In the news

https://doi.org/10.1038/s41571-023-00838-y

From ESMO 2023: advances in lung cancer

Among the many transformative developments reported at this year's ESMO Congress, advances in the management of patients with lung cancer were particularly prominent and encompassed several different disease stages and settings.

For resectable non-small-cell lung cancer (NSCLC), data from the phase III CheckMate 77T study, comparing neoadjuvant nivolumab plus chemotherapy followed by adjuvant nivolumab versus neoadjuvant chemotherapy, revealed improved median event-free survival (EFS) with the former (not reached (NR) versus 18.4 months, HR 0.58, 95% CI 0.42–0.81; $P = 0.00025$). Longer follow-up data from KEYNOTE-671, which tested pembrolizumab in a similar setting, indicate that improved EFS can lead to improved overall survival (median NR versus 52.4 months, HR 0.72, 95% CI 0.56–0.93; $P = 0.0052$). For patients with resected *ALK*-positive NSCLC, the phase III ALINA trial demonstrated improved median disease-free survival (DFS) with adjuvant therapy with the ALK inhibitor alectinib versus 4 cycles of chemotherapy (median NR vs 41.3 months, HR 0.24 (95% CI 0.13–0.43; $P < 0.0001$).

With regard to unresectable disease, early data from KRYSTAL-7 indicate promising activity of adagrasib plus pembrolizumab as first-line therapy for patients with advanced-stage $KRAS^{G12C}$-mutant PD-L1-high NSCLC (PD-L1 tumour-proportion score ≥50%), with an ORR of 63% and survival data awaited at a median follow-up duration of 10.1 months. For patients with advanced-stage *EGFR*-mutant disease (comprising exon 19 deletions or L858R) receiving first-line therapy, the phase III MARIPOSA study demonstrated the superiority of the EGFR–MET bispecific antibody amivantamab plus lazertinib versus osimertinib (median progression-free survival (mPFS) 23.7 months versus 16.6 months, HR 0.70, 95% CI 0.58–0.85; $P < 0.001$). The addition of amivantamab plus lazertinib or amivantamab alone to chemotherapy also improved mPFS in patients with disease progression on prior osimertinib in MARIPOSA-2 (mPFS 8.3 months and 6.3 months versus 4.2 months, respectively, $P < 0.001$ for both comparisons).

Other novel therapies included datopotamab deruxtecan, an antibody–drug conjugate targeting TROP-2, in patients with pretreated advanced-stage NSCLC, which improved mPFS relative to docetaxel (median 4.4 months versus 3.7 months, HR 0.75, 95% CI 0.62–0.91; $P = 0.004$). Finally, evidence of activity of the DLL3-targeted bispecific T cell engager tarlatamab in advanced-stage small-cell lung cancer was presented (mPFS 4.9 months, median overall survival 14.3 months with a 10-mg dose).

These findings further expand the range of therapeutic options available for patients with lung cancer. However, costs are likely to limit the ability of many patients to access these therapies.

Peter Sidaway

Original article: Passaro, A. et al. Amivantamab plus chemotherapy with and without lazertinib in *EGFR*-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase 3 MARIPOSA-2 study. *Ann Oncol.* **21**, https://doi.org/10.1016/j.annonc.2023.10.117 (2023); Ahn, M.-J. et al. Tarlatamab for patients with previously treated small-cell lung cancer. *N. Engl. J. Med.* **20**, https://doi.org/10.1056/NEJMoa2307980 (2023)