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LUNG CONNECT

TROP2-DIRECTED ADCs IN LUNG CANCER: OPTIMISING THE TREATMENT EXPERIENCE

Monday 11th May 2026

ADC, antibody-drug conjugate

DEVELOPED BY LUNG CONNECT

This programme is developed by LUNG CONNECT, an international group of experts in the field of thoracic oncology and brought to you alongside PRECISION ONCOLOGY CONNECT, an international group of experts in the field of Precision Oncology

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Acknowledgement and disclosures

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- **Prof. Nicolas Girard** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: Abbvie, Accord, Amgen, AstraZeneca, BeOne, Bristol Myers Squibb, Daiichi-Sankyo, Ipsen, J&J, Lilly, Merck Sharp & Dohme, Natera, Pfizer, Pharmamar, Pierre Fabre, Regeneron, Summit
- **Dr Louise Lim** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: AstraZeneca, Astellas, BMS, Gilead, MSD, Merck-Serono, Pfizer, Roche
- **Dr Jacob Sands** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: Abbvie, Amgen, AstraZeneca, Boehringer Ingelheim, Catalyst, Daiichi Sankyo, Fosun, Genentech, Gilead, Jazz Pharmaceuticals, Lilly, Merck, Novartis, Pfizer, Pharma Mar, Sanofi
- **Mrs Stephanie McDonald** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: Amgen, AstraZeneca, Bayer, Pfizer

INTRODUCING THE SCIENTIFIC COMMITTEE

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EDUCATIONAL OBJECTIVES

- **Assess the clinical relevance** of TROP2-targeted antibody–drug conjugates (ADCs) in NSCLC and their **role in evolving treatment strategies**
- **Recognise the potential adverse events** associated with TROP2-directed ADCs in metastatic NSCLC, including Dato-DXd
- **Be able to implement strategies to prevent, minimise and manage adverse events** associated with TROP2-directed ADCs to achieve optimal outcomes for NSCLC patients

ADC, antibody-drug conjugates; Dato-DXd, datopotamab deruxtecan; NSCLC, non-small cell lung cancer

AGENDA

THE EVOLVING TROP2-DIRECTED ADC LANDSCAPE IN METASTATIC NSCLC AND STRATEGIES TO OPTIMISE THE TREATMENT EXPERIENCE

Topic	Facilitator
The relevance of TROP2 in metastatic NSCLC	Louise Lim
Clinical overview of TROP2-directed ADCs in NSCLC • Without actionable genomic alterations • With actionable genomic alterations	Nicolas Girard Louise Lim
Optimising the treatment experience: proactive AE monitoring & management	Jacob Sands and Stephanie McDonald
Best practice management: panel discussion and audience questions	All panellists (Facilitator: Nicolas Girard)
Summary and key takeaways	Louise Lim

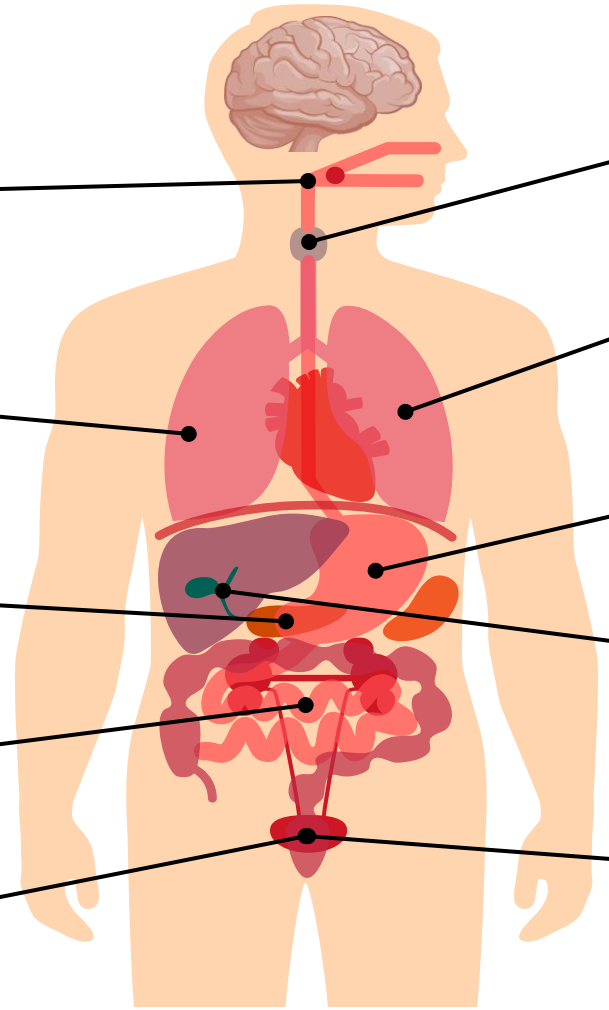
ADC, antibody-drug conjugate; AE, adverse event; (m)NSCLC, (metastatic) non-small cell lung cancer

THE RELEVANCE OF TROP2 IN METASTATIC NSCLC

Dr Louise Lim
Barts Health NHS Trust, UK

NSCLC, non-small cell lung cancer

TROP2: AN ADC TARGET OVEREXPRESSED IN MULTIPLE SOLID TISSUES



Oral SCC
62.57%
SGC
44%

NSCLC
64% of AC
75% of SCC

Pancreatic cancer
55%

Colon cancer
68.4%

Prostate cancer
71%

Thyroid cancer
82.5%

Breast cancer
62.4% of BC
78.1% of TNBC

Gastric cancer
66.3%

Gallbladder cancer
56%

Ovarian cancer
47%

Cervical cancer
88.7%

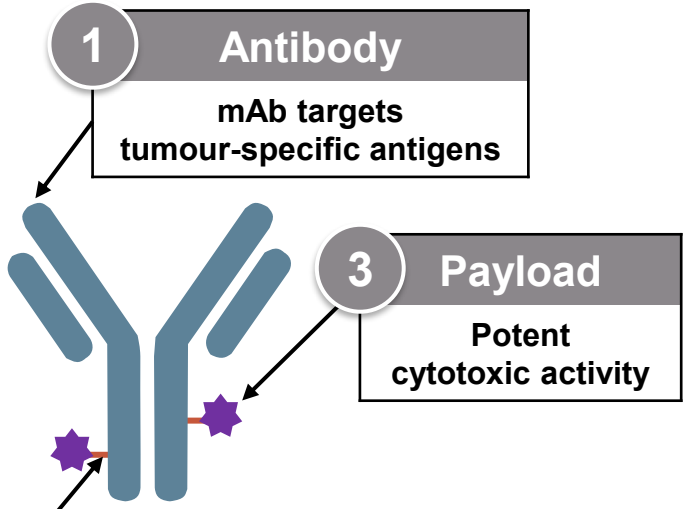
AC, adenocarcinoma; BC, breast cancer; NSCLC, non-small cell lung cancer; SCC, squamous cell carcinoma; SGC, salivary gland carcinoma; TNBC, triple negative breast cancer

Liu X, et al. Pharmacol Ther. 2022:239:108296

WHAT ARE ANTIBODY-DRUG CONJUGATES (ADCs)?

Drug-conjugate structures are based on three components[1-4]

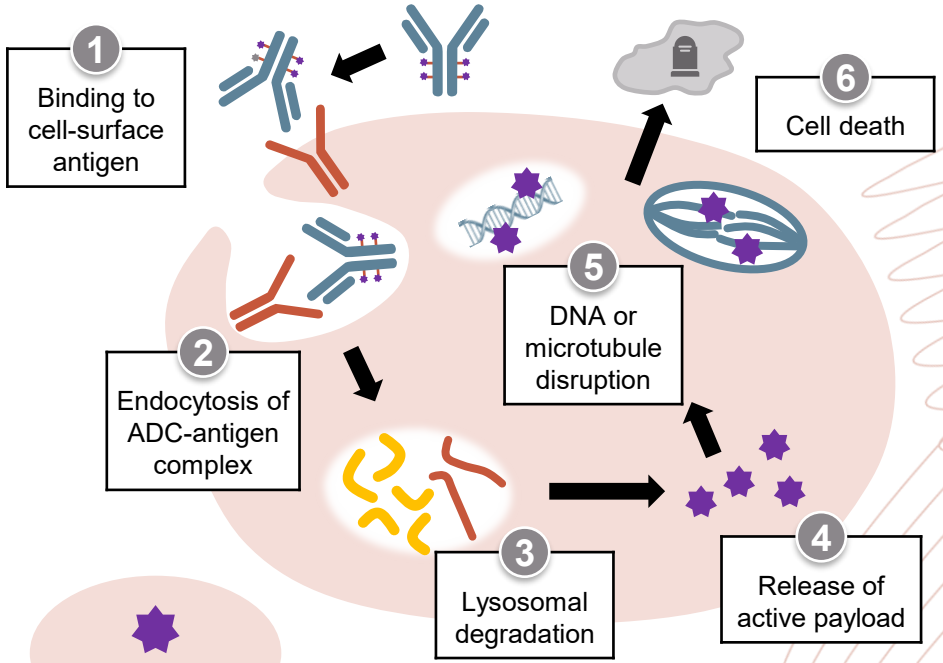
Antibody characteristics
- IgGs with high affinity for antigens[1,2]
- Chimeric/humanised to **lower immunogenicity**[1,2]
- Long serum half-life[1,2]
- High molecular weight[4]



Linker characteristics
- Prevents premature payload release in non-target tissues[1,2]
- **Stable** in circulation[2,3]
- Payload release at **target** site[2]
- Cleavable (pH or protease sensitive) or non-cleavable[1,2]
- Stochastic or site-specific conjunction[3,4]

Payload characteristics
- **Potent** cytotoxics[1]
- DNA (e.g., TOP1) or tubulin inhibitors or immunomodulators[4]
- Optimal DAR: 2-8 units per antibody[1]

MOA[2,5]



Bystander effect: killing of antigen-negative cancer cells; depends on:[1,3,6,7a]
- Use of pH- or protease-cleavable linker
- Hydrophobicity / membrane permeability of the free drug
- Extent of ADC internalization after antigen binding
- Payload release before internalization and from apoptotic cells

[a] Not all ADCs exhibit a bystander effect

ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; Ig, immunoglobin; mAb, monoclonal antibody; MOA, mechanism of action; TOP1, topoisomerase 1

1. Somme LB, et al. BioDrugs. 2024;38:487-97; 2. Shastry M, et al. Am Soc Clin Oncol Educ Book. 2023;43:e390094;
3. Tarantino P, et al. Nat Rev Clin Oncol. 2023;20:558-76; 4. Fu Z, et al. Signal Transduct Target Ther. 2022;7:93; 5. Tsuchikama K, An Z Protein Cell. 2016;9:33-46;
6. Zhou L, et al. Exp Hematol Oncol. 2024;13:26; 7. Staudacher AH, et al. Br J Cancer. 2017;117:1736-42

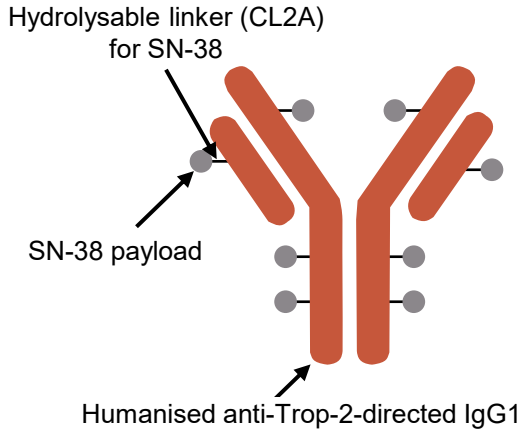
Adapted from Tsuchikama K et al (2016) and Gilead Sciences Inc. Satellite Symposium, ELCC 2026

TROP2-DIRECTED ADCs FOR NSCLC
CURRENT PHASE 3 GLOBAL DEVELOPMENT

ADCs in development for TROP2 differ in their characteristics

Sacituzumab govitecan (SG)[1-5]

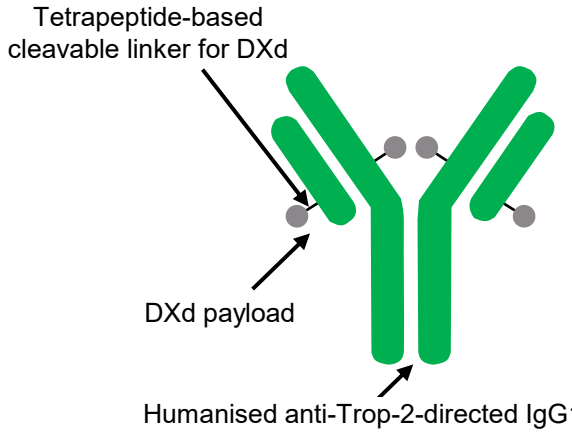
DAR ≈ 7.6:1



- Payload MOA: TOP1 inhibitor
- Bystander antitumour effect

Datopotamab deruxtecan (Dato-DXd)[1,6,7]

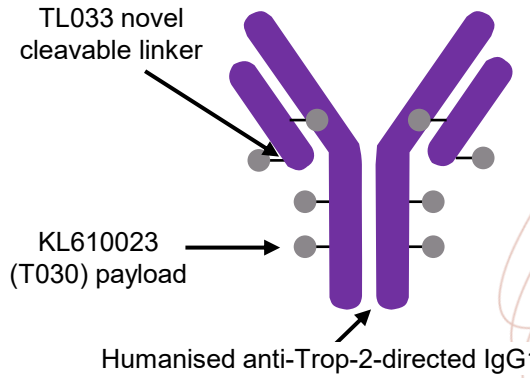
DAR ≈ 4:1



- Payload MOA: TOP1 inhibitor
- Bystander antitumour effect

Sacituzumab tirumotecan (Sac-TMT)[8-10]

DAR ≈ 7.4:1



- Payload MOA: TOP1 inhibitor
- Bystander antitumour effect

ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; Dato-DXd, datopotamab deruxtecan; Ig, immunoglobin; mAb, monoclonal antibody; MOA, mechanism of action; NSCLC, non-small cell lung cancer; Sac-TMT, Sacituzumab tirumotecan; SG, Sacituzumab govitecan; TOP1, topoisomerase 1; TROP2, trophoblast cell surface antigen 2

1. Parisi C, et al. Cancer Treat Rev. 2023;102572; 2. Shastry M, et al. Am Soc Clin Oncol Educ Book. 2023;43:e390094; 3. Paz-Ares LG, et al. J Clin Oncol. 2024;42:2860-2872; 4. TRODELVY® summary of product characteristics 2023.

Available from: Trodelvy, INN-sacituzumab govitecan (accessed 05 May 2026); 5. TRODELVY® Prescribing Information. 03/2025. Available from trodelvy_pi.pdf (Accessed 05 May 2026). 6. DATROWAY® Prescribing Information. Jun 2025. Available from getPIContent (Accessed 05 May 2026); 7.Sands J, et al. J Clin Oncol. 2025;43:1254-1265; 8. Cheng Y, et al. Front Oncol. 2022;12:951589; 9. FDA Grants Breakthrough Therapy Designation to Sacituzumab Tirumotecan (sac-TMT) for the Treatment of Certain Patients With Previously Treated Advanced or Metastatic Nonsquamous Non-Small Cell Lung Cancer With EGFR Mutations (accessed 05 May 2026); 10. Fang W, et al. N Engl J Med. 2025;394:13-26

Figure partially from Parisi C, et al. Cancer Treat Rev. 2023;118:102572 and Gilead Sciences Inc. Satellite Symposium, ELCC 2026

TAKE-HOME MESSAGES

1) **TROP2 is common in NSCLC**

   64% of adenocarcinoma and 75% of squamous cell carcinomas show some expression[1]

2) **Three late-stage ADCs differ mainly by payload and linker**

   SG (SN-38), Dato-DXd (DXd), Sac-TMT (belotecan-derived) — all aim to improve outcomes beyond docetaxel in later lines;[2-4] combinations and biomarker strategies are the next frontier

ADC, antibody-drug conjugate; Dato-DXd, datopotamab deruxtecan; EGFRm, EGFR mutation; NSCLC, non-small cell lung cancer; Sac-TMT, sacituzumab tirumotecan; SG, sacituzumab govitecan

1. Hsu R. Transl Cancer Res. 2025;14(2):679-84; 2. Paz-Ares LG, et al. J Clin Oncol 42:2860-2872; 3. Ahn M-J, et al. J Clin Oncol. 2025;43:260-72; 4. Fang W, et al. N Engl J Med. 2026;394:13-26

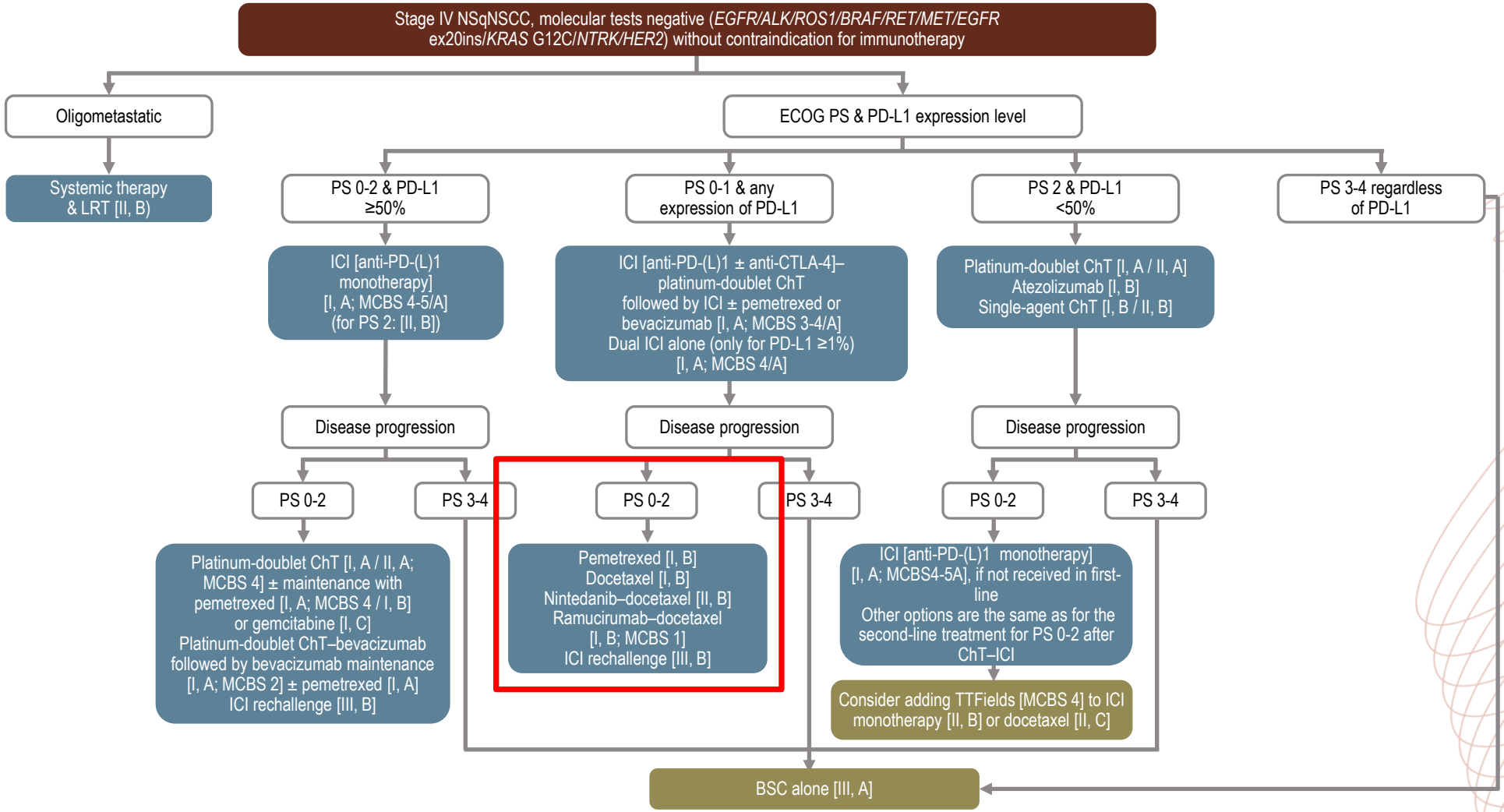
CLINICAL OVERVIEW OF TROP2-DIRECTED ADCs IN NSCLC

WITHOUT ACTIONABLE GENOMIC ALTERATIONS

Prof. Nicolas Girard
Institute Curie,
France

ADC, antibody-drug conjugate; NSCLC, non-small cell lung cancer

ESMO CLINICAL PRACTICE GUIDELINES (V1.2 JAN 2025)



BSC, best supportive care; ChT, chemotherapy; ESMO, European Society for Medical Oncology; ICI, immune checkpoint inhibitor; LRT, local radical therapy; MCBS, ESMO Magnitude of Clinical Benefit Scale; NsqNSCC nonsquamous non-small cell carcinoma; PS, performance status (Eastern Cooperative Oncology Group)

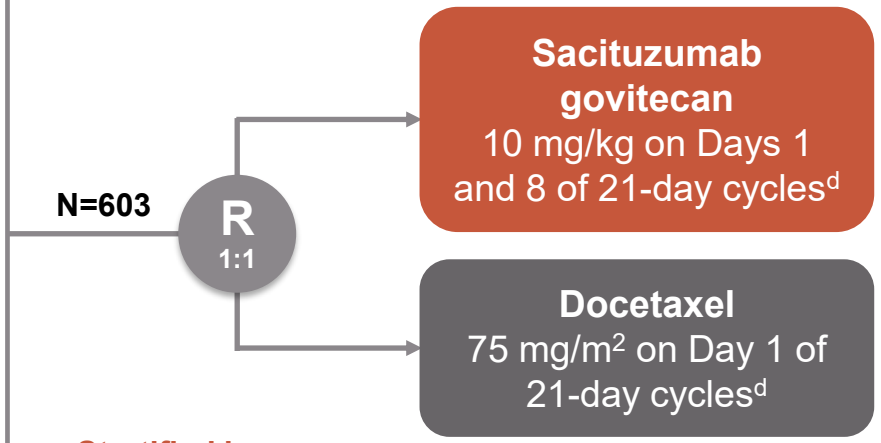
1. Hendriks L, et al. Ann Oncol. 2023;34:358-76; 2. Hendriks L, et al. Ann Oncol. 2025;36(19):1223-7 [ESMO Non-Oncogene-Addicted Metastatic Non-Small-Cell Lung Cancer Living Guideline, v1.2 – January 2025. Available here (accessed April 14, 2026)]

EVOKE-01: SACITUZUMAB GOVITECAN IN PRE-TREATED ADVANCED/METASTATIC NSCLC

GLOBAL, RANDOMISED, OPEN-LABEL, PHASE 3 STUDY

Key eligibility criteria:

- Measurable stage IV NSCLC
- ECOG PS score 0-1
- Radiographic progression after platinum-based and anti-PD-(L)1–containing regimen[a]
- In addition, patients with known AGAs must have received ≥1 approved TKI[b]
  - *EGFR/ALK* test required. Testing of other AGAs recommended[c]
- Previously treated stable brain metastases were included
- No prior treatment with Topo-1 inhibitors, TROP-2–targeted therapies, or docetaxel



Endpoints:

Primary:

- OS

Secondary:

- PFS, ORR, DoR, and DCR by INV per RECIST v1.1
- Safety and tolerability
- QoL using NSCLC-SAQ

Stratified by:

- **Histology** (squamous vs nonsquamous
- **Response to last anti-PD-(L)1–containing regimen** (responsive [best response CR/PR] vs nonresponsive [PD/SD])
- **Received prior targeted therapy for AGA** (yes vs no)

At data cutoff (29 November 2023), the study median follow-up was 12.7 months (range, 6.0-24.0)

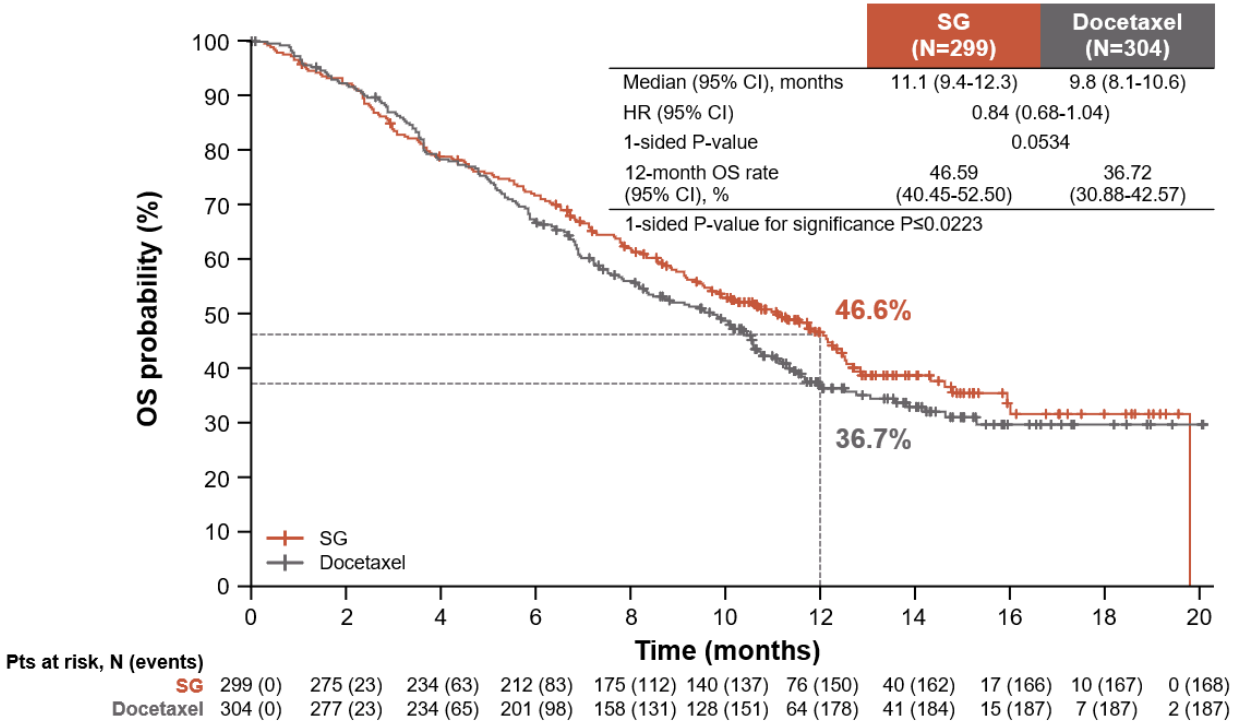
[a] (Neo)adjuvant therapy counted if progression within 6 months of platinum treatment and while on maintenance with checkpoint inhibitor agent; [b] If local approval exists for targeted therapy to that genomic alteration; [c] Based on local SoC and availability of testing/approved targeted agent; [d] Until PD or unacceptable toxicity

AGA, actionable genomic alteration; CR, complete response; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; INV, investigator; (a/m)NSCLC, (advanced/metastatic) non-small cell lung cancer; NSCLC-SAQ, NSCLC-Symptom Assessment Questionnaire; ORR, objective response rate; OS overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; QoL, quality of life; R randomisation; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SD, stable disease; SoC, standard of care; TKI, tyrosine kinase inhibitor; Topo-1, topoisomerase-1

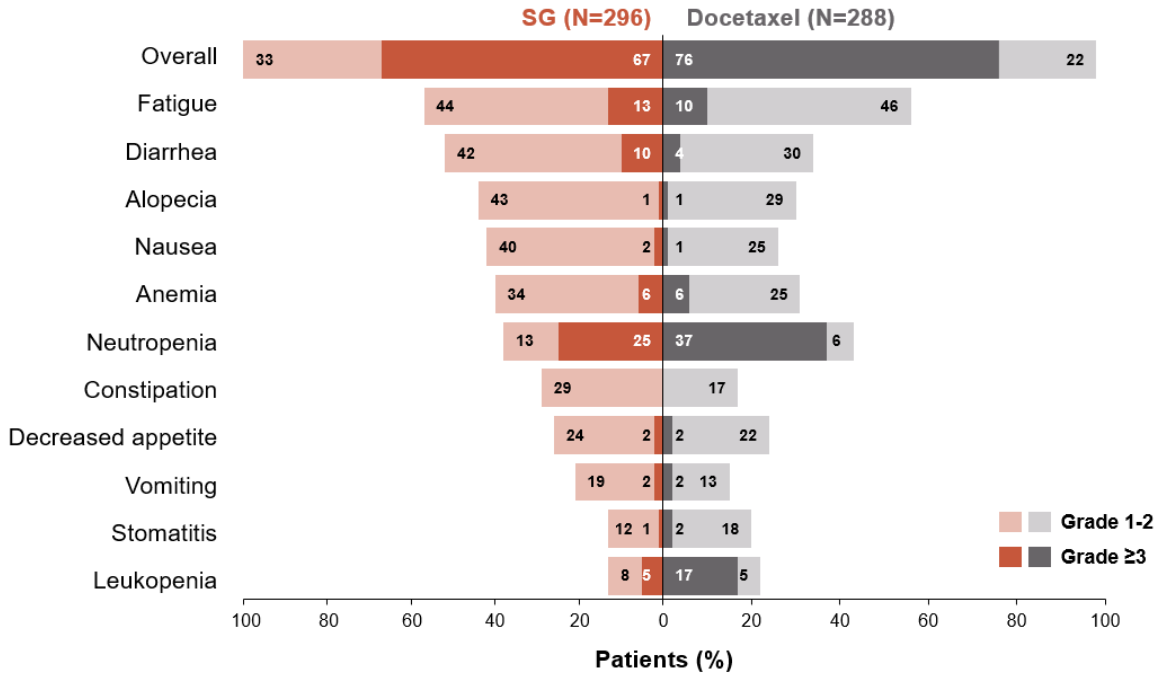
Paz-Ares L, et al. J Clin Oncol. 2024;42:2860-72 (ASCO 2024, oral presentation)

EVOKE-01: SACITUZUMAB GOVITECAN IN PRE-TREATED ADVANCED/METASTATIC NSCLC

OVERALL SURVIVAL (ITT)



TEAEs IN ≥20% OF PATIENTS



CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; NSCLC, non-small cell lung cancer; OS, overall survival; Pts, patients; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event

Paz-Ares L, et al. J Clin Oncol. 2024;42:2860-72 (ASCO 2024, oral presentation)

TROPION-LUNG01: DATO-DXd IN PRE-TREATED ADVANCED/METASTATIC NSCLC

RANDOMISED, PHASE 3, OPEN-LABEL, GLOBAL STUDY (NCT04656652)

Key eligibility criteria:

- NSCLC (stage IIIB, IIIC, or IV)
- ECOG PS of 0 or 1
- No prior docetaxel

Without actionable genomic alterations

- 1 or 2 prior lines, including platinum CT and anti–PD-(L)1 mAb therapy

With actionable genomic alterations

- Positive for *EGFR, ALK, NTRK, BRAF, ROS1, MET* exon 14 skipping, or *RET*
- 1 or 2 prior approved targeted therapies + platinum-based CT, and ≤1 anti–PD-(L)1 mAb

R 1:1

Dato-DXd 6 mg/kg Q3W (N=299)

Docetaxel 75 mg/m^2 Q3W (N=305)

Dual primary endpoints:

- PFS by BICR
- OS

Secondary endpoints:

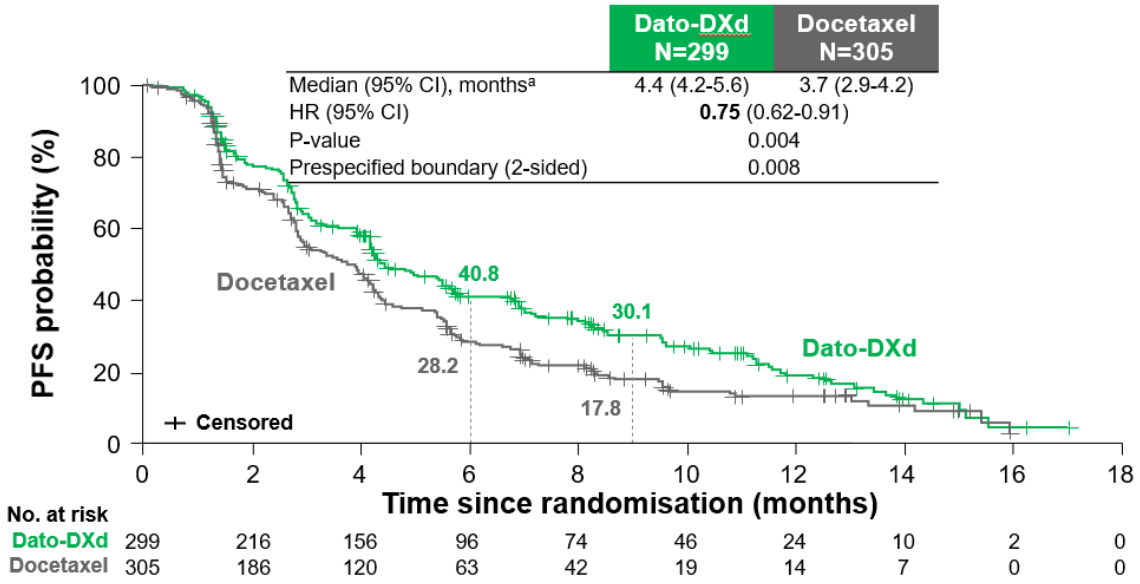
- ORR by BICR
- DoR by BICR
- Safety

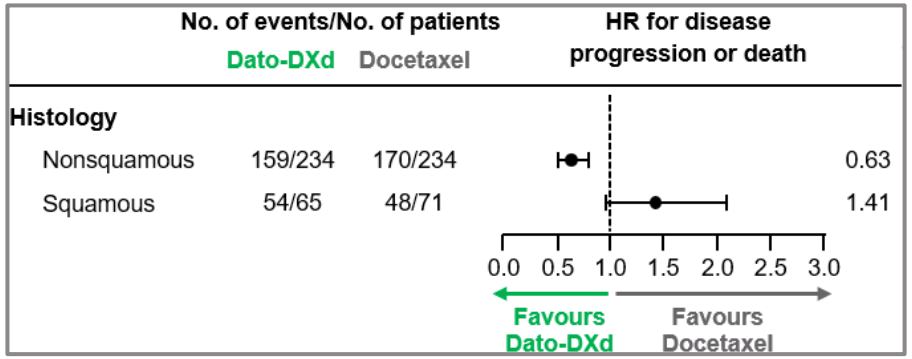
BICR, blinded independent central review; CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; mAb, monoclonal antibody; (a/m)NSCLC, (advanced/metastatic) non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomisation

Ahn M-J, et al. J Clin Oncol. 2025;43:260-272 (including protocol); Ahn M-J, et al. Annals of Oncol. 2023:34 (S2): S1305_LBA12 (oral presentation, presented by Lisberg A. ESMO 2023)

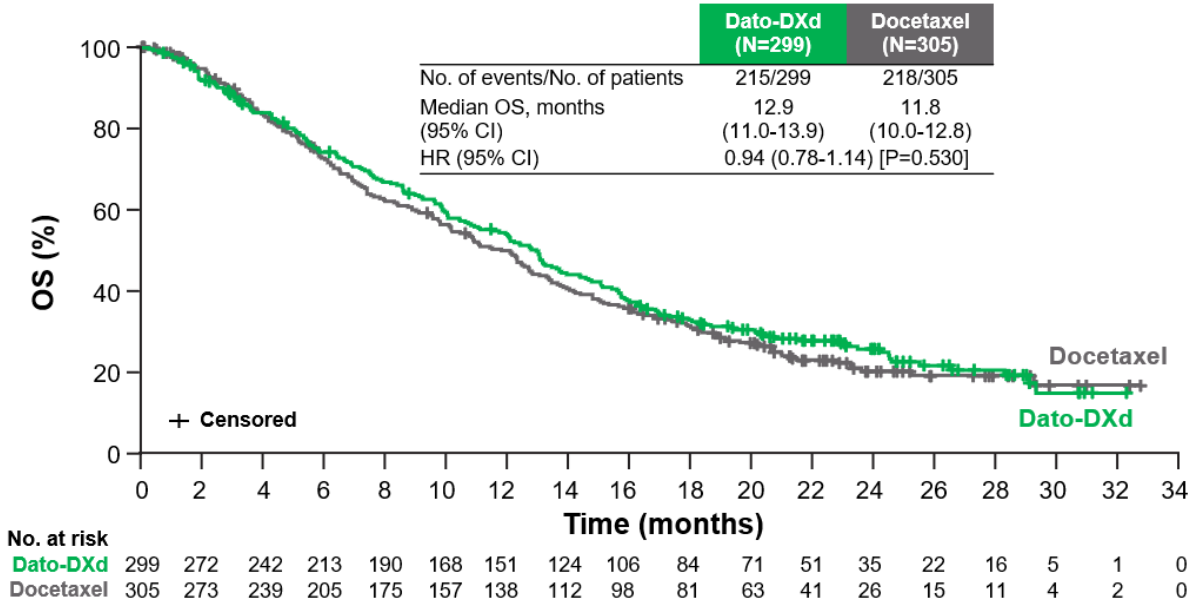
TROPION-LUNG01: EFFICACY OF DATO-DXd IN PRE-TREATED ADVANCED/METASTATIC NSCLC

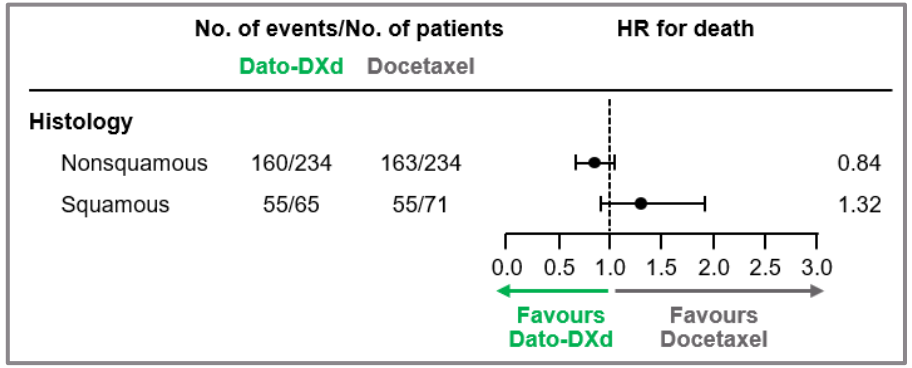
PROGRESSION-FREE SURVIVAL





OVERALL SURVIVAL





[a] Median PFS follow-up was 10.9 (95% CI, 9.8-12.5) and 9.6 (95% CI, 8.2-11.9) months for Dato-DXd and docetaxel respectively; [b] Included 4 CRs and 75 PRs for Dato-DXd and 39 PRs for docetaxel. CI, confidence interval; CR, complete response; Dato-DXd, datopotamab deruxtecan; HR, hazard ratio; mDoR, median duration of response; mo, months; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response

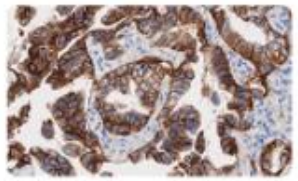
Ahn M-J, et al. J Clin Oncol. 2025;43:260-72

ASSESSING TROP2 AS A BIOMARKER (NMR QCS)?

TROP2 NORMALISED MEMBRANE RATIO (NMR) MEASURED BY QUANTITATIVE CONTINUOUS SCORING (QCS)

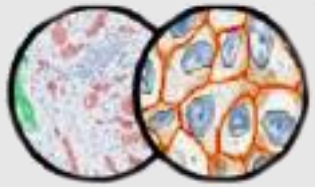
QCS is a novel, fully-supervised computational pathology approach that precisely quantifies and locates targets like TROP2

1 IHC with TROP2 Assay



2 Whole Slide Imaging

3 Automated Image Analysis (QCS)

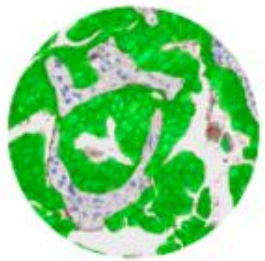


4 Patient Biomarker Status Determination

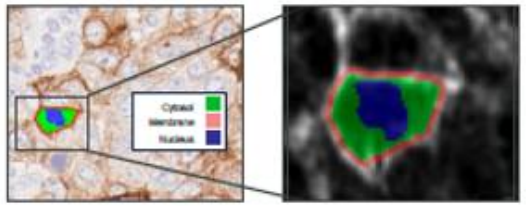
\+ ≥75% of tumour cells with TROP2 NMR ≤0.56

– <75% of tumour cells with TROP2 NMR ≤0.56[a]

Differentiates tumour from non-tumour



Measures OD in each tumour cell



Membrane and cytoplasm optical density (OD)

Calculates TROP2 NMR for every tumour cell

$$\frac{\text{Membrane OD}}{\text{Membrane OD + Cytoplasm OD}}$$

Lower NMR → high cytoplasm proportion

[a] Or >25% of cells with an NMR >0.56

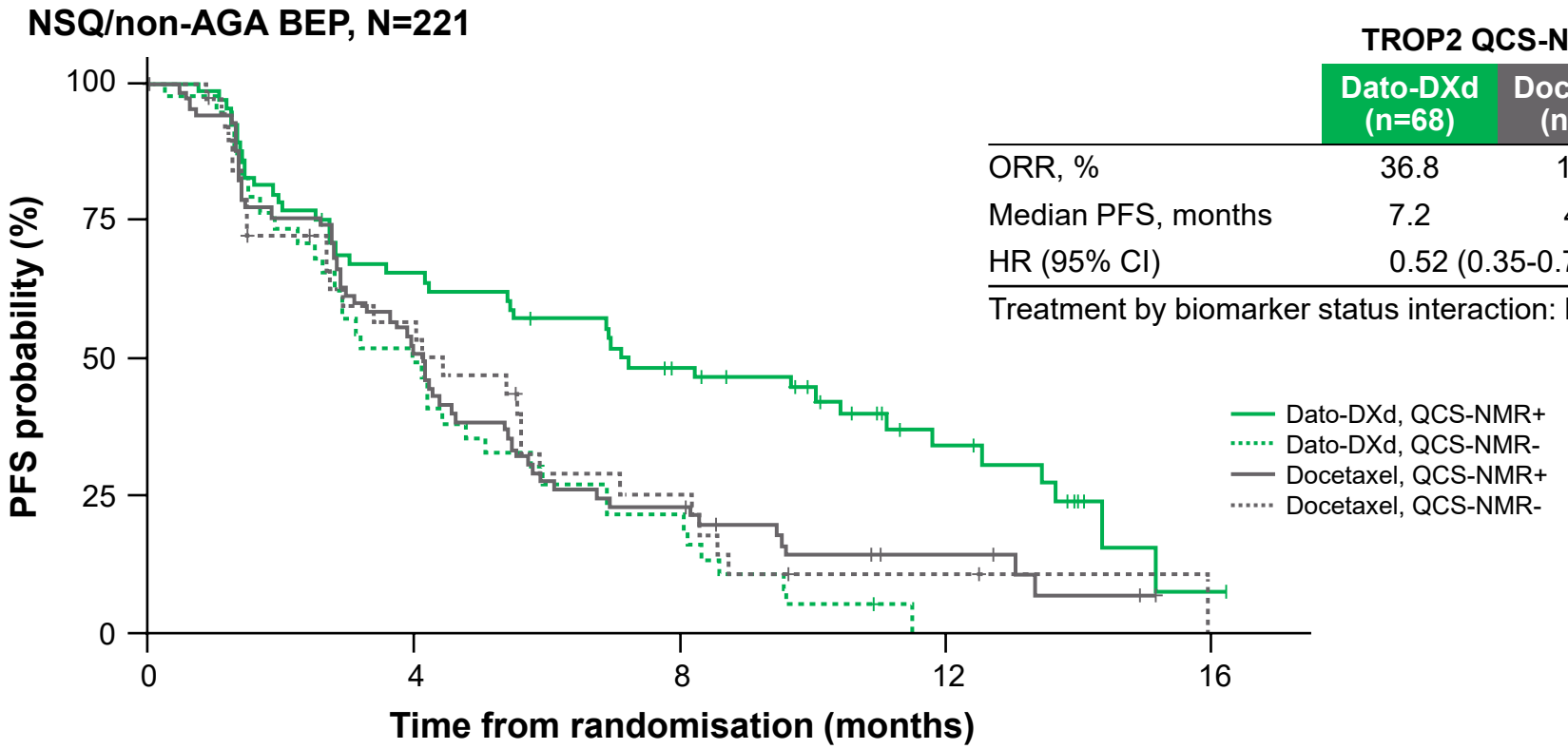
IHC, immunohistochemistry; NMR, normalised membrane ratio; OD, optical density; QCS, quantitative continuous scoring

Garassino, M.C. et al. Journal of Thoracic Oncology, 2024; Volume 19, Issue 10, S2 - S3 (oral presentation, WCLC 2024, PL02.11.)

TROP2 NMR QCS: TROPION-LUNG01

NSQ/NON-AGA BEP: EFFICACY BY TROP2 QCS-NMR STATUS

TROP2 QCS-NMR positivity is predictive for longer PFS with Dato-DXd in the NSQ/non-AGA biomarker-evaluable population



	TROP2 QCS-NMR+		TROP2 QCS-NMR–	
	Dato-DXd (n=68)	Docetaxel (n=72)	Dato-DXd (n=40)	Docetaxel (n=41)
ORR, %	36.8	15.3	22.5	12.2
Median PFS, months	7.2	4.1	4.0	4.4
HR (95% CI)	0.52 (0.35-0.78)		1.22 (0.74-2.00)	

Treatment by biomarker status interaction: P=0.0098

Data cutoff: March 29, 2023. PFS HR (95% CI) by TROP2 QCS-NMR status (+ vs -) within treatment: Dato DXd: 0.40 [0.25-0.64]; Docetaxel: 0.94 [0.60-1.49]

AGA, actionable genomic alteration; BEP, biomarker evaluable population; CI, confidence interval; Dato-DXd, datopotamab deruxtecan; HR, hazard ratio; NMR, normalised membrane ratio; NSQ, nonsquamous; ORR, objective response rate; PFS, progression-free survival; QCS, quantitative continuous scoring

Garassino, M.C. et al. Journal of Thoracic Oncology, 2024; Volume 19, Issue 10, S2 - S3 (oral presentation, WCLC 2024, PL02.11.)

TROPION-LUNG01: SAFETY OF DATO-DXd IN PRE-TREATED ADVANCED/METASTATIC NSCLC

TRAEs OCCURRING IN ≥15% OF PATIENTS

System organ class Preferred term, n (%)	Dato-DXd N=297		Docetaxel N=290	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Gastrointestinal disorders[a]				
Stomatitis	141 (47.5)	20 (6.7)	45 (15.5)	3 (1.0)
Nausea	101 (34.0)	7 (2.4)	48 (16.6)	3 (1.0)
Diarrhea	30 (10.1)	1 (0.3)	55 (19.0)	4 (1.4)
Hematologic disorders[a]				
Anemia[b]	44 (14.8)	12 (4.0)	60 (20.7)	12 (4.1)
Neutropenia[c]	14 (4.7)	2 (0.7)	76 (26.2)	68 (23.4)
Leukopenia[d]	9 (3.0)	0	45 (15.5)	38 (13.1)
Skin and subcutaneous[a]				
Alopecia	95 (32.0)	0	101 (34.8)	1 (0.3)
Metabolism and nutrition[a]				
Decreased appetite	68 (22.9)	1 (0.3)	46 (15.9)	1 (0.3)
General disorders[a]				
Asthenia	56 (18.9)	8 (2.7)	56 (19.3)	5 (1.7)
Adjudicated drug-related ILD or pneumonitis	26 (8.8)[e]	11 (3.7)	12 (4.1)	4 (1.4)

Data cut-off: March 1, 2024. [a] No grade 5 events occurred with Dato-DXd or docetaxel; [b] Grouped PTs of anemia, hemoglobin decreased, and RBC count decreased; [c] Grouped PTs of neutropenia and neutrophil count decreased; [d] Grouped PTs of leukopenia and WBC count decreased. [e] 2 (0.7%) G1 events, 13 (4.4%) G2 events, 3 (1.0% G3, 1 (0.3% G4, 7 (2.4%) G5 events; AESI, adverse event of special interest; Dato-DXd, datopotamab deruxtecan; G, grade; ILD, interstitial lung disease; NSCLC, non-small cell lung cancer; PT, preferred term; TRAE, treatment-related adverse event; WBC, white blood cell

Ahn MJ, et al. J Clin Oncol. 2025;43(3):260-72 (including Supplementary appendix)

ADVERSE EVENTS OF SPECIAL INTEREST

AESI, n (%)	Dato-DXd N=297	Docetaxel N=290
Stomatitis/oral mucositis		
All grades	164 (55.2)	60 (20.7)
Grade ≥3	20 (6.7)	4 (1.4)
Ocular events		
All grades	64 (21.5)	27 (9.3)
Grade ≥3	7 (2.4)	0
Adjudicated drug-related ILD		
All grades	26 (8.8)	12 (4.1)
Grade ≥3	11 (3.7)	4 (1.4)
Grade 5	7 (2.4)	1 (0.3)

AESIs listed in this table are treatment emergent regardless of causality. Some patients may have had more than one event.

Dato-DXd related events:

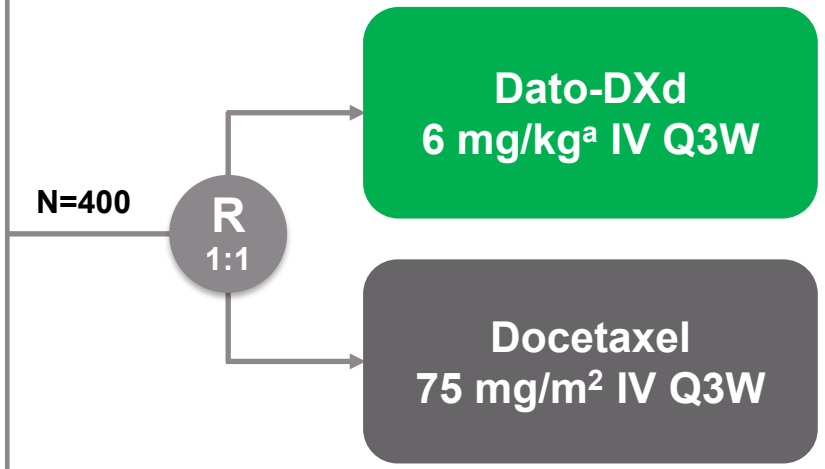
- Stomatitis/oral mucositis resulted in a low rate of treatment discontinuation (0.7%)
- Most frequent ocular surface events: lacrimation increased (23 [7.7%]) and dry eye (21 [7.1%]), all mild or moderate. Any-grade and grade ≥3 keratitis occurred in 12 (4.0%) and 4 (1.3%) patients, respectively
- Seven adjudicated drug-related grade 5 ILD events: primary cause of death in 4 out of 7 was attributed to disease progression by investigator

TROPION-LUNG17: DATO-DXd IN PRE-TREATED ADVANCED/METASTATIC NSCLC

ONGOING PHASE 3 TRIAL IN TROP2 NMR POSITIVE NSQ NSCLC WITHOUT AGA

Patients:

- Aged ≥18 years
- Pathologically documented non-squamous NSCLC (stage IIIB, IIIC, or IV, per AJCC Staging Manual, 9th Edition) without AGA
  - Negative for *EGFR*, *ALK*, and *ROS1* mutations
  - No known AGAs including *KRAS* G12C, *NTRK*, *BRAF*, *MET* exon14 skipping, *RET*, or *HER2* mutations
- TROP2 NMR positive
- Prior receipt of platinum-based chemotherapy and anti-PD-(L)1 monoclonal antibodies
- ≥1 measurable lesion per RECIST v1.1
- ECOG PS 0 or 1
- Stable or asymptomatic brain metastases permitted



Dual primary endpoints:

- PFS by BICR
- OS

Stratified by:

- Duration of prior anti-PD-(L)1 therapy (<6 months vs ≥6 months)
- Geographical region
- (US, Europe, Canada vs other geographic regions)

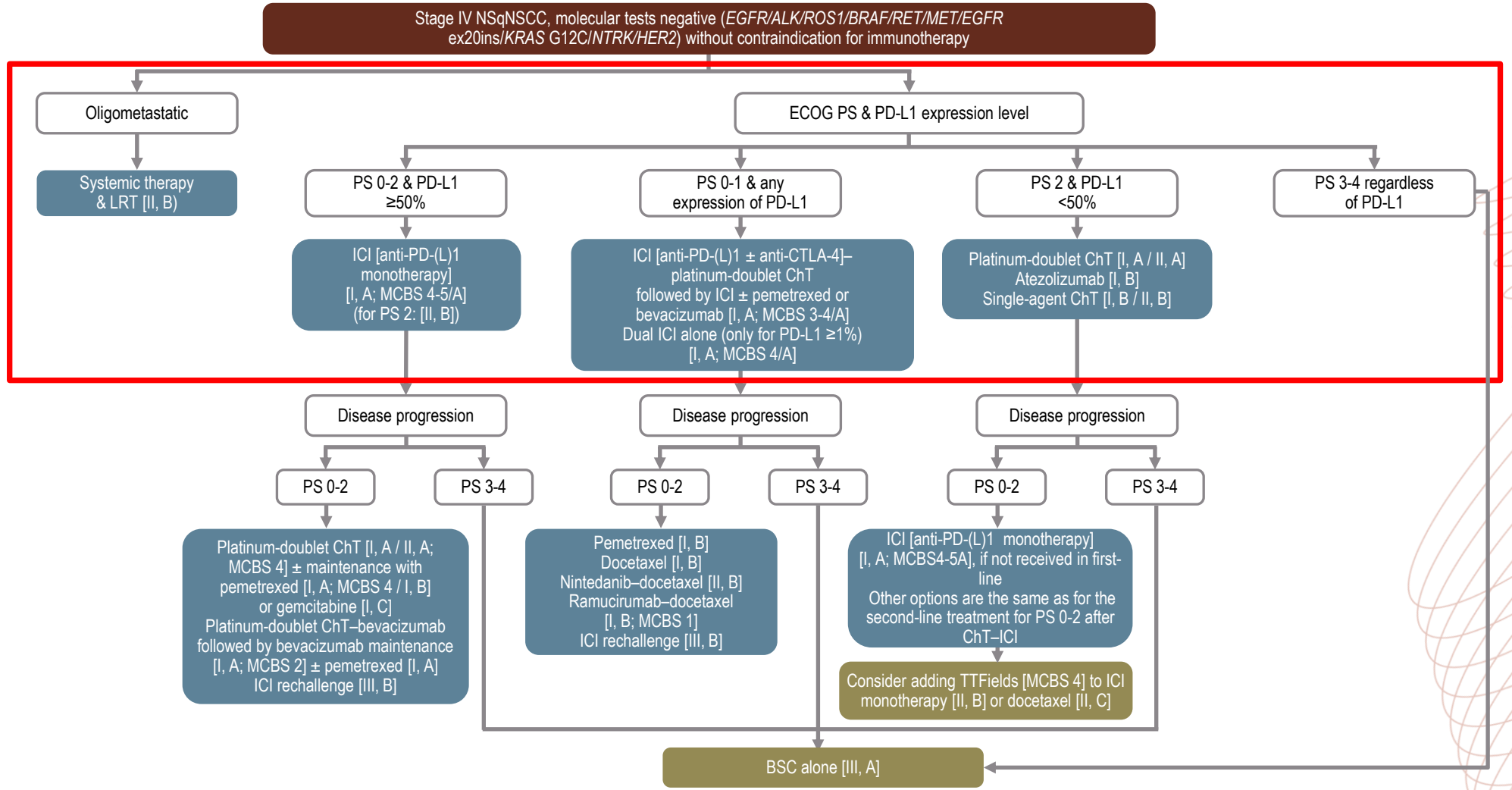
Treatment will continue until investigator assessed radiological progression per RECIST v1.1, unacceptable toxicity, withdrawal of consent, or any other discontinuation criterion is met

[a] Up to a maximum of 540 mg for patients ≥90 kg

AJCC, American Joint Committee on Cancer; AGA, actionable genomic alterations; BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; NMR, normalised membrane ratio; NSCLC, non-small cell lung cancer; NSQ, non-squamous; OS, overall survival; PD-(L)1, programmed cell death-(ligand) 1; PFS, progression-free survival; PS, performance status; Q3W, every three weeks; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; TROP2, trophoblast cell surface antigen 2; US, United States

Sands J, et al. ESMO Open. 2026;11 (suppl_3):106452.(ELCC 2026, poster #145TiP)

ESMO CLINICAL PRACTICE GUIDELINES (V1.2 JAN 2025)

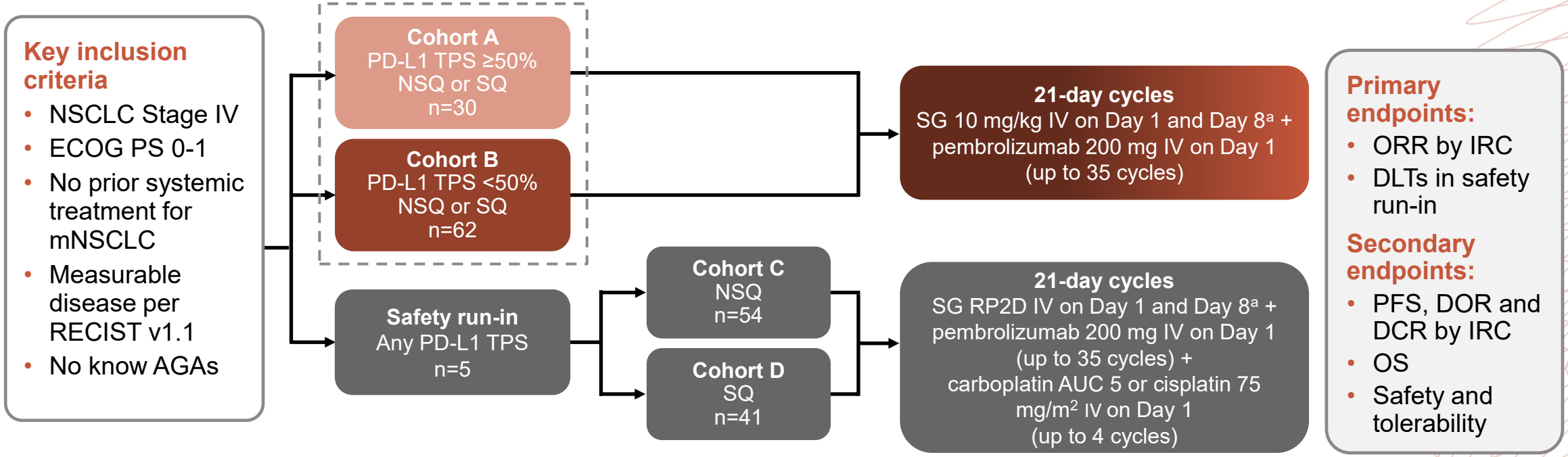


BSC, best supportive care; ChT, chemotherapy; ESMO, European Society for Medical Oncology; ICI, immune checkpoint inhibitor; LRT, local radical therapy; MCBS, ESMO Magnitude of Clinical Benefit Scale; NsqNSCC nonsquamous non-small cell carcinoma; PS, performance status (Eastern Cooperative Oncology Group)

1. Hendriks L, et al. Ann Oncol. 2023;34:358-76; 2. Hendriks L, et al. Ann Oncol. 2025;36(19):1223-7 [ESMO Non-Oncogene-Addicted Metastatic Non-Small-Cell Lung Cancer Living Guideline, v1.2 – January 2025. Available here (accessed April 14, 2026)]

EVOKE-02: SACITUZUMAB GOVITECAN (SG) COMBINATIONS AS 1L TREATMENT FOR ADVANCED/METASTATIC NSCLC

PHASE 2 STUDY



[a] Until PD or unacceptable toxicity

1L, first-line; AGA, actionable genomic alteration; AUC, area under the curve; DCR, disease control rate; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; IV, intravenous; (m)NSCLC, (metastatic) non-small cell lung cancer; NSQ, non-squamous cell; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; RP2D, recommended phase 2 dose; SG, sacituzumab govitecan; SQ, squamous cell; TPS, tumour proportion score

Reck M, et al. J Thorac Oncol. 2026;21:103509; EVOKE-02.pdf (accessed May 02, 2026); NCT05186974

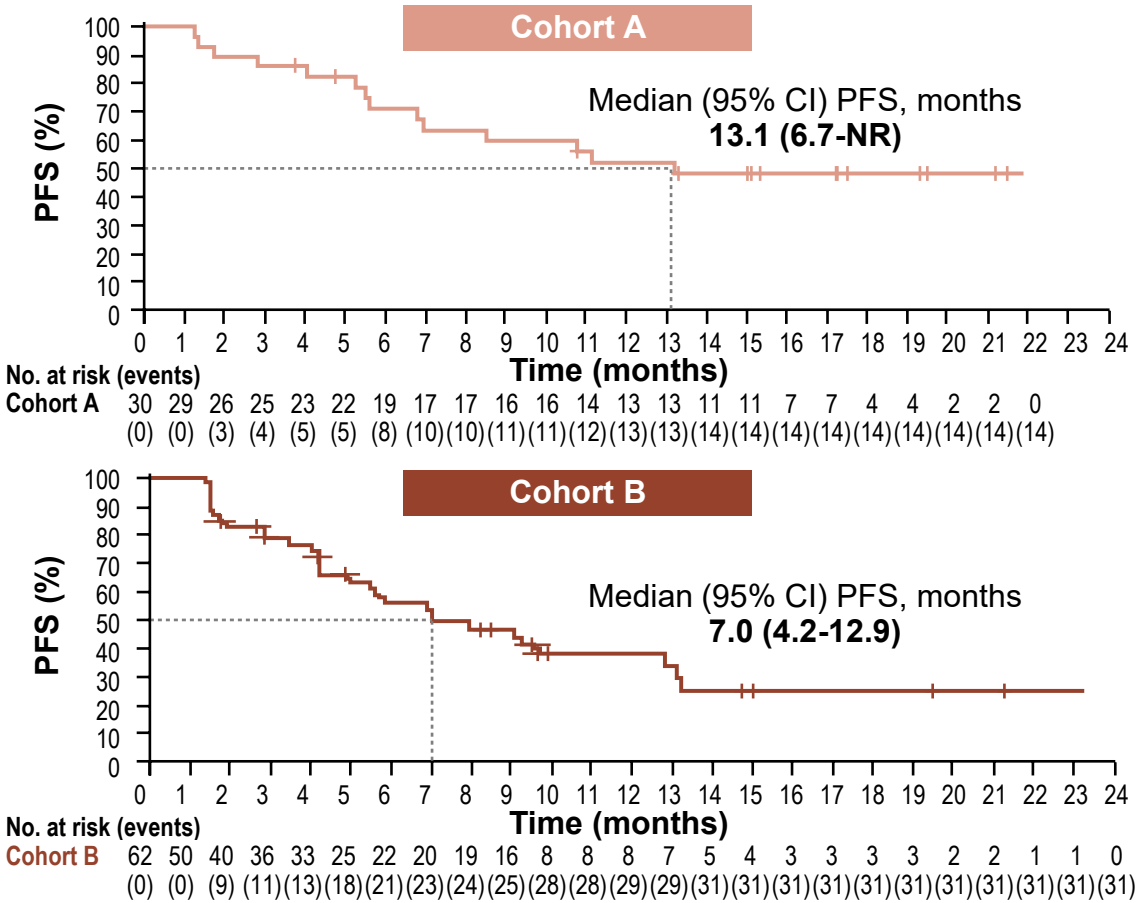
EVOKE-02: SG COMBINATIONS AS 1L TREATMENT FOR ADVANCED/METASTATIC NSCLC (EFFICACY)

EFFICACY BY INVESTIGATOR ASSESSMENT[1a]

Response rates	Cohort A (PD-L1 TPS ≥50%) SG + pembrolizumab (N=30)	Cohort B (PD-L1 TPS <50%) SG + pembrolizumab (N=62)
ORR (95% CI), %[a]	66.7 (47.2-82.7)	29.0 (18.2-41.9)
CR, n (%)	1 (3.3)	0
PR, n (%)	19 (63.3)	18 (29.0)
SD, n (%)	6 (20.0)	23 (37.1)
PD, n (%)	3 (10.0)	9 (14.5)
NE, n (%)[b]	1 (3.3)	12 (19.4)
Median PFS (95% CI),[a] months	13.1 (6.7-NR)	7.0 (4.2-12.9)
Median DoR (95% CI),[a] months	NR (9.4-NR)	11.9 (6.9-NR)

Data cutoff date: 3 June 2024
Study median (range) follow up: 16.6 (8.5-23.8)

PFS BY IRC[1]



[a] Per IRC; [b] Includes not assessed

1L, first-line; CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NE, not evaluable; NR, not reached; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PR, partial response; SG, sacituzumab govitecan; SD, stable disease; TPS, tumour proportion score

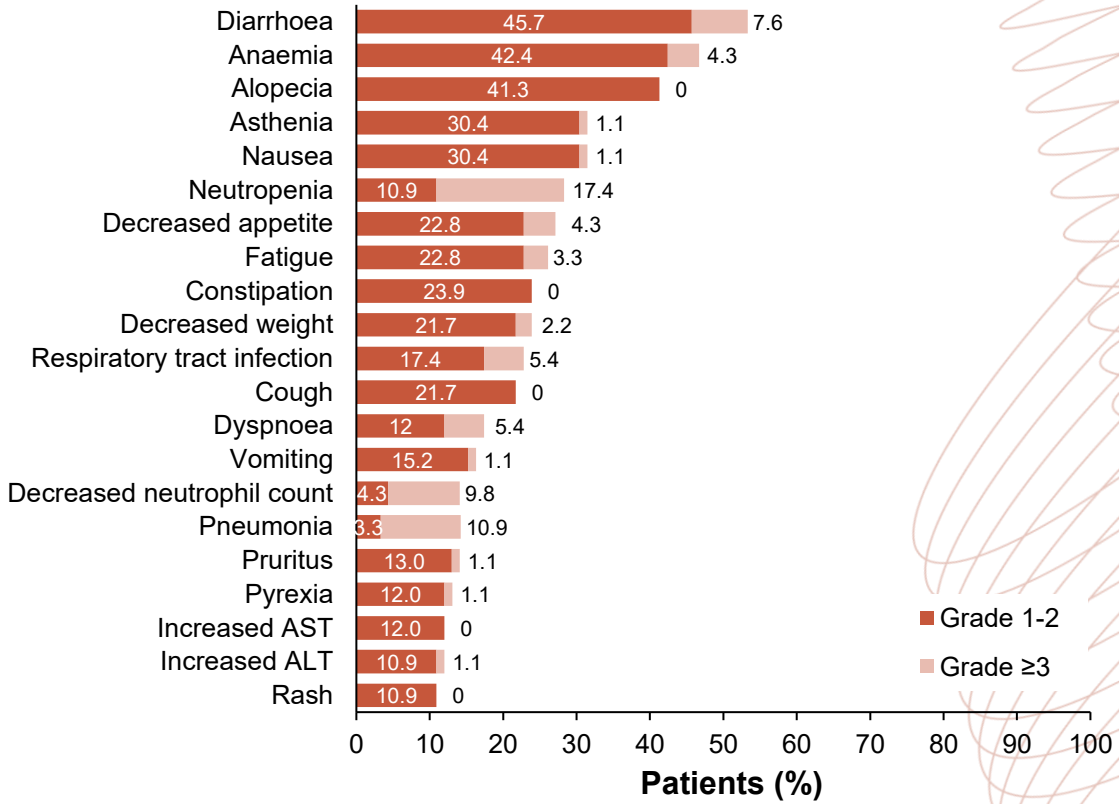
Reck M, et al. J Thorac Oncol. 2026;21:103509

EVOKE-02: SG COMBINATIONS AS 1L TREATMENT FOR ADVANCED/METASTATIC NSCLC (SAFETY)

SAFETY SUMMARY[1]

TEAEs, n (%)	Total SG + pembrolizumab (N=92)
Any-grade TEAEs	92 (100)
Grade ≥3 TEAES	70 (76.1)
TEAEs related to any study drug	84 (91.3)
Grade ≥3 TEAEs related to any study drug	42 (45.7)
Serious TEAEs	58 (63.0)
Related to any study drug	19 (20.7)
TEAEs leading to treatment discontinuation of any study drug	25 (27.2)
TEAEs leading to discontinuation of SG	22 (23.9)
TEAEs leading to discontinuation of pembrolizumab	21 (22.8)
TEAEs leading to dose reduction of SG	16 (17.4)
TEAEs leading to dose interruption of any study drug	65 (70.7)
TEAEs leading to dose interruption of SG	64 (69.6)
TEAEs leading to dose interruption of pembrolizumab	51 (55.4)
TEAEs leading to death	8 (8.7)
TEAEs related to any study drug leading to death[a]	3 (3.3)

ANY-GRADE TEAEs REPORTED IN ≥10% OF PATIENTS[1]



[a] Two patients had neutropenic sepsis, one patient had sepsis

1L, first-line; ALT, alanine aminotransferase; AST, aspartate aminotransferase; NSCLC, non-small cell lung cancer; SG, sacituzumab govitecan; TEAEs, treatment-emergent adverse events

1. Reck M, et al. J Thorac Oncol. 2026;21:103509

EVOKE-03: SG COMBINATIONS AS 1L TREATMENT FOR ADVANCED/METASTATIC NSCLC (ONGOING)

Phase 3, study evaluating SG + pembrolizumab vs pembrolizumab monotherapy for 1L treatment of patients with mNSCLC with PD-L1 TPS ≥50%

Key inclusion criteria:

- Stage IV mNSCLC
- No prior systemic treatment for mNSCLC
- PD-L1 TPS ≥50%
- No pneumonitis/ILD
- *EGFR/ALK/ROS1*-directed primary therapy not indicated
- No active CNS metastases and/or carcinomatous meningitis

N=614

R
1:1

21-day cycles
SG 10 mg/kg Q1W IV
on Day 1 and Day 8 of a 21-day cycle
+
pembrolizumab 200 mg Q3W IV
on Day 1 for up to 35 cycles

21-day cycles
Pembrolizumab 200 mg Q3W IV
on Day 1 for up to 35 cycles

Primary endpoints:

- PFS
- OS

Secondary endpoints:

- ORR
- DOR
- Safety
- PROs using EORTC QLC-C30

1L, first-line; CNS, central nervous system; DOR, duration of response; EORTC QLQ-C30, The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ILD, interstitial lung disease; IV, intravenous; (m)NSCLC, (metastatic) non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; PROs, patient reported outcomes; R, randomisation; SG, sacituzumab govitecan; TPS, tumour proportion score; Q'X'W, every 'x' weeks

EVOKE-03.pdf; Moskovitz M, et al. Cancer Res 2023; 83 (8_Supplement): CT067 (AACR 2023 poster); NCT05609968

EXPLORING DATO-DXd COMBINATIONS AS 1L TREATMENT IN ADVANCED/METASTATIC NSCLC

TROPION-Lung02[1,2]

Phase 1b study of Dato-DXd + pembrolizumab ± Pt-ChT for a/mNSCLC without AGAs[a]

Key eligibility:
- a/mNSCLC
- Dose escalation:[b]
  - ≤2 lines of prior therapy[c]
- Dose expansion
  - ≤1 line of Pt-ChT (Cohorts 1 and 2)[c]
  - Treatment naïve (Cohort 2)[c,d]
  - Treatment naïve (Cohorts 3-6)[c]

Primary endpoints:
- DLTs and TEAEs

Secondary endpoints:
- ORR, DOR, PFS, OS

1L patients only	Dato-DXd Q3W IV	+	Pembro Q3W IV	±	Pt-ChT Q3W IV	
Cohort 1 (n=2)	4 mg/kg	+	200 mg			Doublet
Cohort 2 (n=40)	6 mg/kg	+	200 mg			Doublet
Cohort 3 (n=14)	4 mg/kg	+	200 mg	+	carboplatin AUC 5	Triplet
Cohort 4 (n=26)	6 mg/kg	+	200 mg	+	carboplatin AUC 5	Triplet
Cohort 5 (n=8)	4 mg/kg	+	200 mg	+	cisplatin 75 mg/m^2	Triplet
Cohort 6 (n=6)	6 mg/kg	+	200 mg	+	cisplatin 75 mg/m^2	Triplet

TROPION-Lung04[3,4]

Phase 1b, open-label, multicentre, dose-escalation / dose-confirmation and dose-expansion study evaluating Dato-DXd + durvalumab ± ChT in a/mNSCLC

Key eligibility:
- Previously treated or treatment-naïve a/mNSCLCe
- No AGAs
- ECOG PS 0-1

Primary endpoints:
- Safety and tolerability

Key secondary endpoints:
- ORR, DCR, DOR, PFS (investigator assessment)

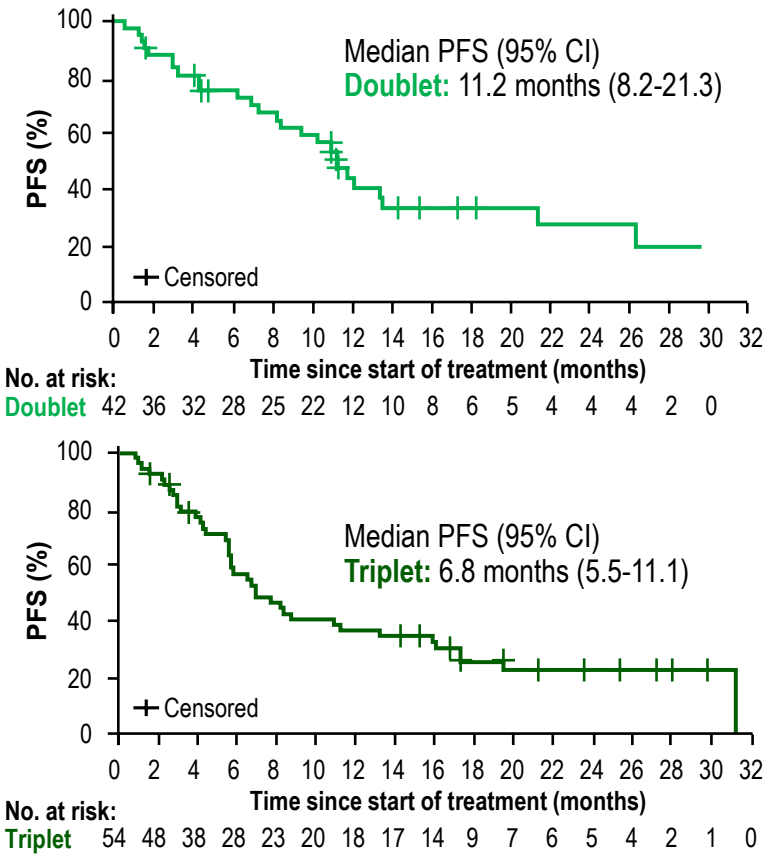
	Part 1: Sequential dose escalation[f]	Part 2: Dose expansion	
Cohort 1	Dato-DXd 4 mg/kg + durvalumab 1120 mg Q3W		Doublet
Cohort 2	Dato-DXd 6 mg/kg + durvalumab 1120 mg Q3W (1L; n=1)	Dato-DXd 6 mg/kg + durvalumab 1120 mg Q3W (1L; n=14)	Doublet
Cohort 3[g]	Dato-DXd 4 mg/kg + durvalumab 1120 mg + 4 cycles of carboplatin AUC 5 Q3W		Triplet
Cohort 4	Dato-DXd 6 mg/kg + durvalumab 1120 mg + 4 cycles of carboplatin AUC 5 Q3W (1L; n=6)	Dato-DXd 6 mg/kg + durvalumab 1120 mg + 4 cycles of carboplatin AUC 5 Q3W (1L; n=31)	Triplet

[a] Patients with known AGAs were not eligible for this study; [b] The first 3-6 patients in each cohort were enrolled to confirm acceptable safety/DLT rate, the remaining are considered part of dose expansion; [c] Prior therapy requirements are for the a/m setting; [d] enrolment after 30 Jun 2022; [e] Patients in Cohort 1 and one patient in Cohort 2 had received ≥1 platinum-based chemotherapy regimen and anti-PD-1/PD-L1 therapy as per an earlier version of the clinical study protocol. Subsequent patients were treatment-naïve or had ≤1 prior line of systemic chemotherapy without concomitant immune checkpoint inhibitors. [f] Dose escalation was guided by a mTPI-2 design and conducted sequentially from Cohort 1 to 2 (Dato-DXd 4 mg/kg to 6 mg/kg) and Cohort 2 to 4 (doublet to triplet combination); [g] Cohort 3 was skipped as there were sufficient data available from the Dato-DXd development program to conclude that 4 mg/kg Dato-DXd in combination with immunotherapy and carboplatin had an acceptable safety profile. 1L, first-line; a/m, advanced/metastatic; AGA, actionable genomic alterations; AUC, area under the curve; ChT, chemotherapy; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; pembro, pembrolizumab; PFS, progression-free survival; Pt, platinum; Q3W, every 3 weeks; TEAE, treatment-emergent adverse event

1. Levy B, et al. J Thorac Oncol. 2026;21:103688; 2. NCT04526691; 3. Cuppens K, et al. Annals of Oncology, 2025; 10 (suppl_2): 1-7. 10.1016/esmoop/esmoop104162 (ESMO TAT 2025; oral presentation); 4. NCT04612751

TROPION-LUNG02: DATO-DXd 1L COMBINATIONS IN ADVANCED/METASTATIC NSCLC (EFFICACY)

EFFICACY BY TREATMENT ARM[1]



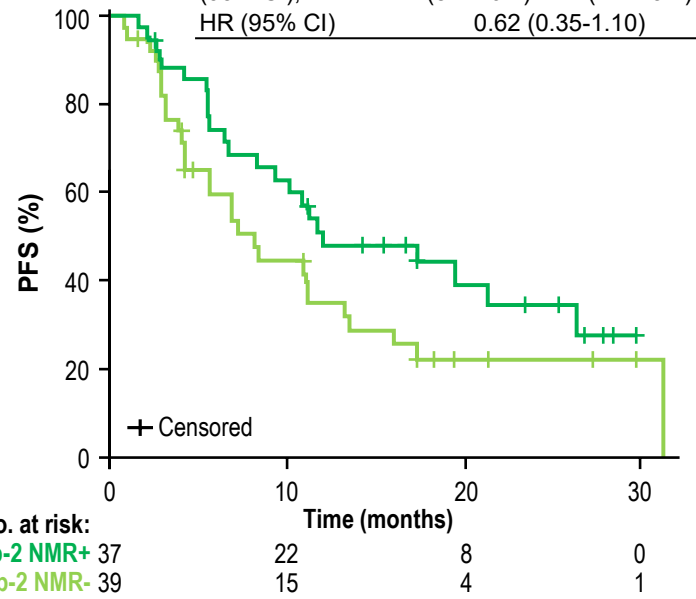
EFFICACY BY PD-L1 STATUS[1]

	Doublet (N=42)		Triplet (N=54)	
	PD-L1 <50%	PD-L1 ≥50%	PD-L1 <50%	PD-L1 ≥50%
N	30	5	40	10
ORR, %	53.3	100	55.0	60.0
BOR, %				
CR	3.3	0	2.5	10.0
PR	50.0	100	52.5	50.0
DOR, months	12.0	NE	14.6	NE
DCR, %	96.7	100	87.5	90.0
Median PFS, months	11.1	NE	6.4	6.8
Median OS, months	NE	NE	13.3	NE

Dato-DXd + pembro ± Pt-ChT showed durable antitumour activity across PD-L1 subgroups

EFFICACY BY TROP-2 NMR[1]

	Trop-2 NMR+ (N=37)	Trop-2 NMR- (N=39)
Median PFS (95% CI), months	12.0 (8.2-26.2)	8.1 (4.2-13.2)
HR (95% CI)	0.62 (0.35-1.10)	



Exploratory TROP-2 NMR biomarker analysis showed a trend toward prolonged PFS in patients who were biomarker positive compared with biomarker negative[1]

1L, first-line; BOR; best overall response; ChT, chemotherapy; CI, confidence interval; CR, complete response; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DOR, duration of response; HR, hazard ratio; NMR, normalised membrane ratio; NSCLC, non-small cell lung cancer; ORR, objective response rate; NE, not evaluable; OS, overall survival; PD-L1, programmed death ligand 1; pembro, pembrolizumab; PFS, progression-free survival; PR, partial response; Pt, platinum

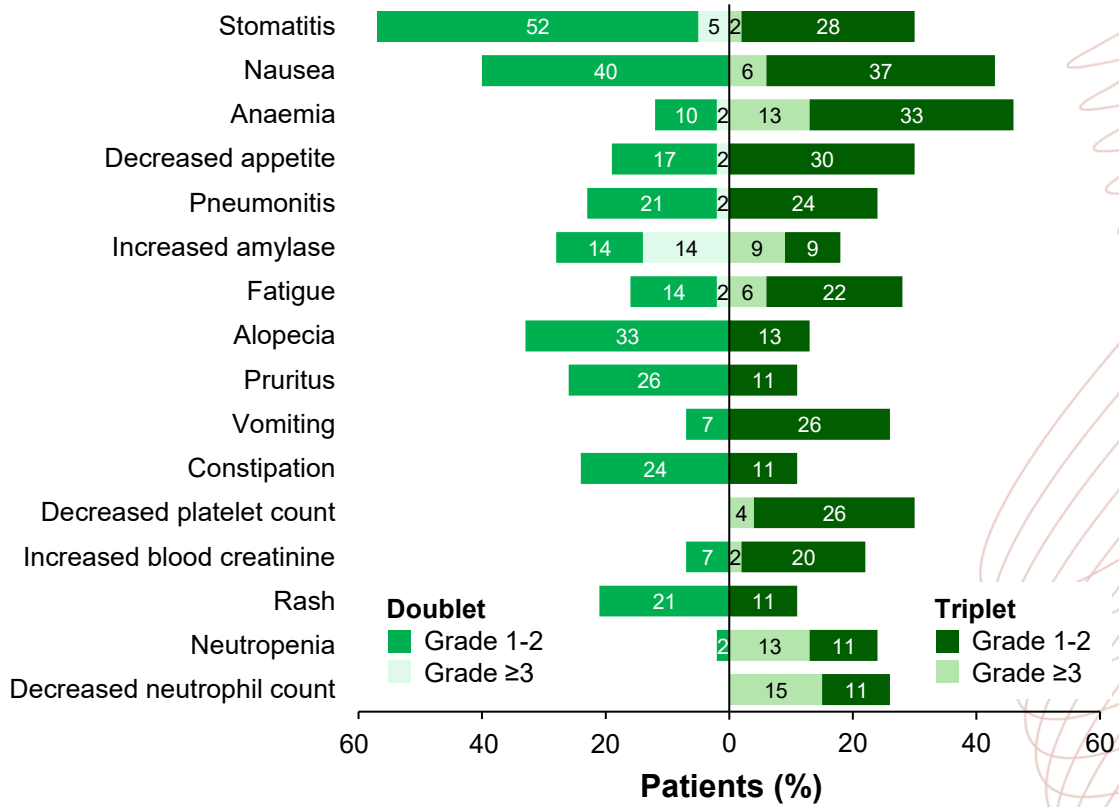
1. Levy B, et al. J Thorac Oncol. 2026;21:103688

TROPION-LUNG02: DATO-DXd 1L COMBINATIONS IN ADVANCED/METASTATIC NSCLC (SAFETY)

SAFETY SUMMARY, 1L PATIENTS[1]

Event, n (%)	Doublet (N=42)	Triplet (N=54)
TRAEs	39 (92.9)	54 (100)
Grade ≥3	17 (40.5)	30 (55.6)
Associated with death	0	0
TRAEs associated with dose modifications		
Dose reduction of any drug	8 (19.0)	14 (25.9)
Dose reduction of Dato-DXd	8 (19.0)	7 (13.0)
Discontinuation of any drug	14 (33.3)	20 (37.0)
Discontinuation of Dato-DXd	13 (31.0)	16 (29.6)
Serious TRAEs	5 (11.9)	12 (22.2)
Grade ≥3	4 (9.5)	9 (16.7)
AESIs		
Oral mucositis/stomatitis	26 (61.9)	22 (40.7)
Grade 3	2 (4.8)	1 (1.9)
Adjudicated drug-related ILD/pneumonitis	11 (26.2)	14 (25.9)
Grade 3	2 (4.8)	1 (1.9)
Ocular surface events	9 (21.4)	18 (33.3)
Grade 3	1 (2.4)	2 (3.7)

TEAEs REPORTED IN ≥10% OF PATIENTS[1]



Grade 3 TRAEs were more frequent in the triplet cohort than the doublet cohort.
No Grade 4 or 5 events were observed[1]

1L, first-line; AESI, adverse event of special interest; Dato-DXd, datopotamab deruxtecan; ILD, interstitial lung disease; NSCLC, non-small cell lung cancer; TEAEs, treatment-emergent adverse events; TRAE, treatment-related adverse event

1. Levy B, et al. J Thorac Oncol. 2026;21:103688

TROPION-LUNG04: DATO-DXd 1L COMBINATIONS IN ADVANCED/METASTATIC NSCLC (EFFICACY)

ANTITUMOUR ACTIVITY

Durable responses were observed for both the doublet and triplet combinations[1]

Response in patients in the 1L setting,[a] n (%)	Cohort 2 doublet (N=15)	Cohort 4 triplet (N=37)
Confirmed ORR, % [95% CI]	53.3 [26.6-78.7]	56.8 [39.5-72.9]
BOR, n (%)		
CR	1 (6.7)	0
PR	7 (46.7)	21 (56.8)
SD	5 (33.3)	12 (32.4)
PD	2 (13.3)	3 (8.1)
Median PFS, months [95% CI]	7.3 [2.0-29.5]	8.7 [5.6-10.1]
Median DOR, months [95% CI]	15.0 [4.5-28.8]	8.8 [5.8-NE]
DCR,[b]% [95% CI]	86.7 [59.5-98.3]	89.2 [74.6-97.0]

Data cutoff: 24 Oct 2024

[a] Investigator assessed per RECIST v1.1; [b] Defined as patients with CR + PR + SD; SD includes unconfirmed CR/PR or SD ≥5 weeks

1L, first-line; BOR; best overall response; CI, confidence interval; CR, complete response; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DOR, duration of response; NE, not evaluable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease

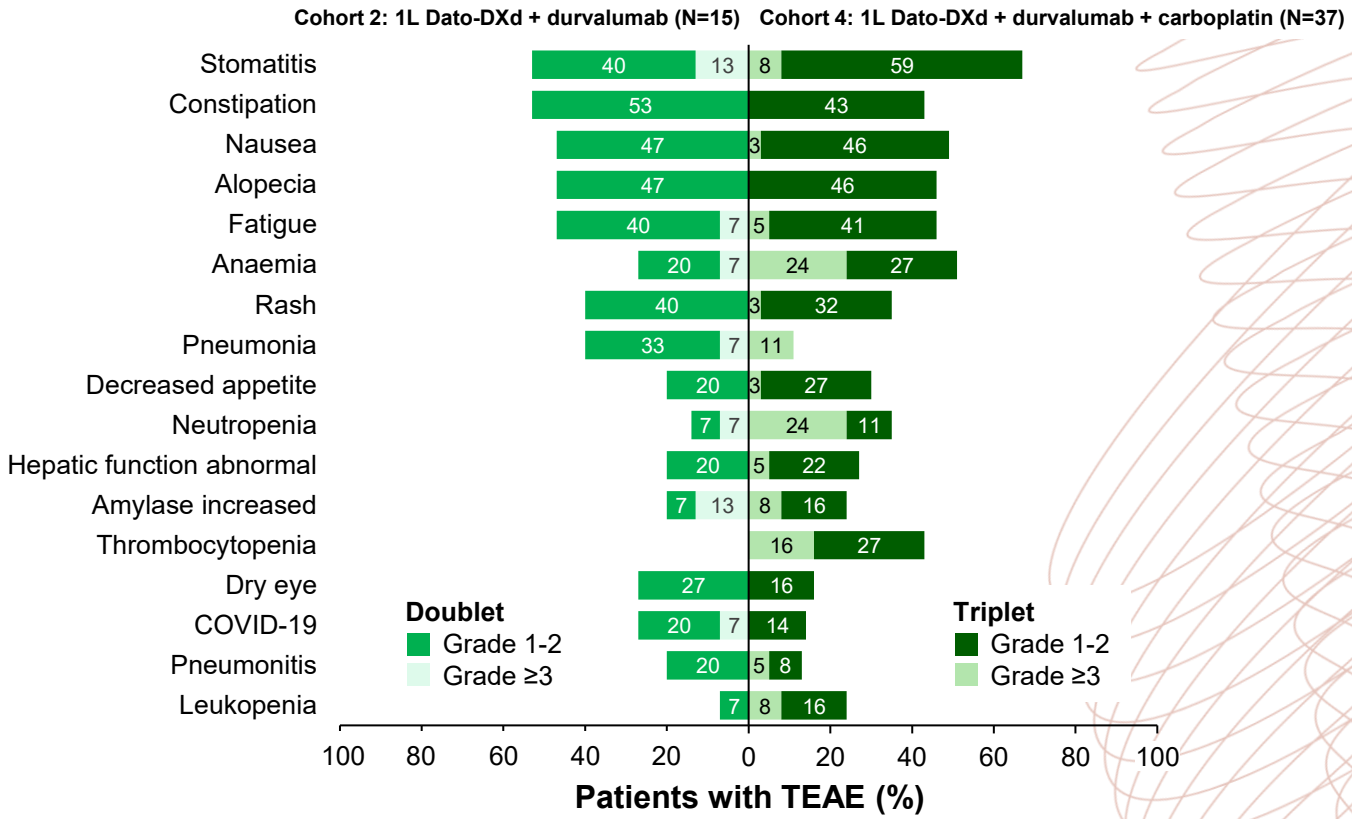
Cuppens K et al. ESMO Open. 2025;10(supplement 2):104164 (ESMO TAT 2025; oral presentation)

TROPION-LUNG04: DATO-DXd 1L COMBINATIONS IN ADVANCED/METASTATIC NSCLC (SAFETY)

SAFETY SUMMARY

Events, n (%)	Cohort 2 1L doublet (N=15)	Cohort 4 1L triplet (N=37)
TEAEs	15 (100)	37 (100)
Treatment related	15 (100)	37 (100)
Grade ≥3 TEAEs	9 (60.0)	26 (70.3)
Treatment related	7 (46.7)	23 (62.2)
SAEs	7 (46.7)	19 (51.4)
Treatment related	6 (40.0)	10 (27.0)
TEAEs associated with:		
Death	0	2 (5.4)[a]
Discontinuation of any drug	4 (26.7)	9 (24.3)
Discontinuation of Dato-DXd	4 (26.7)	8 (21.6)
Adjudicated drug-related ILD, pneumonitis[b]	3 (20.0)	6 (16.2)
Grade ≥3	1 (6.7)[c]	1 (2.7)[d]

TEAEs IN ≥15%[e] OF PATIENTS



[a] Grade 5 pneumonitis (adjudicated as drug-related) and grade 5 dyspnea; [b] ILD/pneumonitis is comprised only of events adjudicated as drug-related ILD and based on a list of 55 preferred terms; [c] Grade 4, patient received sotorasib after PD/discontinuation of study treatment; [d] Grade 5, adjudicated as being study treatment-related'; [e] ≥15% of grade 1/2 TEAEs in either cohort.

1L, first-line; Dato-DXd, datopotamab deruxtecan; ILD, interstitial lung disease; NSCLC, non-small cell lung cancer; PD, progressive disease; SAE, serious adverse event; TEAE, treatment-emergent adverse event

Cuppens K et al. ESMO Open. 2025;10(supplement 2):104164 (ESMO TAT 2025; oral presentation)

Dato-DXd 1L COMBINATION TRIALS

ONGOING PHASE 3 STUDIES IN THE 1L NSQ NSCLC SETTING WITHOUT AGA

AVANZAR
Dato-DXd + durvalumab + carboplatin[1,2] (N=1000)

Key inclusion criteria
- ECOG PS: 0-1
- No AGAs (*EGFR/ALK/ROS1* negative)
- No prior systemic therapy in the a/m setting
- Stage IIIB, IIIC[a] or IV NSCLC

R 1:1

- Dato-DXd + durvalumab + carboplatin Q3W IV for 4 cycles; Dato-DXd + Durvalumab Q3W IV
- Histology-specific ChT + pembrolizumab Q3W IV

Primary endpoints:
- PFS[b] and OS (NSQ; Trop-2 NMR+)
- PFS[b] and OS (NSQ)

Secondary endpoints:
- PFS,[b-d] OS,[c,d] ORR,[b-e] DOR,[b-e] PFS,[c-f] PFS2,[c-e] safety and tolerability, PK, immunogenicity

TROPION-Lung07
Dato-DXd + pembrolizumab ± Pt-ChT[3,4] (N=975)

Key inclusion criteria
- PD-L1 expression <50%
- No AGAs (*EGFR/ALK/ROS1* negative)
- No prior systemic therapy in the a/m setting
- Stage IIIB, IIIC[a] or IV NSCLC

R 1:1:1

- Dato-DXd Q3W + pembrolizumab Q3W IV + cisplatin or carboplatin Q3W IV (max 4 cycles)
- Dato-DXd Q3W IV + pembrolizumab Q3W IV
- Pembrolizumab Q3W IV + pemetrexed Q3W IV + cisplatin or carboplatin Q3W IV (max 4 cycles)

Primary endpoints:
- PFS[b] and OS (ITT population)
- PFS[b] and OS (Trop-2 NMR+)

Secondary endpoints:
- Key: ORRb
- Other: PFS,[f] ORR,[f] DOR,[b-f] TTR,[b,f] DCR,[b,f] PFS2, TTD, safety, immunogenicity

TROPION-Lung08
Dato-DXd + pembrolizumab vs pembrolizumab[5-7] (N=740)

Key inclusion criteria
- PD-L1 TPS ≥50%
- No AGAs (*EGFR/ALK/ROS1* negative)
- No prior systemic therapy in the a/m setting
- Stage IIIB, IIIC[a] or IV NSCLC

R 1:1

- Dato-DXd Q3W IV + pembrolizumab Q3W IV
- Pembrolizumab Q3W IV

Primary endpoints:
- PFS[b] (NSQ)
- OS (NSQ)

Secondary endpoints:
- Key: OS,[d,e] PFS,[d,e] ORR[b,d,e]
- Other: PFS,[e,f] PFS2,d,e ORR,[d-f] DOR,[b,d-f] DCR,[b,d,f] TTD,[b,d-f] safety, immunogenicity

TROPION-Lung10
Dato-DXd + rilvegostomig vs rilvegostomig vs pembrolizumab[8] (N=675)

Key inclusion criteria
- PD-L1 expression ≥50%
- No AGAs (*EGFR/ALK/ROS1* negative)
- No prior systemic therapy in the a/m setting
- Stage IIIB, IIIC or IV NSCLC[a]

R 1:1:1

- Dato-DXd Q3W IV + rilvegostomig Q3W IV
- Rilvegostomig Q3W IV
- Pembrolizumab Q3W IV

Primary endpoints:
- PFS[b] (Trop-2 NMR+)
- OS (Trop-2 NMR+)

Secondary endpoints:
- PFS,[b,g] OS,[g] ORR,[b,c,g] DOR,[b,c,g] PROs,[c,g] PK, immunogenicity, PFS2[c,f,g]

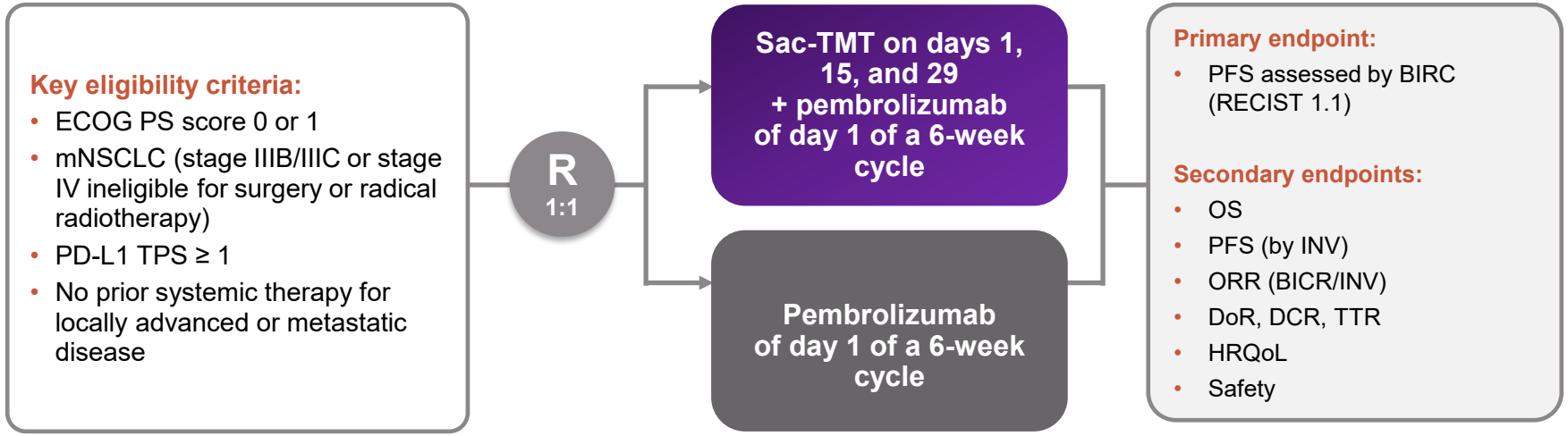
[a] Not a candidate for surgical resection or definitive chemoradiation; [b] By BICR; [c] Trop-2 biomarker-positive population by QCS-NMR assay; [d] ITT population; [e] NSQ population; [f] By investigator; [g] Full analysis set population 1L first line

AGA, actionable genomic alteration, a/m, advanced/metastatic; BICR, blinded independent central review; ChT, chemotherapy; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention-to-treat; IV, intravenous; max, maximum; NMR, normalised membrane ratio; NSCLC, non-small cell lung cancer; NSQ, non-squamous; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PFS2, second progression-free-survival; PK, pharmacokinetics; PRO, patient reported outcome; Pt, platinum; Q3W, every 3 weeks; QCS, Quantitative Continuous Scoring; R, randomisation; TPS, tumour proportion score; TTD, time to deterioration; TTR, time to response

1. Aggarwal C, et al. Poster presented at WCLC 2023 (Abstract P2 04-02); 2. NCT05687266. Updated 10 Dec 2025. Available from: https//clinicaltrials.gov/study/NCT05687266 (Accessed 2 Feb 2026); 3. Okamoto I, et al. Poster presented at ESMO 2023 (Abstract 1505TiP); 4. NCT05555732. Updated 19 Feb 2026. Available from https//clinicaltrials.gov/study/NCT05555732 (Accessed 2 Mar 2026); 5. Zhou C, et al. Poster presented at WCLC 2023 (Abstract P2 08-01); 6. Levy BP, et al. Future Oncol. 2023;19:1461-72; 7. NCT05215340. Updated 7 Jan 2026. Available from: https//clinicaltrials.gov/study/NCT05215340 (Accessed 2 Feb 2026); 8. NCT06357533. Updated 27 Oct 2025. Available from: https//clinicaltrials.gov/study/06357533 (Accessed 2 Feb 2026)

OptiTROP-LUNG05: Sac-TMT 1L COMBINATIONS IN ADVANCED/METASTATIC NSCLC[1,2]

- **At interim analysis:**
  - Sac-TMT plus pembrolizumab significantly improved PFS vs pembrolizumab alone in PD-L1–positive advanced NSCLC
  - The combination showed a positive OS trend



1L, first-line; BIRC, blinded independent review committee; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; HRQoL, health-related quality of life; INV, investigator; IV, intravenously; (m)NSCLC, (metastatic) non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; Sac-TMT, sacituzumab tirumotecan; TPS, tumour proportion score; TTR, time to response

1. Kelun-Biotech Biopharmaceutical Co., Ltd. Press release. November 24, 2025. Available here (accessed May 06, 2026); 2. ClinicalTrials.gov. Identifier NCT06448312

Sac-TMT 1L COMBINATION TRIALS

ONGOING PHASE 3 STUDIES IN THE 1L NSCLC SETTING WITHOUT AGA

TroFuse-007 (Phase 3):[1] Phase 3, randomised, open-label study evaluating Sac-TMT + pembrolizumab compared with pembrolizumab monotherapy for 1L treatment of patients with NSQ or SQ mNSCLC with PD-L1 TPS ≥50%[1]

Key inclusion criteria:
- mNSCLC
- ECOG PS: 0-1
- No prior systemic treatment for mNSCLC
- PD-L1 TPS ≥50%
- No pneumonitis/ILD
- *EGFR/ALK/ROS1*-directed primary therapy not indicated

N=614

R 1:1

- Sac-TMT IV on Days 1, 15 and 29 of each 6-week cycle + Pembrolizumab 400 mg Q6W IV on Day 1 for 18 cycles
- Pembrolizumab 400 mg Q6W IV on Day 1

Primary endpoint:
- OS

Secondary endpoints:
- PFS, OR, DOR
- Safety
- PROs

TroFuse-023 (Phase 3):[2] Phase 3, randomised, open-label study evaluating pembrolizumab + carboplatin / taxane followed by pembrolizumab ± maintenance Sac-TMT for 1L treatment of patients with SQ mNSCLC[2]

Key inclusion criteria:
- SQ mNSCLC
- ECOG PS: 0-1
- No prior systemic treatment for mNSCLC
- No pneumonitis/ILD

Induction phase

Pembrolizumab 200 mg Q3W + carboplatin AUC 6 mg/mL/min Q3W + paclitaxel 200 mg/m^2 Q3W or nab-paclitaxel 100 mg/m^2 weekly (4 cycles)

N=851

R 1:1

Maintenance phase

- Sac-TMT 4 mg/kg Q2W IV + Pembrolizumab 400 mg Q6W IV for 96 weeks
- Pembrolizumab 400 mg Q6W IV for 96 weeks

Primary endpoint:
- OS

Secondary endpoints:
- PFS
- Safety
- PROs

1L, first-line; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ILD, interstitial lung disease; IV, intravenous; (m)NSCLC, (metastatic) non-small cell lung cancer; OR, objective response; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; PROs, patient reported outcomes; SQ, squamous cell; TPS, tumour proportion score; Q'X'W, every 'x' weeks

1. Frost N, et al. J Thorac Oncol. 2024;1910 Suppl):S389-S390 (presented at WCLC 2024, Abstract P4.11D.02); 2. Garassino MC, et al. Cancer Res. 2025;85 (8_Supplement_2): CT250 (presented at AACR 2025)

CLINICAL OVERVIEW OF TROP2-DIRECTED ADCs IN NSCLC

WITH ACTIONABLE GENOMIC ALTERATIONS

Dr Louise Lim
Barts Health NHS Trust, UK

NSCLC, non-small cell lung cancer

TROP2 EXPRESSION IN *EGFR*-MUTANT VS WILD-TYPE NSCLC

EGFR wild-type NSCLC

- TROP2 detected in the majority of tumours (adenocarcinoma and squamous)[1]
- Supports TROP2 directed ADC trials[1]
- Interest in development of potential biomarkers[1] (e.g. quantitative IHC/AI scoring)

EGFR-mutant NSCLC

- Reports show higher TROP2 IHC expression in *EGFR*m vs *EGFR*-wild-type NSCLC[2]
- TROP2 can be enriched in TKI-resistant states (incl. drug-tolerant persister cells)[3]
- *EGFR* mutation has been linked to increased internalisation/activity for some TROP2 ADCs in preclinical work[4]

EGFR wild-type = broad TROP2 expression
_EGFR_m = often higher TROP2 expression and biologically enriched during resistance

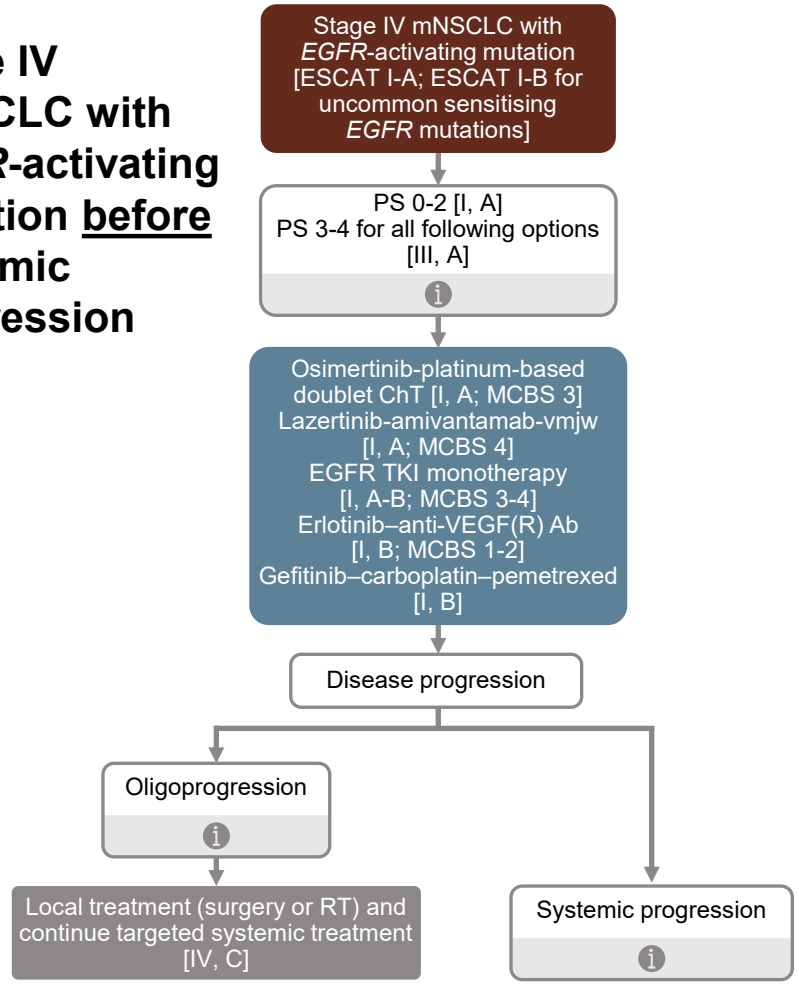
ADC, antibody-drug conjugate; AI, artificial intelligence; EGFRm, EGFR mutation; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

1. Kuo P, et al. PLoS One. 2025;20(4):e0321555; 2. Baldacci S, et al. J Thorac Oncol. 2024;19 (10)_Suppl S80:19S80 (WCLC 2024, Abstract MA07.06); 3. Baldacci S, et al. Cancer Discov. 2025;15(11):2235-50; 4. Zhao S, et al. Nat Med. 2025;31:1976-86

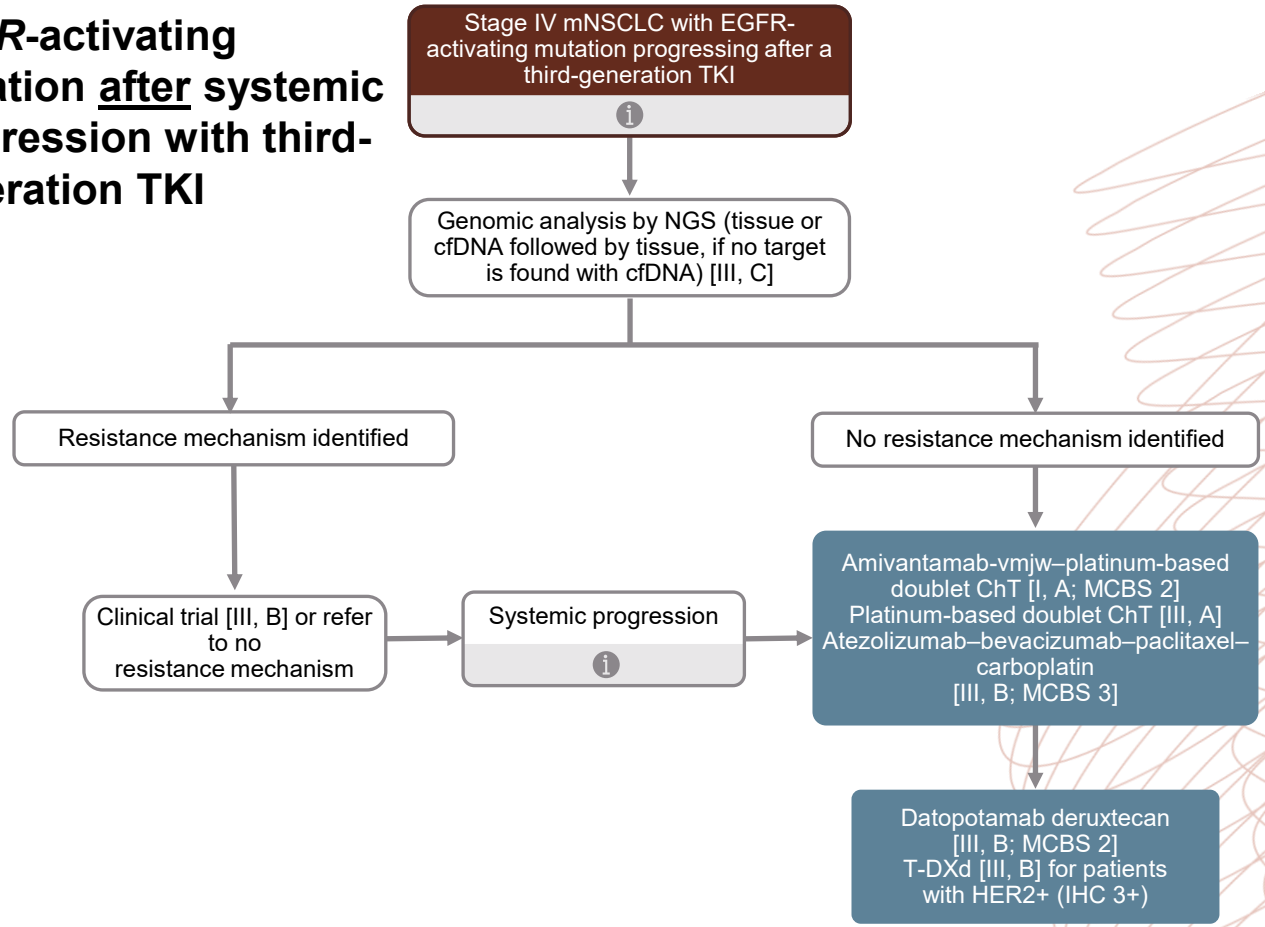
ESMO CLINICAL PRACTICE GUIDELINES: *EGFR*-MUTANT NSCLC

V1.3 Feb 2026

Stage IV mNSCLC with *EGFR*-activating mutation before systemic progression



EGFR-activating mutation after systemic progression with third-generation TKI



Ab, antibody; cfDNA, cell-free DNA; ChT, chemotherapy; ESCAT, ESMO Scale for Clinical Actionability of molecular Targets; ESMO, European Society for Medical Oncology; MCBS, ESMO Magnitude of Clinical Benefit Scale; (m)NSCLC, (metastatic) non-small cell lung cancer; NGS, next-generation sequencing; PS, performance status (Eastern Cooperative Oncology Group); RT, radiotherapy; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor

1. Hendriks L, et al. Ann Oncol. 2023;34:339-357; 2. Hendriks L, et al. ESMO Oncogene-Addicted Metastatic NSCLC Living Guideline, v1.3 – February 2026. Available here (accessed March 16, 2026)

DATO-DXd IN PRE-TREATED *EGFR*-MUTANT NSCLC

TROPION-LUNG05 AND TROPION-LUNG01 POOLED ANALYSIS

Patients with *EGFR*m NSCLC who received Dato-DXd 6 mg/kg Q3W were included in the pool

TROPION-Lung05 (Phase 2 study)

- **Presence of ≥1 actionable genomic alteration** (*EGFR, ALK, ROS1, NTRK, BRAF, MET* exon 14 skipping, or *RET*)
  - ≥1 line of targeted therapy
  - 1-2 prior cytotoxic agent–containing therapies including Pt-CT in the metastatic setting
  - Radiographic disease progression after most recent therapy

TROPION-Lung01 (Phase 3 study)

- **In those with actionable genomic alterations** (*EGFR, ALK, ROS1, NTRK, BRAF, MET* exon 14 skipping, or *RET*)
  - 1-2 prior approved targeted therapies + Pt-CT, and ≥1 anti–PD-(L)1 mAb
  - No prior docetaxel

R 1:1

- **Dato-DXd 6 mg/kg Q3W[a] (N=137)**
- **Dato-DXd 6 mg/kg Q3W[b] (N=299)**
- **Docetaxel 75 mg/kg² Q3W[b] (N=305)**

***EGFR*m Pool: N=117**

TROPION-Lung05 (n=78)

TROPION-Lung01 (n=39)

Endpoints:

- ORR per BICR
- BOR per BICR
- DCR per BICR
- DoR per BICR
- PFS per BICR
- OS
- Safety

[a] Data cutoff: December 14, 2022; [b] Data cutoff: March 1, 2024 (OS and safety) or March 29, 2023 (all other efficacy endpoints)

ADC, antibody-drug conjugate; BICR, blinded independent central review; BOR, best overall response; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DoR, duration of response; EGFRm, EGFR mutation; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Pt-CT, platinum-based chemotherapy; Q3W, once every 3 weeks; R, randomised

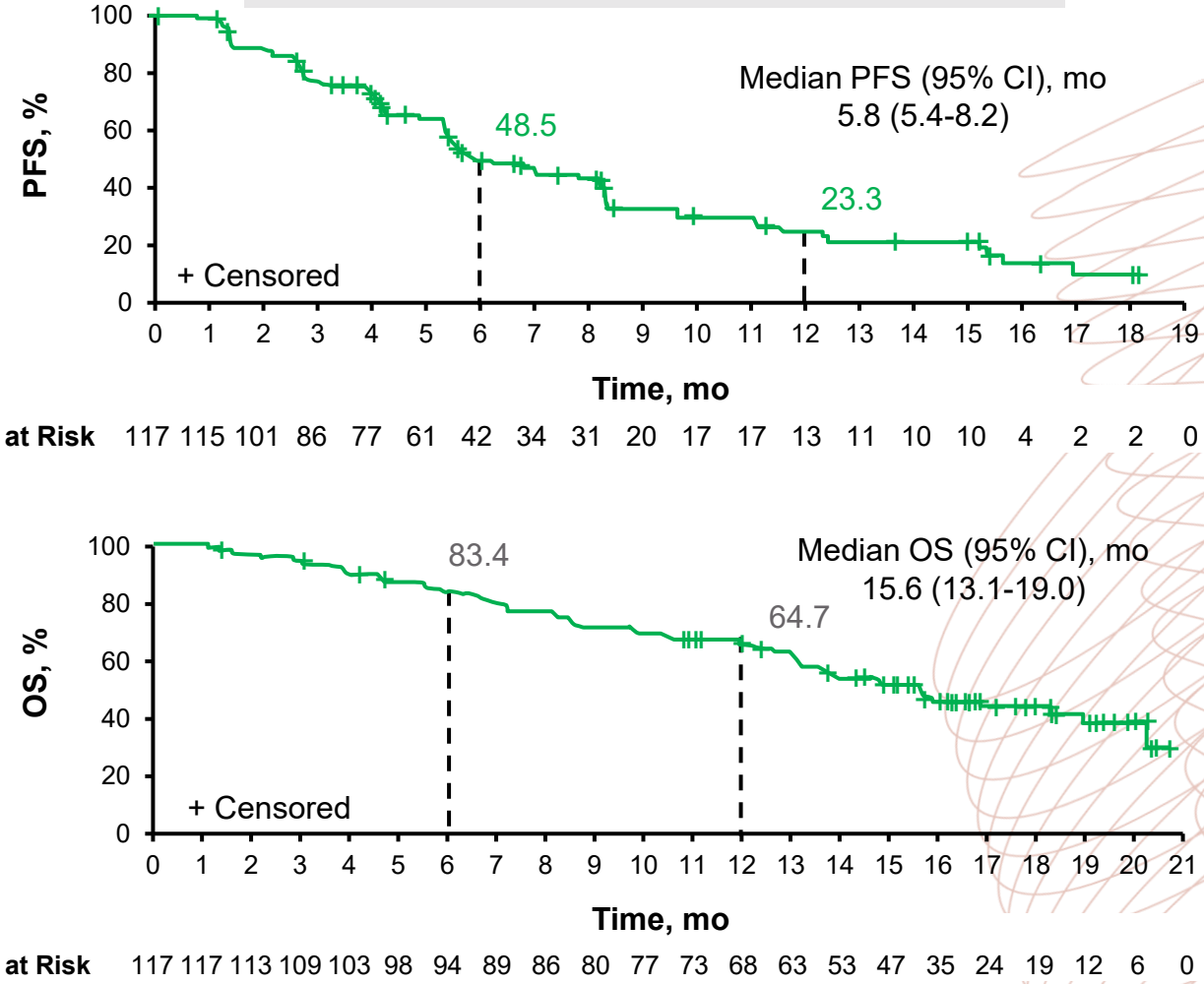
Ahn M-J, et al. Ann Oncol. 2024;35 (Suppl 4):S1630-S1631 (oral presentation, ESMO Asia 2024)

DATO-DXd IN PRE-TREATED *EGFR*-MUTANT NSCLC

TROPION-LUNG05 AND TROPION-LUNG01 EFFICACY

Response	EGFRm Pool (N=117)	Prior Osimertinib (N=96)
Confirmed ORR, n (%) (95% CI)	50 (42.7) (33.6-52.2)	43 (44.8) (34.6-55.3)
BOR, n (%)		
CR	5 (4.3)	4 (4.2)
PR	45 (38.5)	39 (40.6)
SD	48 (41.0)	37 (38.5)
Non-CR/non-PD	3 (2.6)	2 (2.1)
PD	12 (10.3)	10 (10.4)
NE	4 (3.4)	4 (4.2)
Median DoR (95% CI), mo	7.0 (4.2-9.8)	6.9 (4.2-9.8)
DCR, n (%) (95% CI)	101 (86.3) (78.7-92.0)	82 (85.4) (76.7-91.8)
Median PFS (95% CI), mo	5.8 (5.4-8.2)	5.7 (5.4-7.9)
Median OS (95% CI), mo	15.6 (13.1-19.0)	14.7 (13.0-18.3)

PFS and OS in the *EGFR*m Pool (N=117)



ADC, antibody-drug conjugate; BOR, best overall response; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; EGFRm, EGFR mutated; mo, months; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease

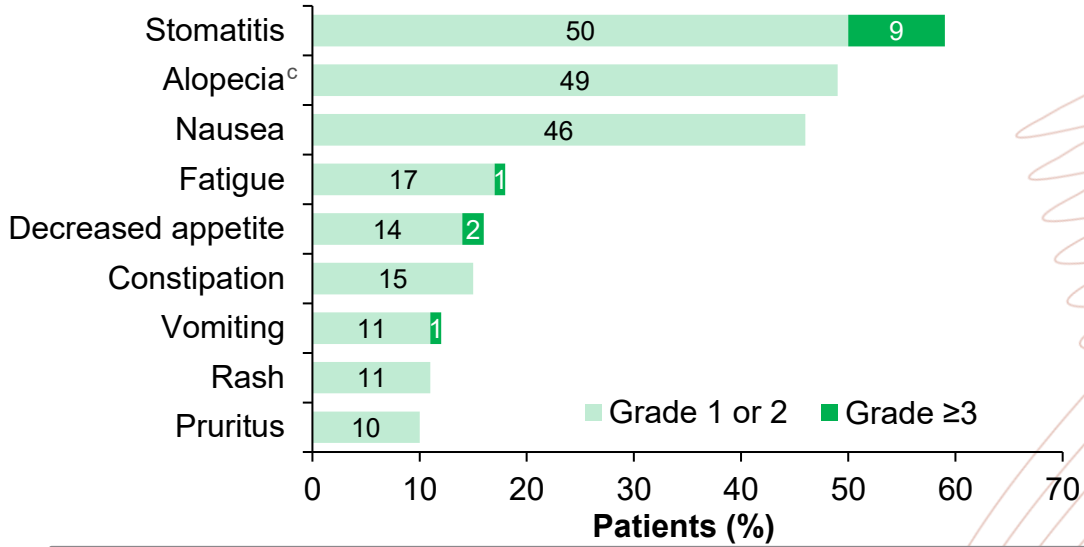
Ahn M-J, et al. Ann Oncol. 2024;35 (Suppl 4):S1630-S1631 (oral presentation, ESMO Asia 2024)

DATO-DXd IN PRE-TREATED *EGFR*-MUTANT NSCLC

TROPION-LUNG05 AND TROPION-LUNG01 SAFETY

	EGFRm Pool (N=117)
TRAEs, n (%)	111 (95)
Grade ≥3	27 (23)
Associated with dose reduction	26 (22)
Associated with dose delay	27 (23)
Associated with treatment discontinuation	6 (5)
Associated with death	0 (0)
Serious TRAEs	9 (8)
AESIs,[a] n (%)	
Stomatitis/oral mucositis	81 (69)
Grade 3[b]	11 (9)
Ocular surface events	38 (32)
Grade 3[b]	3 (3)
Adjudicated drug-related ILD	5 (4)
Grade 3[b]	1 (1)

TRAEs occurring in ≥10% of *EGFR*m pool (N=117)



- Median Dato-DXd treatment duration: **6.1 months**

- Overall safety profile consistent with TROPION-Lung 01 and 05
- No grade 4 or 5 adjudicated drug-related ILD
- Ocular surface events[a] were primarily dry eye (12%), vision blurred and keratitis (each 7%)
- No TRAEs associated with death

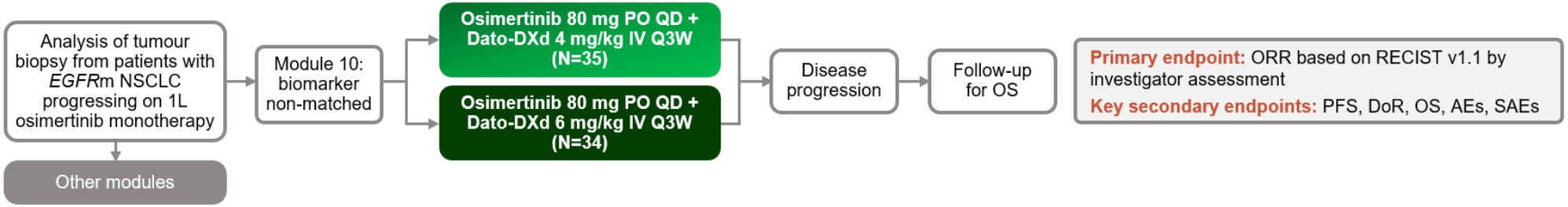
[a] AESIs listed are treatment emergent and include all preferred terms that define the medical concept. Some patients may have had >1 event;
[b] No grade 4 or 5 events occurred; [c] Includes an event incorrectly reported as grade 3 per CTCAE grades

AESI, adverse event of special interest; CTCAE, Common Terminology Criteria for Adverse Events; Dato-DXd, datopotamab deruxtecan; EGFRm, EGFR mutation; ILD, interstitial lung disease; TRAE, treatment-related adverse event

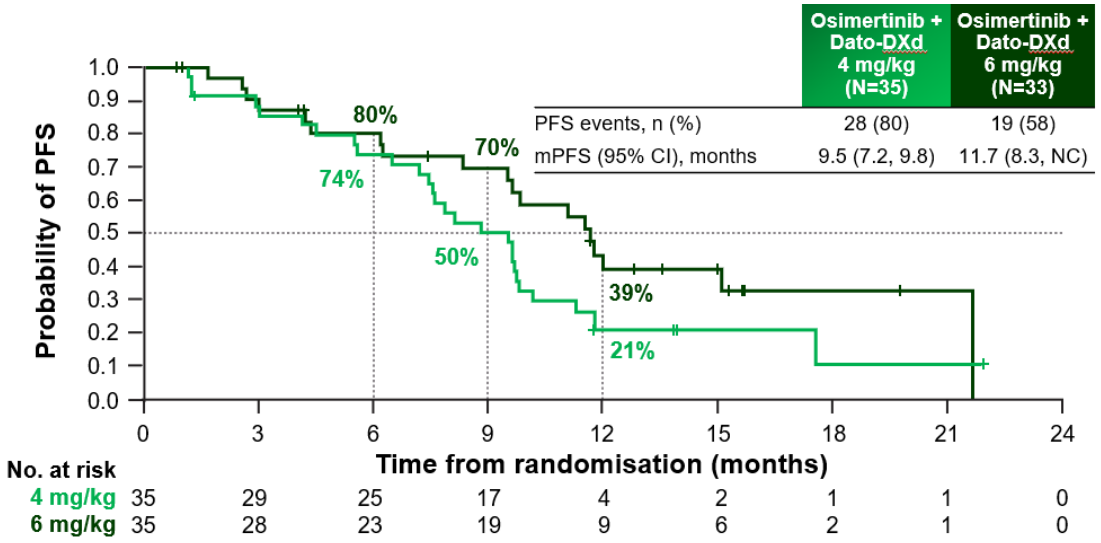
Ahn M-J, et al. Ann Oncol. 2024;35 (Suppl 4):S1630-S1631 (oral presentation, ESMO Asia 2024)

DATO-DXd COMBINATIONS IN POST-OSIMERTINIB *EGFR*-MUTANT NSCLC

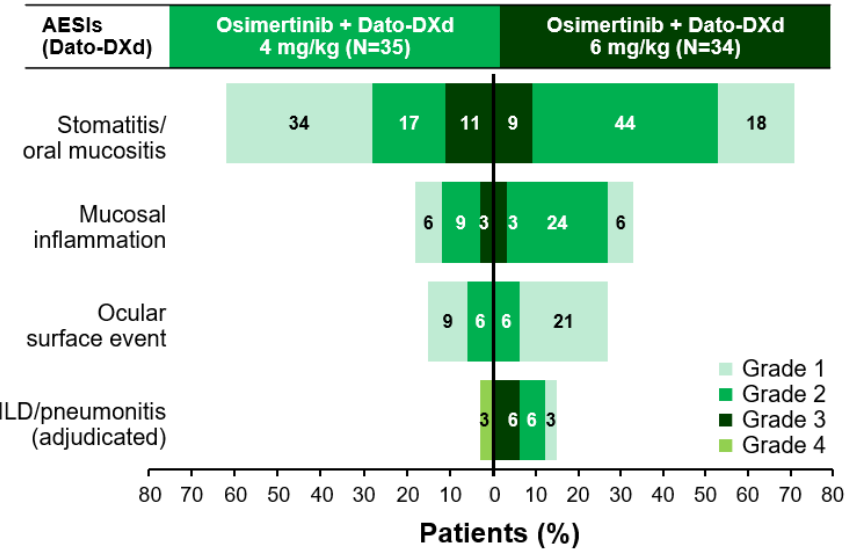
ORCHARD: MODULE 10 STUDY DESIGN AND RESULTS



Progression-free survival



Safety Summary



1L, first-line; ADC, antibody-drug conjugate; AE, adverse event; AESI, adverse event of special interest; CI, confidence interval; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; EGFRm, EGFR mutation; ILD, interstitial lung disease; IV, intravenous; NC, not calculable; NSCLC, non-small cell lung cancer; (m)PFS, (median) progression-free survival; ORR, objective response rate; OS, overall survival; PO, orally; Q3W, every 3 weeks; QD, once daily; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SAE, serious AE

Le X, et al. J Thorac Oncol. 2025;20(3):S2-S4. ELCC 2025 (oral presentation, Abstr 1O)

DATO-DXd IN POST-OSIMERTINIB *EGFR*-MUTANT NSCLC

TROPION-LUNG15: PHASE 3, ONGOING TRIAL

Key eligibility criteria:

- Aged ≥ 18 years
- ECOG or WHO PS score 0 or 1
- Histologically or cytologically confirmed NSQ, locally advanced or metastatic
- Documented EGFR-TKI sensitive mutations
- ≤ 2 prior lines of EGFR-TKIs
- Radiological progression on prior osimertinib monotherapy

Stratification:

- Brain metastases baseline (yes vs no)
- Prior Osi: adjuvant vs post-CRT/1L vs 2L
- Race: Chinese Asian vs non-Chinese Asian vs non-Asian

R 1:1:1

N=630

- **Dato-DXd** (6 mg/kg IV, Q3W)
- **Dato-DXd** (6 mg/kg IV, Q3W) **+ Osi**
- **Platinum-based chemotherapy**

Dual primary endpoints:

- **PFS by BICR**
  Dato-DXd vs Pt-CT
  Dato-DXd + Osi vs Pt-CT

Key secondary endpoints:

- OS
- CNS-PFS by BICR
- Safety

NCT06417814

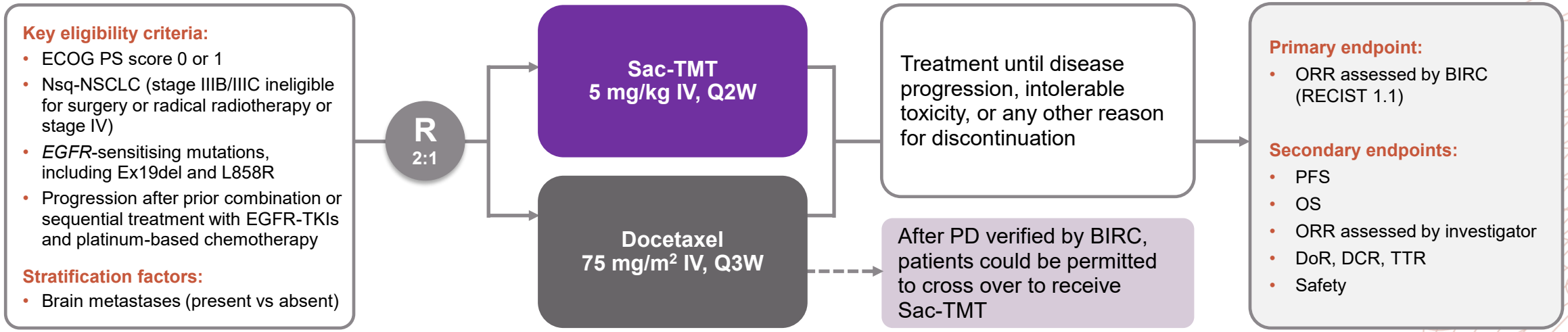
1L/2L, first/second-line; BICR, blinded independent central review; CNS, central nervous system; CRT, chemoradiotherapy; Dato-DXd, datopotamab deruxtecan; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; NSCLC, non-small cell lung cancer; NSQ, non-squamous; OS, overall survival; Osi, osimertinib; PFS, progression-free survival; PS, performance status; Pt-CT, platinum-based chemotherapy; Q3W, every 3 weeks; R, randomisation; Sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitors; WHO, World Health Organization

Nadal E, et al. J Thorac Oncol. 2025;20 (3, supplement 1):S87-S88 (ELCC 2025, Poster 124TiP); Tan DS, et al. Ther Adv Med Oncol. 2025;17: doi: 10.1177/17588359251385410

Sac-TMT IN *EGFR*-MUTANT NSCLC POST-EGFR TKI AND Pt-CT

OptiTROP-LUNG03: STUDY DESIGN

Open-label, randomised, multicentre, registrational trial (NCT05631262)



ADC, antibody-drug conjugate; BIRC, blinded independent review committee; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; Ex19del, exon 19 deletion; IV, intravenous; (Nsq-)NSCLC, nonsquamous non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; Pt-CT, platinum chemotherapy; PFS, progression-free survival; Q2/3W, every 2 or 3 weeks; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; Sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor; TTR, time to response

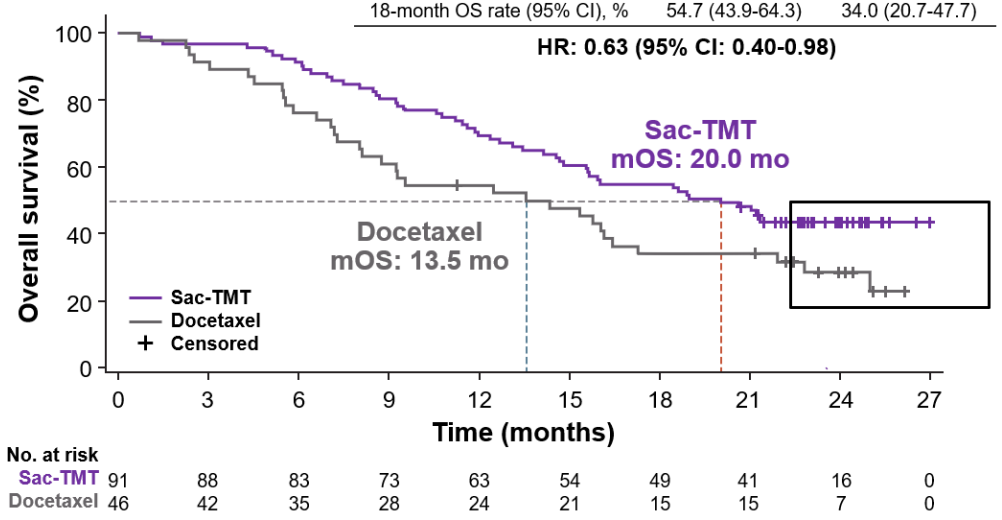
Zhang L, et al. J Clin Oncol 2025;43(suppl 16). Abstr 8507 (ASCO 2025, oral presentation)

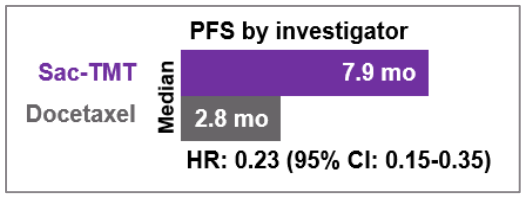
OptiTROP-LUNG03: Sac-TMT IN *EGFR*-MUTANT NSCLC POST-EGFR TKI AND Pt-CT

EFFICACY

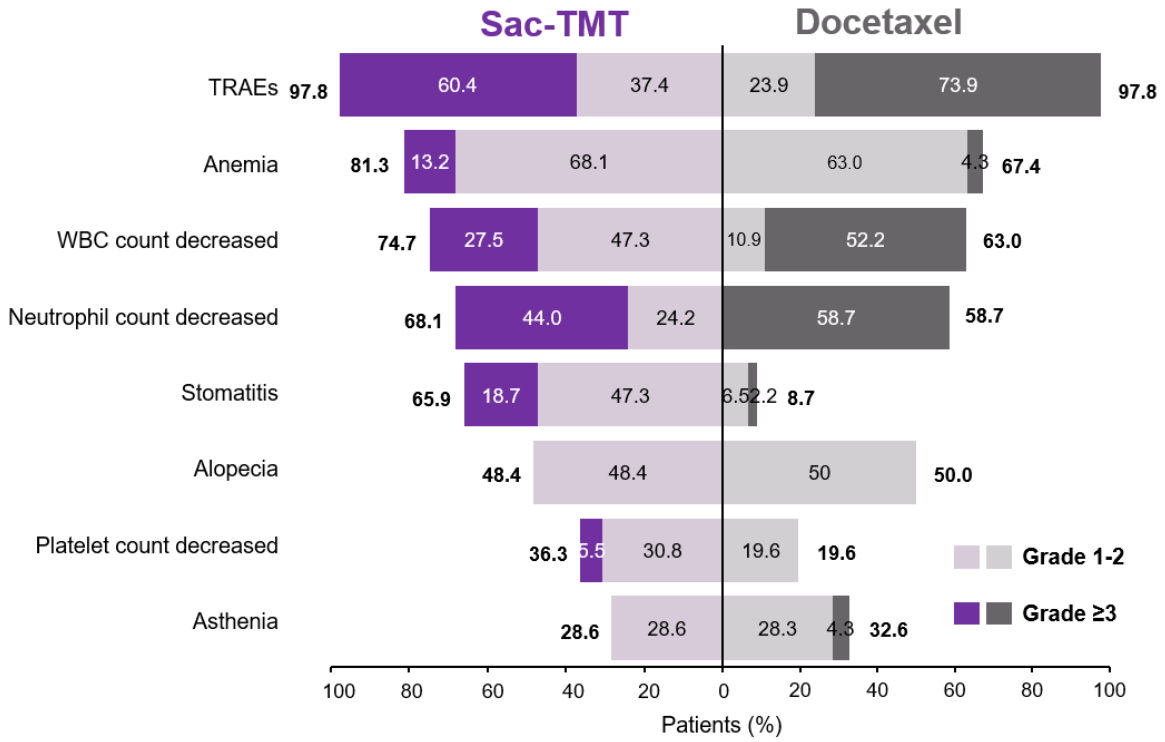
	Sac-TMT (N=91)	Docetaxel (N=46)
OS events, n (%)	51 (56.0)	33 (71.7)
Median OS (95% CI), months	**20.0** (14.8-NE)	**13.5** (8.0-17.2)
18-month OS rate (95% CI), %	54.7 (43.9-64.3)	34.0 (20.7-47.7)

HR: 0.63 (95% CI: 0.40-0.98)





ANY GRADE TRAEs WITH INCIDENCE ≥30%



- The most common TRAEs for both Sac-TMT and docetaxel were hematologic toxicities
  - Febrile neutropenia: none in the Sac-TMT group and 19.6% of patients in the docetaxel group
- ILD/pneumonitis were reported as 2.2% in both groups
- No TRAEs led to treatment discontinuation or death in the Sac-TMT group

Data cut-off: 11 December 2025 (23.8 months follow-up)

CI, confidence interval; HR, hazard ratio; ILD, interstitial lung disease; mo, months; NE, not estimable; NSCLC, non-small cell lung cancer; (m)OS, (median) overall survival; PFS, progression-free survival; Pt-CT, platinum-based chemotherapy; Sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event; WBC, white blood cell

Yang Y, et al. Abstract LBA4, ELCC 2026 (oral presentation)

Sac-TMT IN *EGFR*-MUTANT NSCLC POST-EGFR TKI

OptiTROP-LUNG04: STUDY DESIGN

Open-label, randomised, multicentre, phase 3 trial (NCT05870319)

Key eligibility criteria:

- ECOG PS score 0 or 1
- Nsq-NSCLC (stage IIIB/IIIC or stage IV)
- *EGFR*-sensitive mutations
- Progression after 3rd gen TKI therapy or progression after 1st or 2nd gen TKIs with negative T790M

Stratification factors:

- Prior EGFR-TKI therapy (3rd gen TKI in 1st line vs in 2nd line vs no 3rd gen TKI)
- Brain metastases (yes vs no)

R 1:1

- **Sac-TMT 5 mg/kg IV, Q2W**
- **Pemetrexed 500 mg/m² + carboplatin AUC 5, or Cisplatin 75 mg/m² Q3W for up to 4 cycles**
- **Pemetrexed 500 mg/m² maintenance, Q3W**

Treatment until disease progression, intolerable toxicity, or any other reason for discontinuation

Primary endpoint:

- PFS assessed by BIRC (RECIST 1.1)

Secondary endpoints:

- OS (key secondary endpoint)
- PFS (assessed by investigator)
- ORR, DoR, DCR, etc.
- Safety

ADC, antibody-drug conjugate; AUC, area under the curve; BIRC, blinded independent review committee; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; gen, generation; IV, intravenous; (Nsq-)NSCLC, nonsquamous non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; Q2/3W, every 2 or 3 weeks; R, randomisation; Sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor

Zhang L, et al. Ann Oncol. 2025;36, S1613-S1614 (LBA5, ESMO 2025, oral presentation); Fang W, et al. N Engl J Med 2026;394:13-26

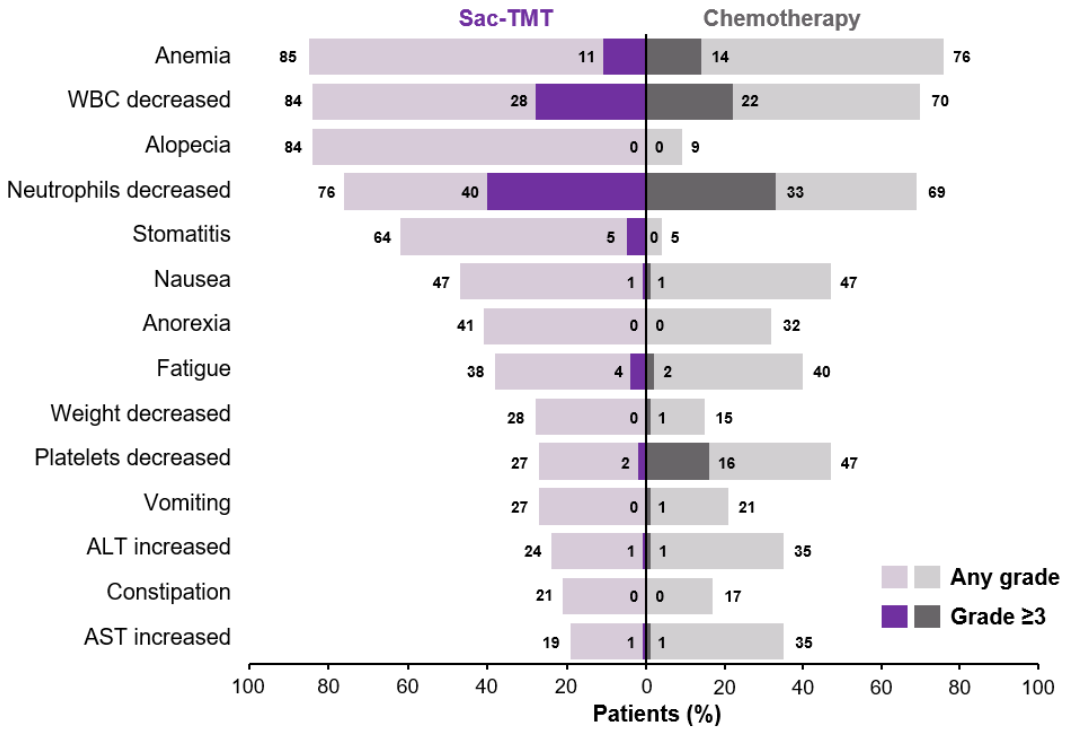
OPTITROP-LUNG04: Sac-TMT IN *EGFR*-MUTANT NSCLC POST-EGFR TKI

EFFICACY

	Sac-TMT (n=188)	CT (n=188)
Median PFS[a] (95% CI), months	**8.3** (6.7-9.9)	**4.3** (4.2-5.5)
HR (95% CI) p value	0.49 (0.39-0.62) <0.0001	
12-month PFS rate (95% CI), %,	32.3 (25.5-39.2)	7.9 (4.4-12.8)
Median OS (95% CI), months	**NR** (21.5-NE)	**17.4** (15.7-20.4)
HR (95% CI) p value	0.60 (0.44-0.82) 0.001[b]	
ORR[a] (95% CI), %	**60.6** (53.3-67.7)	**43.1** (35.9-50.5)
Median DoR[a] (95% CI), months	8.3 (6.2-10.0)	4.2 (3.0-4.4)
DCR[a] (95% CI), %	87.2 (81.6-91.6)	80.3 (73.9-85.7)

A consistent OS and PFS and benefit of Sac-TMT over chemotherapy was observed across all predefined subgroups

ANY GRADE TRAES WITH INCIDENCE ≥20%



- No drug-related ILD/ pneumonitis occurred in either arm
- Ocular surface toxicity occurred in 9.6% of patients in the Sac-TMT group (all grade 1 or 2)

Data cutoff: July 11, 2024, for PFS IA and July 6, 2025 for safety analysis/preplanned IA of OS and final PFS analysis

[a] By BIRC; [b] Two-sided p-value by stratified log-rank test, based on pre-specified OS IA, 2-sided P value was less than the pre-specified efficacy boundary to achieve statistically significant improvement

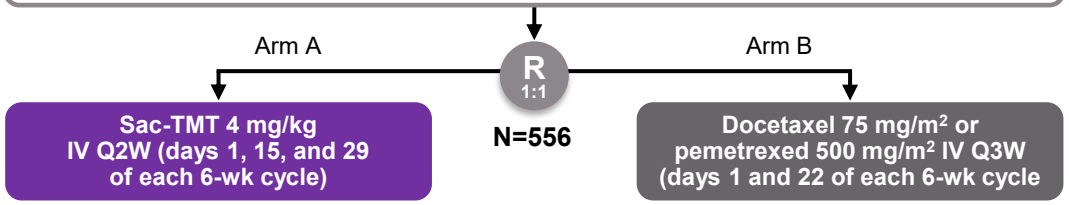
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BICR, blinded independent central review; CI, confidence interval; CT, chemotherapy; DCR, disease control rate; DoR, duration of response; HR, hazard ratio; ; IA, interim analysis; ILD, interstitial lung disease; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Sac-TMT, sacituzumab tirumotecan; TRAE, treatment related adverse event; WBC, white blood cell

Zhang L, et al. Ann Oncol. 2025;36, S1613-S1614 (LBA5, ESMO 2025, oral presentation); Fang W, et al. N Engl J Med 2026;394:13-26

SAC-TMT ONGOING GLOBAL PHASE 3 TRIALS IN PRE-TREATED *EGFR*-MUTANT NSCLC

TroFuse-004 (NCT06074588)[1]

Study population:
- Age ≥18 years
- Histologically/cytologically documented advanced[a] or metastatic nonsquamous NSCLC
- Presence of ex19del or exon 21 L858R *EGFR*m or other genomic alterations[b]
- Documented disease progression following 1 or 2 prior lines of TKIs plus 1 platinum-based chemotherapy ± anti–PD-(L)1
- Measurable disease per RECIST version 1.1



Primary endpoints:
- PFS by BICR
- OS (in patients with *EGFR*m)

Secondary endpoints:
- PFS, OS, ORR, DOR, PROs ,Safety

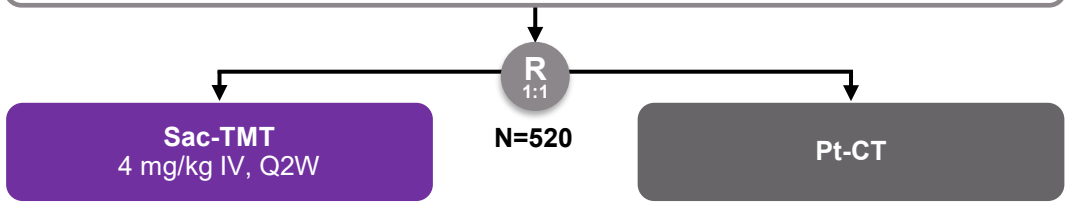
Stratification factors:
- *EGFR*m prior treatment (*EGFR*m with third-generation TKI vs *EGFR*m without third-generation TKI vs other genomic alterations)
- Brain metastasis (yes vs no)
- TROP2 expression (low vs medium vs high)

[a] Stage III disease not eligible for resection or curative radiation;

[b] Including alterations in *ALK, ROS1, BRAF V600E, NTRK, MET* exon 14 skipping, or *RET* and less common *EGFR* mutations (exon 20 S768I, exon 21 L861Q, and/or exon 18 G719X)

TroFuse-009 (NCT06305754)[2]

Study population:
- Age ≥18 years
- Histologically/cytologically documented stage III (not eligible for surgical resection or curative chemoradiation) or stage IV non-squamous NSCLC
- Presence of exon 19del, L858R, G719X, S7681, or L861Q
- Documented disease progression on prior EGFR TKI
- Measurable disease per RECIST version 1.1



Primary endpoints:
- PFS by BICR
- OS

Secondary endpoints:
- ORR
- DoR
- PROs
- Safety

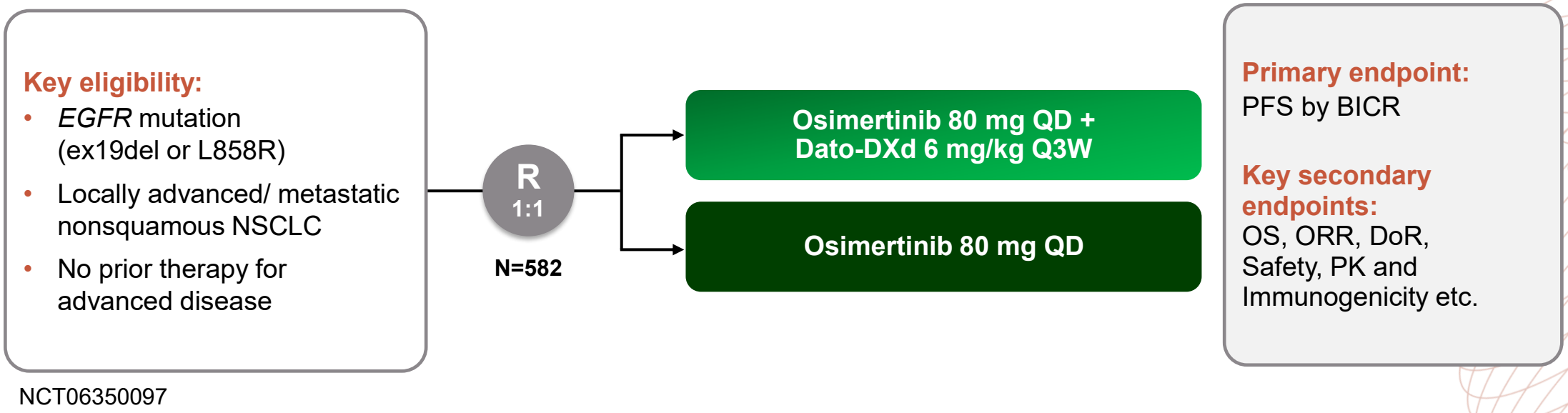
Stratification factors:
- Brain metastases baseline (yes vs no)
- EGFR TKI 1L: 3rd gen vs 1st/2nd gen, including 3rd gen in 2L
- TROP2 expression: no or low vs medium vs high

1L/2L, first/second-line; BICR, blinded independent central review; DoR, duration of response; ex19del, exon 19 deletion; gen, generation; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PROs, patient reported outcomes; Pt-CT, platinum-chemotherapy; Q2/3W, every 2 or 3 weeks; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; Sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitors;

1. Garon EB, et al. J Thorac Oncol. 2024;19 (10, supplement):S245-S246) (WCLC 2024, Abstract P2.10A.06;
2. Leighl NB, et al. J Thorac Oncol. 2024;19(10, supplement): S246-S247 (WCLC 2024, Abstract P2.10A.07)

DATO-DXd AS 1L TREATMENT IN *EGFR*-MUTANT NSCLC

TROPION-LUNG 14: PHASE 3, ONGOING TRIAL



NCT06350097

1L, first-line; BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; ex19del, exon 19 deletion; gen, generation; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; QD, once daily; R, randomisation

Lu S, et al. J Clin Oncol 2025; 43: TPS8647

FUTURE LANDSCAPE & STRATEGIC IMPLICATIONS

- Will ADC + IO replace IO monotherapy in PD-L1 ≥50%?
- Triplet intensification vs biomarker selection strategies
- Will OS improvement justify toxicity?
- Potential need for TROP2 expression stratification
- Impact on second-line ADC positioning
- Competitive pressure from bispecifics and next-generation ADCs

ADC, antibody-drug conjugate; IO, immunotherapy; PD-L1, programmed death ligand 1

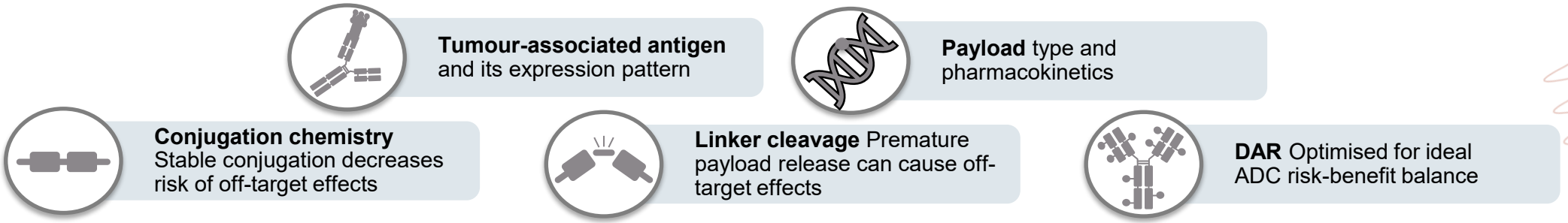
OPTIMISING THE TREATMENT EXPERIENCE: PROACTIVE AE MONITORING & MANAGEMENT

Dr Jacob Sands
Dana-Farber
Cancer Institute, US

Mrs Stephanie McDonald
Dana-Farber
Cancer Institute, US

SAFETY CONSIDERATIONS FOR ADCs

AEs can be on- or off-target and are influenced by:



- **Safety considerations**
- Toxicities relate to payload class and linker behaviour:[2,3]
- Myelosuppression (e.g., neutropenia)
- GI toxicity (e.g., diarrhea)
- Mucositis/stomatitis and ocular surface events[4]
- Interstitial lung disease/pneumonitis

ADC, antibody-drug conjugate; GI, gastrointestinal; NSCLC, non-small cell lung cancer

1. Nguyen TD, et al. Cancers (Basel). 2023;15:713; 2. Ballestin P, et al. Pharmaceutics. 2025;17:258; 3. Lisberg A, et al. Oncologist. 2025;30:oyaf225; 4. Meric-Bernstam F, et al. Oncologist. 2025;30:oyaf031

ORAL MUCOSITIS/STOMATITIS

STOMATITIS EVENTS ACROSS TROP2-ADCs IN NSCLC[a]

	Grade	EVOKE-01[1] SG (N=296) n (%)	TROPION-Lung01[2] Dato-DXd (N=297) n (%)	OptiTROP-Lung03[3] Sac-TMT (N=91) n (%)
 **Stomatitis**	Any grade	13.2	47.5	65.9
	Grade ≥ 3	1.0	6.7	18.7

- **Stomatitis/oral mucositis** often occurs earlier during the course of ADC therapy but can occur at anytime throughout treatment
- It is usually grade 1-2 and can usually be managed with dose reduction/delay
- **Prevention is key!**

[a]Events are treatment emergent for the EVOKE-01 study and treatment-related for TROPION-Lung01 and OptiTROP-Lung03

ADC, antibody drug conjugate; Dato-Dxd, datopotamab deruxtecan; NSCLC, non-small cell lung cancer; Sac-TMT, sacituzumab tirumotecan; SG, sacituzumab govitecan

1. Paz-Ares L, et al. J Clin Oncol. 2024;42,2860-72; 2. Ahn MJ, et al. J Clin Oncol. 2025;43(3):260-72; 3. Fang WF, et al. ESMO Open. 2026;11(Suppl 3):106960 (presented at ELCC 2026, LBA4)

RECOGNISING MUCOSITIS/STOMATITIS

Signs and symptoms of Mucositis/Stomatitis

Symptoms include:

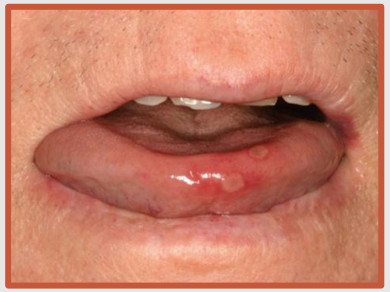
Ulceration	White discoloration in mouth
Mouth and throat pain	Thickening of the saliva
Dry mouth	Bleeding of the oral mucosa
Red, shiny, swollen mouth/ gums	Trouble swallowing, talking, or eating

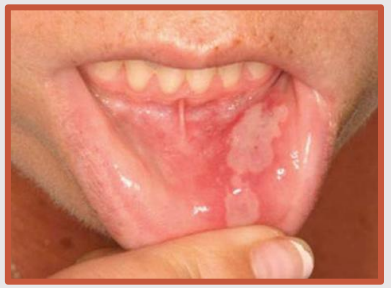
Mucositis/Stomatitis risk factors

- Age (youngest and oldest patients more at risk)
- Pre-existing systemic conditions (e.g. autoimmune disease)
- Poor oral health
- Diet
- History of smoking
- Prior treatment with chemotherapy or ICI agents

Potential questions for patients to monitor for mucositis/ stomatitis

- Does your mouth feel dry or swollen?
- Is it hard to eat due to pain, bleeding, or burning sensations?
- Are there any changes in your eating habits?
- Are you having trouble swallowing or talking?





Bell A, Kasi A. Oral Mucositis. [Updated 2023 May 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK565848/; Gupta A and West HJ. JAMA Oncol. 2016;2:1379; Cleveland Clinic. Mucositis. Available here (accessed March 27, 2026); Meric-Bernstam F, et al. Oncologist. 2025;30:oyaf031

STOMATITIS/MUCOSITIS PROPHYLAXIS

Good oral hygiene

Routine actions to prevent infections and provide oral comfort[1]

Gentle brushing of teeth after meals and at bedtime using a soft toothbrush and a bland fluoride-containing toothpaste

Daily flossing, unless it causes pain or bleeding[1]

Bland rinse[1,2]

- Saline or sodium bicarbonate mouthwash

Hydration and lubrication[1] of oral surfaces

- Oral moisturisers
- Lip lubrication (petrolatum, lip balm, or lip cream)

Prophylaxis

Oral cryotherapy[1]
Ice chips or ice water held in the mouth throughout the infusion

Daily use of a corticosteroid-containing mouthwash,[2,4]
e.g., dexamethasone oral solution

Oral or topical antifungal may be used after the steroid-containing mouthwash[2,4]

Topical analgesic for pain management[2,4]

Nutritional support

Avoidance of:[1]

Smoking

Alcohol

Hot drinks

Acidic, spicy, hot, or raw food

Drink ample amounts of fluids[1,2]
(~2L or ≥64 oz/day)

Monitoring for Stomatitis/Mucositis

- **Regular oral exams** by oncology care team to **detect mucositis** early[1,3]
- **Oral sensitivity, inflammation and tenderness** of the oral mucosa can occur without the appearance of sores[1]

1. Lisberg A, et al. Oncologist. 2025;30:oyaf225; 2. Meric-Bernstam F, et al. Oncologist. 2025;30:oyaf031; 3. Lightfoot MDS, et al. Int J Gynecol Cancer. 2025;35:101997; 4. Villa A, et al. Support Care Cancer 2024; 549: https://doi.org/10.1007/s00520-024-08689-8

PATIENT CASE

Patient Profile

- 65-year-old male, no smoking history
- ECOG PS 0
- Biopsy → lung adenocarcinoma
- PET CT showed liver and bone mets; MRI of brain showed no mets
- Biomarker testing: ***EGFR* exon 19 deletion**

Treatment

- Initiated 1L FLAURA2 osi and chemo (carboplatin + pemetrexed), progressed after 20 months
- Switched treatment to **Dato-DXd** 6 mg/kg Q3W IV
- At C2, patient experienced 4 days of painful (Grade 2) mucositis symptoms
- Able to tolerate soft solids, and weight is stable

Educational case study

1L, first-line; C2, cycle 2; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; mets, metastases; MRI, magnetic resonance imaging; osi, osimertinib; PET CT, positron emission tomography/computed tomography; Q3W, every 3 weeks

POLLING QUESTION

UPON EXAMINATION, THE PATIENT RECEIVING DATO-DXd HAS SOME EVIDENCE OF MUCOSITIS BUT NO SYMPTOMS, CONSISTENT WITH GRADE 1 MUCOSITIS. WHAT IS THE BEST NEXT STEP?

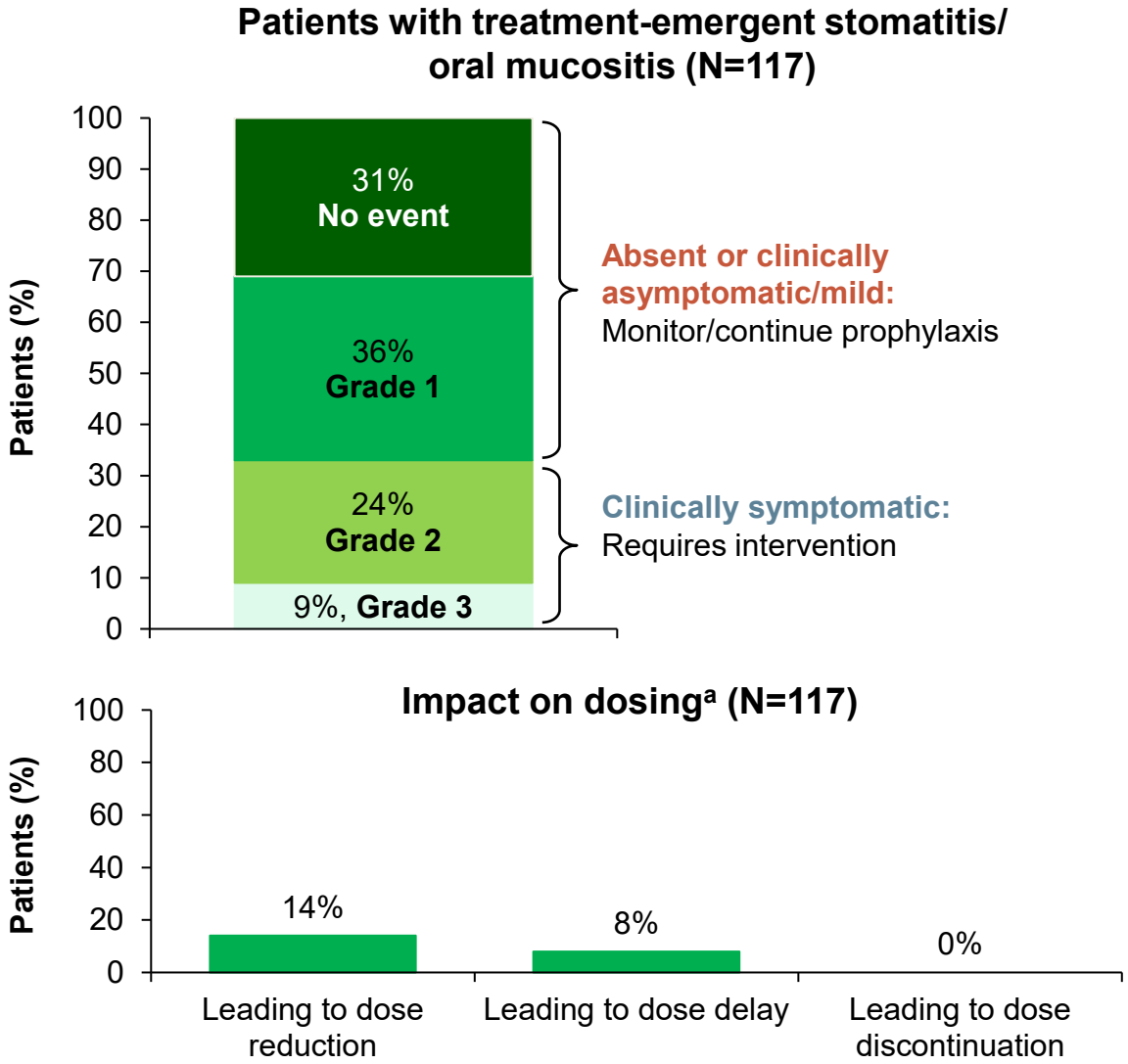
A. Hold treatment and start steroid mouth wash

B. Start antibiotics

C. **Continue treatment, initiate intensive oral care (including steroid mouthwash, oral hygiene, cryotherapy)**

D. Permanently discontinue Dato-DXd

STOMATITIS/ORAL MUCOSITIS WITH DATO-DXd



- Median time to onset:[b] **29 days**
- Median time to asymptomatic resolution:[c] **50 days**

- **Stomatitis/oral mucositis** often occurs earlier during the course of Dato-DXd therapy but can occur at anytime throughout treatment
- Majority of cases are grade 1, asymptomatic and no intervention is required
- Grade 2 and above requires intervention/dose management
- **Prevention is key!**

[a] For Gr 2 events, dose reductions or delays considered if clinically indicated; [b] Of Gr ≥2events;
[c] Of first Gr ≥2 stomatitis event from clinically symptomatic to asymptomatic (Gr 1 or resolved); [d] 32 of 39 events. Gr, grade

1. Ahn M, et al, et al. Ann Oncol. 2024;35(Suppl):S1630–S1631 (presented at ESMO Asia Congress 2024, LBA7); 2. Lisberg A, et al. Oncologist. 2025;30:oyaf225

STOMATITIS/MUCOSITIS MANAGEMENT

SUPPORTIVE CARE DURING DATO-DXd TREATMENT

- Increase the frequency of **bland mouth rinses** up to every hour, if necessary and applicable[1]
- Provide adequate **pain management** (e.g. lidocaine-based mouthwash, topical clobetasol gel)[1]
- As soon as oral pain, inflammation, and/or ulceration develops, strongly consider **steroid-containing mouth rinses** (e.g. dexamethasone 0.1 mg/mL, 10 mL 4 times daily, swish for 1–2 minutes, then spit out, or local alternative)[1,2]
- May consider **oral nystatin suspension or other topical antifungal** ≥15 minutes after the steroid-containing mouthwash, according to clinician preference based on institutional/local guidelines[2]
- Consider **cryotherapy** (ice chips or ice water held in the mouth) throughout the infusion[2]
- For severe and/or persistent events, consider referral to a **dentist, oral surgeon, oral medicine expert or dermatologist**[2]

Dato-Dxd, datopotamab deruxtecan

1. Lisberg A, et al. Oncologist. 2025;30:oyaf225; 2. Meric-Bernstam F, et al. Oncologist. 2025;30:oyaf031

STOMATITIS/MUCOSITIS MANAGEMENT

DOSE MODIFICATIONS WITH DATO-DXd

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic or mild symptoms	Moderate pain or ulcer that does not interfere with oral intake	Severe pain; interfering with oral intake	Life threatening consequences; urgent intervention indicated
Maintain dose	**Optimise** prophylactic and supportive **medications**	If prophylactic and supportive medications have **not yet been optimised**, **delay dose** until resolved to grade ≤1 or baseline, **optimise medications**, and then **maintain dose**	**Discontinue** patient from study treatment
Optimise prophylactic and supportive **medications**	Consider **a dose delay or reduction** if clinically indicated	If prophylactic and supportive medications have **already been optimised**, delay dose until resolved to grade ≤1 or baseline, **then reduce dose by 1 level**	

Dato-DXd, datopotamab deruxtecan

Lisberg A, et al. Oncologist. 2025;30:oyaf225; Meric-Bernstam F, et al. Oncologist. 2025;30:oyaf031; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events v6.0

OCULAR SURFACE EVENTS

OCULAR SURFACE EVENTS ACROSS TROP2-ADCs IN NSCLC[a]

Ocular surface events	Grade	EVOKE-01[1] SG (N=296) n (%)	TROPION-Lung01[2] Dato-DXd (N=297) n (%)	OptiTROP-Lung03[3] Sac-TMT (N=91) n (%)
	Any grade	NR	21.5	NR
	Grade ≥ 3	NR	9.3	NR

- ADCs are associated with various ocular AEs: keratitis, blurred vision, cataract, conjunctivitis, dry eye, photophobia
- Most ADC-associated ocular AEs are reversible with dose delay or dose reduction
- Management of ocular AEs requires a multidisciplinary approach to minimise treatment discontinuation and optimise clinical outcomes

[a]Events are treatment emergent for the EVOKE-01 study and treatment-related for TROPION-Lung01 and OptiTROP-Lung03

ADC, antibody drug conjugate; AE, adverse event; Dato-DXd, datopotamab deruxtecan; NR, not reported; NSCLC, non-small cell lung cancer; Sac-TMT, sacituzumab tirumotecan; SG, sacituzumab govitecan

1. Paz-Ares L, et al. J Clin Oncol. 2024;42,2860-72; 2. Ahn MJ, et al. J Clin Oncol. 2025;43(3):260-72 (supplementary appendix); 3. Fang WF, et al. ESMO Open. 2026;11(Suppl 3):106960 (presented at ELCC 2026, LBA4)

RECOGNISING OCULAR SURFACE EVENTS (OSE)

Signs and symptoms of OSE

Symptoms include:

Increased lacrimation	Red eye
Ocular pain	Visual disturbances (decreased or blurred vision)
Foreign body sensation	Dry eyes
Photophobia	

Baseline and ongoing ophthalmic assessment must be performed by a licensed eye care provider (e.g., ophthalmologist or optometrist)

- **Refer to a licensed eye care provider** (e.g., ophthalmologist or optometrist), if any symptoms warrant ophthalmological assessment: **for any grade ≥2 OSEs (consider referral for grade 1 OSEs)**
- **Notify prescribing oncologist:**
- If there are any contraindications to prescribing ADC (e.g., if the patient presents with clinically significant corneal disease)
- If eye condition is suspected due to any new or worsening signs and symptoms
- **For any grade ≥1 OSEs**

Potential questions for patients to help identify OSE

- Have you noticed your eyes watering more than usual?
- Are you experiencing any pain or discomfort in or around your eyes?
- Have you had any problems with your vision, such as blurriness, seeing double, or difficulty focusing recently?
- Does it feel like there is something in your eye, such as a grain of sand or an eyelash, even though nothing is there?
- Do you find your eyes are unusually sensitive to light, or do bright lights make your eyes feel uncomfortable?
- Have you noticed any redness in your eyes that is not related to tiredness or allergy?
- Are your eyes feeling dry, scratchy, or gritty, especially during the day or when you wake up?
- *(Additional)* Do you have any new eye symptoms, or worsening of existing symptoms, since your last visit?

ADC, antibody-drug conjugate

Dy GK, et al. Oncologist. 2024;29:e1435-e1451; Lindgren ES, et al. Curr Ophthalmol Rep. 2024;12:13-22; Lisberg A, et al. Oncologist. 2025;30:oyaf225

PATIENT CASE

Patient Profile

- 64-year-old female, no smoking history, hypertension, seasonal allergies
- ECOG PS 0
- Biopsy → lung adenocarcinoma
- PET CT showed lung, bone and adrenal metastasis
- Biomarker testing; ***EGFR* exon 19 deletion**

Treatment

- Initiated 1L **carboplatin + pemetrexed,** progressed after 8 months
- Switched treatment to **Dato-DXd 6 mg/kg Q3W IV** on clinical trial
- At C4, patient experienced **gritty sensation both eyes, mild burning and tearing, no loss of vision or eye pain**

Educational case study

1L, first-line; C4, cycle 4; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; PET CT, positron emission tomography/computed tomography; Q3W, every 3 weeks

POLLING QUESTION

PATIENT RECEIVING DATO-DXd REPORTS GRITTY SENSATION, MILD BURNING, TEARING IN BOTH EYES WITHOUT VISION LOSS OR EYE PAIN. WHAT IS THE MOST APPROPRIATE INITIAL MANAGEMENT?

A. Continue treatment without intervention and re-assess at the next cycle

B. **Optimise supportive care with preservative-free lubricating eye drops and refer to eye care provider**

C. Start topical antibiotic eye drops and hold treatment

D. Permanently discontinue Dato-DXd

OCULAR SURFACE EVENTS - PROPHYLAXIS AND MONITORING

PROPHYLAXIS

- It should be strongly recommended that subjects/participants avoid the use of contact lenses starting on the day of the first **Dato-DXd** dose and to use artificial tears (preferably preservative-free) 4 times/day as a preventative measure and up to 8 times/day if clinically needed[1]

MONITOR

- Refer patients to an eye care professional (optometrist or ophthalmologist) for an **ophthalmic exam** prior to treatment initiation, annually while on treatment, at end of treatment, and as clinically indicated[1,2]
  - Including visual acuity testing, intraocular pressure, fundoscopy, slit lamp exam with fluorescein staining[2]
- **Monitor patients for ocular adverse reactions** during treatment (i.e. redness, pain, teary eyes, blurred vision). If present, promptly **refer patients to an eye care professional**[2]
- **Eye care professional to provide an objective assessment for the prescribing oncologist:**[3]
  - so that they may decide if the next dose of the ADC can be given as scheduled, delayed, reduced, or discontinued

ADC, antibody drug conjugate; Dato-DXd, datopotamab deruxtecan; OSE, ocular surface events

1. Heist RS, et al. Cancer Treat Rev. 2024;125:102720; 2. Lisberg A, et al. Oncologist. 2025;30:oyaf225; 3. Berkenstock MK, et al. https://www.aao.org/education/clinical-statement/antibody-drug-conjugates-ocular-toxicities-call-st (Accessed 17-April-2026)

OCULAR SURFACE ADVERSE EVENTS/KERATITIS MANAGEMENT

WITH DATO-DXd TREATMENT

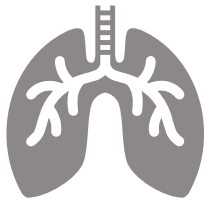
Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or ≤3 lines decreased vision from known baseline)	Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or >3 lines of decreased vision from known baseline, up to 20/200); corneal ulcer; limiting self-care activities of daily living	Perforation; best corrected visual acuity of 20/200 or worse in the affected eye
Consider obtaining an **ophthalmological assessment** Ensure use of **artificial tears** daily (or increase frequency to 8 times daily)	Obtain an **ophthalmological assessment** Delay dose until resolved to grade ≤1, then **maintain dose**	Obtain an **ophthalmological assessment** Delay dose until resolved to grade ≤1, then **reduce dose by 1 level**	Obtain an urgent **ophthalmological assessment** **Discontinue** Dato-DXd treatment

Dato-DXd, datopotamab deruxtecan

Lisberg A, et al. Oncologist. 2025;30:oyaf225; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events v6.0

INTERSTITIAL LUNG DISEASE

ILD/PNEUMONITIS EVENTS ACROSS TROP2-ADCs IN NSCLC[a]



Adjudicated drug-related ILD/ pneumonitis

Grade	EVOKE-01[1] SG (N=296) n (%)	TROPION-Lung01[2,b] Dato-DXd (N=297) n (%)	OptiTROP-Lung03[3] Sac-TMT (N=91) n (%)
Any grade	NR	8.8	2.2
Grade ≥ 3	NR	3.7	NR

- Diagnosing ILD early and initiating prompt treatment is critical to assure patient safety
- Multidisciplinary management of ILD is important!
- Pulmonologists are key members of the MDT once ILD is suspected
- Nurses and APPs play a critical role in counseling patients on early identification, closely monitoring patient symptoms

[a]Events are treatment emergent for the EVOKE-01 study and treatment-related for TROPION-Lung01 and OptiTROP-Lung03; [b]Among the 26 patients (8.8%) in the Dato-DXd group who had adjudicated drug-related ILD or pneumonitis, two (0.7%) had grade 1 events, 13 (4.4%) had grade 2 events, three (1.0%) had grade 3 events, one (0.3%) had a grade 4 event, and seven (2.4%) had grade 5 events

ADC, antibody drug conjugate; APP, advanced practice provider; Dato-DXd, datopotamab deruxtecan; ILD, interstitial lung disease; MDT, multidisciplinary team; NR, not reported; NSCLC, non-small cell lung cancer; Sac-TMT, sacituzumab tirumotecan; SG, sacituzumab govitecan

1. Paz-Ares L, et al. J Clin Oncol. 2024;42,2860-72; 2. Ahn MJ, et al. J Clin Oncol. 2025;43(3):260-72; 3. Fang WF, et al. ESMO Open. 2026;11(Suppl 3):106960 (presented at ELCC 2026, Abstract LBA4)

RECOGNISING INTERSTITIAL LUNG DISEASE (ILD)

Signs and symptoms of ILD

Symptoms include:

- Cough (often dry)
- Fever
- Asthenia (weakness)
- Fatigue
- Chest pain or tightness
- Dyspnea (shortness of breath)

ILD risk factors

- Patient has a history of **non-infectious ILD/pneumonitis**, including radiation pneumonitis, that required steroids, has current ILD/pneumonitis, or has suspected ILD/pneumonitis that cannot be ruled out by imaging at screening
- Patient has **severe pulmonary function compromise**
- Previous thoracic radiotherapy or chemotherapy

Potential questions for patients to assess for ILD

- Have you been coughing recently?
- Is it a dry cough?
- Have you had any shortness of breath, especially during or after physical activity?
- Have you experienced any new breathing or respiratory problems?
- If you already have respiratory problems, have they gotten worse?
- Have you had a fever?
- Have you been feeling tired?
- Have you lost weight?

Lisberg A, et al. Oncologist. 2025;30:oyaf225; Shi J, et al. Ther Adv Respir Dis. 2024:18:1-15; Swain SM, et al. Cancer Treat Rev. 2022;106:102378; Johkoh T, et al. Clin. Lung Cancer. 2014;15(6):448-54; Sato Y, et al. Chest. 2022;162(5):1188-98; Shibaki R, et al. Cancer Med. 2022;11(20):3743-50; Chen X, et al. Support. Care Cancer. 2022;30(8):6515-24

CLINICAL EVALUATIONS: INTERSTITIAL LUNG DISEASE (ILD)

Evaluations

Evaluations include:

High-resolution CT	Pulmonologist consultation
Bronchoscopy and BAL if indicated and feasible	Infectious disease consultation if indicated
Clinical Laboratory tests	Pulmonary function tests (FVC and CO and SpO2)

Differential diagnosis

- Infection
- Progression of underlying disease
- Pulmonary Effusion
- Pericardial Effusion
- COPD flare
- Other pulmonary disorder of unknown origin

- ***65-year-old man with metastatic adenocarcinoma initially treated with carboplatin, pemetrexed, and pembrolizumab started 2nd line treatment on Dato-DXd (on clinical trial). Baseline scan:***

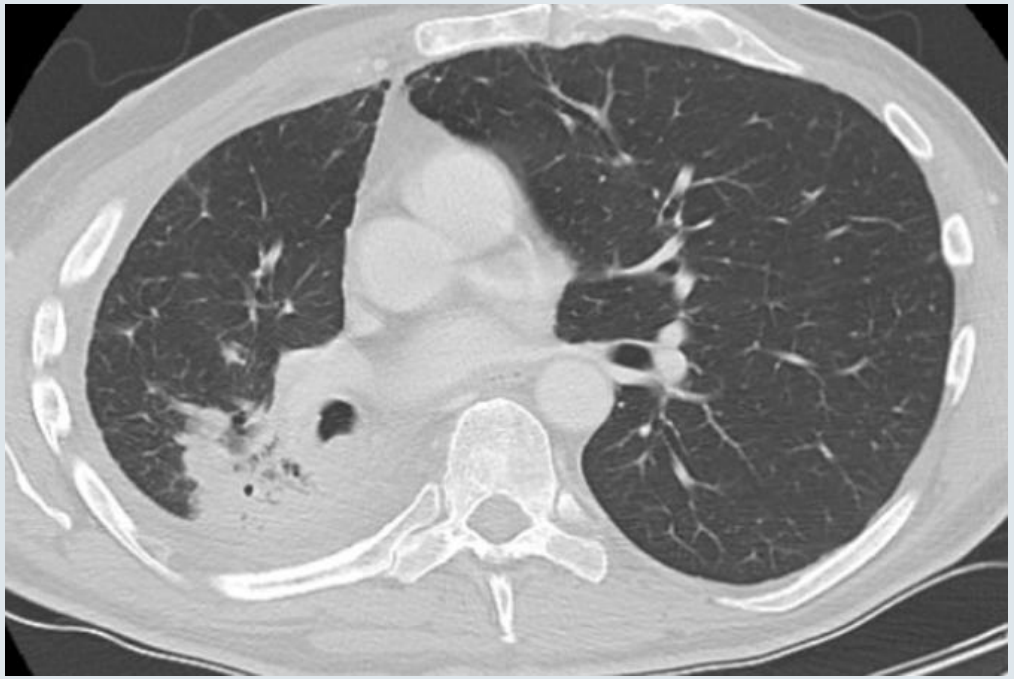


Image provided by Jacob Sands, MD

BAL, bronchoalveolar lavage; CO, carbon monoxide; COPD, chronic obstructive pulmonary disease; CT, computed tomography; Dato-DXd, datopotamab deruxtecan; FVC, forced vital capacity; Sp02, peripheral capillary oxygen saturation

CLINICAL EVALUATIONS: INTERSTITIAL LUNG DISEASE (ILD)

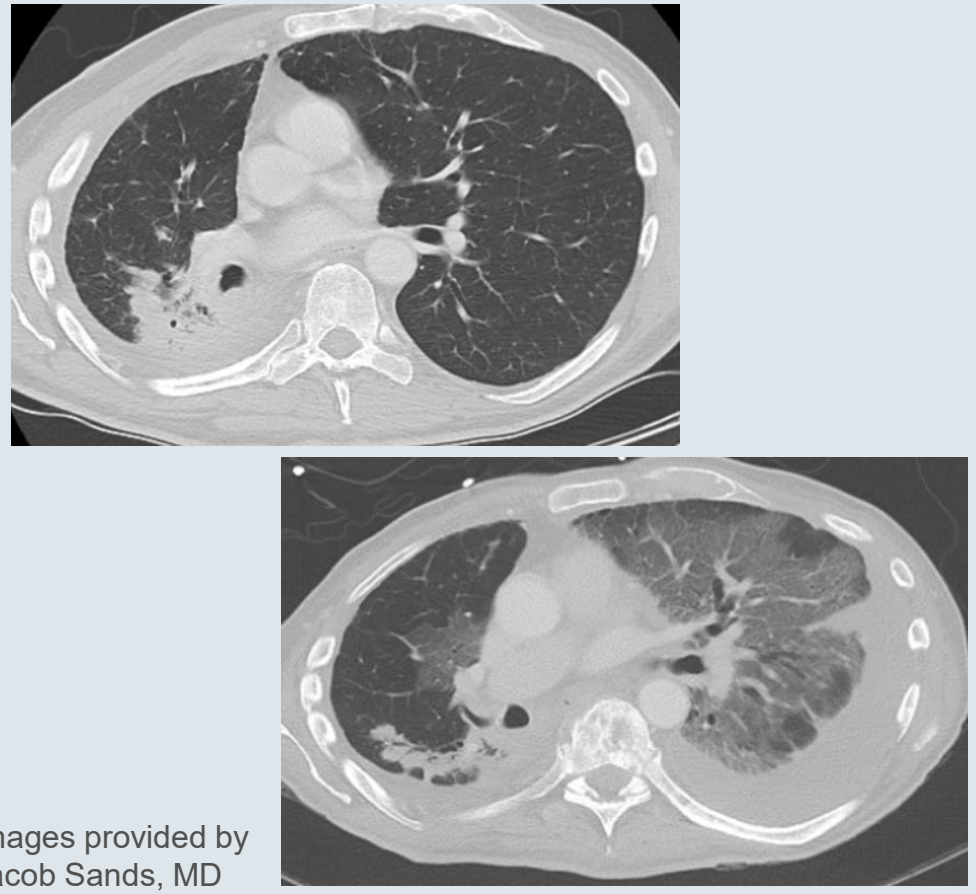
Evaluations

High-resolution CT	Pulmonologist consultation
Bronchoscopy and BAL if indicated and feasible	Infectious disease consultation if indicated
Clinical Laboratory tests	Pulmonary Function Tests (FVC and CO and SpO2

Management ILD

1. **Screen** – monitor for patients that have a h/o ILD
2. **Scan** – baseline and every 6-12 weeks
3. **Synergy** – collaborate with medical team and patients to monitor closely for symptoms of ILD and use multidisciplinary approach once ILD is suspected
4. **Suspend treatment** – once ILD is suspected hold treatment
5. **Steroids** – adapt dose and taper based on grade

- ***After 2+ months on treatment:***

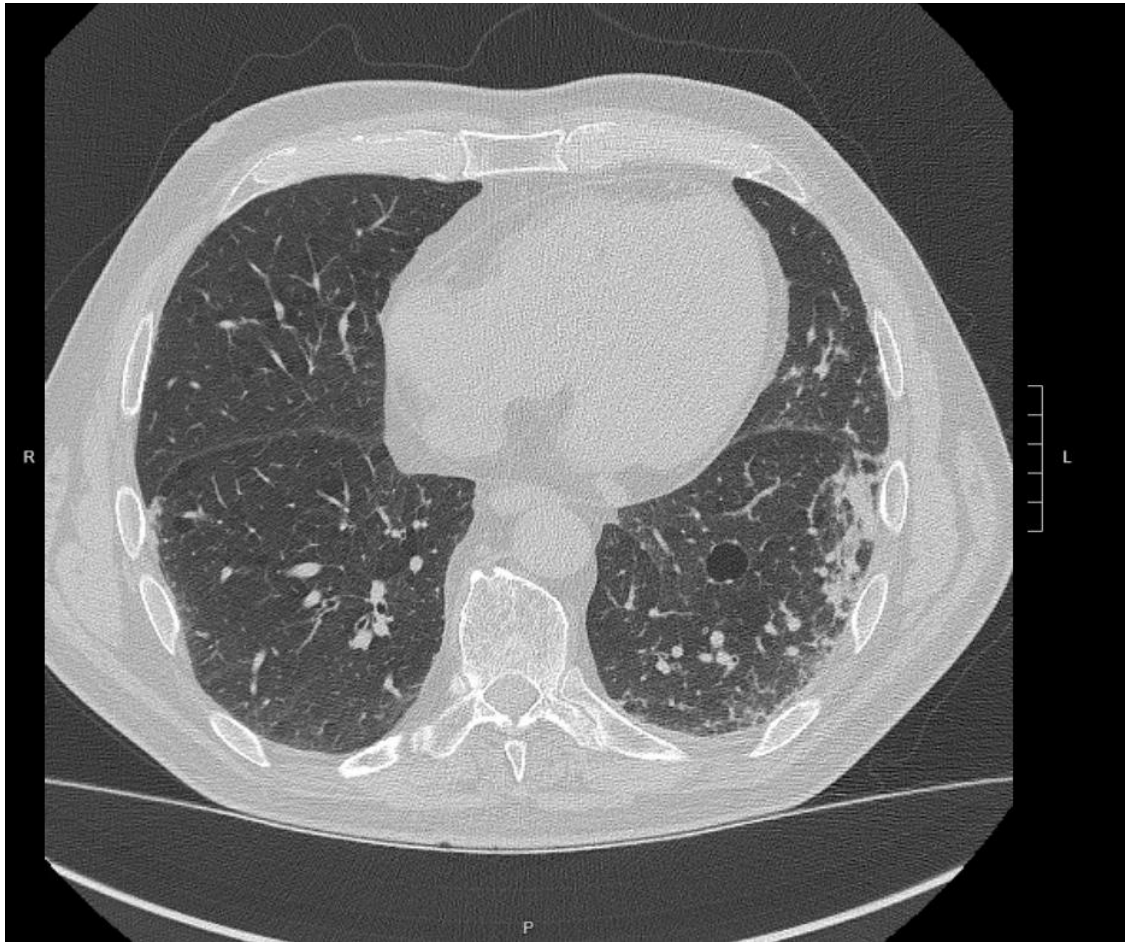


Images provided by Jacob Sands, MD

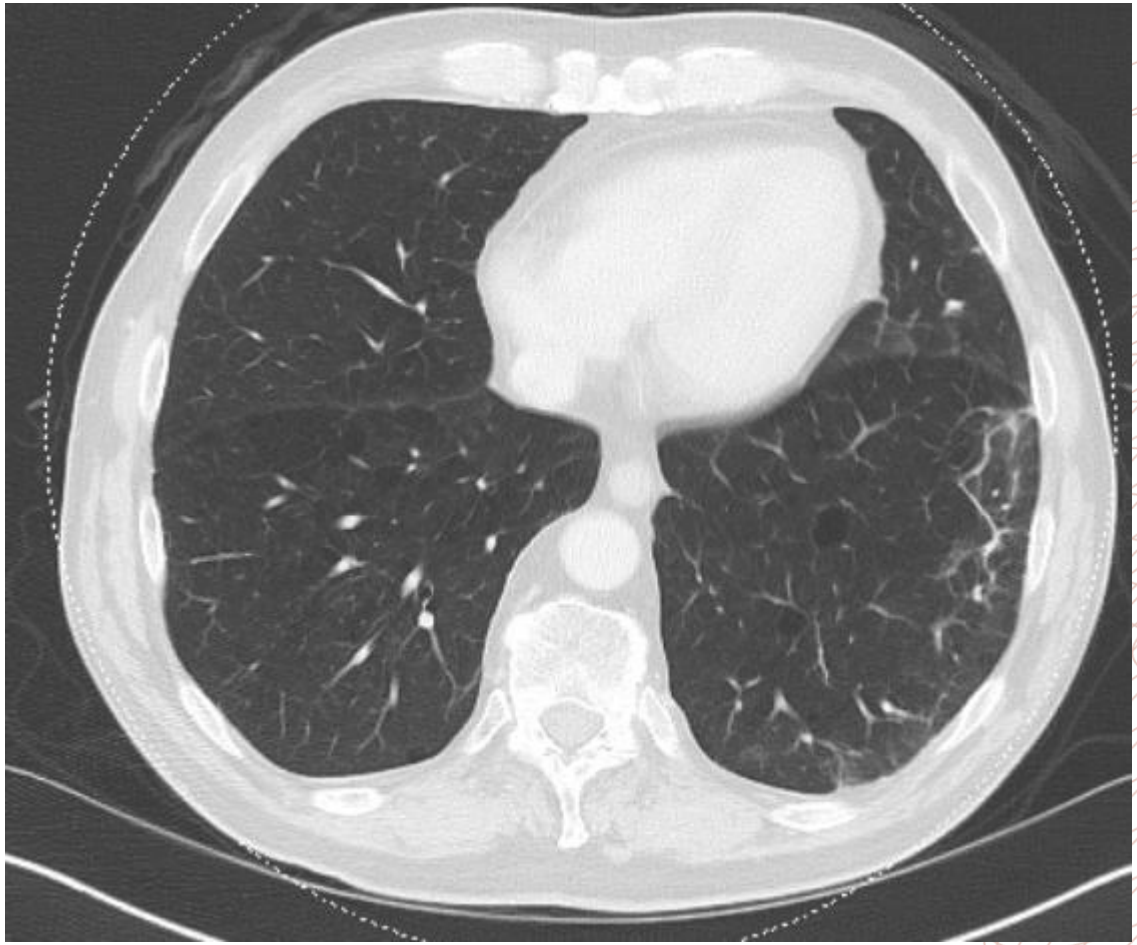
BAL, bronchoalveolar lavage; CO, carbon monoxide; CT, computed tomography; FVC, forced vital capacity; h/o, history of; Sp02, peripheral capillary oxygen saturation

Swain SM, et al. Cancer Treat Rev. 2022;106:102378; Tarantino P and Tolaney SM. JCO Oncol Pract. 19:526-527

BUT ILD CAN BE A MORE COMPLICATED SCENARIO...



March 2025 – Grade II pneumonitis



May 2025

Images provided by Jacob Sands, MD

ILD, interstitial lung disease

INTERSTITIAL LUNG DISEASE WITH ADC THERAPY

ILD

- **ADC-related ILD is not fully understood:**
- Bystander effect: a high affinity of the target antibody (HER2, TROP2, and HER3) for tumour cells *might* lead to increased exposure of normal lung tissue to the payload
  - ADC *may* activate immune mediators leading to inflammatory processes and finally development of ILD
- Rare but serious condition: it is essential that patient understand signs and symptoms
- Requires expedited work up to rule out other causes, steroids mainstay of therapy ILD
- **Permanently discontinue for grade 2 or higher**

ADC, antibody-drug conjugate; ILD, interstitial lung disease

Ahn M, et al, et al. Ann Oncol. 2024;35(Suppl):S1630–S1631 (presented at ESMO Asia Congress 2024, LBA7); Lisberg A, et al. Oncologist. 2025;30:oyaf225; Liu R, et al. Front Oncol. 15:1638054; Rosner SI, et al. Am Soc Clin Oncol Educ Book. 2023;43:e389968; Shi J, et al. Ther Adv Respir Dis. 2024:18:1-15; Swain SM, et al. Cancer Treat Rev. 2022;106:102378

INTERSTITIAL LUNG DISEASE MANAGEMENT

DOSE MODIFICATIONS WITH DATO-DXD

Grade 1 Asymptomatic; clinical or diagnostic observations only	Grade 2 Symptomatic; medical intervention indicated; limiting instrumental activities of daily living	Grade 3-4 **G3:** Severe symptoms; limiting self-care activities of daily living; oxygen indicated; **G4:** Life-threatening respiratory compromise; urgent intervention indicated (eg, tracheotomy or intubation)
Consider a consultation with a **pulmonologist** • Monitor and closely **follow-up in 2-7 days** for onset of clinical symptoms and SpO2 • Consider follow-up **imaging in 1-2 weeks** (or as clinically indicated) • Consider starting **systemic corticosteroids** (e.g. at least 0.5 mg/kg/day prednisone or equivalent) until improvement, followed by gradual taper over at least 4 weeks • **Pause Dato-DXd** until resolved to grade 0, then: • **If resolved in ≤28 days** from day of onset, maintain dose • **If resolved in >28 days** from day of onset, reduce dose by one level	Permanently **discontinue treatment** • Consider a consultation with a **pulmonologist** • Promptly start **systemic corticosteroids** (e.g. ≥ 1.0 mg/kg/day prednisone or equivalent) for at least 14 days or until complete resolution of clinical symptoms and chest CT findings, followed by gradual taper over ≥4 weeks • **Monitor symptoms** closely and re-image as clinically indicated. • If clinical or diagnostic observations worsen or do not improve in 5 days: – Consider **increasing corticosteroid dose** (e.g. 2 mg/kg/day prednisone or equivalent) and switching to IV administration (e.g. methylprednisolone) – Reconsider **additional workup** for alternative etiologies – **Escalate care** as clinically indicated	Permanently **discontinue treatment** • Consider a consultation with a **pulmonologist** • **Hospitalisation** required • Promptly initiate **intensive corticosteroid treatment** empiric high-dose methylprednisolone IV treatment (e.g. 500-1000 mg/day for 3 days), followed by prednisone ≥1.0 mg/kg/day (or equivalent) for ≥14 days or until complete resolution of clinical symptoms and chest CT findings, followed by gradual taper over ≥4 weeks • **Re-image** as clinically indicated • If still no improvement within 3-5 days: – Reconsider **additional workup** for alternative etiologies – Consider other **immunosuppressants** and/or treat per local practice

CT, computed tomography; Dato-DXd, datopotamab deruxtecan; IV, intravenous; SpO2, capillary peripheral oxygen saturation

Lisberg A, et al. Oncologist. 2025;30:oyaf225

OTHER ADVERSE EVENTS

- HEMATOLOGICAL EVENTS
- GI EVENTS

GI, gastrointestinal

GI AND HEMATOLOGICAL EVENTS ACROSS TROP2-ADCs IN NSCLC[a]

		EVOKE-01[1] SG (N=296) n (%)		TROPION-Lung01[2] Dato-DXd (N=297) n (%)		OptiTROP-Lung03[3,4b] Sac-TMT (N=91) n (%)	
		Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Hematological events	Anemia	40.2	6.4	14.8	4.0	81.3	13.2
	WBC decreased	NR	NR	NR	NR	74.7	27.5
	Neutropenia	37.5	24.7	4.7	0.7	68.1	44.0
	Leukopenia	12.8	5.1	3.0	0	NR	NR
	Thrombocytopenia	NR	NR	NR	NR	36.3	5.5
GI events	Diarrhea	52.7	10.5	10.1	0.3	2	0
	Nausea	41.6	1.7	34.0	2.4	19	0
	Vomiting	20.9	2.4	NR	NR	NR	NR
	Constipation	29.1	0	NR	NR	NR	NR

[a]Events are treatment emergent for the EVOKE-01 study and treatment-related for TROPION-Lung01 and OptiTROP-Lung03; [b]GI events not reported in Fang et al (2026), taken from an earlier publication (Fang et al (2025)

ADC, antibody drug conjugate; Dato-DXd, datopotamab deruxtecan; GI, gastrointestinal; NR, not reported; NSCLC, non-small cell lung cancer; Sac-TMT, sacituzumab tirumotecan; SG, sacituzumab govitecan; WBC, white blood cell

1. Paz-Ares L, et al. J Clin Oncol. 2024;42,2860-72; 2. Ahn MJ, et al. J Clin Oncol. 2025;43(3):260-72; 3. Fang WF, et al. ESMO Open. 2026;11(Suppl 3):106960 (presented at ELCC 2026, LBA4); 4. Fang W, et al. BMJ 2025;389:e085680

PATIENT CASE

Patient Profile

- 64-year-old male with **metastatic NSCLC (adenocarcinoma)**
- Molecular testing: **EGFR/ALK/ROS1 negative, KRAS G12C negative**
- **PD-L1 <1%**
- Metastases: lung, liver, bone

Prior Therapy

- Platinum-based chemotherapy + pembrolizumab → progression
- Docetaxel → progression

Current Treatment

- **Sacituzumab govitecan 10 mg/kg Days 1 & 8,** every 21 days on clinical trial

Baseline Status

- ANC 2.1 K/μL | Hgb 11.2 g/dL | Platelets 210 K/μL
- Normal bowel habits

Early Treatment Course

- **After Cycle 1 Day 1**:
  - Onset of **loose stools (5–6/day)**
  - Mild abdominal cramping, fatigue
- **Cycle 1 Day 8 labs:**
  - **ANC 1.1 K/μL**
  - Treatment administered

Educational case study

ANC, absolute neutrophil count; NSCLC, non-small cell lung cancer

PATIENT CASE: NSCLC ON SACITUZUMAB GOVITECAN

TOXICITY ESCALATION – SETS UP DX & MANAGEMENT

Post–Cycle 1 Day 8 (Day +5)

- ≥8 watery stools/day, nocturnal symptoms
- Poor oral intake, dizziness, weakness
- Afebrile

Clinic Evaluation

- Mild hypotension, tachycardia
- **ANC 0.7 K/µL (Grade 3 neutropenia)**
- Hemoglobin 9.6 g/dL
- **Electrolyte abnormalities (hypokalemia)**
- Stool studies pending

Clinical Challenge

- Overlapping **GI and hematologic toxicity**
- Need to distinguish:
  - Drug-related diarrhea vs infectious vs immune-mediated
- Decision points:
  - **Hold therapy**
  - Supportive care
  - Growth factor consideration
  - Future **dose modification**

Educational case study

ANC, absolute neutrophil count; Dx, diagnosis; GI, gastrointestinal

POLLING QUESTION

WHICH SUPPORTIVE CARE STRATEGY HELPS REDUCE RISK OF NEUTROPENIA WITH SACITUZUMAB GOVITECAN?

A. Give antibiotics to all patients

B. **Use G-CSF in high-risk patients**

C. Give steroids before all treatments

D. Hydration only

RECOGNISING HEMATOLOGIC TOXICITIES

Symptoms include:

Often asymptomatic	Fatigue
Fever ≥ 38.3°C (101°F)	Dyspnea
Chills, rigors	Pallor
Oral ulcers	Tachycardia
Easy bruising	Gum bleeding

Risk factors

- Baseline cytopenias
- Older age
- ECOG PS >2
- Nutritional deficiencies (iron, b12, folate)
- Renal or hepatic dysfunction
- Extensive bone marrow involvement
- Heavily pre-treated patients
- Short interval from prior cytotoxic chemotherapy
- Prior platinum, topoisomerase inhibitors or ADC exposure

Potential questions for patients to monitor

- Any fevers, chills since last visit?
- Recent ED visits, antibiotics or hospitalisations?
- Mouth sores or sore throat?
- New cough, dysuria, or skin changes?
- Any change in energy, shortness of breath or dizziness?
- Any limitations to your daily activities outside your baseline?
- Any new palpitations or chest pain?
- Any easy bruising or bleeding?
- Any nosebleeds or gum bleeding?
- Any blood in urine or stool?

ADC, antibody-drug conjugate; ECOG PS, Eastern Cooperative Oncology Group performance status; ED, emergency department

Fang W, et al. N Engl J Med. 2026;394(1):13-26; Wang S, et al. Expert Opinion on Drug Safety 2025; 25(4), 767-75; Merck Manual Professional Edition (Accessed 07 April 2026); Common Terminology Criteria for Adverse Events (CTCAE) v6.0 (MedDRA 28.0) ; Zhao X, et al. Front. Immunol. 2025; 16:1634688

HEMATOLOGIC ADVERSE EVENTS – SACITUZUMAB GOVITECAN (NSCLC)

Common Hematological AEs

- **Neutropenia** (most frequent; can be severe)
- Anemia
- Less commonly thrombocytopenia

Diagnosis & Grading

- CBC with differential **prior to each dose**
- **CTCAE grading:**
- ANC <1.0 K/µL → **Grade ≥3 neutropenia**
- Evaluate for:
- Fever or infection
- Cumulative myelosuppression from prior therapies

Management

- **Hold sacituzumab govitecan** for Grade ≥3 neutropenia
- Initiate **G-CSF** for:
  - Prolonged or recurrent Grade ≥3 neutropenia
  - Prior neutropenic complications
- Resume treatment **after recovery**:
  - ANC ≥1.5 K/µL

Dose Modification

- **Dose reduction** recommended for recurrent Grade 3–4 neutropenia
- Strong consideration for **secondary G-CSF prophylaxis**

Clinical Pearl

- **Proactive ANC monitoring and early growth-factor support help maintain treatment continuity in heavily pretreated NSCLC patients**
- Multidisciplinary coordination improves safety (registered nurse, nurse practitioner/physician assistant, physician, pharmacy)

AE, adverse event; ANC, absolute neutrophil count; CBC, complete blood count; CTCAE, Common Terminology Criteria for Adverse Events; G-CSF, granulocyte colony-stimulating factor; NSCLC, non-small cell lung cancer

Fleming PJ Jr, et al. J Adv Pract Oncol. 2021;12:747-52; Gilead Sciences. TRODELVY® (sacituzumab govitecan-hziy) prescribing information. Revised March 2025; National Cancer Institute CTCAE v5.0. 2017; Zhang Y, et al. Front Oncol. 15:1624386; Bardia A, et al. N Engl J Med 2021; 384:1529-41; National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0

RECOGNISING GASTROINTESTINAL ADVERSE EVENTS

Signs and symptoms of nausea and vomiting

Symptoms include:

Abdominal pain	Bloated or swollen belly
Headache	Fatigue
Lack of appetite	Weight loss
Dizziness or weakness	Not making as much urine as usual

Nausea and vomiting risk factors

- Younger age
- Female sex
- Anxiety
- Travel sickness or nausea during pregnancy
- Previous treatments
- Insufficient sleep before chemotherapy
- Duration of chemotherapy-induced nausea and vomiting

Potential questions for patients to monitor for nausea and vomiting

- Have you begun losing weight, eating or drinking less, or feeling dehydrated?
- How frequently do you vomit or feel the need to vomit?
- Do you feel discomfort in the chest, upper abdomen, or throat?

1. American Cancer Society. Understanding Nausea and Vomiting. Available here (accessed March 27, 2026);
2. Jordan K, et al. Eur. J. Cancer. 2025;222:115451

GASTROINTESTINAL TOXICITY – DIARRHEA MANAGEMENT (SN-38 PAYLOAD)

Mechanism

- SN-38–mediated intestinal mucosal injury
- Typically **early onset** after dosing

Diagnosis

Grade diarrhea using **CTCAE**:

- ≥7 stools/day or nocturnal symptoms → **Grade 3**

Rule out:

- Infectious causes (C. diff, GI panel)
- Immune-mediated colitis (less likely without ICI)

Management

- **Hold sacituzumab govitecan** for Grade ≥3 diarrhea
- **Aggressive antidiarrheal therapy:**
  - Loperamide at first loose stool ± escalation
- IV fluids and **electrolyte repletion**
- Monitor hydration status and renal function

Rechallenge & Prevention

- Resume therapy only when diarrhea ≤ Grade 1
- **Dose reduction** for recurrent severe diarrhea

Patient education:

- Early reporting
- Hydration and diet counselling

Clinical Pearl

Early intervention prevents dehydration, hospitalisation, and unnecessary treatment discontinuation

CTCAE, Common Terminology Criteria for Adverse Events; GI, gastrointestinal; ICI, immune checkpoint inhibitor; IV, intravenous

Benson AB 3rd, et al. J Clin Oncol. 2004;24:2918-2926; National Cancer Institute CTCAE v5.0. 2017; TRODELVY® (sacituzumab govitecan-hziy) prescribing information. Revised March 2025; Ocean AJ, et al. Cancer. 2017;123:3843-3853; Sahi N, et al. Loperamide. [Updated 2024 Feb 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557885/; Sun R, et al. Toxicol Appl Pharmacol. 2020;389:115032; https://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf (Accessed 07 Apr 2026)

MANAGING GASTROINTESTINAL ADVERSE EVENTS

To help control nausea

- Eat **small meals** throughout the day
- **Avoid foods** that can cause nausea (e.g. foods with strong smells)
- **Sit upright** or lie with **head raised** for 1 hour after a meal
- Eat food at **room temperature**
- **Drink** plenty of **water** and other fluids in **slow sips** throughout the day
- Seek a **dietitian** or **specialist nutritionist**
- **Alternative treatments** including relaxation techniques, acupuncture, hypnosis, or music therapy

To help manage vomiting

- **Lie on side** to prevent inhalation of vomit
- Try **frozen liquids** such as ice chips
- Once **vomiting stops**, start taking in small amounts of clear liquids slowly and increase as tolerated
- **Call HCP** if:
  - Vomiting persists for 2-3 days
  - Cannot take medication
  - Cannot take in more than 4 cups of liquid or ice chips in a day
  - Hasn't eaten for more than 2 days

Keeping a diary of when and why nausea occurs may also be helpful

HCP, healthcare professional

1. National Cancer Institute. Nausea and Vomiting and Cancer Treatment. Updated March 10, 2025. Available here (accessed March 27, 2026); 2. American Cancer Society. Managing Nausea and Vomiting at Home. Available here (accessed March 27,2026); 3. National Cancer Institute. Nutrition in Cancer Care (PDQ®)–HCP Version. Updated October 15, 2024. Available here (accessed March 27, 2026)

MULTIDISCIPLINARY MANAGEMENT IS ESSENTIAL!

MULTIDISCIPLINARY COLLABORATION FOR MANAGING ADC-RELATED ADVERSE EVENTS

Healthcare team and patient education[1]

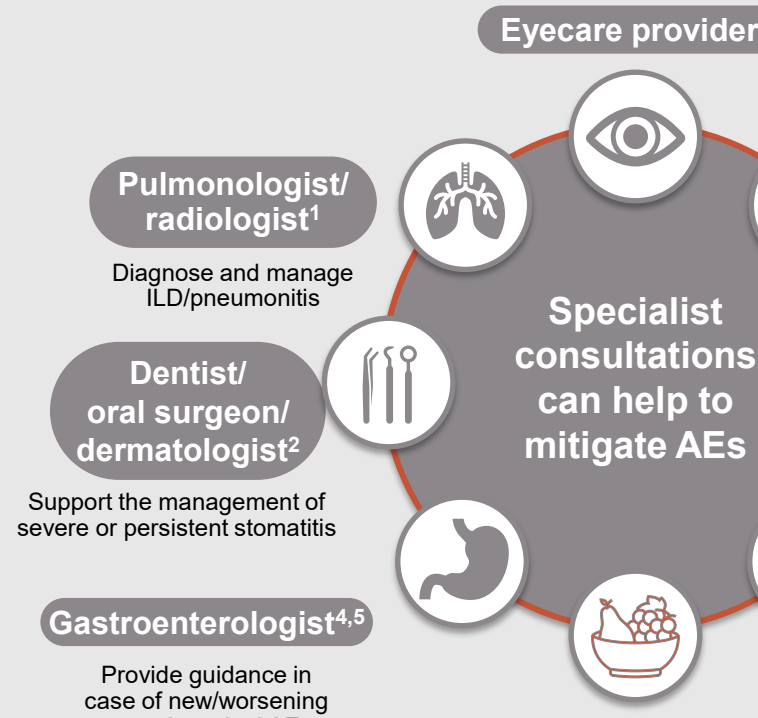
Adherence to any recommended prophylaxis guidance[2]

Vigilance and early intervention[1]

Healthcare team coordination[1,3]

Close communication between oncologist and the wider healthcare team is critical to optimise patient experience with ADCs

Oncologist **Nurse** **Pharmacist**



Eyecare provider[1]
Perform ophthalmologic assessments when indicated; provide guidance on prophylaxis; support ocular AE diagnosis, care, and resolution

Pulmonologist/ radiologist[1]
Diagnose and manage ILD/pneumonitis

Cardiologist[10]
Support early diagnosis and management of cardiac AEs

Dentist/ oral surgeon/ dermatologist[2]
Support the management of severe or persistent stomatitis

Hematologist[9]
Provide guidance on hematological AEs

Gastroenterologist[4,5]
Provide guidance in case of new/worsening gastrointestinal AEs

Neurologist[8]
Diagnose and treat peripheral neuropathy and provide guidance on other ocular AEs (e.g. optic neuritis) when indicated

Dietitian/nutritionist[6,7]
Perform baseline nutritional assessments where indicated; provide recommendations to maintain patient nutritional status during treatment as indicated

ADC, antibody drug conjugate; AE, adverse event; ILD, interstitial lung disease

1. Lisberg A, et al. Oncologist. 2025;30:oyaf225; 2. Meric-Bernstam F, et al. Oncologist. 2025;30:oyaf031; 3. Zhang J, et al. Asia Pac J Oncol Nurs. 2024;11:100595; 4. Kovac MB and Seruga B. Radiol Oncol. 2024;58:170-178; 5. Professional Committee on Clinical Research of Oncology Drugs, Chinese Anti-Cancer Association, et al. Cancer Innov. 2022;1:3-24; 6. National Cancer Institute. Nutrition in Cancer Care (PDQ®). Available here (accessed April 10, 2026); 7. Mahmood I. Antibodies (Basel). 2021;10:40; 8. Velasco R, et al. Cancer (Basel). 2021;13:6125; 9. Rao M, et al. PLoS 2025; 20(10): e0334513; 10. Long P, et al. Front Pharmacol. 2024;15:1378010

STEPS TO OPTIMISING TREATMENT WITH ADCs

Understanding ADCs

It's important that the healthcare team, including oncology nurses, understand how ADCs work and can describe this simply to patients[1-6]

Data awareness

ADC efficacy and safety profiles differ[1,7]; awareness of the most common AEs for the relevant ADCs and how to mitigate them can help optimise the patient experience[1,6]

Access to prophylactic medications

Many potential AEs, such as nausea / vomiting, dry eye, or stomatitis, may require prophylactic medications.[1,6,8] Prevention and management of AEs is critical for optimising prognosis[1]

Referral/consultation pathways

Managing ADC-related AEs sometimes requires support from other specialties.[1,8] Timely specialist referral and multidisciplinary management are recommended[1]

Patient materials

Educational resources can help patients recognise AEs related to ADC treatment and provide practical guidance on managing them[2,9]

ADC, antibody-drug conjugate; AE, adverse event

1. Professional Committee on Clinical Research of Oncology Drugs, Chinese Anti-Cancer Association, et al. Cancer Innov. 2022;1:3-24; 2. Wolters Kluwer. Five strategies for providing effective patient education. Available here (accessed April 10, 2026); 3. Trail PA, et al. Pharmacol Ther. 2018;181:126-142; 4. Passaro A, et al. J Clin Oncol. 2023;41:3747-3761; 5. Clark C and Komo I. Clin J Oncol Nurs. 2024;28:188-196; 6. D'Arienzo A, et al. eClinicalMedicine. 2023;62:102113; 7. Woodford R, et al. ESMO Open. 2025;10:105573; 8. Lisberg A, et al. Oncologist. 2025;30:oyaf225; 9. Managing Side Effects of Antibody–Drug Conjugate (ADC) Therapy: A Guide for Patients With Metastatic Breast Cancer (accessed April 20, 2026)

BEST PRACTICE MANAGEMENT PANEL DISCUSSION AND AUDIENCE QUESTIONS

Prof. Nicolas Girard
Institute Curie, France

Dr Louise Lim
Barts Health NHS Trust, UK

Dr Jacob Sands
Dana-Farber
Cancer Institute, US

Mrs Stephanie McDonald
Dana-Farber
Cancer Institute, US

KEY CLINICAL TAKEAWAYS AND CLOSE

Dr Louise Lim
Barts Health NHS Trust, UK

ADC, antibody-drug conjugate; NSCLC, non-small cell lung cancer

KEY CLINICAL TAKEAWAYS

- **TROP2-ADCs are emerging as a promising therapeutic option** across multiple treatment settings in NSCLC
- **Datopotamab deruxtecan** has received **FDA approval**, while **sacituzumab tirumotecan** is **approved in China**, reflecting growing global adoption of this class
- **TROP2-ADCs demonstrate generally consistent and manageable safety profiles**, with commonly observed adverse events including stomatitis, nausea, fatigue, and hematologic toxicities
- These agents are associated with **specific toxicities that require a multidisciplinary approach**, early recognition, and timely intervention
- **Proactive prophylaxis and structured toxicity management are essential** to support treatment continuity and optimise patient outcomes
- **Ongoing phase 3 trials will further clarify the efficacy, safety, and positioning** of TROP2-ADCs within the NSCLC treatment landscape

ADC, antibody drug conjugate; Dato-Dxd, datopotamab deruxtecan; GI, gastrointestinal; NR, not reported; NSCLC, non-small cell lung cancer; Sac-TMT, sacituzumab tirumotecan; SG, sacituzumab govitecan

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