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Introduction & Objectives: Several immune checkpoint inhibitor (ICI) combinations as well as ICI / VEGF TKI combinations are currently under investigation for the treatment of front-line metastatic renal cell carcinoma (mRCC). The outcome of patients who progress on these new combination regimens is however largely unknown.

Materials & Methods: This is a multicenter retrospective analysis of patients with clear-cell mRCC who received front-line treatment with and progressed on either axitinib/pembrolizumab or axitinib/avelumab combination therapies and received subsequent targeted therapy. Data was collected from 4 institutions (Bart's Cancer Institute, Cleveland Clinic, CHU de Québec, Central Clinical Hospital, Moscow) in compliance with IRB guidelines of each participating institution.

Results: 14 patients had progression of disease on ICI / VEGF TKI and received subsequent targeted therapy. The median age was 59 (range 44-75). All patients were male; 71% had KPS \geq 80. IMDC risk groups for favorable, intermediate and poor were 14%, 57% and 29%, respectively. Prior ICI/VEGF TKI therapy included axitinib/pembrolizumab (64%) and axitinib/avelumab (36%). All patients received at least 1 subsequent therapy (57% cabozantinib, 29% sunitinib, 7% lenvatinib and 7% pazopanib). The overall best response rate to first subsequent therapy was 36% partial response (PR), 21% stable disease (SD) and 43% progression of disease (PD). The median progression free survival (PFS) for first subsequent therapy was 9 months (95%CI 0,7 – 18) and median overall survival (OS) 14 months (95% CI 10 –NR).

Conclusions: Subsequent TKI therapy after initial ICI/VEGF TKI combination shows modest activity and should be the subject of further investigation. Additional data is expected in the near future.