Late-breaking abstract: Relationship of aquaporin 1, 3 and 5 expression in lung cancer cells to cellular differentiation, invasive growth and metastasis potential

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An oncogenic capacity of aquaporins (AQPs), transmembrane channels for water, was recently proposed. This study seeks to elucidate the involvement of AQP1, 3 and 5 in the development and progression of lung cancer. Expression analyses of AQP1, 3 and 5 by immunohistochemistry, western blot and real time RT-PCR in 160 lung cancers showed that AQP1, 3 and 5 were expressed in tumors of cells 71, 40 and 56%, of lung cancers, respectively. AQP expression was frequent in adenocarcinomas (ADCs), while AQP1 and AQP3 expressions were absent in squamous cell carcinomas. Bronchioalveolar carcinoma (BAC) cells exhibited an apical AQP1 and apical or basolateral AQP5 localization in non-mucinous type and apical AQP1 and 5 and basolateral AQP3 expression in mucinous type, which corresponded to AQPs expression of non-neoplastic lung tissue. Basolateral AQP5 expression was acquired during tumorigenesis of non-mucinous BAC. In contrast, invasive ADC tumor cells, either with fibroblastic reaction or papillary growth in the alveolar space, overexpressed AQP1 and 5 with loss of subcellular polarization and with an intracytoplasmic distribution. Overexpression of AQP1 correlated with high postoperative ADC metastasis ratios and unfavorable disease-free survival rates (p=0.031). We conclude that expression patterns of AQP1, 3 and 5 in lung cancer cells are mostly associated with cellular differentiation. However, the expression of AQP1 and 5 is up-regulated in invading lung cancer cells, particularly in ADCs, and the overexpression of AQP1 with loss of subcellular polarization is suggested to be involved in their invasive and metastatic potential.

Methods: After central randomisation, patients received either GIP (gemcitabine 1mg/m2 D1-8, ifosfamide 3g/m2, cisplatin 50 mg/m2), IG (gemcitabine 1mg/m2 D1-8, ifosfamide 3g/m2) or GP (dextemet 75 mg/m2, cisplatin 50 mg/m2). According to the ELCAP experience, an increase of the 1 year survival rate from 35% in the IG arm to 50% in the two cisplatin arms will require to observe 360 deaths.

Results: From 12/2003 to 03/2009, 693 eligible patients were randomised. Main characteristics were: median age 58 years, male/female 523/170, squa- mous/adenocarcinoma/other 152/386/155, Karnofsky PS 60-70/80-100 157/536, stage IIIB-IIIIV 129/564. The main results are:

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<th>IG GIP</th>
<th>GP</th>
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<tbody>
<tr>
<td>Response rate (95% CI)</td>
<td>27% (21-33)</td>
<td>33% (27-39)</td>
</tr>
<tr>
<td>Median PFS (95% CI)</td>
<td>3.6 (2.8-4.4)</td>
<td>4.1 (3.4-4.8)</td>
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<tr>
<td>1-year survival (95% CI)</td>
<td>38% (31-45%)</td>
<td>35% (29%-41%)</td>
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<tr>
<td>Median survival (95% CI)</td>
<td>8.9 (7.2-10.6)</td>
<td>9.6 (7.7-10.2)</td>
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</table>

Conclusions: In this large phase III trial, a non-platinum CT regimen (ifosfamide-gemcitabine) had similar activity to cisplatin-based CT in terms of survival, PFS and response rates with a favourable toxicity profile.
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Use of erlotinib in management of advanced non-small cell lung cancer (NSCLC): The Czech Republic experience with the treatment of a non-selected population of 1735 patients (pts)
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Erlotinib is the first EGFR TKI to be approved in Czech Republic for use in advanced NSCLC. This analysis presented examines data of all pts treated in Czech republic between 12/2005 and 12/2010. Data of all 1735 patients were summarised and retrospective analyses were carried out to determine if any associations were seen between specific characteristics and outcomes.

Of the 1735 pts with advanced NSCLC 35.6% were female and 64.4% male, 21.6% non-smokers, 39.5% former smokers and 38.9% current smokers. Median age was 65 years. Erlotinib was used as 1st line therapy in 14.4%, as 2nd line in 47.3% and as 3rd line in 38.3% pts. PS 0 was in 7.6%, PS 1 in 56.3%, PS 2 in 33.5% and PS 3 in 2.6% pts. Adenocarcinoma was confirmed in 45.9%, squamous-cell carcinoma in 39.2%, large-cell carcinoma in 4.0% and non specified carcinoma in 9.4% pts. CR was confirmed in 0.6%, PR in 123 7.1% pts, SD in 44.1% of pts; 23% of pts progressed and 25.2% pts were not evaluated. Skin toxicity was in 56.7%. Median survival (95% CI) was 7.5 months, PFS (95% CI) was 2.9 months. The differences between groups of pts according to PS (0 vs > 2) were statistically significant (p < 0.001). The best median survival (17.6 month) was in the group of pts with PS 0. Statistically significantly longer (p = 0.001) was mOS and mPFS survival in patients with skin toxicity, in female pts, in non-smokers and in pts with adenocarcinoma.

Erlotinib in this non-selected group of pts with advanced NSCLC was well tolerated and the results from Czech Republic are better then the data from BR.21 study and comparable with the results of TRUST.

Materials and methods: Two groups of consecutive patients with inoperable lung adenocarcinoma were investigated. Group A consisted of 20 patients that received initially carboplatin-paclitaxel with bevacizumab as first line chemotherapy and thereafter bevacizumab alone as maintenance therapy until progression. Group B consisted of 22 patients that received carboplatin-paclitaxel alone. Both groups had similar smoking history and comorbidities. Treatment options were assessed in terms of time to progression and side effects.

Results: Our patient groups consisted of 13 females and 29 males with a mean age of 61.8 years (range 42-82). Twenty seven patients were in stage IV. All patients were ex smokers with equivalence in regard with the smoking habit, the disease stage and the application of radiotherapy between groups A and B. The side effects were similar to both groups of patients (p>0.10). Time to progression was strongly associated with the therapeutic regimens; Group B presented with longer time to progression than Group A (p=0.002).

Conclusions: The addition of bevacizumab to carboplatin-paclitaxel in the treatment of consecutive patients with inoperable lung adenocarcinoma does not seem to confer a significant improvement in progression free survival and response rate.

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Intraoperative photodynamic therapy as a part of combined radical treatment for stage III NSCLC
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Background: Incomplete resections for lung cancer remain an important problem. To increase the radicalism we proposed an intraoperative photodynamic therapy (PDT) of resection margins.

Methods: 16 patients with central NSCLC (12 men, 4 women) were prospectively included in the study (10 – IIb, 6 – IIa). Hystological types were: squamous cell – 10, adenoc – 4, large cell – 2. At the time of diagnosis all patients were considered as unresectable or inoperable, reasons were tracheal involvement (7), functional intolerance to pneumonectomy (3) and N3 disease (2). Preoperative treatment included three cycles of chemotherapy and two courses of endobronchial PDT. During operation, after lung resection (pneumonectomy – 11, lobectomy – 5) intraoperative PDT of resection margins (bronchial and vascular stumps, mediastinum) was done. Chlorin e6 complex was used as a photosensitizer in dose of 2 mg/kg. The interval between the injection and illumination was 2 hours. Red light at 662±1 nm wavelength was used to achieve a total illumination dose of 250 j/cm².

Results: After preoperative treatment partial response of tumor was achieved in all cases and patients underwent surgery with radical intent. There was no post PDT complication. 14 operations were R0, 2 – R1. No major postoperative complications noted except cardiac arrhythmia in 3 patients (19%). Average period of follow-up was 16 months (4 to 30 months), all patients are alive without any signs of recurrence.

Conclusion: The first experience of the combined treatment including intraoperative PDT for locally advanced NSCLC demonstrates safety and effectiveness. Additional studies are needed to prove the value of intraoperative PDT.

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Carboplatin-paclitaxel alone or with bevacizumab in stage III-IV lung adenocarcinoma
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Introduction: Bevacizumab, a monoclonal antibody against vascular endothelial growth factor, has been shown to benefit lung adenocarcinoma patients when added to standard chemotherapy.

Aims and objectives: To assess the clinical efficacy of Bevacizumab in lung adenocarcinoma stage III-IV when added to standard chemotherapy with carboplatin and paclitaxel in a pragmatic tertiary healthcare setting.

Materials and methods: Two groups of consecutive patients with inoperable lung adenocarcinoma were investigated. Group A consisted of 20 patients that received initially carboplatin-paclitaxel with bevacizumab as first line chemotherapy and thereafter bevacizumab alone as maintenance therapy until progression. Group B consisted of 22 patients that received carboplatin-paclitaxel alone. Both groups had similar smoking history and comorbidities. Treatment options were assessed in terms of time to progression and side effects.

Results: Our patient groups consisted of 13 females and 29 males with a mean age of 61.8 years (range 42-82). Twenty seven patients were in stage IV. All patients were ex smokers with equivalence in regard with the smoking habit, the disease stage and the application of radiotherapy between groups A and B. The side effects were similar to both groups of patients (p>0.10). Time to progression was strongly associated with the therapeutic regimens; Group B presented with longer time to progression than Group A (p=0.002).

Conclusions: The addition of bevacizumab to carboplatin-paclitaxel in the treatment of consecutive patients with inoperable lung adenocarcinoma does not seem to confer a significant improvement in progression free survival and response rate.