TPS3649 Poster Session

AZUR-4, a phase 2, open label, randomized study of neoadjuvant dostarlimab plus capecitabine plus oxaliplatin (CAPEOX) versus CAPEOX alone in previously untreated T4N0 or stage III mismatch repair proficient/microsatellite stable resectable colon cancer.

Gertjan Rasschaert, Allyson Peddle, Sabine Tejpar, Nick West, Jenny Ross, Julie C. Switzky, Ken Edwards, Gabor Kari, Suzanne Griffin, Chiuwa Emily Luk, Daniel N. Cohen, Emily Hammatt, Edmund Moon; Department of Gastroenterology/Digestive Oncology, University Hospital Leuven, Leuven, Belgium; Department of Digestive Oncology, University Hospital Leuven and KU Leuven, Leuven, Belgium; Department of Oncology, KU Leuven, Leuven, Belgium; Department of Histopathology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; ICON Central Laboratories, New York, NY; GSK, Collegeville, PA; GSK, Stevenage, United Kingdom

Background: Colon cancer is the third most common cancer globally, with a standard of care in the nonmetastatic setting that includes surgery followed by adjuvant chemotherapy. Results of recent clinical trials suggest that neoadjuvant therapy may be beneficial in locally advanced colon cancer. Neoadjuvant immunotherapy has shown impressive responses in mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) disease with pathological complete responses of up to 67% and 3-year disease-free survival of 100% reported in the NICHE 2 trial. However, most colon cancer (85%–90%) is mismatch repair proficient (MMRp)/microsatellite stable (MSS), which has been shown to have poor response to conventional immunotherapy. Dostarlimab, a programmed cell death protein-1 (PD-1) inhibitor, has a high affinity for binding to PD-1, blocking the interaction between PD-1 and its ligands (PD-L1 and PD-L2). Dostarlimab monotherapy has been approved in the US for the treatment of adults with dMMR advanced/recurrent solid tumors. The AZUR-4 trial (NCT06567782) evaluates dostarlimab + CAPEOX versus CAPEOX alone as neoadjuvant treatment to identify early signals of efficacy in resectable MMRp/MSS colon cancer. The study will assess the relationship between conventional and advanced blood- and tumor-based immune response to better understand the contribution of dostarlimab to pathological response. **Methods:** AZUR-4 is a multicenter, randomized, open-label phase 2 study in MMRp/MSS resectable colon cancer. Approximately 120 patients will be enrolled and randomized 3:1 to the dostarlimab + CAPEOX and CAPEOX arms, respectively, in which they will receive 4 cycles of Q3W neoadjuvant therapy. Key eligibility criteria include age ≥18 years, confirmed resectable MMRp/MSS colon adenocarcinoma with no prior treatment, clinically staged as T4N0 or stage III, Eastern Cooperative Oncology Group performance status of 0 or 1, and required tissue biopsies providing fresh tumor tissue either at prescreening or screening. Primary endpoints are major pathologic response rate (mPR) assessed at ≤10% residual viable tumor (RVT) and treatment-emergent adverse events (AEs), serious AEs, immune-mediated AEs, and AEs leading to death or discontinuation of study drug. Secondary endpoints include primary tumor resection not being excluded by either disease progression or treatment-related toxicities, and pathological response categories that include complete pathological response (cPR) and partial pathologic response (pPR). Exploratory endpoints include overall survival, event-free survival, effects on circulating tumor DNA dynamics, and pathological response rate in biomarker subsets. Clinical trial information: NCT06567782. Research Sponsor: GSK.