TPS4204 Poster Session

ARTEMIDE-Gastric01: A phase 3 randomized study of rilvegostomig with fluoropyrimidine and trastuzumab deruxtecan (T-DXd) as first-line (1L) treatment for locally advanced or metastatic HER2-positive gastric or gastroesophageal junction cancer (GC/GEJC).

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Background: Patients with GC/GEJC often present with advanced disease, and prognosis for these patients is poor, with a 5-year relative survival rate of ~5%, highlighting a need for new treatment options. HER2 overexpression/amplification occurs in ~20% of cases. Adding immune checkpoint inhibition to trastuzumab (anti-HER2 monoclonal antibody) and chemotherapy has shown clinical benefit in patients with advanced HER2-positive GC/GEJC (Janjigian YY, et al. *N Engl J Med* 2024), and led to the approval of pembrolizumab (programmed cell death-1 [PD-1] inhibitor), trastuzumab, and chemotherapy for HER2-positive GC/GEJC with programmed cell death ligand-1 combined positive score (PD-L1 CPS) ≥1. T-DXd (a HER2-directed antibody-drug conjugate) is approved for the treatment of patients with locally advanced/metastatic HER2-positive GC/GEJC who have received a prior trastuzumab-based regimen. In addition, dual inhibition of PD-1 or PD-L1 and the immune checkpoint T cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) has shown encouraging results across multiple tumor types, without major increases in high-grade toxicity compared with PD-1 or PD-L1 inhibition alone. Rilvegostomig is a monovalent, bispecific, humanized IgG1 monoclonal antibody targeting both PD-1 and TIGIT receptors that has shown encouraging efficacy with manageable safety as monotherapy in non-small-cell lung cancer (Hiltermann TJN, et al. WCLC 2024. Oral presentation 1751) and with chemotherapy in HER2-negative GC/GEJC (Herrero FR, et al. *Ann Oncol* 2024. Abs 1422P). **Methods:** ARTEMIDE-Gastric01 (NCT06764875) is a phase 3, randomized, open-label, sponsor-blinded, multicenter, global study that will assess the efficacy and safety of rilvegostomig with T-DXd and chemotherapy as 1L treatment in HER2-positive GC/GEJC with PD-L1 CPS ≥1. Approximately 840 participants (pts) will be randomized to Arm A: rilvegostomig + T-DXd + investigator's (INV) choice of capecitabine or 5-fluorouracil (5-FU); Arm B: pembrolizumab + trastuzumab + INV choice of 5-FU and cisplatin (FP) or capecitabine and oxaliplatin (CAPOX); Arm C: rilvegostomig + trastuzumab + INV choice of FP or CAPOX. Eligible pts will have previously untreated, unresectable, histologically confirmed, locally advanced/metastatic HER2-positive and PD-L1 CPS ≥1 GC/GEJC and an ECOG performance status of 0 or 1. Dual-primary endpoints are progression-free survival (RECIST v1.1; blinded independent central review) and overall survival in all randomized pts. Secondary endpoints include safety/tolerability, objective response rate, and duration of response. Enrollment is planned across ~25 countries in Asia, Australia, Europe, and North and South America. Clinical trial information: NCT06764875. Research Sponsor: AstraZeneca.