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Final Analysis of Landmark IPASS Study Confirms That IRESSA (Gefitinib) is a Valuable Option for the First-Line Treatment of Patients With Advanced NSCLC With EGFR Activating Mutations

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Mature data from the IPASS study, presented today at the 2010 ESMO congress, showed that overall survival (OS) was similar, with no significant difference, between IRESSA (an EGFR tyrosine kinase inhibitor (TKI)) and carboplatin/paclitaxel (doublet chemotherapy) in the overall population (HR=0.90, 95% CI 0.79-1.02, p=0.11, median OS 18.8 vs. 17.4 months). Neither was there a significant difference between treatment arms for OS in the subgroups defined by EGFR mutation status: EGFR mutation-positive patients (HR=1.00, 95% CI 0.76-1.33, median OS 21.6 vs. 21.9 months); EGFR mutation-negative patients (HR=1.18, 95% CI 0.86-1.63, median OS 11.2 vs. 12.7 months); and patients whose EGFR mutation status was unknown (HR=0.82, 95% CI 0.70-0.96, median OS 18.9 vs. 17.2 months).[1]

(Photo: http://www.newscom.com/cgi-bin/prnh/20101011/412970-a)

(Photo: http://www.newscom.com/cgi-bin/prnh/20101011/412970-b)

The mature IPASS OS data confirm that patients with EGFR mutation-positive advanced non-small cell lung cancer (NSCLC) had better outcomes, regardless of which treatment arm they were in, compared to patients with EGFR mutation-negative disease. Median survival times were around 22 months for EGFR mutation-positive patients, but only 11-12 months for EGFR mutation-negative patients.[1] The majority of EGFR mutation-positive patients in IPASS received an EGFR-TKI at some point as 64% of those randomised to carboplatin/paclitaxel later received an EGFR-TKI as subsequent therapy.

"I believe that progression-free survival is a better endpoint than overall survival for evaluation of treatment effect in the first-line setting," said IPASS investigator, Professor James Yang from National Taiwan University Hospital. "However, the IPASS data show that EGFR mutation-positive patients have better survival outcomes than EGFR mutation-negative patients, regardless of whether they were randomised to IRESSA or chemotherapy. Lung cancer patients should be tested to determine their EGFR mutation status, as EGFR mutation-positive patients benefit from treatment with IRESSA through longer progression-free survival, improved control of their symptoms and better quality of life, compared with doublet chemotherapy. It's important to consider very carefully when choosing a first-line treatment for advanced NSCLC, as many patients in clinical practice will not receive further active treatment."

Analysis of the primary endpoint of IPASS in 2008 demonstrated that IRESSA was superior to carboplatin/paclitaxel in terms of progression-free survival (PFS) in the overall population (HR 0.74, 95% CI 0.65-0.85, p<0.001).[2] Further analysis of the data demonstrated that IRESSA's PFS superiority in the overall population was driven by the effect of IRESSA vs. carboplatin/paclitaxel in the subgroup of EGFR mutation-positive patients.[2] In these patients, compared with carboplatin/paclitaxel, IRESSA reduced the risk of progression by 52% (HR=0.48, 95% CI 0.36-0.64, p<0.001) and median progression-free survival was increased from 6.3 to 9.5 months. In addition, IRESSA provided significant benefits in objective response rate, quality of life and symptom improvement compared with carboplatin/paclitaxel in EGFR mutation-positive patients.[2,3]

"IPASS is a landmark study, which changed the way the oncology community viewed lung cancer," said Alison Armour, Medical Science Director for AstraZeneca. "It was anticipated that the significant IRESSA progression-free survival benefit may not translate into an overall survival benefit, due to the large amounts of subsequent treatment that patients could have received following disease progression on their randomised first-line treatment. IPASS data reinforce that there should be a move towards recognising that lung cancer is a complex disease with distinct subtypes requiring targeted medicines."

The IPASS data from 2008[2] formed part of the data package leading to the current indication for IRESSA in Europe.[4] The ESMO Clinical Practice Guidelines[5] for metastatic NSCLC state that first-line treatment with a TKI is an option in patients with tumours harbouring an activating EGFR mutation. IRESSA is currently indicated in Europe for the treatment of patients with EGFR mutation-positive advanced NSCLC.[4] Outside of Europe, IRESSA is licensed in a further 44 countries, labelled indications vary from country to country.

Editors Notes

About IPASS[2]

IRESSA Pan-ASia Study (IPASS) was a Phase III open label, randomised, parallel-group study that assessed the efficacy, safety and tolerability of IRESSA versus standard doublet chemotherapy (carboplatin/paclitaxel) as first-line treatment in a clinically selected population of 1,217 patients from Asia. The patients had advanced NSCLC and had not received prior chemotherapy for advanced disease. Their tumours were of adenocarcinoma histology. They had either never smoked, or were former light smokers (ceased smoking at least 15 years ago and <= 10 pack-years exposure).

The primary endpoint was progression-free survival (PFS: length of time a patient lives without their cancer growing or spreading).

The secondary endpoints included overall survival, objective response rate, quality of life and safety.

IPASS was published in The New England Journal of Medicine and marked the first time a targeted monotherapy has demonstrated significantly longer PFS than doublet chemotherapy in the first-line treatment of EGFR mutation-positive advanced NSCLC.

About IRESSA (gefitinib)

Mode of Action: gefitinib is an EGFR-TKI (epidermal growth factor receptor tyrosine kinase inhibitor), which targets and blocks the activity of the EGFR-TK, an enzyme that regulates intracellular

signalling pathways implicated in cancer cell proliferation and survival. Growth factor signalling has been identified as a key driver of tumour growth and spread in a wide range of cancers.

IRESSA (250 mg) is a once-daily oral therapy.

IRESSA is approved in the EU for the treatment of patients with locally advanced or metastatic NSCLC with activating mutation of EGFR-TK. Outside of Europe, IRESSA is licensed in a further 44 countries - labelled indications vary from country to country.

IRESSA has a well-established, generally well-tolerated side effect profile and is not typically associated with the cytotoxic side-effects commonly seen with chemotherapy. The most commonly seen side-effects of IRESSA are mild-to-moderate rash and diarrhoea.

To view an IRESSA MOA video, please click here: http://www.egfr-mutation.com/EGFR-lung-cancer

To date, the number of patients who have taken IRESSA is over 300,000 and the maximum time a patient has remained on gefitinib therapy is in excess of eight years.[6]

About EGFR mutation testing

Epidermal growth factor receptor (EGFR) is a protein found on the surface of cells to which proteins or ligands such as epidermal growth factor (EGF) bind. When EGF attaches to EGFR, it activates the tyrosine kinase enzyme, triggering reactions that cause the cells to grow and multiply.

The EGFR gene can have mutations that cause the EGFR to be permanently activated, which in turn activates the tyrosine kinase enzyme, triggering reactions that cause the cells to grow and multiply. Those patients who have these mutations have EGFR mutation-positive disease.

NSCLC is the more common of the two forms of lung cancer. The other is small-cell lung cancer (SCLC), which accounts for 15% of cases, whereas NSCLC accounts for approximately 85%.[7]

Approximately 10-15% of NSCLC patients in Europe[4,8,9] and 30-35% of NSCLC patients in Asia will have EGFR mutation-positive NSCLC. [10,11]

EGFR mutation-positive NSCLC can be identified through biopsy testing at the point of diagnosis. This is an additional test that the oncologist requests along with other standard diagnostic tests (histology testing) to identify what kind of lung cancer a patient has. If done at the same time, this can avoid any delay in the start of treatment.

A number of different laboratory tests are currently available for this purpose, including DNA sequencing, Clamp (especially in Japan) and Melt analysis. In addition, there is a mutation detection technique called the TheraScreen EGFR29(R) (DxS).

For more information on EGFR mutation testing, please visit: http://www.egfr-mutation.com

About AstraZeneca

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