# Biomarkers predict benefit of targeted therapy in metastatic renal-cell cancer

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MedWire News: In metastatic renal-cell cancer, the level of cytokines and angiogenic factors (CAF) identify those patients with an aggressive disease course who derive the greatest benefit from treatment with the molecular-targeted therapy pazopanib, a retrospective analysis of clinical trials shows.

By contrast, clinical classifications offer prognostic information but do not predict treatment benefit.

The findings "support the use of CAF profiling to define biologically distinct subgroups of patients," study co-author John Heymach (University of Texas MD Anderson Cancer Center, Houston, USA) and colleagues comment in *TheLancet Oncology*.

Pazopanib targets the increased expression of vascular endothelial growth factor (VEGF) is associated with increased angiogenesis and is prognostic of overall survival in renal-cell carcinoma.

Heymach and team assessed the prognostic and predictive associations of pretreatment plasma concentrations of CAFs with data from a phase II and a phase III trial of pazopanib treatment.

They first screened 17 CAFs in 129 patients who had the greatest or least tumour shrinkage in a phase II trial of 215 patients treated with pazopanib. From this, five candidate markers emerged - interleukin 6, interleukin 8, hepatocyte growth factor (HGF), tissue inhibitor of metalloproteinases 1(TIMP-1), and E-selectin.

Confirmatory analyses in the full 215 patients identified associations of interleukin 6, interleukin 8, VEGF, osteopontin, E-selectin, and HGF with continuous tumour shrinkage or progression-free survival (PFS) in patients treated with pazopanib.

These markers were then validated in a separate phase III trial of 344 patients, in which those treated with pazopanib who had high concentrations (relative to median) of interleukin 8, osteopontin , HGF, and TIMP-1 had shorter PFS than did those with low concentrations.

By contrast, high concentrations of interleukin 6 were predictive for improved relative PFS benefit from pazopanib compared with placebo.

"This juxtaposition suggests that patients with tumours that have greater angiogenic drive fare worse than do patients without such tumours, but that this deleterious effect can be at least partially abrogated by pazopanib treatment," Heymach et al comment.

Indeed, other examples exist of markers whose expression leads to poor prognosis but improved relative benefit from specific therapy, for example, in breast cancer, HER2 and targeting with agents such as trastuzumab or lapatinib.

In conclusion, the authors say CAF profiling has several advantages including straightforward and relatively noninvasive sample collection, availability of several robust analytical platforms, and the ability to monitor changes during treatment or disease progression.