Poster 552P

# TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd) in Asian patients with previously treated non-small cell lung cancer (NSCLC) with actionable genomic alterations


Myung-Ju Ahn,[1] Byoung Chul Cho,[2] **Yasushi Goto**,[3] Kiyotaka Yoh,[4] Wu-Chou Su,[5] Junichi Shimizu,[6] Jong-Seok Lee,[7] Satoshi Oizumi,[8] James Chih-Hsin Yang,[9] Hidetoshi Hayashi,[10] Hong Zebger-Gong,[11] Koichi Sugiura,[12] Lan Lan,[13] Chelsea Liu,[13] Satoru Kitazono[14]

[1]Samsung Medical Center, Seoul, South Korea; [2]Severance Hospital, Seoul, South Korea; [3]National Cancer Center Hospital, Tokyo, Japan; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]National Cheng Kung University Hospital, Tainan, Taiwan; [6]Aichi Cancer Center Hospital, Japan, [7]Seoul National University Bundang Hospital, South Korea; [8]Hokkaido Cancer Center, Japan; [9]National Taiwan University Hospital, Taiwan; [10]Kindai University Hospital, Japan; [11]Daiichi Sankyo Europe GmbH, Munich, Germany; [12]Daiichi Sankyo Co., Ltd, Tokyo, Japan; [13]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [14]The Cancer Institute Hospital of JFCR, Tokyo, Japan


## Objective

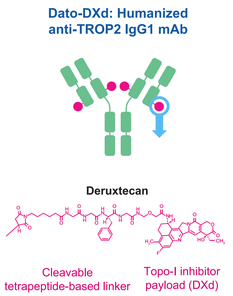
- To assess the efficacy and safety of Dato-DXd in Asian patients with previously treated advanced/metastatic NSCLC with actionable genomic alterations

## Conclusions

- In Asian patients with heavily pretreated advanced/metastatic NSCLC and actionable genomic alterations, Dato-DXd showed encouraging antitumor activity, with clinically meaningful overall responses
- The safety profile was manageable and consistent with prior studies of Dato-DXd in NSCLC
  - TEAEs were primarily grade 1 or 2, with stomatitis and nausea being the most frequently reported
- Results in this Asian subpopulation of TROPION-Lung05 are consistent with the global populations of TROPION-Lung05 and the phase 3 TROPION-Lung01 trial[2,3]

## Introduction

- Dato-DXd is an ADC composed of a TROP2-directed IgG1 mAb covalently linked to a highly potent cytotoxic topoisomerase I inhibitor payload via a plasma-stable, tumor-selective, tetrapeptide-based cleavable linker[1]
- In the phase 3 TROPION-Lung01 study (NCT04656652), Dato-DXd showed promising efficacy in patients with advanced or metastatic NSCLC with or without actionable genomic alterations, significantly improving PFS compared to docetaxel, with no new safety signals[2]
  - The HR for PFS with Dato-DXd vs docetaxel was 0.75 for the overall TROPION-Lung01 study population; for the subgroup of individuals with actionable genomic alterations (n=47), the HR was 0.38
- TROPION-Lung05 (NCT04484142) is a global phase 2 study evaluating Dato-DXd in patients with advanced/metastatic NSCLC with actionable genomic alterations who have progressed on or after targeted therapy and platinum-based chemotherapy[3]
- Here, we report results from patients enrolled in Asia from TROPION-Lung05







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Corresponding author email address: silkahn@skku.edu


# Methods

## Study design

- TROPION-Lung05 (NCT04484142) is a phase 2, multicenter, single-arm, open-label study (**Figure 1**)
- This is a post hoc analysis of patients enrolled from participating study sites in Asia

**Figure 1. TROPION-Lung05 study design**

**Key inclusion criteria**

- Adults with advanced/metastatic NSCLC
- Presence of actionable genomic alterations (e.g. *EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
- Previous treatment with:
  - ≥1 line of targeted therapy
  - 1 or 2 prior cytotoxic agent–containing therapies including platinum-based therapy in the metastatic setting
- ECOG PS = 0 or 1
- Radiographic disease progression on/after most recent treatment for advanced/ metastatic disease

**Treatment**
Dato-DXd 6 mg/kg Q3W

Asian subpopulation, n=66
Total study population, N=137

**Endpoints[a]**
**Primary:**
- ORR by BICR

**Secondary:**
- DoR by BICR
- DCR by BICR
- PFS by BICR
- Safety

[a]The primary completion date will occur when all patients have had either a minimum of 9 months of follow up since first receiving Dato-DXd or have discontinued from the study.

# Results

## Patients

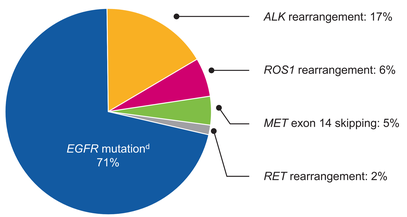
**Table 1. Demographics and baseline characteristics**

| Characteristic | Asian population (N=66) |
|---|---|
| **Age**, median (range), years | 64 (34–77) |
| **Female**, n (%) | 38 (58) |
| **Adenocarcinoma histology**, n (%) | 63 (96) |
| **History of brain metastases**, n (%)[a] | 30 (46) |
| **Prior lines of therapy**, n (%)[b] | |
| Prior targeted therapy for indicated actionable genomic alteration for adv/met disease | 66 (100) |
| Prior platinum chemotherapy | 66 (100) |
| ≥3 lines of systemic therapy for adv/met disease | 45 (68) |
| ≥2 lines of targeted therapy for indicated actionable genomic alteration for adv/met disease | 35 (53) |
| Anti–PD-1/anti–PD-L1 immunotherapy | 23 (35) |

[a]Patients with clinically inactive brain metastases and patients with treated brain metastases who are no longer symptomatic, require no treatment with corticosteroids or anticonvulsants, and have recovered from radiotherapy may be included in the study. [b]Patients may have received ≥1 type of prior therapy.

- Of 137 patients enrolled in TROPION-Lung05, 66 patients were enrolled in Asia and included in this analysis (Japan, n=32; South Korea, n=26; Taiwan, n=8)
- At the time of data cutoff (December 14, 2022), 11 (16.7%) patients had treatment ongoing and 55 (83.3%) patients had discontinued from the study drug; primary cause of treatment discontinuation was disease progression (PD + clinical progression; 72.7%)
- The median study duration was 15.7 (range, 9.7–20.5) months and the median treatment duration was 5.7 (range, 0.7–20.0) months
- Demographics and baseline characteristics are shown in **Table 1**

**Figure 2. Summary of alteration types[a–c]**




[a]Patients whose tumors harbor *KRAS* mutations, in the absence of the genomic alterations *EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, and *RET*, were excluded from the study. [b]One patient had tumors with *MET* amplification. [c]Patients had co-occurring alteration types; thus, percentages do not sum to 100%. [d]Protocol requires enrollment of ≈50% of patients with *EGFR*-mutated tumors, among whom 80% should have received prior osimertinib.

- The most common types of alterations were *EGFR* mutations (71.2%) and *ALK* rearrangements (16.7%) (**Figure 2**)
  - The most common types of *EGFR* mutations were exon 19 deletion (37.9%), exon 20 T790M (25.8%), and exon 21 L858R (22.7%)

## Efficacy

**Table 2. Tumor response by BICR**

| Patients, n (%) | All patients (N=66) | *EGFR*m (n=47) |
|---|---|---|
| **ORR** | 28 (42.4) | 23 (48.9) |
| [95% CI[a]] | [30.3, 55.2] | [34.1, 63.9] |
| CR | 2 (3.0) | 2 (4.3) |
| PR | 26 (39.4) | 21 (44.7) |
| **DoR**, median (95% CI), months | 4.4 (4.0, 14.0) | 4.4 (4.0, 14.0) |
| **Non-CR/non-PD** | 2 (3.0) | 2 (4.3) |
| **SD** | 23 (34.8) | 16 (34.0) |
| **NE[b]** | 2 (3.0) | 0 |
| **DCR** | 53 (80.3) | 41 (87.2) |
| [95% CI[a]] | [68.7, 89.1] | [74.3, 95.2] |
| **PD** | 11 (16.7) | 6 (12.8) |

[a]The 2-sided 95% CIs are based on the Clopper-Pearson exact binomial method. [b]Patients were not evaluable due to a lack of adequate post-baseline tumor assessment (n=1) or due to SD occurring <5 weeks after the start of the study treatment (n=1).

- The ORR was 42.4% (48.9% in the subset of patients with *EGFR* mutations) and the DCR was 80.3% (87.2% in patients with *EGFR* mutations) (**Table 2**)
- The median DoR was 4.4 months in the overall Asian population and 4.4 months in the subset of patients with *EGFR* mutations

**Figure 3. (A) Antitumor activity by BICR and (B) Percent change from baseline in the sum of diameters in target lesions in patients with confirmed CR/PR by BICR**

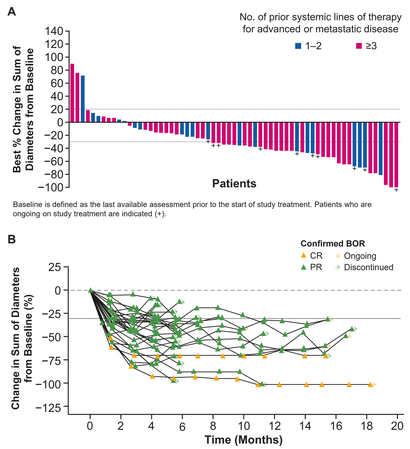
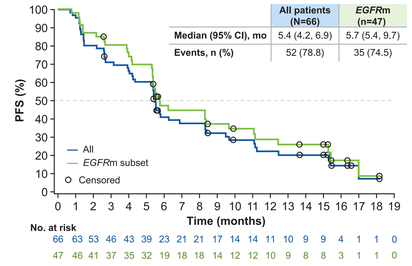



**Figure 4. PFS by BICR**




| | All patients (N=66) | *EGFR*m (n=47) |
|---|---|---|
| Median (95% CI), mo | 5.4 (4.2, 6.9) | 5.7 (5.4, 9.7) |
| Events, n (%) | 52 (78.8) | 35 (74.5) |

- Median PFS was 5.4 months in the overall Asian population and 5.7 months in the subset of patients with *EGFR* mutations (**Figure 4**)

## Safety

**Table 3. Summary of TEAEs**

| Patients, n (%) | Dato-DXd (N=66) |
|---|---|
| **TEAEs** | |
| Any grade | 66 (100) |
| Grade ≥3 | 24 (36.4) |
| Treatment-related | 59 (89.4) |
| Grade ≥3 | 17 (25.8) |
| **Serious TEAEs** | |
| Any grade | 10 (15.2) |
| Grade ≥3 | 8 (12.1) |
| Treatment-related | 3 (4.5) |
| Grade ≥3 | 2 (3.0) |
| **Dose adjustments due to AEs** | |
| Dose reduction | 11 (16.7) |
| Treatment-related | 10 (15.2) |
| Dose delay | 24 (36.4) |
| Treatment-related | 16 (24.2) |
| Dose withdrawn | 5 (7.6) |
| Treatment-related | 3 (4.5) |
| **TEAEs associated with death** | 1 (1.5) |
| Treatment-related | 0 |

- Any grade and grade ≥3 TEAEs were observed in 66 (100%) and 24 (36.4%) patients, respectively
  - One (1.5%) grade 5 TEAE (dyspnea) was associated with disease progression and reported as unrelated to Dato-DXd (**Table 3**)

## Abbreviations

ADC, antibody-drug conjugate; AESI, adverse events of special interest; BICR, blind independent central review; BOR, best overall response; CI, confidence interval; CR, complete response; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*m, *EGFR* mutation-positive; HR, hazard ratio; ILD, interstitial lung disease; IRR, infusion-related reaction; mAb, monoclonal antibody; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; SD, stable disease; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event; TROP2, trophoblast cell surface antigen 2.


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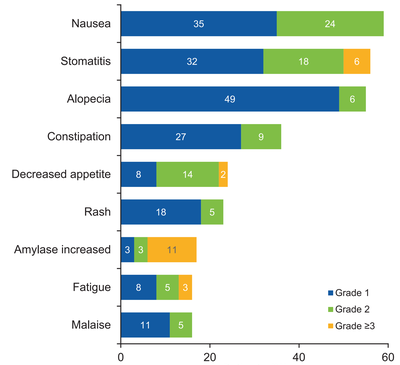
**Figure 5. All-cause TEAEs in ≥15% of patients**




- The most common TEAEs were nausea (59.1%), stomatitis (56.1%), and alopecia (54.5%) (**Figure 5**)
  - The most common grade ≥3 TEAEs were amylase increased (10.6%), stomatitis (6.1%), and anemia (4.5%)

**Table 5. AESIs[a]**

| Patients, n (%) | AESIs (N=66) Any grade | Grade 1 | Grade 2 | Grade 3[b] | AESIs associated with Dose reduction | Dose delay | Dose with-drawn |
|---|---|---|---|---|---|---|---|
| Oral mucositis/ stomatitis | 38 (57.6) | 21 (31.8) | 13 (19.7) | 4 (6.1) | 5 (7.6) | 6 (9.1) | 0 |
| Ocular events | 16 (24.2) | 11 (16.7) | 2 (3.0) | 3 (4.5) | 1 (1.5) | 3 (4.5) | 0 |
| IRR | 9 (13.6) | 8 (12.1) | 1 (1.5) | 0 | 0 | 0 | 0 |
| Adjudicated drug-related ILD | 2 (3.0) | 1 (1.5) | 1 (1.5) | 0 | 0 | 0 | 2 (3.0) |

[a]AESIs listed include all preferred terms defined by the medical concept. [b]There were no cases of grade 4–5 AESIs.

- The overall incidence of oral mucositis/stomatitis was high (58%), but the majority (52%) were grade 1–2 (**Table 5**)
- The majority of cases of ocular events (e.g. dry eye) and IRR were low grade
- There were 2 (3.0%) cases of adjudicated drug-related ILD, both grade 1–2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## References


1. Okajima D, et al. *Mol Cancer Ther*. 2021;20:2329–2340.
2. Ahn M, et al. Presented at ESMO 2023, October 20–24, 2023, Madrid, Spain.
3. Paz-Ares L, et al. Presented at ESMO 2023, October 20–24, 2023, Madrid, Spain.