

# Lung Cancer Treatment Research Enters a New Era

Better outcomes were achieved with combinations of experimental new drugs targeting common and rare tumour mutations.

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- Advances in lung cancer treatment highlight importance of tumour testing at diagnosis.
- Research presented at the ESMO Congress 2023 sets potential major changes in first-line treatment for patients with NSCLC with targetable tumour cell mutations.

More people with non-small cell lung cancer (NSCLC) are likely to benefit from new drugs that target molecular alterations in tumor cells, with less need for chemotherapy, following results of multiple landmark clinical trials reported for the first time in late-breaking presentations at the ESMO Congress 2023 (, LBA2, LBA4, LBA5, LBA1, LBA12). Better outcomes were achieved with combinations of experimental new drugs targeting common and rare tumour mutations than with standard treatments, with improvements seen in both early and late-stage NSCLC – the type of lung cancer responsible for approximately eight out of 10 cases of the disease ([ESMO. Non-small-cell lung cancer: A guide for patients](#)).

“The results are very impressive and mean that we can expect major changes in first-line treatment for patients with NSCLC with these targetable tumor cell alterations, and in the way we care for patients whose previous treatment has stopped working,” said Professor Alessandra Curioni-Fontecedro, University of Fribourg, Switzerland. “As a result, it will be more important than ever that lung cancer is diagnosed and treated by lung cancer specialists with access and understanding of molecular testing and findings,” she added.

Dr Elene Mariamidze, Todua Clinic, Tbilisi, Georgia, agreed: “We are entering an era of personalized medicine in NSCLC where we are using combinations of novel, targeted agents, and it will be essential to know the whole mutational burden of each patient at diagnosis so we can properly plan the most effective and least toxic approach. The future of lung cancer care lies in finding the right combination of targeted treatment, or chemotherapy with immunotherapy for each patient.”

Both Curioni-Fontecedro and Mariamidze highlighted data from studies using a new combination of targeted drugs in patients with advanced or metastatic NSCLC who had an EGFR mutation – one of the most common tumour mutations. When people were given the combination as first-line treatment, progression-free survival (PFS) was significantly better than with the current most effective treatment for the mutation (abstracts LBA14). In people who had already progressed on this current standard of care, the new targeted drugs, combined with chemotherapy, significantly improved PFS compared with chemotherapy alone (abstract LBA15).

“We still need to see that the new combination leads to improved overall survival compared with current treatment. We also need to understand more about the effects in patients with brain metastases as it appears that one of the newer EGFR-targeting agents used in these studies has good penetration of brain tissue,” commented Curioni-Fontecedro.

“These studies show that patients now have a potentially new drug combination for their treatment that works partly by targeting EGFR mutations, and partly by directing immune cells to destroy cancer cells. The fact that the combination worked better than the current standard of care, not just better than placebo, shows tangible benefits for this new approach,” added Mariamidze.

Results of NSCLC studies presented at the ESMO Congress 2023 also suggest that using mutation-targeted treatment can reduce the need for chemotherapy in some patients, including those with some rarer tumour alterations for which targeted treatment options have previously been limited. These include patients with operable, early stage ALK-positive NSCLC (abstract LBA2), those with RET-mutated advanced NSCLC (abstract LBA4), and those with the less common, more difficult to treat EGFR mutation, Exon 20 insertion, advanced NSCLC (abstract LBA5).

In addition, study data reinforce the value of adding immunotherapy to chemotherapy in some types of NSCLC, including the use of this treatment before surgery for patients with operable cancers to shrink tumours and indicate likely response to further treatment after surgery (so called, neoadjuvant treatment) (abstract LBA1).

“We know that patients have a better prognosis if pre-surgical treatment of lung cancer leads to tumour disappearance on pathology reports after surgery (pCR-pathologic complete response) than if there are still obvious cancer cells present in post-surgical material. The new results show that adding immunotherapy to chemotherapy before surgery, and then continuing with maintenance immunotherapy for a year after surgery, is more effective than just giving chemotherapy before surgery,” Mariamidze pointed out.

Even for patients with advanced or metastatic NSCLC who have relapsed following previous treatments and can only be given chemotherapy, there is good news. Directing chemotherapy more precisely at tumors using antibody drug conjugates, namely antibodies that recognise specific proteins commonly found in lung cancers significantly improved PFS compared to currently used chemotherapy (abstract LBA12).

“The approach using these antibody drug conjugates will make a big difference for the majority of

patients with advanced or metastatic NSCLC who have stopped responding to first and second-line treatments, irrespective of whether they have targetable mutations. We need to know more about the side-effects of this approach but these findings are likely to change the standard of care for these patients,” predicted Curioni-Fontecedro.

Following such promising NSCLC data presented at ESMO 2023, the next step for both Curioni-Fontecedro and Mariamidze is to better understand the sequence of treatments that will give the best outcomes for patients.

“We still face the dilemma of what we do after patients have had these promising new drugs and need further treatment. It will be very important to understand the sequencing of treatment now that we have so many more options for treating NSCLC so that we can achieve the best possible results for each patient,” said Curioni-Fontecedro.

“Very few patients benefit from one therapy alone, and most will need combinations of treatments at different times in their lung cancer care. We need further research to show when and how to target different mutations, possibly including new targets, and to help establish the ideal treatment plan for patients with lung cancer who develop extensive disease,” concluded Mariamidze.

This [news release](#) was published by ESMO on October 17, 2023.