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Treatment beyond progression in primary refractory mRCC during 1L systemic therapy (Meet-Uro 33)

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Introduction

The optimal management of metastatic renal cell carcinoma (mRCC) patients (pts) experiencing progressive disease (PD) at the 1st radiological assessment during 1st line therapy (primary refractory pts) remains undefined. While treatment beyond progression (TBP) may be appropriate for selected pts with clinical benefit, evidence on pts selection and survival outcomes in this setting is limited.

Methods

Meet-Uro 33 is an ongoing Italian multicenter retrospective/prospective observational study of mRCC pts receiving 1st line ICI-ICI, ICI-TKI or TKI. Among primary refractory pts, we compared clinical

characteristics, overall survival (OS) and 2nd line therapy between pts receiving TBP and those who did not (non-TBP).

Results

Of 2027 pts enrolled, 242 (12%) were primary refractory: 46 (19%) TBP pts and 196 (81%) non-TBP pts. TBP pts were more likely to have IMDC favorable-risk (26% *vs* 5%) and Meet-URO score group 1 (23% vs 4%) (both: $p < 0.001$), a lower metastatic burden (41% *vs* 27% for 1 metastatic site, $p = 0.04$) and more frequently received nivo+cabo or pembro+lenva (28% *vs* 12%, 11% *vs* 7%; $p = 0.02$) compared to non-TBP pts. In TBP pts, subsequent best response was PD in 56.5%, while disease control (response or stable disease) in 17.4% pts. The mOS of all primary refractory pts was 8.3 months: TBP pts had significantly longer OS than non-TBP pts (7.3 *vs* 14.1 months, $p = 0.0004$). Overall, 122/242 pts (50%) received 2nd line therapy, including 19/46 TBP pts (41%) and 103/196 (53%) non-TBP pts. No statistically significant difference in 2nd line therapy choice ($p = 0.13$) was observed, although 2nd line TKI use was numerically higher in non-TBP (92% *vs* 79%).

Conclusions

Among primary refractory pts, TBP was preferentially adopted in pts with favorable prognosis, low tumor burden and in those receiving highly active ICI-based combinations. TBP was associated with longer OS, despite a lower rate of subsequent 2nd line therapy. These findings support the potential role of TBP in carefully selected patients with ongoing clinical benefit despite early radiological progression. Future studies are warranted to define optimal selection criteria and validate the survival impact of this strategy.