World Cancer Research Journal WCRJ 2014; 1 (4): e343

METASTATIC RENAL CANCER PROGNOSTIC AND PREDICTIVE BIOMARKERS. REVIEW

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Sorafenib was approved by the US food and Drug Administration in 2005, and since then significant progress in systemic therapy of metastatic renal cell carcinoma (mRCC) has been made[1]. Although our armamentario can now rely on a plethora of targeted agents approved in such a clinical setting, a portion of mRCC patients do not respond to these treatments yet. Moreover, prediction of clinical outcome by means of validated biomarkers is currently lacking[2]. The most widely used score system are the Memorial Sloan Kettering Cancer Center (MSKCC) – or Motzer- criteria, which stratify patients according to five prognostic factors (i.e., LDH; Karnofsky performance status less than 80; time elapsed between diagnosis and treatment of less than 1 year; and haemoglobin and calcium serum levels) that significantly correlates with overall survival (OS). This model identified six clinical parameters useful to stratify patients into *good, intermediate, and poor prognosis groups*[3]. We therefore read with interest, in this issue of the WCRJ, D'Aniello et al's review on the prognostic and predictive role of biomarkers in mRCC. Their aim was to describe the main biological and clinical factors that have a substantial impact on treatment decision-making[4]. Since RCC is a heterogeneous tumour that involves several molecular pathways in its development, it is difficult to predict individual response to treatment and clinical benefits. The main difficulty for the definition of specific and generalized tumour characteristics concerns the intra-tumour heterogeneity, and the lack of tumour specimens for translational research. The authors describe the most studied biomarkers, tissues, clinical and genetic factors useful for early identification and to better select the optimal therapy in each stage of disease development. Interestingly, the prognostic impact of tissue factors was also evaluated. Among clinical factors, arterial hypertension is reported to be associated with anti-VEGF therapy, and it appears to be a class effect. Data suggest that hypertension secondary to treatment with sunitinib is associated with improvement in clinical outcomes (i.e., objective response rate, PFS, and OS) and similar results have been observed with other anti-VEGF agents. mTOR inhibitors, for instance, may also have antiangiogenic activity, and treatment emergent hypertension has been observed as a consequence of treatment with non-VEGF therapy. Noteworthy from the review, hypothyroidism and the hand-foot syndrome show a significant predictor value too. Finally, the authors recorded the impact of genetic factors, particularly the expression of selected genes such as VHL, and proteins such as VEGF and CAIX. In conclusion, the review by D'Aniello and colleagues represents an exhaustive and useful tool for clinicians, and it further highlights the importance of a thorough clinical and biological evaluation of mRCC patients treated with a targeted agent.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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