EMORY WINSHIP CANCER INSTITUTE
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ASCO 2017: Myeloma update

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Daratumumab + KRd in Newly Diagnosed MM: Study Design

- Multicenter, open-label phase Ib study

Transplant-eligible and transplant-ineligible pts with newly diagnosed MM, no clinically significant cardiac disease (N = 22)

→

Daratumumab: cycle 1: 8 mg/kg on Days 1-2; cycles 1-2: 16 mg/kg Q1W; cycles 3-6: 16 mg/kg Q2W; cycles > 6: 16 mg/kg Q4W
Carfilzomib: cycle 1, Day 1: 20 mg/m^2; cycle 1, Day 8+: escalated to 70 mg/m^2 weekly (Days 1, 8, 15)
Lenalidomide: 25 mg on Days 1-21
Dexamethasone: 40 mg weekly*
(N = 22)

→

Until elective discontinuation for ASCT or ≤ 13 cycles

*Pre- and postinfusion: dexamethasone 20 mg, diphenhydramine 25-50 mg, paracetamol 650-1000 mg, montelukast 10 mg.

- Primary endpoints: safety, tolerability
- Secondary endpoints: ORR, DoR, TTR, IRR
- Exploratory endpoint: PFS

Jakubowiak AJ, et al. ASCO 2017. Abstract 8000.

Daratumumab + KRd in Newly Diagnosed MM: Tolerability and Infusion-Related Reactions

- Median follow-up: 10.8 mos (range: 4.0-12.5)
- Median cycles: 11.5 (range: 1.0-13.0)
- 19/22 pts escalated carfilzomib to 70 mg/m^2 by cycle 2, Day 1
- 8/22 pts (36%) discontinued tx
  - ASCT: 6 (27%)
  - AE: 1 (5%)
  - PD: 1 (5%)
- 27% of pts experienced IRR
  - No grade 3/4
  - With first infusion: 5 pts (23%)
  - With later infusions: 1 pt (5%)
- Lower IRR rate with first dosing split over Days 1-2

Jakubowiak AJ, et al. ASCO 2017. Abstract 8000.

Daratumumab + KRd in Newly Diagnosed MM: Nonhematologic and Hematologic TEAEs

Nonhematologic TEAE in ≥ 30% Pts,* %	Daratumumab + KRd (N = 22)	
	All Grade	Grade 3/4
Diarrhea	73	14
URTI	59	0
Cough	55	5
Constipation	50	0
Fatigue	50	5
Dyspnea	46	0
Insomnia	46	5
Nausea	41	0
Rash	41	0
Back pain	41	0
Muscle spasm	36	0
Vomiting	32	0
Pain in extremity	32	0

Hematologic TEAE in ≥ 30% Pts, %	Daratumumab + KRd (N = 22)	
	All Grade	Grade 3/4
Lymphopenia	68	64
Thrombocytopenia	55	9
Anemia	46	9
Leukopenia	41	9
Neutropenia	32	14

*Also included hyperglycemia (all grade: 32%; no grade 3/4) and increased ALT (all-grade: 32%; grade 3/4: 9%).

Jakubowiak AJ, et al. ASCO 2017. Abstract 8000.

Daratumumab + KRd in Newly Diagnosed MM: Serious TEAEs

Serious TEAE, n	Pts (N = 22)
Pulmonary embolism*	3
Pyrexia	2
Influenza	2
Abdominal pain	1
Chest pain	1
Dyspnea	1
Allergic dermatitis	1

Serious TEAE, n	Pts (N = 22)
Presyncope	1
Gastroenteritis	1
Lobular pneumonitis	1
Bacterial pneumonia	1
Tachycardia	1
Congestive heart failure	1
Hypertension	1

*1 pt had bilateral deep vein thrombosis and pulmonary embolism.

- 10/22 pts (46%) experienced serious TEAEs; all pts on aspirin prophylaxis
  - Likely related to: daratumumab, n = 3 (14%), carfilzomib, n = 5 (23%), lenalidomide, n = 5 (23%), dexamethasone, n = 2 (9%)
  - 1 pt (5%) d/c for pulmonary embolism considered unrelated to daratumumab or carfilzomib
- No change in LVEF measurements over time

Jakubowiak AJ, et al. ASCO 2017. Abstract 8000.

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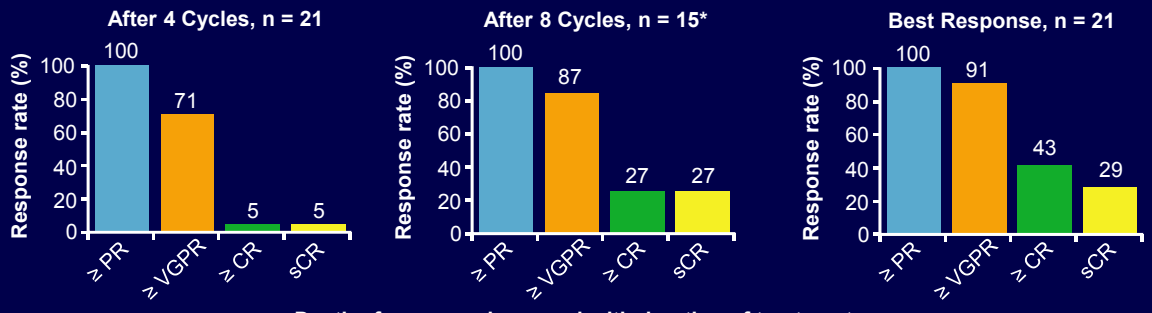
Daratumumab + KRd in Newly Diagnosed MM: Response

- Median number of treatment cycles: 11.5 (range: 1.0-13.0)



Depth of response improved with duration of treatment

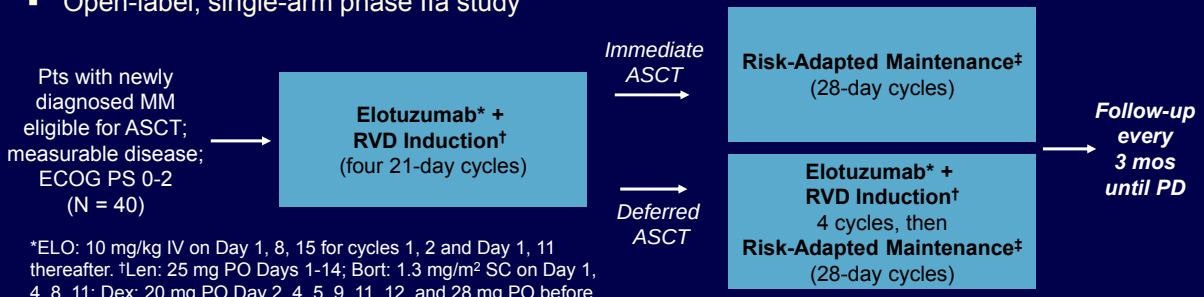
*5 pts who proceeded to ASCT before cycle 8 and 1 pt who discontinued due to PD at cycle 7 were excluded.

- Median follow-up: 10.8 mos (range: 4.0-12.5)
- OS: 100% at follow-up

Jakubowiak AJ, et al. ASCO 2017. Abstract 8000. Reproduced with permission.

Elotuzumab + RVD in ND MM: Study Design

- Open-label, single-arm phase IIa study



*ELO: 10 mg/kg IV on Day 1, 8, 15 for cycles 1, 2 and Day 1, 11 thereafter. †Len: 25 mg PO Days 1-14; Bort: 1.3 mg/m^2 SC on Day 1, 4, 8, 11; Dex: 20 mg PO Day 2, 4, 5, 9, 11, 12, and 28 mg PO before ELO infusion; 8 mg IV Day 1, 8, 15 before ELO infusion.

‡High risk (ISS stage III and/or high-risk cytogenetics): ELO + RVD; standard risk (ISS stage I/II w/o high-risk cytogenetics): ELO + Len/Dex.

- Primary objective: response rate after 4 cycles of ELO + RVD
- Secondary objectives: proportion of pts with SC mobilization after 4 cycles ELO + RVD; proportion with dose modification within 4 cycles ELO + RVD; safety; clinical activity

Laubach J, et al. ASCO 2017. Abstract 8002.

Slide credit: clinicaloptions.com

Elotuzumab + RVD in ND MM: Risk-Adapted Maintenance Strategies

Pts With ASCT	Pts Deferring ASCT
High risk: ISS stage III and/or high-risk cytogenetics	High Risk: ISS Stage III and/or high-risk cytogenetics
▪ Elotuzumab: 20 mg/kg IV on Day 1 ▪ Bortezomib: 1.3 mg/m^2 SC on Day 1, 15 ▪ Lenalidomide: 10 mg PO Days 1-21, then 7-day rest ▪ Dexamethasone: 8 mg IV Day 1 before elotuzumab infusion	▪ Elotuzumab: 20 mg/kg IV on Day 1 ▪ Bortezomib: 1.3 mg/m^2 SC on Day 1, 15 ▪ Lenalidomide: dose tolerated during induction; PO Days 1-21, then 7-day rest ▪ Dexamethasone: 8 mg IV Day 1 before elotuzumab infusion
Standard risk: ISS stage I or II without high-risk cytogenetics	Standard risk: ISS stage I or II without high-risk cytogenetics
▪ Elotuzumab: 20 mg/kg IV on Day 1 ▪ Lenalidomide: 10 mg PO Days 1-21, then 7-day rest ▪ Dexamethasone: 8 mg IV Day 1 before elotuzumab infusion	▪ Elotuzumab: 20 mg/kg IV on Day 1 ▪ Lenalidomide: dose tolerated during induction; PO Day 1-21, then 7-day rest ▪ Dexamethasone: 8 mg IV Day 1 before elotuzumab infusion

- All pts received antiviral prophylaxis; PCP prophylaxis recommended

Laubach J, et al. ASCO 2017. Abstract 8002.

Slide credit: clinicaloptions.com

Elotuzumab + RVD in ND MM: Efficacy

- N = 40 pts evaluable for response
  - Received study therapy, ≥ 1 follow-up assessment
- Median time to first response ≥ PR: 25 days (95% CI: 22-29)
- Median DoR: NR

Response After 4 Cycles, %	All Pts (N = 40)	Pts With ASCT (n = 20)	Pts Deferring ASCT (n = 20)
ORR	82	95	70
PR	28	25	30
VGPR	40	45	35
CR	15	25	5

Response, n (%)	All Pts (N = 40)		Pts Completing 4 Cycles (n = 34)	
	After 4 Cycles	Best Response	After 4 Cycles	Best Response
ORR (≥ PR)	33 (82)	34 (85)	33 (97)	33 (97)
VGPR (≥ VGPR)	22 (55)	28 (70)	22 (65)	29 (88)
CR + sCR	6 (15)	14 (35)	6 (15)	14 (41)

Laubach J, et al. ASCO 2017. Abstract 8002.

Slide credit: clinicaloptions.com

Elotuzumab + RVD in ND MM: Grade ≥ 3 AEs

Hematologic AE, %	Pts (N = 40)		
	Grade 3	Grade 4	Grade 5
Thrombocytopenia	10	5	0
Anemia	5	0	0
Febrile neutropenia	5	0	0
Lymphopenia	2	0	0
Neutropenia	2	0	0

Nonhematologic AE, %	Pts (N = 40)		
	Grade 3	Grade 4	Grade 5
Hypophosphatemia	12	0	0
Back pain	10	0	0
Fatigue	10	0	0
Lung infection	10	0	0
Hypertension	8	0	0
Syncope	8	0	0
Increased ALT	5	0	0
Fever	5	0	0
Hyperglycemia	2	2	0
Hypotension	5	0	0
Rash	5	0	0
Sepsis	0	2	2
Cardiac arrest	0	2	0
Respiratory failure	0	2	0

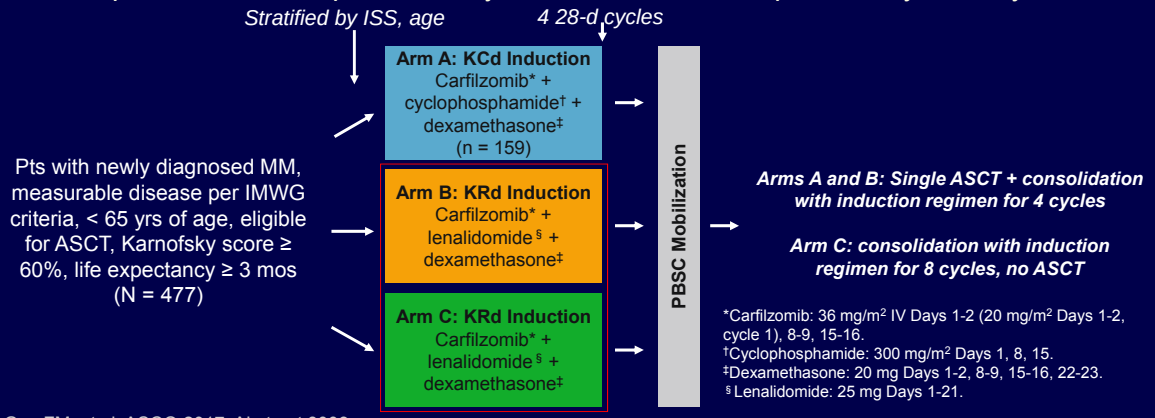
- 7 pts discontinued treatment
  - All no immediate ASCT
  - 2 pts died (sepsis, 1 on study, 1 > 30 days after discontinuation of treatment)

Laubach J, et al. ASCO 2017. Abstract 8002.

Slide credit: clinicaloptions.com

FORTE: Study Design

- Multicenter, randomized, open-label phase II study
- Endpoints: induction phase safety, PBSC mobilization, preliminary efficacy



*Carfilzomib: 36 mg/m^2 IV Days 1-2 (20 mg/m^2 Days 1-2, cycle 1), 8-9, 15-16.
†Cyclophosphamide: 300 mg/m^2 Days 1, 8, 15.
‡Dexamethasone: 20 mg Days 1-2, 8-9, 15-16, 22-23.
§Lenalidomide: 25 mg Days 1-21.

Gay FM, et al. ASCO 2017. Abstract 8003.
ClinicalTrials.gov. NCT02203643.

Current report analyzed Arm B + Arm C together (n = 318)

FORTE: Induction Phase Safety

Hematol. AEs, %	Grade 1/2		Grade 3/4 or SAE	
	KCd	KRd	KCd	KRd
≥ 1 AE	13	16	6	7
Thrombo-cytopenia	3*	8*	1	2
Neutropenia	1	3	5	6
Anemia	10	10	3	2

*P = .05 for comparison between arms.

- AE-related d/c: KCd, 2%; KRd, 4%
- Fewer dose reductions with KCd vs KRd (6% vs 15%; P = .005)
- AE-related deaths: KCd, 2 cases (1 each of pneumonia, sudden death); KRd, 3 cases (1 each of sudden death during sepsis, infection, cardiac arrest after d/c for renal failure)

Nonhematol. AEs, %	Grade 1-2		Grade 3/4 or SAE	
	KCd	KRd	KCd	KRd
≥ 1 AE	38*	55*	16*	32*
Dermatologic	3*	17*	1*	8*
Renal	3	3	2	1
Fever	11	17	1	4
Infections	6	10	3	5
GI	12*	28*	1	2
Hepatic	5	11	1*	8*
DVT	2†	8†	0	1
Hypertension	4	4	2	3
Cardiac	3	2	2	1

*P < .001 for comparison between arms.
†P = .01 for comparison between arms.

Gay FM, et al. ASCO 2017. Abstract 8003.

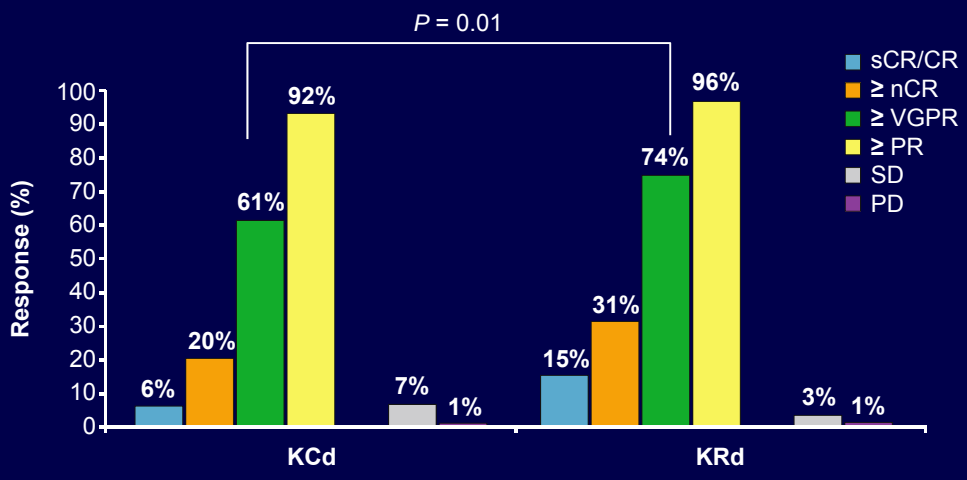
FORTE: PBSC Mobilization

Parameter	KCd	KRd	*P* Value
Median PBSC, 10^6/kg (IQR)	8.6 (7.0-11.3)	6.3 (4.5-8.8)	< .001
PBSC harvest, % ▪ ≥ 4 x 10^6/kg ▪ ≥ 2 and < 4 x 10^6/kg ▪ < 2 x 10^6/kg (mobilization failure)	 97 2 1	 88 8 4	 .002 .02 Ns
Pts requiring plerixafor, %	6	28	< .001

- Poor PBSC mobilization (harvest < 4 x 10^6/kg and/or requiring plerixafor) more likely with KRd vs KCd
  - OR: 6.55 (95% CI: 2.88-14.91; *P* < .001)

Gay FM, et al. ASCO 2017. Abstract 8003.

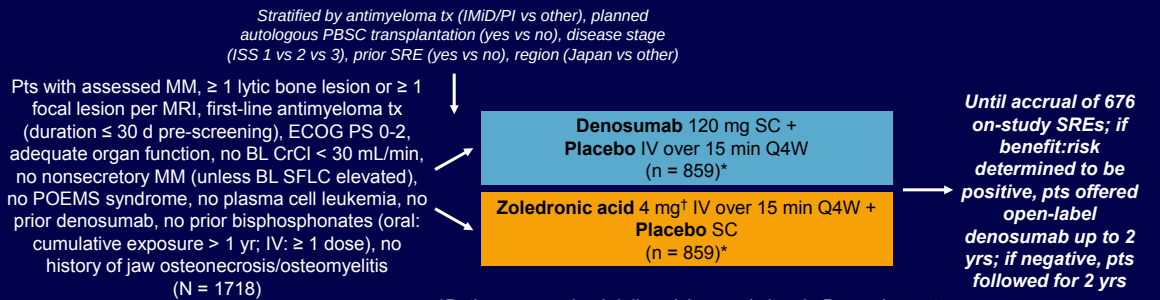
FORTE: Preliminary Efficacy



Gay FM, et al. ASCO 2017. Abstract 8003. Reproduced with permission.

Denosumab vs ZA in Newly Diagnosed MM: Study Design

- International, randomized, double-blind phase III trial (primary analysis cutoff: July 19, 2016; enrollment ended: March 29, 2016)



*Both arms received daily calcium and vitamin D supplements.
†ZA dose adjusted per BL CrCl, with subsequent dose intervals dictated by serum CrCl.

- Primary endpoint: time to first on-study SRE (noninferiority)
- Secondary endpoints: time to first on-study SRE (superiority), time to first-and-subsequent on-study SRE (superiority), OS, PFS (exploratory), safety

Raje NS, et al. ASCO 2017. Abstract 8005. ClinicalTrials.gov. NCT01345019.

Denosumab vs ZA in Newly Diagnosed MM: Time to SRE

- Primary endpoint met: denosumab noninferior to ZA for time to first on-study SRE
  - Denosumab not superior to ZA for time to first on-study SRE or time to first-and-subsequent on-study SRE

On-study Endpoint	Denosumab (n = 859)	ZA (n = 859)	Difference (95% CI)	*P* Value		
				Noninferior	Superior	Superior (Adj.*)
Time to first SRE						
▪ Crude incidence, n (%)	376 (43.8)	383 (44.6)	HR: 0.98 (0.85-1.14)	.01	.82	.84
▪ KM median, mos (95% CI)	22.83 (14.72-NE)	23.98 (16.56-33.31)				
Time to first-and-subsequent SRE†			RR: 1.01 (0.89-1.15)	--	.84	.84
▪ Events, n	565	565				
▪ Mean events per pt, n	0.66	0.66				

*Per protocol: if denosumab noninferior to ZA, time to first on-study SRE (superiority) and time to first-and-subsequent on-study SRE tested simultaneously with Hochberg procedure to control overall type I error at α = 0.05. †21-d window applied.

Raje NS, et al. ASCO 2017. Abstract 8005.

Denosumab vs ZA in Newly Diagnosed MM: OS, PFS

Endpoint	Denosumab (n = 859)	ZA (n = 859)	HR (95% CI)
OS ▪ Deaths, n (%)	121 (14.1)	129 (15.0)	0.90 (0.70-1.16) *P* = .41
mPFS, mos (95% CI)	46.09 (34.30-NE)	35.38 (30.19-NE)	0.82 (0.68-0.99) *P* = .036*

*Descriptive *P* value for PFS exploratory endpoint.

Raje NS, et al. ASCO 2017. Abstract 8005.

Denosumab vs ZA in Newly Diagnosed MM: Bone and Renal AEs

- Median cumulative exposure: denosumab, 15.75 mos; ZA, 14.78 mos
- Significantly lower rate of renal TEAEs with denosumab vs ZA
  - Creatinine increase observed in 12.5% of pts receiving denosumab vs 20.8% receiving ZA
- Significantly higher rate of hypocalcemia with denosumab vs ZA
  - Most events grade 1-2 (no grade 5 events)

AE, n (%)	All Pts		Pts With BL CrCl ≤ 60 mL/min	
	DMB (n = 850)	ZA (n = 852)	DMB (n = 233)	ZA (n = 220)
Renal TEAE	85 (10.0)*	146 (17.1)*	30 (12.9)*	58 (26.4)*
Creatinine > 2 mg/dL, n/N_1‡ (%)	31/824 (3.8)†	54/823 (6.6)†	20/216 (9.3)	32/203 (15.8)
Creatinine doubled from BL, n/N_2§ (%)	28/841 (3.3)†	55/840 (6.5)†	6/233 (2.6)†	16/220 (7.3)†
Hypocalcemia TEAE	144 (16.9)†	106 (12.4)†	46 (19.7)	28 (12.7)
Jaw osteonecrosis (positively adjudicated)	35 (4.1)	24 (2.8)	10 (4.3)	4 (1.8)

*P < .001 between arms. †P < .05. ‡N_1: pts with BL serum creatinine ≤ 2 mg/dL. §N_2: pts without missing BL serum creatinine values.

Raje NS, et al. ASCO 2017. Abstract 8005.

Denosumab vs ZA in Newly Diagnosed MM: Safety

AE, n (%)	Denosumab (n = 850)	ZA (n = 852)
All AEs	816 (96.0)	825 (96.8)
▪ AEs grade ≥ 3	562 (66.1)	575 (67.5)
▪ Serious AEs	391 (46.0)	403 (47.3)
▪ Fatal AEs	89 (10.5)	93 (10.9)
▪ AE-related IP d/c	110 (12.9)	98 (11.5)
▪ AE-related study d/c	17 (2.0)	9 (1.1)
TEAEs	217 (25.5)	222 (26.1)
▪ AEs grade ≥ 3	44 (5.2)	49 (5.8)
▪ Serious AEs	27 (3.2)	28 (3.3)
▪ Fatal AEs	0	1 (0.1)
▪ AE-related IP d/c	36 (4.2)	36 (4.2)
▪ AE-related study d/c	5 (0.6)	1 (0.1)
Most common AEs*		
▪ Diarrhea	285 (33.5)	276 (32.4)
▪ Nausea	268 (31.5)	259 (30.4)

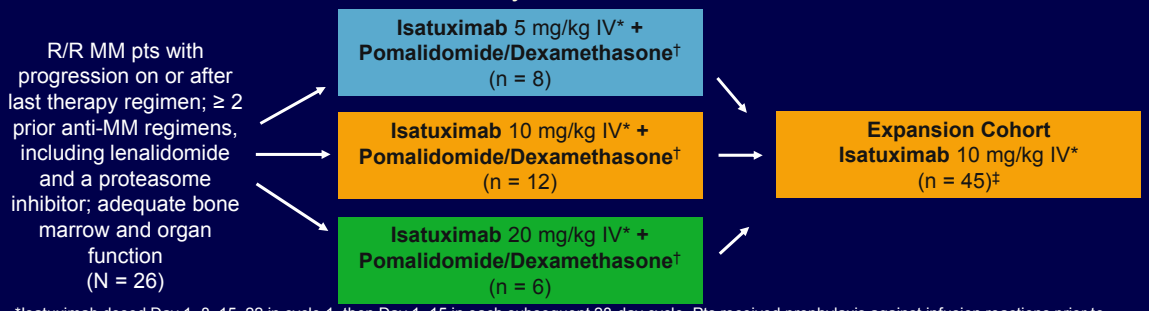
*AEs in ≥ 25% of pts in denosumab arm.

AE of Interest, n (%)	Denosumab (n = 850)	ZA (n = 852)
Atypical femur fracture (positively adjudicated)	0	0
AE possibly related to hypersensitivity	219 (25.8)	189 (22.2)
▪ Serious AE	5 (0.6)	9 (1.1)
Musculoskeletal pain	407 (47.9)	425 (49.9)
Infections and infestations	537 (63.2)	500 (58.7)
▪ Serious infections and infestations	165 (19.4)	163 (19.1)
New primary malignancy	22 (2.6)	12 (1.4)
Acute phase reactions	46 (5.4)	74 (8.7)

Raje NS, et al. ASCO 2017. Abstract 8005.

TCD14079: Study Design

- Phase Ib 3 + 3 dose escalation study



*Isatuximab dosed Day 1, 8, 15, 22 in cycle 1, then Day 1, 15 in each subsequent 28-day cycle. Pts received prophylaxis against infusion reactions prior to administration. †Pomalidomide 4 mg on Days 1-21 in each 28-d cycle; dexamethasone 40 mg (or 20 mg if ≥ 75 yrs of age) on Day 1, 8, 15, 22 in each 28-day cycle. ‡Includes 45 pts total including pts from dose-finding arms.

- Primary objective: recommended dose of isatuximab in combination with pomalidomide/dexamethasone
- Secondary objectives: safety, tolerability, pharmacokinetics, efficacy

Mikhael J, et al. ASCO 2017. Abstract 8007.

TCD14079: TEAEs

TEAE, n	All Grades (≥ 30% of Pts)				Grade ≥ 3 (≥ 5% of Pts)			
	ISA 5 mg/kg (n = 8)	ISA 10 mg/kg* (n = 12)	ISA 20 mg/kg (n = 6)	All Pts (n = 26)	ISA 5 mg/kg (n = 8)	ISA 10 mg/kg* (n = 12)	ISA 20 mg/kg (n = 6)	All Pts (n = 26)
Any	8	12	6	26	8	8	5	21
Fatigue	5	8	4	17	1	1	0	2
Dyspnea	5	4	3	12	1	0	1	1
Infusion reaction	4	7	1	12	0	1	0	1
Diarrhea	2	5	3	10	0	0	0	0
URTI	4	3	3	10	0	0	0	0
Constipation	4	3	2	9	0	0	0	0
Acute renal injury	1	1	0	2	1	1	0	2
Pneumonia	0	1	1	2	0	1	1	2

*Pts from dose escalation cohort (n = 9) and expansion cohort (n = 3) combined.

- Isatuximab dose omission in 9 of 26 pts (35%), pomalidomide reduction/omission in 17 of 26 pts (65%) due to AEs; 1 pt in 10-mg/kg arm died of perforated bowel due to light chain deposition disease

Mikhael J, et al. ASCO 2017. Abstract 8007.

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TCD14079: Hematologic Lab Abnormalities

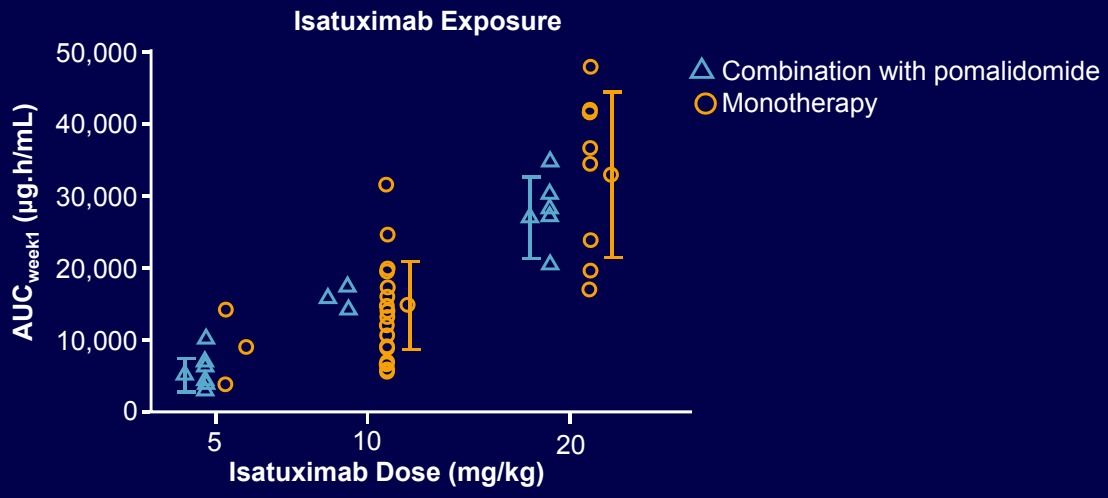
Lab Abnormality, n	All Grades				Grade ≥ 3			
	ISA 5 mg/kg (n = 8)	ISA 10 mg/kg* (n = 11)	ISA 20 mg/kg (n = 6)	All Pts (n = 25)	ISA 5 mg/kg (n = 8)	ISA 10 mg/kg* (n = 11)	ISA 20 mg/kg (n = 6)	All Pts (n = 25)
Anemia	8	11	6	25	0	1	2	3
Leukopenia	8	11	6	25	7	9	5	21
Lymphopenia	8	11	6	25	7	9	4	20
Neutropenia	8	10	6	24	7	10	6	23
Thrombocytopenia	7	11	5	23	2	2	4	8

*Pts from dose escalation cohort (n = 9) and expansion cohort (n = 3) combined.

- Isatuximab dose omission in 3 pts and pomalidomide dose reduction in 9 pts due to neutropenia, but no treatment discontinuations or withdrawals
- DLTs leading to dose omission/reduction: grade 4 neutropenia, n = 1 in 5-mg/kg arm; grade 4 neutropenic infection, n = 1 in 10-mg/kg arm; grade 3 confusion, n = 1 in 20-mg/kg arm

Mikhael J, et al. ASCO 2017. Abstract 8007.

TCD14079: Isatuximab Pharmacokinetics



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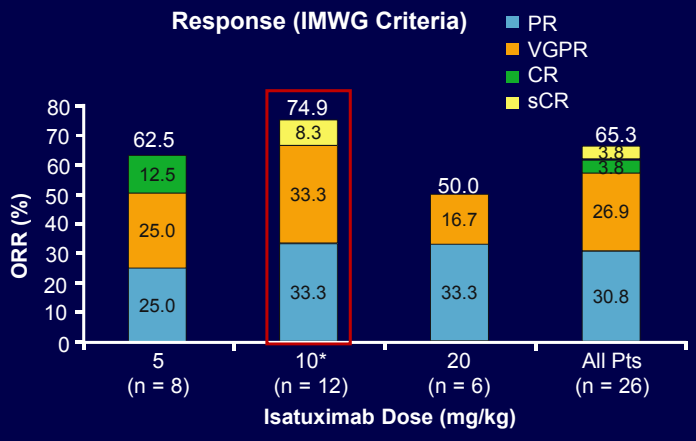
TCD14079: Efficacy



*Pts from dose escalation cohort (n = 9) and expansion cohort (n = 3) combined.

- Median DoR: 36.1 wks
- Median TTR: 4.3 wks
- Of 5 pts with high-risk cytogenetics (del[17p] or t[4:14]), 1 obtained VGPR, 1 PR, 1 minimal response
- ORR of 60%, 50%, and 47%, observed in pts who were refractory to lenalidomide, PI, or IMiD + PI, respectively

Mikhael J, et al. ASCO 2017. Abstract 8007. Reproduced with permission.

Durable remissions with BCMA specific chimeric antigen receptor (CAR)-modified T cells in patients with refractory/relapsed multiple myeloma

Wanhong Zhao (alternative presenter)

Frank (Xiaohu) Fan [1], Wanhong Zhao [2] Jie Liu [2], Aili He [2], Yinxia Chen [2], Xingmei Cao [2], Nan Yang [2], Baiyan Wang [2], Pengyu Zhang [2], Yilin Zhang [2], Fangxia Wang [2], Bo Lei [2], Liufang Gu [2], Xugeng Wang [2], Qiuchuan Zhuang [1] and Wanggang Zhang [2]

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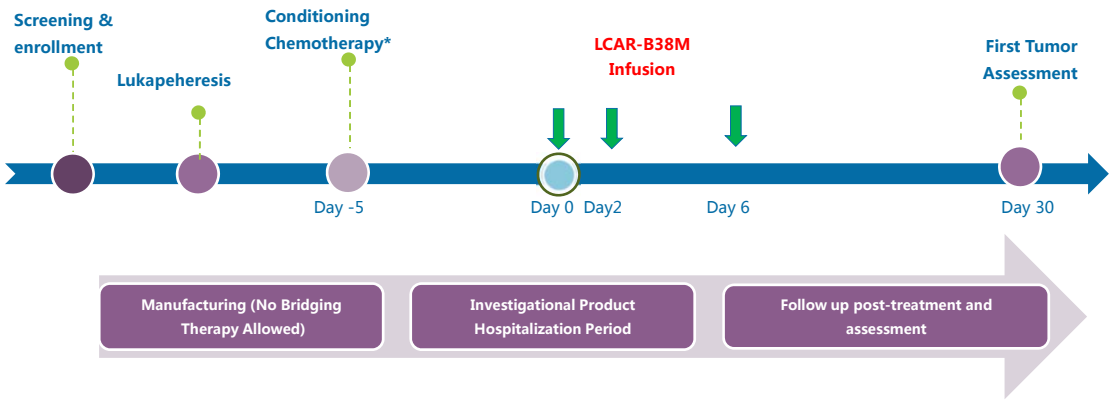
[2]Hematology Division, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

Legend LCAR-B38M Treatment Scheme

Clinicaltrials.gov/NCT03090659

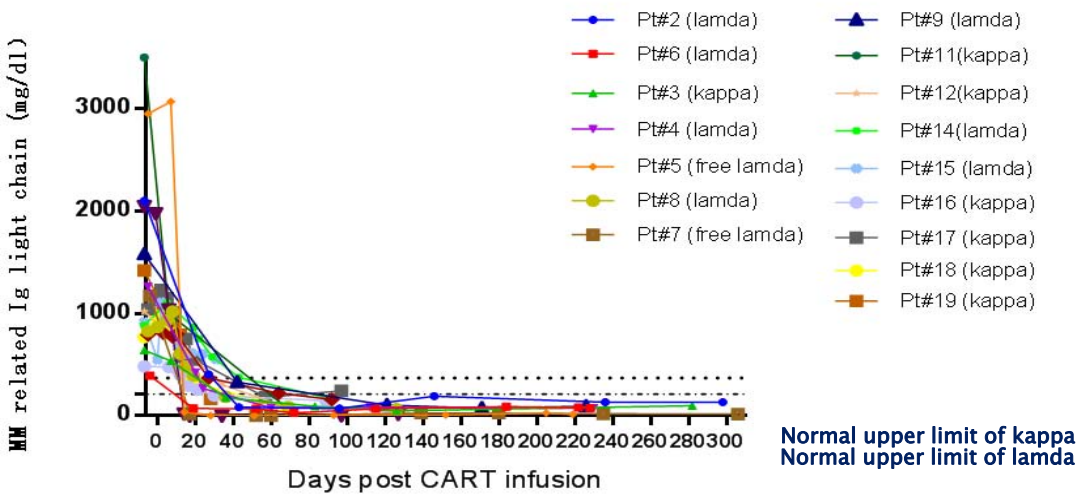


Summary of Patient Characteristics

Clinicaltrials.gov/NCT03090659

Characteristic	Cohort
r/r MM patient, total number enrolled	35
Median age (range), years	55 (43-72)
Male, n(%)	19(54)
Durie-Salmon stage, n(%) I/IIA/IIIA/IIIB	1(3)/4(11)/ 25 (71)/ 5 (14)
Number of prior lines of therapy, n(%) 3/4/≥5	14 (40)/ 16 (46)/ 5 (14)
Refractory subgroup, n(%) Refractory to ≥ 2nd line therapy	35(100)

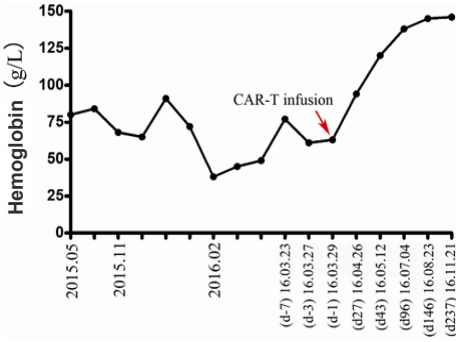
Clinical efficacy of LCAR-B38M product



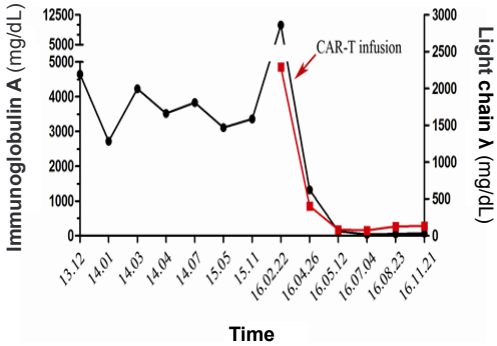
Legend's first CR case in MM CAR-T clinical trial

- **Patient #2 follow-up (two months after CAR-T therapy)**

Hb

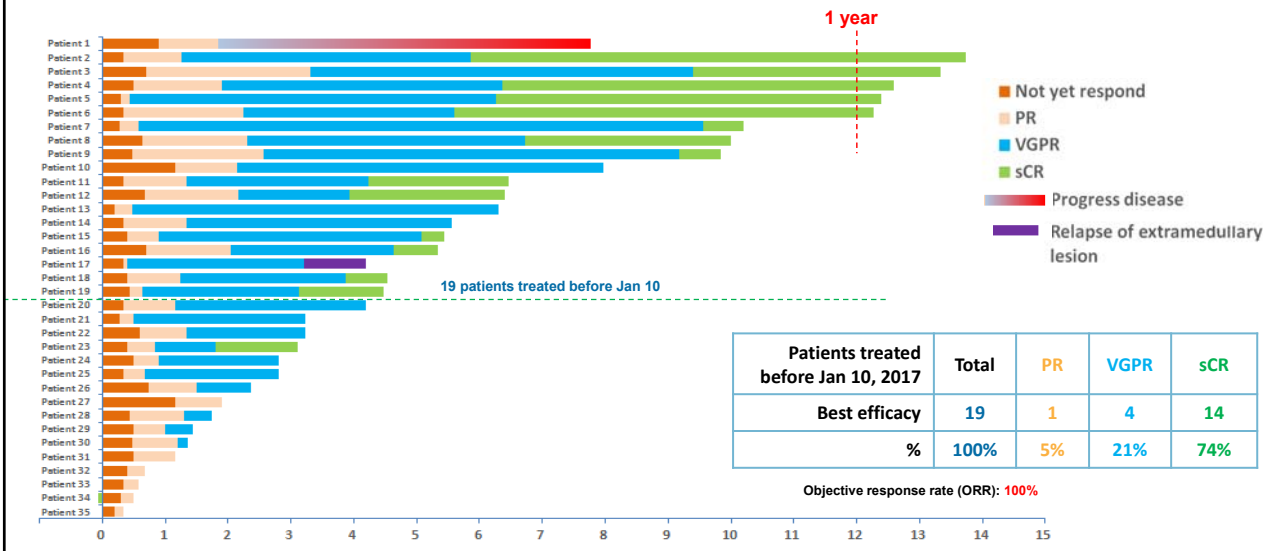


IgA (Lamda light chain)



- ✓ All Hematology indexes recovered as normal;
- ✓ Tumor cells in bone marrow disappeared completely;
- ✓ Abnormal immunoglobulin disappeared.

Efficacy follow-up of LCAR-B38M CAR-T cells



Patients treated before Jan 10, 2017	Total	PR	VGPR	sCR
Best efficacy	19	1	4	14
%	100%	5%	21%	74%

Objective response rate (ORR): 100%

All about Safety

- **Adverse effects**
  - **Cytokine release syndrome, CRS)** — **MILD**
    - IL-6R mAb (tocilizumab)
  - **Neurological toxicity** — **None**
    - Cerebral edema, lethal
    - Confusion, seizure, delirium, aphasia
    - Never happened to Legend' s product
  - **B cell aplasia (hypogammaglobulinemia)** — **Recoverable**
    - IVIG repletion every 2 months

Table 2. CRS revised grading system

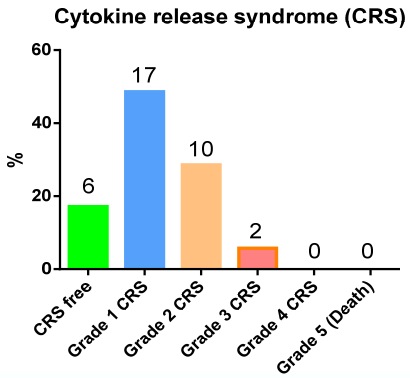
Grade	Toxicity
Grade 1	Symptoms are not life threatening and require symptomatic treatment only, eg, fever, nausea, fatigue, headache, myalgias, malaise
Grade 2	Symptoms require and respond to moderate intervention Oxygen requirement <40% or Hypotension responsive to fluids or low dose[2] of one vasopressor or Grade 2 organ toxicity
Grade 3	Symptoms require and respond to aggressive intervention Oxygen requirement ≥40% or Hypotension requiring high dose* or multiple vasopressors or Grade 3 organ toxicity or grade 4 transaminitis
Grade 4	Life-threatening symptoms Requirement for ventilator support or Grade 4 organ toxicity (excluding transaminitis)
Grade 5	Death

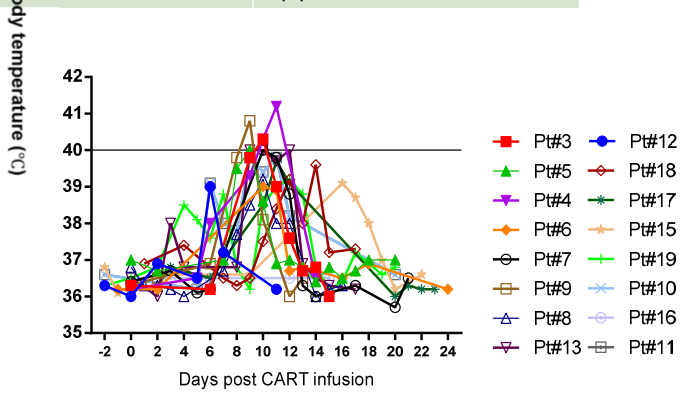
Grades 2-4 refer to CTCAE v4.0 grading.

Daniel W. Lee, Rebecca Gardner, David L. Porter, Chrystal U. Louis, Nabil Ahmed, Michael Jensen, Stephan A. Grupp, Crystal L. Mackall Blood. 2014 Jul 10; 124(2): 188–195.

Safety: Major adverse events is cytokine release syndrome (CRS)

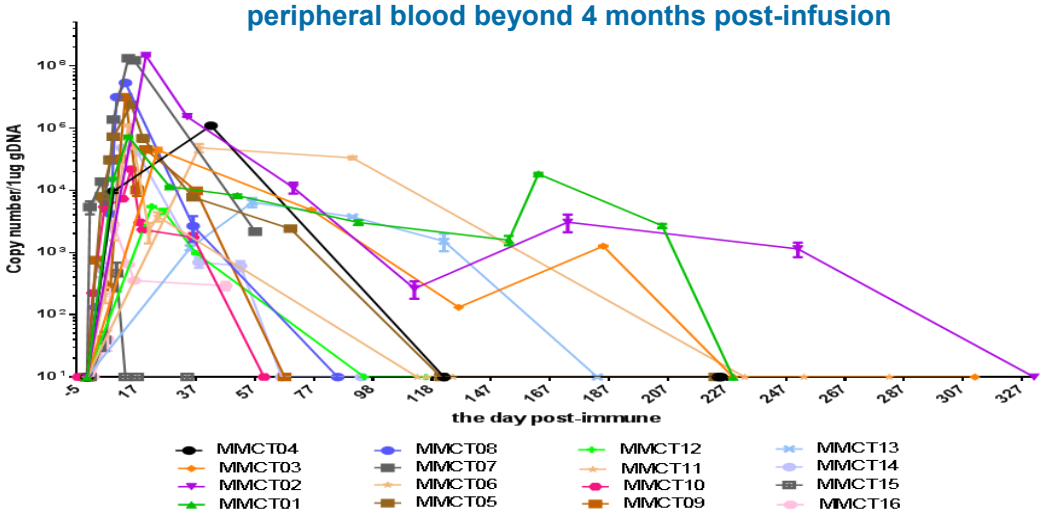
Adverse Event, n (%)	Patients (N=35)
Grade ≥3 adverse event	2 (5.7%)
Serious adverse event	0 (0)
Fatal events excluding disease progression	0 (0)



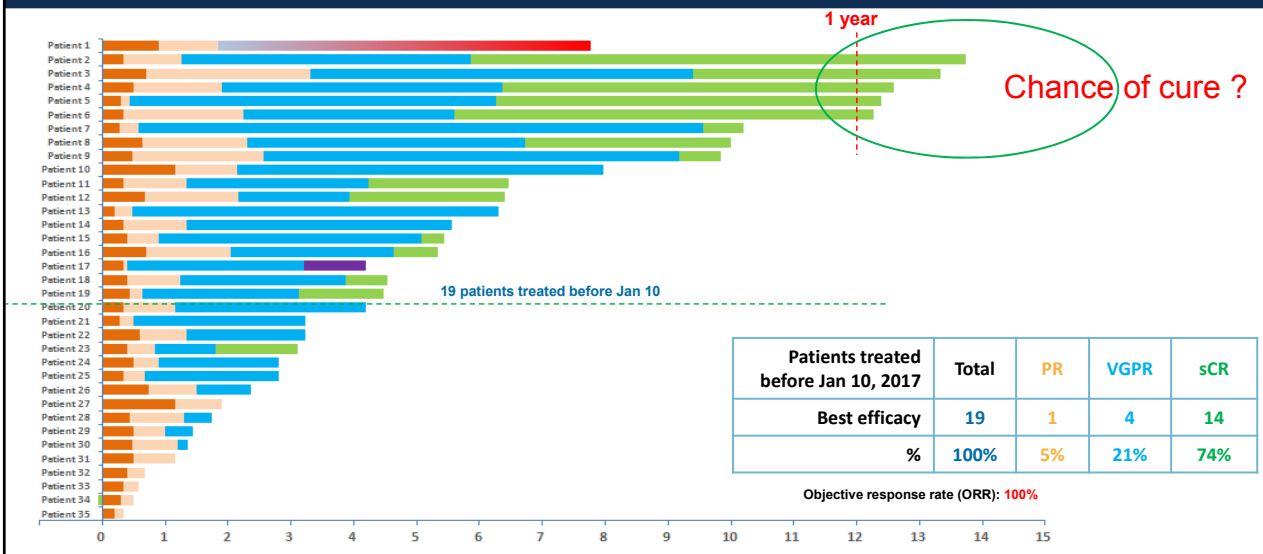


Persistence of infused LCAR-B38M cells

For majority of patients, LCAR-B38M cells are undetectable in peripheral blood beyond 4 months post-infusion



Efficacy follow-up of LCAR-B38M CAR-T cells



Patients treated before Jan 10, 2017	Total	PR	VGPR	sCR
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Conclusions

- **LCAR-B38M CAR-T technology exert quick and reproducible therapeutic effects in refractory and relapsed multiple myeloma patients.**
- **>12 months follow-up of early patients shows durable and stringent complete remission which raises hopes of cure.**
- **LCAR-B38M technology not only demonstrate outstanding efficacy, but also suggest a great safety profile.**
- **US clinical trial is under way and the technology will be fully validated under "American (FDA) standard".**