

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

Clinical summary for Module 3: Bringing it together for optimal care For more information, visit: <u>www.touchONCOLOGY.com</u>

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

Oncology nurses are uniquely qualified to offer a wide range of support¹



"In the MDT discussion it's important that everybody has some input, especially the nurses because they often know the patients best and they can explain what they feel the patient would be able to tolerate and what the patient's individual wishes are."

Faculty and topics

Jackie Fenemore presented key considerations for supporting patients with NSCLC through their treatment journey to improve outcomes and QoL



With treatment advances, patients are living longer, placing a growing

emphasis on supportive care that preserves or improves patient QoL during and after active care¹



- Adopt principles of prehabilitation to improve or maintain PS²
- Signpost to support groups and charities for emotional and physical help¹

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 reporting⁴
- Education for primary care physicians and local teams⁵



Communication

- Ensure patient's care team are kept abreast of any developments, e.g. local admission to hospital⁶
- Ensure good communication links, e.g. if side effects occur⁶



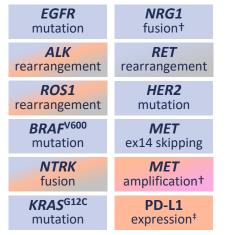
Bringing it together: Implications of novel treatments on the shifting biomarker landscape

Biomarker testing driven by availability of targeted therapies⁷

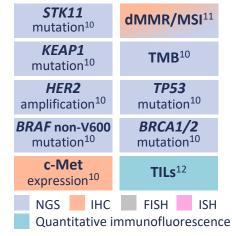


"I think in the near future we will have to test for more, in particular more immunohistochemical markers, as ADCs will become more important and we will have to test for the targets of these ADCs, which are mainly protein markers that are on the cell surface or intracellular protein markers."

ESMO⁸ and NCCN⁹ biomarker testing recommendations*



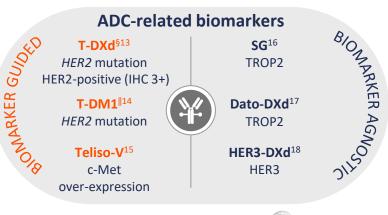
Examples of emerging biomarkers



Faculty and topics

Prof. Dr Egbert Smit presented on the rationale, recommendations and challenges associated with biomarker testing in patients with NSCLC







*For advanced/metastatic NSCLC. [†]Recommended by ESMO only.⁸ [‡]ESMO recommends PD-L1 is systematically determined in advanced NSCLC;⁸ NCCN recommends targeted therapy for the oncogenic driver takes precedence over treatment with an immune checkpoint inhibitor.⁹ [§]FDA- and EMA-approved.^{19,20} [¶]Not approved but NCCN recommended.⁹

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

The importance of biomarker testing to guide treatment decisions

20°

"Ultimately, we are going to need to identify biomarkers to help with risk-stratifying our patients to help us make these treatment decisions in the first-line setting. It becomes important because what we treat patients with in the first-line setting really dictates what treatment options are available in the second-line setting."

EGFR-mutant NSCLC

- Osimertinib is the preferred first-line option^{8,9}
- Promising data in the first-line setting for approved combinations from FLAURA2²¹ and MARIPOSA²²
- Second-line treatment is based on resistance mechanisms (clinical trial),⁸ SoC Pt-ChT or atez + bev + Pt-ChT⁸ or amivantamab + ChT^{9,23,24}
- Promising data in the second-line setting from MARIPOSA-2,²⁵ HERTHENA-Lung01,²⁶ HERTHENA-Lung02,²⁷ HARMONi-A²⁸ and PALOMA-3²⁹

EGFR-wildtype NSCLC

- ICI monotherapy is considered SoC⁸ and is a preferred **first-line** option when PD-L1 TPS \geq 50%*;^{8,9} ICI + Pt-ChT preferred when PD-L1 TPS <50%^{†8,9}
- Promising long-term data in the first-line from CheckMate 9LA,³⁰ POSEIDON,³¹ and EMPOWER-Lung 3;³²
- New data from HARMONi-2³³ and EVOKE-02³⁴
- Options **after progression** on first-line therapy are limited^{8,9,35}
- Promising data using ADCs (e.g. EVOKE-01³⁶ and TROPION-Lung01)³⁷

Bringing it together

- Importance of the MDT for optimizing care
- Oncology nurses, as part of the wider MDT, can offer a wide range of support to patients, including prehabilitation, education, identification of AEs and managing side effects¹
- Importance of biomarker testing to help guide treatment decisions
- Shift towards large-panel NGS¹⁰
 Potential for expanding the
- scope of IHC testing³⁸

Faculty and topics

Dr Helena Yu, CD provided a summary of key learnings from across the three modules, as well as an update of recently presented data



Outstanding practice gaps and future directions³⁹

- Biomarkers to help risk-stratify patients and improved treatment options for addressing CNS metastases
- 2. Second-line treatment options after disease progression on IO or chemo-IO
- 3. Universal comprehensive biomarker testing practices with better collaboration across medical disciplines



*Anti-PD-1/PD-L1; ICI + Pt-ChT is also a preferred option.^{8,9} [†]ESMO recommends anti-PD-1/PD-L1 ± anti-CTLA-4 + Pt-doublet ChT followed by ICI ± pemetrexed or bev;⁸ NCCN recommends Pt-doublet ChT + either pembro or cemiplimab as the preferred first-line options (additional recommended options include atez + bev + Pt-doublet ChT and anti-PD-1/PD-L1 + anti-CTLA-4 ± Pt-ChT, among others).⁹

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

EGFR-mutant NSCLC		EGFR-wildtype NSCLC		
Phase III: MARIPOSA ²² Amivantamab + lazertinib vs osimertinib	Phase III: MARIPOSA-2 ²⁵ Amivantamab + ChT vs ChT	Phase III: HARMONi-2 ³³ Ivonescimab vs pembro	Phase II: EVOKE-02 ³⁴ SG + pembro + carboplatin	Phase III: TROPION-Lung01 ³⁷ Dato-DXd vs dtx
First line	After progression on osimertinib	First line	First line	Previously treated patients
Amivantamab + lazertinib continued to show a trend towards improved OS vs osimertinib over a longer follow-up	OS did not reach prespecified significance threshold at the second interim OS analysis Median follow-up 18 months	PFS benefit of ivo vs pembro consistent across pre-specified groups* at a pre- planned interim analysis	Efficacy of SG seen across histology and PD-L1 subgroups Median follow-up 14 months mPFS (months)	Second dual primary endpoint of OS showed a numerical improvement with Dato-DXd vs docetaxel
(vs interim OS analysis) Median follow-up 31 months mOS (months) Amivantamab + lazertinib: NE Osimertinib: 37 HR 0.77; 95% CI 0.61–0.96	mOS (months) Amivantamab + ChT: 18 ChT: 15 HR 0.73; 95% CI 0.54–0.99 p=0.039	Median follow-up 9 months mPFS (months) Ivonescimab: 11 Pembro: 6 ORR (%) Ivonescimab: 50 Pembro: 39	SQ: 8 NSQ: 8 PD-L1 TPS <1%: 8 PD-L1 TPS 1-49%: 7 PD-L1 TPS ≥50%: NR Recommended dose for SG: 7.5 mg/kg	Median follow-up 23 months mOS (months) Dato-DXd: 13 Dtx: 12 SQ Dato-DXd: 8 Dtx: 9 NSQ
p=0.019 61% of patients treated with amivantamab + lazertinib alive at 3 years vs 53% with osimertinib	Amivantamab + ChT significantly prolonged post-progression outcomes vs ChT	Safety profile of ivonescimab consistent with prior studies and was well tolerated	TEAEs manageable with appropriate supportive measures	Dato-DXd: 15 Dtx: 12 Overall safety profile consistent with prior PFS data cutoff

*SQ, NSQ, PD-L1 TPS 1–49%, PD-L1 TPS ≥50%, with liver metastases, with brain metastases.

Abbreviations

ADC, antibody–drug conjugate; AE, adverse event; atez, atezolizumab; bev, bevacizumab; c-Met, cellular mesenchymal epithelial transition factor receptor; CD, course director; chemo-IO, chemoimmunotherapy; ChT, chemotherapy; CI, confidence interval; CNS, central nervous system; dato-DXd, datopotamab deruxtecan; dMMR, mismatch repair deficient; dtx, docetaxel; EGFR, epidermal growth factor receptor; ESMO, European Society for Medical Oncology; ex14, exon 14; FISH, fluorescence *in situ* hybridization; HER2, human epidermal growth factor receptor 2; HER3, human epidermal growth factor receptor 3; HER3-DXd, patritumab deruxtecan; HR, hazard ratio; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; IO, immunotherapy; ISH, *in situ* hybridization; MDT multidisciplinary team; MET, mesenchymal epithelial transition factor receptor; m, median; MSI, microsatellite instability; NCCN, National Comprehensive Cancer Network®; NE, not evaluable; NGS, next-generation sequencing; NR, not reached; NSCLC, non-small cell lung cancer; NSQ, non-squamous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand-1; pembro, pembrolizumab; PFS, progression-free survival; PS, performance status; Pt-ChT, platinum-based chemotherapy; QoL, quality of life; SG, sacituzumab govitecan; SoC, standard of care; SQ, squamous; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; teliso-V, telisotuzumab vedotin; TIL, tumour infiltrating lymphocyte; TMB, tumour mutational burden; TPS, tumour proportion score; TROP2, trophoblast cell-surface antigen 2.

The guidance provided by this clinical summary is not intended to directly influence patient care. Clinicians should always evaluate their patients' conditions and potential contraindications and review any relevant manufacturer product information or recommendations of other authorities prior to consideration of procedures, medications or other courses of diagnosis or therapy included here. Our clinical summary coverage does not constitute implied endorsement of any product(s) or use(s). touchONCOLOGY cannot guarantee the accuracy, adequacy or completeness of any information, and cannot be held responsible for any errors or omissions.



References

- 1. Ovesen L. Oncol Nurs News. 2023;17.
- 2. Fenemore J, Roberts J. Nurs Times. 2021;117:30–3.
- Canadian Cancer Society. 2024. Available at: <u>https://cancer.ca/en/treatments/treatment-types/supportive-drugs</u> (accessed 8 November 2024).
- 4. Snively A. ONS. Available at: <u>https://voice.ons.org/news-and-views/12-</u> 2023/personalized-patient-education (accessed 8 November 2024)
- 5. Faculty (Fenemore J) expert perspectives from personal communication 5 September 2024.
- 6. Naito T. Asia Pac J Oncol Nurs. 2024;11:100370.
- 7. Hendriks LE, et al. Ann Oncol. 2023;34:339–57.
- ESMO. Lung & Chest Cancers Pocket Guideline 2024. Available at: <u>https://bit.ly/3pRPTDp</u> (accessed 8 November 2024).
- NCCN Clinical Practice Guidelines in Oncology. NSCLC Version 11.2024 — October 15, 2024. Available at: NCCN.org (accessed 8 November 2024).
- 10. de Jager VD, et al. Lancet Reg Health Eur. 2024;38:100839.
- 11. Qin J, et al. J Clin Oncol. 2022;40(Suppl. 16):e21142.
- 12. Lopez de Rodas M, et al. J Immunother Cancer. 2022;10:e004440.
- 13. Goto K, et al. J Clin Oncol. 2023;41:4852–63.
- 14. Li BT, et al. J Clin Oncol. 2018;36:2532-7.
- 15. Camidge DR, et al. J Clin Oncol. 2024;42(Suppl. 16):103.
- 16. Patel JD, et al. J Clin Oncol. 2024;42(Suppl. 16):8592.
- 17. Girard N, et al. Presented at: ELCC 2024, Prague, Czechia. 20–23 March 2024. 59P.
- ClinicalTrials.gov. NCT03260491. Available at: <u>https://clinicaltrials.gov/study/NCT03260491</u> (accessed 8 November 2024).
- 19. FDA. Trastuzumab deruxtecan PI. Updated April 2024. Available at: <u>https://bit.ly/4d4PjWd</u> (accessed 8 November 2024).
- 20. EMA. Trastuzumab deruxtecan SmPC. Updated October 2024. Available at: https://bit.ly/4bmhRtk (accessed 8 November 2024).
- 21. Planchard D, et al. N Engl J Med. 2023;389:1935-48.

- 22. Gadgeel S, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. OA02.03.
- 23. FDA. Amivantamab PI. Updated September 2024. Available at: <u>https://bit.ly/4eLIKsA</u> (accessed 8 November 2024).
- 24. EMA. Amivantamab SmPC. Updated September 2024. Available at: <u>https://bit.ly/4hc1KCi</u> (accessed 8 November 2024).
- 25. Popat S, et al. Presented at: ESMO 2024. Barcelona, Spain. 13–17 September 2024. LBA54.
- 26. Yu HA, et al. J Clin Oncol. 2023;41:5363–75.
- 27. Flaherty C. OncLive. 2024. Available at: <u>https://bit.ly/4ep2EIR</u> (accessed 8 November 2024).
- 28. Zhang L, et al. J Clin Oncol. 2024;42(Suppl. 16):8508.
- 29. Leighl NB, et al. J Clin Oncol. 2024;42:3593-605.
- 30. Reck M, et al. Eur J Cancer. 2024;211:114296.
- 31. Peters S, et al. Presented at: ESMO Immuno-Oncology 2023, Geneva, Switzerland. 6–8 December 2023. LBA3.
- 32. Baramidze A, et al. Presented at: ELCC 2024, Prague, Czechia. 20–23 March 2024. 64P.
- Zhou C, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. PL02.04.
- Gray J, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. OA08.07.
- 35. Insa A, et al. Crit Rev Oncol Hematol. 2022;169:103538.
- Reinmuth N, et al. Presented at: ESMO 2024. Barcelona, Spain. 13–17 September 2024. 1314P.
- Sands J, et al. Presented at: WCLC 2024. San Diego, CA, USA. 7–10 September 2024. OA08.03.
- 38. Ren S, et al. ESMO Open. 2022;7:100395.
- 39. Faculty (Yu HA) expert perspectives from personal communication 10 October 2024.

