Highlights from
IMS 20th meeting 2023

Martina Pennisi

CAR-T anti-BCMA: esperienze nel *setting* della RW

30-31 gennaio 2024
BOLOGNA, Royal Hotel Carlton

Disclosures

- Honoraria: Bristol Myers Squibb
- Advisory Board: Nektar Therapeutics

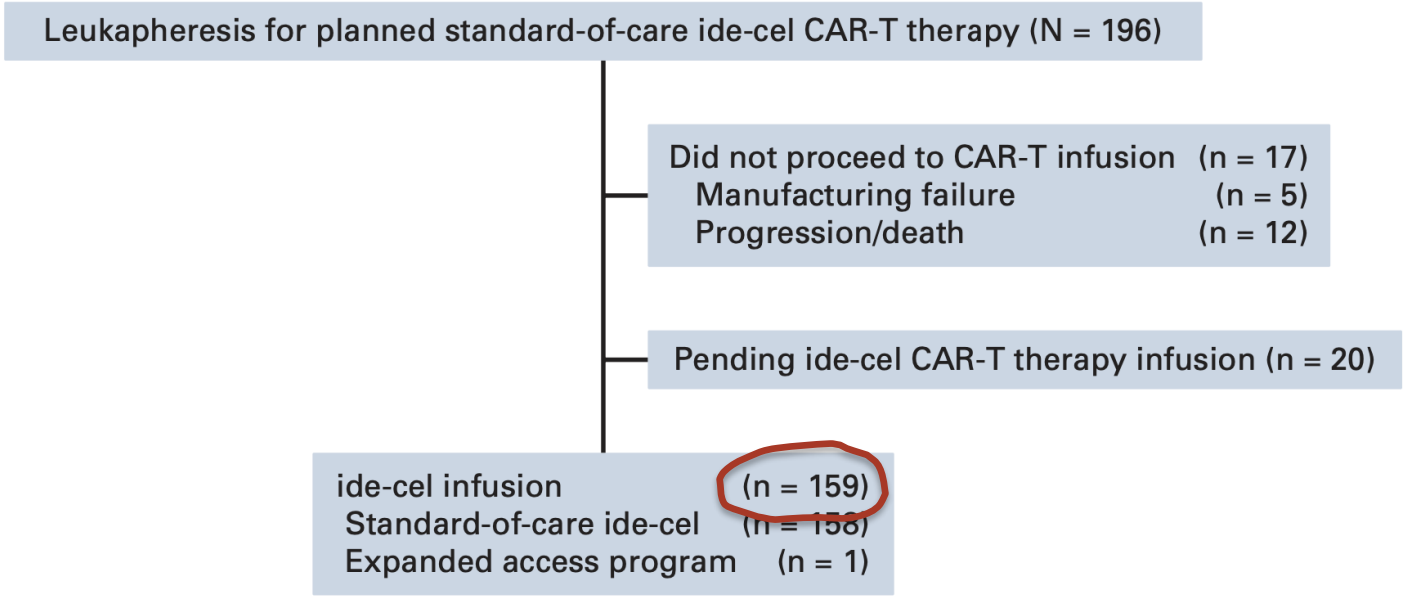
IDECABTAGENE VICLEUCEL *Ide-cel*

- FDA Approval March 2021
- EMA Approval August 2021

CILTACABTAGENE AUTOLEUCEL *Cilta-cel*

- FDA Approval February 2022
- EMA Approval May 2022

Real-World Experience From the Myeloma CAR T Consortium
Data on SoC IDE-CEL at 11 US centers



115 of 129 (89%) patients who were alive had follow-up within a data cutoff of 3 months

Hansen DK, et al. JCO Jan 2023

Characteristic	No. (%)
Patients, No.	159
Age, years	
< 65	82 (52)
≥ 65	77 (48)
Median (range)	64 (36-83)
Sex, male	91 (57)
Extramedullary disease	76 (48)
High marrow burden	36 (25)
Unknown	13
ECOG PS	
0-1	127 (81)
2-4	29 (19)
Unknown	31
R-ISS disease stage	
I	22 (17)
II	71 (55)
III	35 (27)
Unknown	31
Myeloma subtype	
Intact immunoglobulin	121 (76)
Light chain	36 (23)
Oligo-/nonsecretory	2 (1)

Characteristic	No. (%)
Cytogenetic abnormality	
Any high-risk cytogenetics	49 (35)
Unknown	18
del(17p)	32 (22)
Unknown	13
t(4;14)	19 (14)
Unknown	19
t(14;16)	6 (4)
Unknown	19
Bridging therapy	123 (77)
Response to bridging therapy	
PR or better	13 (11)
SD/PD	101 (82)
Unknown response	9 (7)

Median time
leukapheresis → infusion
47 days (range 34-91)

Adapted from Hansen DK, et al. JCO Jan 2023

Characteristic	No. (%)
Prior therapies	
Prior antimyeloma therapies, No., median (range)	7 (4-18)
Refractory disease	107 (67)
Relapsed disease	45 (28)
Prior autologous SCT	134 (84)
Prior allogeneic SCT	9 (6)
Prior anti-BCMA therapy	33 (21)
PI	148 (93)
Anti-CD38 antibody	148 (93)
Double-refractory	141 (89)
Triple-refractory	134 (84)
Penta-refractory	70 (44)
CAR T-cell dose (million cells), median (range)	407.0 (154.1-456.4)
Unknown	4

Characteristic	No. (%)
CAR T-cell dose (million cells)	
< 400	64 (41)
≥ 400	91 (59)
Unknown	4
KarMMa exclusion criteria at the time of leukapheresis	
No. of patients who met exclusion criteria	120 (75)
1 criterion	47 (30)
≥ 2 criteria	73 (46)
Organ dysfunction[a] (renal, cardiac, and hepatic)	45 (28)
Prior anti-BCMA therapy	33 (21)
Platelets < 50,000/μL	33 (21)
Hemoglobin < 8 g/dL	25 (16)
ECOG PS ≥ 2	28 (18)
Unknown	3
ANC < 1,000/uL	22 (14)
PCL, POEMS, amyloidosis, nonsecretory myeloma	11 (7)
History of CNS myeloma and other CNS pathology	13 (8)
Prior allogeneic SCT	9 (6)
Other malignancies	10 (6)
Chronic immunosuppression	2 (1)

Adapted from Hansen DK, et al. JCO Jan 2023

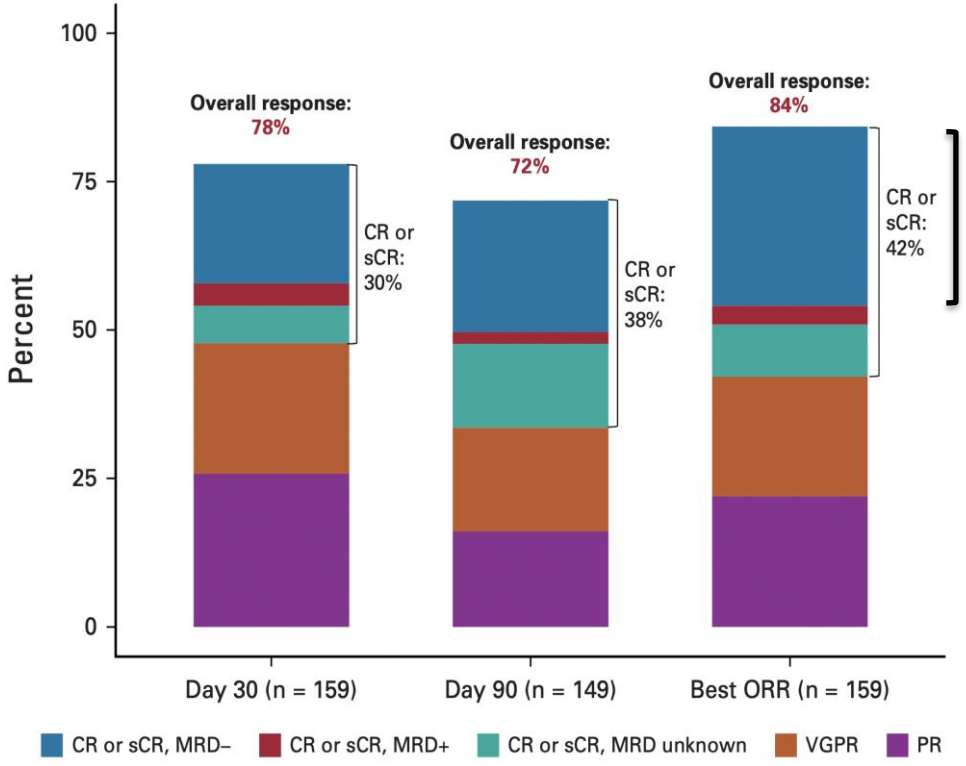
Rates of CRS and ICANS similar to KarMMa

Event and grade	No (%)	
	US CART Consortium (n= 159)[1]	KarMMa (n=128)[2]
CRS		
Any	131 (82)	107 (84)
Grade 1	99 (62)	61 (48)
Grade 2	27 (17)	39 (30)
Grade ≥ 3	5 (3)	7 (5)
ICANS / NT		
Any	29 (18)	23 (18)
Grade 1	12 (8)	12 (9)
Grade 2	8 (5)	7 (5)
Grade ≥ 3	9 (6)	4 (3)

Event and grade	No (%)	
	US CART Consortium (n= 159)[1]	KarMMa (n=128)[2]
Cytopenias ≥ 30 days		
Grade ≥ 3 Neutropenia	70 (60)	52 (41)
Grade ≥ 3 Anemia	42 (38)	-
Grade ≥ 3 Thrombocytopenia	70 (59)	62 (48)
Infections		
Any	52 (34)	88 (69)
Grade ≥ 3	-	28 (22)

[1]Hansen DK, et al. JCO Jan 2023 and [2]Munshi NC, et al. NEJM 2021

Best ORR and CR/sCR were 84% and 42%, compared to 73% and 33% in KarMMa



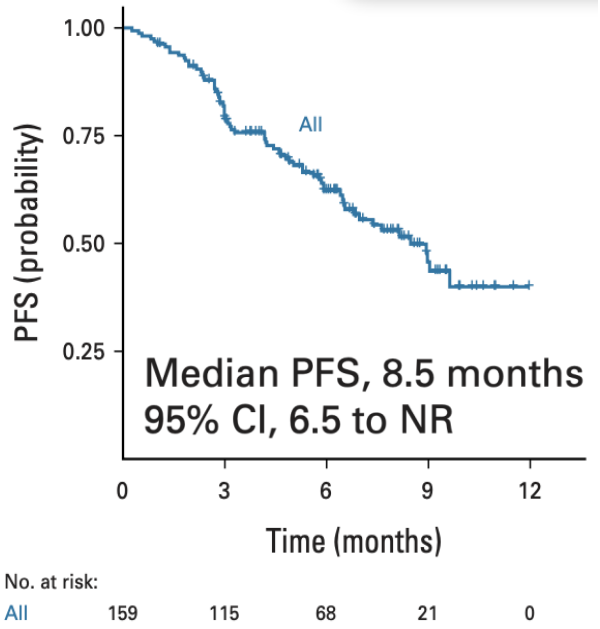
72% MRD-neg (10^{-5})

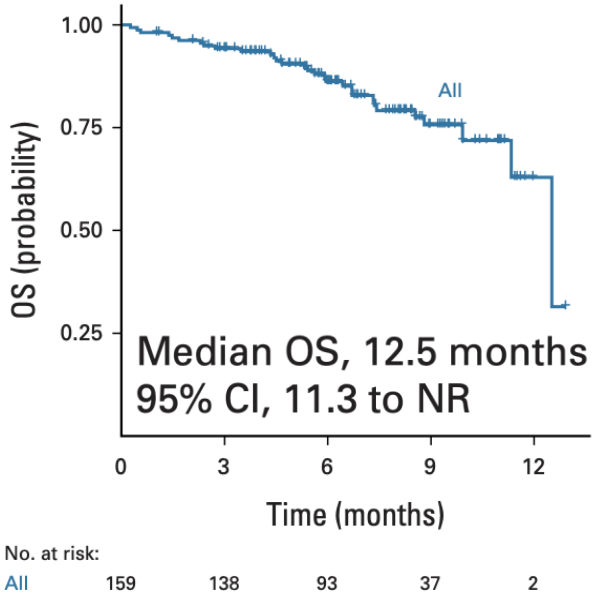
Median time to response = 30 days

Extramedullary, penta-refractory and prior anti-BCMA Tx predicted ↓ response (p .03, p .009, p .04)

Hansen DK, et al. JCO Jan 2023

Median follow-up 6.1 months from CAR T infusion





Adapted from Hansen DK, et al. JCO Jan 2023

Characteristic	N (event N)	HR (95% CI)	P
Prior BCMA-TT			**.003**
No	104 (42)	1.00 (referent)	
Yes	31 (18)	2.81 (1.44 to 5.51)	
High-risk cytogenetics			
No	86 (33)	1.00 (referent)	**.003**
Yes	49 (27)	2.31 (1.34 to 3.97)	
Extramedullary disease			.06
No	70 (25)	1.00 (referent)	
Yes	65 (35)	1.68 (0.97 to 2.90)	
CAR T-cell dose			.6
$< 400 \times 10^6$	57 (26)	1.00 (referent)	
$\geq 400 \times 10^6$	78 (34)	0.86 (0.50 to 1.47)	
ECOG PS at LD			**.02**
0-1	108 (42)	1.00 (referent)	
2-4	27 (18)	2.19 (1.16 to 4.14)	
Penta-refractory			.8
No	76 (33)	1.00 (referent)	
Yes	59 (27)	0.92 (0.53 to 1.58)	
Patient age	135 (60)	0.97 (0.95 to 1.00)	**.04**

Prior exposure to anti-BCMA tx (belantamab, BiTEs, CART), high risk cytogenetics, ECOG PS ≥ 2 and younger age predicted inferior PFS

Hansen DK, et al. JCO Jan 2023

US Consortium: outcomes in pts with renal impairment (RI) (CrCl < 50 ml/min) treated with Ide-cel

	Overall N=214	CrCl < 50 ml/min N=28	CrCl ≥ 50 ml/min N=186	P-value
	Median (range) or N (%)	Median (range) or N (%)	Median (range) or N (%)	
Age	64 years (36, 83)	69 years (50, 83)	63 years (36, 83)	**0.001**
Age, ≥ 65 years	103 (48%)	20 (71%)	83 (45%)	**0.008**
Sex, Female	86 (40%)	19 (68%)	67 (36%)	**0.001**
Extramedullary disease	96 (45%)	13 (46%)	83 (45%)	0.9
BMPCs (≥ 50%)	58 (30%)	9 (32%)	49 (29%)	0.7
Marrow PCs Unknown	18	0	18	
ECOG PS 2-4 , N=206	35 (17%)	6 (23%)	29 (16%)	0.4
R-ISS at CAR-T infusion, N=163				**0.03**
I	36 (22%)	1 (4.3%)	35 (25%)	
II	83 (51%)	12 (52%)	71 (51%)	
III	44 (27%)	10 (43%)	34 (24%)	
High-risk cytogenetics, N=187	62 (33%)	12 (48%)	50 (31%)	0.09
Laboratory Data				
ANC < 1000/uL	26 (12%)	2 (7.1%)	24 (13%)	0.5
Hemoglobin < 8 g/dL	33 (15%)	6 (21%)	27 (15%)	0.4
Platelets < 50,000/uL	41 (19%)	9 (32%)	32 (17%)	0.06
Beta-2-microglobulin, mg/L	3.0 (0.7, 15.3)	4.2 (2.4, 13.5)	2.9 (0.7, 15.3)	**0.004**
Albumin, g/dL	3.6 (1.7, 4.8)	3.3 (2.4, 4.7)	3.7 (1.7, 4.8)	**0.005**
Prior Therapy				
Prior lines of therapy	6 (3, 19)	8 (5, 15)	6 (3, 19)	**0.03**
Prior autologous SCT	180 (84%)	23 (82%)	157 (84%)	0.8
Prior allogeneic SCT	10 (5%)	2 (7%)	8 (4%)	0.6
Prior anti-BCMA therapy	53 (25%)	7 (25%)	46 (25%)	>0.9
Triple Refractory	178 (83%)	26 (93%)	152 (82%)	0.2
Penta Refractory	93 (43%)	10 (36%)	83 (45%)	0.4
Bridging Therapy	166 (78%)	26 (93%)	140 (75%)	**0.04**
CAR-T cell dose, median (range)*	406 (154, 459)	416 (156, 455)	406 (154, 459)	0.6
Fludarabine dose reduction, yes	61 (29%)	22 (79%)	39 (21%)	**<0.001**
Fludarabine dose reduction %				
≤ 20%	22 (36%)	3 (14%)	19 (49%)	
21-40%	16 (26%)	7 (32%)	9 (23%)	**0.018**
>40%	23 (38%)	12 (55%)	11 (28%)	

Adapted from Sidana S et al, Haematologica 2023

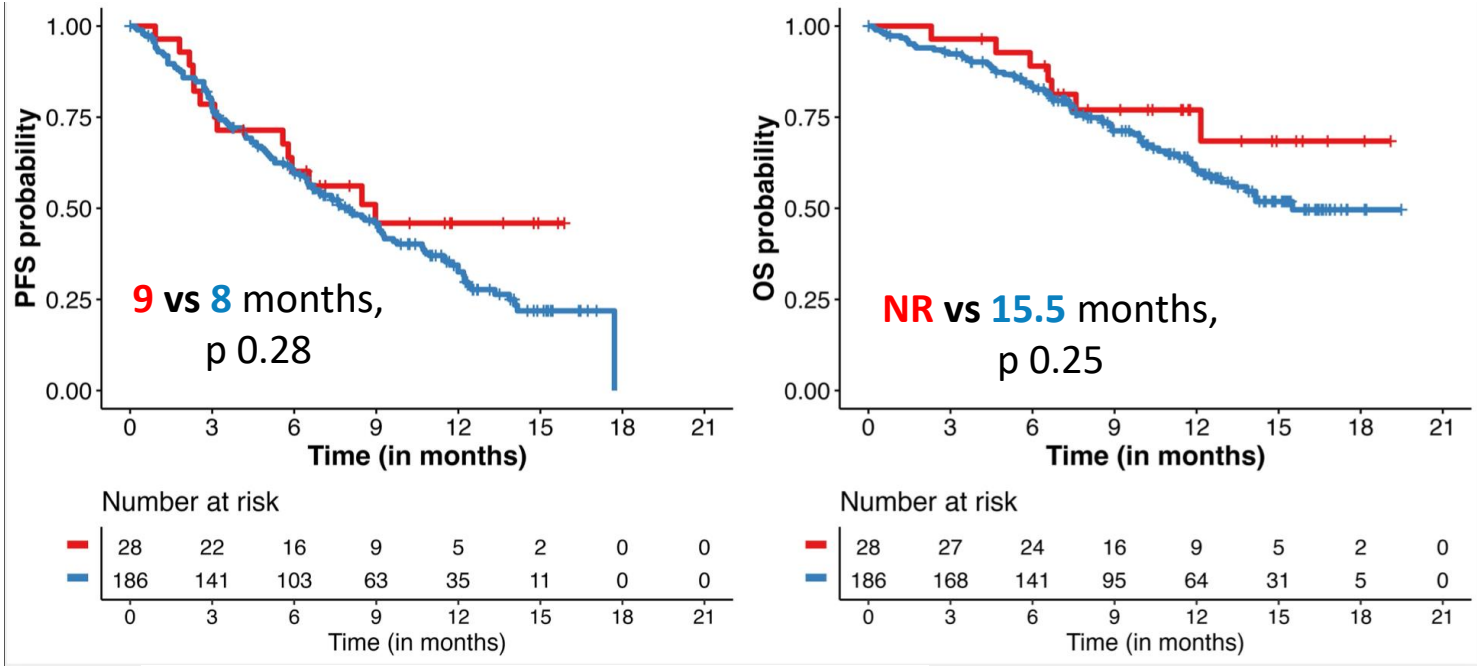
US Consortium: outcomes in pts with renal impairment (RI) (CrCl < 50 ml/min) treated with Ide-cel

	Overall N=214	CrCl < 50 ml/min N=28	CrCl ≥ 50 ml/min N=186	P-value
	Median (range) or N (%)	Median (range) or N (%)	Median (range) or N (%)	
Age	64 years (36, 83)	69 years (50, 83)	63 years (36, 83)	**0.001**
Age, ≥ 65 years	103 (48%)	20 (71%)	83 (45%)	**0.008**
Sex, Female	86 (40%)	19 (68%)	67 (36%)	**0.001**
Extramedullary disease	96 (45%)	13 (46%)	83 (45%)	0.9
BMPCs (≥ 50%)	58 (30%)	9 (32%)	49 (29%)	0.7
Marrow PCs Unknown	18	0	18	
ECOG PS 2-4 , N=206	35 (17%)	6 (23%)	29 (16%)	0.4
R-ISS at CAR-T infusion, N=163				**0.03**
I	36 (22%)	1 (4.3%)	35 (25%)	
II	83 (51%)	12 (52%)	71 (51%)	
III	44 (27%)	10 (43%)	34 (24%)	
High-risk cytogenetics, N=187	62 (33%)	12 (48%)	50 (31%)	0.09
Laboratory Data				
ANC < 1000/uL	26 (12%)	2 (7.1%)	24 (13%)	0.5
Hemoglobin < 8 g/dL	33 (15%)	6 (21%)	27 (15%)	0.4
Platelets < 50,000/uL	41 (19%)	9 (32%)	32 (17%)	0.06
Beta-2-microglobulin, mg/L	3.0 (0.7, 15.3)	4.2 (2.4, 13.5)	2.9 (0.7, 15.3)	**0.004**
Albumin, g/dL	3.6 (1.7, 4.8)	3.3 (2.4, 4.7)	3.7 (1.7, 4.8)	**0.005**
Prior Therapy				
Prior lines of therapy	6 (3, 19)	8 (5, 15)	6 (3, 19)	**0.03**
Prior autologous SCT	180 (84%)	23 (82%)	157 (84%)	0.8
Prior allogeneic SCT	10 (5%)	2 (7%)	8 (4%)	0.6
Prior anti-BCMA therapy	53 (25%)	7 (25%)	46 (25%)	>0.9
Triple Refractory	178 (83%)	26 (93%)	152 (82%)	0.2
Penta Refractory	93 (43%)	10 (36%)	83 (45%)	0.4
Bridging Therapy	166 (78%)	26 (93%)	140 (75%)	**0.04**
CAR-T cell dose, median (range)*	406 (154, 459)	416 (156, 455)	406 (154, 459)	0.6
Fludarabine dose reduction, yes	61 (29%)	22 (79%)	39 (21%)	**<0.001**
Fludarabine dose reduction %				
≤ 20%	22 (36%)	3 (14%)	19 (49%)	
21-40%	16 (26%)	7 (32%)	9 (23%)	**0.018**
>40%	23 (38%)	12 (55%)	11 (28%)	

Renal function did not deteriorate in any pt with baseline RI.
Renal function improved in some pts.

Adapted from Sidana S et al, Haematologica 2023

Patients with RI had similar response and safetyrates compared to those without RI
Renal function did not impact PFS and OS



Adapted from Sidana S et al, Haematologica 2023

US Consortium: analysis of risk factors for early progression after ide-cel

Characteristic	Study Cohorts			p-value
	Overall, N = 211	Progressed ≤ 3 months, N = 43	Did not progress ≤ 3 months, N = 168	
Patient Age, Median (Range) [IQR]	64.0 (36.0, 83.0) [57.0, 69.0]	61.0 (43.0, 78.0) [55.5, 66.5]	65.0 (36.0, 83.0) [58.0, 69.0]	0.090
Male Sex, n (%)	127 (60%)	28 (65%)	99 (59%)	0.5
Race and ethnicity, n (%)				**0.030**
Hispanic	22 (10%)	10 (23%)	12 (7.1%)	
Non-Hispanic Black	36 (17%)	5 (12%)	31 (18%)	
Other	8 (3.8%)	1 (2.3%)	7 (4.2%)	
Non-Hispanic White	145 (69%)	27 (63%)	118 (70%)	
Plasma cell leukemia, n (%)	12 (6%)	6 (14%)	6 (4%)	**0.018**
Extramedullary disease, n (%)	95 (45%)	26 (60%)	69 (41%)	**0.023**
High Marrow Burden (>= 50%), n (%)	58 (30%)	13 (35%)	45 (29%)	0.4
Unknown	17	6	11	
ECOG at LD of 0-1, n (%)	169 (83%)	31 (76%)	138 (85%)	0.14
Unknown	8	2	6	
R-ISS stage at CAR T infusion, n (%)				0.4
I	37 (23%)	5 (14%)	32 (25%)	
II	82 (50%)	20 (57%)	62 (48%)	
III	44 (27%)	10 (29%)	34 (27%)	
Unknown	48	8	40	
High-risk cytogenetics, n (%)	60 (33%)	16 (42%)	44 (30%)	0.2
Unknown	27	5	22	

Hashmi H et al, Haematologica 2023

Characteristic	Study Cohorts			p-value
	Overall, N = 211	Progressed ≤ 3 months, N = 43	Did not progress ≤ 3 months, N = 168	
t(4;14) at Infusion, n (%) Unknown	21 (11%) 27	8 (21%) 6	13 (8.9%) 21	**0.046**
Deletion 17p at infusion, n (%) Unknown	40 (21%) 21	10 (26%) 4	30 (20%) 17	0.4
t(4;16) at infusion, n (%) Unknown	7 (4%) 27	1 (3%) 6	6 (4%) 21	>0.9
Bridging Therapy, n (%)	162 (77%)	38 (88%)	124 (74%)	**0.044**
Number of prior lines of therapy, Median (Range) [IQR]	6.0 (3.0, 19.0) [5.0, 9.0]	7.0 (4.0, 18.0) [5.0, 9.5]	6.0 (3.0, 19.0) [5.0, 8.0]	0.075
> 4 prior lines of therapy, n (%)	180 (85%)	40 (93%)	140 (83%)	0.11
Prior treatment with BCMA-targeted therapy, n (%)	52 (25%)	17 (40%)	35 (21%)	**0.011**
Triple-refractory, n (%)	176 (83%)	36 (84%)	140 (83%)	>0.9
Penta-refractory, n (%)	90 (43%)	20 (47%)	70 (42%)	0.6

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Extramedullary disease, high ferritin at LD and plasma cell leukemia were indepent risk factors for PFS and OS

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	PFS			OS		
Early progression risk factors	**N (N event)**	**HR (95% CI)**	**p-value**	**N (N event)**	**HR (95% CI)**	**p-value**
Prior BCMA therapy						
No	135 (79)	1.00 (Referent)		134 (42)	1.00 (Referent)	
Yes	49 (38)	1.64 (1.08, 2.50)	**0.02**	49 (23)	1.56 (0.90, 2.71)	0.1
Extramedullary disease						
No	100 (53)	1.00 (Referent)		99 (28)	1.00 (Referent)	
Yes	84 (64)	1.71 (1.16, 2.51)	**0.006**	84 (37)	1.69 (1.00, 2.86)	**0.048**
Baseline ferritin at LD						
Normal	100 (53)	1.00 (Referent)		100 (22)	1.00 (Referent)	
≥ ULN	84 (64)	1.95 (1.33, 2.88)	**<0.001**	83 (43)	2.56 (1.51, 4.35)	**<0.001**
Bridging therapy						
No	40 (19)	1.00 (Referent)		40 (6)	1.00 (Referent)	
Yes	144 (98)	1.42 (0.84, 2.38)	0.2	143 (59)	2.23 (0.94, 5.26)	0.07
Race and ethnicity						
Non-Hispanic White	126 (81)	1.00 (Referent)		126 (45)	1.00 (Referent)	
Non-Hispanic Black	33 (21)	1.48 (0.90, 2.46)	0.1	32 (12)	1.45 (0.75, 2.79)	0.3
Hispanic	19 (12)	1.15 (0.60, 2.17)	0.7	19 (7)	1.45 (0.61, 3.25)	0.4
Other	6 (3)	0.56 (0.18, 1.81)	0.3	6 (1)	0.27 (0.04, 2.04)	0.2
Plasma cell leukemia						
No	175 (108)	1.00 (Referent)		174 (58)	1.00 (Referent)	
Yes	9 (9)	4.27 (2.06, 8.87)	**<0.001**	9 (7)	3.97 (1.66, 9.46)	**0.002**
t(4;14) at infusion						
No	163 (98)	1.00 (Referent)		162 (52)	1.00 (Referent)	
Yes	21 (19)	1.82 (1.07, 3.09)	**0.03**	21 (13)	1.58 (0.80, 3.11)	0.2

Extramedullary disease, high ferritin at LD and plasma cell leukemia were indepent risk factors for PFS and OS

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	PFS			OS		
Early progression risk factors	**N (N event)**	**HR (95% CI)**	**p-value**	**N (N event)**	**HR (95% CI)**	**p-value**
Prior BCMA therapy						
No	135 (79)	1.00 (Referent)		134 (42)	1.00 (Referent)	
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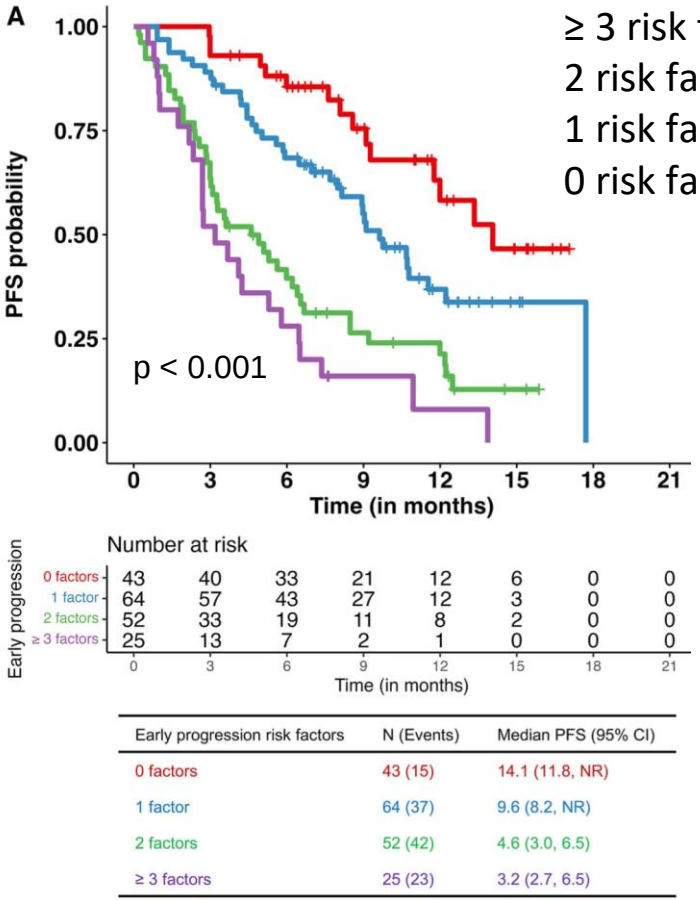
Extramedullary disease						
No	100 (53)	1.00 (Referent)		99 (28)	1.00 (Referent)	
Yes	84 (64)	1.71 (1.16, 2.51)	**0.006**	84 (37)	1.69 (1.00, 2.86)	**0.048**
Baseline ferritin at LD						
Normal	100 (53)	1.00 (Referent)		100 (22)	1.00 (Referent)	
≥ ULN	84 (64)	1.95 (1.33, 2.88)	**<0.001**	83 (43)	2.56 (1.51, 4.35)	**<0.001**
Bridging therapy						
No	40 (19)	1.00 (Referent)		40 (6)	1.00 (Referent)	
Yes	144 (98)	1.42 (0.84, 2.38)	0.2	143 (59)	2.23 (0.94, 5.26)	0.07
Race and ethnicity						
Non-Hispanic White	126 (81)	1.00 (Referent)		126 (45)	1.00 (Referent)	
Non-Hispanic Black	33 (21)	1.48 (0.90, 2.46)	0.1	32 (12)	1.45 (0.75, 2.79)	0.3
Hispanic	19 (12)	1.15 (0.60, 2.17)	0.7	19 (7)	1.45 (0.61, 3.25)	0.4
Other	6 (3)	0.56 (0.18, 1.81)	0.3	6 (1)	0.27 (0.04, 2.04)	0.2
Plasma cell leukemia						
No	175 (108)	1.00 (Referent)		174 (58)	1.00 (Referent)	
Yes	9 (9)	4.27 (2.06, 8.87)	**<0.001**	9 (7)	3.97 (1.66, 9.46)	**0.002**
t(4;14) at infusion						
No	163 (98)	1.00 (Referent)		162 (52)	1.00 (Referent)	
Yes	21 (19)	1.82 (1.07, 3.09)	**0.03**	21 (13)	1.58 (0.80, 3.11)	0.2



Early progression risk factors	N (Events)	Median PFS (95% CI)
0 factors	43 (15)	14.1 (11.8, NR)
1 factor	64 (37)	9.6 (8.2, NR)
2 factors	52 (42)	4.6 (3.0, 6.5)
≥ 3 factors	25 (23)	3.2 (2.7, 6.5)

≥ 3 risk factors = 3.2 months
2 risk factors = 4.6 months
1 risk factor = 9.6 months
0 risk factors = 14.1 months

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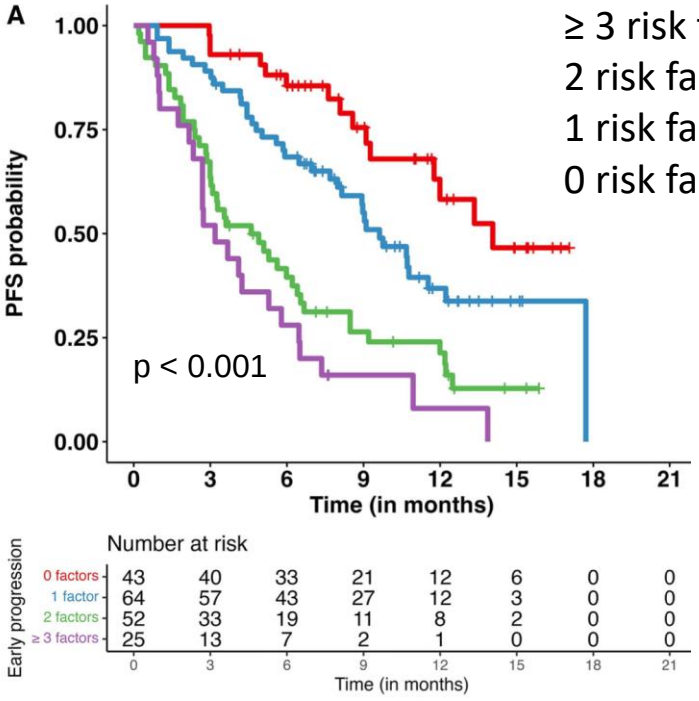
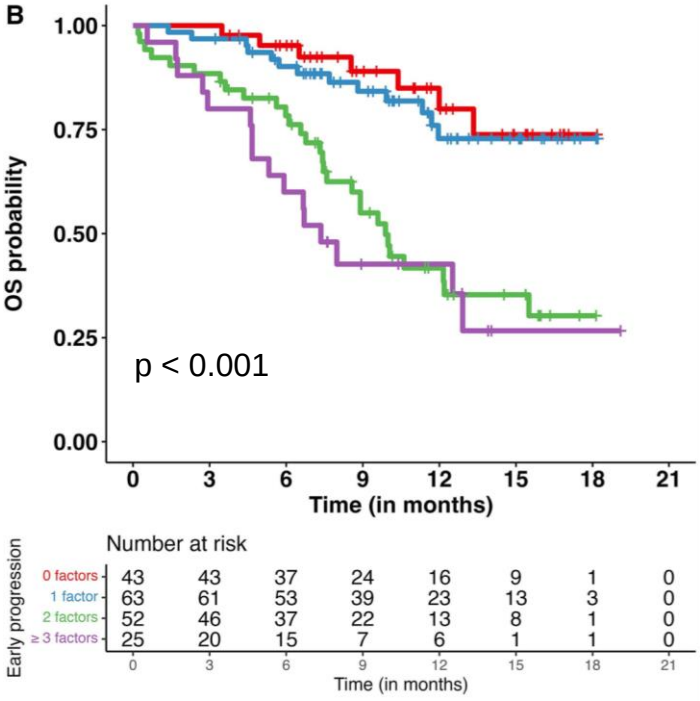
≥ 3 risk factors = 3.2 months
2 risk factors = 4.6 months
1 risk factor = 9.6 months
0 risk factors = 14.1 months



Early progression risk factors	N (Events)	Median PFS (95% CI)
0 factors	43 (15)	14.1 (11.8, NR)
1 factor	64 (37)	9.6 (8.2, NR)
2 factors	52 (42)	4.6 (3.0, 6.5)
≥ 3 factors	25 (23)	3.2 (2.7, 6.5)



Early progression risk factors	N (Events)	Median OS (95% CI)
0 factors	43 (7)	NR (NR, NR)
1 factor	63 (13)	NR (NR, NR)
2 factors	52 (29)	9.9 (8.6, NR)
≥ 3 factors	25 (16)	7.4 (5.3, NR)

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US Consortium: outcomes in pts treated with ide-cel after prior anti-BCMA Tx

239 underwent leukapheresis

↓

56 received prior BCMA-TT

↓

50 infused with Ide-Cel

Ferreri CJ et al, Blood Cancer Journal 2023

US Consortium: outcomes in pts treated with ide-cel after prior anti-BCMA Tx

239 underwent leukapheresis

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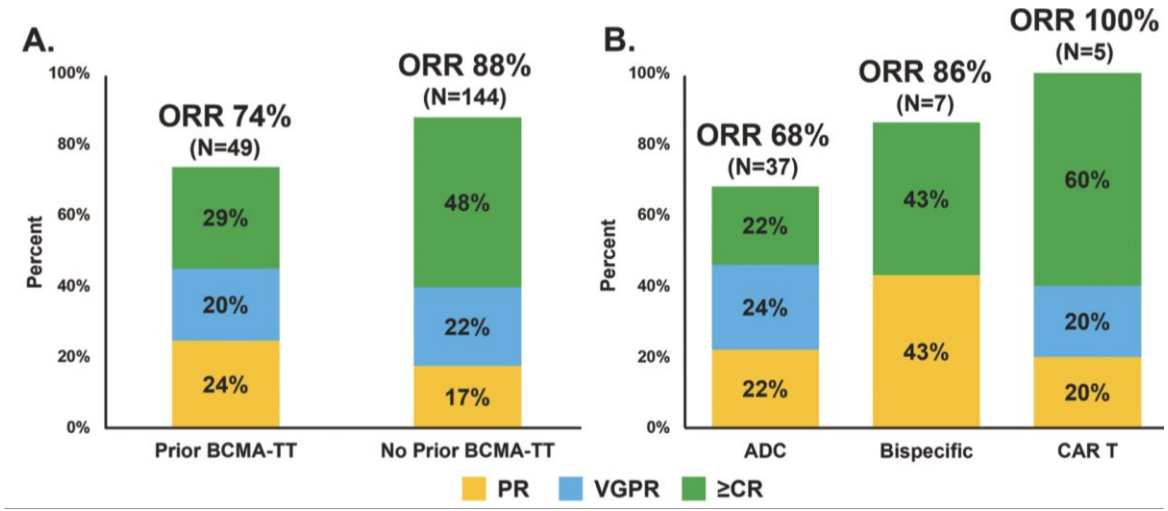
56 received prior BCMA-TT

↓

50 infused with Ide-Cel



Ferreri CJ et al, Blood Cancer Journal 2023

US Consortium: outcomes in pts treated with ide-cel after prior anti-BCMA Tx

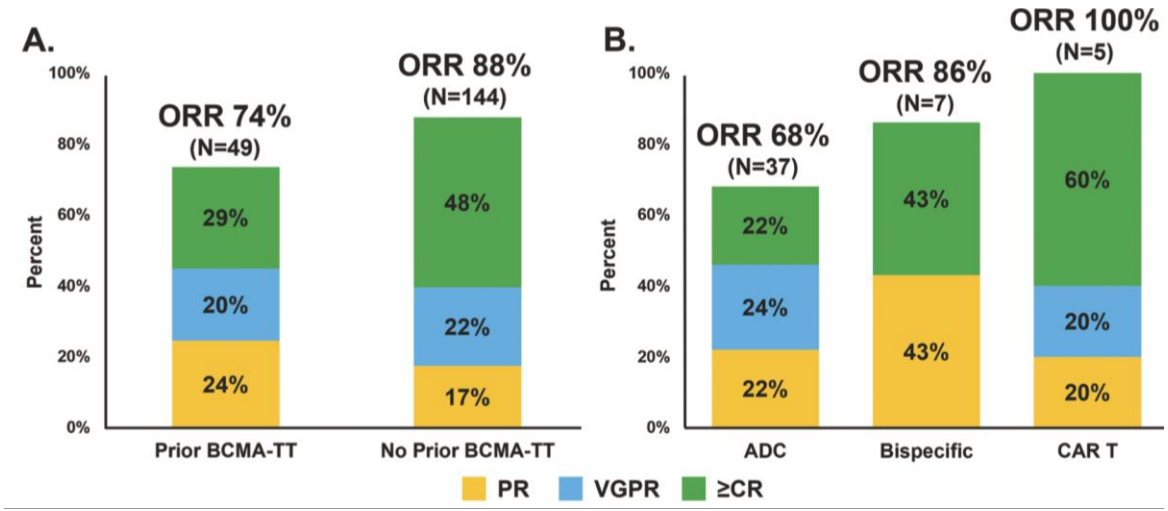
239 underwent leukapheresis

⬇

56 received prior BCMA-TT

⬇

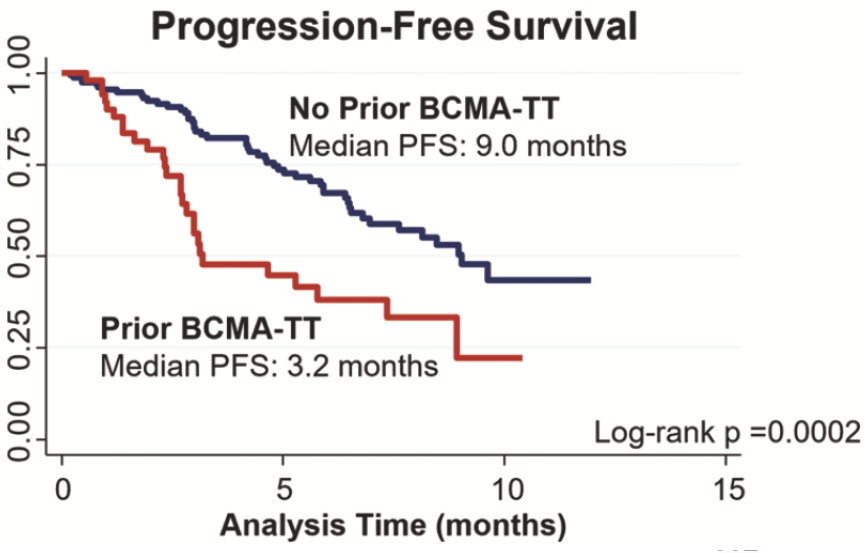
50 infused with Ide-Cel

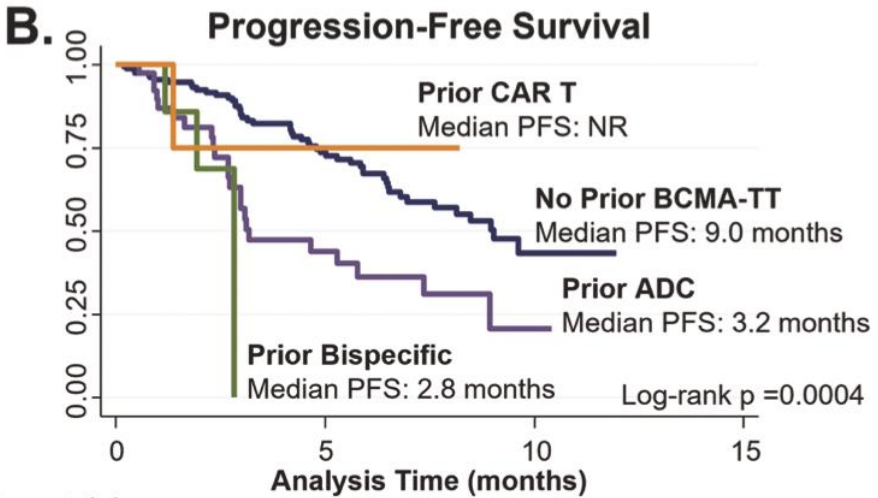


Variable	Responders ($N = 36$)	Non-responders ($N = 13$)	P
Duration of therapy with prior BCMA-TT in days, median (range)[a]	23 (1–208)	63 (1–370)	0.025
Time from last BCMA-TT to apheresis in days, median (range)	169.5 (30–1066)	84 (1–286)	0.017
Time from last BCMA-TT to ide-cel infusion in days, median (range)	209 (16–1118)	128 (32–362)	0.052
Ide-cel cell dose ($\times 10^6$), mean (SD)	392.3 (58.9)	397.7 (43.7)	0.95
Received systemic therapy between last BCMA-TT and apheresis, *n* (%)	28 (78%)	9 (69%)	0.539

[a]Note that prior anti-BCMA CAR T was recorded as 1 day for duration of prior BCMA-TT.

Ferreri CJ et al, Blood Cancer Journal 2023





Number at risk

No Prior BCMA-TT	153	73	7	0
Prior ADC	38	12	1	0
Prior Bispecific	7	0	0	0
Prior CAR T	5	2	0	0

Ferreri CJ et al, Blood Cancer Journal 2023

CIBMTR real-world study: 821 patients treated with SoC ide-cel

N=821	N (%) or Median (Range)
Median age, years	66 years (29-90)
Age ≥ 70 years	251 (31%)
Sex, female	334 (41%)
Race, White Race, Black	652 (79%) 120 (15%)
Ethnicity, Hispanic	55 (7%)
ECOG Performance Status 0-1	728 (89%)
Clinically significant co-morbidity	631 (77%)
ISS Stage (N=420) Stage I Stage II Stage III	 210 (50%) 142 (34%) 68 (16%)
Bone marrow plasma cells > 50%	71/508 (14%)
Non-secretory disease	17 (2%)
High-risk cytogenetics	196/727 (27%)
High-risk cytogenetics including 1q	381/727 (52%)
Extramedullary disease	85/488 (17%)
Plasma cell leukemia	13 (1.6%)

High-risk cytogenetics include del17p, t(4;14) and t(14;16)

N=821	N (%) or Median (Range)
Prior lines of therapy	7 (4-21)
Triple class exposed	776 (97%)
Penta class exposed	490 (60%)
Prior BCMA Therapy • Prior ADC (Belantamab) • Prior CAR-T • Prior bispecific	150 (18%) • 116 (14%) • 36 (4%) • 3 (0.4%)
Bridging therapy	442/799 (54%)
Lymphodepletion Chemotherapy • Fludarabine/Cyclophosphamide • Bendamustine • Cyclophosphamide + Other • Cyclophosphamide • Other/unknown	 741 (90%) 51 (6%) 18 (2%) 8 (1%) 3 (0.3%)
CAR-T cell dose in million cells	409 (307-460)
CAR-T cell dose > 400 million	475 (58%)

Courtesy of Pasquini M, ASH 2023

	CIBMTR N=821	KarMMa[1] N=128	US RWE[2] N=159
CRS - Any grade Grade 3 or higher	80% 3%	84% 5%	82% 3%
ICANS– Any grade Grade 3 or higher	28% 5%	18% 3%	18% 6%
Overall response rate	73%	73%	84%
Very good partial response rate	56%	52%	62%
Complete response rate	25%	33%	42%
Progression free survival, median	9.0 months	8.8 months	8.5 months
Median follow-up	11.6 months	13.3 months	6.1 months

1. Munshi et al. NEJM 2021; 2. Hansen, Sidana et al. JCO 2023

Courtesy of Pasquini M, ASH 2023

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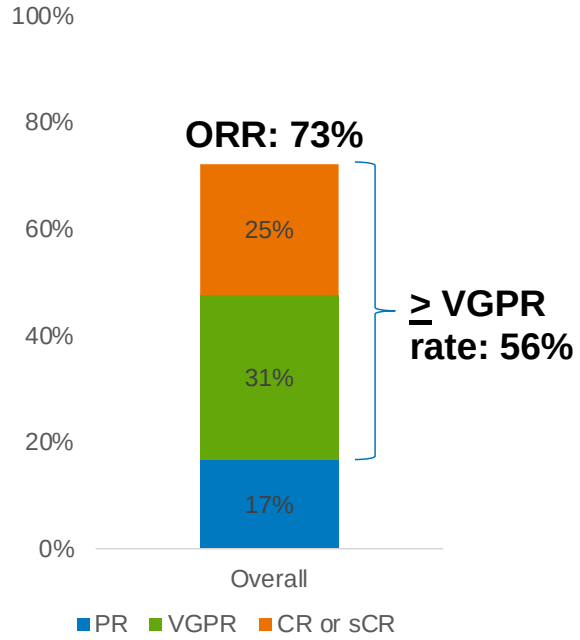

Response data available in 810 patients.

Courtesy of Pasquini M, ASH 2023

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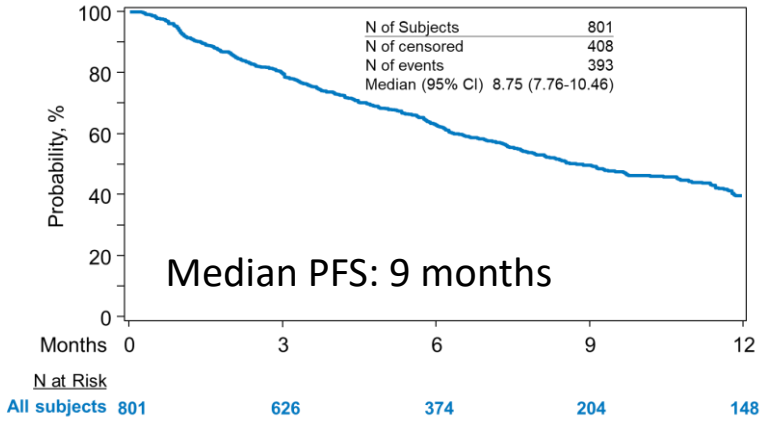
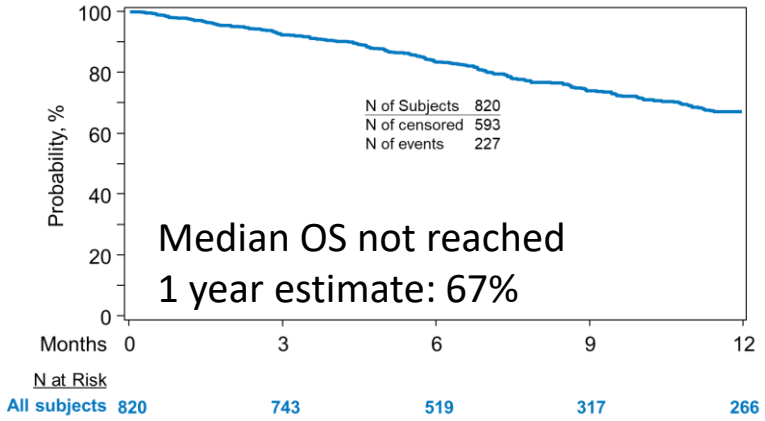
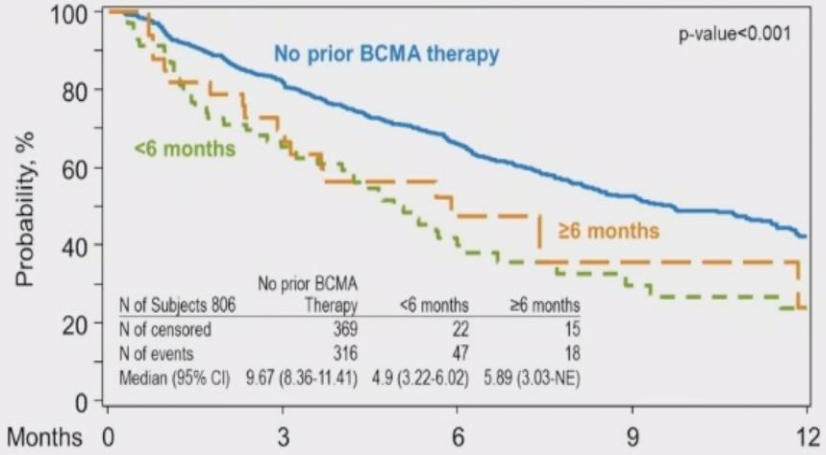




Courtesy of Pasquini M, ASH 2023

Sub-group Analysis: Prior BCMA Therapy

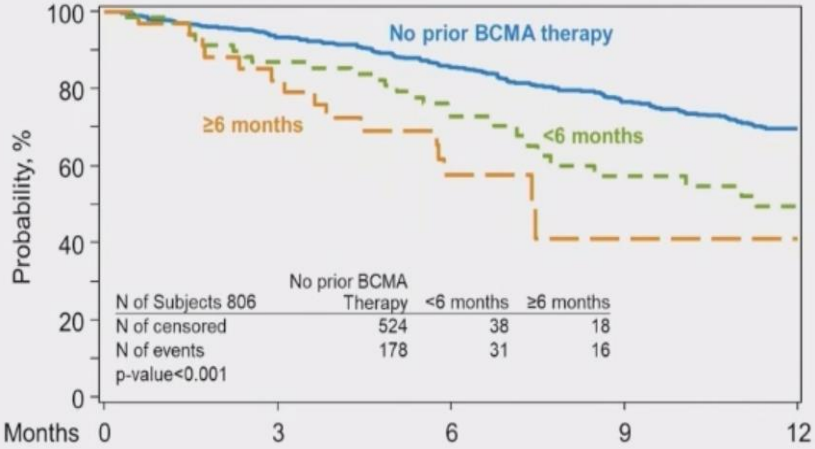
Progression-free Survival



N at Risk

No prior BCMA therapy	685	549	335	186	135
<6 months	69	45	21	10	8
≥6 months	33	22	10	3	2

Overall Survival



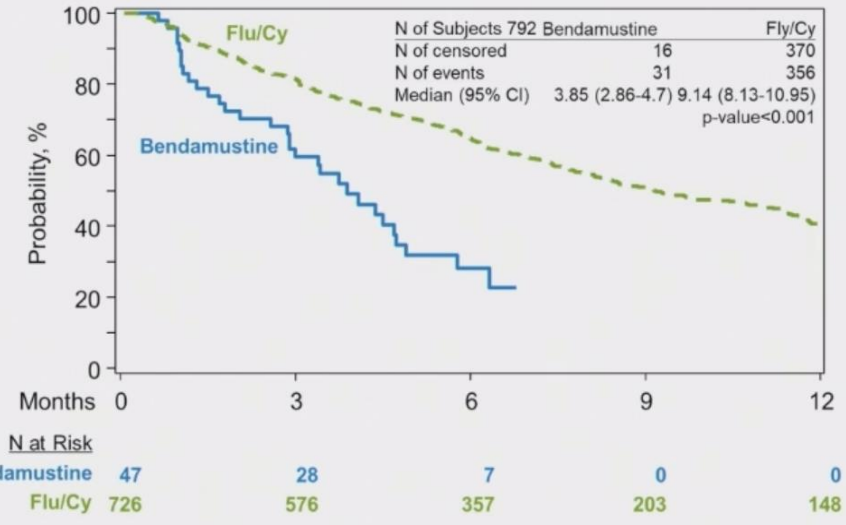
N at Risk

No prior BCMA therapy	702	642	451	281	234
<6 months	69	60	41	22	19
≥6 months	34	27	13	5	5

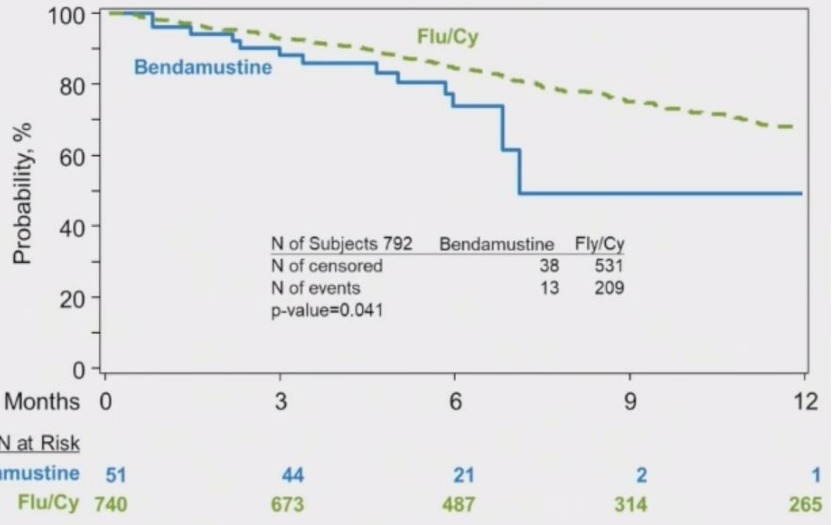
Courtesy of Pasquini M, ASH 2023

Sub-group Analysis: Lymphodepletion Therapy

Progression-free Survival

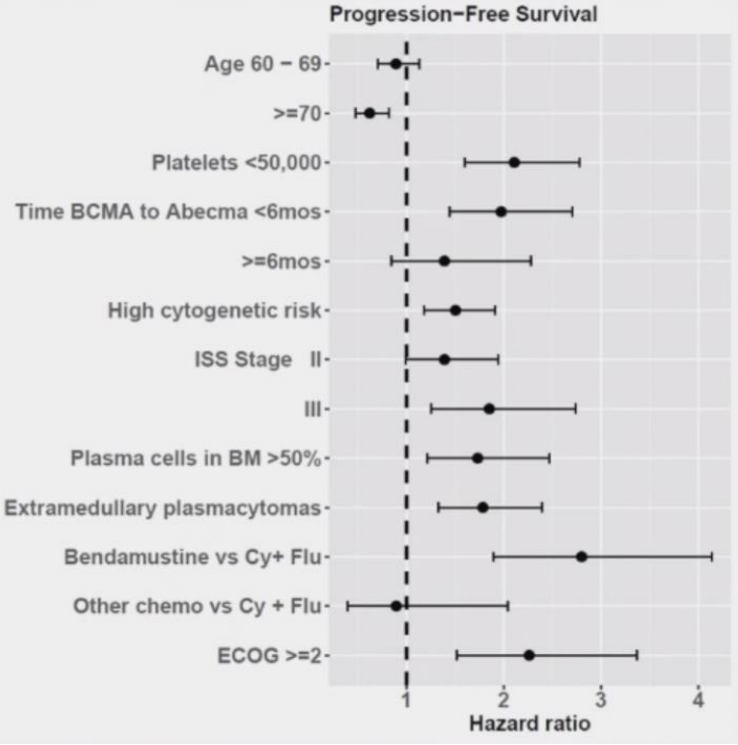


Overall Survival

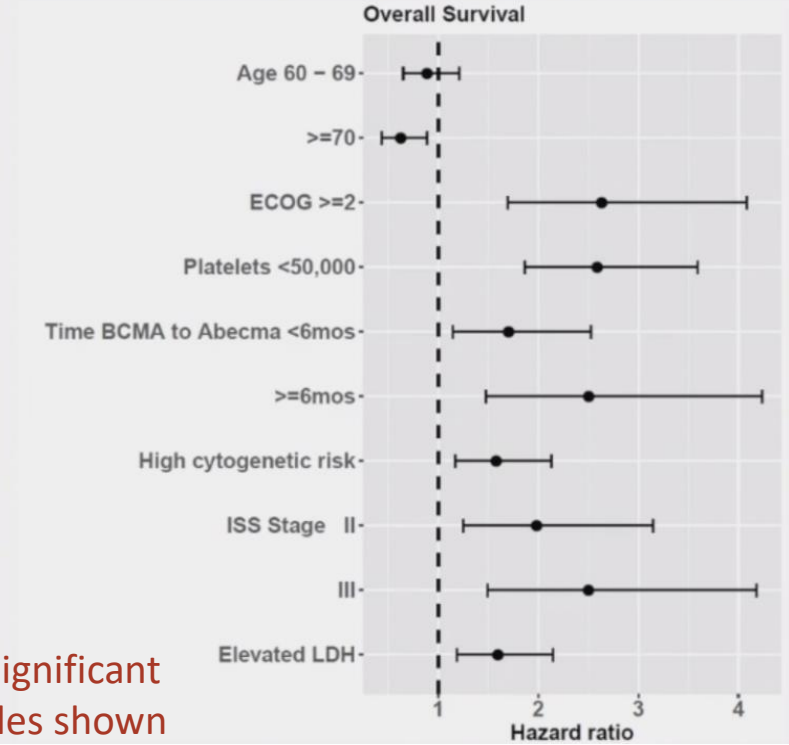


Courtesy of Pasquini M, ASH 2023

Multivariable Analysis for Survival



Only significant variables shown



Courtesy of Pasquini M, ASH 2023

Real-world retrospective study of 163 patients apheresed with intention to be treated with SoC CILTA-CEL at 15 US centers

Pts characteristics	163 apheresed	151 infused
Age, median (range)	64 years (30-79)	64 years (30-79)
Sex, male	95 (58%)	86 (57%)
Extramedullary disease	54 (34%)	48 (32%)
Plasma cell leukemia	14 (9%)	10 (7%)
Oligosecretory/non-secretory MM	31 (19%)	27 (18%)
Marrow burden, ≥ 50% plasma cells	21 (16%)	19 (15%)
ECOG Performance Status	At apheresis	At LD Chemo
0-1	140 (94%)	121 (88%)
2-4	10 (7%)	16 (12%)
Unknown	13	14
R-ISS disease stage		
I	32 (30%)	31 (30%)
II	51 (47%)	48 (47%)
III	25 (23%)	23 (23%)
Unknown	55	49
Any high-risk cytogenetics [del 17p, t(4;14), t(14;16)]	61 (43%)	56 (42%)
Unknown	20	18

Courtesy of Sidana S, IMS 2023

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12 not infused:
- 5 progressions,
- 4 manufact failure,
- 1 MDS,
- 1 out of spec,
- 1 lost to follow-up

Courtesy of Sidana S, IMS 2023

Pts characteristics	163 apheresed	151 infused
Prior therapies		
Median anti-myeloma therapies (range)	5 (3-18)	6 (3-18)
Prior autologous HCT	137 (84%)	126 (83%)
Prior anti-BCMA therapy	18 (11%)	17 (11%)
Refractory status		
Triple-refractory	114 (70%)	105 (70%)
Penta-refractory	54 (33%)	49 (32%)
Bridging therapy (BT)	-	117 (77%)
Response to BT (≥ PR)	-	31/105 (30%)
Lymphodepletion	-	
Fludarabine/Cyclophosphamide	-	125 (83%)
Others	-	26 (17%)
Time from apheresis to infusion	-	71 days (36-161)
CAR T-cell dose (million cells/kg)	-	0.6 (0.2-0.9)
Median follow-up from CAR-T		6.9 months

57% ineligible for CARTITUDE-1

22% received an out of spec product

Courtesy of Sidana S, IMS 2023

Table 2: Toxicity, N=151	N (%) or median (range)
Cytokine Release Syndrome, Any/Grade ≥ 3	120 (79%) / 8 (5%)
Neurotoxicity (ICANS), Any/Grade ≥ 3	26 (18%) / 9 (6%)
Delayed Neurotoxicity	18 (12%)
Parkinsonism	2 (1%)
Bell's Palsy	9 (6%)
Other*	7 (5%)
Delayed neurotoxicity, onset relative to CAR-T	25 days (13-146)
Delayed Neurotoxicity Resolution	7/18 resolved, 3 died with ongoing NT
Time to resolution in days, median (range)	43 days (18-99)
Tocilizumab use	91 (61%)
Corticosteroid use	60 (41%)
Anakinra use	19 (13%)
Infections: Any/severe infections	55 (37%) / 31 (21%)
Deaths due to non-relapse mortality (NRM)**	14 (9%)

* Diplopia (3), dysautonomia (1), polyneuropathy (1), PRES/PML (2)
** Cause of death: Infection, including PML (6), CRS (3), CRS and infection (1), delayed neurotoxicity (2), HLH (1), ICANS (1)

Courtesy of Sidana S, IMS 2023

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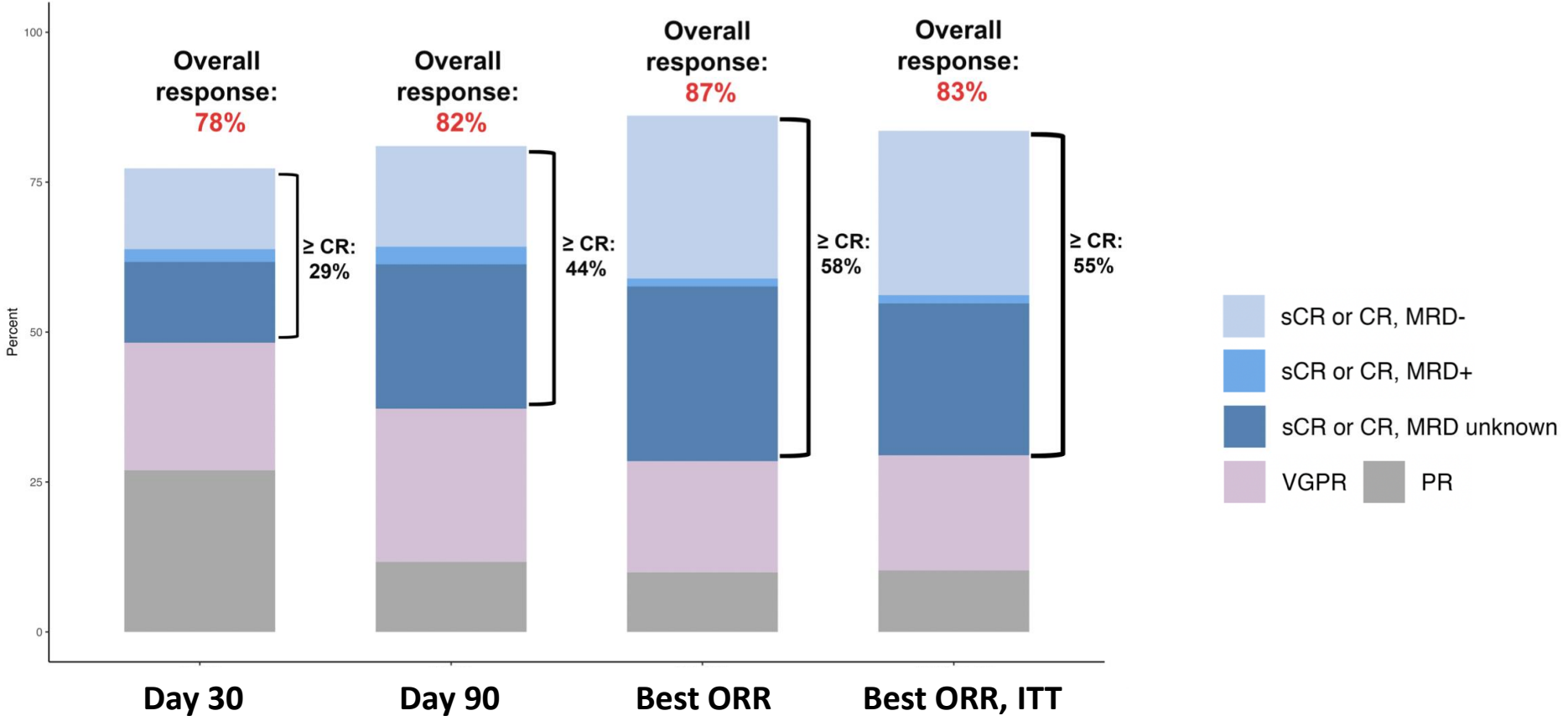
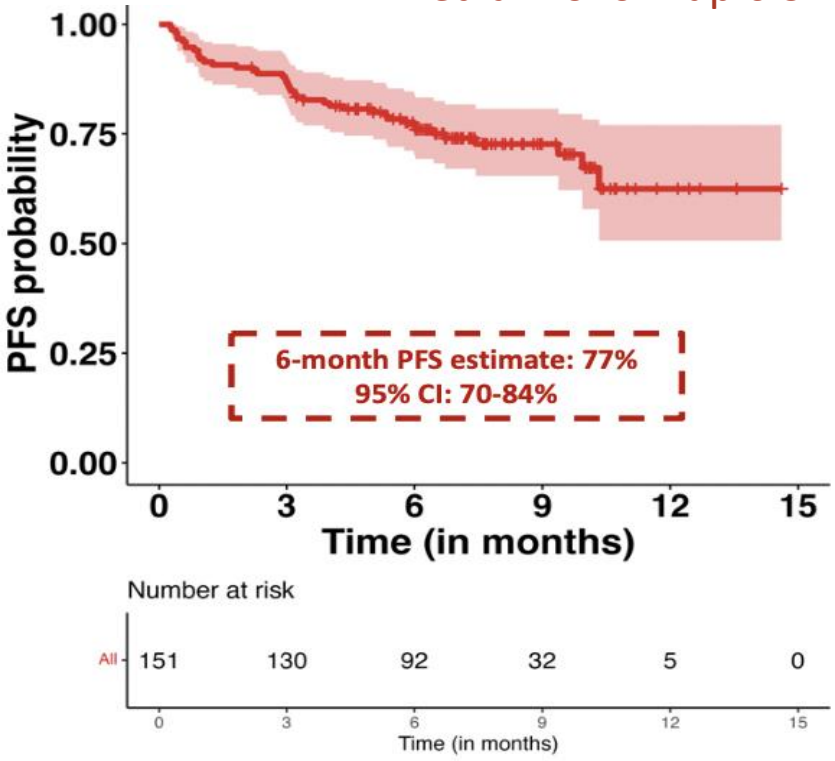
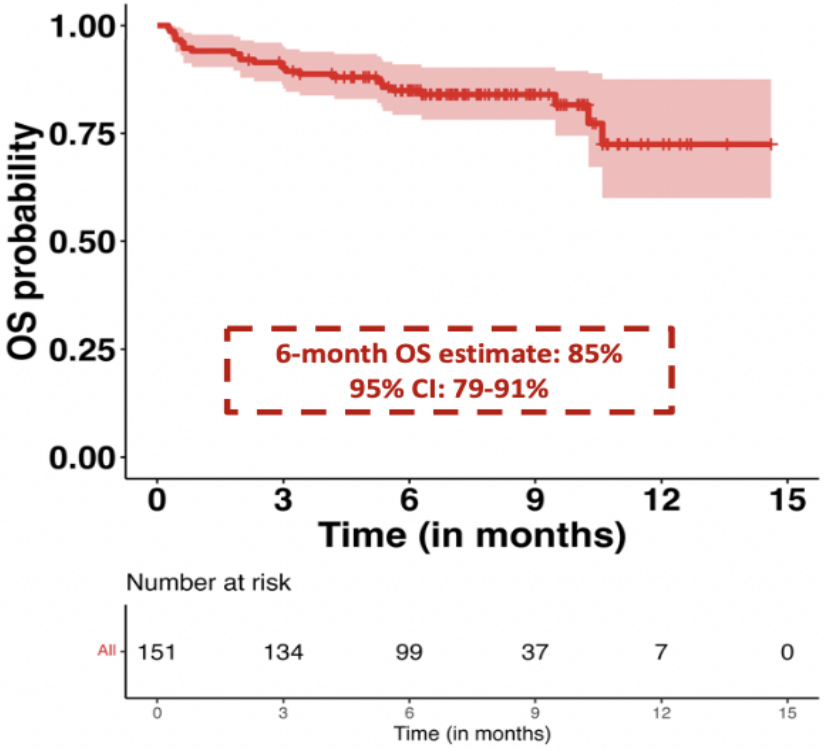
Courtesy of Sidana S, IMS 2023



Courtesy of Sidana S, IMS 2023

Median follow-up 6.9 months from CAR T infusion





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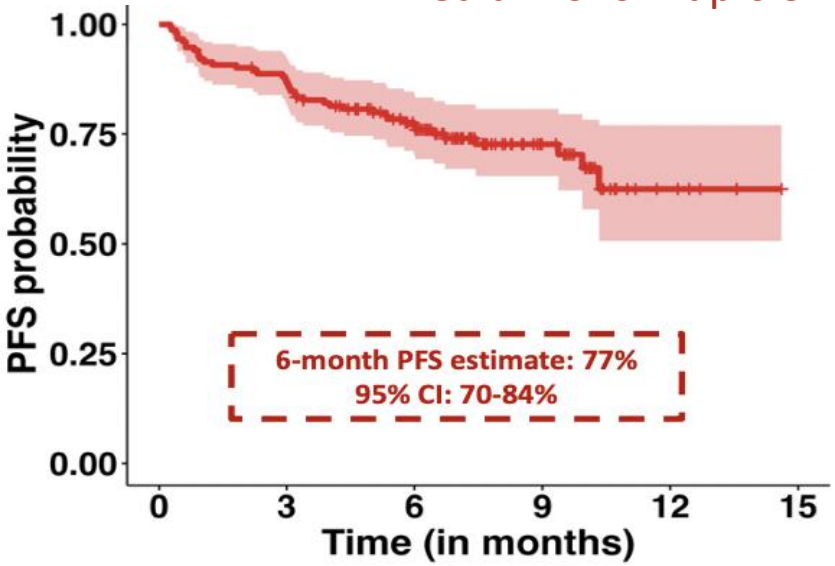

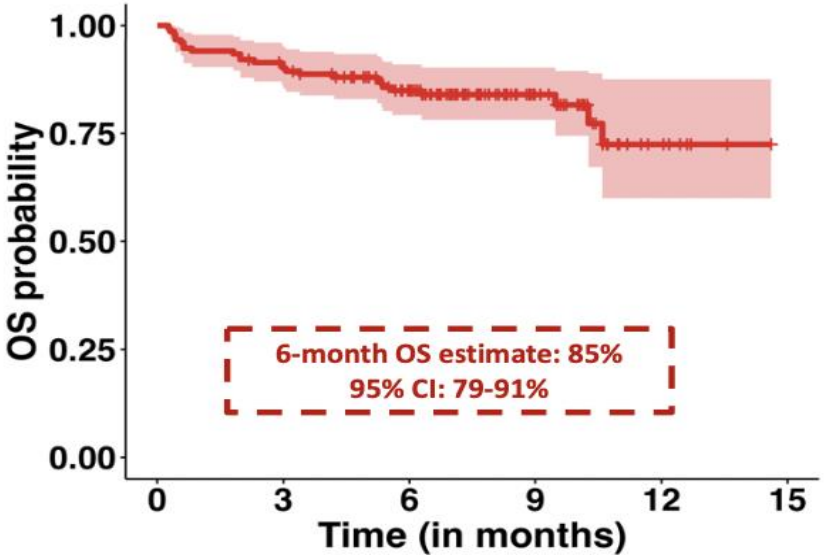

In a multivariable model, only high-risk cytogenetics was an adverse prognostic factor for PFS (HR: 2.73, 95% CI: 1.37-5.44, p=0.004).

Courtesy of Sidana S, IMS 2023

Conclusions

- Real life studies produced efficacy and safety results comparable to those of clinical trials
- Results were favourable despite a significant proportion of patients would not have met exclusion criteria of the clinical trials (57-75%), including patients with more aggressive disease and renal insufficiency, and even with a group receiving out of spec cilta-cel (22%)
- Risk factors for shorter PFS included aggressive disease features, younger age, ECOG ≥2; prior exposure to anti-BCMA tx should be further explored by type of drug used