Supporting Materials

Supporting Table 1 Baseline characteristics in ITT patients

	Intent-to-treat[1,2]	
Characteristic*	**NIVO+IPI (N=550)**	**SUN (N=546)**
Median age (range), years	62 (26–85)	62 (21–85)
Sex, n (%)		
Male	413 (75)	395 (72)
Female	137 (25)	151 (28)
IMDC prognostic score, n (%)		
Favourable (0)	125 (23)	124 (23)
Intermediate (1–2)	334 (61)	333 (61)
Poor (3–6)	91 (17)	89 (16)
Region, n (%)		
United States	154 (28)	153 (28)
Canada/Europe	201 (37)	199 (36)
Rest of the world	195 (35)	194 (36)
Prior radiotherapy, n (%)	63 (11)	70 (13)
Prior nephrectomy, n (%)	453 (82)	437 (80)
No. of sites with target/nontarget lesions, n (%)†		
1	123 (22)	118 (22)
≥2	427 (78)	427 (78)
Quantifiable tumour PD-L1 expression, n (%)	N=499	N=503
<1%	386 (77)	376 (75)
≥1%	113 (23)	127 (25)

*Information shown in the table is based on data collected with the use of an interactive voice-response system.
†The number of target or nontarget lesions at baseline was not reported for one patient in the SUN arm.
IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; NIVO+IPI, nivolumab plus ipilimumab; PD-L1, programmed death ligand 1; SUN, sunitinib.

Supporting Table 2 Subsequent therapy in ITT, I/P-risk and FAV-risk patients

	Intent-to-treat		Intermediate/poor risk		Favourable risk	
Therapy	**NIVO+IPI (N=550)**	**SUN (N=546)**	**NIVO+IPI (N=425)**	**SUN (N=422)**	**NIVO+IPI (N=125)**	**SUN (N=124)**
Any subsequent therapy, n (%)*,†,‡	330 (60.0)	382 (70.0)	249 (58.6)	289 (68.5)	81 (64.8)	93 (75.0)
Subsequent systemic therapy, n (%)§	294 (53.5)	363 (66.5)	218 (51.3)	272 (64.5)	76 (60.8)	91 (73.4)
PD-(L)1 inhibitor, n (%)						
Nivolumab	54 (9.8)	219 (40.1)	33 (7.8)	157 (37.2)	21 (16.8)	62 (50.0)
Pembrolizumab	10 (1.8)	14 (2.6)	7 (1.6)	8 (1.9)	3 (2.4)	6 (4.8)
Atezolizumab	2 (0.4)	3 (0.5)	1 (0.2)	2 (0.5)	1 (0.8)	1 (0.8)
Durvalumab	0	3 (0.5)	0	1 (0.2)	0	2 (1.6)
CTLA-4 inhibitor, n (%)						
Ipilimumab	3 (0.5)	17 (3.1)	3 (0.7)	11 (2.6)	0	6 (4.8)
Investigational antineoplastic	0	1 (0.2)	0	1 (0.2)	0	0
VEGF(R) inhibitor, n (%)						
Aflibercept	0	1 (0.2)	0	1 (0.2)	0	0
Axitinib	99 (18.0)	136 (24.9)	76 (17.9)	105 (24.9)	23 (18.4)	31 (25.0)
Bevacizumab	12 (2.2)	10 (1.8)	10 (2.4)	10 (2.4)	2 (1.6)	0
Cabozantinib	89 (16.2)	89 (16.3)	63 (14.8)	62 (14.7)	26 (20.8)	27 (21.8)
Lenvatinib	26 (4.7)	15 (2.7)	21 (4.9)	9 (2.1)	5 (4.0)	6 (4.8)
Pazopanib	106 (19.3)	39 (7.1)	78 (18.4)	29 (6.9)	28 (22.4)	10 (8.1)
Sorafenib	14 (2.5)	6 (1.1)	12 (2.8)	6 (1.4)	2 (1.6)	0
Sunitinib	129 (23.5)	72 (13.2)	101 (23.8)	46 (10.9)	28 (22.4)	26 (21.0)
mTOR inhibitor, n (%)						
Everolimus	52 (9.5)	70 (12.8)	42 (9.9)	54 (12.8)	10 (8.0)	16 (12.9)
Temsirolimus	5 (0.9)	6 (1.1)	4 (0.9)	4 (0.9)	1 (0.8)	2 (1.6)

*Patient may have received more than one type of subsequent therapy. Subsequent therapy was defined as therapy started on or after first dosing date (randomisation date if patient was never treated).
†Subsequent radiotherapy was given to 15.3% versus 14.3% (ITT), 15.1% versus 14.7% (I/P) and 16.0% versus 12.9% (FAV) of patients.
‡Subsequent surgery was given to 8.9% versus 4.9% (ITT), 7.8% versus 5.9% (I/P) and 12.8% versus 1.6% (FAV) of patients.
§Systemic therapies not included under PD-(L)1, CTLA-4, VEGF(R) or mTOR inhibitors include ALK/EGFR tyrosine kinase inhibitors, cancer vaccine, interferon, interferon alfa, interleukin, interleukin 2, investigational immunotherapy, capecitabine, carboplatin, cisplatin, cobimetinib, cyclophosphamide, doxorubicin, doxorubicin liposomal, epirubicin, etoposide, fluorouracil, gemcitabine, ibrutinib, infliximab, irinotecan, methotrexate, oxaliplatin, tegafur/uracil, vorinostat, investigational antineoplastic, investigational drug, radium 223, budesonide, candesartan, cimetidine, denosumab, medroxyprogesterone, meloxicam, selenium.
CTLA-1, cytotoxic T lymphocyte antigen-4; FAV, favourable risk; I/P, intermediate/poor risk; ITT, intent-to-treat; mTOR, mammalian target of rapamycin; NIVO+IPI, nivolumab plus ipilimumab; PD-(L)1, programmed death (ligand) 1; VEGF(R), vascular endothelial growth factor (receptor); SUN, sunitinib;

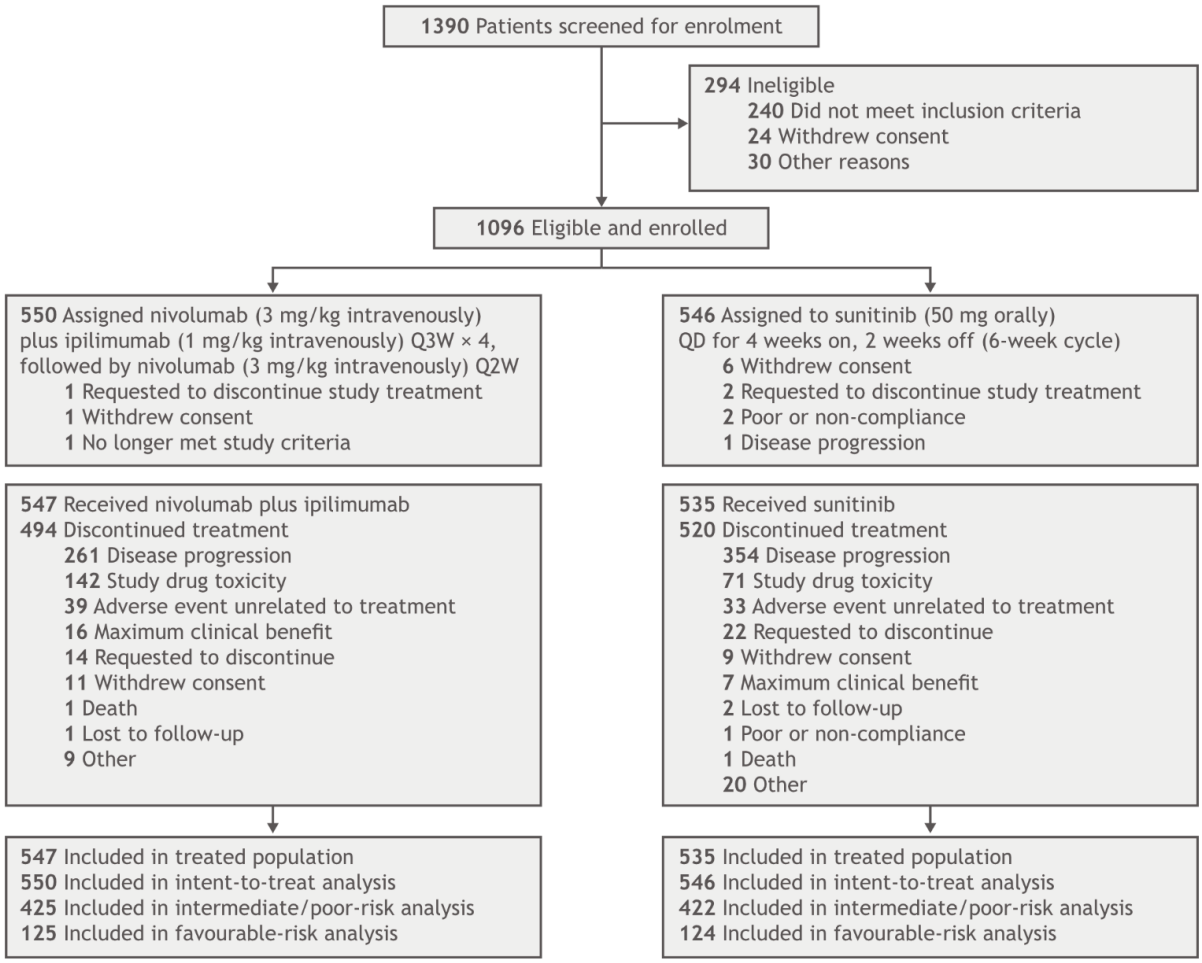
Supporting Table 3 Summary of safety in all treated population

	All treated patients			
Safety parameters; patients, n (%)	**NIVO+IPI (N=547)**		**SUN (N=535)**	
	Any grade	**Grade 3–4**	**Any grade**	**Grade 3–4**
Treatment-related AEs	514 (94)	262 (48)	521 (97)	343 (64)
All treatment-related AEs (any grade >20% in either arm)				
Fatigue	209 (38)	24 (4)	266 (50)	51 (10)
Pruritus	169 (31)	3 (<1)	50 (9)	0
Diarrhoea	155 (28)	21 (4)	284 (53)	31 (6)
Rash	126 (23)	10 (2)	70 (13)	0
Nausea	110 (20)	8 (1)	208 (39)	7 (1)
Hypothyroidism	90 (16)	2 (<1)	143 (27)	1 (<1)
Decreased appetite	76 (14)	7 (1)	135 (25)	6 (1)
Vomiting	61 (11)	4 (<1)	116 (22)	10 (2)
Dysgeusia	26 (5)	0	118 (22)	1 (<1)
Stomatitis	25 (5)	0	151 (28)	14 (3)
Mucosal inflammation	15 (3)	1 (<1)	155 (29)	15 (3)
Hypertension	12 (2)	4 (<1)	220 (41)	91 (17)
Palmoplantar erythema	6 (1)	1 (<1)	234 (44)	50 (9)
All treatment-related select AEs[a]				
Gastrointestinal	163 (30)	28 (5)	284 (53)	31 (6)
Hepatic	107 (20)	48 (9)	79 (15)	20 (4)
Skin	279 (51)	22 (4)	308 (58)	55 (10)
Endocrine	180 (33)	38 (7)	168 (31)	1 (<1)
Pulmonary	38 (7)	6 (1)	2 (<1)	0
Renal	56 (10)	7 (1)	48 (9)	6 (1)

AE, adverse event; NIVO+IPI, nivolumab plus ipilimumab; SUN, sunitinib.

[a]Treatment-related select AEs were prespecified and defined as events that might be immune-mediated, differ from those caused by non-immunotherapeutic drugs, might require immunosuppression for management and whose early recognition might mitigate severe toxicity.

Supporting Figure 1 CONSORT diagram



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