TPS3172 **Poster Session**

Phase IB/II study to evaluate safety and preliminary efficacy of the WEE1 inhibitor Debio 0123 in combination with sacituzumab govitecan (SG) in triple-negative or hormone receptor–positive (HR+)/HER2-negative (HER2–) advanced breast cancer (ABC): The WIN-B study.

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Background: SG is a Trop-2 directed antibody drug conjugate that has shown an overall survival benefit for patients (pts) with HER2- ABC in two phase III trials. Unfortunately, most pts become refractory to this treatment, highlighting a critical need for strategies to overcome resistance to SG and improve therapeutic outcomes. WEE1 is a cyclin-dependent kinase 1 regulator, which delays the G2/M transition and maintains genomic stability during the cell cycle. Debio 0123, a highly selective and brain penetrant WEE1 inhibitor, has demonstrated synergistic activity in breast cancer preclinical models with SG. The aim of the WIN-B study is to evaluate the safety and preliminary efficacy of combining the WEE1 inhibitor Debio 0123 with SG in pts with previously treated HER2- ABC. **Methods:** WIN-B (NCT06612203) is an international, multicenter, open-label, single-arm phase Ib/II trial. In phase Ib, 12-24 pts will be assigned to different Debio 0123 dose cohorts (200, 300, 400, or 520 mg orally once daily on days 1-3 and 8-10) plus standard doses of SG (10 mg/kg intravenously on days 1 and 8) given in 3-week cycles. In phase II, 52 pts will be divided into cohorts A (triple-negative breast cancer [TNBC], n = 26) and B (HR+/HER2– tumors, n = 26), and will be treated with the recommended doses determined during phase Ib. Key inclusion criteria are: pts aged ≥18 with TNBC or HR+/HER2- tumors who have experienced disease progression after 1 or 2 lines of systemic therapy for ABC, ECOG performance status of 0-1, with evaluable (for phase Ib) or measurable (for phase II) disease as per RECIST v.1.1. Pts will receive study treatment until progression, death, unacceptable toxicity, or study discontinuation. Primary objectives are: in phase Ib, to establish the recommended phase 2 dose of the combination of Debio 0123 plus SG and, in phase 2, to assess the objective response rate (ORR) as per RECIST v.1.1. Key secondary endpoints are progression-free survival and overall survival, safety and toxicity. In phase Ib, dose escalation will be performed using a Bayesian Logistic Regression Model with overdose control. In phase 2, A'Hern one-stage design will be set at one-sided type I binomial exact test of 5% to attain 80% power. The primary analyses will estimate ORR (H0: ORR≤29% for TNBC and ORR≤19% for HR+/HER2- tumors vs H1: ORR≥55% for TNBC and ORR≥41% for HR+/HER2- tumors). The phase 2 part of the study will be deemed positive if at least 12 (46.2%) and nine (34.6%) pts with TNBC and HR+/HER2- tumors, respectively, achieve an objective response. Clinical trial information: NCT06612203. Research Sponsor: Debiopharm. Gilead will provide the supply of SG.