Add to My Itinerary

Session CTPL03 - Targeted Therapy and Ovarian Cancer Trials

CT012 - TRX-E-002-1 in treatment-refractory ovarian cancer: Final phase 1 study results from the dose-escalation and dose-expansion cohorts

April 11, 2021, 3:05 PM - 3:20 PM | Channel 10

Presenter/Authors

Jermaine Coward, *Ganessan Kichenadasse*, *Paul Harnett*, *Kathleen Moore*, *Minal Barve*, *James Garner*, *Mary Lopresti*, *Don S. Dizon*. ICON Cancer Centre, South Brisbane, Australia, Flinders Medical Centre, Adelaide, Australia, Crown Princess Mary Cancer Centre, Westmead, Australia, Oklahoma Health Sciences Center, Oklahoma City, OK, Mary Crowley Cancer Research Center, Dallas, TX, Kazia Therapeutics Limited, Sydney, Australia, Lifespan Cancer Institute, Providence, RI

Disclosures

J. Coward: None. G. Kichenadasse: None. P. Harnett: None. K. Moore: ; Advisory Board; Astra Zeneca. ; Advisory Board; Aravive. ; Advisory Board; Eisai. ; Advisory Board; Elevar. ; Advisory Board; GSK/Tesaro. ; Advisory Board; Genentech/roche. ; Advisory Board; Immunogen. ; Advisory Board; Merck. ; Advisory Board; Myriad. ; Advisory Board; Mersana. ; Advisory Board; Sorrento. ; Advisory Board; VBL Therapeutics. ; PTC Therapeutics. ; Lilly. M. Barve: None. J. Garner: ; Kazia Therapeutics Limited. M. Lopresti: None. D.S. Dizon: None.

Abstract

Introduction: For women with advanced ovarian cancer survival outcomes with standard cytotoxic chemotherapy are poor and are thought to reflect the existence of drug-resistant ovarian cancer stem cells. TRX-E-002-1 (Cantrixil), a novel third generation benzopyran molecule has been shown to be effective in a mouse model of recurrent chemotherapy-resistant ovarian cancer. We present the final results of a phase I progressive design trial (Part A dose escalation, Part B dose expansion) of Cantrixil (NCT02903771). The objectives were to establish maximum tolerated dose (MTD) when given in combination with chemotherapy, and to evaluate safety, tolerability and anti-tumour activity of intraperitoneal (IP)-administered Cantrixil. Methods: Women who had completed ≥2 prior regimens and whose disease was platinum-refractory, platinum-resistant or who had documented intolerance to platinum therapy, were eligible. Treatment comprised up to eight 3-week cycles. In the first 2 cycles, patients were dosed weekly with Cantrixil as monotherapy after which investigators were allowed to initiate pre-defined standard intravenous chemotherapy regimens (cycles 3-8). All patients were followed up for 3 months after the end of treatment. Results: Of 32 patients enrolled, 25 received ≥1 Cantrixil dose; 6 patients (24%) completed all 8 treatment cycles. Patients (92% Caucasian, mean age 62.5 years) had a median of 2 prior lines of platinum therapy and a median of 3 prior lines of anticancer therapies (including anti-VEGF; n=13, 52% and PARPi; n=6, 24%). Platinum sensitivity: refractory (n=3,12%), resistant (n=17, 68%), sensitive (n=5, 20%). In Part A (n=11), an MTD of 5mg/kg was established on the dose-limiting toxicity of ileus (n=2) and safety signals of bowel obstruction (n=3) and abdominal pain (n=2). The pharmacokinetic profile was multi-exponential, with rapid increases in systemic concentration and distribution and a slower elimination phase. Drug accumulation was minimal and was not influenced by co-administration of

chemotherapy. Analysis of weight and dose-normalized (to 1 mg/kg) data found no notable trends. Across Parts A and B, 16 patients received ≥1 Cantrixil dose and had a post-baseline efficacy measurement available. The overall response rate was 18%, including one complete response (platinum-resistant; who remains in remission 37.05 months since starting treatment) and two partial responses (one platinum-resistant, one platinum refractory). The median progression free survival was 3.06 months (95% CI:1.28,∞).
Conclusion: IP-administered Cantrixil, a first-in-class, dual acting, anti-cancer therapy has encouraging activity in a cohort of difficult to treat patients with persistent epithelial ovarian, fallopian tube or primary peritoneal cancer who have demonstrated resistance to a range of prior treatments. Disease response compares favorably to a figure of 10% for historical controls.