

Tumoral expression of pyruvate kinase L/R as a predictive marker for treatment of metastatic renal cancer patients with sunitinib and sorafenib



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Patients with metastatic renal cell cancer (mRCC) are commonly treated with the tyrosine kinase inhibitors (TKI) sunitinib and sorafenib. No predictive marker is available to select patients who will gain from these treatments. Tumoral pyruvate kinase L/R (PKLR) is a membrane protein with highly specific expression in the renal tubule. We have previously shown that the tumoral expression of cubilin is associated with progression free survival (PFS) in mRCC patients treated with sunitinib and sorafenib and in the present study; we investigated if PKLR can predict response in these patients. The expression of PKLR was analyzed in tumor tissue from a cohort of patients with mRCC (n=139) using immunohistochemistry. One hundred and thirty-six (136) of these patients were treated with sunitinib or sorafenib in the first or second-line setting. Thirty were censored because of early toxicity leading to the termination of treatment. The remaining patients (n=106) were selected for the current study. Fifty-five (55%) of the tumors expressed membranous PKLR. Patients with PKLR tumor expression experienced a significantly longer PFS compared to patients with no expression (eight vs. five months, p=0.019). In addition, the combined expression of PKLR and cubilin resulted in a higher predictive value than PKLR alone. We show that tumoral PKLR membrane expression is a positive predictive biomarker for sunitinib and sorafenib treatment in patients suffering from mRCC. Our results also indicate that the combined expression with cubilin more accurately than PKLR alone can select patients with no benefit from treatment.

Biography

Marjut Niinivirta is an Oncologist working at the Uppsala University Hospital in Sweden and pursuing PhD at Uppsala University, researching on predictive markers in renal cell cancer.

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Figure 2: Progression free survival for renal cancer patients treated for metastatic disease with sunitinib or sorafenib in the first or second line setting, comparing membranous negative tumors (PKLR-, n=51) versus positive tumors (PKLR+, n=55)

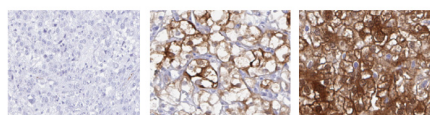


Figure 1: Negative (A), incomplete (B) and complete (C) membranous PKLR staining in primary renal cell carcinoma

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