TPS5623 Poster Session

A single-center, open-label, single-arm, phase I study with dose expansion cohort of sacituzumab govitecan in combination with cisplatin for patients with platinum sensitive recurrent ovarian and endometrial cancer.

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Background: Sacituzumab govitecan (SG) is an antibody-drug conjugate (ADC) composed of the irinotecan active metabolite SN-38 (govitecan) covalently linked to a humanized monoclonal antibody (hRS7) targeting trophoblastic cell-surface antigen-2 (Trop-2). Sacituzumab govitecan has demonstrated in vitro and in vivo activity against multiple solid tumors, including ovarian cancer and endometrial cancer. The Basket Trial, a phase I/II study of single agent sacituzumab govitecan in patients with epithelial cancers, showed clinical efficacy in endometrial cancer patients (n = 18) with an ORR of 22.2% (6.4-47.6) and median OS of 11.9 months (4.7 months – NR). Insufficient ovarian cancer patients were enrolled for response parameters to be met. The combination of platinum agents and topoisomerase inhibitors, such as irinotecan, has showed complementary effects in pre-clinical studies, however, the use in clinical practice has been limited by intolerable toxicity. Early trials have found that compared to irinotecan, a prodrug for SN-38, sacituzumab govitecan allows for improved targeted delivery of SN-38 to tumor tissue and increased therapeutic activity with relatively moderate toxicity. The tempering of the toxicity by this ADC may allow for the combination of cisplatin with sacituzumab govitecan to capitalize on the synergy between platinum agents and topoisomerase I inhibitors. The most common grade $\geq$ 3 adverse events that are seen with sacituzumab govitecan include leukopenia, neutropenia, and thrombocytopenia, thus the less myelosuppressive platinum agent cisplatin is the preferred platinum choice for this combination. **Methods:** Sacituzumab govitecan is being evaluated in combination with cisplatin in an open-label, non-randomized, dose de-escalation (phase 1) study with a planned dose expansion cohort in platinum sensitive, recurrent epithelial ovarian and endometrial cancer patients. Platinum sensitivity for both cancers is defined as cancer recurrence/progression occurring more than 6 months after the last dose of prior platinum therapy. The safety run in phase utilizes a 3+3 design with a de-escalated dose level if the starting dose of sacituzumab govitecan shows toxicity. The primary endpoint for the safety run-in is to determine the dose-limiting toxicity (DLT) and dose expansion cohort dose of sacituzumab govitecan when administered with a fixed schedule of cisplatin. The dose expansion cohort is designed to indicate proof of concept regarding the ORR, CBR, PFS, and safety of the combination regimen at the dose established in the safety run-in phase of the study. The study began enrolling patients October 2024 at our institution and is currently in phase 1 at the starting dose level of sacituzumab govitecan. Clinical trial information: NCT06040970. Research Sponsor: Gilead Sciences, Inc.