Evaluating selpercatinib for the treatment of non-small cell lung cancer

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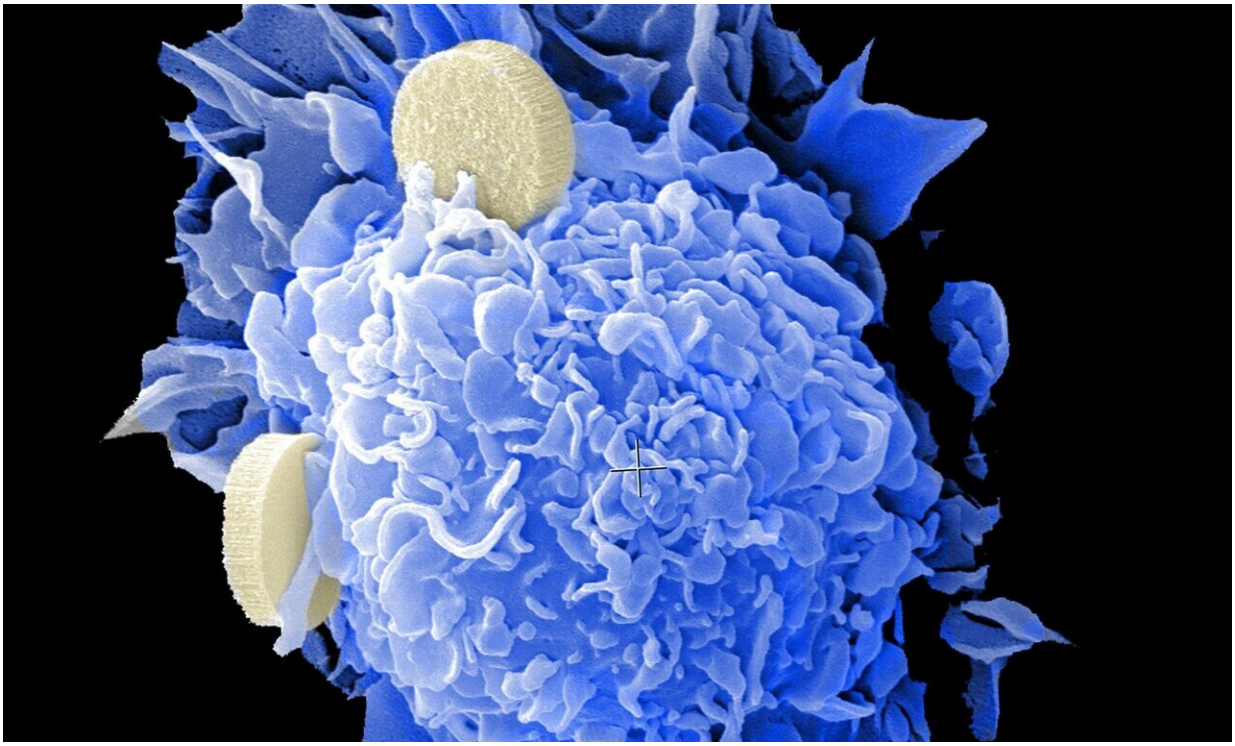

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A phase III LIBRETTO-431 multicenter study has evaluated the efficacy and safety of selpercatinib compared to control treatment, which consisted of platinum-based chemotherapy associated or not with pembrolizumab (immune checkpoint inhibitor) in non-small cell lung cancer (NSCLC).

The research was published in the *New England Journal of Medicine* and included Dr. Milena Perez Mak, D'Or Institute for Research and Education (IDOR) researcher, and clinical oncologist at the São Paulo State Cancer Institute (Icesp).

Lung cancer is one of the most common cancers worldwide and is notable for its high lethality. Among the subtypes of lung cancer, NSCLC is the most common, accounting for approximately 85% of cases. It originates in the cells of the bronchi and alveoli of the lungs.

The study evaluated the efficacy of selpercatinib in patients with NSCLC who had genomic alterations in the RET gene. The therapy in question was based on a RET inhibitor, which aims to block the action of the abnormal gene responsible for the proliferation of cancer cells.

Combining chemotherapy with pembrolizumab is the standard treatment for patients with advanced NSCLC, but its efficacy is uncertain in patients with RET gene translocations. We therefore compared the two therapies to determine which treatment is more effective when used first-line.

The study included 261 patients from 23 countries who had advanced NSCLC with RET gene translocation between March 2020 and August 2022. These patients were randomly assigned to the treatment or control groups. With randomization, the researchers can be more confident that any difference observed in the results is due to the treatment being studied and not to pre-existing differences between the groups.

The results showed that patients who received selpercatinib had a significant gain in cancer progression-free survival, reaching 24.8 months, compared to 11.2 months in the control group.

The researchers also evaluated the effectiveness of the drugs on

intracranial lesions, as many patients with advanced NSCLC can develop metastases in the brain. At the start of the study, 42 patients with brain metastases were identified.

Selpercatinib was able to treat existing metastases in the central nervous system and prevent the formation of new intracranial metastases. This finding is relevant since the treatment of brain metastases is a challenge due to the presence of the blood-brain barrier, which prevents the action of most cancer drugs on lesions in the brain.

Another point evaluated was the safety of the treatment. Patients treated with selpercatinib had adverse effects that differed from chemotherapy, including increased liver enzymes, which were controlled after dose adjustment, and hypertension.

The authors highlighted the importance of performing molecular tests during diagnosis to enable the most appropriate choice of first-line therapy for this patient population.

"This study represents the importance of the appropriate selection of treatment for lung cancer patients according to the molecular characteristics of the tumor. Through the use of precision medicine, it is possible to obtain better results as demonstrated by this study. In addition, the participation of our center reinforces the quality of research in Brazil and the possibility of including Brazilian patients in international clinical studies," says Dr. Milena Mak.

More information: Caicun Zhou et al, First-Line Selpercatinib or Chemotherapy and Pembrolizumab in RET Fusion–Positive NSCLC, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMoa2309457

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