Perspectives on *EGFR*-mutant and wildtype NSCLC: Tailoring treatment advances in late-stage disease

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Bringing it together: Novel strategies, care pathways and side-effect management

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Oncology nurses are uniquely qualified to offer a wide range of support to patients with NSCLC[1]

With treatment advances, patients are living longer, placing a **growing emphasis on supportive care** that preserves or improves patient QoL during and after active care[1]

Supportive care

- Adopt principles of prehabilitation to improve or maintain PS[2]
- Signpost to support groups and charities for emotional and physical help[1]

Supportive medication

- Provide prophylactic supportive medication,[3] e.g. antiemetics for nausea and vomiting; creams for skin reactions; medications for diarrhoea, pain and fatigue

Education

- Personalized patient education on when to contact the treating team about a potential side effect, and encourage early reporting[4]
- Education for GPs/primary care physicians and local teams[5]

Effective communication

- Ensure patient's care team are kept abreast of any developments, e.g. local admission to hospital[6]
- Ensure good communication links, e.g. if side effects occur[6]

GP, general practitioner; NSCLC, non-small cell lung cancer; PS, performance status. 1. Ovesen L. *Oncology Nursing News.* 2023;17;
2. Fenemore J, Roberts J. *Nursing Times.* 2021;117:30–3; 3. Canadian Cancer Society. 2024. Available at: https://cancer.ca/en/treatments/treatment-types/supportive-drugs (accessed 6 September 2024); 4. Snively A. ONS. Available at: https://voice.ons.org/news-and-views/12-2023/personalized-patient-education (accessed 12 September 2024); 5. Faculty (Fenemore J) expert perspectives from personal communication 5 September 2024; 6. Naito T. *Asia Pac J Oncol Nurs.* 2024;11:100370.

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Bringing it together: Implications of novel treatments on the shifting biomarker landscape

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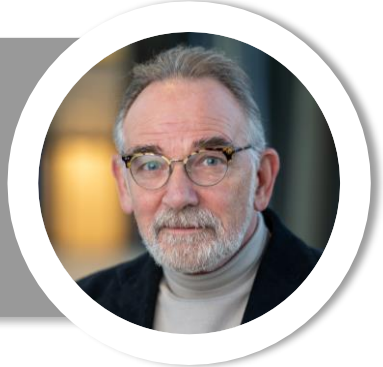

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Recommendations for biomarker testing in advanced/metastatic non-squamous NSCLC

DIAGNOSIS	ESMO[1]	NCCN[2]
Genetic alteration		
EGFR mutation	✓	✓
ALK rearrangement	✓	✓
ROS1 rearrangement	✓	✓
BRAF mutation	✓	✓
NTRK rearrangement/fusion	✓	✓
KRAS mutation	✓	✓
*MET*ex14 skipping	✓	✓
MET amplification	✓	✗
RET rearrangement	✓	✓
HER2 mutation	✓	✓
NRG1 fusion	✓	✗
Other biomarkers		
PD-L1	✓*	✓

*Tested systematically after molecular tests negative.

PROGRESSION

ESMO

Tissue/liquid biopsy in patients with progression who require a change in systemic therapy, to assess for all actionable mechanisms of resistance[3]

Next-generation sequencing (tissue or cfDNA followed by tissue if no target found with cfDNA) for all patients who develop resistance to osimertinib[1]

NCCN

Tissue biopsy of a progressing lesion should be considered to evaluate morphology and biomarker analysis[2]

Re-testing of a sample from a tumour that is actively progressing while exposed to targeted therapy can shed light on appropriate next therapeutic steps[2]

Broad genomic profiling may be the most informative approach to examining potential mechanisms of resistance[2]

cfDNA, cell-free DNA; NSCLC, non-small cell lung cancer; PD-L1, programmed death ligand-1.

1. ESMO. Lung & Chest Cancers Pocket Guideline 2023. Available at: https://bit.ly/3pRPTDp (accessed 30 August 2024); 2. NCCN Clinical Practice Guidelines in Oncology. NSCLC Version 9.2024 — September 9, 2024. Available at: NCCN.org (accessed 12 September 2024);
3. Hendriks LE, et al. *Ann Oncol.* 2023;34:339–57.

Key ADCs in late-stage development for the treatment of NSCLC

Biomarker guided

Trastuzumab deruxtecan*[1]
Patient selection:
Activating *HER2* mutation

Trastuzumab emtansine†[2]
Patient selection:
Activating *HER2* mutation

Telisotuzumab vedotin[3]
Patient selection:
c-Met over-expression

Biomarker agnostic

Sacituzumab govitecan[4]
ADC target:
TROP2

Datopotamab deruxtecan[5]
ADC target:
TROP2

Patritumab deruxtecan[6]
ADC target:
HER3

ADC, antibody–drug conjugate. *FDA- and EMA-approved.[7,8] †Not approved but NCCN recommended.[9]

1. Goto K, et al. *J Clin Oncol.* 2023;41:4852–63; 2. Li BT, et al. *J Clin Oncol.* 2018;36:2532–7; 3. Camidge DR, et al. *J Clin Oncol.* 2024;42(Suppl. 16):103; 4. Patel JD, et al. *J Clin Oncol.* 2024;42(Suppl. 16):8592; 5. Girard N, et al. Presented at: ELCC 2024, Prague, Czechia. 20–23 March 2024. 59P; 6. ClinicalTrials.gov. NCT03260491. Available at: https://clinicaltrials.gov/study/NCT03260491 (accessed 5 September 2024); 7. FDA. Trastuzumab deruxtecan PI. Updated April 2024. Available at: https://bit.ly/4d4PjWd (accessed 4 September 2024); 8. EMA. Trastuzumab deruxtecan SmPC. Updated March 2024. Available at: https://bit.ly/4bmhRtk (accessed 4 September 2024); 9. NCCN Clinical Practice Guidelines in Oncology. NSCLC Version 9.2024 — September 9, 2024. Available at: NCCN.org (accessed 12 September 2024).

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Bringing it together: Optimizing outcomes in late-stage NSCLC: Key learnings

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Overview of course content

Current module

1

***EGFR*-mutant NSCLC**

- Unmet needs
- Latest advances
- Practical insights

2

***EGFR*-wildtype NSCLC**

- Unmet needs
- Latest advances
- Practical insights

3

Bringing it together for optimal care

- Patient management
- Biomarker landscape
- Key learnings

EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer.

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Data updates: *EGFR*-mutant NSCLC

MARIPOSA

Trial population[1]

- Locally advanced/metastatic NSCLC
- *EGFR*-mutated (Ex19del or L858R)
- No prior systemic therapy for advanced disease
- Asymptomatic or stable CNS disease permitted
- ECOG PS 0 or 1

Prior published MARIPOSA data[1]

At a median follow-up of 22.0 months, **amivantamab + lazertinib** significantly improved PFS vs **osimertinib** in the first-line setting (HR 0.70; 95% CI 0.58–0.85; p<0.001)

Longer follow-up data presented at WCLC 2024[2]

First-line **amivantamab + lazertinib** vs **osimertinib**

	Ami + Laz n=429	Osimertinib n=429
Median follow-up: 31.1 months		
mOS	NE	37.3 months
Intracranial PFS	24.9 months	22.2 months
mTTD	26.3 months	22.6 months
PFS2	NE	32.4 months

Amivantamab + lazertinib continued to show a **trend towards improved OS vs osimertinib**

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; mOS, median overall survival; mTTD, median time to treatment discontinuation; NE, not estimable; NSCLC, non-small cell lung cancer; PFS, progression-free survival; PFS2, PFS after first subsequent therapy; WCLC, World Conference on Lung Cancer.

1. Cho BC, et al. *N Engl J Med.* 2024. doi: 10.1056/NEJMoa2403614; 2. Gadgeel S, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. OA02.03.

Data updates: *EGFR*-mutant NSCLC

MARIPOSA-2

Trial population[1]

- Locally advanced/metastatic NSCLC
- *EGFR*-mutated (Ex19del or L858R)
- Disease progression on or after osimertinib monotherapy
- Asymptomatic or stable brain disease permitted
- ECOG PS 0 or 1

Prior published MARIPOSA-2 data[1]

At a median follow-up of 8.7 months, PFS was significantly longer with **amivantamab + ChT** vs **ChT** alone (HR for disease progression or death 0.48; 95% CI 0.36–0.64; p<0.001)

Second interim OS analysis presented at ESMO 2024[2]

Amivantamab + ChT vs **ChT**
after disease progression on osimertinib

	Ami + ChT n=131	**ChT n=263**
Median follow-up: 18.1 months		
mOS	17.7 months	15.3 months
mTTD	10.4 months	4.5 months
PFS2	16.0 months	11.6 months

OS did not reach prespecified significance threshold

Amivantamab + ChT significantly prolonged post-progression outcomes vs **ChT**

ChT, chemotherapy; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; ESMO, European Society for Medical Oncology; HR, hazard ratio; mOS, median overall survival; mTTD, median time to treatment discontinuation; NSCLC, non-small cell lung cancer; PFS, progression-free survival; PFS2, PFS after first subsequent therapy.

1. Passaro A, et al. *Ann Oncol.* 2024;35:77–90; 2. Popat S, et al. Presented at: ESMO 2024. Barcelona, Spain. 13–17 September 2024. LBA54.

Data updates: *EGFR*-wildtype NSCLC

HARMONi-2

Trial design

- Randomized (1:1), double-blind phase III trial
- Patients received treatment until no clinical benefit, unacceptable toxicity or up to 24 months

Trial population

- NSCLC (stage IIIB, IIIC or IV)
- No *EGFR* mutations or *ALK* rearrangement
- No prior systemic therapy for advanced disease
- PD-L1 TPS ≥1%
- ECOG PS 0 or 1

Pre-planned interim analysis presented at WCLC 2024

First-line **ivonescimab** vs **pembrolizumab**

	Ivonescimab n=198	Pembrolizumab n=200
Median follow-up: 8.7 months		
mPFS	11.1 months	5.8 months
ORR	50.0%	38.5%
DCR	89.9%	70.5%
	n=197	n=199
TRAEs	89.8%	81.9%
Grade ≥3 TRAEs	29.4%	15.6%

PFS benefit consistent across pre-specified groups:

Squamous histology, non-squamous histology, TPS 1–49%, TPS ≥50%, with liver metastases, with brain metastases

ALK, anaplastic lymphoma kinase; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; mPFS, median progression-free survival; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD-L1, programmed death ligand-1; TPS, tumour proportion score; TRAE, treatment-related adverse event; WCLC, World Conference on Lung Cancer.

Zhou C, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. PL02.04.

Data updates: *EGFR*-wildtype NSCLC

EVOKE-02

Trial design
- Global, open-label, phase II trial

Trial population
- Advanced/metastatic NSCLC
- No known actionable genomic alterations
- No prior systemic therapy for advanced disease
- Any PD-L1 TPS
- ECOG PS 0 or 1

Efficacy seen across histology and PD-L1 subgroups

Recommended dose for sacituzumab govitecan: 7.5 mg/kg

Initial results presented at WCLC 2024

First-line **sacituzumab govitecan + pembro + carboplatin**

Histology	**Non-squamous (n=51)**	**Squamous (n=41)**
Median follow-up	14.5 months	14.2 months
mPFS	8.1 months	8.3 months
ORR	45.1%	39.0%

PD-L1 TPS	**<1% (n=44)**	**1–49% (n=36)**	**≥50% (n=12)**
mPFS	8.3 months	6.8 months	NR
ORR	43.2%	33.3%	66.7%

Safety	**10 mg/kg (n=29)**	**7.5 mg/kg (n=66)**
Any grade/Grade ≥3 TEAEs	100%/93.1%	100%/86.4%
Leading to discontinuation of SG	31.0%	13.6%
Leading to dose reduction of SG	65.5%	28.8%

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; mPFS, median progression-free survival; NR, not reached; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD-L1, programmed death ligand-1; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TPS, tumour proportion score; WCLC, World Conference on Lung Cancer.

Gray J, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. OA08.07.

Data updates: *EGFR*-wildtype NSCLC

TROPION-Lung01

Trial population[1]

- NSCLC (stage IIIB, IIIC or IV)
- ECOG PS 0 or 1
- No prior docetaxel
- **Without AGAs:** 1 or 2 prior lines, including Pt-ChT and anti-PD-1/PD-L1 therapy
- **With AGAs:** 1 or 2 prior approved targeted therapies + Pt-ChT and ≤1 anti-PD-1/PD-L1 therapy

Prior published TROPION-Lung01 data[1,2]

Dual primary endpoint of PFS met:
Statistically significant improvement with **Dato-DXd** vs **docetaxel**

Final OS data presented at WCLC 2024[1]

Datopotamab deruxtecan vs **docetaxel** in pretreated patients

	Dato-DXd	Docetaxel
Median follow-up: 23.1 months		
mOS: **Intention to treat**	**n=299** 12.9 months	**n=305** 11.8 months
mOS: **Non-squamous**	**n=234** 14.6 months	**n=234** 12.3 months
mOS: **Squamous**	**n=65** 7.6 months	**n=71** 9.4 months

Dual primary endpoint of OS showed a **numerical improvement** with **Dato-DXd** vs **docetaxel** but was **not statistically significant**[1]

AGA, actionable genomic alteration; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; (m)OS, (median) overall survival; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand-1; PFS, progression-free survival; Pt-ChT, platinum-based chemotherapy; WCLC, World Conference on Lung Cancer.

1. Sands J, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. OA08.03; 2. Ahn M-J, et al. *Ann Oncol.* 2023;34(Suppl. 2):S1305–6.