Supplementary Material

Real-world impact of upfront cytoreductive nephrectomy in metastatic non-clear cell renal cell carcinoma treated with first-line immunotherapy combinations or tyrosine kinase inhibitors (a sub-analysis from the ARON-1 retrospective study)

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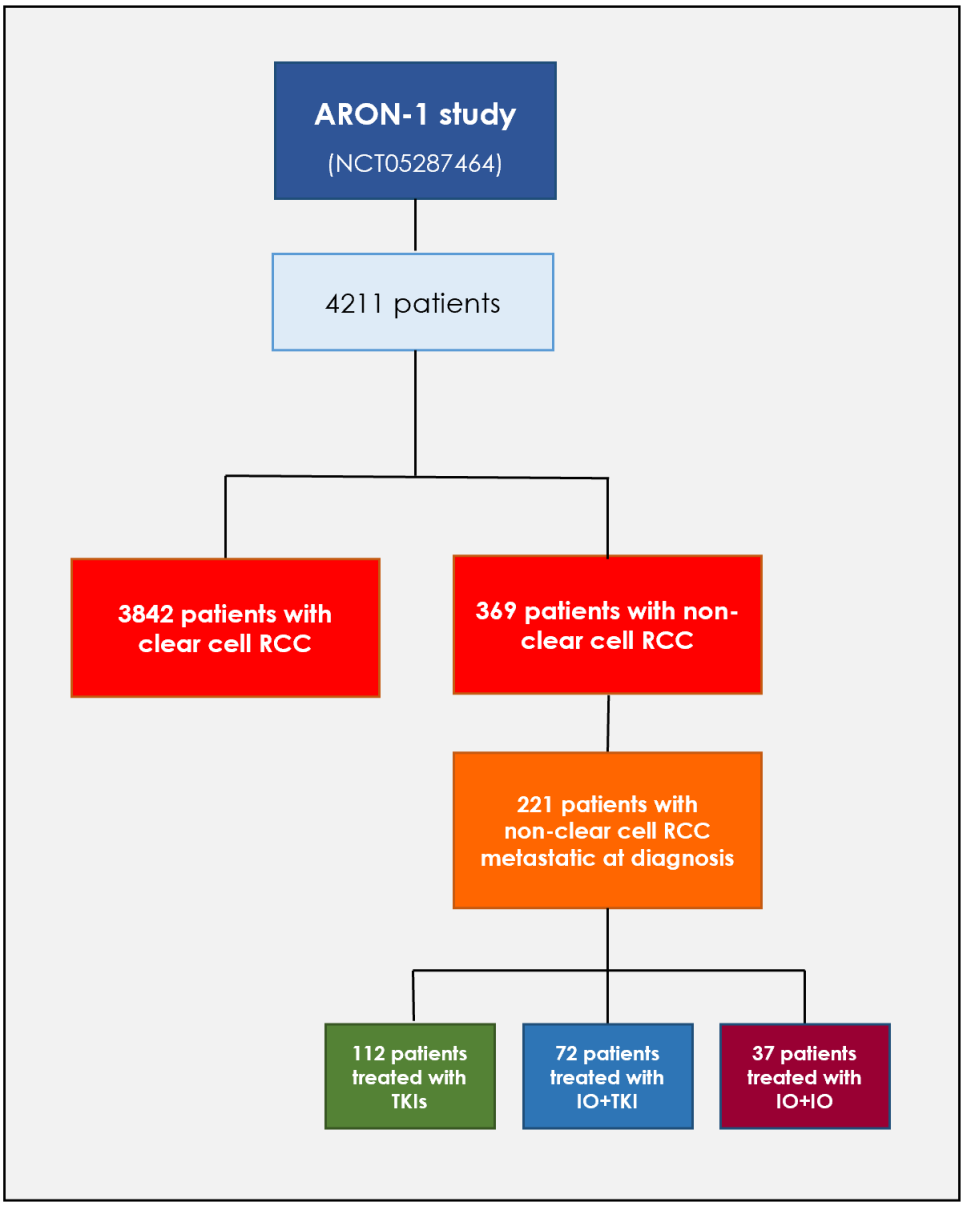
Overall and progression-free survival in specific groups

According to the IMDC risk, intermediate-risk patients showed longer OS compared to poor-risk patients (30.0 months, 95%CI 24.8–41.7 *vs* 13.3 months, 95%CI 9.2–23.9, *p*<0.001, **Figure S2**), while the difference in PFS was not significant (10.0 months, 95%CI 6.6–80.0 *vs* 6.5 months, 95%CI 4.8–10.1, *p*=0.217, **Figure S2**).

Stratified by the first-line therapy, the median OS was 26.9 months (95%CI 22.1–36.8) *vs* 24.9 months (95%CI 22.3–35.3) for patients receiving TKI monotherapy or IO combinations, respectively (*p*=0.579), with a 2y-OS rate of 55% for both subgroups. According to the IMDC risk, in the intermediate-risk patients the median OS was 28.8 months (95%CI 22.3–35.3) for IO combinations *vs* 30.0 months (95%CI 24.9–71.3) for TKI monotherapy (*p*=0.962) and in the poor-risk patients, the median OS was 12.7 months (95%CI 7.0–15.4) for IO combinations *vs* 16.7 months (95%CI 11.0–27.7) for those receiving TKI monotherapy (*p*=0.593). The median PFS was 13.0 months (95%CI 8.3–16.9) for patients treated with IO combinations *vs* 6.5 months (95%CI 5.3–80.0) for those receiving TKI monotherapy (*p*=0.002, **Figure S3**). In the intermediate-risk patients, the median PFS was 15.9 months (95%CI 8.8–26.4) for IO combinations *vs* 6.5 months (95%CI 5.3–80.0) for TKI monotherapy (*p*=0.003, **Figure S3**). In the poor-risk patients, the median PFS was 10.1 months (95%CI 3.2–15.2) for IO combinations *vs* 6.0 months (95%CI 3.9–7.4) for those receiving TKI monotherapy (*p*=0.264).

According to the IMDC risk groups, in the intermediate-risk and poor-risk patients, the median OS with IO+TKI was 31.1 months (95%CI 20.8–40.5) and 15.4 months (95%CI 7.0–15.4), while IO+IO combination showed median OS 28.8 months (95%CI 7.8–28.8, *p*=0.628) and 7.7 months (95%CI 2.6–11.9, *p*=0.100) in the two IMDC groups, respectively. In the intermediate-risk patients, the median PFS was 16.8 months (95%CI 12.8–18.6) for IO+TKI and 8.3 months (95%CI 4.1–47.6) for IO+IO (*p*=0.213). In the poor-risk patients, the median PFS was 12.7 months (95%CI 3.2–23.5) for IO+TKI *vs* 6.0 months (95%CI 2.0–15.0) for IO+IO (*p*=0.382).

Figure S1. Patients' selection process from the ARON-1 study.


ARON-1 study
(NCT05287464)
4211 patients
3842 patients with clear cell RCC
369 patients with non-clear cell RCC
221 patients with non-clear cell RCC metastatic at diagnosis
112 patients treated with TKIs
72 patients treated with IO+TKI
37 patients treated with IO+IO

RCC = renal cell carcinoma; IO = immuno-oncology; TKI = tyrosine kinase inhibitor

Figure S2. Kaplan-Meier estimates of progression-free survival and overall survival according to IMDC risk.

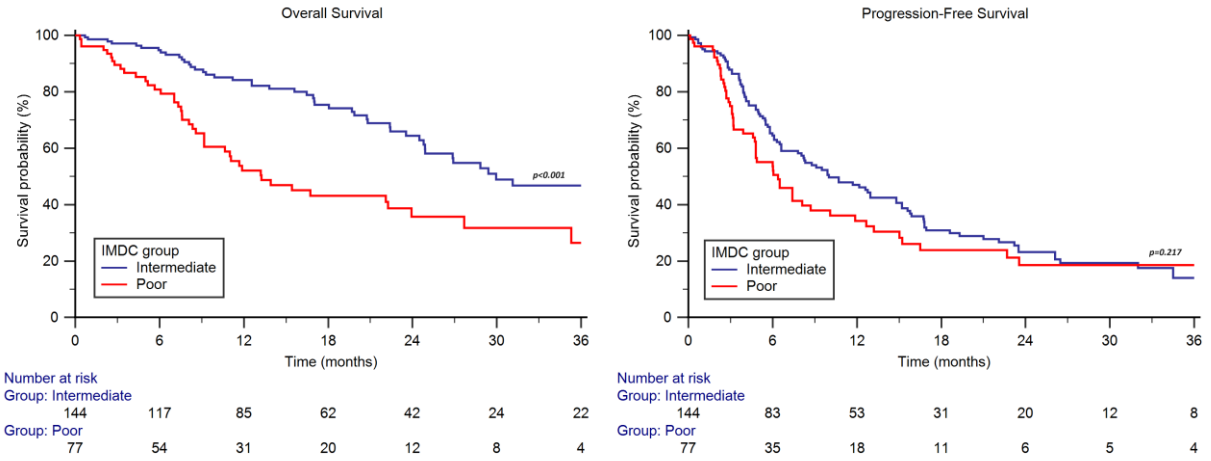


Figure S3. Kaplan-Meier estimates of progression-free survival according to the type of first-line therapy. Comparison between tyrosine kinase inhibitor (TKI) monotherapy and immuno-oncology (IO) combinations.