Clinical outcome of multiple myeloma patients with relapsed disease after BCMA-targeted CAR T treatment.

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Disclosure

I have no financial disclosure or conflicts of interest with the presented material in this presentation.

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Background

- **CAR T** and **bispecific antibodies** offer hope to heavily pretreated patients
- Deep responses with possibly **profound impact on disease course**
- Most patients with relapsed/refractory myeloma eventually relapse
- Important questions remain after relapse on these novel agents

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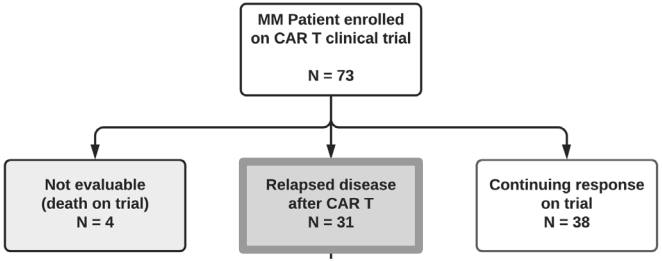
BCMA-targeted CAR T study cohort



- 73 patients treated with BCMA-targeted CAR T
- **N = 31 patients with relapsed disease**
- Time of relapse after CAR T = start of analysis

- 3 different CAR T products

- Median **age** 61 years (range 35-75)
- Median **time from diagnosis** 74 months (range 22-282)
- 84% with **high-risk** characteristics on FISH
- Median 5 **prior treatment lines** (range 1-18)

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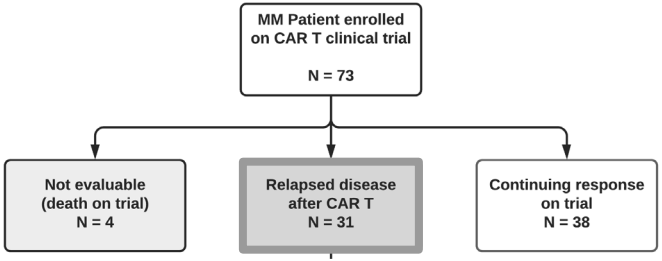
BCMA-targeted CAR T study cohort



- 73 patients treated with BCMA-targeted CAR T
- **N = 31 patients with relapsed disease**
- Prior treatment exposure:

TREATMENT	% EXPOSED	% REFRACTORY
ASCT	90%	-
Lenalidomide	100%	74%
Pomalidomide	87%	84%
Bortezomib	90%	61%
Carfilzomib	94%	87%
Ixazomib	23%	23%
CD38 mAb	97%	97%
Alkylating agents	100%	54%
Venetoclax	19%	19%
Selinexor	19%	19%
Bispecific antibodies	13% (n = 4)	13%
Triple-class refractory	-	84%

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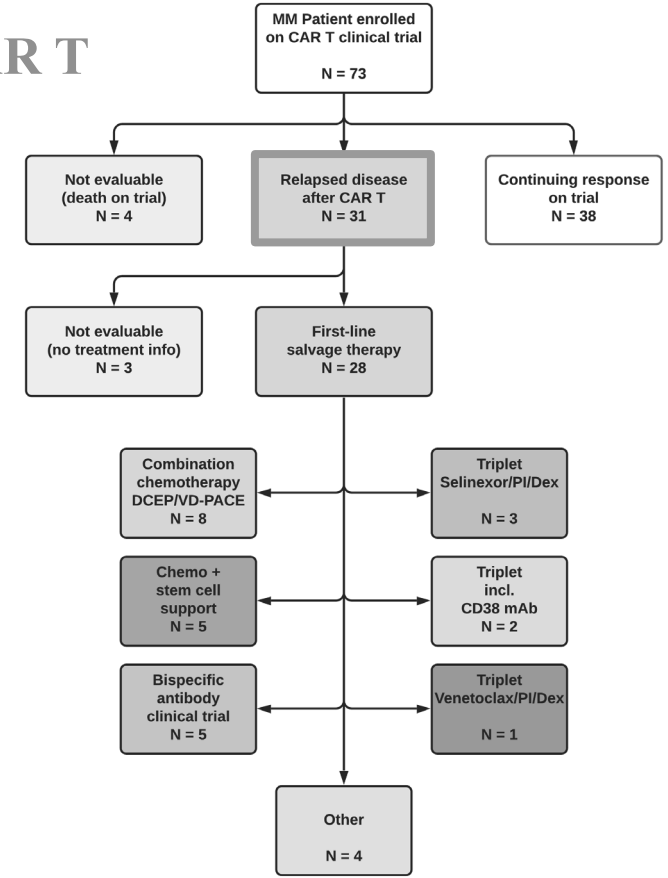
Outcome after relapse on BCMA-targeted CAR T

- 28 patients received salvage therapy
- Median time from relapse to subsequent treatment: 30 days (range 0-201)
- Median of 2 additional treatment lines (range 0-8)
- **Most common <u>initial</u> treatment:**
  - DCEP±V or VD(T)-PACE: 8/28 (29%)
  - Chemo → stem cell support: 5/28 (18%)
  - Bispecific antibody: 5/28 (18%)
  - Selinexor + doublet: 3/28 (11%)
  - CD38 mAb + doublet: 2/28 (7%)
  - Venetoclax + doublet 1/28 (4%)
  - Other 4/28 (14%)



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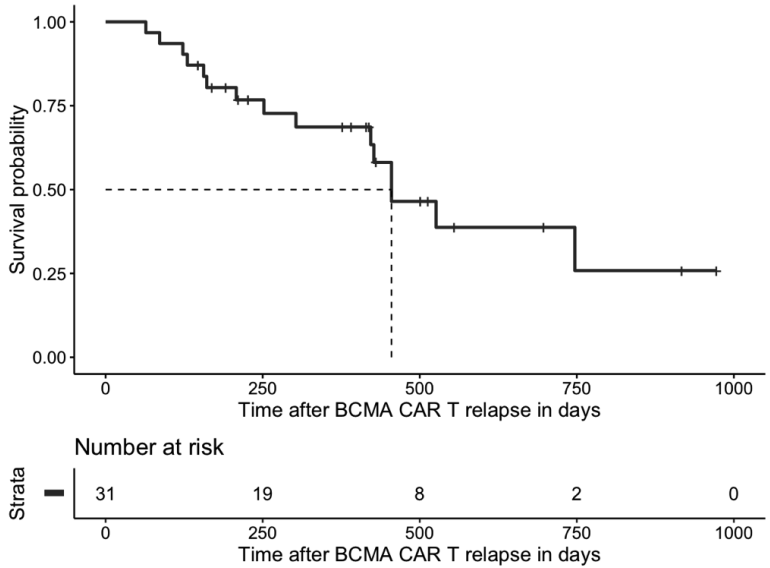
Outcome after relapse on BCMA-targeted CAR T

- ORR of initial treatment: 46%
  - 7 CR, 5 VGPR, 1 PR, 7 SD, 8 PD

- **Median PFS of first-line salvage treatment:**
  105 days (95% CI: 78-204 days)

- **Median OS:**
  455 days (15 mo) with median FU of 501 days



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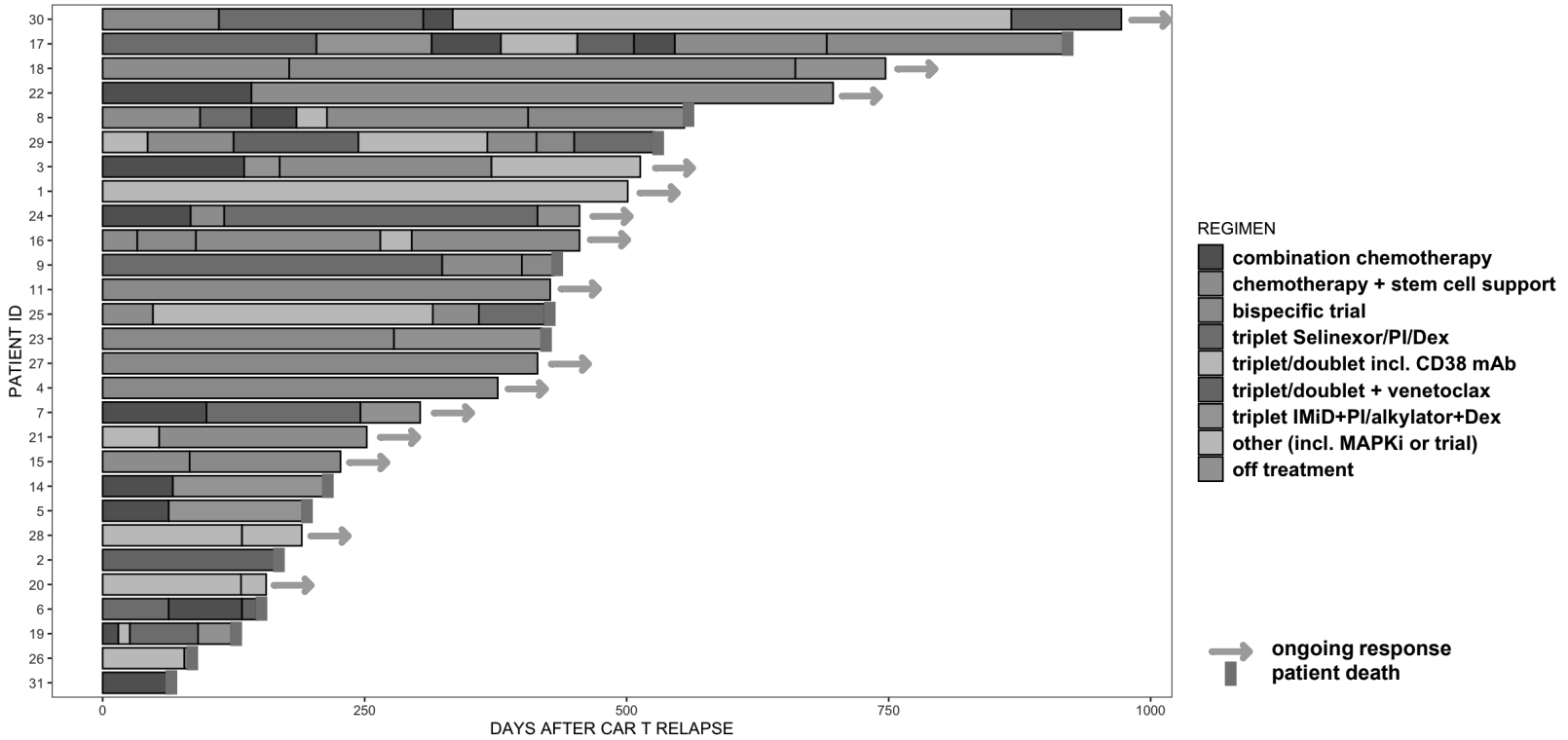
Post-CAR T salvage treatments & duration of response



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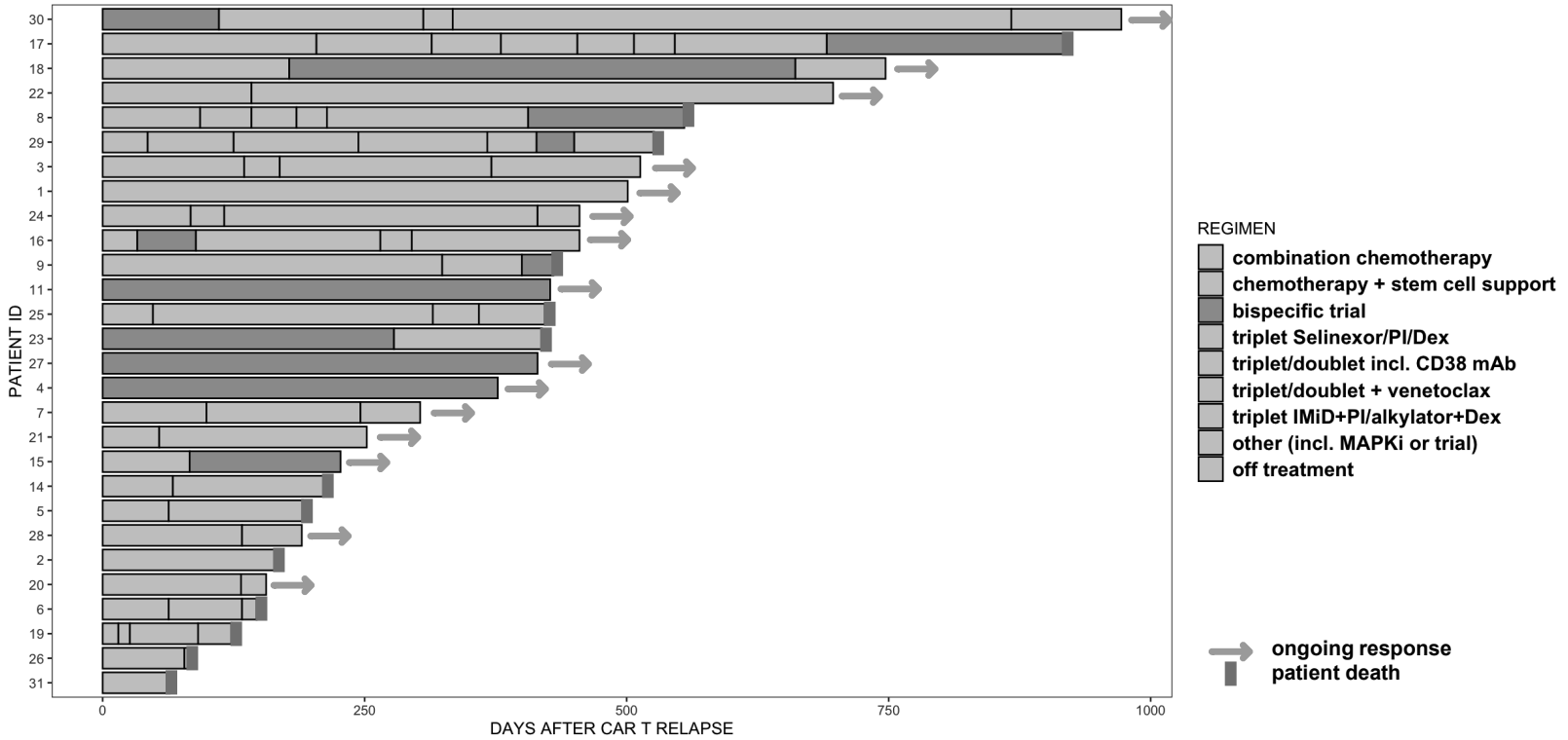
Post-CAR T salvage treatments & duration of response



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Durable responses after relapse on BCMA-targeted CAR T

- 33 occurrences of **responses > 120 days (range 128-555 days)** at various treatment lines post-relapse

- **Durable response treatment regimens:**
  - Chemo + stem cell support N = 8
  - **Bispecific antibodies** (incl. BCMA-targeted) N = 8
  - Selinexor + doublet N = 5
  - MAPK inhibition ± other N = 3 *

** Also see poster abstract P-090: Agte S. et al. BRAF V600E Multiple Myeloma Patient Salvaged With Triple MAPK Inhibition After CAR T Relapse*

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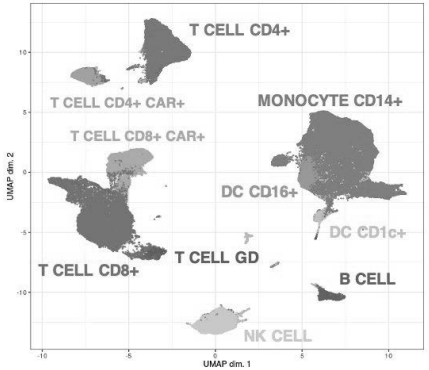
Single-cell pipeline to characterize CAR T relapse

- Collection of peripheral blood mononuclear cells (PBMC) and bone marrow aspirates (BMA)
  - Screening
  - Various timepoints post-infusion (e.g. CRS)
  - Relapse

- Deconvolute different contributing factors to relapse:
  - Clinical characteristics
  - Tumor genomics (WGS, Tapestri)
  - Micro-environment (CyTOF, CITE-seq)
  - Cytokine milieu (Olink)
  - Antigen loss, anti-drug antibodies, …

David Melnekoff

Yogita Ghodke



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Conclusions

- BCMA-targeted CAR T approved for MM, more products in development
- Profound impact on disease course; relapse occurs after CAR T

*There is **"life after CAR T"***

- RRMM patients relapsing after CAR T therapy can be salvaged
- First-line salvage: ORR 46%, PFS 105 days
- Sometimes multiple lines of treatment to contributing to OS of 15 months

- Choice of treatment varies based on patient characteristics
  - Bispecific for patients fit and eligible for clinical trial
  - Patients with cytopenias could benefit from stem cell support
  - Other options incl. triplets with selinexor, venetoclax,… show activity

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Thank you to all patients!

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Thank you for your attention.
Happy to answer any questions!