Lesion detection by ceCT, 89Zr-girentuximab and FDG PET/CT in newly diagnosed patients (pts) with metastatic clear cell renal cell carcinoma (mccRCC)


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Background: As slow disease progression is observed in a subset of mccRCC patients, watchful waiting can be considered, thereby postponing toxicity of systemic treatment. To identify those patients, the IMPACT trial evaluated the role of anti-Carbonic

AdipoR2 was generally lower expressed than AdipoR1 in mRCC tumor sections. Adiponectin expression in tumors was observed by immunohistochemistry. Assays with RCC cell lines were used to examine the signal transduction pathways of adiponectin in RCC.

Results: Investigation of the variations in AdipoR1 and AdipoR2 expression in 230 mRCC tumor samples showed that AdipoR1 expression in mRCC tumor samples was significantly lower than AdipoR2 (Fisher’s exact test, p < 0.001). AdipoR1 expression, but not AdipoR2, was a significant independent predictor of favorable responding to TKI and good survival outcomes. In contrast to AdipoR1, AdipoR2 expression was not associated with progression or survival.

Discussion: Our findings indicate that AdipoR1 is an important receptor for adiponectin in mRCC. These results show that AdipoR1 is a potential prognostic marker for the subset of patients who will respond favorably to TKI therapy. The role of AdipoR2 as a receptor for adiponectin in mRCC needs further investigation.

Conclusion: AdipoR1 expression is a predictor of favorable response to TKI therapy and good survival outcomes in mRCC patients. AdipoR2 expression is not associated with progression or survival. These results suggest that AdipoR1 could serve as a target to impede tumor progression and sensitize tumors to TKI therapy.
Anhydrase IX antibody $^{89}$Zr-girentuximab and $^{18}$F-fluorodeoxyglucose (FDG) PET/CT (PET). Here, we report preliminary analyses of a secondary endpoint: comparison of baseline contrast-enhanced (ce)CT, $^{89}$Zr-girentuximab and FDG PET to detect metastases.

**Methods:** mcrRCC pts with good or intermediate prognosis (according to IMDC) and eligible for watchful waiting were included. Patients underwent 3 scans, i.e. ceCT, $^{89}$Zr-girentuximab and $^{18}$F-FDG PET. So far, baseline scans of 29 of the 40 pts to be accrued were independently reviewed by 3 experienced readers. Lesions by ceCT were defined positive according to RECIST1.1. For lesions with prominent uptake of $^{89}$Zr-girentuximab or $^{18}$F-FDG, maximum Standardized Uptake Values (SUVmax) were calculated. Analyses were performed on a lesion level, taking clustering of data within patients and lesions into account.

**Results:** In total 335 lesions were detected by at least one modality (mean 11(2-33) per pt); ceCT detected 52% (95% CI: 45-58), $^{18}$F-FDG PET 61% (95% CI: 55-67) and $^{89}$Zr-girentuximab PET 69% (95% CI: 63-74). Differences in lesion detection varied across organ sites ($p<0.001$). Lesions were visualized by ceCT and $^{18}$F-FDG PET in all pts, whereas $^{89}$Zr-girentuximab-PET detected lesions in 27 of 29 pts. Compared to ceCT, $^{89}$Zr-girentuximab PET visualized additional lesions in all organ sites. Location was strongly related with $^{89}$Zr-girentuximab uptake; highest uptake in kidney and adrenal gland tumor (mean SUVmax 63.2 and 70.3, resp) and lowest uptake in lung and lymph nodes (mean SUVmax 10.9 and 15.0, resp). After correction for location, no relation was observed between $^{89}$Zr-girentuximab SUVmax and tumor size, as measured by ceCT, and $^{18}$F-FDG SUVmax.

**Conclusions:** $^{89}$Zr-girentuximab and $^{18}$F-FDG PET visualize additional lesions compared to ceCT, however correlation was poor. The addition of $^{89}$Zr-girentuximab or $^{18}$F-FDG PET might aid in deciding to either delay or start systemic treatment.

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