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PHASE IB/II STUDY TO EVALUATE SAFETY AND PRELIMINARY EFFICACY OF THE WEE1 INHIBITOR DEBIO 0123 IN COMBINATION WITH SACITUZUMAB GOVITECAN IN TRIPLE-NEGATIVE OR HORMONE RECEPTOR-POSITIVE (HR+)/HER2-NEGATIVE (HER2–) ADVANCED BREAST CANCER (ABC): THE WIN-B STUDY

Timothy Robinson[1], María Gión[2,3,4], María Isabel Blancas[4,5], Meritxell Aguiló[4], Juliana Carvalho[4], Sandra Santasusagna[4] Michela Verbeni[4], Rui Rui Zhang[4], Esteban Rodrigo Imedio[6], Luke Piggott[6], José Manuel Pérez-García[4,7], Javier Cortés[3,4,7,8,9], Antonio Llombart-Cussac[4,10,11]

[1] University of Bristol, Bristol, England; [2] Hospital Ramón y Cajal, Madrid, Spain; [3] IOB Madrid, Institute of Oncology, Hospital Beata María Ana, Madrid, Spain; [4] Medica Scientia Innovation Research (MEDSIR), Barcelona, Spain and Ridgewood, New Jersey, US; [5] Medical Oncology Department, Hospital Clínico San Cecilio, Granada, Spain; [6] Debiopharm International, Lausanne, Switzerland; [7] International Breast Cancer Center (IBCC), Pangaea Oncology, Quiron Group, Barcelona, Spain; [8] Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain; [9] Oncology Department, Hospital Universitario Torrejón, Ribera Group, Madrid, Spain; [10] Hospital Arnau de Vilanova, FISABIO, Valencia, Spain; [11] Translational Oncology Group, Department of Medicine, Facultad de Ciencias de la Salud, Universidad Cardenal Herrera-CEU, Alfara del Patriarca, Spain.

BACKGROUND

- Sacituzumab govitecan (SG) is a Trop-2 directed antibody-drug conjugate that improves overall survival in patients with advanced HR+/HER2- tumors and triple- negative breast cancer (TNBC)[1].
- Different mechanisms of resistance may be involved in tumor progression after SG use. There is a need to develop new strategies or combinations to improve its efficacy[2].
- WEE1, a cyclin-dependent kinase 1 regulator, delays the G2/M transition and plays a critical role in preserving genomic stability throughout the cell cycle[3].
- Debio 0123, a highly selective and brain-penetrant WEE1 inhibitor, has shown synergistic effects with SG in preclinical breast cancer models[4].
- The rationale of the WIN-B study is to explore the efficacy of the combination of Debio 0123 and SG in previously treated patients with advanced HR+/HER2- tumors and TNBC.

STATISTICS

- The primary endpoint of phase Ib is to determine the recommended phase II dose of Debio 0123 in combination with SG. In phase II, the primary endpoint is to assess the overall response rate (ORR) in each cohort according to RECIST v.1.1.
- In phase Ib, dose escalation will be performed using a Bayesian Logistic Regression Model with overdose control.
- The primary analysis will estimate ORR (H_0: ORR ≤ 29% for TNBC and ORR ≤ 19% for HR+/HER2- tumors vs H_1: ORR ≥ 55% for TNBC and ORR ≥ 41% for HR+/HER2- tumors).
- The hypotheses will be tested in each cohort using an exact binomial test at one-sided 5% significance level, with 80% power.
- The phase II part of the study will be deemed positive if at least 12 (46.2%) patients in the TNBC cohort or 9 patients in the HR+/HER2- tumor cohort achieve an objective response.

TRIAL ENROLLMENT

- The WIN-B started the recruitment in January 2025. As of February 21st , five centers have initiated recruitment.

ACKNOWLEDGEMENTS

The WIN-B team thanks all the patients and their families who will be involved in this study, as well as the trial teams of the participating sites. We also thank Debiopharm and Gilead for funding this trial.

BIBLIOGRAPHY

1. **Hope, S. R.** *et al.* 2020. Future Oncol. 12, 705–715.
2. **Shastry, M.** *et al.* 2022. Breast. 66, 169–177.
3. **Bukhari, A. B.** *et al.* 2022. Front Oncol. 12, 828684.
4. **Piggott, L.** *et al.* 2024. Cancer Res. 84, 3370.

CONTACT INFORMATION

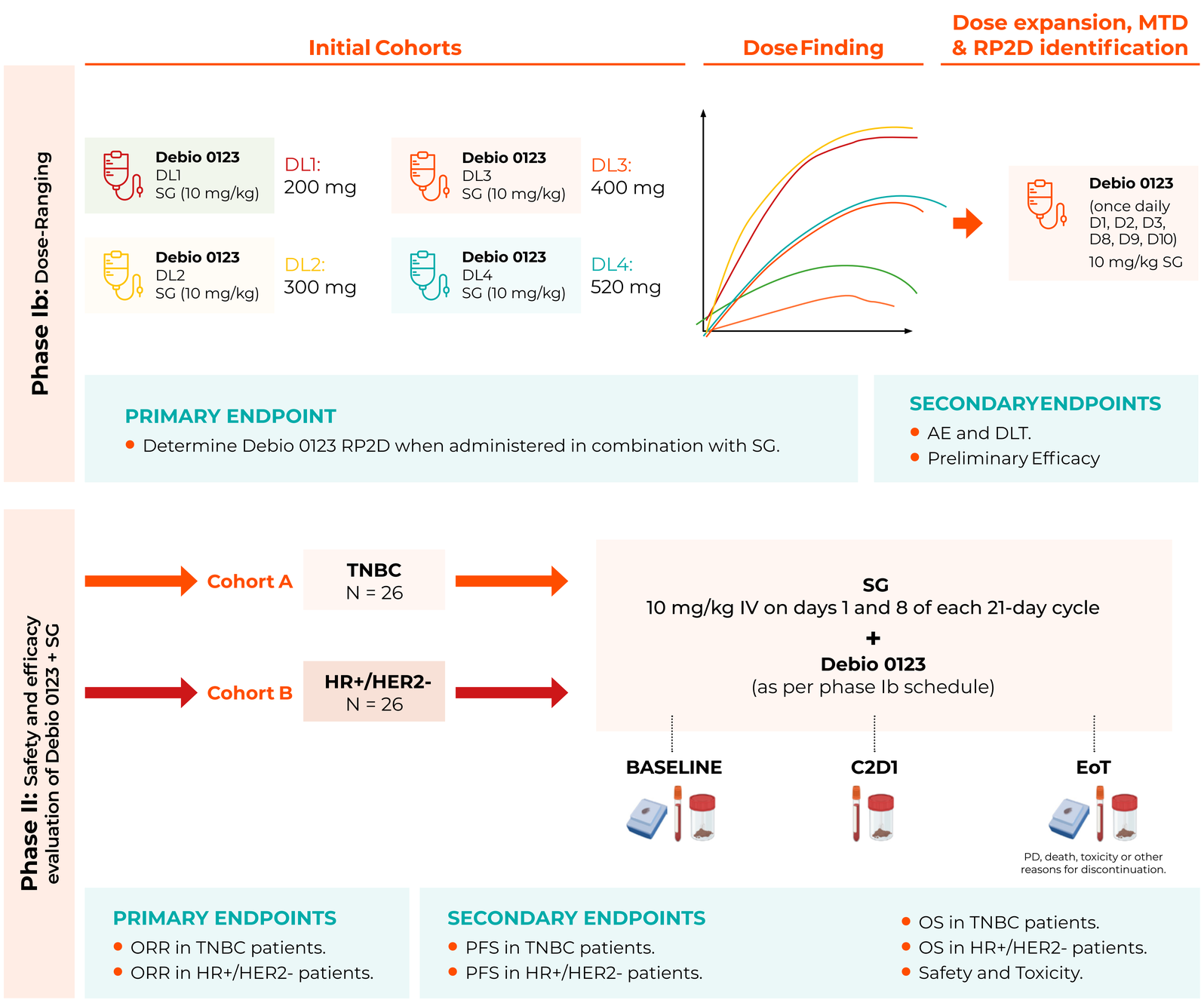
Antonio Llombart-Cussac, MD
Email: antonio.llombart@maj3.health

TRIAL DESIGN

The WIN-B study is an international, multicenter, open-label, single-arm phase Ib/II trial (NCT06612203).

KEY INCLUSION CRITERIA

- ≥18 years of age.
- Advanced HR+/HER2- tumors or TNBC.
- Refractory to at least one and no more than two lines of chemotherapy regimens for ABC.
- HR+/HER2– patients must be refractory to at least 1 prior anti-cancer hormonal treatment for ABC and must have resistance to CDK4/6 inhibitor defined as:
  a. PD while on, or within 12 months after the end of this treatment in the (neo)adjuvant setting;
  b. PD to this treatment during advanced disease.
- No previous Trop-2 ADC or WEE-1 inhibitors are allowed.
- Brain metastasis are allowed if stable in the 4 weeks previous entry into the trial.
- Evaluable (for phase Ib) or measurable (for phase II) disease according to RECIST v.1.1.



PRIMARY ENDPOINT

- Determine Debio 0123 RP2D when administered in combination with SG.

SECONDARY ENDPOINTS

- AE and DLT.
- Preliminary Efficacy

PRIMARY ENDPOINTS

- ORR in TNBC patients.
- ORR in HR+/HER2- patients.

SECONDARY ENDPOINTS

- PFS in TNBC patients.
- PFS in HR+/HER2- patients.
- OS in TNBC patients.
- OS in HR+/HER2- patients.
- Safety and Toxicity.

Scan here to view a plain language summary of this study

Abbreviations: **ABC:** advanced breast cancer; **ADC:** antibody drug conjugate; **AE:** adverse events; **CDK4/6:** cyclin-dependent kinases 4 and 6; **DL:** dose level; **DLT:** dose-limiting toxicities; **ECOG PS:** Eastern Cooperative Oncology Group Performance Status; **EoT:** end of treatment; **H_0:** null hypothesis; **H_1:** alternative hypothesis; **HR:** hormone receptor; **HER2:** human epidermal growth factor receptor 2; **IV:** intravenously; **MTD:** maximum tolerated dose; **ORR:** objective response rate; **OS:** overall survival; **PD:** progressive disease; **PFS:** progression-free survival; **RECIST:** Response Evaluation Criteria In Solid Tumors; **RP2D:** recommended phase II dose; **SG:** Sacituzumab govitecan; **TNBC:** triple-negative breast cancer; **Trop-2:** trophoblast cell surface antigen 2; **WEE1:** WEE1 G2 checkpoint kinase.