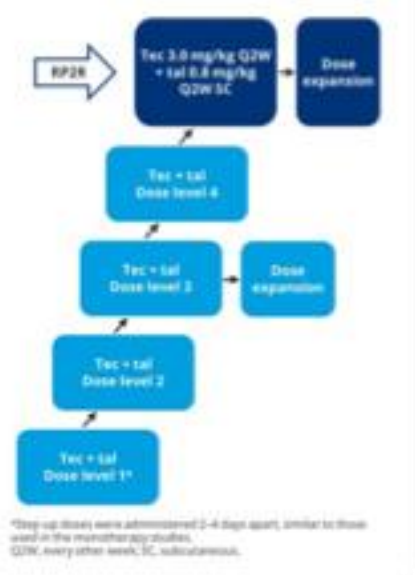
- ORR for EMD in 14 RCT (n=172)
- ORR was 0.86 vs 0.77 for EMD

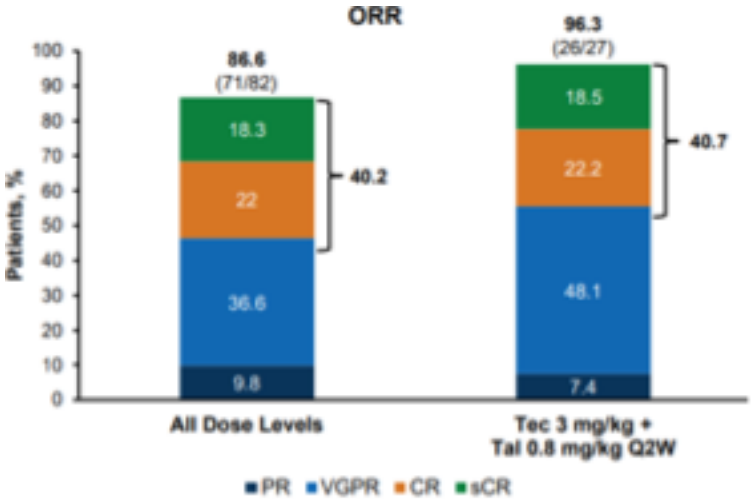
BiAb

- ORR for EMD available in 4 RCT (106 pts)
- ORR was 0.67 vs 0.48 for EMD



EMM Therapy in the last decade (RedirecTT-1 Tec+Tal)





- First results from the phase 1b trial of teclistamab + talquetamab showed a safety profile consistent with each of the monotherapies
- 96% ORR across at RP2R
- 86% ORR in extramedullary disease subgroup (RP2R)

P-069

Liquid biopsy monitoring is more sensitive than alternative techniques in extramedullary multiple myeloma

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Background:

- EMM detection and monitoring include PET/CT scans alternatives to BM biopsies
- consensus response criteria (CRC) are limited
    - EMD is frequently nonsecretory or with minimal BM involvement
- EMD is associated with DM in the MAPK pathway (KRAS, NRAS and BRAF)
- DM are detectable in cell free DNA (cfDNA) in EMD patients

Aim:

- **Clarify the possible role of cfDNA characterisation and monitoring in EMD patients**

Methods:

- DM were identified by WG and WE sequencing
- Dd-PCR was used to detect DM in cfDNA at additional time-points (prior to EMD, after treatment and at relapse)
- 100% of 13 pts had the EMD DM + at the time of EMD with VAF ranging from 0.05% to 37.63%. 8 pts had at least 2 cfDNA time-points
- cfDNA levels after therapy were correlated to PET/CT, Consensus RC and EuroFlow minimal residual disease (MRD)

Results and Conclusions:

- **cfDNA is complementary to PET/CT** (2 had cfDNA + with PET/CT - and 1 cfDNA - but PET/CT +)
- **cfDNA was more sensitive compared to CRC** (cfDNA+ in 3 patients in a CR)
- **cfDNA assessment outperformed MRD** (40% of MRD- with cfDNA +)
- **Patients achieving cfDNA - had the longest PFS** (median 23.5 vs 6 months in cfDNA+ 6 months)
- **cfDNA+ anticipated relapse**
- **DM were detectable in cfDNA prior to the initial development of EMD**

Extramedullary myeloma identification and monitoring

TABLE 1
Elements to Be Specified in ^{18}F-FDG PET/CT MM Reporting

Lesion	Definition
FL	Foci of uptake above surrounding background noise on 2 successive sections with or without osteolysis on computed image, excluding benign etiologies
Extramedullary disease	Tissue invasion without contiguous bone involvement
Paramedullary disease	Soft-tissue invasion with contiguous bone involvement
Diffuse medullary involvement	Homogeneous or heterogeneous diffuse uptake of pelvic-spinal-peripheral skeleton higher than liver background
FL SUV_{max}	SUV_{max} of bone FLs
^{18}F-FDG PET/CT abnormality	Presence of FLs, extramedullary disease lesions, paramedullary disease lesions, or diffuse medullary involvement

TABLE 2
Interpretation Criteria for ^{18}F-FDG PET/CT in MM Response to Therapy Assessment

Status	Definition
Complete metabolic response	Uptake ≤ liver activity in bone marrow sites and FLs previously involved (including extramedullary and paramedullary disease [Deauville score, 1–3])
Partial metabolic response	Decrease in number or activity of bone marrow sites/FLs present at baseline but persistence of lesions with uptake > liver activity (Deauville score, 4 or 5)
Stable metabolic disease	No significant change in bone marrow sites/FLs compared with baseline
Progressive metabolic disease	New FLs compared with baseline consistent with myeloma

Kraeber-Bodere et al; Journal of Nuclear Medicine, 2023

Take home messages

- Extramedullary plasmacytomas confers a dismal prognosis, both at diagnosis (denovo EMM) and even more at relapse (secondary EMM) not overcome by the novel agents
- PET-CT is the best available methods for staging and response definition
- Liquid Biopsy may have a role in the future
- For de novo EMM consider quadruplet therapy plus tandem auto or tandem auto/allo in transplant elegible patients
- For secondary EMM still no standard of care available

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