Background

- Dostarlimab is an investigational anti-PD-1 monoclonal antibody that has shown activity in patients with advanced/recurrent dMMR EC (objective response rate, 42.3%; disease control rate, 57.7%) and an acceptable safety profile.
- The ongoing GARNET trial (NCT02715284) is evaluating dostarlimab in patients with advanced solid tumors.
- PRO assessments measure the experiences of patients with cancer related to an intervention, from the patient’s perspective.
- Regulators increasingly utilize PROs to inform the risks and benefits of new drug candidates, with the US Food and Drug Administration recommending a focus on 3 core concepts:
  - Physical functioning (PF): Activities instrumental for daily living, such as mobility or dexterity
  - Disease-related symptoms (DRS): Symptoms such as pain or fatigue that can or might accompany a disease
  - Symptomatic AEs: Symptoms such as gastrointestinal upset that can or might occur secondary to treatment
- Anti-PD-1 therapies have shown favorable PROs in lung cancer, but there is little PRO data available in patients with EC.

Conclusions

- PROs from the GARNET trial showed that dostarlimab was generally well tolerated, and key disease-related symptoms, such as pain and fatigue, improved or were stable while on treatment.
- These data, along with the efficacy and safety profile of dostarlimab, support further evaluation of dostarlimab in patients with advanced/recurrent EC.

Patient-Reported Outcomes (PROs) in the GARNET Trial in Patients With Advanced or Recurrent Mismatch Repair Deficient/Microsatellite Instability-High (dMMR/MSI-H) Endometrial Cancer (EC) Treated With Dostarlimab

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Objective

- To evaluate PROs from patients treated with the anti-programmed cell death-1 (PD-1) antibody dostarlimab in the single-arm GARNET trial by assessing PF, DRS, and symptomatic adverse events (AEs).

Methods

- Patients with recurrent or advanced dMMR/MSI-H EC that progressed on or after a platinum regimen were enrolled.
- Patients received 500 mg of dostarlimab every 3 weeks (C0D1) for 4 cycles, then 1000 mg every 6 weeks (C0D1) until disease progression or discontinuation.
- PRO assessment, an exploratory endpoint, was conducted using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30).
- PRO data were collected at baseline, each dosing cycle, and after treatment discontinuation for up to 24 weeks.
- For PF and DRS, multi-item descriptive analyses were conducted, including an assessment of change from baseline.
- For symptomatic AEs and tolerability (nausea, vomiting, constipation, diarrhea, tiredness/fatigue), item-level analyses were conducted to understand response distribution and change in response categories from baseline.
- PROs from the GARNET trial showed that dostarlimab was generally well tolerated, and key disease-related symptoms, such as pain and fatigue, improved or were stable while on treatment.
- These data, along with the efficacy and safety profile of dostarlimab, support further evaluation of dostarlimab in patients with advanced/recurrent EC.

Results (cont’d)

- Overall, for patients who experienced symptomatic AEs, nausea, vomiting, constipation, diarrhea, and tiredness remained relatively stable compared with baseline over the course of treatment; 6% to 37% of patients reported an improvement in these symptoms (Figure 2).
- Symptomatic AEs did worsen in some patients: >25% of patients had a single category worsening and >6% of patients had a 2- or 3-category worsening (Figure 2).
- A positive trend was observed early in the treatment cycle for nausea, and EC (objective response rate, 42.3%; disease control rate, 57.7%) and an acceptable safety profile.

- Pain, fatigue, and physical functioning showed a positive trend above baseline starting at cycles 2, 3, and 4, respectively (Figure 1).

Table 1. Completion Rate of EORTC QLQ-C30

<table>
<thead>
<tr>
<th>Item assessed, n (%)</th>
<th>Baseline</th>
<th>Cycle 2, day 1</th>
<th>Cycle 3, day 1</th>
<th>Cycle 4, day 1</th>
<th>Cycle 5, day 1</th>
<th>Cycle 6, day 1</th>
<th>Cycle 7, day 42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>66 (100)</td>
<td>62 (93.9)</td>
<td>56 (87.6)</td>
<td>52 (85.2)</td>
<td>42 (72.2)</td>
<td>29 (63.0)</td>
<td>19 (45.2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>66 (100)</td>
<td>65 (98.4)</td>
<td>60 (93.8)</td>
<td>52 (85.2)</td>
<td>43 (81.1)</td>
<td>31 (67.4)</td>
<td>19 (45.2)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>66 (100)</td>
<td>69.6 (96.9)</td>
<td>60 (93.8)</td>
<td>51 (83.6)</td>
<td>40 (75.5)</td>
<td>30 (65.2)</td>
<td>19 (45.2)</td>
</tr>
<tr>
<td>Constipation</td>
<td>66 (100)</td>
<td>65 (98.4)</td>
<td>61 (95.3)</td>
<td>54 (88.5)</td>
<td>43 (81.1)</td>
<td>30 (65.2)</td>
<td>20 (47.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>66 (100)</td>
<td>64 (96.9)</td>
<td>60 (93.8)</td>
<td>54 (88.5)</td>
<td>43 (81.1)</td>
<td>31 (67.4)</td>
<td>19 (45.2)</td>
</tr>
</tbody>
</table>

Conclusions

- PROs from the GARNET trial showed that dostarlimab was generally well tolerated, and key disease-related symptoms, such as pain and fatigue, improved or were stable while on treatment.
- These data, along with the efficacy and safety profile of dostarlimab, support further evaluation of dostarlimab in patients with advanced/recurrent EC.

Results

- PRO data were available for 66 of 104 patients who received ≥1 dose of dostarlimab (safety population).
- Patient completion rate for the EORTC QLQ-C30 was consistent across all domains assessed, ranging from 100% at baseline to 45% at cycle 7, although compliance was reduced over later cycles (Table 1).
- Compliance is based on the expectation that patients will complete scheduled questionnaires while on study and until their death.

Figure 1. Mean Change From Baseline

- Overall, for patients who experienced symptomatic AEs, nausea, vomiting, constipation, diarrhea, and tiredness remained relatively stable compared with baseline over the course of treatment; 6% to 37% of patients reported an improvement in these symptoms (Figure 2).
- Symptomatic AEs did worsen in some patients: >25% of patients had a single category worsening and >6% of patients had a 2- or 3-category worsening (Figure 2).
- A positive trend was observed early in the treatment cycle for nausea, and there was no worsening by 3 categories, which coincides with no grade ≥3 nausea per National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v4.03 (as measured by physicians).
- There was also an observed early positive trend for constipation; however, after cycle 3, one patient reported a worsening by 3 categories that coincided with the single report of CTCAE grade 3 constipation (as measured by physicians).

References