

1 **Supplementary figure legends**

2 **Figure S1. Additional analysis from TCGA KIRP Cohort (n=271).** A, Boxplots
3 representing MCP-Counter estimation of different immune cell populations according to
4 clusters. p values were obtained using the two-sided Mann-Whitney test (**p<0.001). B,
5 Boxplots representing copy number alterations (CNA) (CDKN2A, Chromosome (chr) 3p and
6 7 between 2 clusters. p values were obtained using the two-sided Mann-Whitney test
7 (**p<0.01; ns: non-significant). C, Boxplots representing gene signature mRNA-based
8 concerning the Cell cycle, Hypoxia, NRF2/ARE, TFE3 fusion, between 2 clusters. p values
9 were obtained using the two-sided Mann-Whitney test (**p<0.001). D, Boxplots
10 representing the Th2 prognostic signature according to the clusters from MCP-Counter
11 (**p<0.001).

12 **Figure S2. Transcriptomic analyses from independent Albiges *et al.* cohort (n=98).** A,
13 Heatmap representing unsupervised analysis from MCP-Counter on the microarray expression
14 data (k=2), identifying the TME subtypes. B, Boxplots representing the expression of 5
15 checkpoint markers according to clusters from the MCP-Counter analysis. C, Boxplots
16 representing the 3 predictive gene signatures of response to treatment described in the clear-
17 cell renal cell carcinoma (angiogenesis, Effector T-cell (Eff T), JAVELIN Renal 101
18 Immuno), according to the clusters from MCP-Counter. p values were obtained using the two-
19 sided Mann-Whitney test (**p<0.01; ***p<0.001).

20 **Figure S3. Additional heatmap from AXIPAP trial cohort (n=38).** Heatmap representing
21 unsupervised analysis based on the immune markers performed in immunohistochemistry
22 (k=2), identifying the “IHC TME subtypes” with the “immune-enriched” group and the
23 “immune-low” group, annotated histological type and angiogenic markers, CD31(AV:
24 vascular architecture; DV: vascular density) and VEGF.

25 **Figure S4. Assessment of response to treatment from AXIPAP trial cohort (n=38).** A,
26 table with objective response rate (ORR) of patients treated with axitinib in 1st line, from
27 AXIPAP trial cohort, according to subgroups from the unsupervised analysis based on IHC
28 immune markers from AXIPAP trial cohort (n=36). B, table with objective response rate
29 (ORR) of patients treated by immunotherapy in 2nd or 3rd line, according to subgroups from
30 the unsupervised analysis based on IHC immune markers from AXIPAP trial cohort (n=12).
31 C, Boxplots representing the 3 predictive gene signatures of response to treatment described
32 in the clear-cell renal cell carcinoma, (angiogenesis, Effector T-cell (Eff T), JAVELIN Renal
33 101 Immuno), according to subgroups from the unsupervised analysis based on IHC immune
34 markers from AXIPAP trial cohort (n=30). p values were obtained using the two-sided Mann-
35 Whitney test (*p<0.05; ns: non-significant).

36 **Figure S5. Gene ontology (GO) terms analysis.** A, The bubble diagram representing
37 Biological Process significantly activated between the clusters from MCP-Counter in TCGA
38 cohort. B, The bubble diagram representing Biological Process significantly activated
39 between subgroups from the unsupervised analysis based on IHC immune markers in
40 AXIPAP trial cohort.