Trastuzumab Deruxtecan in patients with HER2[+] or HER2-Low Advanced Breast Cancer and Pathologically Confirmed Leptomeningeal Carcinomatosis: Results from Cohort 5 of the DEBBRAH Study

Marta Vaz Batista1, José Manuel Pérez-García1, Laia Garrigós1, José Ángel García-Sáez1, Patricia Cortés1, Fabricio Racca2, Salvador Blanch3, Manuel Ruiz-Borrego4, Adela Fernández5, María Fernández-Abad6,7, Vega Iranzo8, María Gio9, Giovanni Marta10, Daniel Alcalá-López11, Judit Pérez-Escudero12, Antoni Llobet-Cortés13, Sofía Naya14, Javier Cortés15

1Hospital Professor Doutor Fernando Fonseca EPE, Lisbon, Portugal, 2Medicina Scientia Innovation Research (MEDSIR), Barcelona, Spain, and Rigshospitalet, New Jersey, US, 3International Breast Cancer Center (IBCC), Pangea Oncology, Quiron Group, Barcelona, Spain, 4Hospital Universitari Dexeus, Barcelona, Spain, 5Hospital Clínico San Carlos, Madrid, Spain, 6Quironina Oncology, Quiron Group, Madrid, Spain, 7IBIO Institute of Oncology, Quiron Group, Madrid and Barcelona, Spain, 8Fundació Hospital VELLER del Raco, Sevilla, Spain, 9Institut Català d’Oncològic de l’Hospital de l’Hospitalet (ICO), Barcelona, Spain, 10Medical Oncology department, Hospital Ramon y Cajal, Madrid, Spain, 11Alcalá de Henares University, Faculty of medicine, Madrid, Spain, 12Consortium Hospital General Universitari de Valencia, Valencia, Spain, 13Hospital Arnau de Vilanova, FSABV, Valencia, Spain, 14Universitat Catòlica de Valencia, Valencia, Spain, 15Universidade Europea de Madrid, Madrid, Spain.

Background
- Leptomeningeal carcinomatosis (LMC) occurs in approximately 10% of patients (pts) with advanced breast cancer (ABC) and represents a devastating complication contributing to poor outcomes (4-50%), with a poor prognosis due to limited available therapeutic options.
- Historically, data have shown that without treatment, median overall survival (OS) of these pts is around 4-6 weeks and, if treated, the median OS can increase to approximately 2.4 months.

Methods
- This is an international, investigator-initiated, open-label, multicenter, single-arm, phase 2 trial (NCT04420598).
- Pts received T-DXd until progressive disease (PD), unacceptable toxicity, consent withdrawal, or death.

Primary endpoint
- To assess the OS of the MD.

Secondary endpoints
- To assess the median progression-free survival (PFS), overall response rate (ORR), clinical benefit rate (CBR), time to response (TTR), duration of response (DOR), and rate of grade ≥3 CTx-related toxicities.

Exploratory endpoints
- To assess patient reported outcomes using the European Organization for Research and Treatment of Cancer quality of life questionnaire (QLQ-C30) and EORTC BR 25 from cohort 5.
- To evaluate predictive and/or prognostic factors on plasma and/or tissue biomarkers and/or cerebrospinal fluid (CSF) samples.

Study assessments
- Tumor imaging of those and abdomen by computed tomography scan or MRI performed at baseline, every 6 weeks for the first 6 months and, thereafter, every 9 weeks until the end of the study visit.
- Brain MRI performed at baseline, every 5 weeks for the first 6 months and every 9 weeks thereafter unless clinically suspected brain progression.
- Assessment by MRI obtained together with spinal tap for CSF collection every 3 weeks for the first 12 weeks, every 6 weeks thereafter, and time of treatment progression or study termination.

Statistics
- Sample size was planned to attain an 85% power at normal level of one-sided α of 0.05 in each cohort (described below for cohort 5).

Results
1. Recruitment and Patient Disposition
- From April 14, 2021, through April 5, 2022, 7 pts were enroled into cohort 5, across 6 hospitals in Spain (Table 1).
- Data cut-off date: April 4, 2022

2. Efficacy in Patients with LMC
- Median OS was 13.3 months (95% CI, 2.5-NR, p=0.001) meeting the primary endpoint (Figure 2).
- Median PFS was 9.8 months (95% CI, 2.1-NR, Figure 2).
- Of the 5 pts who had progressed, none had intracranial progression and/or clinical worsening of leptomeningeal symptoms at the time of treatment failure.
- At data cut-off, 2 (28.6%) pts remained on therapy (Table 3).