Analysis of tumor texture on a pre-treatment CT scan predicts treatment outcome in NSCLC patients

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the only metastatic site in 32 (33.5%) pts or were associated with another site in 36 pts (37.5%) and with at least two other sites in 28 (29%) pts. The Karnofsky Performance Status was > 70% in 77 pts (88%). Radical surgery was performed in 9 pts while 4 pts received a stereotactic radiation surgery. 58 (59%) pts received CT after development of BM: 60% of pts just received one line, 26% had two lines, 14% 3 lines or more. 37 pts had synchronous BM. 54% received CT before RT and 57% after, the median time to the beginning WBRT was 3.6 m. The median overall survival was 8.7 m [4.1−56]. 59 pts developed metachronous BM with a median time of 10 m after diagnosis of the primary tumor, the WBRT begins after a median time of 1.15 m. The median overall survival after the diagnosis of BM was 5.7 m [0.4−44.5].

The median overall survival from time of BM diagnosis for all pts was 6.7 m [0.2−69.6]. Median overall survival since the first diagnosis of metastases (whichever the site) was 11.6 m [0.6−69.6].

Conclusion: Our results suggest that in NSCLC pts with synchronous BM, CT may be beneficial and that the sequence with WBRT should be better define.

9056 POSTER Evaluating the efficacy of zoledronic acid for the prevention of disease progression in patients with non-small cell lung cancer (NSCLC)

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Background: Bisphosphonates are effective inhibitors of bone resorption, and outcomes from preclinical and clinical studies have suggested that they have antitumor activity. Preclinical studies of zoledronic acid (ZOL) have demonstrated its ability to induce tumor cell apoptosis, inhibit angiogenesis, inhibit tumor cell adhesion and invasion, decrease tumor cell proliferation, and activate an immune response. Clinical studies in patients with early stage breast cancer suggest that ZOL improves disease-free survival and recurrence-free survival and may improve bone-metastases-free survival. These findings provide the rationale to investigate whether ZOL can prevent disease progression in patients with early stage NSCLC.

Table 1: Disease events in patients with NSCLC after primary therapy

<table>
<thead>
<tr>
<th>Bone metastases, n (%)</th>
<th>Ongoing treatment, n = 161</th>
<th>Discontinued treatment, n = 188</th>
<th>Total patients, n = 407</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone metastases, n (%)</td>
<td>2 (3.4)</td>
<td>4 (2.5)</td>
<td>20 (10.6)</td>
</tr>
<tr>
<td>Progression/Recurrence, n (%)</td>
<td>19 (32.8)</td>
<td>46 (28.6)</td>
<td>131 (69.7)</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>5 (8.6)</td>
<td>0</td>
<td>110 (58.5)</td>
</tr>
<tr>
<td>Progression/Recurrence/Death, n (%)</td>
<td>21 (36.2)</td>
<td>46 (28.6)</td>
<td>155 (82.4)</td>
</tr>
</tbody>
</table>

Currently the median follow-up of patients in this study is 12.9 months (range, 0.03−36.2 months). Updated preliminary safety and efficacy results from this trial will be presented.

9057 POSTER New dendritic cell immunotherapy approach: randomized phase II study in IIB-IIIA stage non-small cell lung cancer patients

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Background: Ex vivo-generated dendritic cells (DC) loaded with tumor vaccines have been used as vaccines to improve antitumor immunity in patients with different types of cancer since 1996. Currently, extensive studies to improve the immunotherapy approach based on DC-vaccine have been performed. Great emphasis is paid to finding new more efficient ways to load DC with tumor antigens. Our preclinical findings indicate that the mechanically heterogenized tumor cells (MHTC) used for DC loading is a very effective and promising approach. We report a phase II trial in non-small cell lung cancer (NSCLC) patients treated with DC pulsed with MHTC, following successful phase I results.

Material and Methods: Seventy-one patients with IIB-IIIA stage NSCLC, ECOG 0−1, without autoimmune disorders were enrolled. 28 patients had received DC-therapy in adjuvant regimen (4−9x10⁶ per injection), 43 patients underwent surgery (lobectomy, pneumonectomy) only. In the trial were used autologous DC of monocytic origin with expression of surface markers CD86 and HLA-DR at least 70%, CD83 ~ 50% obtained by flow cytometry. Adjuvant therapy with DCs loaded with MHTC was carried out in post-operative period for prevention metastasis development and recurrence of disease. DCs were injected i.v. in 1−2 courses. One course consisted of 5 injections with one-month interval. Groups of comparison were similar by histology stages, age, clinical and immunological monitoring of DC-vaccine therapy was performed. Special attention was focused on antigen specific antitumor immune response.

Results: DC-immunotherapy was well tolerated without significant toxicity. DC-therapy has improved of 3-year survival of patients. Overall survival of NSCLC patients for 3 year in the group with vaccine therapy was 66% vs 30%. During 3 year follow-up period in a group with DC-vaccine treatment disease progression occurred in 9 patients (32.1%), in a group with surgical treatment alone – in 28 patients (60.5%), 95% of patients showed significant antigen specific immune response after 3−5 DC-vaccinations. In responding to DC-vaccination patients, immunotherapy significantly boosted the IFN-γ and IL-2 producing T-cell response to autologous tumor challenge. Moreover, the increased functionality of T-cells, indicated by increased expression of markers for CTL activation, differentiation and proliferation was revealed.

Conclusions: There was clear evidence of clinical benefit of immunother-apy by DC pulsed with MHTC for NSCLC patients. This approach warrants further study.

9058 POSTER Analysis of tumor texture on a pre-treatment CT scan predicts treatment outcome in NSCLC patients

E. Rios Velazquez1, J.H. Aerts1, C. Dehing-Oberij1, S. Petit1, H. Eikelker2, D. De-Ruyscher3, A.N. Rief2, P. Lambin1, 1MAASTRO, Radiation Oncology, Maastricht, The Netherlands; 2Eindhoven University of Technology, Biomedical Engineering, Eindhoven, The Netherlands

Background: Early identification of patients at risk of treatment failure is an essential step to improve current treatments. We hypothesized that texture and shape attributes of the tumor on a pre-treatment CT scan correlate with patient outcome. We therefore developed a semi-automated recognition system for prediction of 2-years survival, after radiotherapy based on CT scans image traits.

Methods: 129 patients (38 women and 91 men) with inoperable NSCLC (stage IIIB-IV), treated with radical (chemo-)radiotherapy were included in this study. The primary gross tumor volume was delineated on a pre-treatment CT scan and was defined as the region of interest (ROI). A set of 30 image traits assessing gray level intensity and spatial distribution, size and shape of the tumor were extracted from this ROI. The cohort was randomly divided into five equally sized groups. In a combinatorial feature selection procedure a support vector machine model was built and validated using a five-fold cross validation approach. The model performance was expressed as the mean AUC assessed by the 5-fold cross validation. The combination of variables with the highest classification accuracy was included in the final model. Patient outcome was defined as 2-years survival calculated from the start of treatment.

Results: From the 30 extracted image features, 5 were included in the final predictive model: contrast, mean gray value, kurtosis, long run emphasis and compactness. These features encode textural and shape information.
of the tumor region on the pre-treatment CT scan. The AUC of the ROC curve of the final model on the validation set was 0.77 (95% CI, 0.69–0.85). Conclusion: Our results indicate that meaningful and reliable image traits extracted from the pre-treatment CT scan can predict patient outcome after treatment. The prediction of two year survival with our approach may be an important tool for the analyst in oncology to extract informative CT image traits that can assist them in the decision of treatment choice, allowing them with the possibility of treatment individualization.

Results: Our results demonstrate that patients carrying the GG CCND1 genotype present an increased risk for the development of NSCLC (OR = 1.57; 95% CI 1.17–2.10, P = 0.003). This genetic polymorphism was even more evident when considering the epidermoid histological type (OR = 1.84, 95% CI 1.30–4.07, P = 0.005). Multivariate logistic regression analysis adjusted by gender, age and tobacco smoke confirmed this association, indicating that individuals carrying two G-alleles present an increased risk of 2.7-fold for the development of lung cancer (aOR = 2.68, 95% CI 1.54–4.69, P = 0.001).

Conclusions: In conclusion, our results may be important in the definition of a biological predictive profile for the development of NSCLC within our population. Furthermore, the knowledge of the mechanisms involved in NSCLC carcinogenesis may help to identify targets for the development of chemoprevention or therapeutic strategies.

Lung cancer patients with bone metastasis in a US managed care plan

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Background: For lung cancer patients with bone metastasis, skeletal complications including fractures are common and cause considerable morbidity, reduce quality of life, and reduce survival. This study was designed to assess the impact of zoledronic acid (ZOL) and intravenous bisphosphonate (IVBP), in patients with solid tumor cancers, including lung cancer.

Methods: A claims-based analysis using commercial and Medicare Advantage data from over 45 US managed care plans was used to evaluate the relation between treatment persistence and follow-up duration in patients treated with ZOL compared with those who were not (non-IVBP). A secondary analysis assessing the effect of time to treatment with ZOL will also be conducted. Persistence was defined as the absence of a >45 day gap between ZOL treatments. Index date was set at bone metastasis or first ZOL fill. Age 18+ with a lung cancer and a bone metastasis diagnosis between 01/01/01 and 12/31/06, continuous enrollment in the health plan for 6 months pre-index, with no evidence of bone metastasis or IVBP in the pre-index period was required. Patients were followed until disenrollment (including mortality) or end of study (12/31/07). ANOVA tests were used to compare follow-up duration, a proxy for survival, between ZOL persistence groups.

Results: The study sample included 10,513 lung cancer patients; 1,729 in the ZOL cohort and 8,784 in the non-IVBP cohort. Mean age was 62.4 years (+11.24) and 59.0% of patients were male. 78.5% of patients were commercial enrollees. Mean Charlson was 4.67 (+2.95). Treatment persistence groups included in the analysis were 31–90 days (N = 475), 91–180 days (N = 239), 181–365 days (N = 133), >366 days (N = 44).

Persistent use of ZOL was associated with longer follow-up duration. There was a statistically significant difference (p < 0.001) in the unadjusted mean follow-up duration for the non-IVBP cohort, 216 days (+304), compared with 236 (+233; 95% 90–90 days persistence group); 330 (+259; 91–180 days); 425 (+237; 181–365 days); and 729 days (+418; >366 days). Persistent use of ZOL was associated with longer follow-up duration. There was a statistically significant difference (p < 0.001) in the unadjusted mean follow-up duration for the non-IVBP cohort, 216 days (+304), compared with 236 (+233; 95% 90–90 days persistence group); 330 (+259; 91–180 days); 425 (+237; 181–365 days); and 729 days (+418; >366 days).

Conclusions: This study showed that in cancer patients with lung cancer and bone metastasis, patients with longer periods of persistence with ZOL achieved the better outcomes in terms of longer follow-up duration in the health plans.