

Highlights from IMS 20th meeting 2023

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Malattia
extramidollare

30-31 gennaio 2024
BOLOGNA, Royal Hotel Carlton

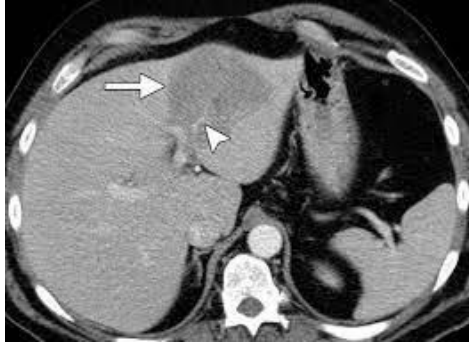
Disclosures

	<u>Speaking fees</u>	<u>Advisory boards</u>	<u>Research support</u>
Amgen	X	X	
<u>BMS/Celgene</u>	X	X	X
GSK		X	
<u>Karyopharm</u>		X	
Janssen	X	X	X
Sanofi	X	X	X
<u>Takeda</u>	X	X	

DEFINITIONS

Plasmocytoma

Monoclonal proliferation of plasma cells forming a tumor mass



Extramedullary Plasmocytoma

Plasma cell tumor of soft tissue

Parosseous Plasmocytoma

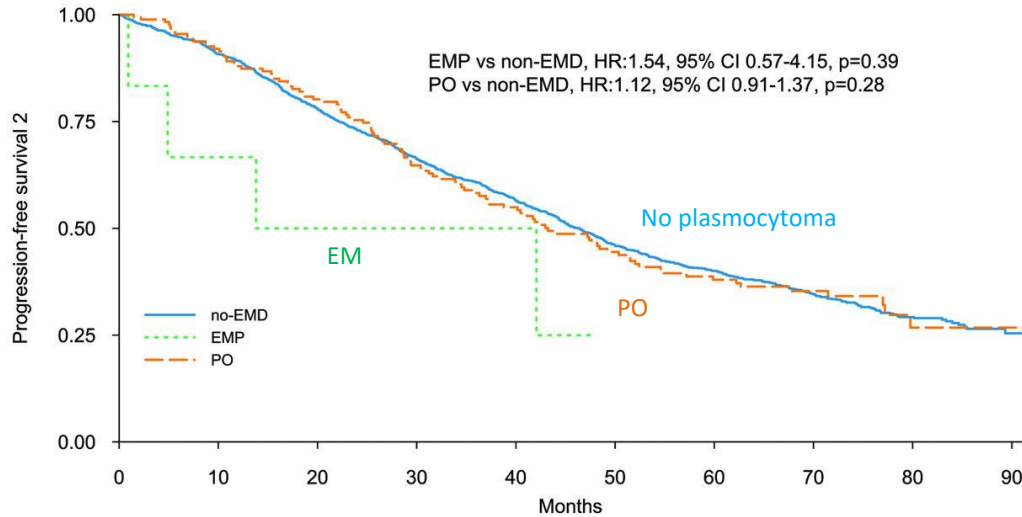
Plasmocytoma that arises from skeletal focal lesions, disrupts the cortical bone and grows as extra-bone masses

CLINICAL FEATURES OF EXTRAMEDULLARY PLASMOCYTOMAS

PFS 2

2332 relapsed pts

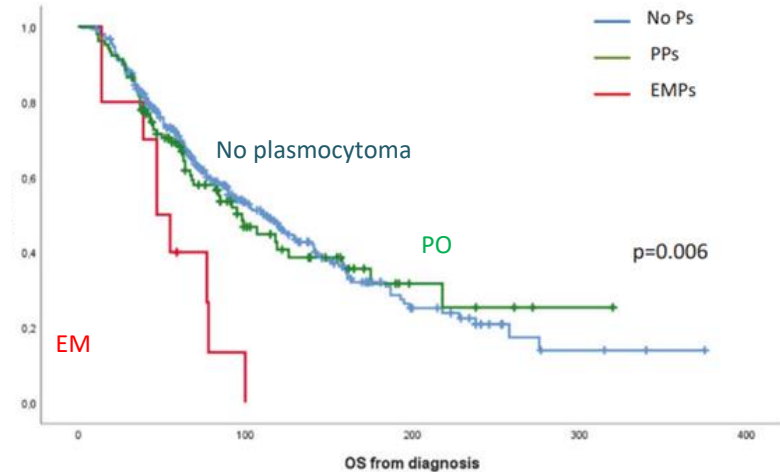
EMP vs non-EMD, HR:1.54, 95% CI 0.57-4.15, p=0.39
PO vs non-EMD, HR:1.12, 95% CI 0.91-1.37, p=0.28



no-EMD	1523	1297	1074	886	725	559	434	293	121	19
EMP	6	4	3	3	2	0	0	0	0	0
PO	180	159	133	102	81	63	49	31	9	3
	Number at risk									

OS from diagnosis

1304 pts



BIOLOGICAL FEATURES OF EXTRAMEDULLARY PLASMOCYTOMAS

Extramedullary disease is characterised by:

- High incidence of high risk FISH, in particular: **del(17p)**, **amp(1q)** and **t(4;14)**
- **High ki67**
- Abnormal expression of **adhesion proteins**

BIOLOGICAL FEATURES OF EXTRAMEDULLARY PLASMOCYTOMAS

In particular:

- **del (17p)** → 34% in EMD vs 11% in MM
- **Ki-67** → 67% (range, 30–90%)
- **CD56** → lower expression in EMD respect to MM (15% vs 80%)

BIOLOGICAL FEATURES OF EXTRAMEDULLARY PLASMOCYTOMAS

Reduced expression of therapeutic targets

22 MM pts with EMD

3 at diagnosis

CD38 expression

BM 79% EMD 55%

CD56 expression

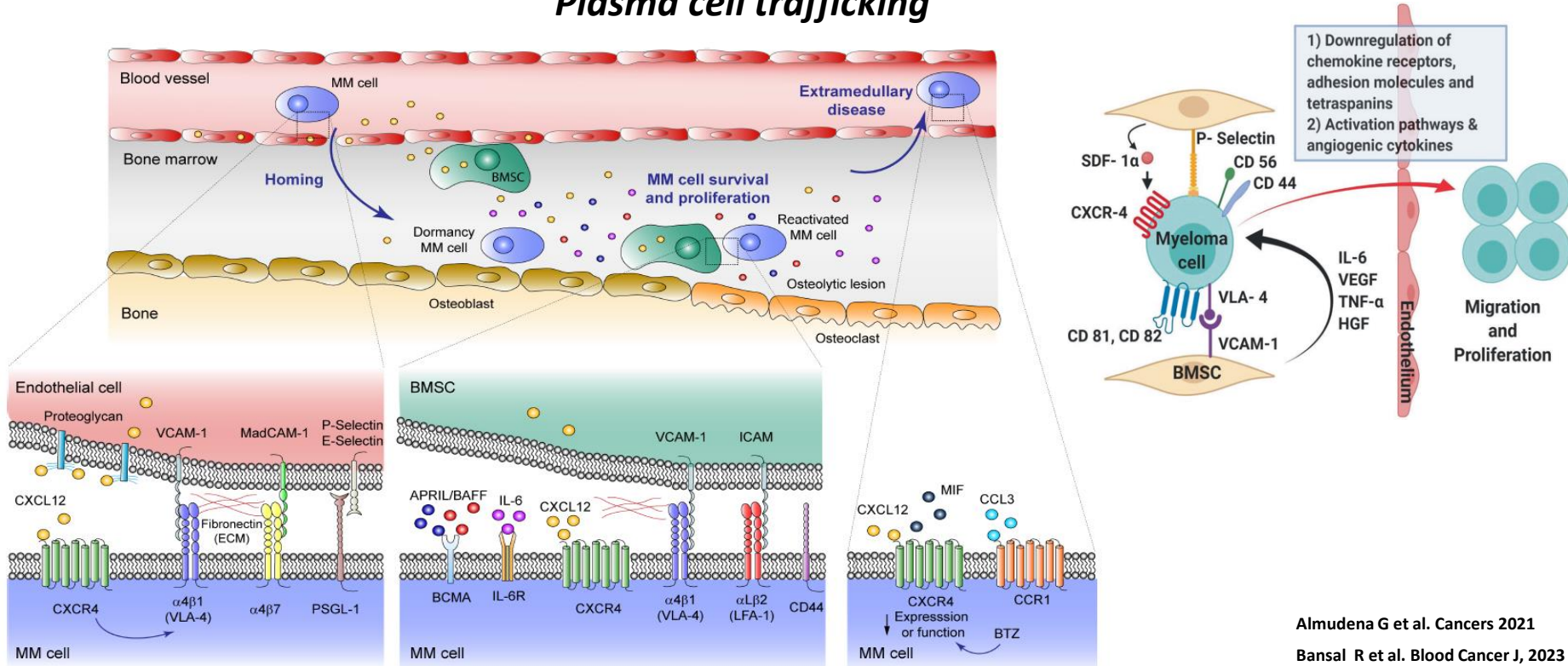
EMD 28%

CD44 expression

EMD 63%

BIOLOGICAL FEATURES OF EXTRAMEDULLARY PLASMOCYTOMAS

Plasma cell trafficking

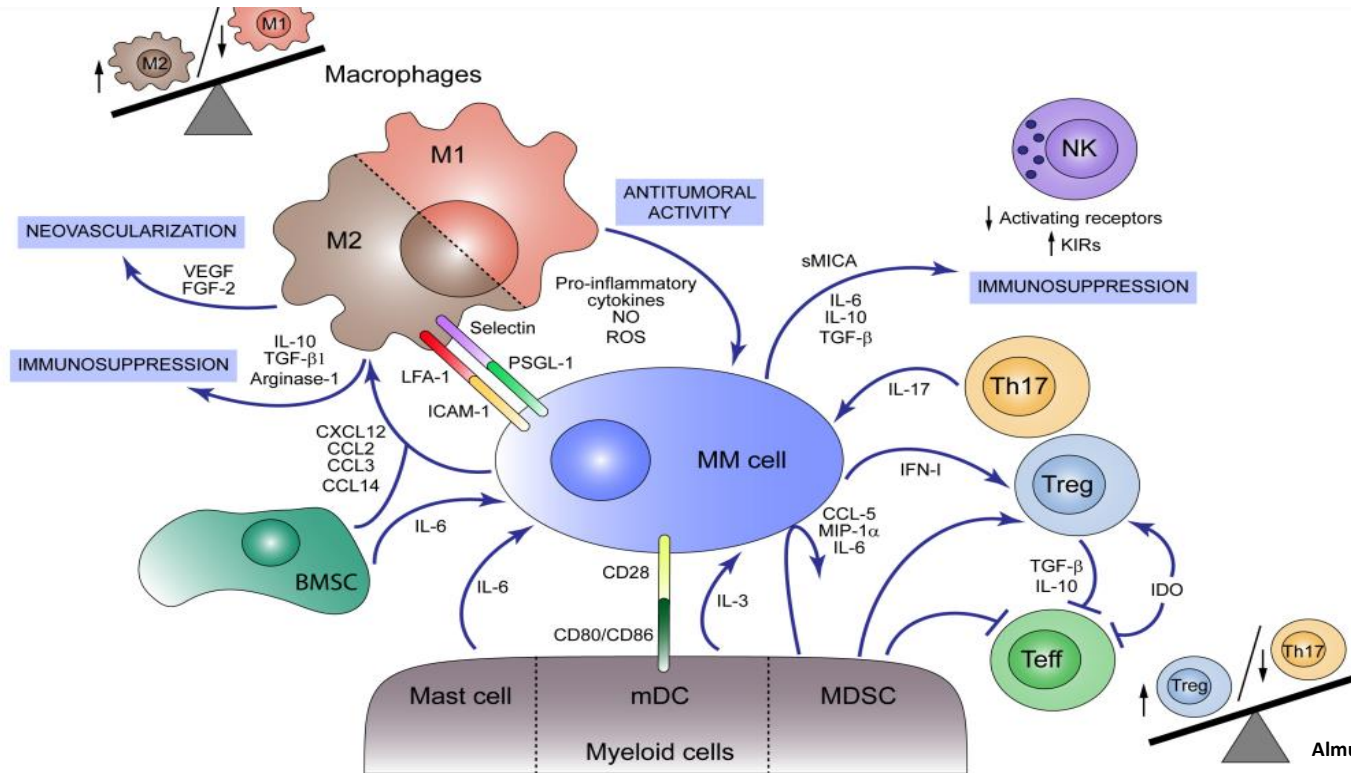


Almudena G et al. *Cancers* 2021

Bansal R et al. *Blood Cancer J*, 2023

BIOLOGICAL FEATURES OF EXTRAMEDULLARY PLASMOCYTOMAS

Immunoediting of the tumor microenvironment



IMiDs-treated relapsed MM with EMD

Thalidomide → Ineffective

Lenalidomide → Ineffective

Pomalidomide → Not very effective

CELLMoDs → No data

Isatuximab-treated relapsed MM with EMD (IsaPd vs Pd – Ikaria study)

154 pts in Isa-Pd → 24 pts with EMD

153 pts in Pd → 24 pts with EMD

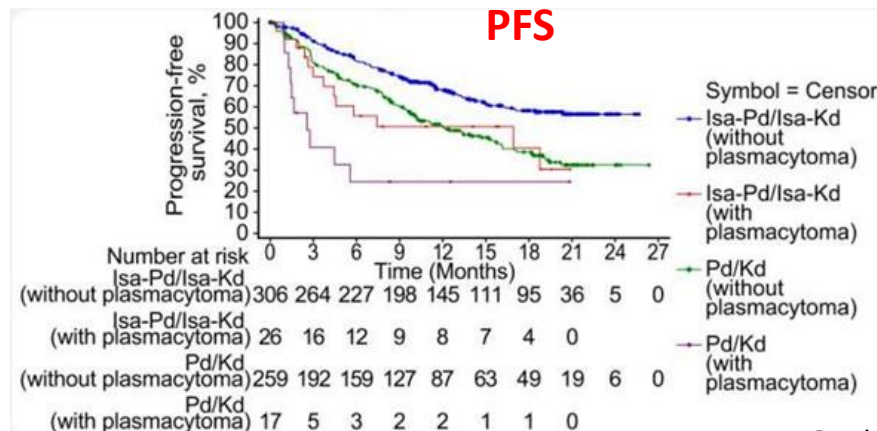
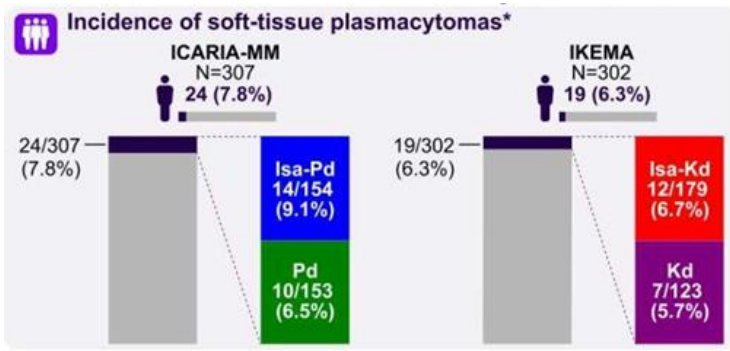
PFS

Median **4.6 months**

Median **1.6 months**

HR 0.2

Isatuximab-treated relapsed MM with EMD (IsaKd vs Kd – Ikema study)



Daratumumab-treated relapsed MM with EMD (retrospective monocentric experience)

13 pts with relapsed MM and EMD **Median PFS 6,5 months**

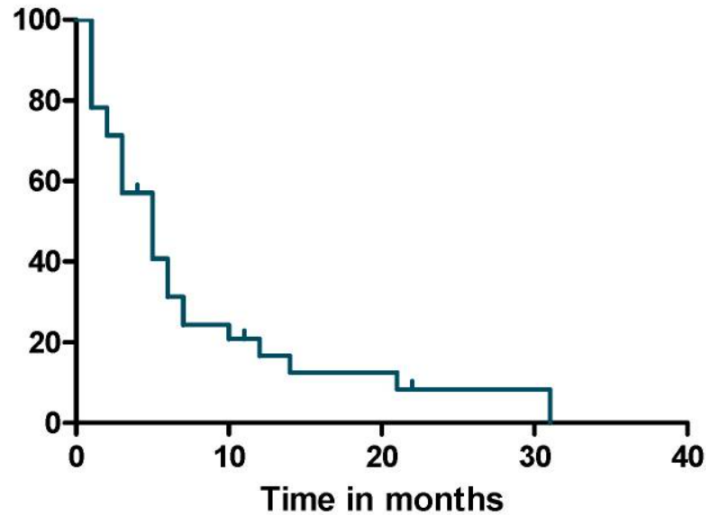
Daratumumab-treated relapsed MM with EMD (Sirius subgroup analysis)

14 pts with relapsed MM and EMD **ORR 3 (21%) pts**

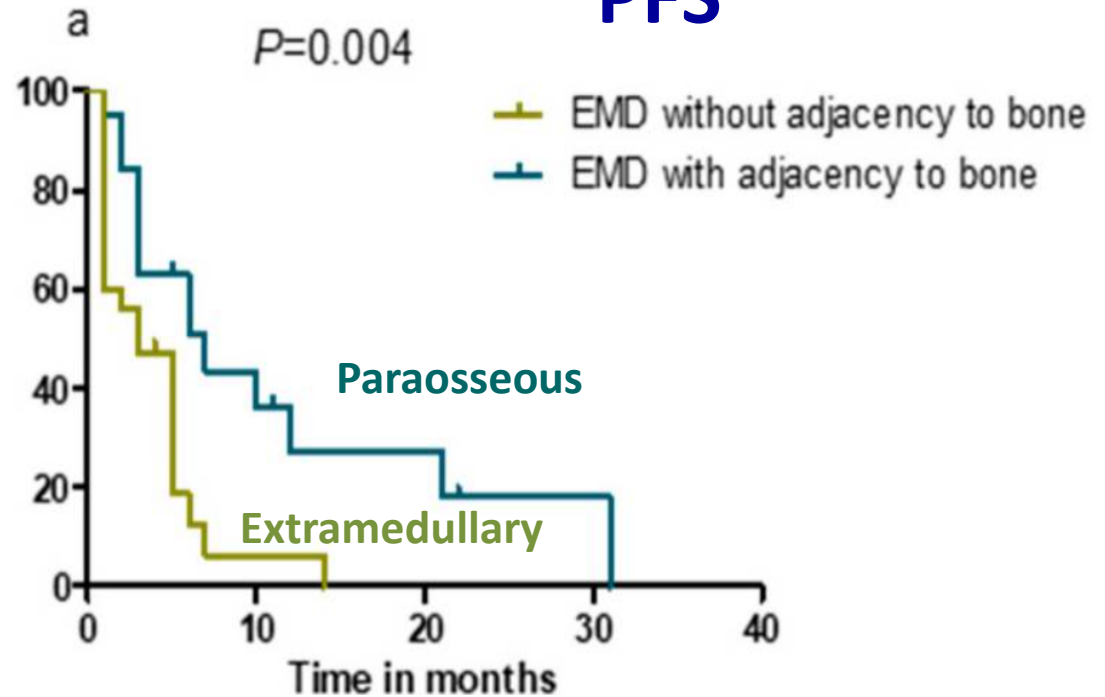
Carfilzomib-treated relapsed MM with plasmacytomas

45 pts

PFS



PFS



Selinexor-treated relapsed MM with EMD (SelDex – STORM study)

122 penta-refractory patients enrolled in the study.

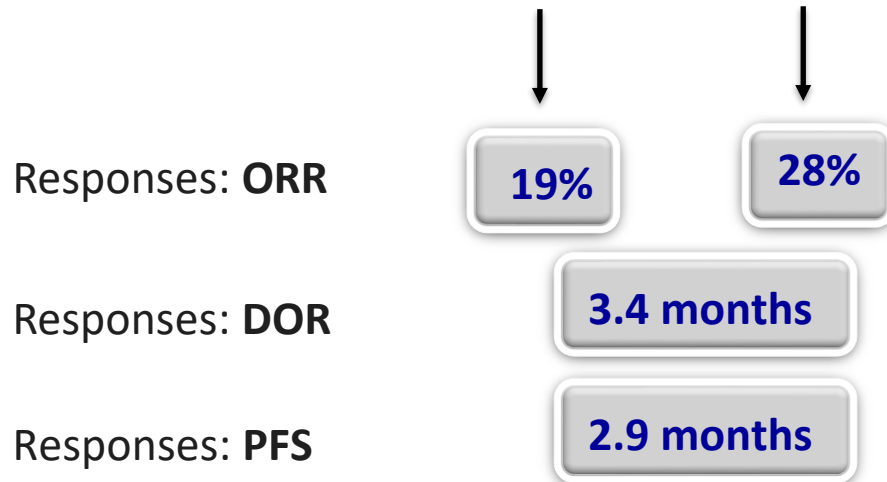
27 patients with plasmocytoma: 22 EMD + 5 paraosseous disease

16 evaluable patients: 4 PR + 1 VGPR

Melflufen-treated relapsed MM with EMD (MelflufenDex – Horizon study)

121 triple refractory patients enrolled in the study.

44 patients with plasmacytoma: 26 EMD + 18 paraosseous disease



Bispecific-treated relapsed MM with EMD (Teclistamab – Majestec study)

165 pts dosed with **teclistamab**

28 pts (17%) had EMD

ORR **69%** no-EMD
 36% EMD

Bispecific-treated relapsed MM with EMD (Real world evidence)

106 pts treated with **teclistamab** in the real world setting

100% triple-class exposed

64% were penta-class refractory

53% previously treated with an BCMA-directed therapy

66% overall

68% pentarefractory

29% EMD

Responses: **ORR**

In multivariate analysis EMD was a strong predictor of lower PFS

Talquetamab-treated relapsed MM with EMD (MonumenTAL1 study)

143 pts treated with **talquetamab** at full dose

100% triple-class exposed

98% were penta-class exposed

24% had EMD

Responses: **ORR**

74% overall

48% EMD

CiltaCel-treated relapsed MM with EMD (Cartitude 1 study)

113 pts (97 infused) treated with CiltaCell

19 pts with plasmocytoma (EMD + PO)

ORR

98% overall

100% (Plasmocytoma)

Median DOR*

NE

12 months

2-yrs PFS

60%

47%

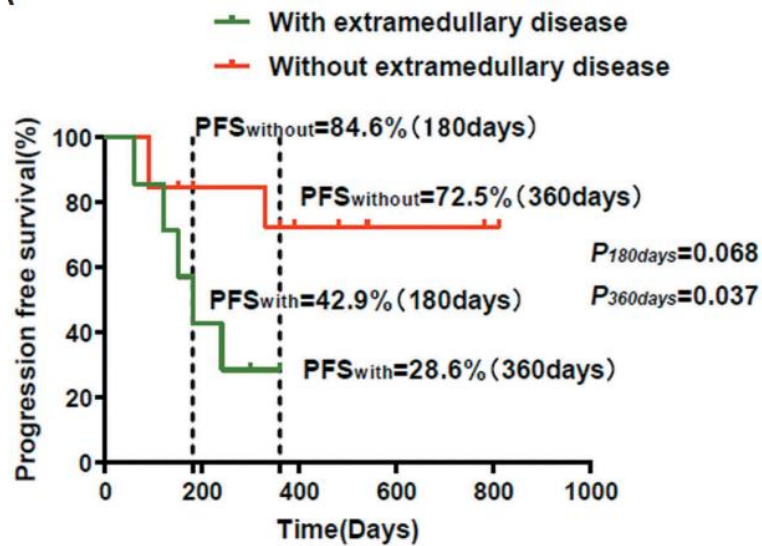
*Median follow-up 22 months

Jakubowiak A et al. ASH 2021

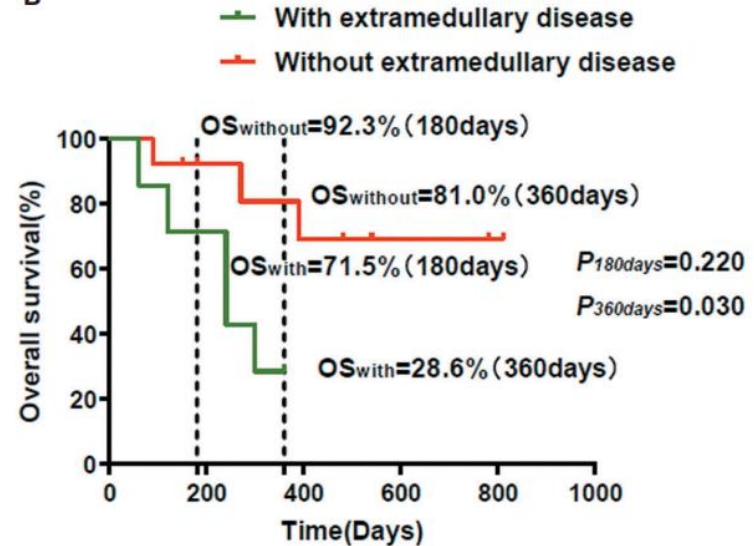
Humanized anti-BCMA CAR-T

Small experience in 20 heavily-treated MM pts

PFS



OS



Mayo Clinic Real world experience

20 pts with secondary EMD treated with **CAR-T**.

ORR

75%

PFS

4.9 months

12 pts with secondary EMD treated with **Bispecific antibodies**.

ORR

75%

PFS

2.9 months

CONCLUSIONS

EMD represents the worst challenge in MM patients.

EMD recapitulates the worst adverse biological factors (FISH, high proliferative rate....

EMD is well equipped to withstand immunotherapy.

EMD is uncommon, and this impairs the clinical research.