Dostarlimab is a programmed death 1 (PD-1) receptor monoclonal antibody that blocks interaction with the PD-1 ligands, PD-L1 and PD-L2.

In the EU, dostarlimab is approved as a monotherapy in adult patients with recurrent or advanced mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) endometrial cancer (EC) that has progressed on or after 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 after a platinum-containing regimen.

GARNET (NCT02715284) is a phase 1, single-arm study of dostarlimab monotherapy in multiple tumor types, including 2 EC cohorts. Tumor mutational burden (TMB) has been studied as a predictor of response to anti-PD-1 therapy, although with limited data for EC.

Conclusions

- TMB-high (TMB-H) status and dMMR/MSI-H status show substantial overlap in the patient population with EC.
- TMB-H and dMMR/MSI-H EC have similar response rates.
- Notably, the objective response rate (ORR) of patients with mismatch repair proficient (dMMR) and TMB-E was comparable to the ORR of patients with dMMR/MSI-H and TMB-H.
- TMB-H status in the patients with MMRp EC was not due to MSI-H (hypomethylated) or POML2-mutated (ultramethylated) status.
- The study was not powered to assess antitumor activity by TMB status, and interpretation is limited by the small number of patients in each subgroup.

Objective

To examine the antitumor activity of dostarlimab in patients with dMMR/MSI-H or dMMR/microsatellite instability-high (MSI-H) EC by TMB status.

Methods

GARNET (NCT02715284) is a phase 1, single-arm study of dostarlimab monotherapy in expanded cohorts in multiple tumor types (Figure 1).

Results

- 129 patients with dMMR/MSI-H EC and 161 patients with MMRp/MSI-H EC had been enrolled and treated as of the data cutoff date of March 1, 2020; these patients constitute the safety populations of cohorts A1 and A2, respectively.
- The primary efficacy population included those patients with ≥24 weeks of follow-up time in the study and with ≥1 measurable lesion at baseline per blinded independent central review.
- In total, 105 patients with dMMR/MSI-H EC and 156 patients with MMRp/MSI-H EC had data available and were included in this analysis (Table 1).

Safety

- Safety on these patients has been previously reported.

Conflicts of Interest

Dr. Oken, R. is a consultant for Deciphera Pharmaceuticals and receives personal fees from Mersana Therapeutics. He has served on advisory boards for Mersana Therapeutics, Deciphera Pharmaceuticals, Advaxis Inc, Aron Zenith, Arano Therapeutics-AQ, BioMarin Pharmaceuticals, and Genentech/Roche. Dr. Kwon has served on advisory boards for Immunomedics, Genentech/Roche, and Genentech/Roche. Dr. Kim has received support from Amgen, Genentech/Roche, and the Korean government...