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

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International Myeloma Workshop 2021, Vienna
Disclosure

I have no financial disclosure or conflicts of interest with the presented material in this presentation.
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
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)
BCMA-targeted CAR T study cohort

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

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>% EXPOSED</th>
<th>% REFRACTORY</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCT</td>
<td>90%</td>
<td>-</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>100%</td>
<td>74%</td>
</tr>
<tr>
<td>Pomalidomide</td>
<td>87%</td>
<td>84%</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>90%</td>
<td>61%</td>
</tr>
<tr>
<td>Carfilzomib</td>
<td>94%</td>
<td>87%</td>
</tr>
<tr>
<td>Ixazomib</td>
<td>23%</td>
<td>23%</td>
</tr>
<tr>
<td>CD38 mAb</td>
<td>97%</td>
<td>97%</td>
</tr>
<tr>
<td>Alkylating agents</td>
<td>100%</td>
<td>54%</td>
</tr>
<tr>
<td>Venetoclax</td>
<td>19%</td>
<td>19%</td>
</tr>
<tr>
<td>Selinexor</td>
<td>19%</td>
<td>19%</td>
</tr>
<tr>
<td>Bispecific antibodies</td>
<td>13% (n = 4)</td>
<td>13%</td>
</tr>
<tr>
<td>Triple-class refractory</td>
<td>-</td>
<td>84%</td>
</tr>
</tbody>
</table>
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 initial 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%)
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
Post-CAR T salvage treatments & duration of response

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REGIMEN
- combination chemotherapy
- chemotherapy + stem cell support
- bispecific trial
- triplet Selinexor/PI/Dex
- triplet/doublet incl. CD38 mAb
- triplet/doublet + venetoclax
- triplet IMiD+PI/alkylator+Dex
- other (incl. MAPKi or trial)
- off treatment

ongoing response
patient death
Post-CAR T salvage treatments & duration of response

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ongoing response
patient death
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
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, …
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
Acknowledgements

Parekh Lab
Sarita Agte
Adolfo Aleman
David Melnekoff
Yogita Ghodke
Bhaskar Upadhyaya
Alessandro Laganà
Samir Parekh

Fellows & residents
Tarek H. Mouhieddine
Darren Pan
Guido Lancman
Megan Metzger

Myeloma Center of Excellence
Sundar Jagannath
Shambavi Richard
Ajai Chari
Larysa Sanchez
Hearn Cho
Joshua Richter
Cesar Rodriguez
Adriana Rossi
All nurses and clinical staff

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