

## The prognostic role of nephrectomy in patients (pts) with metastatic renal cell carcinoma (mRCC) treated with immunotherapy according to the novel prognostic Meet-URO score: Subanalysis of the Meet-URO 15 study.

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**Background:** Most of mRCC pts with favorable and intermediate prognosis, according to the IMDC classification, are offered a nephrectomy. However, in the immunotherapy era, the role of nephrectomy is still unclear. In the Meet-URO 15 study we reported the higher prognostic accuracy of the Meet-URO score compared to the IMDC score, by the addition of the neutrophil-to-lymphocyte ratio (NLR) and the presence of bone metastases to the IMDC score, identifying five categories with progressively worse prognosis. For this reason, we aimed to explore the prognostic impact of the previous nephrectomy (PN) on mRCC pts receiving immunotherapy and according to the Meet-URO score groups. **Methods:** The Meet-URO 15 study was a multicentric retrospective analysis on 571 pretreated mRCC pts receiving nivolumab. Univariable analysis of the correlation between PN and overall survival (OS) and multivariate analysis adjusted for IMDC score, therapy line, NLR and metastatic sites were performed. The interaction of PN with the Meet-URO prognostic groups was then evaluated. **Results:** 503/571 pts (88%) underwent PN. A reduced risk of death (HR = 0.44; 95% CI: 0.32-0.60;  $p < 0.001$ ) and higher mOS and OS rate were observed in pts with PN than without (mOS: 36 vs 13 months; 1-year-OS 72% vs 52% and 2-year-OS 57% vs 24%, respectively). The reduced risk of death for pts who underwent PN was confirmed at the multivariate analysis (HR = 0.69; 95% CI: 0.49-0.97;  $p = 0.032$ ). The percentage of pts receiving PN progressively reduced through the five Meet-URO prognostic groups (PN: group 1: 98%, group 2: 95%, group 3: 84%, group 4: 79%, group 5: 59%). No significant interaction was observed between the PN and Meet-URO score when all the five groups were considered ( $p = 0.17$ ). A significant interaction was observed when the Meet-URO groups 1, 2 and 3 were taken together (HR = 0.40; 95% CI: 0.25-0.63;  $p < 0.001$ ), highlighting the significant protective role of the PN on OS for these three groups. For the Meet-URO groups 4 and 5, the interaction was indeed not significant (HR = 0.81; 95% CI: 0.51-1.30;  $p = 0.39$ ). **Conclusions:** PN has a favourable prognostic impact on pretreated mRCC pts receiving immunotherapy. This benefit may be limited to mRCC pts with more favorable diseases as belonging to Meet-URO prognostic groups 1, 2 and 3. Further analysis of the type of PN (i.e., radical vs cytoreductive) is ongoing and confirmatory prospective evaluations are warranted. Research Sponsor: Italian Ministry of Health (Ricerca Corrente 2018 - 2021 grants).