Prospective evaluation of circulating VEGF in patients with advanced non-small cell lung cancer treated with bevacizumab, pemetrexed and cisplatin in the trial SAKK19/09

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Background: Bevacizumab is a monoclonal antibody directed against the vascular endothelial growth factor (VEGF). The previous phase II trial ABIGAIL (Reck, 2010) suggested circulating VEGF as a prognostic, but not predictive, biomarker for patients (pts) with non-small cell lung cancer (NSCLC) treated with bevacizumab. We prospectively measured VEGF in the multicenter phase II trial SAKK19/09 (NCT01116219).

Methods: SAKK19/09 enrolled 77 evaluable patients (pts) with previously untreated, advanced nonsquamous NSCLC and EGFR wild type. Pts received 4 cycles of cisplatin 75mg/m2 (or carboplatin AUC5), pemetrexed 500mg/m2 and bevacizumab 7.5mg/kg, followed by maintenance therapy with pemetrexed and bevacizumab until progression by RECIST1.1. Follow-up CT scans were performed every 6 weeks until week 54 and every 12 weeks thereafter. Baseline EDTA blood samples were sent by same-day courier to the central laboratory for centrifugation, aliquoting, and freezing. Upon completion of enrollment, aliquots were thawed, and VEGF quantification was performed centrally using Luminex® Performance Assay Human Base Kit A (R&D Systems, Abingdon, UK). The mean value was used to stratify pts into two groups (low versus high VEGF). Best response rate assessed by RECIST1.1 (CR+PR versus SD+PD).

Results: Clinical results of the SAKK19/09 trial were reported previously (Gautschi, 2013). Baseline plasma VEGF was detectable in 71 of 77 (92%) evaluable patients treated with chemotherapy and bevacizumab. The mean value was 74.9 pg/ml, the median 47.5 pg/ml, and the range 3.55 to 310 pg/ml. Using the mean as a predefined cutoff value, 50 patients had low VEGF levels and 21 patients had high VEGF levels. High VEGF was significantly associated with shorter PFS (4.1 vs 8.3 months, HR=2.56; 95%CI: 1.43- 4.57; p=0.0015) and OS (8.7 vs 17.5 months, HR=2.67; 95%CI: 1.37-5.20; p=0.0041), but not with best response rate (p=0.2256).

Conclusions: Consistent with the ABIGAIL trial, circulating VEGF was prognostic, but not predictive for response, in the current trial. Further work is ongoing to identify potentially predictive biomarkers for bevacizumab, using comprehensive proteomic analyses.

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