Supplementary Appendix

Supplement to: Choueiri TK, Hessel C, Halabi S, et al. Cabozantinib versus sunitinib as initial therapy for metastatic renal cell carcinoma of intermediate or poor risk (Alliance A031203 CABOSUN trial): progression-free survival by independent review and overall survival update.

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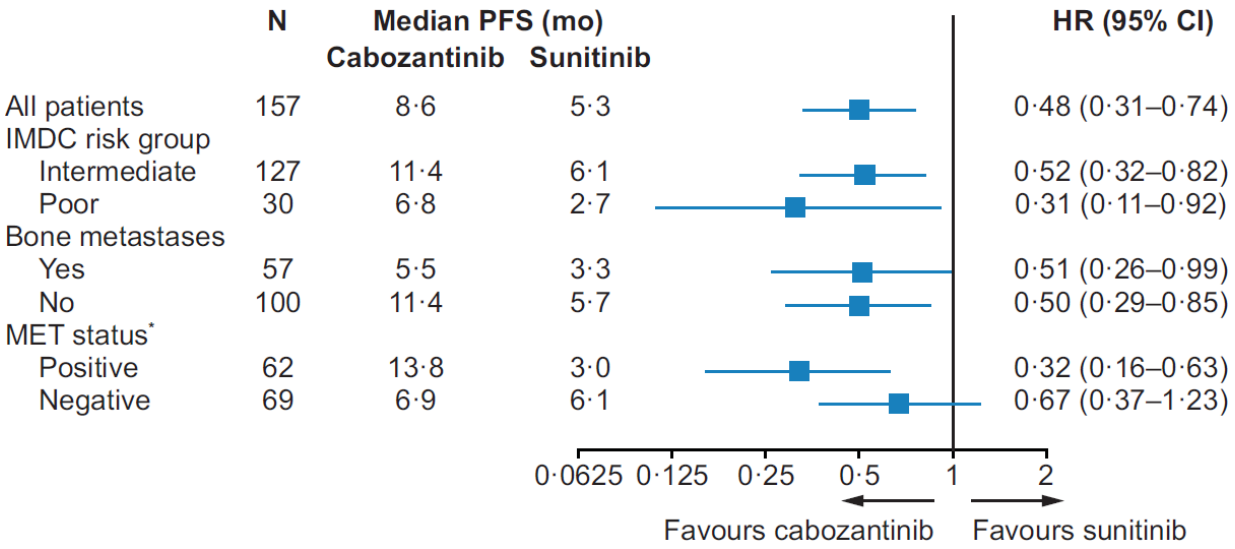
Figure S1. Forest plot of progression-free survival per independent radiology review committee



HR, hazard ratio; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; PFS, progression-free survival. Data are as of September 15, 2016. All randomised patients were included in the analyses. Hazard ratios are unstratified with the exception of the analysis for all patients.
*Eight patients in the cabozantinib group and 18 patients in the sunitinib group had unknown MET status.

Table S1. Tumour response per investigator

	Cabozantinib (N=79)	**Sunitinib (N=78)**
Objective response rate (95% CI)	33% (23% – 44%)	12% (5% – 21%)
Best overall response		
Confirmed complete response	1 (1%)	0
Confirmed partial response	25 (32%)	9 (12%)
Stable disease	34 (43%)	29 (37%)
Progressive disease	14 (18%)	19 (24%)
Unevaluable or missing*	5 (6%)	21 (27%)

Data are % or n (%) and are as of September 15, 2016.

*Unevaluable or missing for the following reasons: cabozantinib: adverse event (4), withdrew consent (1); sunitinib: adverse event (7), death (2), disease progression (2), withdrew consent (9), other (referred to hospice treatment; 1)

Table S2. Study disposition and baseline characteristics by best overall response per independent radiology committee

	Sunitinib		Cabozantinib	
	Response Assessment was PR/SD/PD (N = 60)	**Response Assessment was Missing/UE (N = 18)**	**Response Assessment was PR/SD/PD (N = 73)**	**Response Assessment was Missing/UE (N = 6)**
Discontinued study treatment	60 (100%)	18 (100%)	73 (100%)	6 (100%)
Disease progression	40 (67%)	1 (6%)	44 (60%)	0
Adverse events	10 (17%)	6 (33%)	11 (15%)	5 (83%)
Alternative therapy	1 (2%)	0	1 (1%)	0
Patient off-treatment for other complicating disease	1 (2%)	0	1 (1%)	0
Death	1 (2%)	2 (11%)	2 (3%)	0
Withdrawn consent	4 (7%)	9 (50%)	3 (4%)	1 (17%)
Other	1 (2%)	0	1 (1%)	0
Age (years)	63 (45-84)	66 (31-87)	62 (40-82)	68 (53-79)
Male	45 (75%)	12 (67%)	61 (84%)	5 (83%)
Female	15 (25%)	6 (33%)	12 (16%)	1 (17%)
Ethnic origin				
White	57 (95%)	18 (100%)	66 (90%)	4 (67%)
Black or African American	2 (3%)	0	3 (4%)	0
Other	1 (2%)	0	54 (7%)	2 (33%)
ECOG PS				
0	28 (47%)	8 (44%)	35 (48%)	1 (17%)
1	26 (43%)	6 (33%)	31 (42%)	2 (33%)
2	6 (10%)	4 (22%)	7 (10%)	3 (50%)
IMDC risk group				
Intermediate	50 (83%)	13 (72%)	61 (84%)	3 (50%)
Poor	10 (17%)	5 (28%)	12 (16%)	3 (50%)
Bone metastases per IxRS				
Yes	21 (35%)	7 (39%)	25 (34%)	4 (67%)
No	39 (65%)	11 (61%)	48 (66%)	2 (33%)
Nephrectomy	47 (78%)	13 (72%)	54 (74%)	3 (50%)

	Sunitinib		Cabozantinib	
	Response Assessment was PR/SD/PD (N = 60)	**Response Assessment was Missing/UE (N = 18)**	**Response Assessment was PR/SD/PD (N = 73)**	**Response Assessment was Missing/UE (N = 6)**
Number of metastatic sites per investigator				
0	0	0	0	0
1	20 (33%)	6 (33%)	15 (21%)	2 (33%)
2	16 (27%)	4 (22%)	34 (47%)	3 (50%)
≥3	24 (40%)	8 (44%)	24 (33%)	1 (17%)

Data are n (%) or median (range). CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; IMDC, International metastatic renal cell carcinoma Database Consortium; IRC, independent radiology review committee; IxRS, interactive voice/web response system; PD, progressive disease; PR, partial response; SD, stable disease; UE, unable to evaluate.

Table S3. Subsequent anticancer therapy

	Cabozantinib (N=79)	**Sunitinib (N=78)**
Any subsequent anticancer therapy	51 (65%)	50 (64%)
Radiotherapy	10 (13%)	14 (18%)
Surgery	5 (6%)	6 (8%)
Systemic therapy	48 (61%)	48 (62%)
Tyrosine kinase inhibitors	38 (48%)	37 (47%)
Axitinib	18 (23%)	16 (21%)
Pazopanib	14 (16%)	10 (13%)
Sunitinib	11 (14%)	10 (13%)
Sorafenib	1 (1%)	2 (3%)
Cabozantinib	1 (1%)	6 (8%)
Lenvatinib	1 (1%)	0
mTOR inhibitors	15 (19%)	18 (23%)
Everolimus	8 (10%)	15 (19%)
Temsirolimus	7 (9%)	4 (5%)
PD-1 checkpoint inhibitors	14 (18%)	15 (19%)
Cytokines	3 (4%)	1 (1%)

PD-1, programmed cell death-1.