Topics: CTCs / CECs (circulating tumor cells/ circulating epithelial cells)

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Abstract

Title

Early increase of Circulating Endothelial Cells (CECs) predict treatment effectiveness in metastatic renal cell carcinoma (mRCC) under tyrosine-kinase inhibitors (TKIs)

Authors

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**Background**

Oral TKIs improved mRCC outcome, in both progression-free survival (PFS) and overall survival (OS). However, biology of mRCC and response to VEGFR-targeted agents are heterogeneous, and clinicians lack marker of treatment effectiveness.

We planned a prospective non-interventional study, to evaluate prevalence and prognostic/predictive value of CECs in mRCC receiving first line TKI.

**Patients and methods**

After the Ethics Committee approval at IOV-IRCCS and participating hospitals, from June 2008 and December 2015 we enrolled 246 mRCC patients, upon signed informed consent.

Blood samples were collected at baseline (T0) before the first dose of TKI, then at day 28 (T1), at day 56 (T2) and then at progression or at 12 months in the absence of progression (T3).

According to manufactures instructions, we quantified CECs by CellSearch platform, as cells exhibiting the phenotype CD146+, CD105+, DAPI+ and CD45-, and expressed as CEC number per 4 ml peripheral blood (PB).

**Results and conclusion**

Study primary objective was the prognostic value of Circulating Tumor Cells (CTCs) on PFS and OS of mRCC under a first-line TKI. Pilot study data (n=53) has been elsewhere published (Rossi et al., BJC 2012), whilst the CTC results of the overall cohort (n=246) have been submitted for publication.

In 135 out of 246 patients, we analyzed CEC at baseline and at least 1 subsequent time-point of blood draws schedule.

As previously reported, baseline CTC number >_ 3 cells was prognostic of shorter PFS and OS, (Basso et al., JCO 2017), conversely the baseline CEC level did not.
Here we showed that CEC number increased from T0 (median = 19) to T1 (median = 25), and T2 (median = 31). Noteworthy, at T1 (n=123) by using the 3rd quartile as cut-off value (48 CECs/4 ml PB) we found a significant association between CEC level and longer OS (1624 and 777 days, for > and < 48 CECs, respectively, according to Kaplan-Meier, log-rank test, p=0.012).

Our data confirm that CTCs at baseline are prognostic for mRCC, whilst the CECs number at 28° day is a predictor of treatment efficacy in patients receiving TKIs.

OS according to CEC level at T1 (n=123)