TTP and OS were female gender, the absence of smoking history, and adenocarcinoma histology. As expected, those treated with Erlotinib in the first line setting had significantly longer TTP than further lines (7.4 vs. 4.4; p<0.001). In the multivariate analysis only non smoking history remained as predictive factor for longer TTP and survival (p<0.0001).

Most frequent reported adverse events were rash (62.9%; 12.9% grade 3/4), asthenia (37.1%; 9.2% grade 3/4) and diarrhea (33.3%; 6.1% grade 3/4).

Conclusions: This interim analysis of a subset of elderly patients with advanced or metastatic NSCLC treated with Erlotinib in a real-life clinical setting confirms the good tolerability and promising activity. It is worthwhile mentioning the benefit in survival obtained by chemonaïve elderly patients. Therefore Erlotinib is an effective treatment for elderly patients with advanced NSCLC, even as a first-line treatment. A randomized phase III study intended for elderly patients with Erlotinib is warranted.

P3-062 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Wood-smoke exposure as a survival predictor in non-small cell lung cancer with response to erlotinib: an open label phase II study

Arrieta, Oscar[1] Tellez, Eduardo[2] Martinez, Luis[3] De-La-Cruz-Vargas, Jhony[4] Flores-Estrada, Diana[5] Silva-Godinez, Juan-Carlos[6] Morales-Barrera, Rafael[7] de la Garza, Jaime[5]

[1] Instituto Nacional de Cancerologia / Universidad Nacional Autonoma de Mexico, Mexico D.F., Mexico [2] ISSSTEP, Puebla, Mexico, Mexico [3] Instituto Nacional de Enfermedades Respiratorias, Mexico, Mexico [4] Grupo Oncologico Acapulco, Acapulco, Mexico [5] Instituto Nacional de Cancerologia, Mexico, Mexico [6] Universidad Nacional Autonoma de Mexico / Instituto Nacional de Cancerologia, Mexico, Mexico [7] Instituto Nacional de Cancerologia, Mexico D.F., Mexico

Background: Erlotinib, a tyrosine kinase inhibitor, has been shown to improve the survival and quality of life in patients with non-small cell lung cancer (NSCLC) after first or second-line chemotherapy. Asian origin, adenocarcinoma histologic type, female gender, lack of tobacco use, and expression of EGFR have been described as significant independent predictors of response to erlotinib. Although tobacco use is considered a major cause of NSCLC, other factors are involved in its pathogenesis. In underdeveloped countries such as Mexico, wood and other solid fuels are still used for cooking and heating. The pathophysiolocial mechanisms of wood smoke exposure (WSE) as a potential risk factor for the development of NSCLC are still unknown.

Methods: In this study, 135 patients with histologically proven NSCLC with poor performance status were treated with erlotinib after first or second-line chemotherapy. Clinical and pathological characteristics were associated with response to treatment.

Results: We found a global response to erlotinib in 45 patients (31.3%, CI 95% 23.5-39.1), stable disease in 31.9% and progression in 30.6%. Clinical improvement was observed in 56.5%. The clinical features associated with response to erlotinib in the univariate analysis were female gender (44.4 vs. 20.6%, p=0.003), no tobacco use (48.4 vs. 19.7%, p<0.001). Borderline statistical significance was observed with adenocarcinoma histological type (34.3 vs. 16%, p=0.086). However, in the logistic regression analysis only the histological type (p=0.049) and WSE (p=0.001) showed statistical significance. The factors associated to an improved progression-free survival(PFS) in the Cox multivariate analysis were adenocarcinoma histologic type (7.9±0.7 vs 2.2±0.4 months, p= 0.02), female gender (8.4±0.7 vs 4.4±1.6 months, p= 0.02) and WSE (17.56±4.17 vs 4.8±0.7 months, p< 0.001).

Conclusion: WSE is associated with response to erlotinib in patients with NSCLC and may indicate an improvement in PFS. The EGFR mutation is probably involved in the development of NSCLC in non-smokers with WSE.

P3-063 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

The role of IL-20 in lung cancer: A new epigenetic target?

Baird, Anne-Marie[1,3] Al-Sarraf, Nael[2] Gray, Steven G.[3,1] O'Byrne, Kenneth J.[3,1]

[1] Trinty College, Dublin, Ireland [2] Cardiothoracic Surgery, St. James's Hospital, Dublin, Ireland [3] Trinity College, Dublin, Ireland

Background: IL-20 is a pleiotrophic member of the IL-10 family and plays a role in skin inflammation and the development of haematopoietic cells. It has potent angiogenic, inflammatory and chemo-attractive characteristics with an involvement in rheumatoid arthritis and atherosclerosis. It activates STAT3, which in turn promotes proliferation, apoptosis resistance and immune tolerance. STAT3 activation is recognised as an important link between inflammation and cancer. It can function through IL-20Rα, IL-20Rβ and IL-22R1. Decreased expression of IL-20Rα in lung tissues of non-small lung cancer patients correlated with an increase in disease free survival.

Methods: A panel of cell lines were examined for the expression of IL-20, IL-20Rα and IL-20Rβ at the mRNA and protein level. This included three normal (HBEC 3, 4 & 5) and two lung cancer (A549-adenocarcinoma & SK-MES-1- squamous cell carcinoma) cell lines. The effects of a histone deacetylase inhibitor, Trichostatin A, (TSA-250ng/ml) and cycloheximide (10μg/ml) on the expression of the IL-20 family were examined. A CHiP assay was carried out to investigate the effect of TSA on the IL-20 promoter. Tumour and normal matched tissue from patients were examined at the mRNA and protein level for the IL-20 receptors.

Results: The mRNA expression pattern of IL-20 was different in the normal and lung cancer cell lines. There was moderate to high expression in the three normal cell lines compared with low to moderate levels in the cancer cell lines. A similar trend was observed with IL-20Rα and IL-20Rβ. The anti-angiogenic properties of IL-20 have previously been demonstrated in the lung. We investigated the effect of TSA on IL-20 expression. IL-20 was induced by TSA treatment in all cell lines and super-induced by cycloheximide in A549 and HBEC 4. Results from a CHiP assay performed on A549 cells demonstrates that the effect of TSA is and early and immediate response. The effect of TSA on the two receptors at mRNA level was much less pronounced on the cell lines with the exception of HBEC 4, which showed a minor increase of both with treatment. Further analysis of IL-20 and the receptors in clinical (adenocarcinoma and squamous cell carcinoma) samples revealed a somewhat different pattern between the two lung cancer types. At the mRNA level, IL-20 was downregulated in adenocarcinoma and upregulated in squamous samples. There was an increase in IL-20Rβ mRNA and protein in both tumour types. A significant difference was observed in IL-20Rα expression between the tumour types. In adenocarcinomas, IL-20Rα was predominantly downregulated at the mRNA level, with minimum detection at the protein level. However, in squamous samples the receptor was upregulated in tumours at both the mRNA and protein level.