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

Satoru Kitazono,[1] Luis Paz-Ares,[2] Myung-Ju Ahn,[3] Aaron Lisberg,[4] Byoung Chul Cho,[5] George Blumenschein Jr,[6] Elaine Shum,[7] Elvire Pons Tostivint,[8] Yasushi Goto,[9] Kiyotaka Yoh,[10] Rebecca Heist,[11] Paul Baas,[12] David Planchard,[13] Maurice Pérol,[14] Enriqueta Felip,[15] Wu-Chou Su,[16] Hong Zebger-Gong,[17] Lan Lan,[18] Chelsea Liu,[18] Jacob Sands[19]

[1]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [2]Hospital Universitario 12 de Octubre, Madrid, Spain; [3]Samsung Medical Center, Seoul, South Korea; [4]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [5]Severance Hospital, Seoul, South Korea; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]NYU Langone Health Perlmutter Cancer Center, New York, NY, USA; [8]University Hospital of Nantes, Nantes, France; [9]National Cancer Center Hospital, Tokyo, Japan; [10]National Cancer Center Hospital East, Kashiwa, Japan; [11]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [12]The Netherlands Cancer Institute, Amsterdam, the Netherlands; [13]Gustave Roussy, Villejuif, France; [14]Centre Léon Bérard, Lyon, France; [15]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [16]National Cheng Kung University Hospital, Tainan, Taiwan; [17]Daiichi Sankyo Europe GmbH, Munich, Germany; [18]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [19]Dana-Farber Cancer Institute, Boston, MA, USA

Declaration of Interests

Satoru Kitazono

- **Speaker fees**: Pfizer, Ono Pharmaceutical Co., Chugai Pharmaceutical Co.
- **Funding for the current study** provided by Daiichi Sankyo Inc, and AstraZeneca

AACR, American Association for Cancer Research; AECC, American-European Consensus Conference; ASCO, American Society of Clinical Oncology; ASEICA, Spanish Association for Cancer Research; ESMO, European Society for edical Oncology.

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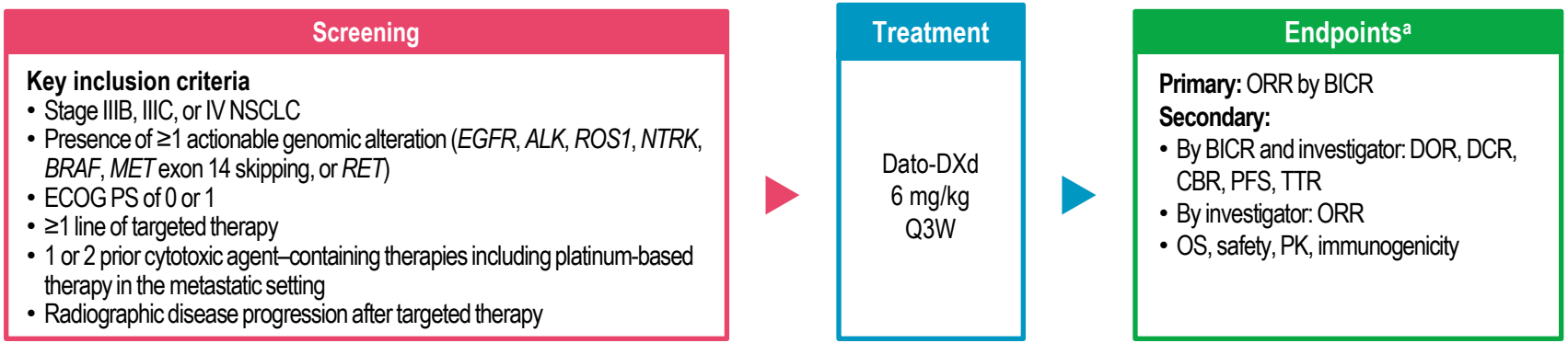
Introduction and Study Design

- **Dato-DXd** is a TROP2-directed ADC consisting of a humanized anti-TROP2 IgG1 monoclonal antibody covalently linked to a highly potent topoisomerase I inhibitor payload via a plasma-stable, tumor-selective, tetrapeptide-based cleavable linker[1]
- In the **phase 1 TROPION-PanTumor01** study, Dato-DXd showed promising efficacy in patients with actionable genomic alterations[2]
- TROPION-Lung05 (NCT04484142) is a **phase 2**, single-arm study evaluating Dato-DXd in patients with **advanced or metastatic NSCLC with actionable genomic alterations** that progressed on or after targeted therapy and platinum-based chemotherapy



ADC, antibody-drug conjugate; BICR, blinded independent central review; CBR, clinical benefit rate; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IgG1, immunoglobulin G1; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; TROP2, trophoblast cell-surface antigen 2; TTR, time to response.

[a]The primary completion date will occur when all patients have had either a minimum of 9 months of follow-up after the start of study treatment or have discontinued from the study.

1. Okajima D, et al. *Mol Cancer Ther*. 2021;20:2329-2340. **2.** Shimizu T, et al. *J Clin Oncol*. Published online June 16, 2023.

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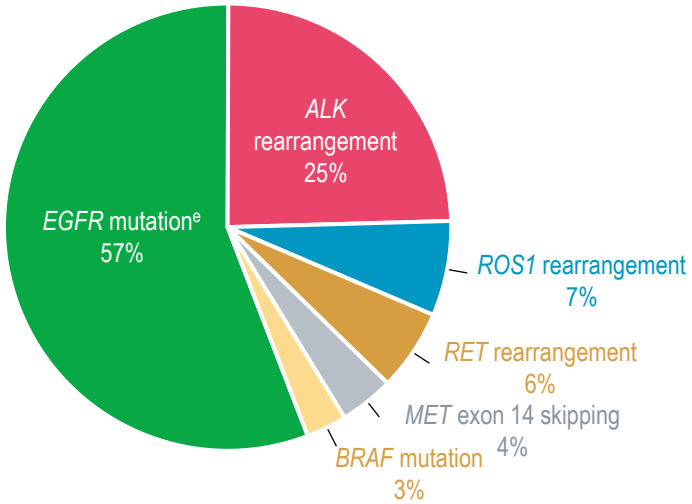
Patient Characteristics and Disposition

Demographic characteristics	Dato-DXd (N=137)
Median age (range), years	60 (29-79)
Female, n (%)	83 (61)
Histology, n (%)	
Adenocarcinoma	130 (95)
History of brain metastasis, n (%)[a]	70 (51)
Median prior lines of therapy for adv/met disease	3
Prior lines of therapy, n (%)	137 (100)
≥3 prior lines of therapy for adv/met disease	98 (72)
Prior platinum chemotherapy	137 (100)
Prior anti–PD-1/anti–PD-L1 immunotherapy	49 (36)
≥2 prior lines of targeted therapies for indicated genomic alteration	82 (60)

Relative Frequency of Genomic Alterations[b-d]



Disposition

At the time of data cutoff (December 14, 2022):

- Median (range) treatment duration was 4 (1-21) months
- 60 participants (44%) were ongoing in study
- 20 participants (15%) were ongoing on study treatment

adv/met, advanced/metastatic; Dato-DXd, datopotamab deruxtecan; PD-1, programmed cell death 1 protein; PD-L1, programmed cell death 1 ligand 1.

[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 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. [c]Three patients had tumors with *MET* amplification. [d]Patients had co-occurring alteration types; thus, percentages do not sum to 100%. [e]Protocol requires enrollment of ≈50% of patients with *EGFR*-mutated tumors, among whom 80% should have received prior osimertinib.

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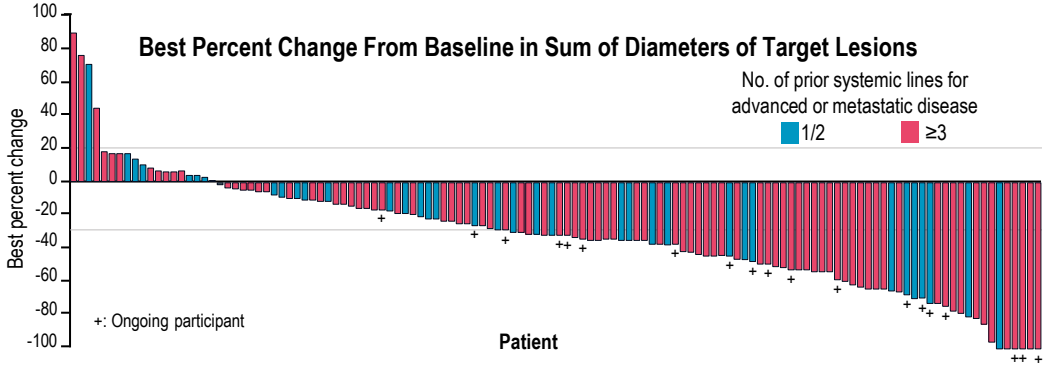
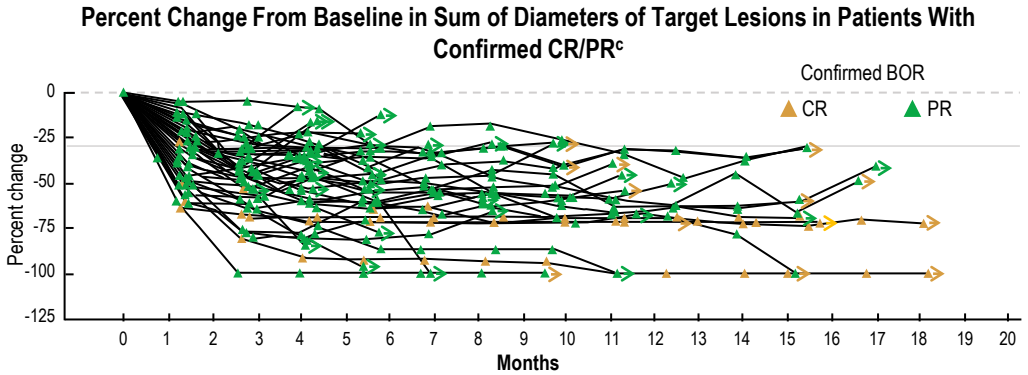
Efficacy Summary

Response per BICR	All treated patients (N=137)	Patients with *EGFR* mutations (N=78)	Patients with *ALK* rearrangement (N=34)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]	34 (43.6) [32.4-55.3]	8 (23.5) [10.7-41.2]
Median DOR (95% CI), months	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]	64 (82.1) [71.7-89.8]	25 (73.5) [55.6-87.1]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)

BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations, the ORR was 49.1% in those previously treated with osimertinib (n=55)





BICR, blinded independent central review; BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; ORR, objective response rate; PFS, progression-free survival; PR, partial response.

[a]The 2-sided 95% CIs are based on the Clopper-Pearson exact binomial method. [b]Median PFS and PFS probabilities are based on the Kaplan-Meier method. [c]Per BICR.

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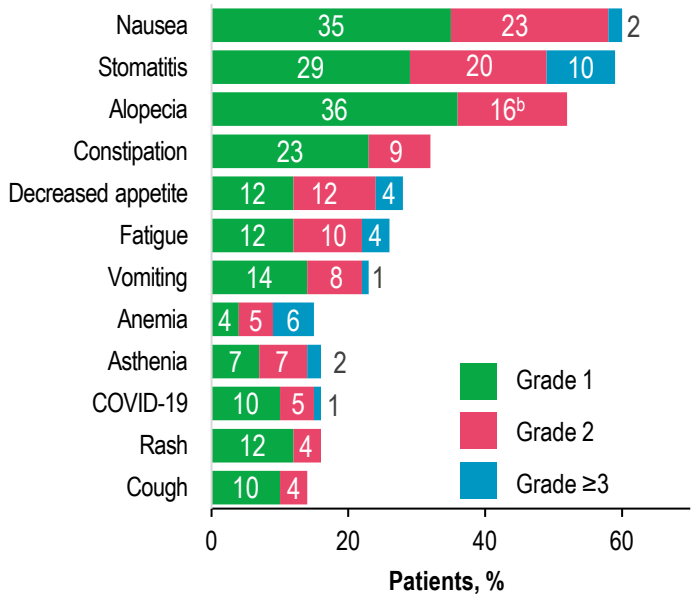
Safety Summary

TEAEs Occurring in ≥15% of Patients; All Grades (N=137)[a]



- 137 patients (100%) experienced **TEAEs** (grade ≥3, 47%)
  - 129 (94%) experienced **treatment-related TEAEs** (grade ≥3, 29%)
  - 34 (25%) experienced **serious AEs** (grade ≥3, 5%)
- 30 (22%), 13 (10%), and 2 (2%) patients experienced TEAEs associated with **dose reduction, dose withdrawal, and death**,[c] respectively

AESI Incidence by Grade[d]

n (%)	Total	Grade 1	Grade 2	Grade ≥3
Oral mucositis/stomatitis	90 (66)	45 (33)	30 (22)	15 (11)
Ocular surface toxicity[e]	36 (26)	26 (19)	7 (5)	3 (2)[f]
IRR	22 (16)	15 (11)	7 (5)	0
Adjudicated drug-related ILD	5 (4)	1 (1)	3 (2)	1 (1)[g]

AE, adverse event; AESI, adverse event of special interest; CTCAE, Common Terminology Criteria for Adverse Events; ILD, interstitial lung disease; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event. [a]Due to rounding, summed rates may not reflect total percentage of TEAEs. [b]Includes an event reported as grade 3 incorrectly per CTCAE grades. [c]Two deaths were associated with disease progression, unrelated to study drug by investigator. [d]AESIs listed in this slide include all preferred terms defined by the medical concept. [e]Dry eye was the most commonly reported ocular surface toxicity (n=15 [11%]). [f]Patients with grade 3 ocular surface toxicity had corneal disorder, cornea verticillata, and punctate keratitis. [g]One case of ILD was reported as a grade 3 event by investigator, and the patient died due to disease progression per investigator. The same event was adjudicated as a grade 5 event.

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Conclusions

Encouraging antitumor activity was observed with **Dato-DXd treatment** in a **heavily pretreated** NSCLC population with **actionable genomic alterations**, including patients with ***EGFR* mutations and *ALK* rearrangements**

Dato-DXd had a **manageable safety profile,** characterized by a low incidence of hematologic or drug-related grade ≥3 toxicities. Nausea and stomatitis were the predominant AEs seen, consistent with previously reported data in NSCLC

The findings are consistent with the **phase 3 TROPION-Lung01** study (NCT04656652), assessing Dato-DXd vs docetaxel in patients with pretreated adv/met NSCLC and including those with actionable genomic alterations, which recently met its dual primary endpoint of superior PFS for Dato-DXd

adv/met, advanced/metastatic; AE, adverse event; Dato-DXd, datopotamab deruxtecan; NSCLC, non-small cell lung cancer.

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Acknowledgments

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