

Crizotinib (Xalkori®) for the treatment of anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer (NSCLC)

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An activating mutation of the anaplastic lymphoma kinase (ALK) fusion gene is responsible for 1-7% of non-small lung cancer (NSCLC). In Austria approximately 30 to 200 patients will be newly diagnosed with ALK-positive NSCLC per year.

Crizotinib, a selective adenosine triphosphatase-competitive small-molecule inhibitor of ALK, was licensed for the treatment of adults with ALK-positive advanced NSCLC in the U.S. in August 2011. In Europe this approval is restricted to second line therapy for ALK-positive NSCLC patients with disease progression after chemotherapy only.

To date, interim results of 2 single arm Phase II trials and 1 randomized controlled phase III trial were published. All of these trials are still ongoing. In the phase III trial (Profile 1007) crizotinib is investigated in comparison to standard chemotherapy in 347 patients with advanced ALK-positive NSCLC. After a median follow-up of about 12 months a statistically significant better progression free survival and objective response rate for the crizotinib group were reported. Although the overall survival rates were comparable in both groups, there was an increased number of deaths related to disease progression in the crizotinib group.

Significant benefits for patients treated with crizotinib were reported in terms of lung cancer symptoms and quality of life. On the other hand, different types of vision disorders occurred in a higher proportion of patients in the crizotinib group, but all of them seemed to be of lower grades. The rates of adverse events of higher grade were similar in both groups.

Despite the seemingly positive interim results of the Profile 1007 trial, the effectiveness and toxicity of crizotinib remains uncertain and the results have to be confirmed by the final results of the study and by further RCTs, as demanded by the European and US regulatory authorities. As crizotinib affects only ALK-positive NSCLC patients, a reliable ALK-testing prior to treatment initiation is crucial for patient selection. Therefore, reliable test results and a rigorous quality assessment are of maximum importance to ensure an appropriate patient selection.

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