## EURTAC first-line phase III randomized study in advanced non-small cell lung cancer: Erlotinib works also in European population

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Activating epidermal growth factor receptor (EGFR) mutations represent the first target for which specific tyrosine kinase inhibitors (TKIs) are clinically available for the personalized treatment of advanced non-small cell lung cancer (NSCLC) patients. Until few months ago, three randomized phase III studies investigated the role of two EGFR-TKIs inhibitors, gefitinib (1-3) and erlotinib (4), as first-line treatment compared with standard platinum-based chemotherapy, in patients affected by advanced NSCLC harboring EGFR activating mutations. In all these trials the main endpoint was reached with EGFR-TKIs reporting a significant improvement in progression-free survival (PFS) and overall response rate (ORR). The overall survival (OS) where available, was similar between TKIs and chemotherapy arm due to the high percentage of cross-over treatment. Nevertheless, OS reached about 30 months, results which were never seen in trials addressed to advanced NSCLC patients. All these studies were performed in Asian population and this is the main reason explaining, at the moment, that gefitinib is licensed for the treatment of patients affected by advanced NSCLC harbouring activating EGFR mutations in any line of therapy worldwide but in United States.

EURopean TArceva vs. Chemotherapy (EURTAC) study is the first trial with a TKI addressed to European population affected by advanced NSCLC harbouring activating EGFR mutations (exon 19 deletion or L858R mutation in exon 21). In this trial erlotinib, at the oral dose of 150 mg daily, was compared with platinum-based doublets (cisplatin or carboplatin plus gemcitabine or docetaxel) in 174 eligible patients. Erlotinib scored significantly better than

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No main differences were reported in terms of PFS when comparing the results reported by the three studies addressed to the Asians and the EURTAC trial in both arms of treatment. In the EURTAC trial the ORRs of both arms were lower than those reported in the other trials. Indeed, these results may be affected by the influence of the characteristics of randomized patients as for example the mutations type or smoking status.

Another important issue is the toxicity. EGFR-TKIs were better tolerated with lower percentage of severe toxicities than chemotherapy arm in all studies. But, erlotinib seems to be better tolerated in Chinese population (grade 3-4 toxicities 17%) then in European patients (grade 3-4 toxicities 45%). Overall gefitinib resulted more hepatotoxic while erlotinib resulted more toxic in terms of rash and diarrhoea. To date we have no large prospective phase III studies comparing gefitinib and erlotinib. However, a randomized phase II study in secondline setting confirmed the above mentioned different toxicity profile of the two drugs (6).

Overall, the EURTAC trial underlined the importance of genotyping patients to personalizing the therapeutic approach for treatment of NSCLC regardless their ethnicity. Of importance is the need to have an adequate amount of tumor tissue for biomarker analyses. When available in the market, the choice of the EGFR-TKIs in clinical practice should be guided by clinical experience and manageability in the use of the drug. Comparisons in advanced NSCLC harbouring an activating EGFR mutation between gefitinb and erlotinib and even new irreversible TKI's inhibitor such as afatinib are challenging in terms of efficacy and toxicity.

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