370 TIME COURSE OF TREATMENT-RELATED ADVERSE EVENTS (TRAES) DURING DOSTARLIMAB THERAPY IN THE GARNET TRIAL

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Background Dostarlimab is a humanized programmed death 1 (PD-1) receptor monoclonal antibody that blocks interaction with the ligands PD-L1 and PD-L2. Dostarlimab is approved as a monotherapy in adult patients (pts) with mismatch repair deficient (dMMR; US) or dMMR/microsatellite-instability high (EU) recurrent or advanced endometrial cancer that has progressed progressing on or following prior treatment with a platinum-containing regimen. GARNET is a phase 1 study assessing antitumor activity and safety of dostarlimab monotherapy in pts with solid tumors.

Methods Pts with dMMR solid tumors, mismatch repair proficient endometrial cancer, and non-small cell lung cancer that progressed on or after prior therapy received 500 mg of dostarlimab IV every 3 weeks (Q3W) for 4 cycles, then 1000 mg IV every 6 weeks (Q6W) for up to 2 years or until disease progression or discontinuation. Here, we report TRAEs by cycle.

Results A total of 515 pts were included. Of these pts, 60 (11.7%) experienced TRAEs leading to treatment interruption, and 25 (4.9%) experienced TRAEs leading to discontinuation. TRAEs of any grade with overall incidence of ≥10% of pts are shown (table 1). The majority of TRAEs occurred during cycles 1–3, with highest incidence during cycle 1. Grade 3 or 4 TRAEs were rare; those seen in ≥1% of pts are shown. Immune-related (ir) TRAEs of any grade with overall incidence of ≥2% of pts are shown. Most cases (96.9%) of irTRAEs occurred during cycles 1–8. The peak incidence of hypothyroidism occurred during cycle 4; in addition, frequency was increased during cycles 5–8, compared with cycles 1–4. No deaths were attributed to dostarlimab.

Abstract 370 Table 1 Time course of adverse events in the GARNET trial

Preferred term, n (%)	Overall N=515	500 mg Q3W C1 N=515	C2 N=468	C3 N=421	C4 N=382	1000 mg Q6W C5 N=322	C6 N=250	C7 N=214	C8 N=195
Any-grade TRAEs occurring in ≥10% of pts									
Fatigue	77 (15.0)	34 (6.6)	11 (2.4)	7 (1.7)	4 (1.0)	3 (0.9)	5 (2.0)	2 (0.9)	0
Diarrhea	66 (12.8)	27 (5.2)	15 (3.2)	9 (2.1)	4 (1.0)	2 (0.6)	3 (1.2)	3 (1.4)	0
Asthenia	59 (11.5)	27 (5.2)	12 (2.6)	7 (1.7)	6 (1.6)	2 (0.6)	2 (0.8)	1 (0.5)	1 (0.5)
Nausea	56 (10.9)	23 (4.5)	12 (2.6)	8 (1.9)	5 (1.3)	3 (0.9)	2 (0.8)	1 (0.5)	1 (0.5)
Grade ≥3 TRAEs occurring in ≥1% of pts									
Anemia	9 (1.7)	2 (0.4)	3 (0.6)	1 (0.2)	1 (0.3)	0	1 (0.4)	0	0
Fatigue	8 (1.6)	2 (0.4)	1 (0.2)	1 (0.2)	0	3 (0.9)	0	0	0
Lipase increased	7 (1.4)	0	2 (0.4)	2 (0.5)	0	1 (0.3)	0	0	0
Alanine aminotransferase increased	5 (1.0)	2 (0.4)	0	0	1 (0.3)	1 (0.3)	0	0	1 (0.5)
Diarrhea	5 (1.0)	0	1 (0.2)	2 (0.5)	1 (0.3)	0	1 (0.4)	0	0
Any-grade irTRAEs occurring in ≥2% of pts									
Hypothyroidism	34 (6.6)	0	2 (0.4)	3 (0.7)	13 (3.4)	2 (0.6)	5 (2.0)	5 (2.3)	3 (1.5)
Diarrhea	19 (3.7)	3 (0.6)	8 (1.7)	2 (0.5)	3 (0.8)	0	2 (0.8)	0	0
Alanine aminotransferase increased	11 (2.1)	4 (0.8)	0	0	3 (0.8)	2 (0.6)	1 (0.4)	0	1 (0.5)

C, cycle.

Conclusions No new safety signals were detected with dostarlimab compared to other anti–PD-1 inhibitors. Most TRAEs were low grade. The majority of TRAEs and grade ≥3 TRAEs occurred in the first 3 cycles (first 12 weeks), but some cases occurred later, suggesting a need for ongoing monitoring. Few increases in the incidence of TRAEs were seen during cycle 5 following the transition to the 1000-mg Q6W dosing schedule; the TRAEs with increased incidence after the transition were fatigue and lipase increased. An increase in the frequency of the irTRAE hypothyroidism was seen after transitioning to the 1000-mg Q6W schedule.

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