TPS1133 Poster Session

Adaptive designed eniluracil + capecitabine phase 2 trial in advanced or metastatic breast cancer patients.

David Young, Sian Elizabeth Bigora, Mary Nyberg, Shanique Smythe-Peterkin, Yvonne Madden, Mridula Annette George; Processa Pharmaceuticals, Inc., Hanover, MD; Processa Pharmaceuticals.com, Hanover, MD; Rutgers Cancer Institute of New Jersey, New Brunswick, NJ

Background: Ethynyl-uracil (eniluracil or 6422), an irreversible inhibitor of the dihydropyrimidine dehydrogenase enzyme that metabolizes 5-FU to catabolites, eliminates the formation of 5-FU catabolites and catabolite side effects while exposing cancer cells to more 5-FU and more cancer killing 5-FU anabolites. The combination of a single 40 mg day 1 dose of 6422 followed by Day 2 Capecitabine (6422+Cap) on a 7 day on + 7 day off schedule (7+7) of Capecitabine (Cap) is being evaluated. The dose of Cap used in 6422+Cap will be approximately 15% of the therapeutic dose of Cap used in clinical practice for breast cancer. A Phase 1B study in patients with refractory gastrointestinal (GI) cancer has been completed. The Maximum Tolerated Dose of Cap in 6422+Cap was determined to be 225 mg BID. The Recommended Phase 2 Dose Range of Cap in 6422+Cap was determined to be from 75 mg BID to 225 mg BID. based on the FDA's Optimal Design Guidance and Project Optimus initiative to define the dose-response relationship for both safety and efficacy. Since FDA believed that determining the optimal dosage regimen following the Principles of Project Optimus would be extremely difficult for 6422+Cap in GI cancer given the standard combination chemotherapeutic treatments, the target population was changed to breast cancer patients. FDA also determined that a Phase 1B study in breast cancer would not be required given the GI cancer Phase 1B data. **Methods:** Several Project Optimus focused Phase 2 designs were evaluated. Based on guidance from the FDA, an adaptive, 3 arm, 30 patients/arm, phase 2, open-labelled, randomized trial was selected which would compare 2 regimens of 6422+Cap vs. standard dose of Cap alone. The study would initially enroll patients into 2 treatment arms. The 2 arms are: a 1000 mg/m2 BID monotherapy Cap control group and a 6422+Cap regimen of 40 mg on day 1 followed by day 2 Cap dose of 150 mg BID on 7+7 schedule. Upon completing the enrollment and evaluation of 9-10 patients in each of the first 2 arms, an interim analysis will be conducted to determine the Cap dose to be used in the 6422+Cap 3rd arm. Depending on the interim results, Cap dose in the 3rd arm will either be increased to 225 mg BID or decreased to 75 mg BID. Patients with triple-negative or HR positive/HER2 negative, advanced or metastatic breast cancer are eligible for the study. Patients should have measurable disease in accordance with RECIST 1.1. Patients with stable brain metastases are eligible. The primary endpoint of the study is Objective Response Rate. This will be assessed based on the null hypothesis that the endpoint in each 6422+Cap arm is less than or equal to the monotherapy arm. Additionally, safety will be assessed by the incidence and severity of adverse events across treatment groups. The pharmacokinetics of Cap, 5-FU, and the FBAL catabolite will be evaluated using population PK analysis. Currently 3 patients have been enrolled in the study. Clinical trial information: NCT06568692. Research Sponsor: Processa Pharmaceuticals Inc.