Author's response to reviews

Title: Circulating endothelial cells are an early predictor of tumor response in renal cell carcinoma patients treated with sunitinib

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Author's response to reviews: see over
Dear Dr. Norton,

Please find enclosed a revised version of our original article, which I submit on behalf of my co-authors. The major reviewers criticism was based on the limited number of patients and the difficulties, which arise from such a small cohort. The definition of groups according to RECIST criteria into PD, SD and PR/CR has also been questioned.

We therefore calculated the median PFS for sunitinib treatment and divided our population equally into subgroups with either superior (PFS above the median) or inferior (PFS below the median) clinical outcome. CEC, sVEGFR2 and monocyte counts have been re-calculated for both cohorts and implemented in the paper. Indeed, the reviewers’ concerns regarding the significance of pre-therapeutic measures of sVEGFR2 and monocytes as a predictor of clinical outcome were confirmed in this current analysis. However, the increase of CEC compared to baseline remained significant in the group with PFS above the median, only. Despite the small cohort of patients tested in our study, we believe that the current analysis reflects more robust results due to stratification of patients by either superior or inferior clinical outcome.

For previous figures 2A and 4A it has also been suggested to display patients with repeated measurements only. We therefore amended the design of the current figures accordingly (now 3A and 5A). Furthermore, we enclosed a figure displaying CEC counts in patients with distinct clinical response (based on PFS), as previously suggested. Another figure depicting PFS by Kaplan-Meier curve has been added as Fig. 2.

Response by histology has been added into the text, measures for response and baseline CEC counts have been evaluated in clear cell RCC and others. There is a slight imbalance between histology groups in favor of ccRCC (OR+SD 83 vs. 60%), which is pronounced by the small numbers of these histologies (failures in 4 ccRCC vs 2 others).

Sincerely,
Yours,
Dr. med. Viktor Grünwald