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Introduction & Objectives: Non-clear cell renal cell carcinomas (non-ccRCC) account for about 20% of malignant renal tumours in adults, including several histologies with different biological behavior and are underrepresented in clinical trials, which limits our evidence for their treatment. We aim to study the clinical outcomes of non-ccRCC metastatic patients treated with targeted therapy in a Portuguese oncology reference center.

Materials & Methods: Retrospective study of non-ccRCC metastatic patients treated from January 2007 to December 2018. Demographic, pathological and clinical data were collected from clinical records. Primary endpoint was overall survival (OS) and secondary endpoint was progression-free survival (PFS) to first (1st) and second (2nd) line targeted therapy.

Results: We identified 232 patients with metastatic RCC treated in our oncological center and 49 (21,1%) had a non-ccRCC, from those 38 were male (77,6%) and median age was 62 years (29-88).

Papillary histological type was the most common (40,8%), followed by unclassified non-ccRCC (38,8%), chromophobe (16,3%), one case of MiT family translocation and another of succinate dehydrogenase-deficient RCC. 42,9% patients had stage IV disease at diagnosis. Lymph nodal and lung metastasis were the most frequent (42,9% and 40,8%, respectively), followed by bone (24,5%) and liver (20,4%) metastasis. 65,3% had undergone nephrectomy and five patients were treated with metastasectomy. In 1st line, most of the patients were treated with anti-vascular endothelial growth factor (VEGF) therapy, including sunitinib (46,9%), pazopanib (10,2%) and sorafenib (4,1%), followed by temsirolimus (18,4%), interferon (16,3%) and best supportive care for 2 patients. Twenty-five patients received 2nd line therapy, mainly with anti-VEGF therapy (72,0%) and the remaining with mammalian target of rapamycin (mTOR) inhibitors. The median OS of metastatic disease was 24,2 months (95%CI 15,2–33,2). The median PFS to 1st line therapy was 11,2 months (95%CI 10,2–12,1) with no statistical differences between anti-VEGF (11,2 months, 95%CI 6,5–15,9), mTOR inhibitor (10,5 months, 95%CI 0,8–20,2) and interferon (11,2 months, 95%CI 0,04–22,3), $p=0,413$. The median PFS to 2nd line therapy was 5,8 months (95%CI 0,9–10,7), namely 10,3 months with anti-VEGF therapy and 2,8 months with mTOR inhibitors ($p=0,108$).

Conclusions: Our results confirm the poorer prognosis of metastatic non-ccRCC and evidences the evolution of treatments for RCC during the last decade. There was no statistical difference between 1st line treatments which can be reflection of our small sample size. The results obtained with interferon may suggest that immunotherapy may be a future therapeutic option, although the characteristics and heterogeneity of our retrospective study are a limitation. Clinical trials or larger observational studies of non-ccRCC are warranted.