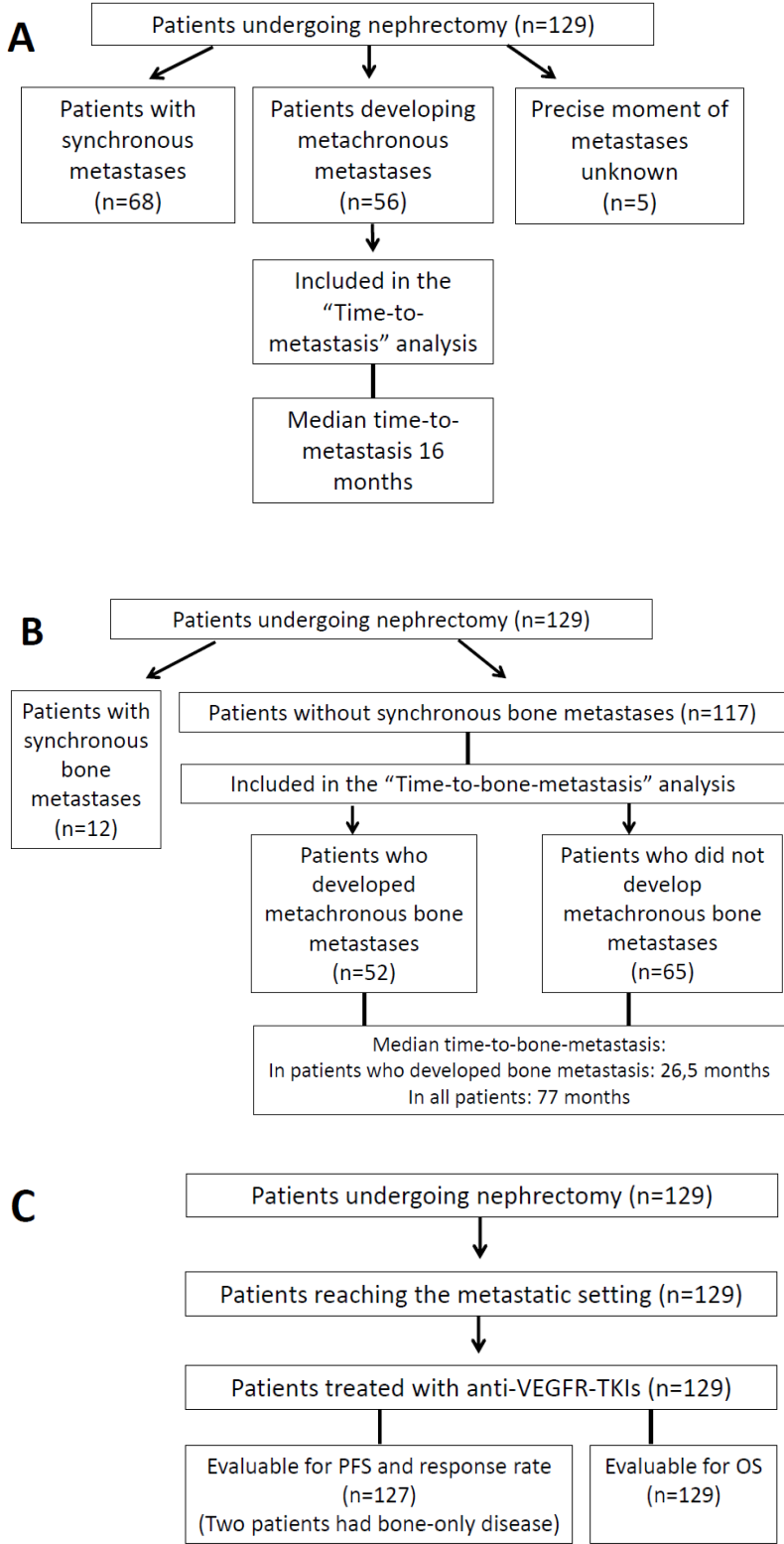


SUPPLEMENTAL FIGURE 1: FLOWCHART WITH THE INCLUDED PATIENTS

PANEL A: Patients included in the time-to-metastasis analysis

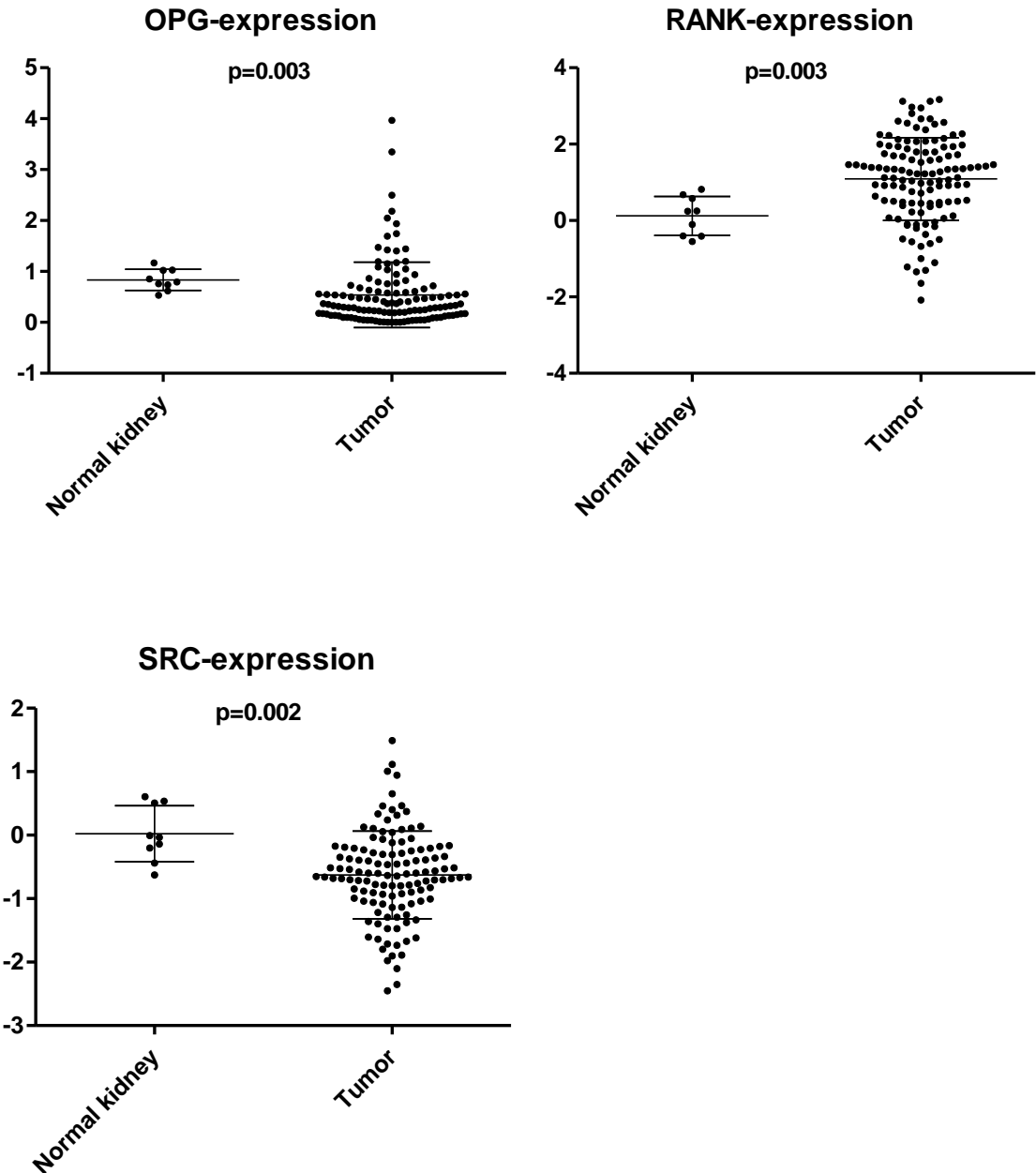
PANEL B: Patients included in the time-to-bone-metastasis analysis

PANEL C: Patients included in the analysis of efficacy of anti-VEGFR-TKIs

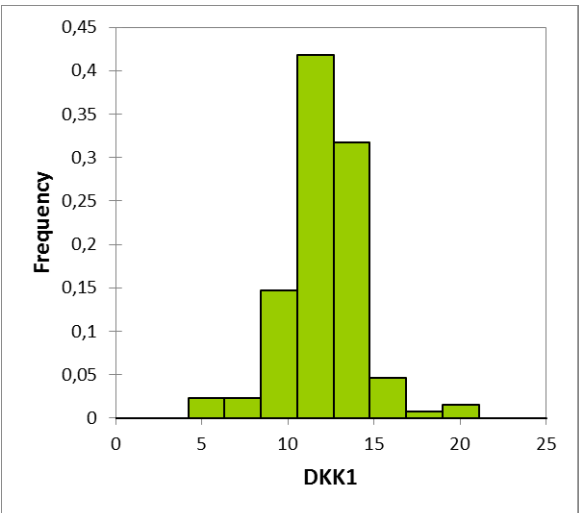
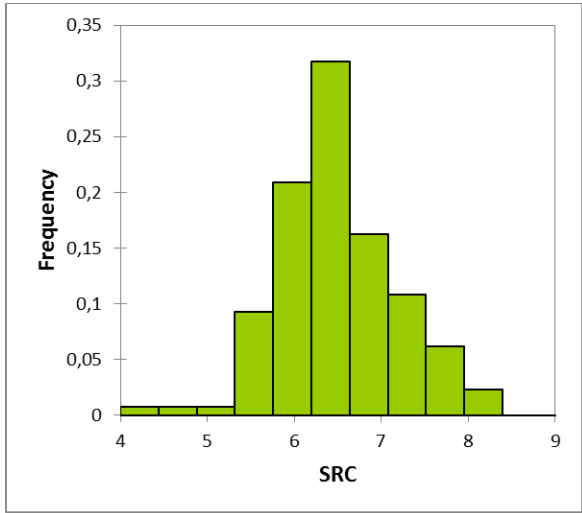
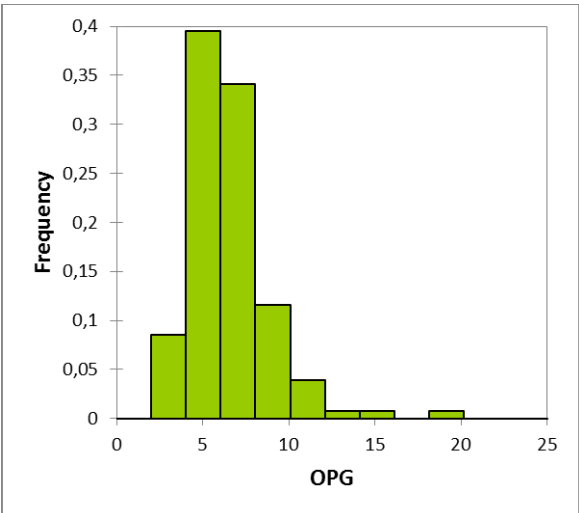
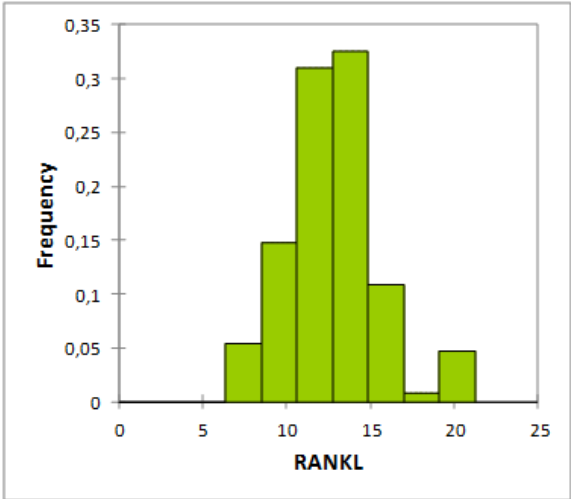
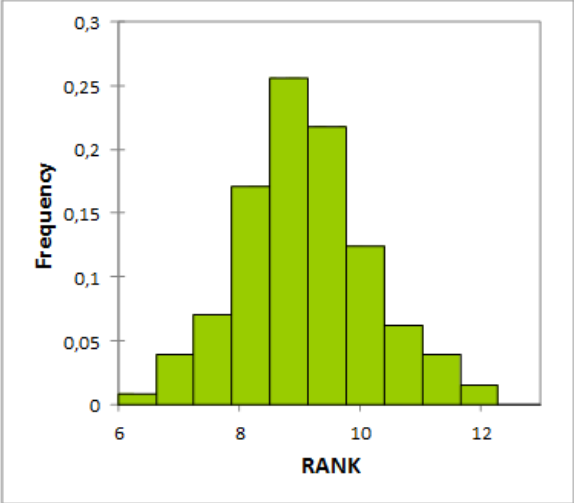


SUPPLEMENTAL FIGURE 2: OPG, RANK AND SRC-EXPRESSION LEVELS IN TUMOR COMPARED TO NORMAL KIDNEY TISSUE.

Expression levels, as defined by 2-delta-delta-CT ACTB, were compared by Mann-Whitney test. We observed higher RANK- ($p=0.003$), lower SRC- ($p=0.002$) and lower OPG-expression ($p=0.003$) in tumors ($n=129$) compared to normal kidney ($n=9$).



SUPPLEMENTAL FIGURE 3: HISTOGRAM SHOWING THE GAUSSIAN DISTRIBUTION OF THE EXPRESSION LEVELS OF RANK, RANKL, OPG, SRC AND DKK1 IN THE PRIMARY KIDNEY TUMORS



SUPPLEMENTAL TABLE 1: GENE SYMBOL, GENE NAME AND APPLIED BIOSYSTEMS ASSAY ID-NUMBER FOR THE GENES STUDIED

Gene Symbol	Gene name	Assay ID
ACTB	Actine B	Hs01060665_g1
TNFSF11	Receptor activator of NF-kB ligand	Hs00243522_m1
DKK1	Dickkopf WNT signaling pathway inhibitor-1	Hs00183740_m1
TNFRSF11B	Osteoprotegerin	Hs00900360_m1
TNFRSF11A	Receptor activator of NF-kB	Hs00921374_m1
SRC	Src	Hs01082246_m1

SUPPLEMENTAL TABLE 2: PEARSON CORRELATION OF THE EXPRESSION LEVELS OF THE DIFFERENT GENES

Among the total series of samples, the expression of the different genes was not correlated except for OPG- and SRC-expression, that were weakly correlated ($r^2=0.138$, $p<0.0001$).

R ² (p-value if <0.05)	RANK	OPG	RANKL	SRC	DKK1
RANK	1				
OPG	0.006	1			
RANKL	0.000	0.036 (p=0.03)	1		
SRC	0.005	0.138 (p<0.0001)	0.003	1	
DKK1	0.012	0.037 (p=0.03)	0.000	0.023	1