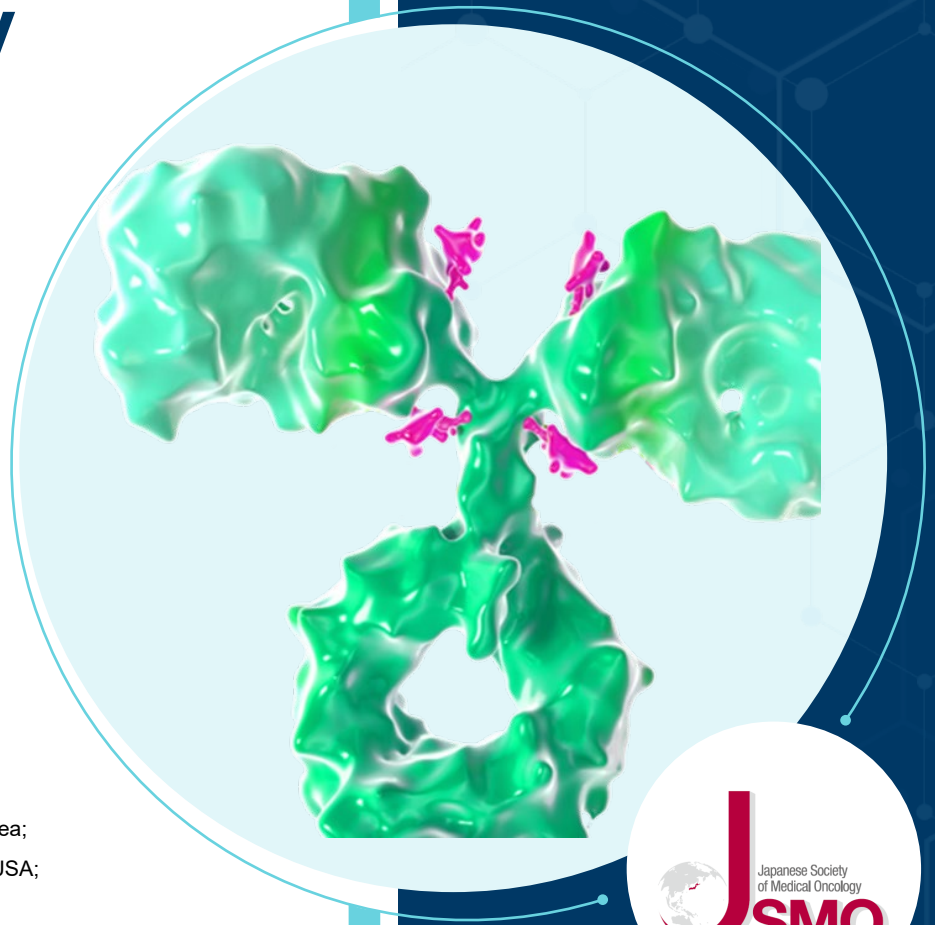
#OS11-1

TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd) in previously treated NSCLC with actionable genomic alterations (AGAs)



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Conflict of Interest disclosure slide for representative speakers or investigators

Research fund	**□scientific research fund □contract □donation ■other （Clinical Trial） □N/A**	**Sponsor**	**Daiichi Sankyo**
Name of lead presenter	**Satoru Kitazono**	**Institution or company/position**	**The Cancer Institute Hospital of JFCR, Tokyo, Japan**

	No	**If yes, please specify the name of company, organization, your status.**
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Introduction

- **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; IgG1, immunoglobulin G1; NSCLC, non-small cell lung cancer; TROP2, trophoblast cell-surface antigen 2

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.

Study Design: TROPION-Lung05 (NCT04484142)

Screening

Key inclusion criteria

- Stage IIIB, IIIC, or IV NSCLC
- Presence of ≥1 actionable genomic alteration (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
- ECOG PS of 0 or 1
- ≥1 line of targeted therapy
- 1 or 2 prior cytotoxic agent–containing therapies including platinum-based therapy in the metastatic setting
- Radiographic disease progression after targeted therapy

Treatment

Dato-DXd
6 mg/kg
Q3W

Endpoints[a]

Primary: ORR by BICR

Secondary:

- By BICR and investigator: DOR, DCR, CBR, PFS, TTR
- By investigator: ORR
- OS, safety, PK, immunogenicity

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; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; TROP2; 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.

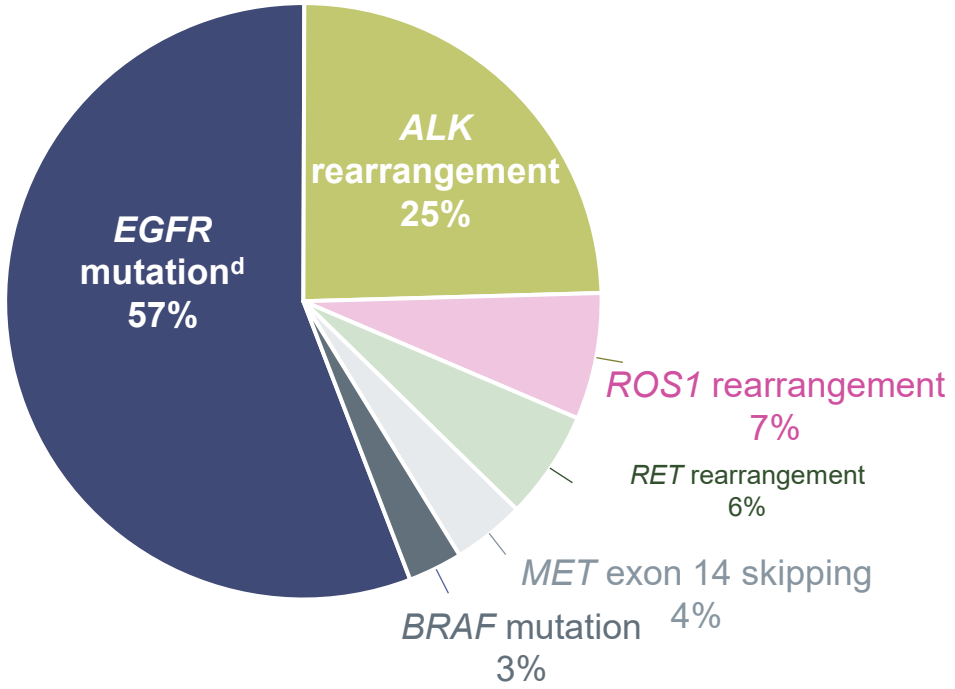
Patient Characteristics

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)

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

Patient Disposition

Relative Frequency of Genomic Alterations[a-c]



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

[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]Three patients 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.

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)

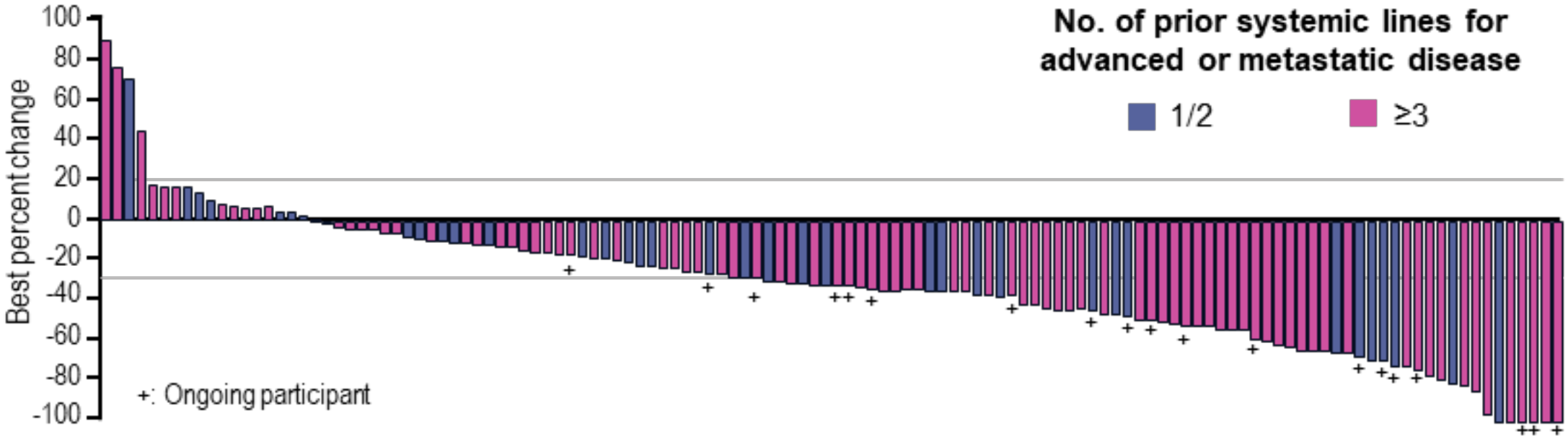
BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations (N=68), the ORR was 49.1% in those previously treated with osimertinib

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.

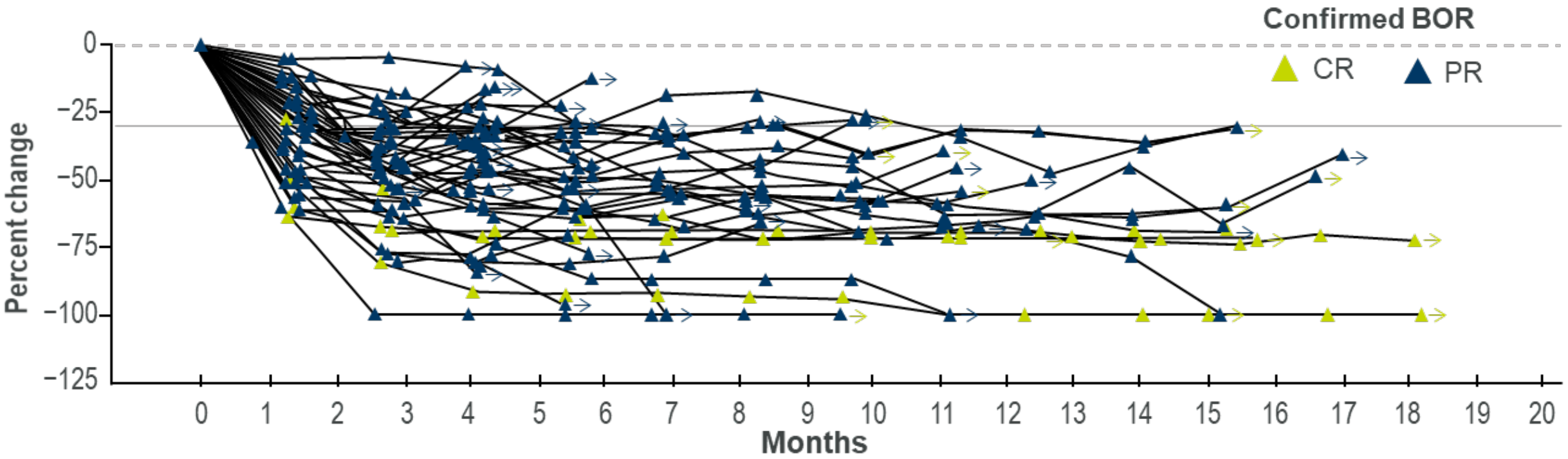
Antitumor Activity

Best Percentage Change From Baseline in Sum of Diameters in Target Lesions



Antitumor Activity

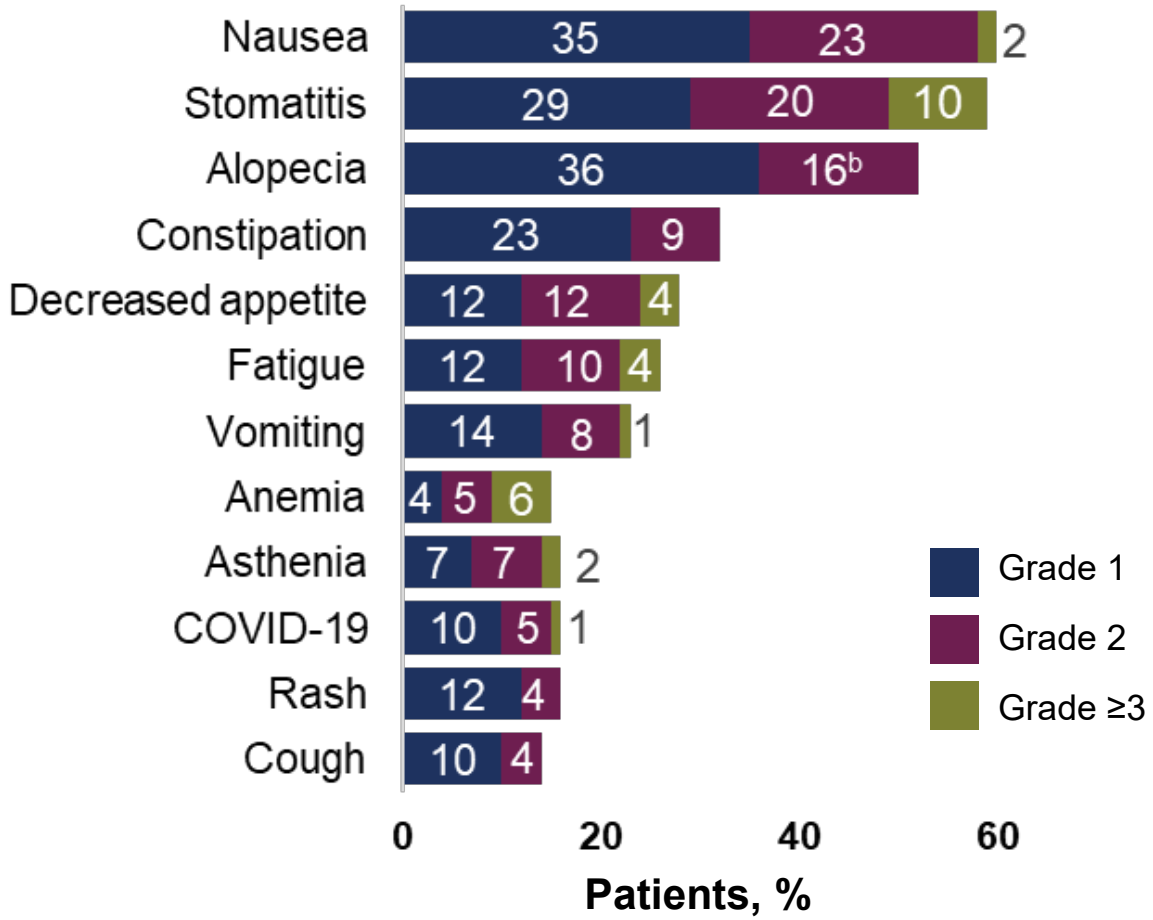
Percent Change From Baseline in Sum of Diameters of Target Lesions in Patients With Confirmed CR/PR[a]



BOR, best overall response; CR, complete response; PR, partial response. [a]Per blinded independent central review (BICR).

Safety Summary

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



- 137 (100%) patients 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

AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; 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.

Safety Summary

AESI Incidence by Grade[a]

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

AESI, adverse event of special interest; ILD, interstitial lung disease; IRR, infusion-related reaction

[a]AESIs listed in this slide include all preferred terms defined by the medical concept. [b]Dry eye was the most commonly reported ocular surface toxicity (n=15 [11%]). [c]Patients with grade 3 ocular surface toxicity had corneal disorder, cornea verticillata, and punctate keratitis. [d]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

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 ongoing, randomized, **phase 3 TROPION-Lung01** study (NCT04656652) is assessing Dato-DXd vs docetaxel in patients with pretreated adv/met NSCLC, including those with actionable genomic alterations

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

Acknowledgments

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