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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Model parameters: baseline values, ranges, and distributions for sensitivity analysis

Variable	Baseline value	Range		Reference for baseline value	Distribution (parameters)
		Minimum	Maximum		
HR of IN versus sunitinib for OS	0.63	0.44	0.89	[5]	Normal (-0.46, 0.18)*
HR of IN versus sunitinib for PFS	0.82	0.64	1.05	[5]	Normal (-0.20, 0.13)*
Log-logistic PFS survival model with sunitinib	λ=0.04128308, γ=1.452671	-	-	[5]	-
Weibull OS survival model with sunitinib	λ=0.01974261, γ=1.09098	-	-	[5]	-
Weibull OS survival model with nivolumab plus ipilimumab	λ=0.012437844, γ=1.09098	-	-	[5]	-
Background mortality rate	Age specific			[9]	
Rate of treatment discontinuation due to AEs					
IN	0.220	0.170	0.260	[5]	Beta (118,429)
Sunitinib	0.120	0.090	0.140	[5]	Beta (63,472)
IN AEs incidence					
Fatigue	0.040	0.030	0.050	[5]	Beta (23,524)
Hypertension	0.070	0.060	0.080	[5]	Beta (4, 543)
Thrombocytopenia	0	0	0	[5]	-
Palmar-Plantar Erythrodysesthesia	0	0	0	[5]	-
Sunitinib AEs incidence					
Fatigue	0.090	0.070	0.110	[5]	Beta (49, 486)
Hypertension	0.160	0.130	0.190	[5]	Beta (85, 450)
Thrombocytopenia	0.050	0.040	0.060	[5]	Beta (25, 510)
Palmar-Plantar Erythrodysesthesia	0.090	0.070	0.110	[5]	Beta (49,486)
IN second-line therapy proportion					
Sunitinib	0.20	0.160	0.240	[5]	Beta (111, 439)
Pazopanib	0.130	0.104	0.156	[5]	Beta (72,478)
Cabozantinib	0.060	0.048	0.072	[5]	Beta (261, 4089)
Sunitinib second-line therapy proportion					

Nivolumab	0.270	0.216	0.324	[5]	Beta (147,399)
Axitinib	0.190	0.152	0.228	[5]	Beta (106,440)
Cabozantinib	0.080	0.064	0.096	[5]	Beta (255, 2938)
Utility (SD)					
In the first-line sunitinib	0.73	0.58	0.88	[10]	Beta (26, 10)
In the first-line IN	0.82	0.65	0.98	[5, 10]	Beta (17, 4)
In second-line therapy	0.66	0.52	0.79	[11]	Beta (33, 17)
Patients' weight, kg	70	40	200	[14]	Gamma (8, 0.1)
Drug cost, $/per cycle					
IN	32213.44	25770.75	38656.13	[15]	Gamma (100,0.003)
Nivolumab (maintenance phase)	19551.60	15641.28	23461.92	[15]	Gamma (100,0.005)
Axitinib	16703.40	13362.72	20044.08	[16]	Gamma (100,0.006)
Cabozantinib	19249.86	15399.89	23099.83	[16]	Gamma (100,0.005)
Sunitinib	10761.52	8609.22	12913.82	[17]	Gamma (100,0.009)
Pazopanib	9982.56	7986.05	11979.07	[17]	Gamma (100,0.010)
AEs cost, $US					
Fatigue	0	0	0	[18]	-
Hypertension	61.90	49.52	74.28	[18]	Gamma (100,1.616)
Thrombocytopenia	9400.00	7520.00	11280.00	[19]	Gamma (100,0.011)
Palmar-Plantar Erythrodysesthesia	43.64	34.91	52.37	[20]	Gamma (100,2.291)
Administration	139.61	111.69	167.53	[22]	Gamma (100,0.716)

HR= hazard ratio; IN= nivolumab plus ipilimumab; OS= overall survival; PFS= progression free survival; AE=adverse event;

*A lognormal distribution was used for hazard ratio: a normal distribution was firstly fit to log hazard ratio and then the result was exponentiated.

eTable 2 Background mortality rate

Estimates of background mortality rate or each age were provided in the US life table available in the following publication.

Arias E, Heron M, Xu J. United States Life Tables, 2014. Natl Vital Stat Rep. 2017;66:1-64.

Age	Background mortality rate	Age	Background mortality rate	Age	Background mortality rate
21	0.000795	51	0.004484	81	0.055475
22	0.000858	52	0.004874	82	0.061509
23	0.000898	53	0.005302	83	0.068675
24	0.000923	54	0.005771	84	0.076701
25	0.000943	55	0.006274	85	0.085469
26	0.000968	56	0.006793	86	0.095935
27	0.000994	57	0.007321	87	0.107533
28	0.001024	58	0.007854	88	0.120347
29	0.001058	59	0.008403	89	0.134457
30	0.001095	60	0.008999	90	0.149939
31	0.001132	61	0.009652	91	0.166861
32	0.001171	62	0.010341	92	0.185276
33	0.001213	63	0.011056	93	0.205223
34	0.00126	64	0.011804	94	0.226719
35	0.001319	65	0.012598	95	0.24976
36	0.001389	66	0.013484	96	0.274312
37	0.001467	67	0.014501	97	0.300311
38	0.00155	68	0.015701	98	0.327661
39	0.001639	69	0.017146	99	0.356235
40	0.001743	70	0.018855	100	1
41	0.001864	71	0.020762		
42	0.002001	72	0.022816		
43	0.002159	73	0.02501		
44	0.002345	74	0.027353		
45	0.002547	75	0.029897		
46	0.002778	76	0.03287		
47	0.003059	77	0.036315		
48	0.003391	78	0.040253		
49	0.003753	79	0.044908		
50	0.004118	80	0.049974		

eTable 3: Drug dose and costs

Drug	Dose	Unit price ($)	Cost for 1 model cycle ($, 6 wks)
Nivolumab (induction phase)	3 mg/kg * 70 kg every 3 weeks for 4 doses	27.155/mg	11405.10
Nivolumab (maintenance phase)	240 mg every 2 weeks	27.155/mg	19551.60
Ipilimumab	1 mg/kg * 70 kg every 3 weeks for 4 doses	148.631/mg	20808.34
Nivolumab plus ipilimumab cost per cycle	Nivolumab (induction phase) + ipilimumab		32213.44
Sunitinib	50 mg/d for 4 weeks followed by 2 weeks off treatment	384.340/50mg	10761.52
Cabozantinib	60mg/d	458.330/60mg	19249.86
Pazopanib	800mg/d	59.420/200mg	9982.560
Axitinib	5mg twice/d	198.850/5mg	16703.40

**eTable 4 Results for subgroup analyses**

Subgroup	Sample size		OS HR (95% CI)	ICER (95% CI)	Cost-effectiveness probability at WTP	
	Nivolumab +Ipilimumab	Sunitinib			$100,000/QALY	$150,000/QALY
Age						
< 65 yr	265	259	0.53 (0.40–0.71)	95,460 (52,547 to 177,323)	56%	93%
≥ 65 and < 75 yr	125	133	0.86 (0.58–1.27)	178,565 (-1,082,934 to 1,325,930)	20%	42%
≥ 75yr	35	30	0.97 (0.48–1.95)	313,117 (-1,160,294 to 1,226,019)	18%	34%
Sex						
Male	314	301	0.71 (0.55–0.92)	123,292 (44,941 to 374,534)	31%	68%
Female	111	121	0.52 (0.34–0.78)	94,405 (52,061 to 191,668)	59%	92%
Region						
United States	112	110	0.64 (0.40–1.00)	109,951 (37,371 to 393,168)	42%	76%
Canada and Europe	148	147	0.70 (0.49–1.01)	121103 (34,322 to 487,429)	35%	69%
Rest of the world	165	165	0.63 (0.45–0.89)	108,363 (46,968 to 275,286)	43%	80%
Baseline IMDC prognostic risk						
Intermediate	314	317	0.66 (0.50–0.87)	113,336 (48,503 to 279,532)	37%	77%
Poor	102	97	0.57 (0.39–0.82)	100,060 (50,266 to 227,695)	51%	87%
Previous nephrectomy						
Yes	341	319	0.69 (0.53–0.89)	119,022 (46,473 to 347,110)	36%	72%
No	84	103	0.63 (0.42–0.94)	108,363 (46,511 to 339,422)	43%	79%
Baseline PD-L1 expression						
<1%	284	278	0.73 (0.56–0.96)	124719 (-89,051 to 182,742)	32%	67%
≥1%	100	114	0.45 (0.29–0.71)	86,390 (42,372 to 129,817)	72%	97%
Bone metastases						
Yes	84	89	0.71 (0.47–1.08)	123,292 (-92,494 to 551,413)	34%	66%
No	341	333	0.64 (0.49–0.82)	109951 (49,056 to 250,882)	40%	81%
Liver metastases						

Yes	88	89	0.64 (0.42–0.96)	109,951 (41,516 to 373,075)	42%	78%
No	337	333	0.66 (0.51–0.85)	113,336 (48,419 to 273,130)	38%	78%
Lung metastases						
Yes	294	296	0.61 (0.47–0.78)	105,378 (50,172 to 217,535)	45%	86%
No	131	126	0.81 (0.53–1.22)	153,568 (-733,088 to 1,122,851)	23%	49%
Lymph-node metastases						
Yes	190	216	0.79 (0.59–1.07)	145,916 (-251,792 to 726,544)	24%	53%
No	235	206	0.55 (0.40–0.76)	97,680 (52,546 to 196,330)	53%	91%

OS= overall survival; HR= hazard ratio; CI= confidence interval/credible intervals; ICER=incremental cost-effectiveness ratio; WTP=willingness-to-pay; QALY= quality-adjusted life year;

eFigure 1 Markov model simulating outcomes for the CheckMate 214 trial
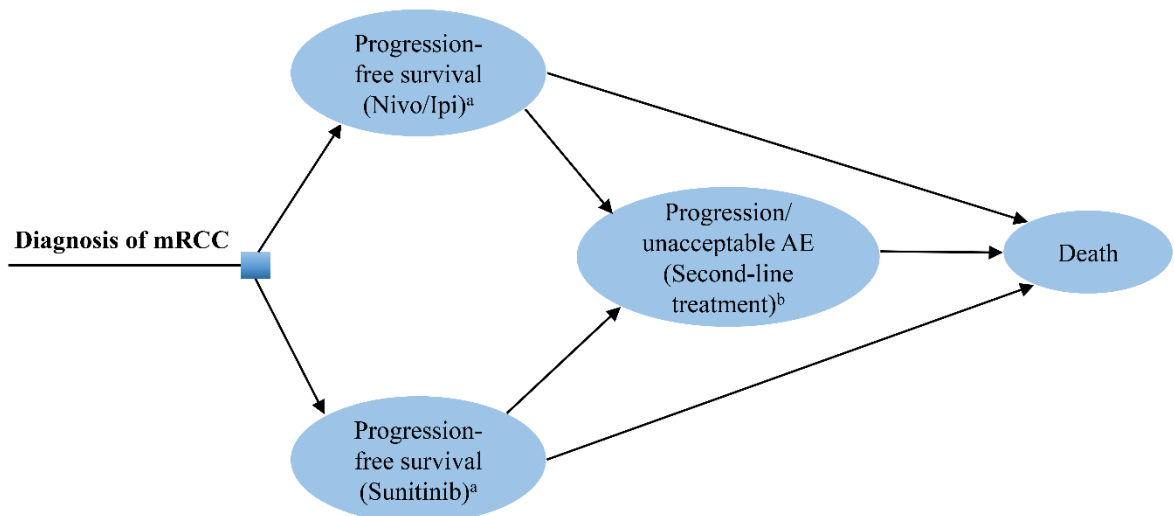
aRegimen in the parentheses represent the treatments the patients received until disease progression or unacceptable toxicity. bUpon progression of the disease or unacceptable toxicity, both groups could receive second-line treatment until death. mRCC, metastatic renal cell carcinoma; Nivo, nivolumab; Ipi, ipilimumab; AE, adverse event.

eFigure 2 Results of two-way sensitivity analyses for utility values

**Sensitivity Analysis on Utility_IN and Utility_Sun
(Net Benefit, WTP=$150,000/QALY)**
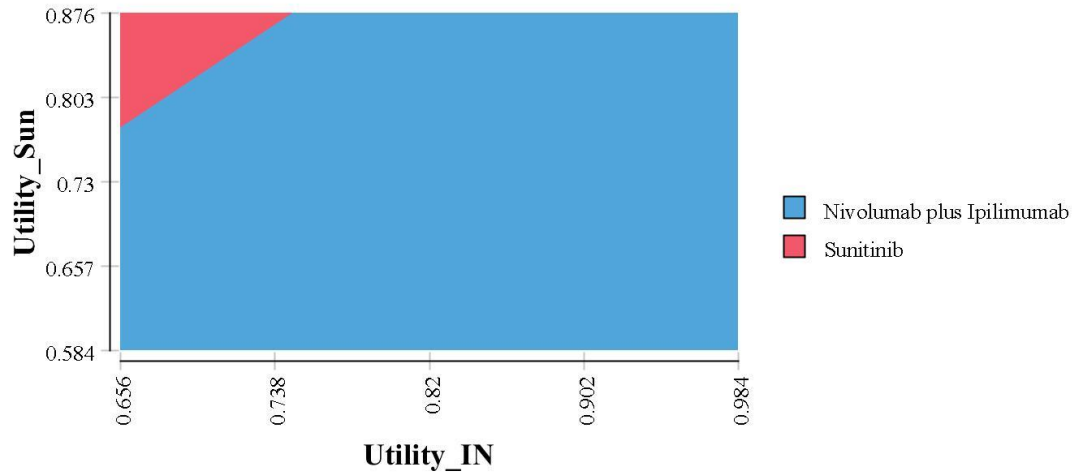
When the utility value for sunitinib was 0.782, if the value of nivolumab plus ipilimumab was greater than 0.656, the ICER will be lower than $150,000/QALY, suggesting that nivolumab plus ipilimumab is likely to be cost effective across the majority of utility combinations at a WTP threshold of $150,000/QALY.