Safety and Efficacy of Daratumumab with Lenalidomide and Dexamethasone in Relapsed or Relapsed and Refractory Multiple Myeloma.

Torben Plesner¹, Hendrik-Tobias Arkenau², Henk M. Lokhorst³, Peter Gimsing⁴, Jakub Krejcik¹, Charlotte Lemech², Monique Minnema³, Ulrik Niels Lassen³, Tahamtan Ahmadi⁵, Howard Yeh⁵, Mary Guckert⁵, Huaibao Feng⁵, Nikolai C. Brun⁶, Steen Lisby⁶, Linda Basse⁶, Antonio Palumbo⁷, Paul G. Richardson⁸

¹Vejle Hospital, Vejle, Denmark; ²Sarah Cannon Research Institute, London, United Kingdom; ³Department of Hematology, University Medical Center Utrecht, Utrecht, Netherlands; ⁴Rigshospitalet, Copenhagen, Denmark; ⁵Janssen Research & Development, USA; ⁶Genmab A/S, Copenhagen, Denmark; ⁷University of Torino, Azienda Ospedaliero-Universitaria (AOU) S. Giovanni Battista Torino, Torino, Italy; ⁸Dana-Farber Cancer Institute, Boston, MA
Daratumumab

- A human CD38 mAb with broad-spectrum killing activity of CD38-expressing tumor cells
- DARA+LEN enhanced killing of MM cells *in vitro* and is hypothesized to lead to synergistically higher efficacy in clinical setting.

Study Objective

- To evaluate safety and efficacy of DARA+LEN+DEX in patients with relapsed, or relapsed and refractory (RR) MM

Presented by: Torben Plesner
Study Design

Part 1 - Dose Escalation
Open-label weekly iv infusion, Dose escalation: 3+3 scheme

- 2-16 mg/kg
- Cycle 1
- Cycle 2
- Cycle 3-6
- Cycle 7-24
- Follow-Up

Part 2 - Expansion Cohort
Open-label single arm iv infusion at 16 mg/kg

- 16 mg/kg
- Cycle 1
- Cycle 2
- Cycle 3-6
- Cycle 7-24
- Follow-Up

Daratumumab infusions, (First infusion includes pre-dose the day before)
Lenalidomide treatment day 1-21 25 mg po
Dexamethasone weekly 40 mg

Table:

<table>
<thead>
<tr>
<th></th>
<th>2 mg/kg (N=3)</th>
<th>4 mg/kg (N=3)</th>
<th>8 mg/kg (N=4)</th>
<th>16 mg/kg Part 1 (N=3)</th>
<th>16 mg/kg Part 2 (N=9)</th>
<th>Total (N=12)</th>
<th>Total (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusions per patient, Median (range)</td>
<td>21.0 (13; 26)</td>
<td>23.0 (22; 24)</td>
<td>20.0 (17; 21)</td>
<td>11.0 (10; 16)</td>
<td>2.0 (1; 4)</td>
<td>2.5 (1; 16)</td>
<td>12.0 (1; 26)</td>
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<tr>
<td>Duration of infusion (hours), n, Median (range)</td>
<td>60 (5.8; 11.9)</td>
<td>69 (5.7; 10.3)</td>
<td>78 (5.6; 9.3)</td>
<td>36 (5.8; 8.5)</td>
<td>19 (5.8; 12.2)</td>
<td>55 (5.8; 12.2)</td>
<td>262 (5.6; 12.2)</td>
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Results

Demographics and Baseline Characteristics

• Data from 22 patients (16 men, 6 women) are evaluable to date.
• Median age 62 (48-76) years
• Median prior therapies: 2.5 (1-4)
• 13 patients had ECOG status 0; 8 patients had ECOG status 1
• 3 patients (1 in 4 mg/kg group and 2 in 8 mg/kg group) LEN refractory.

Safety

• AEs (>30% patients): neutropenia, diarrhea
• MTD not reached
• No DLTs reported in any dose cohort
• Infusion reactions (grade 1 and 2) reported in 4 patients
**Efficacy**
- All patients followed up for at least 2 weeks
- Marked decrease in M-protein
- PR or better: 15/20 patients
- 3 CR, 6 VGPR
- Median time to response-4.3 weeks (2.1-11.3)
Conclusions

- DARA+LEN+DEX treatment demonstrated a favorable safety profile with manageable toxicities in relapsed and RR MM patients.
- MTD was not reached in part 1; RP2D was determined by PK/PD, safety and efficacy evaluation.
- ORR was 75% (15/20) combining all patients (part 1 and 2); ORR was 92.3% (12/13) for part 1 patients, who had at least 2 months of follow-up.
- Encouraging early activity was seen with marked reduction in M-protein; 3 CR and 6 VGPR.
- Among the 3 patients refractory to prior LEN, all achieved a response (2 PR, 1 VGPR).
- Further clinical development of DARA in combination with LEN+DEX is merited.