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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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[1]
  - 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[2,3]
- Here, we report on PRO measures collected from patients enrolled in the dMMR/MSI-H EC expansion cohort of GARNET, following protocol amendment 3

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

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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 (Q3W) for 4 cycles, then 1000 mg every 6 weeks (Q6W) until disease progression or discontinuation
- PRO assessment, an exploratory endpoint, was measured 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
  - Patients reported their symptoms as 1 of 4 categories (not at all, a little, quite a bit, very much), which were then correlated to a change from baseline (improved, stable, and 1-, 2-, or 3-category worsening)

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/or until time of death

Results *(cont'd)*

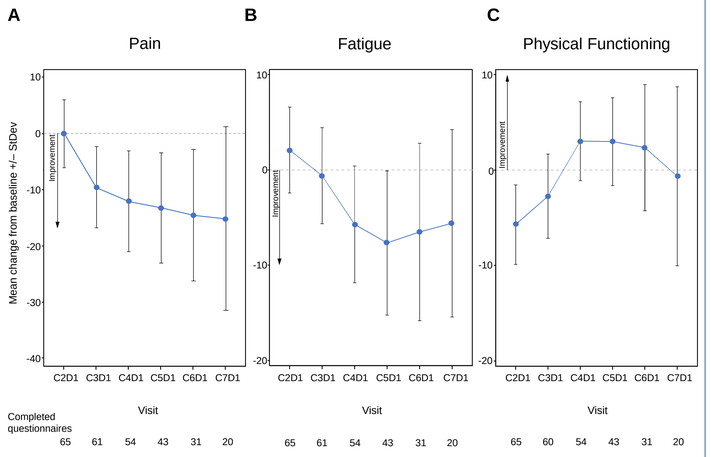
Table 1. Completion Rate of EORTC QLQ-C30

Item assessed, n (%)	Baseline n=66	Cycle 2, day 1 n=66	Cycle 3, day 1 n=64	Cycle 4, day 1 n=61	Cycle 5, day 1 n=53	Cycle 6, day 1 n=46	Cycle 7, day 1 n=42
Physical functioning	66 (100)	62 (93.9)	56 (87.5)	52 (85.2)	42 (79.2)	29 (63.0)	19 (45.2)
Pain	66 (100)	65 (98.4)	60 (93.8)	52 (85.2)	43 (81.1)	31 (67.4)	19 (45.2)
Fatigue	66 (100)	64 (96.9)	60 (93.8)	51 (83.6)	40 (75.5)	30 (65.2)	19 (45.2)
Nausea and vomiting	66 (100)	65 (98.4)	61 (95.3)	54 (88.5)	43 (81.1)	31 (67.4)	20 (47.6)
Constipation	66 (100)	65 (98.4)	61 (95.3)	54 (88.5)	43 (81.1)	30 (65.2)	19 (45.2)
Diarrhea	66 (100)	64 (96.9)	60 (93.8)	54 (88.5)	43 (81.1)	31 (67.4)	19 (45.2)

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

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

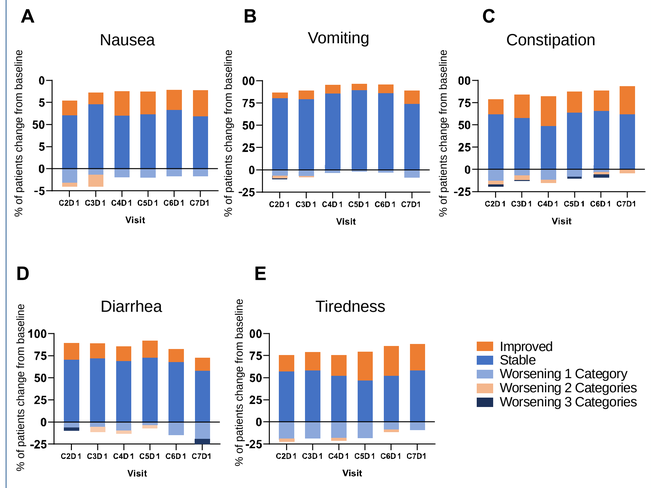
Figure 1. Mean Change From Baseline



C, cycle; D, day; StDev, standard deviation.

- 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)
  - Of patient-reported symptomatic AEs, gastrointestinal worsening occurred most often in this cohort of patients
  - 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)

Figure 2. Change in Response From Baseline



C, cycle; D, day.

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