TPS5633 Poster Session

Sapanisertib and serabelisib (PIKTOR) with paclitaxel and a diet substudy in patients with advanced/recurrent endometrial cancer (GOG-3111).

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Background: Patients with advanced/recurrent endometrial cancer have limited 2L+ treatment options. The PI3K/mTOR pathway regulates glucose homeostasis downstream of insulin/insulin receptor signaling and is mutated in >80% of endometrial cancer. Multi-node inhibition of this pathway with the combination of sapanisertib, an mTORC1/2 inhibitor, and serabelisib, a PI3Kα inhibitor, (PIKTOR) achieves more complete PI3K pathway blockade compared to single node inhibition in preclinical models. In a Phase 1b trial (NCT03154294) of triplet combination paclitaxel, serabelisib, and sapanisertib, the combination led to an overall response rate of 80% with 3 CR and 1 PR in 5 patients with advanced, treatment refractory endometrial cancer. This study evaluates whether PIKTOR with paclitaxel improves efficacy outcomes in participants with advanced/recurrent endometrial cancer with mutation(s) in the PI3K/AKT/mTOR pathway and who have failed prior systemic therapies. **Methods:** GOG-3111 is a Phase 2 (ClinicalTrials.gov ID NCT06463028), multi-center, open-label, single-arm trial evaluating the efficacy and safety of PIKTOR plus paclitaxel in participants with advanced/recurrent endometrial cancer. Approximately 40 participants will be enrolled in the main study and up to 50% of participants will have the option to receive triplet combination therapy with a diet. Eligible participants will have histologically confirmed diagnosis of advanced/recurrent endometrioid endometrial carcinoma and documented genetic mutation(s) in the PI3K/AKT/mTOR pathway by next generation tumor testing. Participants must have received >1 but no more than 3 prior systemic therapies for advanced/recurrent disease (ie, including platinum-based therapy and an immune checkpoint inhibitor either together or separately). Study interventions are 28-day cycles with: Paclitaxel: 80 mg/m2 IV weekly on Days 1, 8, and 15; PIKTOR (sapanisertib [1] 3mg and serabelisib [2] 100 mg) oral with food on Days 2-4, 9-11, 16-18, and 23-25. Radiographic imaging and RECIST v1.1 response assessment will be performed every 8 weeks starting at C1D1. The primary objective is to evaluate the objective response rate (ORR) and secondary objective is to evaluate efficacy via progression-free survival (PFS), PFS at 6 months, overall survival, clinical benefit rate, duration of response; and safety/tolerability of PIKTOR + paclitaxel. The substudy rationale is to evaluate the impact of diet on treatment tolerability and efficacy. Clinical trial information: NCT06463028. Research Sponsor: Faeth Therapeutics.