

Supplementary materials

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

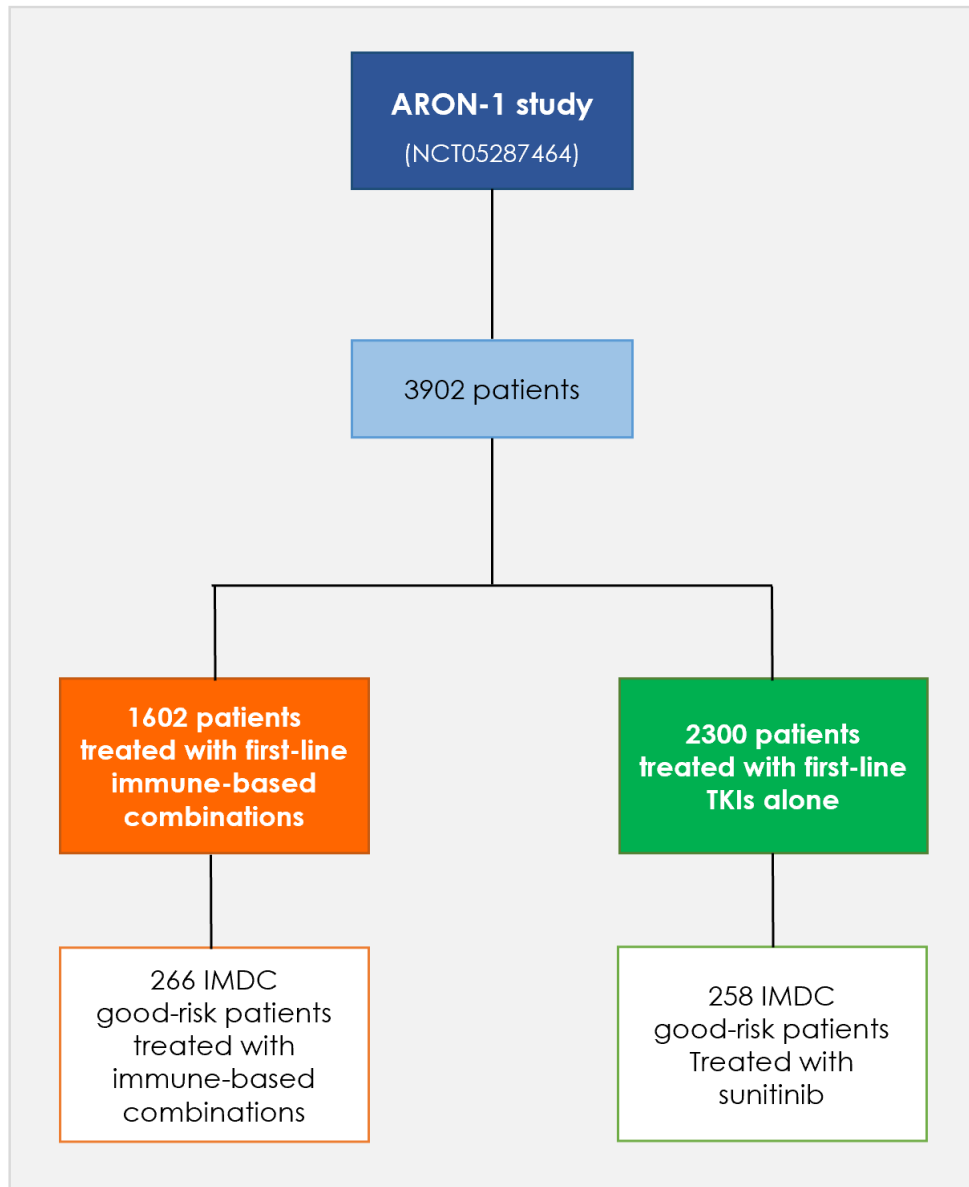


Figure Supplementary 2. Duration of response of first-line therapy.

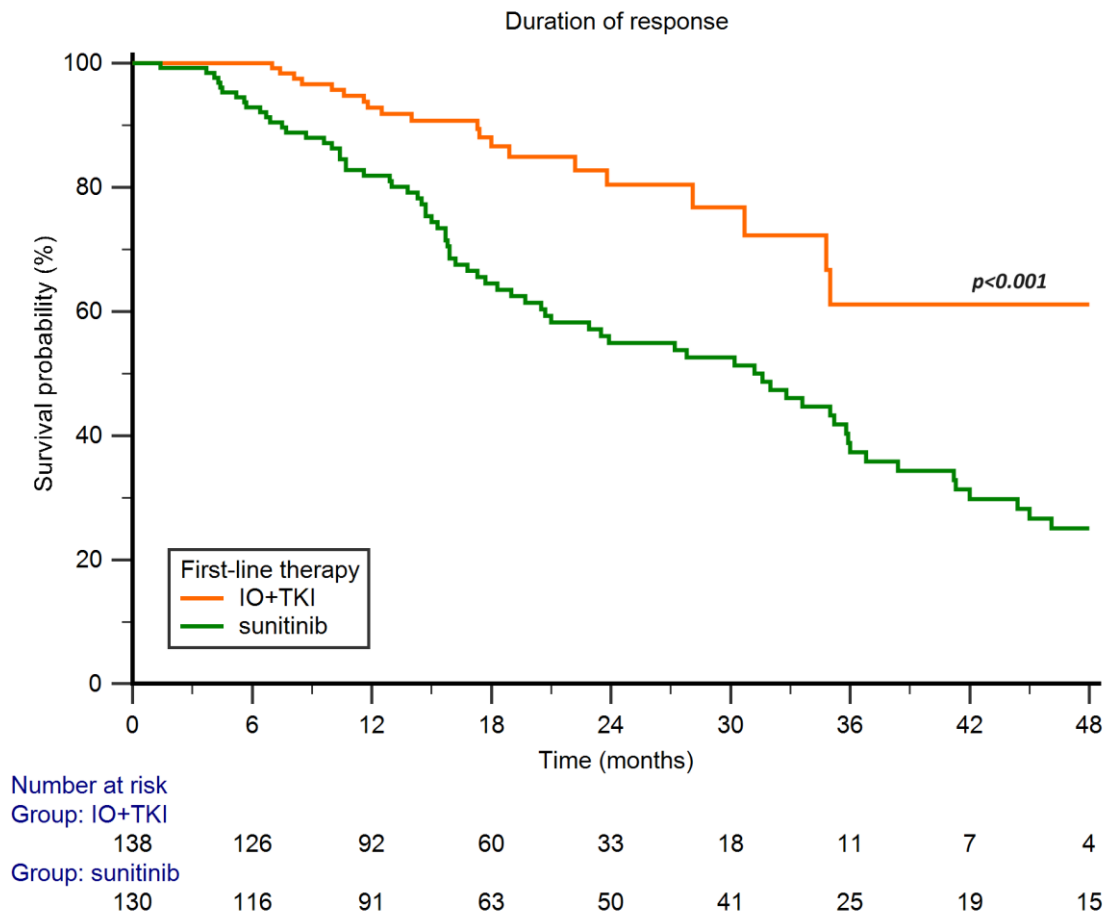
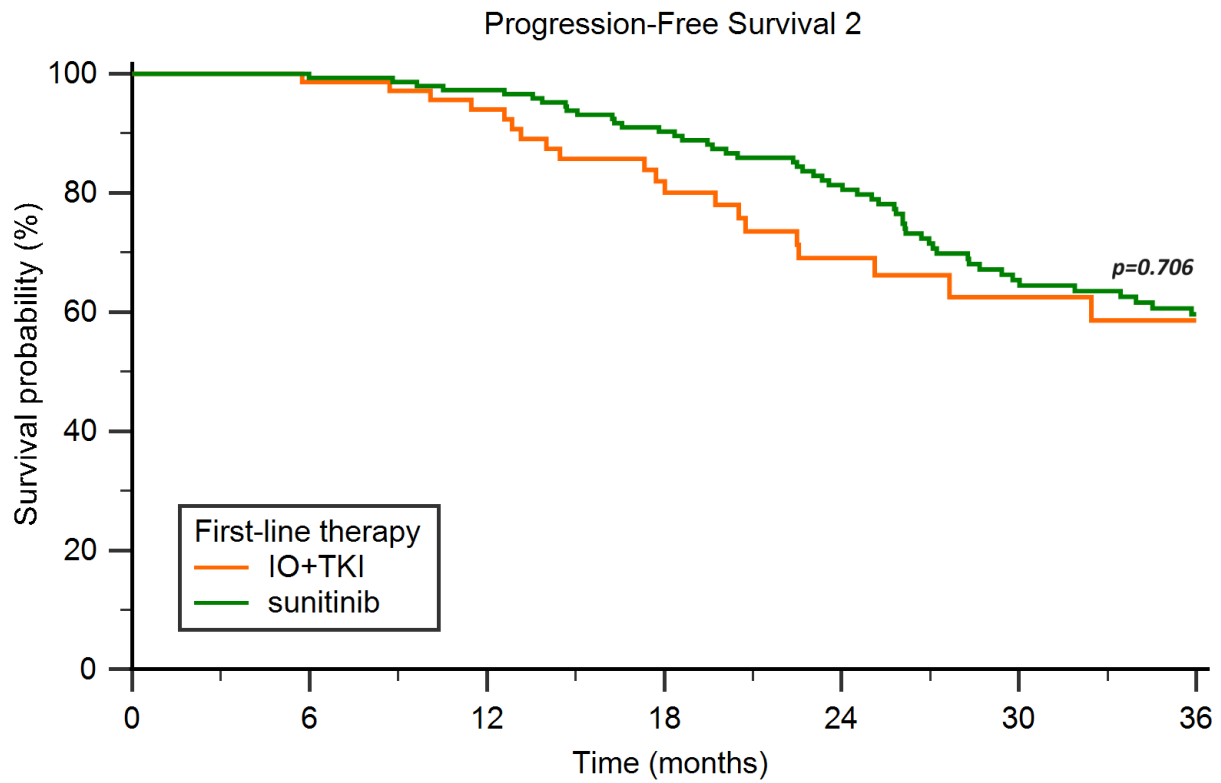


Figure Supplementary 3. Progression-Free Survival 2 in favorable-risk patients treated by IO + TKI or sunitinib.



Number at risk

Group: IO+TKI

| | | | | | | |
|----|----|----|----|----|----|----|
| 77 | 71 | 57 | 43 | 29 | 16 | 14 |
|----|----|----|----|----|----|----|

Group: sunitinib

| | | | | | | |
|-----|-----|-----|-----|-----|----|----|
| 149 | 147 | 142 | 125 | 103 | 72 | 61 |
|-----|-----|-----|-----|-----|----|----|

Figure Supplementary 4. Ideal candidate to IO+TKI or TKI basing on the 2y-OS rate in favorable-risk RCC patients.

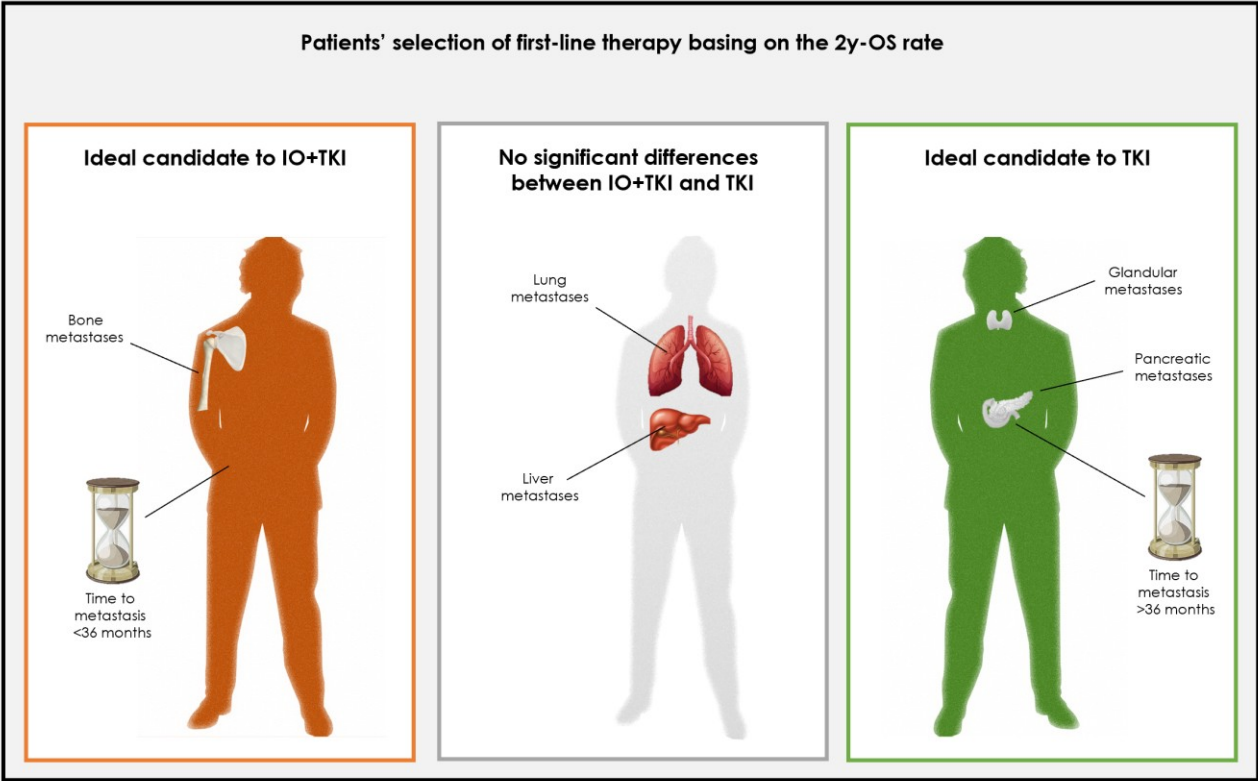


Table Supplementary 1. Univariate and multivariate analysis in favorable-risk RCC patients treated with IO+TKI.

| Overall Survival | Univariate Cox Regression | | Multivariate Cox Regression | |
|--|---------------------------|-------------------|-----------------------------|---------|
| | HR (95%CI) | p-value | HR (95%CI) | p-value |
| Gender (females vs males) | 1.09 (0.77–1.43) | 0.798 | | |
| Age ($\geq 65y$ vs $< 65y$) | 1.42 (0.92–1.69) | 0.421 | | |
| Nephrectomy (yes vs no) | 0.39 (0.15–1.03) | 0.057 | | |
| Histology (nccRCC vs ccRCC) | 2.13 (0.80–5.66) | 0.131 | | |
| Sarcomatoid features (yes vs no) | 1.13 (0.87–2.27) | 0.189 | | |
| Lung metastases (yes vs no) | 0.95 (0.45–2.04) | 0.901 | | |
| Bone metastases (yes vs no) | 1.03 (0.43–2.46) | 0.940 | | |
| Liver metastases (yes vs no) | 3.04 (1.15–8.06) | 0.026 | | |
| Brain metastases (yes vs no) | 0.93 (0.10–5.36) | 0.753 | | |
| Glandular metastases (yes vs no) | 1.22 (0.49–3.01) | 0.678 | | |
| Time from RCC diagnosis to metastasis >36 vs ≤ 36 months | 0.95 (0.45–2.01) | 0.903 | | |
| Progression-Free Survival | Univariate Cox Regression | | Multivariate Cox regression | |
| | HR (95%CI) | p-value | HR (95%CI) | p-value |
| Gender (females vs males) | 1.16 (0.83–1.67) | 0.478 | | |
| Age ($\geq 65y$ vs $< 65y$) | 1.10 (0.91–1.62) | 0.313 | | |
| Nephrectomy (yes vs no) | 1.44 (0.58–3.57) | 0.432 | | |
| Histology (nccRCC vs ccRCC) | 1.58 (0.81–3.09) | 0.184 | | |
| Sarcomatoid features (yes vs no) | 0.63 (0.19–2.01) | 0.431 | | |
| Lung metastases (yes vs no) | 1.31 (0.81–2.10) | 0.274 | | |
| Bone metastases (yes vs no) | 1.09 (0.64–1.85) | 0.752 | | |
| Liver metastases (yes vs no) | 4.08 (2.22–7.49) | < 0.001 | | |
| Brain metastases (yes vs no) | 0.71 (0.22–2.27) | 0.566 | | |
| Glandular metastases (yes vs no) | 1.15 (0.66–1.98) | 0.627 | | |
| Time from RCC diagnosis to metastasis >36 vs ≤ 36 months | 0.93 (0.59–1.47) | 0.765 | | |
| ccRCC = clear cell Renal Cell Carcinoma; IMDC = International Metastatic RCC Database Consortium; nccRCC = non-clear cell Renal Cell Carcinoma | | | | |

Table Supplementary 2. Univariate and multivariate analysis in favorable-risk RCC patients treated with sunitinib.

| Overall Survival | Univariate Cox Regression | | Multivariate Cox Regression | |
|--|---------------------------|-------------------|-----------------------------|--------------|
| | HR (95%CI) | p-value | HR (95%CI) | p-value |
| Gender (females vs males) | 1.05 (0.83–1.76) | 0.764 | | |
| Age (≥ 65y vs < 65y) | 1.32 (0.89–1.76) | 0.341 | | |
| Nephrectomy (yes vs no) | 1.10 (0.35–3.47) | 0.868 | | |
| Histology (nccRCC vs ccRCC) | 1.14 (0.73–1.78) | 0.565 | | |
| Sarcomatoid features (yes vs no) | 2.06 (1.18–3.60) | 0.012 | 1.67 (0.96–2.90) | 0.071 |
| Lung metastases (yes vs no) | 0.95 (0.67–1.35) | 0.782 | | |
| Bone metastases (yes vs no) | 1.08 (0.71–1.66) | 0.712 | | |
| Liver metastases (yes vs no) | 1.80 (1.19–2.72) | 0.005 | 1.89 (1.29–2.78) | 0.001 |
| Brain metastases (yes vs no) | 0.98 (0.45–2.11) | 0.962 | | |
| Glandular metastases (yes vs no) | 0.71 (0.40–1.26) | 0.245 | | |
| Time from RCC diagnosis to metastasis >36 vs ≤36 months | 0.74 (0.53–1.03) | 0.071 | | |
| Progression-Free Survival | Univariate Cox Regression | | Multivariate Cox regression | |
| | HR (95%CI) | p-value | HR (95%CI) | p-value |
| Gender (females vs males) | 1.18 (0.88–1.77) | 0.589 | | |
| Age (≥ 65y vs < 65y) | 1.17 (0.95–1.56) | 0.653 | | |
| Nephrectomy (yes vs no) | 1.96 (0.62–6.15) | 0.249 | | |
| Histology (nccRCC vs ccRCC) | 2.15 (1.43–3.24) | < 0.001 | | |
| Sarcomatoid features (yes vs no) | 1.61 (0.84–3.10) | 0.153 | | |
| Lung metastases (yes vs no) | 1.02 (0.73–1.41) | 0.929 | | |
| Bone metastases (yes vs no) | 1.30 (0.89–1.90) | 0.170 | | |
| Liver metastases (yes vs no) | 1.29 (0.86–1.92) | 0.216 | | |
| Brain metastases (yes vs no) | 1.26 (0.68–2.33) | 0.459 | | |
| Glandular metastases (yes vs no) | 0.84 (0.54–1.32) | 0.453 | | |
| Time from RCC diagnosis to metastasis > 36 vs ≤ 36 months | 0.74 (0.53–1.02) | 0.220 | | |
| ccRCC = clear cell Renal Cell Carcinoma; IMDC = International Metastatic RCC Database Consortium; nccRCC = non-clear cell Renal Cell Carcinoma | | | | |