Background

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

- In the US, dostarlimab is approved as a monotherapy in adult patients with dMMR recurrent or advanced endometrial cancer that has progressed on or after a platinum-containing regimen.

- In the EU, dostarlimab is approved as a monotherapy in adult patients with recurrent or advanced dMMR/instability-high endometrial cancer that has progressed on or after treatment with a platinum-containing regimen.

- Dostarlimab has demonstrated antitumor activity across multiple tumor types in patients with dMMR advanced/recurrent solid tumors, with an objective response rate of 41.6% (34.3–48.6%) in the combined cohort A1 + F population.

- Consistent antitumor activity was seen across endometrial and non-endometrial tumor types, such as colorectal cancer.

- The median duration of response was 34.7 (2.63 to 35.78) months in the combined cohort A1 + F population.

- Dostarlimab demonstrated a manageable safety profile across different tumor types.

Abstract #2564

The authors present the GARNET study, which is a phase 1, single-arm study of dostarlimab monotherapy in multiple tumor types. In part 2B, dostarlimab was administered at the recommended therapeutic dose determined from parts 1A and 2A (Figure 1).

Figure 1. GARNET Study Dosing Schedule

Objective

- To report objective response rate (ORR) and duration of response (DOR), by individual cohort and as an overall population, in patients with dMMR tumors.

Methods

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

- In part 2B, dostarlimab was administered at the recommended therapeutic dose determined from parts 1A and 2A (Figure 1).

Figure 2. Histology of Cohorts A1 + F Tumors

Results

- 143 patients in cohort A1 and 173 patients in cohort F were enrolled and treated as of the data cut-off date as of March 1, 2020, with an update on duration of response and safety taken on or after treatment with a platinum-containing regimen.

- Ongoing response was seen across tumor types and there was no evidence of disease progression in 16 (15.5%) patients in cohort F and 12 (11.7%) patients in cohort A1 by data cutoff date as of March 1, 2020, with an update on duration of response and safety taken on or after treatment with a platinum-containing regimen.

- 103 patients in cohort A1 and 106 patients in cohort F met this criteria (Figure 2).

Conclusions

- Dostarlimab was well tolerated, with an adverse event profile similar to other drugs in this class (Table 4).

- The grade 3 immune-related treatment-related adverse events had an incidence of 5% each (Table 4).

- There were 2 (0.6%) reports of grade 3 treatment-related colitis.

References


GARNET Trial Design

Part 1
Dose finding

Part 2A
Fixed-dose safety run-in

Part 2B
Expansion cohorts

A1: dMMR EC
(N=143)

A2: MMRp EC

E: NSCLC

F: Non-endometrial
dMMR basket
(N=173)

G: PROC

Key inclusion/exclusion criteria for cohorts A1 and F:
- Patients with dMMR/MSI-H solid tumors (cohort F was also open to patients with POLx-mutated solid tumors)
- Patients could be screened based on MMR/MSI testing results using IHC, PCR, or NGS performed in a certified local laboratory, but patient eligibility was determined by MMR IHC results for this analysis
- Patients must have measurable disease at baseline
- Patients must be anti-PD-(L)1 naïve
- Patients must submit 2 scans demonstrating PD based on BICR per RECIST v1.1 prior to the first dose of dostarlimab

Additional key inclusion/exclusion criteria for cohort A:
- Patients must have progression on or after platinum doublet therapy
- Patients must have received ≤2 prior lines of treatment for recurrent or advanced disease

Additional key inclusion/exclusion criteria for cohort F:
- Patients must have progression following systemic therapy and have no satisfactory alternative treatment options
- Patients with CRC must have PD after, or been intolerant to, fluoropyrimidine, oxaliplatin, and irinotecan

BICR, blinded independent central review; CRC, colorectal cancer; dMMR, mismatch repair deficient; EC, endometrial cancer; IHC, immunohistochemistry; MMR, mismatch repair; MMRp, mismatch repair proficient; MSI, microsatellite instability; MSI-H, microsatellite instability high; NGS, next-generation sequencing; NSCLC, non–small cell lung cancer; PCR, polymerase chain reaction; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PROC, platinum-resistant ovarian cancer; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.