LEUKEMIA & LYMPHOMA SOCIETY®

UNDERSTANDING MY TREATMENT OPTIONS: MULTIPLE MYELOMA

Sagar Lonial, MD, FACP
Professor and Chair
Department of Hematology and Medical Oncology
Chief Medical Officer
Winship Cancer Institute of Emory University
Anne and Bernard Gray Family Chair in Cancer
Emory University School of Medicine
Atlanta, GA

1

WELCOMING REMARKS

UNDERSTANDING MY TREATMENT OPTIONS: MULTIPLE MYELOMA

Lizette Figueroa-Rivera, MA
Senior Director, Education & Support
The Leukemia & Lymphoma Society
Rye Brook, NY

2

LEUKEMIA & LYMPHOMA SOCIETY®

2

WELCOMING REMARKS

UNDERSTANDING MY TREATMENT OPTIONS: MULTIPLE MYELOMA

This program is supported by

Bristol Myers Squibb™ | Genentech, A Member of the Roche Group | Biogen | GSK

janssen Oncology, PHARMACEUTICAL COMPANIES OF Johnson & Johnson | LEGEND BIOTECH | Karyopharm® Therapeutics

3

LEUKEMIA & LYMPHOMA SOCIETY®

3

PRESENTATION

UNDERSTANDING MY TREATMENT OPTIONS: MULTIPLE MYELOMA

Sagar Lonial, MD, FACP
Professor and Chair
Department of Hematology and Medical Oncology
Chief Medical Officer
Winship Cancer Institute of Emory University
Anne and Bernard Gray Family Chair in Cancer
Emory University School of Medicine

4

LEUKEMIA & LYMPHOMA SOCIETY®

4

DISCLOSURES

UNDERSTANDING MY TREATMENT OPTIONS: MULTIPLE MYELOMA

Sagar Lonial, MD, FACP

Consultant/advisor/speaker: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Novartis, Takeda, Pfizer

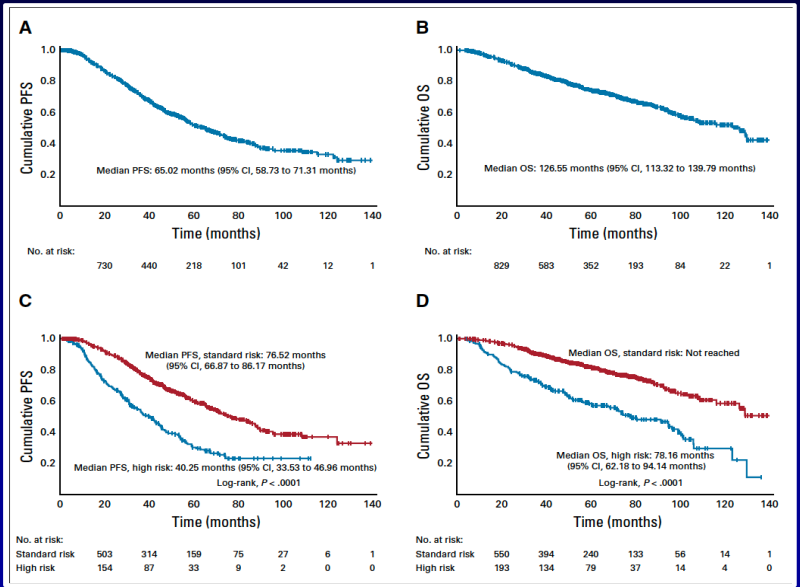
Researcher: Bristol-Myers Squibb, Janssen, Novartis, Takeda

Board member with stock: TG Therapeutics.

LEUKEMIA & LYMPHOMA SOCIETY®

5

What is the current state of the art?



Joseph et al, JCO 2020

6

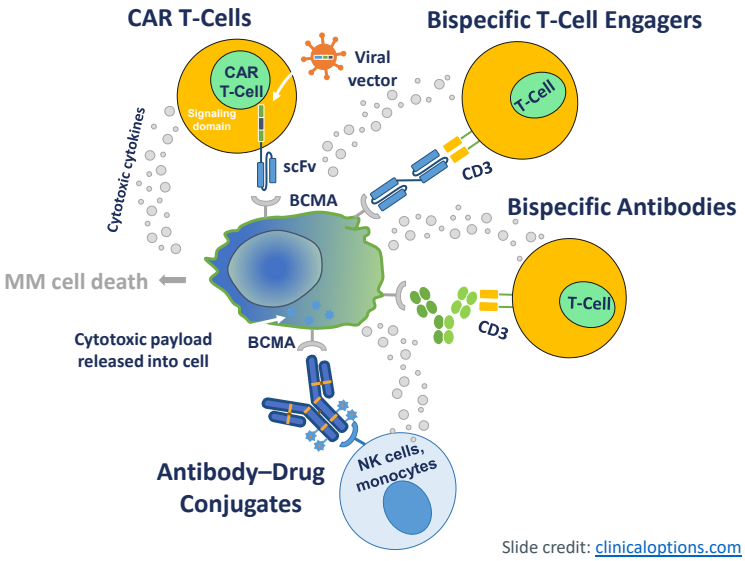
Topics to Cover

- Immune therapy and targets
- Precision Medicine and MM
- New versions of existing agents

7

BCMA in Multiple Myeloma

- Expressed on late memory B-cells committed to PC differentiation and PCs
- BCMA plays a role in survival of long-lived PCs
- γ-secretase cleaves BCMA from the cell surface, yielding soluble BCMA

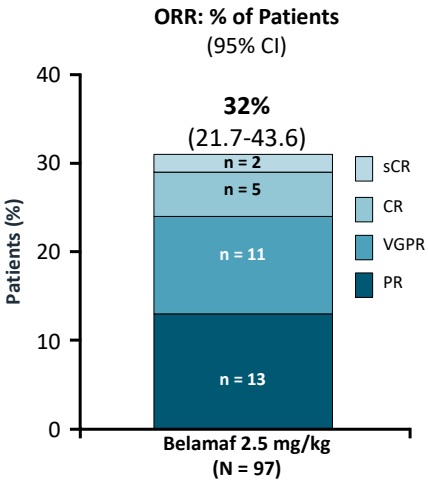


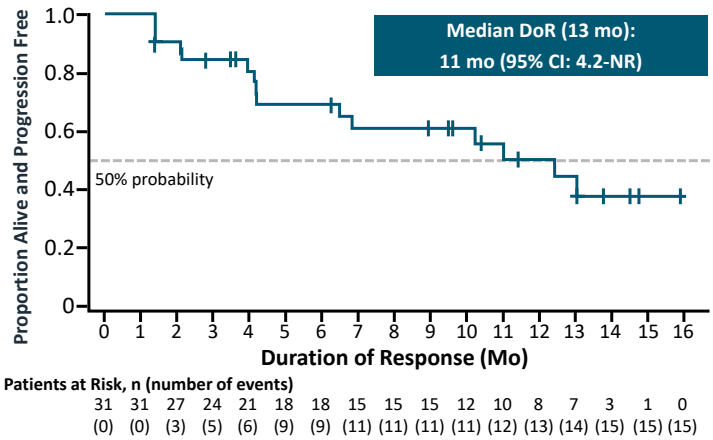
Cho. Front Immunol. 2018;10:1821.

Slide credit: clinicaloptions.com

8

Phase II DREAMM-2: Response and DoR at 13 Mo of Follow-up, Belantamab Mafodotin 2.5 mg/kg





Lonial. Cancer 2021;[Epub].

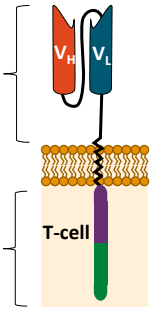
9

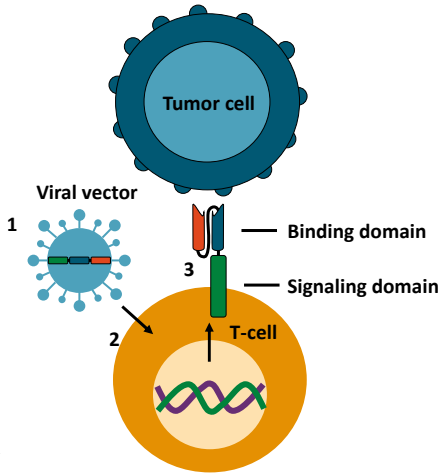
CAR T-Cell Structure

Tumor antigen–binding domain

Fusion protein

- T-cell costimulatory receptor signaling domain
- TCRζ activation domain





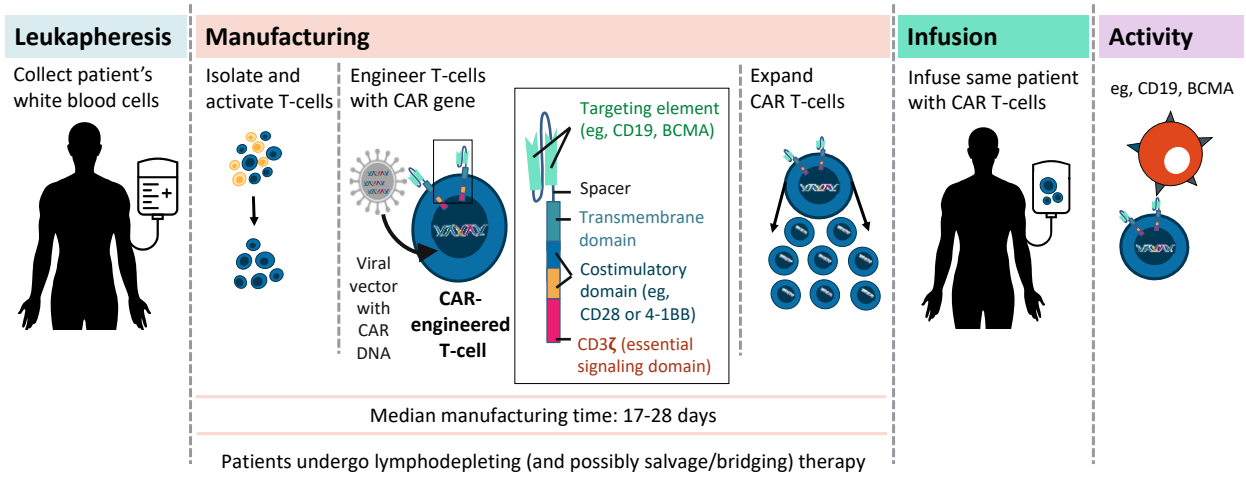
BCMA-directed CAR T-cell

- Comprising a BCMA antigen–binding domain, a costimulatory domain (generally CD28 or 4-1BB), and CD3-ζ signaling domain

Bruno. Haematologica. 2021;106: 2054. Morgan. Biomedicines. 2016;4:9.

10

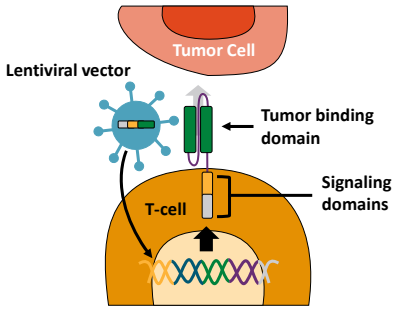
Autologous CAR T-Cell Therapy: Underlying Principles



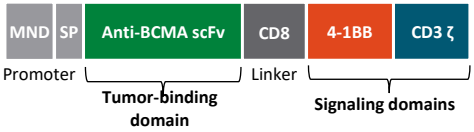
Majors. EHA 2018. Abstr PS1156. Lim. Cell. 2017;168:724. Sadelain. Nat Rev Cancer. 2003;3:35.
Brentjens. Nat Med. 2003;9:279. Park. ASH 2015. Abstr 682. Axicabtagene ciloleucel PI. Tisagenlecleucel PI.

11

Phase II KarMMA: Idecabtagene Vicleucel (Ide-cel) in Relapsed/Refractory MM



Idecabtagene CAR design



Patients with R/R MM and ≥3 prior regimens each with ≥2 consecutive cycles, prior IMiD, PI, and anti-CD38 mAb, and refractory to last therapy by IMWG criteria
(N = 158)

↓

Leukapheresed
n = 140

↓

Idecabtagene vicleucel (n = 128)
150 x 10^6 CAR T-cells (n = 4)
300 x 10^6 CAR T-cells (n = 70)
450 x 10^6 CAR T-cells (n = 54)

↓

Median Follow-Up, mo
150 x 10^6 CAR T-cells: 18.0
300 x 10^6 CAR T-cells: 15.8
450 x 10^6 CAR T-cells: 12.4
Total: 24.8

- **Primary endpoint:** ORR
- **Secondary endpoints:** CRR, safety, DoR, PFS, OS, PK, MRD, QoL, HEOR
- **Exploratory endpoints:** immunogenicity, BCMA expression/loss, cytokines, T-cell immunophenotype, GEP in BM

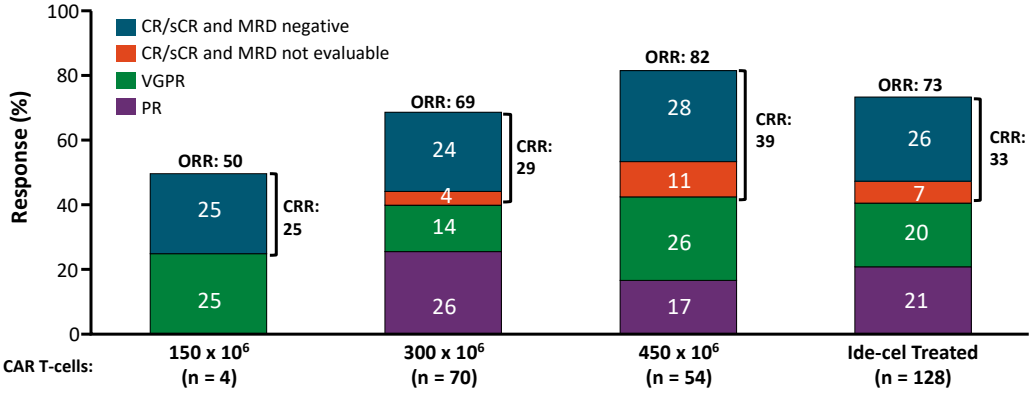
Baseline characteristics:
- High-risk cytogenetics: 35%
- Extramedullary disease: 39%
- Median no. of prior therapies: 6 (range: 3-16)
- Triple refractory: 84%

Anderson. ASCO 2021. Abstr 8016. Munshi. NEJM. 2021;384:705.

Slide credit: clinicaloptions.com

12

Phase II KarMMa Update: Clinical Response of Idecabtagene Vicleucel in R/R MM



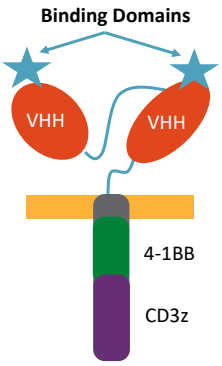
- Median time to first response: 1.0 mo (range: 0.5-8.8); median time to CR: 2.8 mo (range: 1.0-11.8)
- Median follow-up of 13.3 mo across target dose levels
- MRD-negative ($<10^{-5}$) in all treated patients (n = 128) was 26% and 79% in evaluable patients with ≥CR (n = 42)

Anderson. ASCO 2021. Abstr 8016. Munshi. NEJM. 2021;384:705.

Slide credit: clinicaloptions.com

13

CARTITUDE-1: Ciltacabtagene Autoleucel for R/R MM



- Contains 2 BCMA-targeting single-chain antibody designed to confer avidity
- Identical to the CAR construct used in the LEGEND-2 study

- Single-arm, open-label phase Ib/II trial

Patients with R/R MM per IMWG and ≥3 prior regimens or double refractory to IMiD and PI and had received IMiD, PI, and anti-CD38 mAb
(N = 113)

↓

Lymphodepletion
n = 101

↓

Ciltacabtagene autoleucel (n = 97)
Target 0.75 x 10^6 CAR T-cells (range 0.5-1 x 10^6)

Median administered dose:
0.71 x 10^6 (0.51 – 0.95 x 10^6) CAR+ viable T cells/kg

- Primary endpoints: Phase Ib: AEs; phase II: ORR

Baseline characteristics:
- High-risk cytogenetics: 23.7%
- Extramedullary disease: 13.4%
- Median no. of prior therapies: 6 (range: 3-18)
- Triple refractory: 87.6%

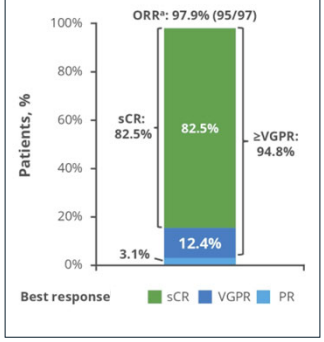
Berdeja. Lancet. 2021;398:314. Martin. JCO. 2022;[EPub]

Slide credit: clinicaloptions.com

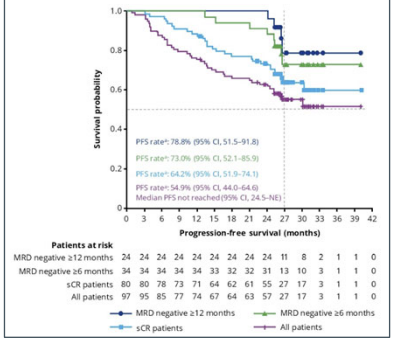
14

Landmark 2 Years Post-Last Patient-in Results of the CARTITUDE-1 Phase 1/2 Study of Cilta-Cel in Patients With RRMM: Efficacy[1,2]

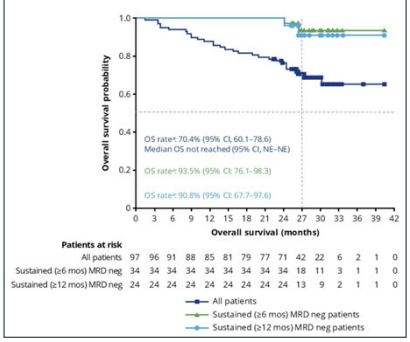
ORR BY IRC



PFS BY MRD AND RESPONSE STATUS



OS BY MRD STATUS



- Median DOR: NE (95% CI, 23.3 months-NE)
- Of 61 patients evaluable, 91.8% were MRD neg (10^{-5})
- DOR, PFS, and/or OS were shorter in subgroups with high-risk cytogenetics, ISS stage III, and high tumor burden, as well as presence of plasmacytomas

Data cutoff: January 11, 2022. Median follow-up: 27.7 months.
[a] 27-month PFS and OS rates.
1. Usmani SZ, et al. ASCO 2022. Abstract 8028. 2. Lin Y, et al. EHA 2022. Abstract P961.

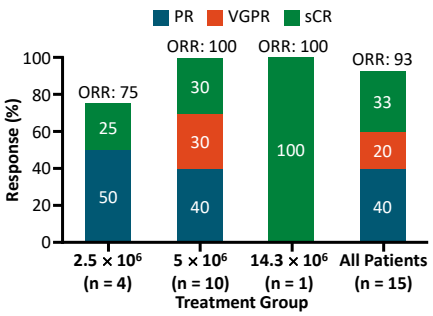
15

15

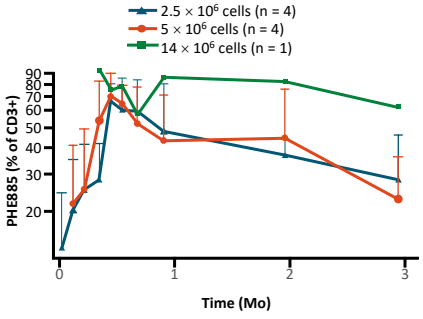
Phase I Trial of PHE885 in R/R MM: Fully Human BCMA CAR T-Cell Therapy

- PHE885: anti-BCMA CAR T-cells manufactured ex vivo with culture time of approximately 24 hr; time to manufacture final product is <2 days, relying entirely on in vivo expansion after CAR T-cell infusion
- Phase I study in heavily pretreated patients with R/R MM

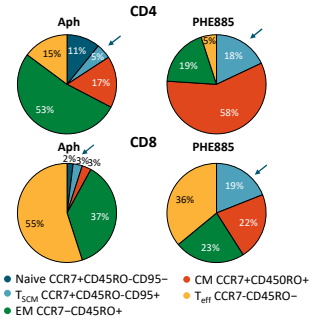
Tumor Response by Dose



Cellular Kinetics of PHE885 by Flow Cytometry



Manufacturing Process Preserves T-Cell Stemness



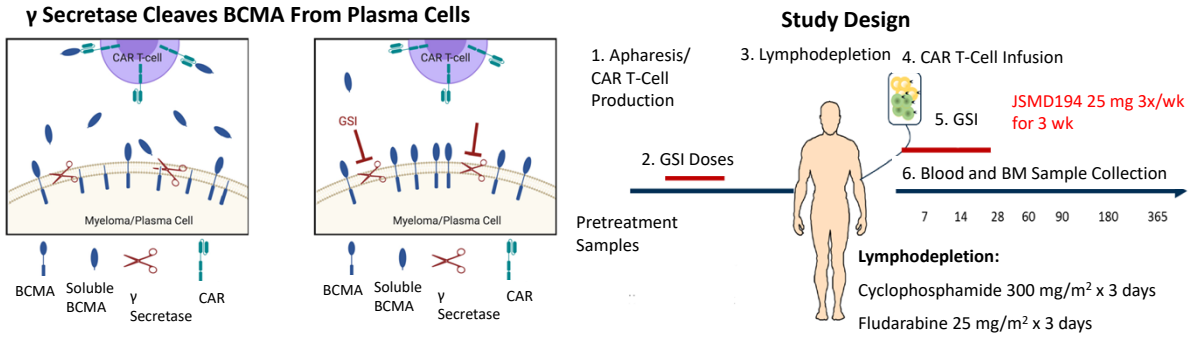
- Following PHE885 treatment, there is a shift toward naive/T_{SCM} phenotype
- Shift to T_{SCM}/T_{naive} population observed in CD4+ and CD8+ T-cells in patients with ≥ VGPR but not with PD

Sperling. ASH 2021. Abstr 3864.

Slide credit: clinicaloptions.com

16

Fully Human BCMA CAR T-Cells Combined With γ Secretase Inhibitor to Increase BCMA Expression in R/R MM



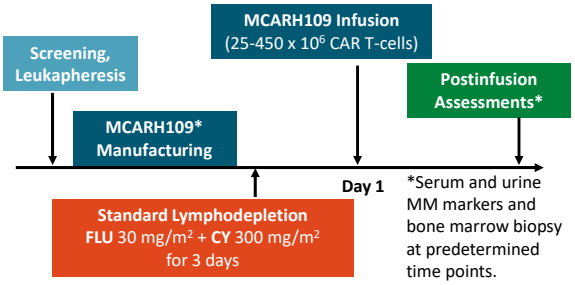
Pont. Blood. 2019;134:1585. Cowan. ASH 2021. Abstr 551.

Slide credit: clinicaloptions.com

17

GPRC5D-Targeted CAR T-Cell Therapy MCARH109 in R/R MM

- MCARH109: human-derived scFv targeting $GPRC_5D$ with 4-1BB costimulatory domain and lentiviral vector for transduction; production starts with 1:1 ratio of CD4+ and CD8+ cells
- Open-label, 3 + 3 dose-escalation phase I study enrolling adults with R/R MM after ≥3 lines of tx including PI, IMiD, and CD38 Ab
- 16 evaluable patients



Dose escalation cohorts: 25 x 10^6 → 50 x 10^6 → 150 x 10^6 → 450 x 10^6 CAR+ T-cells

Response, n (%)	25 x 10^6 CAR+ T-Cells (n = 3)	50 x 10^6 CAR+ T-Cells (n = 3)	150 x 10^6 CAR+ T-Cells (n = 5)	450 x 10^6 CAR+ T-Cells (n = 5)	Total (N = 16)
≥ PR	1 (33)	3 (100)	2 (40)	5 (100)	11 (69)
≥ VGPR	1 (33)	2 (67)	0	4 (80)	7 (44)
≥ CR	0	1 (33)	0	3 (60)	4 (25)
BM MRD negativity	2 (67)	2 (67)	2 (40)	2 (50)	8 (50)

Response, n (%)	Prior BCMA-Targeted Tx (n = 10)	Prior CAR T-Cell Tx (n = 8)
≥ PR	8 (80)	6 (75)
≥ CR	3 (30)	3 (38)
BM MRD negativity†	5 (50)	2 (25)

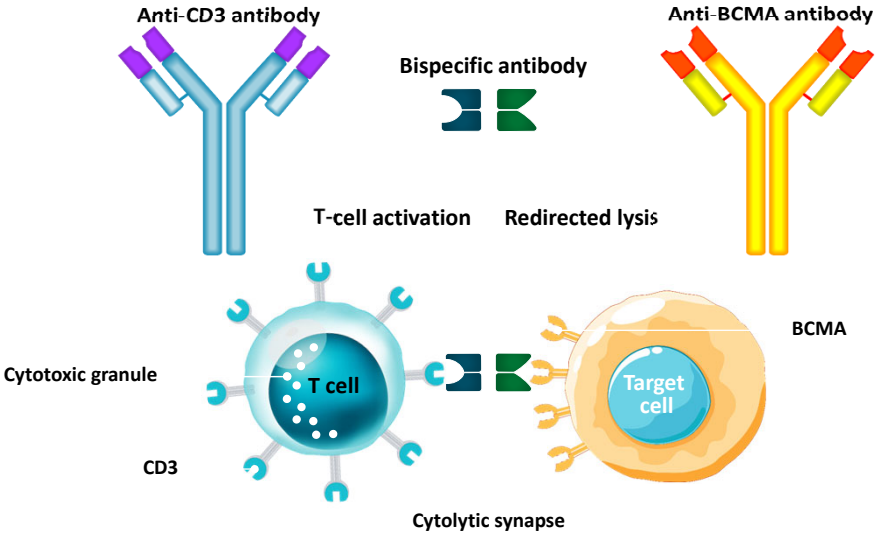
†MRD assessment by flow cytometry, sensitivity: 1 in 10^5.

Mailankody. ASH 2021. Abstr 827.

Slide credit: clinicaloptions.com

18

Bispecific T Cell Engagers

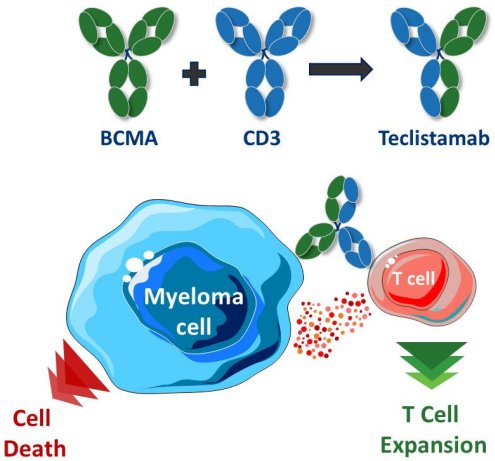


Baeuerle PA, et al. *Cancer Res*. 2009;69:4941-4944.

19

Teclistamab: BCMA x CD3 Bispecific DuoBody® Antibody

- Teclistamab (JNJ-64007957) is a humanized IgG-4 bispecific DuoBody® antibody that binds to BCMA and CD3
- Teclistamab redirects CD3+ T cells to BCMA-expressing myeloma cells to induce cytotoxicity of the targeted cells in preclinical studies[1,2]
- Teclistamab potently kills myeloma cell lines and primary myeloma cells from heavily pretreated patients[2]
- A Phase 1 first-in-human study is underway to evaluate safety and antitumor activity of teclistamab in patients with RRMM (NCT03145181)

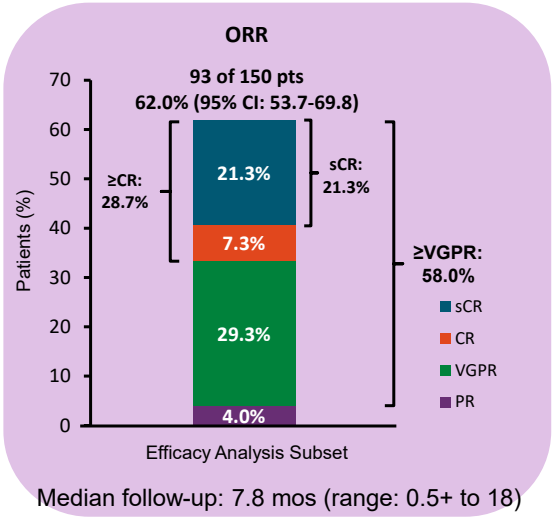


Teclistamab includes technology licensed from GenMab. [1]Labrijn AF et al. *Proc Natl Acad Sci USA*. 2013;110:5145. [2]Frerichs KA et al. *Clin Cancer Res*. 2020; doi:10.1158/1078-0432.CCR-19-2299. BCMA=B-cell maturation antigen; MM=multiple myeloma; RR=relapsed or refractory

56th ASCO Annual Meeting 2020, Usmani SZ, et al. Abstract #100 3

20

MajesTEC-1: Efficacy Outcomes



Event	All Patients (N = 165)
MRD negativity, n (%, 95% CI) ▪ At 10^{-5} ▪ At 10^{-6}	(n = 150) 37 (24.7; 18.0-32.4) 25 (16.7; 11.1-23.6)
MRD negativity with ≥CR, %	41.9
Median TTR, mo (range)	1.2 (0.2-5.5)
Median DoR, mo	Not yet reached
EFS rates, % (95% CI) ▪ 6-Mos ▪ 9-Mos	 92.5 (80.6-97.2) 85.9 (70.0-93.7)
PFS rates, % (95% CI) ▪ 6-Mos ▪ 9-Mos	 64.4 (56.0–71.7) 58.5 (48.8–67.0)
Median OS	Not yet reached

Moreau. ASH 2021. Abstr 896.

21

BCMA x CD3 Bispecific Antibodies: Summary

Therapy	Characteristics	N	Population	Safety	Response	DOR/PFS
Teclistamab[1]	▪ Bispecific ▪ IV/SC (RP2D: 1500µg/kg SC) ▪ Weekly and every other week in f/u	157	▪ At SC cohorts: ▪ Median of 5PL ▪ 79% triple refractory ▪ 38% penta refractory	▪ At RP2D: ▪ CRS 70% G1-2 ▪ Neurotox 1% (G1) ▪ Infections 50%	At RP2D, ORR: 65% with 40% sCR/CR	No mature data
AMG701[2]	▪ BiTE modified ▪ IV ▪ Weekly	82	▪ Median of 6PL ▪ 62% triple refractory	▪ CRS 55%, G3-4: 9% ▪ No ICANS ▪ 20% cytopenias	83% ORR at the top dose level and 50% VGPR	No mature data
REGN5458[3]	▪ Bispecific ▪ IV ▪ Weekly and every other week C4->	49	▪ Median of 5PL ▪ 100% triple refractory ▪ 57% penta refractory	▪ CRS 39%, no G3-4 ▪ ICANS 12% ▪ cytopenias 47% and infections 18%	62.5% at 96 mg and 95% of responders were VGPR. Some CR in lower dose levels	Preliminary median DOR: 6m
TNB-383B[4]	▪ Triple chain anti-BCMA bispecific ▪ IV fixed doses ▪ Every 3 weeks	58	▪ Median of 6PL ▪ 64% triple refractory ▪ 34% penta refractory	▪ CRS 45% and no G3-4 ▪ No ICANS ▪ Cytopenias 21% and infections 14%	80% (13% CR) at the dose levels 40-60 mg	No mature data
PF-3135[5]	▪ Bispecific ▪ SC and weekly ▪ RP2D: 1000 µg/kg	30	▪ Median of 8PL ▪ 87% triple refractory ▪ 23% prior BCMA-based therapy	▪ CRS 73% and no G3-4 ▪ ICANS 20% ▪ ISR 50%	83% ORR at RP2D	No mature data

1. Usmani SZ et al. Lancet 2021. 2. Harrison SJ, et al. Presented at ASH 2020. Abstract 181. 3. Madduri D, et al. Presented at ASH 2020. Abstract 291. 4. Rodriguez C, et al. Presented at ASH 2020. Abstract 293.5. Bahlis NJ, et al. Presented at ASCO 2021. Abstract 8006.

22

22

Updated Results From the MonumenTAL-1 Phase 1 Study of Talquetamab in Patients With RRMM: Study Design and Patients[1,2]

Key Eligibility Criteria
- RR or intolerant to established MM therapies
- Prior BCMA-targeted therapy was permitted

Dosing Schedule at RP2D
- Required premedications[a] were limited to step-up doses and 1st full dose
- MTD was not reached
- Collective data supported 2 RP2Ds for talquetamab

PHASE 1 (N=130)

- **SUBQ Talquetamab (n=30)**: 405 µg/kg SUBQ QW[b] for ≥2-3 step-up doses given prior to 1st full dose (21-day cycles)
- **SUBQ Talquetamab (n=44)**: 800 µg/kg SUBQ Q2W[b] for ≥2-3 step-up doses given prior to 1st full dose (28-day cycles)

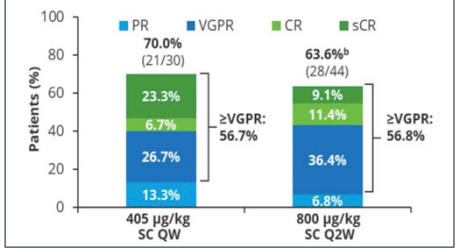
Key Objectives: RP2D (Part 1), RP2D safety/tolerability (Part 2), antitumor activity, PK, PD

Patient Characteristics		405 µg/kg QW (n=30)	800 µg/kg Q2W (n=44)
Median age, years (range)		61.5 (46-80)	64.0 (47-84)
BM plasma cells ≥60%, n (%)		6 (20.7)	5 (12.2)
Extramedullary plasmacytomas ≥1, n (%)		11 (36.7)	15 (34.1)
High-risk cytogenetics,[b] n (%)		3 (11.1)	9 (22.5)
ISS stage, n (%)	I	12 (41.4)	16 (37.2)
	II	13 (44.8)	18 (41.9)
	III	4 (13.8)	9 (20.9)
Median years since diagnosis (range)		5.6 (1.7-19.6)	6.4 (0.8-21.3)
Median prior lines of therapy (range)		6 (2-14)	5 (2-17)
Prior SCT, n (%)		27 (90.0)	33 (75.0)
Exposure status, n (%)	Triple-class	30 (100)	43 (97.7)
	Penta-drug	24 (80.0)	30 (68.2)
	BCMA	9 (30.0)	12 (27.3)
Refractory status, n (%)	Triple-class	23 (76.7)	34 (77.3)
	Penta-drug	6 (20.0)	12 (27.3)

Data cutoff: April 6, 2022.
[a] Glucocorticoid, antihistamine, antipyretic, and steroids. [b] del(17p), t(4;14), and/or t(14;16); calculated from n=27 for 405 µg/kg SUBQ QW and n=40 for 800 µg/kg SUBQ Q2W.
1. Minnema MC, et al. ASCO 2022. Abstract 8015. 2. Minnema MC, et al. EHA 2022. Abstract S182.

Updated Results From the MonumenTAL-1 Phase 1 Study of Talquetamab in Patients With RRMM: Efficacy and Summary[1,2]

ORR[a]



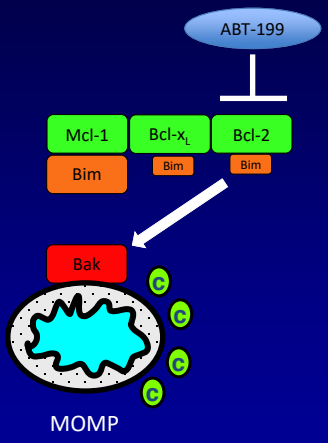
Response	405 µg/kg QW (n=30)	800 µg/kg Q2W (n=44)
Median follow-up, months (range)	13.2 (1.1-24.0)	7.7 (0.7-16.0)
ORR, n (%)	21 (70.0)	28 (63.6)
Triple-class refractory, n/N (%)	15/23 (65.2)	23/34 (67.6)
Penta-drug refractory, n/N (%)	5/6 (83.3)	9/12 (75.0)
Median time to first confirmed response, months, (range)	0.9 (0.2-3.8)	1.2 (0.3-6.8)
Median DOR, months (95% CI)	10.2 (3.0-NE)	13.0 (5.3-NE)

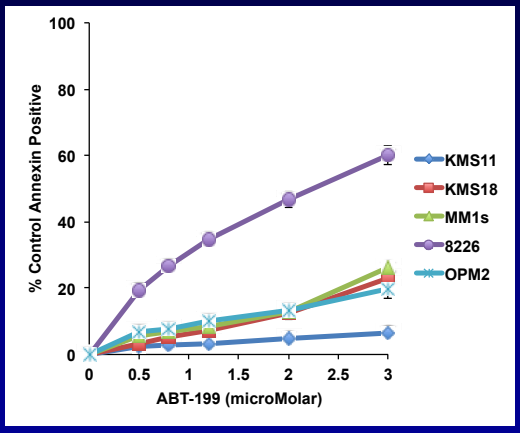
PK and PD Summary
- For both regimens, PK and PD profiles were comparable
- 17.6% of patients (13/74) had low titer antidrug Ab, which did not impact safety, efficacy, or PK
- Both regimens were associated with peripheral induction of PD-1+ T cells and consistent induction of cytokines

Authors' Conclusions
- Both doses of talquetamab had comparable safety, efficacy, and PK/PD profiles in patients with RRMM
- Longer follow-up ORR results (64% to 70%) across triple-class– and penta-drug–refractory patients confirm the efficacy of QW or Q2W schedules
- A phase 2 expansion study of both RP2Ds and phase 1 studies evaluating talquetamab combination therapy are ongoing

Data cutoff: April 6, 2022.
[a] Investigator assessment of evaluable patients per 2011 IMWG response criteria; includes unconfirmed responses.
[b] Due to rounding, individual response rates do not sum to the ORR.
1. Minnema MC, et al. ASCO 2022. Abstract 8015. 2. Minnema MC, et al. EHA 2022. Abstract S182.

Venatoclax in MM

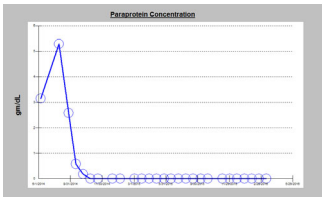




Shannon Matulis

25

The opportunity to learn from the n=1 experience



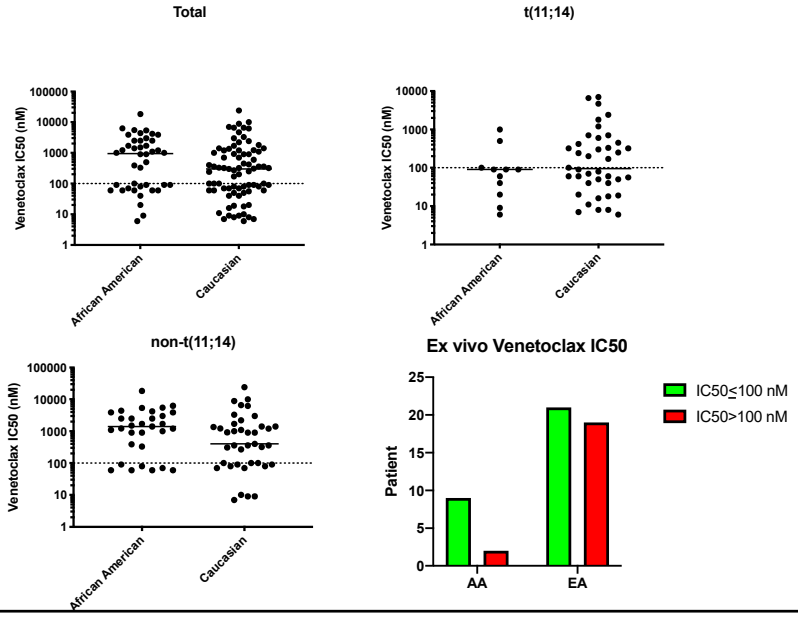
Samples	ABT-199	ABT-737	t(11;14)
MM80	0.04	ND	+
MM76-2	0.05	0.06	+
MM76-1	0.06	0.05	+
MM67	0.06	0.06	+
MM70-1	0.06	0.06	-
MM81	0.06	0.08	-
MM82	0.07	0.17	-
MM78	0.09	0.09	-
MM72	0.1	0.41	-
MM59	0.2	0.07	+
MM58-1	0.25	0.07	+
MM69	0.27	0.64	-
MM60	0.3	0.26	+
MM51	0.32	0.08	N/A
MM75	0.36	0.3	-
MM73	0.36	0.1	-
MM71	0.39	0.24	-
MM56	0.45	0.2	+
MM74	1.4	0.7	-
MM54	1.4	1.1	-
MM68	1.4	2	-
MM55	1.7	0.1	-
MM58 - 2	1.98	ND	+
MM54-2	2	1	-
MM64	2.2	1.1	-
MM52	2.3	0.69	-
MM65	2.5	2.4	-
MM66	3.3	2.4	-
MM62	4.2	1.2	-
MM61	4.7	2.7	+
MM49	6.7	4.1	N/A
MM70-2	7	0.4	-
MM79	10	5.6	-
MM77	12	ND	+
MM63	30.2	18.4	-

IC50 (µM)

EMORY WINSHIP CANCER INSTITUTE

26

AA t(11;14) myeloma trend towards Venetoclax sensitivity

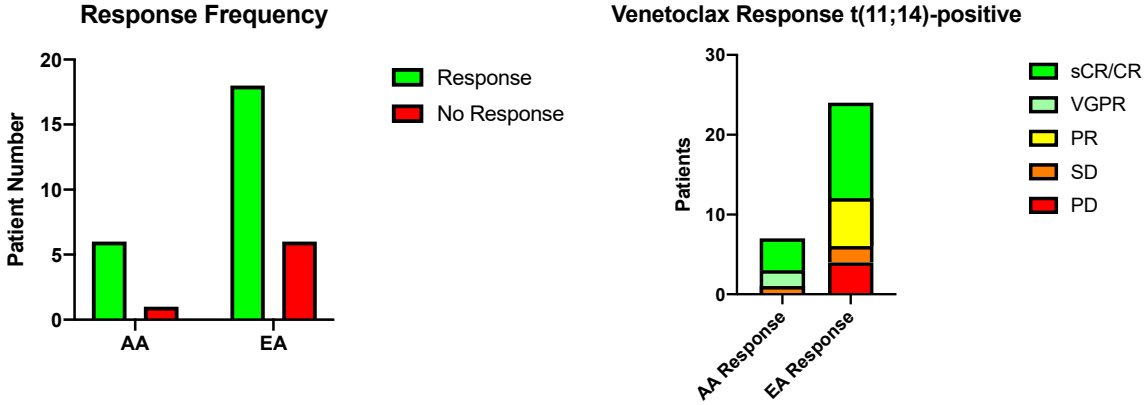


EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center

Shannon Matulis
Vikas Gupta
Ajay Nooka

27

Responses of t(11;14) patients to Ven-containing regimens



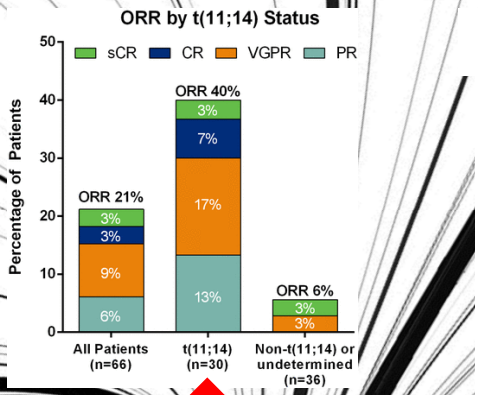
Patient	Response Rate	VGPR or better
EA	75%	50%
AA	86%	86%

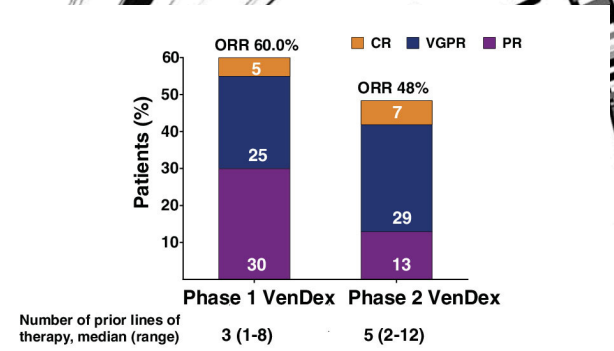
EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center

Shannon Matulis
Vikas Gupta
Ajay Nooka

28

TARGETING BCL2 IS EFFECTIVE IN PATIENTS WITH t(11;14) MYELOMA





Kaufman *et al., Am. J. Hematol.*, 2021

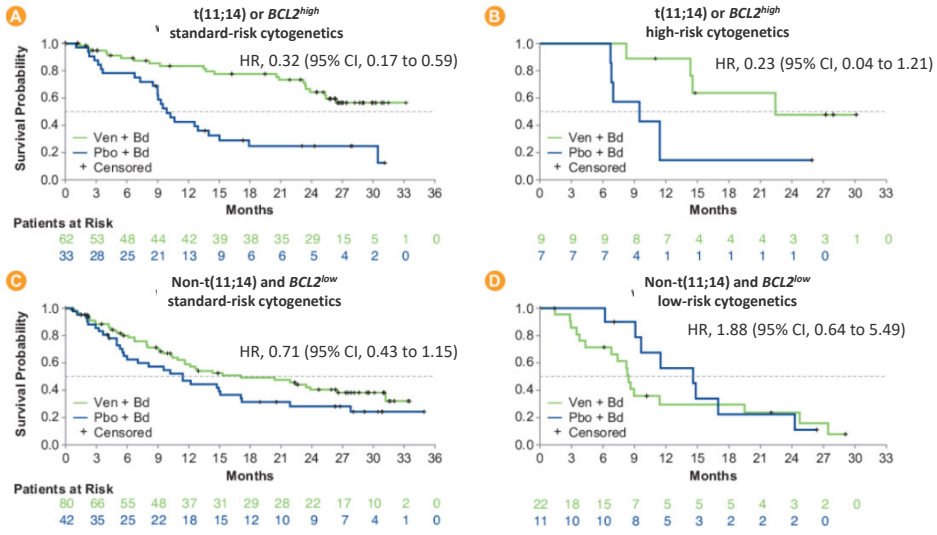
Kumar *et al., Blood*, 2018

Jonathan Kaufman
Sagar Kumar

WINSHIP CANCER INSTITUTE OF EMORY UNIVERSITY | NCI Designated Comprehensive Cancer Center

29

PFS Is Significantly Prolonged with Venetoclax in Patients With t(11;14) or *BCL2*^{high}, but Not in Patients With Non-t(11;14), *BCL2*^{low} MM

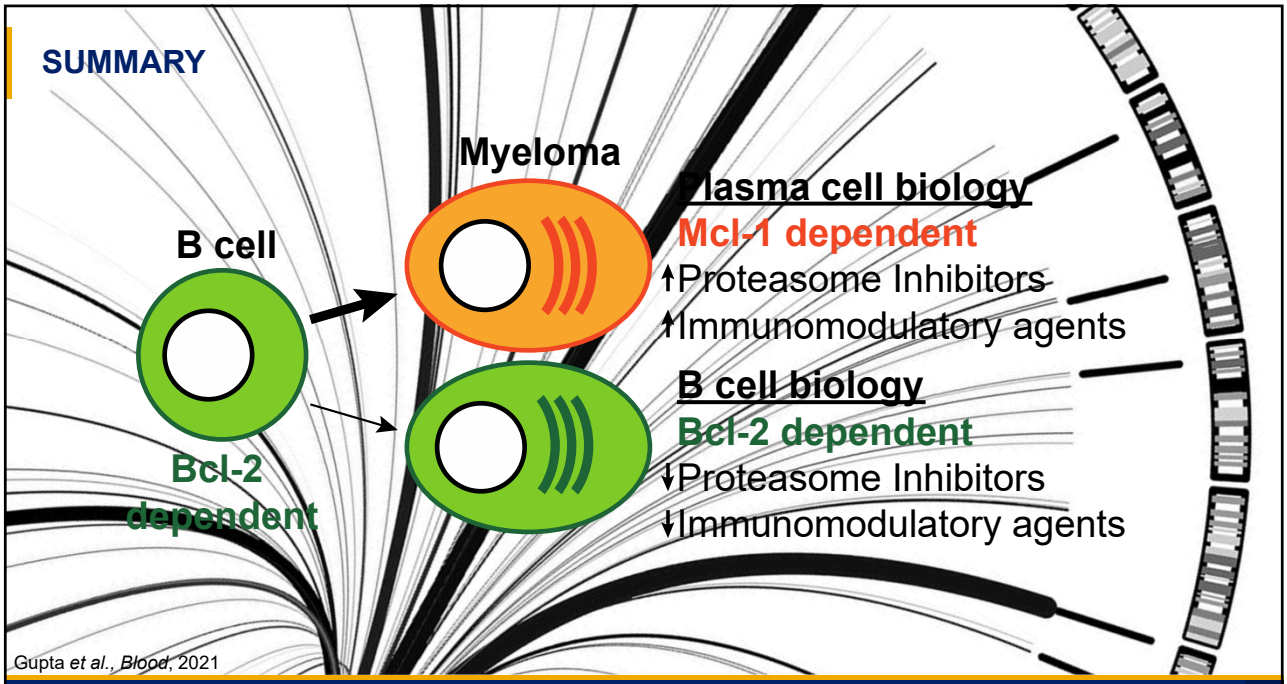


Kumar S, et al. EHA 2020. Abstract EP939. High *BCL2* gene expression was determined by qPCR.

30

30

SUMMARY



Gupta *et al.*, *Blood*, 2021

31

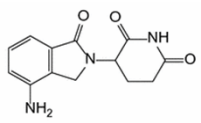
New CELMoD® agents in development

- LEN and POM (a subgroup of CELMoD® agents) helped to transform therapy and drive survival in MM[1-3]
- Rational selection of molecules based on **deep scientific understanding of CRBN and MM biology: IBER and CC-92480**[4-6]

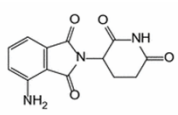
2019 and 2020:

First clinical data for new CELMoD® agents (IBER and CC-92480) in MM

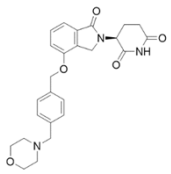
LEN



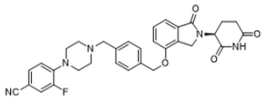
POM



IBER



CC-92480



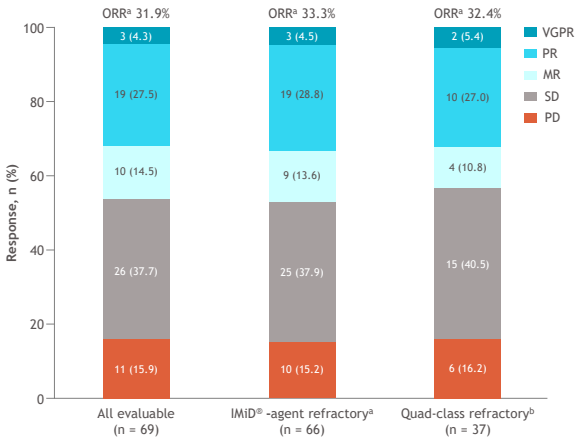
IBER (CC-220) and CC-92480 are investigational products, currently not approved by any regulatory agency.

CELMoD®, cereblon E3 ligase modulator; CRBN, cereblon; IBER, iberdomide; LEN, lenalidomide; MM, multiple myeloma; POM, pomalidomide.

1. Rajkumar SV, et al. *Lancet Oncol* 2010;11:29-37; 2. Facon T, et al. *Blood* 2018;131:301-310; 3. Durie BGM, et al. *Blood Cancer J* 2020;10:53; 4. Ito T, Handa H. *Int J Hematol* 2016;104:293-299; 5. Matyskiela ME, et al. *J Med Chem* 2018;61:535-542; 6. Hansen JD, et al. *J Med Chem* 2020;63:6648-6676.

32

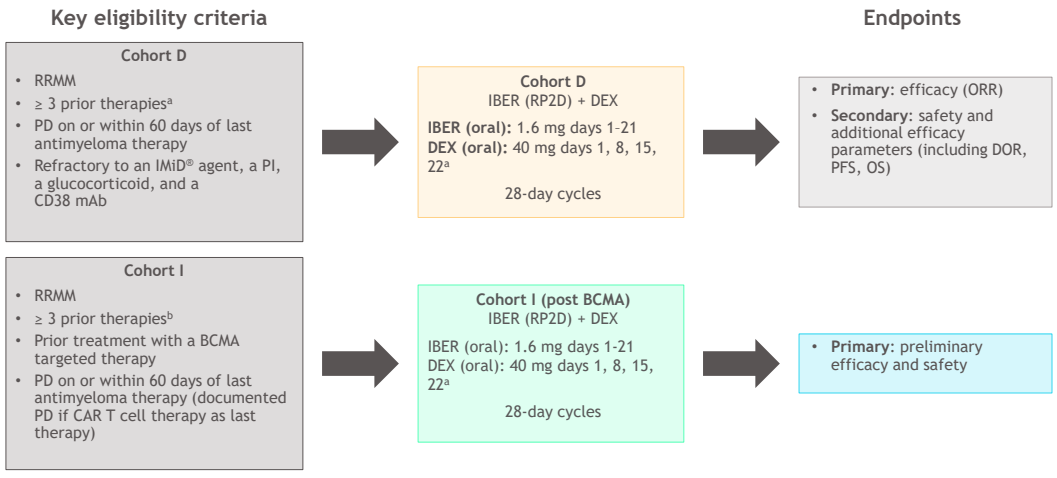
CC-220-MM-001: Response rates and safety



Common (> 20% all grade) TEAEs and events of interest, n (%)	Cohort B (IBER + DEX) (N = 75)		
	All grade	Grade 3	Grade 4
Anaemia	32 (42.7)	20 (26.7)	1 (1.3)
Neutropenia	30 (40.0)	13 (17.3)	12 (16.0)
Febrile neutropenia	4 (5.3)	4 (5.3)	0
Thrombocytopenia	13 (17.3)	3 (4.0)	5 (6.7)
Infection	38 (50.7)	16 (21.3)	1 (1.3)
Fatigue	26 (34.7)	0	1 (1.3)
Insomnia	23 (30.7)	0	0
Back pain	16 (21.3)	6 (8.0)	0
Muscle spasms	15 (20.0)	0	0
Diarrhoea	15 (20.0)	0	0
Constipation	11 (14.7)	1 (1.3)	0
Peripheral sensory neuropathy	4 (5.3)	1 (1.3)	0
Deep vein thrombosis	1 (1.3)	0	0
Pulmonary embolism	1 (1.3)	1 (1.3)	0

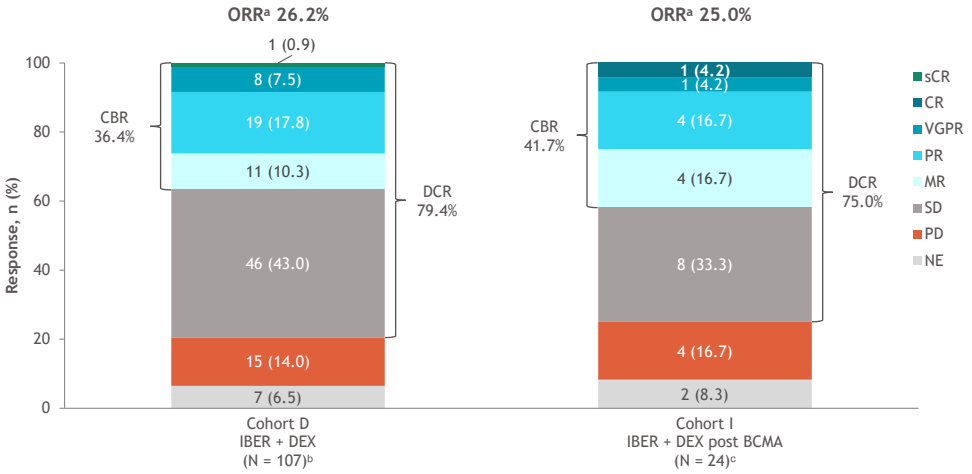
IBER (CC-220) is an investigational product, currently not approved by any regulatory agency.
[a]PR or better
Evaluable patients include patients who have received ≥ 1 dose of IBER, had measurable disease at baseline, and ≥ 1 post-baseline response assessment; [a] Refractory to LEN or POM; [b] Refractory to ≥ 1 IMiD® agent, 1 PI, 1 anti-CD38 mAb, and 1 steroid. MR, minimal response; ORR, overall response rate; PR, partial response; SD, stable disease; TEAE, treatment-emergent adverse event; VGPR, very good partial response. Lonial S, et al. Oral presentation at ASCO 2019; abstract 8006; Lonial S, et al. *Blood* 2019;134(suppl 1). Abstract 3119.

CC-220-MM-001: dose-expansion phase; Cohorts D and I



IBER (CC-220) is an investigational product, currently not approved by any regulatory agency.
[a] Including LEN, POM, a PI, a glucocorticoid, and an anti-CD38 mAb; [b] Including LEN or POM, a PI, an anti-CD38 mAb, and a BCMA therapy.
CAR, chimeric antigen receptor; DOR, duration of response; OS, overall survival; PFS, progression-free survival.
Lonial S, et al. Oral presentation at ASH 2021; abstract 162.

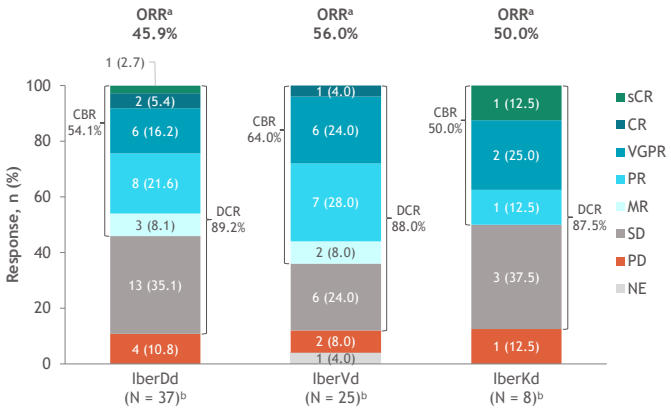
CC-220-MM-001: response



IBER (CC-220) is an investigational product, currently not approved by any regulatory agency.
[a] PR or better; [b] 2 patients in SD and MR discontinued treatment because of death due to COVID-19; [c] Includes all treated patients who have post-baseline efficacy assessment or have discontinued treatment before any post-baseline efficacy assessment (2 patients were in C1 with no post-baseline efficacy assessments so were excluded from analysis).
C, cycle; CBR, clinical benefit rate; COVID, coronavirus disease; CR, complete response; DCR, disease control rate; NE, not evaluable; sCR, stringent complete response.
Lonial S, et al. Oral presentation at ASH 2021; abstract 162.

CC-220-MM-001: IBER in combination with DEX and DARA, BORT, or CFZ (Cohorts E, F and G) in patients with RRMM

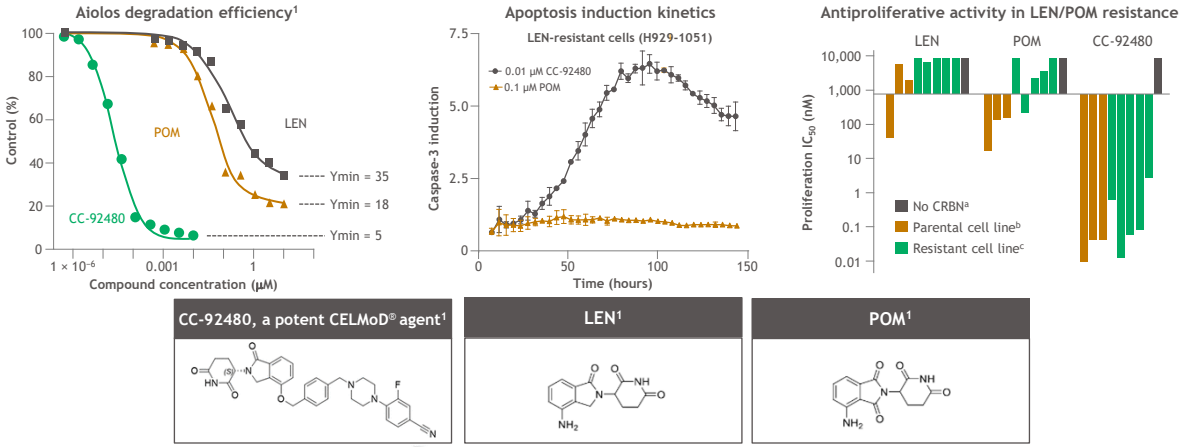
- IBER + DEX in combination with DARA or BORT or CFZ showed a favourable safety profile in patients with heavily pretreated RRMM; TEAEs were mainly hematologic and well manageable
- The RP2D was determined at 1.6 mg in the IberDd cohort, while dose evaluation continues in the IberVd and IberKd cohorts
- Promising efficacy was observed even among patients refractory to IMiD® agents, DARA, and PIs



IBER (CC-220) is an investigational product, currently not approved by any regulatory agency.
[a] PR or better; [b] Excludes treated patients who did not reach any post-baseline efficacy assessment and were still on treatment at time of data cut-off.
Lonial S, et al. Oral presentation at EHA 2021; abstract S187.

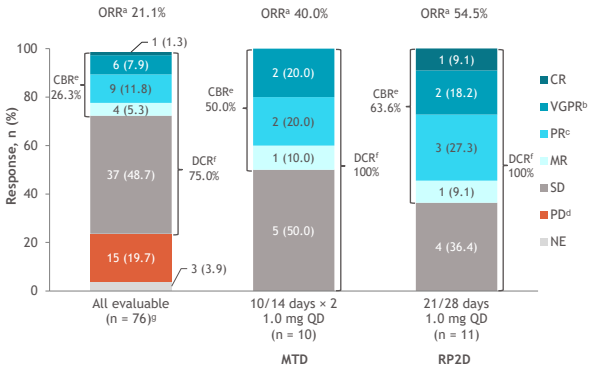
CC-92480 is a novel CELMoD® agent[1,2]

Efficient substrate degradation leading to apoptosis and potent antiproliferative activity in LEN and POM resistance[3]



CC-92480 is an investigational product, currently not approved by any regulatory agency.
[a] DF15R; [b] DF15, H929, and OPM-2; [c] H929R1, H929R2, OPM-2R1, OPM-2R2, and OPM-2R3. IC_{50}, 50% inhibitory concentration; Ymin, maximum degradation point.
1. Hansen JD, et al. *J Med Chem* 2020;63:6648-6676; 2. Wong L, et al. *Blood* 2019;134(suppl 1). Abstract 1815; 3. Richardson PG, et al. Oral presentation at ASCO 2020; abstract 8500.

CC-92480-MM-001: efficacy and safety in patients with heavily pretreated RRMM



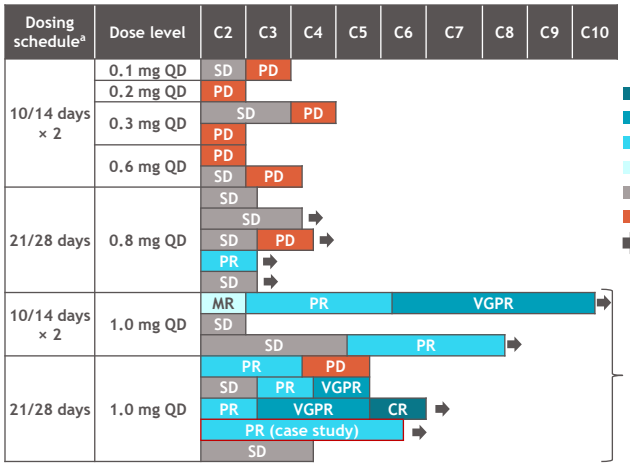
Common (> 20% all grade) TEAEs and events of interest, n (%)	All doses (N = 76)	
	Grade 3	Grade 4
Neutropenia	23 (30.3)	26 (34.2)
Febrile neutropenia	4 (5.3)	1 (1.3)
Anaemia	24 (31.6)	-
Thrombocytopenia	5 (6.6)	7 (9.2)
Fatigue	7 (9.2)	-
Pyrexia	3 (3.9)	-
Peripheral sensory neuropathy	-	-
Diarrhoea	1 (1.3)	-
Nausea	1 (1.3)	-
Deep vein thrombosis	-	-
Infections	25 (32.9)	2 (2.6)
Pneumonia[h]	11 (14.5)	-

- Prophylactic G-CSF was not permitted during C1
- Neutropenia was managed with dose interruption/reduction and G-CSF
- Dose reduction of CC-92480 occurred in 17 (22.4%) patients
- No patients discontinued due to treatment-related AEs

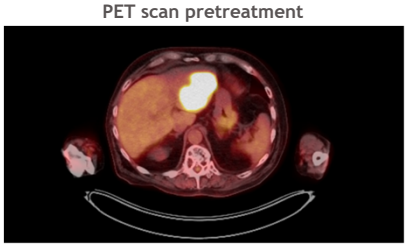
CC-92480 is an investigational product, currently not approved by any regulatory agency.
[a] PR or better; [b] 1 patient in the 21/28-day 1.0-mg QD cohort had an unconfirmed VGPR at time of data cut-off; [c] 2 patients in the 21/28-day 0.8-mg QD cohort had an unconfirmed PR at time of data cut-off; [d] 1 patient in the 21/28-day 0.8-mg QD cohort had an unconfirmed PD at time of data cut-off; [e] CBR defined as MR; [f] DCR defined as SD; [g] 1 patient had a pending response assessment at time of data cut-off; [h] Includes Medical Dictionary for Regulatory Activities Terminology version 22.0 preferred terms pneumonia, pneumocystis jirovecii pneumonia, respiratory syncytial viral pneumonia, and staphylococcal pneumonia. AE, adverse event; G-CSF, granulocyte-colony stimulating factor.
Richardson PG, et al. Oral presentation at ASCO 2020; abstract 8500.

CC-92480-MM-001: responses in patients with extramedullary disease

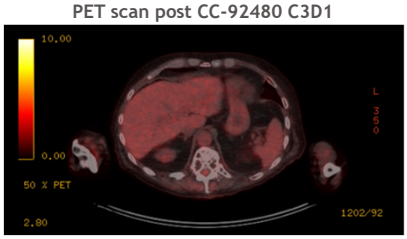
Only patients on continuous schedules are shown



PET scan pretreatment



PET scan post CC-92480 C3D1



CC-92480 is an investigational product, currently not approved by any regulatory agency.

[a] 1 patient in the 21/28-day 1.0-mg QD cohort had an unconfirmed VGPR at time of data cut-off; [b] 1 patient in the 21/28-day 0.8-mg QD cohort had an unconfirmed PR at time of data cut-off; [c] 1 patient in the 21/28-day 0.8-mg QD cohort had an unconfirmed PD at time of data cut-off. EMP, extramedullary plasmacytoma; PET, positron emission tomography.

Richardson PG, et al. Oral presentation at ASCO 2020; abstract 8500.

The Future is Very Bright

- New targets and modalities (CART, TCE, ADC) and others in development have the potential to bring together multiple modalities to eliminate the malignant clone
- Trials testing combinations that rely not only on immune but existing targets such as Pis, IMIDs, steroids, and CD38 will be key
- Precision medicine currently a reality and hopefully will be more important as we develop drugs for common mutations

Patients and Families

Thanks to:

Jonathan Kaufman
Ajay Nooka
Craig Hofmeister
Madhav Dhodapkar
L.T. Heffner
Vikas Gupta
Nisha Joseph
Leon Bernal
Charise Gleason
Donald Harvey
Colleen Lewis
Amelia Langston
Y. Gu
S-Y Sun
Jing Chen
Mala Shanmugan
Larry Boise
Cathy Sharp
Jennifer Shipp

And the Clinical Research Team

IMS

Golfers Against Cancer
T.J. Martell Foundation

And many others who are part of the B-cell team

41

ASK A QUESTION

UNDERSTANDING MY TREATMENT OPTIONS: MULTIPLE MYELOMA

Ask a question by phone:

Press star (*) 1 on your keypad to ask a question
To remove your question press star (*) 2 on your keypad

Ask a question by web:

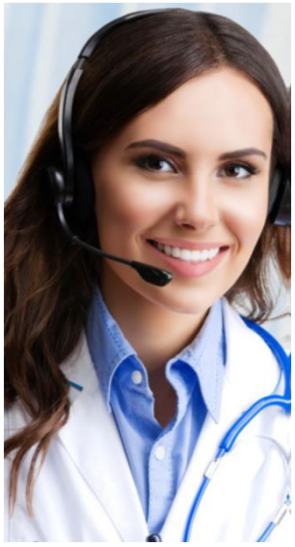
Type your question in the “Ask a question” box under the speaker video window

Due to time constraints, we can only take one question per person.
Once you’ve asked your question, the operator will transfer you back into the audience line.

42

42

LLS EDUCATION & SUPPORT RESOURCES

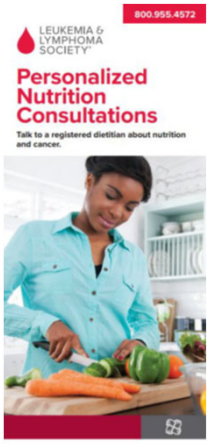


HOW TO CONTACT US:

To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
Email: www.LLS.org/ContactUs
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation



NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLS.org/Consult.

LEUKEMIA & LYMPHOMA SOCIETY

43

LLS EDUCATION & SUPPORT RESOURCES

Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit **www.LLS.org/Chat**.

Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit **www.LLS.org/EducationVideos**.

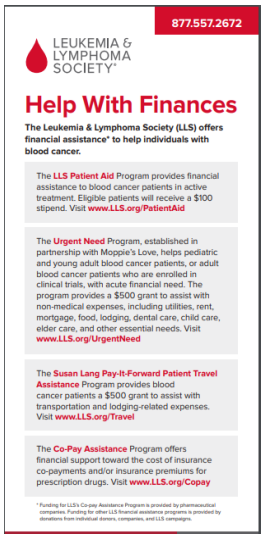
Patient Podcast

The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit **www.TheBloodline.org**.

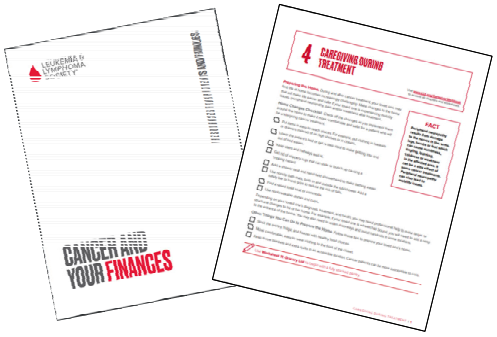
LEUKEMIA & LYMPHOMA SOCIETY

44

LLS EDUCATION & SUPPORT RESOURCES



The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers: www.LLS.org/Finances



To order free materials: **www.LLS.org/Booklets**

LEUKEMIA & LYMPHOMA SOCIETY

45

45

46