1072 A 2-gene panel derived from prostate cancer-enhanced transcripts in whole blood is prognostic for survival and predicts treatment benefit in metastatic castration-resistant prostate cancer

Eur Urol Suppl 2016;15(3);e1072

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INTRODUCTION & OBJECTIVES: Castration-resistant prostate cancer (CRPC) is a heterogeneous disease with enormous variability of survival and treatment response. To determine a prognostic model derived from prostate cancer-enhanced transcripts in whole blood of CRPC patients and explore its applicability as a surrogate of treatment response.

MATERIAL & METHODS: Six out of 23 selected transcripts were identified as specific for detection of metastatic prostate cancer cells in peripheral blood using quantitative polymerase chain reaction (qPCR). Their prognostic value was explored in whole blood samples of a training cohort (n=22 CRPC patients, New York, USA). A resulting 2-gene panel (2GP) including KLK2 and TMPRSS2 was validated in an independent cohort with pretreatment and posttreatment blood draws after 9-16 weeks of systemic treament (n=86 CRPC patients, Munich, Germany). Overall survival (OS), prostate-specific antigen-progression-free survival (PSA-PFS) and clinical PFS were analyzed. Kaplan Meier and cox regression analyses were performed.

RESULTS: An unfavourable 2GP (≥1 marker positive) identified patients with poor survival (median OS 10.0 months [95% CI 5.7-14.2] vs. not reached; p=0.023). This was validated in an independent cohort at pretreatment (median OS 7.8 [95% CI 6.5-9.2] vs. 17.3 months [95% CI 10.7-23.8]; p=0.004) and posttreatment blood draw (median OS 5.0 [95% CI 0.0-10.0] vs. 18.0 months [95% CI 9.5-26.6]; p=0.003). The 2GP independently predicted OS on multivariate analysis (hazard ratio 2.1 [95% CI 1.1-4.0]; p=0.034) and performed better than PSA decline at correlation with OS.
Conversion to favourable 2GP during treatment correlated with improved OS, PSA-PFS and clinical PFS.

CONCLUSIONS: We established a 2GP which is prognostic for survival at pre- and posttreatment blood draw in CRPC patients. Conversion to favourable 2GP predicts treatment benefit which merits further prospective investigation of its use as a surrogate of treatment response.