Safety and Antitumour Activity of Dostarlimab in Patients With Advanced or Recurrent DNA Mismatch Repair Deficient or Proficient Endometrial Cancer: Results From the GARNET Study

Valentina Boni, MD, PhD, Sharad Ghamande, MD, Jodi nlng, MD, Gilbert Peiper, DO, Valentina Boni, MD, PhD, Sharad Ghamande, MD, Jodi nlng, MD, Gilbert Peiper, DO

1. Background

   Endometrial cancer (EC) is the most common gynecologic malignancy in the United States (US) and Europe.

   - EC has a wide frequency of mismatch repair deficiency (dMMR) and microsatellite instability-high (MSI-H) tumours among all tumours (approximately 10%).

   - Treatment options are limited for patients with disease progression that occurs on or after first-line therapy, and overall survival is typically <1 year.

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2. Methods

   - GARNET (NCT02715284) is a phase 1, single-arm study of dostarlimab (dMMR) advanced EC, using objective response rate (ORR) and duration of response (DOR) as the primary endpoints.

   - The study enrolled 129 patients with mismatch repair deficiency (dMMR) endometrial cancer (EC) who had received up to 3 prior systemic treatments.

   - The primary endpoint was ORR and DOR.

3. Results

   - ORR was 30.6% (95% CI, 21.2–41.4) with a confirmed ORR of 17.4% (95% CI, 10.2–27.6).

   - At 6 mos of treatment, 25% of patients had confirmed ongoing responses.

   - The median duration of response was 13.1 mos (95% CI, 8.5–18.7).

4. Conclusions

   - Dostarlimab demonstrated durable antitumour activity in both dMMR and dMMR proficient (dMMRp) patients.

   - Dostarlimab was well tolerated, with an AE profile characteristic of anti-PD-1/PD-L1 therapy.

   - These results support the use of dostarlimab as a potential treatment option for patients with advanced or recurrent EC.

5. Acknowledgements

   - Presenting Author Email: MMRunk

Table 1. Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>n=126</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>median</td>
<td>57.0</td>
<td>range</td>
</tr>
<tr>
<td>Performance status</td>
<td>0</td>
<td>96</td>
<td>1</td>
</tr>
<tr>
<td>Histology</td>
<td>endometrioid</td>
<td>104</td>
<td>serous</td>
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<tr>
<td>MSI HGS stage</td>
<td>I</td>
<td>51</td>
<td>II</td>
</tr>
<tr>
<td>Prior chemotherapy</td>
<td>3+</td>
<td>110</td>
<td>2+</td>
</tr>
<tr>
<td>Number of prior lines of therapy</td>
<td>3</td>
<td>110</td>
<td>2</td>
</tr>
<tr>
<td>Ovarian ablation</td>
<td>yes</td>
<td>110</td>
<td>no</td>
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Table 2. Primary Endpoint Analysis

<table>
<thead>
<tr>
<th></th>
<th>(A) dMMR</th>
<th>(B) dMMRp</th>
</tr>
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<tbody>
<tr>
<td>Patients</td>
<td>110</td>
<td>16</td>
</tr>
<tr>
<td>ORR</td>
<td>30.6% (95% CI, 21.2–41.4)</td>
<td>11.0% (95% CI, 4.2–23.5)</td>
</tr>
<tr>
<td>Confirmed ORR</td>
<td>17.4% (95% CI, 10.2–27.6)</td>
<td>2.5% (95% CI, 0.4–15.2)</td>
</tr>
<tr>
<td>SD</td>
<td>45.8% (95% CI, 36.7–55.2)</td>
<td>65.0% (95% CI, 50.0–79.3)</td>
</tr>
<tr>
<td>DOR</td>
<td>13.1 mos (95% CI, 8.5–18.7)</td>
<td>4.6 mos (95% CI, 3.0–7.5)</td>
</tr>
</tbody>
</table>

Table 3. Safety

<table>
<thead>
<tr>
<th></th>
<th>(A) dMMR</th>
<th>(B) dMMRp</th>
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</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>yes</td>
<td>110</td>
</tr>
<tr>
<td>Any TEAE ≥3</td>
<td>yes</td>
<td>54 (38.0)</td>
</tr>
<tr>
<td>Adverse event, n=14</td>
<td>yes</td>
<td>110</td>
</tr>
<tr>
<td>Asthenia</td>
<td>7 (4.9)</td>
<td>3 (18.7)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>18 (14.3)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>8 (6.3)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>18 (14.3)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (2.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>10 (7.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Rash</td>
<td>22 (17.3)</td>
<td>6 (37.5)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>7 (5.6)</td>
<td>3 (18.7)</td>
</tr>
</tbody>
</table>

Conflict of Interest

- DS, et al. declares personal fees from Immunogen, Eisai, Agenus, and GlaxoSmithKline; consultancy/advisory board members from Immunogen, Genentech, AstraZeneca, and BMS; and other financial or material support from Immunogen, Eisai, Agenus, GlaxoSmithKline, and MedImmune. VM discloses grants, personal fees, and non-commercial support from Immunogen, Genentech, AstraZeneca, and BMS. MG, BK, and AG disclose nothing to disclose.
Figure 3. Best Volume Change in Target Lesions Based on BICR per RECIST 1.1 in (A) dMMR and (B) MMRp EC

In order to use the magnification feature on this figure, please download the poster PDF via the QR code above.

Best change in target lesion size is the maximum reduction from baseline or the minimum increase from baseline in the absence of a reduction.

BICR, blinded independent central review; CR, complete response; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.
Figure 4. Duration of Treatment in Responders in (A) dMMR and (B) MMRp EC

In order to use the magnification feature on this figure, please download the poster PDF via the QR code above.

Data cut-off date 1 March 2020.
CR, complete response; dMMR, mismatch mutation repair deficient; EC, endometrial cancer; MMRp, mismatch mutation repair proficient; mo, months; PD, progressive disease; PR, partial response; SD, stable disease.