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Title: TTF-1 for prediction of response to chemotherapy in patients with locally advanced or metastatic small cell lung cancer (SCLC)

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Body: Background: The thyroid transcription factor-1 (TTF1) plays a crucial role in differentiating primary lung from other cancers, especially in adenocarcinoma (AC). Furthermore, data indicate a possible association between TTF1-status and overall survival (OS) in AC patients. So far, no impact on OS was described in SCLC patients. Besides OS, it is unknown if the TTF1-status influences chemosensitivity of SCLC and might therefore predict response to chemotherapy. Aim: To compare the response to chemotherapy in a population of patients with SCLC stage III/IV according to their TTF1-expression. Methods: We analyzed 294 patients (f, n=110; m, n=184) with SCLC stage III/IV (according to UICC-6, stage IIIA, n=32; IIIB, n=87; IV, n=175) diagnosed in our institution between 01/05 and 12/08. Median age was 65 (± 10) years. TTF1-expression was prospectively determined. Response to treatment was evaluated using the Response Evaluation Criteria in Solid Tumors (RECIST Version 1.0). The overall response rate (ORR) and the disease control rate (DCR) were calculated and compared between the group of TTF1-positive and TTF1-negative SCLC. Results: The information on TTF1 and response to treatment was available in 178 (77%) cases. 150 (84%) had TTF1-positive and 28 (16%) TTF1-negative SCLC. Analyzing the DCR, we observed a better response to treatment for patients with TTF1-expression (DCR 90%) as compared to those with TTF1-negative SCLC (DCR 71%; $p=0.013$). Regarding the ORR, there was no statistically significant difference between both groups (TTF1-pos. 75% vs. TTF1-neg. 71; $p=0.642$). Conclusion: TTF1-expression may be associated with better response to chemotherapy in SCLC.