Date: 24 March 2021

AstraZeneca
Da Vinci Building
Melbourn Science Park
Hertfordshire,· SG8 6HB
United Kingdom

astrazeneca.com

Subject: Reason for the termination of AstraZeneca study DUETTE D6018C00004: A phase II, randomised, multicentre study to investigate the efficacy and tolerability of a second maintenance treatment in patients with platinum sensitive relapsed epithelial ovarian cancer, who have previously received PARPi maintenance treatment.

Following the review of data from an interim analysis in a separate study D5336C00001 (VIOLETTE, NCT03330847), which included the same ceralasertib+olaparib combination as proposed for evaluation in the DUETTE study (ceralasertib 160 mg once daily [qd] orally [po] on Days 1 to 7 plus olaparib 300 mg twice daily [bd] po continuous, 28-day cycle), AstraZeneca decided to terminate the DUETTE study.

VIOLETTE is a Phase II, Open Label, Randomised, Multi-centre Study to Assess the Safety and Efficacy of Agents Targeting DNA Damage Repair in combination with Olaparib versus Olaparib Monotherapy in the Treatment of Metastatic Triple Negative Breast Cancer Patients Stratified by Alterations in Homologous Recombinant Repair-related Genes. The Unblinded Review Committee recommended to terminate the VIOLETTE study at the interim analysis as there was no meaningful benefit from adding ceralasertib to olaparib compared with olaparib monotherapy. It is important to note that this decision was based on lack of efficacy and there are no safety concerns for the combination.

AstraZeneca also reassessed the Ataxia-Telangiectasia mutated and Rad3-related (ATR) target cover using ceralasertib dosed at 160 mg qd on Days 1-7 in combination with olaparib 300 mg bd in a 28-day cycle. Whilst ATR target cover is achieved in each 24 hr dosing period, population PK simulations at steady state suggest that, with the VIOLETTE / DUETTE dose and schedule, there is sub-optimal target cover per cycle as ceralasertib is dosed for 7 days duration only. Therefore, no patient receiving combination treatment with ceralasertib and olaparib can achieve the optimal ATR target cover per cycle using the DUETTE dose and schedule, independent of tumor indication.

A separate ongoing Phase 3 study (OReO, NCT03106987) is assessing the role of PARPi in the second maintenance setting regarding platinum sensitive ovarian cancer patients. This trial is expected to read out in Q2, 2021.

AstraZeneca PLC
Registered in England No. 2723534
Registered office: 1 Francis Crick Avenue
Cambridge Biomedical Campus
Cambridge, CB2 0AA
United Kingdom

At the time the decision to terminate the study was made, some patients had consented to enter pre-screening but none had been treated with olaparib monotherapy or the ceralasertib combination. Therefore, no data will be reported for this study.

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