Study/Registry Title	A prospective, non-interventional study (NIS) with trastuzumab deruxtecan for patients with HER2-low expressing unresectable and/or metastatic breast cancer accompanied by a disease registry of patients treated with conventional chemotherapy (Destiny Breast HER2-low Respond Europe)
Observational plan version identifier	Version 2.0
Date of last observational plan version	29.04.2024
Marketing Authorization Holder	Daiichi Sankyo Europe for T-DXd For conventional chemotherapy: NA
Main Authors	[redacted], Senior Director European Medical Affairs Oncology [redacted], Head of European Clinical Operations both DSE
Rationale and Background	About half of all breast cancer patients show a low-level expression of HER2 (HER2-low), defined as immunohistochemically (IHC) 1+ or 2+ and lack of HER2 gene amplification measured by in situ hybridization (ISH) (IHC1+, IHC2/ISH-). The low HER2 expression is a promising new target for antibody–drug conjugates (ADCs) currently under investigation. Based on DB04 trial results the European Medicines Agency (EMA) assessed the registration for T-DXd and on December 16, 2022, the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion to extend the indication of trastuzumab deruxtecan (T-DXd). Trastuzumab deruxtecan as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-lowbreast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.
Research Question and Objectives	This non-interventional study will investigate the effectiveness of T-DXd, the demographic and clinical characteristics of the patients, treatment patterns, tolerability, management of Adverse Drug Reactions (ADRs), and patient experience of T-DXd, in patients with HER2-low unresectable and/or metastatic breast cancer. Patients will be treated according to the proposed indication statement in the Summary of Product Characteristics (SmPC). In addition, data on conventional chemotherapy (i.e., including but not limited to capecitabine, eribulin, gemcitabine, paclitaxel and nab-paclitaxel) will be collected in a disease registry part of the study. The same inclusion criteria will be applied to patients on conventional chemotherapy. The disease registry part will allow us to understand treatment patterns and outcomes on conventional chemotherapy before the introduction of T-DXd in this patient setting.

Study Design	Multinational, multicenter, prospective observational, non-interventional study
Population	Setting: • 1350 patients from different countries and care settings (primary care and secondary care and different specialties) The study population consists of adult patients with unresectable or metastatic HER2-low breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy
Inclusion/exclusion criteria	Key inclusion criteria: • Adult patient (age ≥ 18 years) with histological or cytological confirmed diagnosis of unresectable and/or mBC • Documented HER2-low status (IHC1+, IHC2+/ISH-) • Patients who have received prior chemotherapy in the metastatic setting or • Patients who have developed disease recurrence during or within 6 months of completing adjuvant chemotherapy • Decision to newly initiate therapy of T-DXd or conventional chemotherapy according to the physician's choice per SmPC • Written Informed Consent (ICF) to participate in the study Key Exclusion criteria: • Pregnancy or breastfeeding • Patients who at time of data collection for this study are participating in or have participated in an interventional study that remains blinded. As this is a non-interventional study, no explicit exclusion criteria are defined. The prescribing behavior will not be influenced.
Data Sources	As this is a non-interventional study, only data on clinical routine practice will be documented. To facilitate accurate recording of data, patients can optionally fill in a memory aid to note important details.
Milestones	First Patient In (FPI) / Start of Data Collection: Q1/2024 Last Patient In (LPI): Q2/2025 Last Patient Out (LPO) (end of treatment): Q2/2027 Last patient completing post treatment: Q3/2028 Final Report: Q4/2028 Timelines may be adapted in case some countries experience major delays of ethics approvals.