The Time Course of Adverse Events During Dostarlimab Treatment in Patients with Recurrent or Advanced Endometrial Cancer in the GARNET Trial

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Purpose
The ongoing GARNET trial (NCT02715284) is evaluating dostarlimab (a programmed death-ligand 1 [PD-L1] checkpoint inhibitor) in metastatic endometrial cancer patients, with or without microsatellite instability (MSI) or mismatch repair deficient (dMMR) status. We report the time of onset of treatment-related adverse events (TRAEs) in the 19 patients evaluable for adverse events (AEs).

Methods
GARNET is a phase 1, single-arm study of dostarlimab monotherapy in multiple tumor types. In part 1, Dostarlimab was dosed at the recommended therapeutic dose determined from parts 1 and 2A. 500 mg intravenously every 3 weeks for 4 cycles, then 1000 mg every 6 weeks, until disease progression or discontinuation (Figure 1).

Results
TRAEs occurring in ≥2% of patients, by cycle

Figure 2. GARNET Trial Design

Figure 3. Enrollment and Outcomes

Figure 4. Primary Endpoint Analysis: DOR

Figure 5. Grade 3a TRAEs Occurring in ≥22% of Patients, by Cycle

Figure 6. Grade ≥3a TRAEs Occurring in ≥22% of Patients, by Cycle

Results (cont’d)

Table 1. Demographics and Baseline Characteristics

The only TRAE seen more in than 5% was hypothyroidism (Figure 6).

Table 2. Primary Endpoint Analysis: DOR

Table 3. Safety Summary

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Background
Endometrial cancer (EC) is the most common gynecological malignancy in the US and EU. EC has demonstrated an approximately 30% rate of microsatellite repair defect (dMMR) and microsatellite instability-high (MSI-H) tumors, the highest among all tumors.

Dostarlimab (TSR-042) is a programmed death-1 (PD-1) PD-L1 pseudosubstrate inhibitor that blocks interaction with PD-L1 and PD-L2.

Dostarlimab has demonstrated clinical activity in advanced solid tumors, including dMMR EC, colorectal cancer, and non-small cell lung cancer.

In the EU, dostarlimab is approved as a monotherapy in advanced adult patients with dMMR/H or recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen.

In the US, dostarlimab is approved as a monotherapy in adult patients with dMMR recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen and in adult patients with dMMR recurrent or advanced solid tumors that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.

The ongoing GARNET trial (NCT02715284) is evaluating dostarlimab in patients with advanced solid tumors.

Objective
Presented here is the evaluation of the time of onset of TRAEs and TRAEs during dostarlimab treatment in patients with dMMR (cohort A) and MMRp (cohort A2) in the GARNET trial.

Conclusions
Dostarlimab has an acceptable safety profile with manageable adverse events when analyzed over the dMMR and mismatch repair-proficient (MMRp) EC safety population of the GARNET trial.

Only 0.5% of patients discontinued treatment because of treatment-related adverse events (TRAEs). TRAEs and immune-related TRAEs (irTRAEs) were seen in a low percentage of patients.

TRAEs and irTRAEs were seen more frequently earlier in the time course of Dostarlimab treatment. irTRAEs were infrequent but could be seen throughout the course of treatment, as careful monitoring is necessary.

No increase in the rate of TRAEs or irTRAEs was seen when changing to the 1000-mg CRVH dosage of dostarlimab.

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