

Press Release

Datopotamab Deruxtecan Late-Breaking Data at ESMO Breast Shows Promising Preliminary Response and Disease Control in Patients with Metastatic Triple Negative Breast Cancer

- Oral presentation highlighting first results from TROPION-PanTumor01 in patients with triple negative breast cancer shows preliminary clinical activity

Tokyo, Munich and Basking Ridge, NJ – (May 8, 2021) – New data from Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca's datopotamab deruxtecan (Dato-DXd), a TROP2 directed DXd antibody drug conjugate (ADC), showed preliminary response and disease control in patients with metastatic triple negative breast cancer (TNBC) with disease progression following standard treatment.

These preliminary data from the TNBC cohort of the TROPION-PanTumor01 phase 1 study were presented as a late-breaking mini oral presentation (Abstract #LBA4) at the 2021 European Society of Medical Oncology (ESMO) Breast Cancer Virtual Congress (#ESMOBreast21).

TNBC accounts for approximately 10 to 15% of breast cancer cases and is associated with higher disease recurrence and worse prognosis compared to other breast cancer subtypes.^{1,2,3} It is estimated that only 12.2% of patients with metastatic TNBC survive five years and median overall survival is generally less than two years.^{2,3}

The preliminary objective response rate (ORR), assessed by blinded independent central review, was 43% in 21 evaluable patients treated with datopotamab deruxtecan [6 mg/kg (n=19) or 8 mg/kg (n=2)]. Five confirmed complete or partial responses (CR/PRs) were seen, with four additional CR/PRs awaiting confirmation at the time of data cut-off of January 8, 2021. A disease control rate of 95% was observed.

“There are currently limited treatment options for patients with previously treated metastatic triple negative breast cancer, historically a very difficult-to-treat subtype of breast cancer,” said Aditya Bardia, MD, MPH, Director of Breast Cancer Research, Mass General Cancer Center, Harvard Medical School. “These initial safety and efficacy results of datopotamab deruxtecan in patients with triple negative breast cancer are encouraging and warrant further development for patients with breast cancer.”

The safety profile of datopotamab deruxtecan seen in the TNBC cohort is consistent with safety that has been previously reported in the non-small cell lung cancer (NSCLC) cohort of TROPION-PanTumor01. No

patients discontinued treatment due to adverse events (AEs); however, dose reductions due to AEs occurred in six patients (25%) and were most commonly due to stomatitis (13%) and mucosal inflammation (8%). Grade 3 or higher treatment emergent adverse events (TEAEs) regardless of causality occurred in 33% of patients. TEAEs grade 3 or higher included stomatitis (13%), fatigue (4%) and anemia (4%) with no grade 3 or higher TEAEs of diarrhea or neutropenia. The most common TEAEs overall in $\geq 25\%$ of patients were stomatitis, nausea, fatigue, vomiting, and alopecia. No cases adjudicated as drug-related interstitial lung disease (ILD) were observed.

“These preliminary results provide proof-of-concept that targeting TROP2 with datopotamab deruxtecan may be an effective treatment strategy for patients with previously treated metastatic triple negative breast cancer,” said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. “We are encouraged by the early tumor responses and disease control seen in these patients and we will continue to explore the potential of datopotamab deruxtecan in several types of breast cancer, including triple negative breast cancer.”

“Triple negative breast cancer is known to be particularly aggressive and fast growing, and after treatment the risk of recurrence is faster and higher than in any other breast cancer subgroup,” said Cristian Massacesi, Senior Vice President, Head of Late Stage Development Oncology R&D, AstraZeneca. “The preliminary results for datopotamab deruxtecan in this cohort of pretreated patients are encouraging for this high-potential targeted ADC.”

Patients were treated with a median of four prior lines of therapy (range, 1-9, including prior lines of therapy in the [neo]adjuvant or metastatic setting) with a majority (88%) receiving more than two previous lines of treatment, including a taxane (83%), platinum-based chemotherapy (50%), immunotherapy (33%), sacituzumab govitecan (8%) and a PARP inhibitor (4%). As of data cut-off on January 8, 2021, 75% of patients remained on treatment with datopotamab deruxtecan.

Summary of TROPION-PanTumor01 Results

Efficacy Measure	Total Evaluable in TNBC Cohort (N=21) ^{i,ii}
ORR, % ^{iii, iv}	43% (n=9)
CR/PR (confirmed)	n=5
CR/PR (pending confirmation)	n=4
DCR, % ^v	95% (n=20)
PD, %	5% (n=1)

CR, complete response; DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PR, partial response

ⁱ Includes response evaluable patients who had ≥ 1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 3 patients at the data cutoff. One patient was not confirmed to have a target lesion per BICR and therefore had a best overall response of non-CR/non-PD.

ⁱⁱ Includes 2 patients that received 8 mg/kg datopotamab deruxtecan prior to selection of the 6-mg/kg dose for dose expansion

ⁱⁱⁱ Includes patients with a best overall response of CR, PR, stable disease, or non-CR/non-PD.

^{iv} ORR is CR+PR; Responses are confirmed (CRs/PRs; n=5) plus those ongoing CRs/PRs too early to be confirmed (n=4).

^v DCR is CR+PR+SD

About TROPION-PanTumor01

TROPION-PanTumor01 is a first-in-human, open-label, two-part, multicenter phase 1 trial designed to evaluate the safety, tolerability and preliminary efficacy of datopotamab deruxtecan in patients with advanced solid tumors refractory to or relapsed from standard treatment or for whom no standard treatment is available, including NSCLC, TNBC and hormone receptor positive (HR+) breast cancer.

The dose escalation part of the study assessed the safety and tolerability of increasing doses of datopotamab deruxtecan to determine the maximum tolerated dose and/or recommended dose for expansion in patients with unresectable advanced NSCLC. The dose expansion part of the study further assessed the safety and tolerability of datopotamab deruxtecan at selected dose levels (4 mg/kg, 6 mg/kg and 8 mg/kg) in patients with NSCLC. Based on the preliminary efficacy and safety, the 6 mg/kg dose has been identified as the recommended dose for the NSCLC cohort.

The TNBC cohort was added in July 2020 and is currently evaluating patients with metastatic TNBC receiving datopotamab deruxtecan (6 mg/kg) with disease relapse or progression with standard treatment. The HR positive/HER2 negative cohort was added in March 2021 and is currently evaluating patients with metastatic HR positive/HER2 negative breast cancer receiving datopotamab deruxtecan (6 mg/kg) with disease relapse or progression with standard treatment.

Safety endpoints include dose limiting toxicities and serious adverse events. Efficacy endpoints include ORR, DCR, duration of response, time to response, progression-free survival and overall survival. Pharmacokinetic, biomarker and immunogenicity endpoints also are being evaluated.

About TROP2 in Triple Negative Breast Cancer

TROP2 (trophoblast cell-surface antigen 2) is a transmembrane glycoprotein that is overexpressed in several types of solid tumors, including breast cancer.⁴ Research indicates that high TROP2 expression is associated with cancer cell growth and proliferation and poor patient survival.^{4,5} While TROP2 is expressed across all breast cancer subtypes, it is overexpressed in approximately 80% of patients with TNBC, making it a promising molecular target for therapeutic development.⁵

Approximately 10 to 15% of patients with breast cancer are considered triple negative because the tumors test negative for estrogen, progesterone hormone receptors (HRs) and human epidermal growth factor 2 receptor (HER2).^{1,2,6} An estimated 260,000 new cases of TNBC were reported globally in 2018 with it being more common in younger women and those who are Black.^{1,2,7} Compared to patients with other breast cancer subtypes, prognosis for patients with metastatic TNBC is generally worse and the disease is more likely to recur following treatment with initial chemotherapy.^{1,3} Five-year survival of metastatic TNBC is estimated at 12.2% and median overall survival is generally less than two years.^{2,3}

About Datopotamab Deruxtecan (Dato-DXd)

Datopotamab deruxtecan (Dato-DXd) is a TROP2 directed antibody drug conjugate (ADC). Designed using Daiichi Sankyo's proprietary DXd ADC technology, datopotamab deruxtecan is one of three lead ADCs in the oncology pipeline of Daiichi Sankyo, and one of the most advanced programs in AstraZeneca's ADC scientific platform.

A comprehensive development program called TROPION is underway globally with trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple solid tumors, including NSCLC, TNBC and HR+ breast cancer. Trials in combination with other anticancer treatments, such as immunotherapy, are also underway.

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize datopotamab deruxtecan in [July 2020](#), except in Japan where Daiichi Sankyo maintains exclusive rights. Daiichi Sankyo is responsible for the manufacturing and supply of datopotamab deruxtecan.

About Daiichi Sankyo Cancer Enterprise

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by our DXd antibody drug conjugate (ADC) technology, our powerful research engines include biologics, medicinal chemistry, modality and other research laboratories in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. For more information, please visit: www.DSCancerEnterprise.com.

About Daiichi Sankyo

Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose “to contribute to the enrichment of quality of life around the world.” In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an “Innovative Global Healthcare Company Contributing to the Sustainable Development of Society.” For more information, please visit www.daiichisankyo.com.

Media Contacts:

Global/US:

Victoria Amari
Daiichi Sankyo, Inc.
vamari@dsi.com
+1 908 900 3010 (mobile)

Japan:

Masashi Kawase
Daiichi Sankyo Co., Ltd.
kawase.masashi.a2@daiichisankyo.co.jp
+81 3 6225 1126 (office)

EU:

Lydia Worms
Daiichi Sankyo Europe GmbH
lydia.worms@daiichi-sankyo.eu
+49 (89) 7808751 (office)
+49 176 11780861 (mobile)

Investor Relations Contact:

DaiichiSankyoIR@daiichisankyo.co.jp

References

- ¹ American Cancer Society. [Triple-negative breast cancer](#). Accessed April 19, 2021.
- ² Sharma P. *Oncologist*. 2016;21:1050-1062.
- ³ National Cancer Institute. [SEER cancer stat facts: female breast cancer subtypes](#). Accessed April 19, 2021.
- ⁴ Goldenberg D, et al. *Oncotarget*. 2018;9(48): 28989-29006.
- ⁵ Zaman S, et al. *Onco Targets Ther*. 2019;12:1781-1790.
- ⁶ Bianchini G, et al. *Nat Rev Clin Oncol*. 2016;13:674-690.
- ⁷ Bray F, et al. *CA Cancer J Clin*. 2018;68:394-424.