

## **COST ESTIMATES**

We considered only direct medical care costs in the analysis, including the drugs, their administration, management of adverse events, monitoring via physical exams, imaging, and lab tests. Per the CDC, the mean US patient weight was 77.34 kg for women and 89.72 kg for men; we chose to use 85 kg as an average to both account for the higher prevalence of RCC amongst males and weight loss effects [14 20]. The cost of nivolumab plus ipilimumab was calculated for intravenous treatment at doses of 3 mg per kg for nivolumab plus doses of 1 mg per kg for ipilimumab administration every 3 weeks for the first 4 doses, then the cost was calculated for nivolumab alone administered every 2 weeks at a dose of 1 mg per kg until disease progression or drug discontinuation [2]. The cost of pembrolizumab plus axitinib was calculated for intravenous treatment at doses of 200 mg of pembrolizumab every 3 weeks and oral administration of doses of 5 mg twice daily of axitinib until disease progression or drug discontinuation [7]. The cost of avelumab plus axitinib was calculated for intravenous avelumab treatment at doses of 10 mg per kg every 2 weeks and oral treatment of doses of 5 mg twice daily of axitinib, until disease progression or drug discontinuation [10]. The costs of second-line therapy was calculated for oral administration of cabozantinib daily until progression or death. We used average wholesale price (AWP) of drugs, as published by UpToDate/Lexicomp [21], to estimate the unit price of all drugs. Intravenous administration costs were obtained from the Centers of Medicare & Medicaid Services (CMS) [22].

Our model accounted for wastage and no vial sharing, using 2 x 50 mg per 10 mL vials for ipilimumab, 1 x 240 mg per 24 mL vials of nivolumab, 2 x 100 mg per 4 mL vials for pembrolizumab, and 4 x 200 mg per 10 mL vials of avelumab. Given the wide range of second-line therapies used as described in each trial, and the fact that they often were not given as single-agents mutually exclusively, we made the assumption that all patients who went on to receive subsequent therapy received cabozantinib alone.

The cost of imaging via bone scans, MRI brains, and CT of the chest, abdomen, and pelvis were considered fixed across the different drug regimens and thus were not included in the analysis. However, physician visits and lab studies were likely to differ between the treatment options because of the dosing schedule and were accounted for accordingly. Physician visit costs and lab costs were estimated based on data obtained from CMS [22]. We included in the model grade 3 and 4 adverse drug events (ADE), with incidence of >1%, that might have an economic impact. An ADE having an economic impact was defined as an adverse event that would require further management with medication or

procedures, or assessment with lab work, imaging, or further procedures. For nivolumab plus ipilimumab, these adverse events were diarrhea and rash; for pembrolizumab plus axitinib, these adverse events were diarrhea, hypertension, hyperthyroidism, transaminitis, dyspnea, and hand-foot syndrome; and for avelumab plus axitinib, these adverse events were diarrhea, hypertension, nausea, dyspnea, infusion reaction, anemia, transaminitis, and hand-foot syndrome. We assumed that grade 3/4 diarrhea would be managed by a several day hospitalization and include a imaging and sigmoidoscopy; grade 3/4 rash would be managed via a topical steroid and antibiotics; grade 3/4 hypothyroidism would require lab testing and addition of daily oral levothyroxine; grade 3/4 hypertension would require addition of two antihypertensive drugs daily; grade 3/4 transaminitis would require lab testing, addition of steroids, and abdominal ultrasound; grade 3/4 dyspnea would require hospitalization for pneumonitis which would include imaging and bronchoscopy; grade 3/4 hyperthyroidism would require lab testing and addition of the beta-blocker propranolol daily; grade 3/4 hand-foot would require addition of topical urea cream; grade 3/4 nausea would require hospitalization for gastroenteritis and addition and multiple antiemetics; grade 3/4 infusion reaction would require hospitalization for allergic reaction; and grade 3/4 anemia would indicate need for a blood transfusion. Drug costs, lab costs, and hospitalization costs via diagnosis related groups (DRGs) were estimated based on data obtained from CMS [22].

**Supplementary Table 1. Weibull Model Parameters for Transition Probabilities**

Treatment	Progression Free Survival	Overall Survival
Pembrolizumab+Axitinib	$\lambda = 0.037113$ ; $\Upsilon = 1.030999$	$\lambda = 0.005973$ ; $\Upsilon = 1.214945$
Avelumab+Axitinib	$\lambda = 0.05919$ ; $\Upsilon = 0.930056$	$\lambda = 0.005602$ ; $\Upsilon = 1.314887$
Nivolumab+Ipilimumab	$\lambda = 0.092746$ ; $\Upsilon = 0.71103$	$\lambda = 0.017709$ ; $\Upsilon = 0.911218$

**Supplementary Table 2. Costs and Increments for Pembrolizumab+Axitinib**

Variable	Baseline Rate	Cost	Time Increment
<b>AEs incidence</b>			
Diarrhea (grade 3/4)	0.091	\$630.52	Overall for Study
ALT/AST (grade 3/4)	0.133	\$103.41	Overall for Study
Dyspnea (grade 3/4)	0.016	\$137.76	Overall for Study
Hyperthyroid (grade 3/4)	0.012	\$0.70	Overall for Study
HTN (grade 3/4)	0.221	\$17	Overall for Study
PPES (grade 3/4)	0.051	\$3	Overall for Study
<b>Visits, Labs, and Imaging</b>			
	1 visit every 3 weeks		
Office Visit		\$272.88	Per 6 week interval
CBC/CMP	1 every 3 weeks	\$40.74	Per 6 week interval
	Once every 6 weeks		
TSH and FT4		\$28.69	Per 6 week interval
<b>Drug cost, \$/per cycle</b>			
Pembrolizumab+Axitinib (and administration cost)		\$32,938	Per 6 week interval for Progression-free State
Second-line therapy (using Cabozantinib for 7.4 months)	0.204	\$33,269	Overall for Progression State

**Supplementary Table 3. Costs and Increments for Avelumab+Axitinib**

Variable	Baseline Rate	Cost	Time Increment
<b>AEs incidence</b>			
Diarrhea (grade 3/4)	0.067	\$464.23	Overall for Study
ALT/AST (grade 3/4)	0.06	\$46.65	Overall for Study
Dyspnea (grade 3/4)	0.03	\$258.30	Overall for Study
HTN (grade 3/4)	0.256	\$19	Overall for Study
PPES (grade 3/4)	0.058	\$3	Overall for Study
Nausea (grade 3/4)	0.014	\$97	Overall for Study
Infusion Rxn (grade 3/4)	0.016	\$152	Overall for Study
Anemia (grade 3/4)	0.016	\$6	Overall for Study
<b>Visits, Labs, and Imaging</b>			
Office Visit	1 visit every 2 weeks	\$409.32	Per 6 week interval
CBC/CMP	1 every 2 weeks	\$60.30	Per 6 week interval
TSH and FT4	Once every 6 weeks	\$28.69	Per 6 week interval
<b>Drug cost, \$/per cycle</b>			
Avelumab+Axitinib (and administrative costs)		\$49,984	Per 6 week interval for Progression-free State
Second-line therapy (using Cabozantinib for 7.4 months)	0.208	\$33,922	Overall for Progression State

**Supplementary Table 4. Costs and Increments for Nivolumab+Ipilimumab**

Variable	Baseline Rate	Cost	Time Increment
<b>AEs incidence</b>			
Diarrhea (grade 3/4)	0.04	\$277.15	Overall for Study
Rash (grade 3/4)	0.01	\$2.92	Overall for Study
<b>Visits, Labs, and Imaging</b>			
Office Visit: First two cycles of "healthy"	1 visit every 3 weeks	\$272.88	Per 6 week interval for "healthy" until progression
Office Visit: After 2 cycles of "healthy"	1 visit every 2 weeks	\$409.32	Per 6 week interval for "healthy" until progression
CBC/CMP: First two cycles of "healthy"	1 every 3 weeks	\$40.20	Per 6 week interval for "healthy" until progression
CBC/CMP: After 2 cycles of "healthy"	1 every 2 weeks	\$61.11	Per 6 week interval for "healthy" until progression
TSH and FT4	Once every 6 weeks	\$28.69	Per 6 week interval
<b>Drug cost, \$/per cycle</b>			
Nivolumab plus ipilimumab (and Administration costs): First 2 cycles	2 doses of IPI and 3 doses of Nivo per 6 weeks	\$58,397	Per 6 week interval for Progression-free State (first 2 cycles)
Nivolumab plus ipilimumab (and Administration costs): After 2 cycles	3 doses of Nivo per 6 weeks	\$23,183	Per 6 week interval for Progression-free State (After 2 cycles)
Second-line therapy (using Cabozantinib for 7.4 months)	0.39	\$63,603	Overall for Progression State

**Supplementary Table 5. Baseline patient demographics across the three trials**

<b>Patient Demographics</b>	<b>Nivolumab plus Ipilimumab (n=550)</b>	<b>Pembrolizumab plus Axitinib (n=432)</b>	<b>Avelumab plus Axitinib (n=442)</b>
<b>Median Age</b>	62 (26-85)	62 (30-89)	62 (29-83)
<b>Age &lt;65</b>		260 (60.2%)	
<b>Male sex</b>	413 (75%)	308 (71.3%)	316 (71.5%)
<b>North America/US</b>	154 (28%)	104 (24.1%)	128 (29%)
<b>Europe/Canada</b>	201 (37%)	106 (24.5%)	128 (29%)
<b>Rest of World</b>	195 (35%)	222 (51.4)	186 (42.1%)
<b>IMDC favorable</b>	125 (23%)	138 (31.9%)	94 (21.3%)
<b>IMDC Intermediate</b>	334 (61%)	238 (55.1%)	271 (61.3%)
<b>IMDC Poor</b>	91 (17%)	56 (13%)	72 (16.3%)
<b>PD-L1 CPS &gt;1</b>	113/499 (23%)	243/410 (59.3%)	
<b>PDL-L1 CPS &lt;1</b>	278/392 (71%)	167/410 (40.7)	
<b>1 Organ with mets</b>	123 (22%)	114 (26.4%)	181 (41%)
<b>&gt;2 organs with mets</b>	427 (78%)	315 (72.9%)	250 (56%)
<b>Lung mets</b>	381 (69%)	312 (72.2%)	
<b>LN mets</b>	246 (45%)	199 (46.1%)	
<b>Bone mets</b>	112 (20%)	103 (23.8%)	
<b>Adrenal gland mets</b>		67 (15.5%)	
<b>Liver mets</b>	99 (18%)	66 (15.3%)	
<b>Prior radiation</b>	63 (11%)	41 (9.5%)	
<b>Prior nephrectomy</b>	453 (82%)	357 (82.6%)	352 (79.6%)

**Supplementary Table 6. Parameters for Pembrolizumab+Axitinib v. Nivolumab+Ipilimumab**

<b>Variable</b>	<b>Value</b>	<b>Lower Range</b>	<b>Upper Range</b>	<b>Interval</b>
Cost of nivolumab and ipilimumab (first 2 cycles, \$ per cycle)	\$ 58,396.94	\$ 46,717.55	\$ 70,076.33	20%
Cost of nivolumab and ipilimumab (after 2 cycles, \$ per cycle)	\$ 23,183.37	\$ 18,546.70	\$ 27,820.04	20%
Cost of pembrolizumab and axitinib (\$ per cycle)	\$ 32,937.60	\$ 26,350.08	\$ 39,525.12	20%
Cost of adverse effects (nivolumab and ipilimumab, \$)	\$ 280.07	\$ 224.06	\$ 336.08	20%
Cost of adverse effects (pembrolizumab and axitinib, \$)	\$ 891.52	\$ 713.22	\$ 1,069.82	20%
Cost of visits: healthy (nivolumab and ipilimumab, first 2 cycles, \$)	\$ 341.77	\$ 273.42	\$ 410.12	20%
Cost of visits: healthy (nivolumab and ipilimumab, after 2 cycles, \$)	\$ 499.12	\$ 399.30	\$ 598.94	20%
Cost of visit: progression (nivolumab and ipilimumab, \$)	\$ 28.69	\$ 22.95	\$ 34.43	20%
Cost of visits (pembrolizumab and axitinib, \$)	\$ 342.31	\$ 273.85	\$ 410.77	20%
$\lambda$ of nivolumab and ipilimumab (progression)	0.0927	0.0788	0.1067	15%
$\lambda$ of pembrolizumab and axitinib (progression)	0.0371	0.0315	0.0427	15%
$\gamma$ of nivolumab and ipilimumab (progression)	0.7110	0.6044	0.8177	15%
$\gamma$ of pembrolizumab and axitinib (progression)	1.0310	0.8763	1.1856	15%
$\lambda$ of nivolumab and ipilimumab (survival)	0.0177	0.0151	0.0204	15%
$\lambda$ of pembrolizumab and axitinib (survival)	0.0060	0.0051	0.0069	15%
$\gamma$ of nivolumab and ipilimumab (survival)	0.9112	0.7745	1.0479	15%
$\gamma$ of pembrolizumab and axitinib (survival)	1.2149	1.0327	1.3972	15%
Utility of nivolumab and ipilimumab	0.8280	0.7452	0.9108	10%
Utility of pembrolizumab and axitinib	0.8700	0.7830	0.9570	10%
Utility of 2nd line Tx	0.7900	0.7110	0.8690	10%
Cost of 2nd line Tx (after nivolumab and ipilimumab, \$)	\$ 63,603.40	\$ 50,882.72	\$ 76,324.08	20%
Cost of 2nd line Tx (after pembrolizumab and axitinib, \$)	\$ 33,269.47	\$ 26,615.58	\$ 39,923.36	20%
Discount rate	3%	2%	4%	20%

**Supplementary Table 7. ICER Sensitivities for Pembrolizumab+Axitinib v. Nivolumab+Ipilimumab**

<b>Variable</b>	<b>ICER LB</b>	<b>ICER UB</b>	<b>Range</b>
Cost of nivolumab and ipilimumab (first 2 cycles, \$ per cycle)	\$(115,713.54)	\$ 20,704.08	\$ 136,417.62
Cost of nivolumab and ipilimumab (after 2 cycles, \$ per cycle)	\$(260,365.77)	\$ 165,356.31	\$ 425,722.08
Cost of pembrolizumab and axitinib (\$ per cycle)	\$ 252,194.86	\$(347,204.32)	\$ (599,399.18)
Cost of adverse effects (nivolumab and ipilimumab, \$)	\$ (47,708.77)	\$ (47,300.69)	\$ 408.09
Cost of adverse effects (pembrolizumab and axitinib, \$)	\$ (46,855.22)	\$ (48,154.24)	\$ (1,299.02)
Cost of visits: healthy (nivolumab and ipilimumab, first 2 cycles, \$)	\$ (47,903.92)	\$ (47,105.54)	\$ 798.39
Cost of visits: healthy (nivolumab and ipilimumab, after 2 cycles, \$)	\$ (52,087.46)	\$ (42,922.00)	\$ 9,165.47
Cost of visit: progression (nivolumab and ipilimumab, \$)	\$ (48,120.98)	\$ (46,888.48)	\$ 1,232.50
Cost of visits (pembrolizumab and axitinib, \$)	\$ (37,580.85)	\$ (57,428.61)	\$ (19,847.76)
$\lambda$ of nivolumab and ipilimumab (progression)	\$ 125,025.11	\$(200,451.62)	\$ (325,476.73)
$\lambda$ of pembrolizumab and axitinib (progression)	\$(243,618.43)	\$ 96,604.44	\$ 340,222.87
$\gamma$ of nivolumab and ipilimumab (progression)	\$ 341,313.71	\$(416,414.50)	\$ (757,728.21)
$\gamma$ of pembrolizumab and axitinib (progression)	\$(867,777.50)	\$ 351,251.53	\$ 1,219,029.03
$\lambda$ of nivolumab and ipilimumab (survival)	\$ 12,391.15	\$ 603,024.48	\$ 590,633.33
$\lambda$ of pembrolizumab and axitinib (survival)	\$ 373,458.55	\$ 4,365.24	\$ (369,093.30)
$\gamma$ of nivolumab and ipilimumab (survival)	\$ 30,884.97	\$ 81,020.74	\$ 50,135.77
$\gamma$ of pembrolizumab and axitinib (survival)	\$ 55,021.97	\$ 34,505.98	\$ (20,515.99)
Utility of nivolumab and ipilimumab	\$ (94,468.08)	\$ (31,730.43)	\$ 62,737.64
Utility of pembrolizumab and axitinib	\$ (32,558.11)	\$ (87,821.33)	\$ (55,263.22)
Utility of 2nd line Tx	\$ (50,641.50)	\$ (44,733.88)	\$ 5,907.62
Cost of 2nd line Tx (after nivolumab and ipilimumab, \$)	\$ (79,410.89)	\$ (15,598.57)	\$ 63,812.32
Cost of 2nd line Tx (after pembrolizumab and axitinib, \$)	\$ (29,498.53)	\$ (65,510.93)	\$ (36,012.40)
Discount rate	\$ (47,491.04)	\$ (47,518.59)	\$ (27.56)



**Supplementary Table 8. Parameters for Nivolumab+Ipilimumab v. Avelumab+Axitinib**

<b>Variable</b>	<b>Value</b>	<b>Lower Range</b>	<b>Upper Range</b>	<b>Interval</b>
Cost of nivolumab and ipilimumab (first 2 cycles, \$ per cycle)	\$ 58,396.94	\$ 46,717.55	\$ 70,076.33	20%
Cost of nivolumab and ipilimumab (after 2 cycles, \$ per cycle)	\$ 23,183.37	\$ 18,546.70	\$ 27,820.04	20%
Cost of avelumab and axitinib (\$ per cycle)	\$ 49,983.63	\$ 39,986.90	\$ 59,980.36	20%
Cost of adverse effects (nivolumab and ipilimumab, \$)	\$ 280.07	\$ 224.06	\$ 336.08	20%
Cost of adverse effects (avelumab and axitinib, \$)	\$ 1,046.22	\$ 836.98	\$ 1,255.47	20%
Cost of visits: healthy (nivolumab and ipilimumab, first 2 cycles, \$)	\$ 341.77	\$ 273.42	\$ 410.12	20%
Cost of visits: healthy (nivolumab and ipilimumab, after 2 cycles, \$)	\$ 499.12	\$ 399.30	\$ 598.94	20%
Cost of visit: progression (nivolumab and ipilimumab, \$)	\$ 28.69	\$ 22.95	\$ 34.43	20%
Cost of visits (avelumab and axitinib, \$)	\$ 498.31	\$ 398.65	\$ 597.97	20%
$\lambda$ of nivolumab and ipilimumab (progression)	0.09275	0.0788	0.1067	15%
$\lambda$ of avelumab and axitinib (progression)	0.05919	0.0503	0.0681	15%
$\gamma$ of nivolumab and ipilimumab (progression)	0.71103	0.6044	0.8177	15%
$\gamma$ of avelumab and axitinib (progression)	0.93006	0.7905	1.0696	15%
$\lambda$ of nivolumab and ipilimumab (survival)	0.01771	0.0151	0.0204	15%
$\lambda$ of avelumab and axitinib (survival)	0.00560	0.0048	0.0064	15%
$\gamma$ of nivolumab and ipilimumab (survival)	0.91122	0.7745	1.0479	15%
$\gamma$ of avelumab and axitinib (survival)	1.31489	1.1177	1.5121	15%
Utility of nivolumab and ipilimumab	0.8280	0.7452	0.9108	10%
Utility of avelumab and axitinib	0.8200	0.7380	0.9020	10%
Utility of 2nd line Tx	0.7900	0.7110	0.8690	10%
Cost of 2nd line Tx (after nivolumab and ipilimumab, \$)	\$ 63,603.40	\$ 50,882.72	\$ 76,324.08	20%
Cost of 2nd line Tx (after avelumab and axitinib, \$)	\$ 33,921.81	\$ 27,137.45	\$ 40,706.18	20%
Discount rate	3%	2%	4%	20%

**Supplementary Table 9. ICER Sensitivities for Nivolumab+Ipilimumab v. Avelumab+Axitinib**

<b>Variable</b>	<b>ICER LB</b>	<b>ICER UB</b>	<b>Range</b>
Cost of nivolumab and ipilimumab (first 2 cycles, \$ per cycle)	\$ (113,694.61)	\$ (79,371.60)	\$ 34,323.01
Cost of nivolumab and ipilimumab (after 2 cycles, \$ per cycle)	\$ (150,089.47)	\$ (42,976.75)	\$ 107,112.73
Cost of avelumab and axitinib (\$ per cycle)	\$ (596.52)	\$ (192,469.70)	\$ (191,873.18)
Cost of adverse effects (nivolumab and ipilimumab, \$)	\$ (96,584.45)	\$ (96,481.77)	\$ 102.68
Cost of adverse effects (avelumab and axitinib, \$)	\$ (96,341.33)	\$ (96,724.88)	\$ (383.55)
Cost of visits: healthy (nivolumab and ipilimumab, first 2 cycles, \$)	\$ (96,633.55)	\$ (96,432.67)	\$ 200.88
Cost of visits: healthy (nivolumab and ipilimumab, after 2 cycles, \$)	\$ (97,686.14)	\$ (95,380.08)	\$ 2,306.05
Cost of visit: progression (nivolumab and ipilimumab, \$)	\$ (96,688.16)	\$ (96,378.06)	\$ 310.10
Cost of visits (avelumab and axitinib, \$)	\$ (93,612.67)	\$ (99,453.55)	\$ (5,840.88)
$\lambda$ of nivolumab and ipilimumab (progression)	\$ (51,368.56)	\$ (134,476.17)	\$ (83,107.61)
$\lambda$ of avelumab and axitinib (progression)	\$ (158,807.27)	\$ (46,298.96)	\$ 112,508.31
$\gamma$ of nivolumab and ipilimumab (progression)	\$ 9,332.05	\$ (184,899.79)	\$ (194,231.83)
$\gamma$ of avelumab and axitinib (progression)	\$ (284,633.91)	\$ 36,226.99	\$ 320,860.90
$\lambda$ of nivolumab and ipilimumab (survival)	\$ (57,617.76)	\$ (163,204.57)	\$ (105,586.81)
$\lambda$ of avelumab and axitinib (survival)	\$ (168,562.82)	\$ (62,031.38)	\$ 106,531.44
$\gamma$ of nivolumab and ipilimumab (survival)	\$ (20,011.70)	\$ 1,016,205.72	\$ 1,036,217.41
$\gamma$ of avelumab and axitinib (survival)	\$ 311,527.91	\$ (3,978.44)	\$ (315,506.36)
Utility of nivolumab and ipilimumab	\$ (110,333.68)	\$ (85,801.08)	\$ 24,532.59
Utility of avelumab and axitinib	\$ (88,440.50)	\$ (106,255.89)	\$ (17,815.39)
Utility of 2nd line Tx	\$ (103,401.35)	\$ (90,520.46)	\$ 12,880.90
Cost of 2nd line Tx (after nivolumab and ipilimumab, \$)	\$ (104,560.78)	\$ (88,505.44)	\$ 16,055.34
Cost of 2nd line Tx (after avelumab and axitinib, \$)	\$ (96,069.91)	\$ (96,996.31)	\$ (926.41)
Discount rate	\$ (96,528.79)	\$ (96,537.48)	\$ (8.69)

**Supplementary Table 10. Parameters for Pembrolizumab+Axitinib v. Avelumab+Axitinib**

<b>Variable</b>	<b>Value</b>	<b>Lower Range</b>	<b>Upper Range</b>	<b>Interval</b>
Cost of pembrolizumab and axitinib (\$ per cycle)	\$ 32,937.60	\$ 26,350.08	\$ 39,525.12	20%
Cost of avelumab and axitinib (\$ per cycle)	\$ 49,983.63	\$ 39,986.90	\$ 59,980.36	20%
Cost of adverse effects (pembrolizumab and axitinib, \$)	\$ 891.52	\$ 713.22	\$ 1,069.82	20%
Cost of adverse effects (avelumab and axitinib, \$)	\$ 1,046.22	\$ 836.98	\$ 1,255.47	20%
Cost of visits (pembrolizumab and axitinib, \$)	\$ 342.31	\$ 273.85	\$ 410.77	20%
Cost of visits (avelumab and axitinib, \$)	\$ 498.31	\$ 398.65	\$ 597.97	20%
$\lambda$ of pembrolizumab and axitinib (progression)	0.0371	0.0315	0.0427	15%
$\lambda$ of avelumab and axitinib (progression)	0.0592	0.0503	0.0681	15%
$\gamma$ of pembrolizumab and axitinib (progression)	1.0310	0.8763	1.1856	15%
$\gamma$ of avelumab and axitinib (progression)	0.9301	0.7905	1.0696	15%
$\lambda$ of pembrolizumab and axitinib (survival)	0.0060	0.0051	0.0069	15%
$\lambda$ of avelumab and axitinib (survival)	0.0056	0.0048	0.0064	15%
$\gamma$ of pembrolizumab and axitinib (survival)	1.2149	1.0327	1.3972	15%
$\gamma$ of avelumab and axitinib (survival)	1.3149	1.1177	1.5121	15%
Utility of pembrolizumab and axitinib	0.8700	0.7830	0.9570	10%
Utility of avelumab and axitinib	0.8200	0.7380	0.9020	10%
Utility of 2nd line Tx	0.7900	0.7110	0.8690	10%
Cost of 2nd line Tx (after pembrolizumab and axitinib, \$)	\$ 33,269.47	\$ 26,615.58	\$ 39,923.36	20%
Cost of 2nd line Tx (after avelumab and axitinib, \$)	\$ 33,921.81	\$ 27,137.45	\$ 40,706.18	20%
Discount rate	3%	2%	4%	20%

**Supplementary Table 11. ICER Sensitivities for Pembrolizumab+Axitinib v. Avelumab+Axitinib**

<b>Variable</b>	<b>ICER LB</b>	<b>ICER UB</b>	<b>Range</b>
Cost of pembrolizumab and axitinib (\$ per cycle)	\$ (213,771.36)	\$ (12,260.39)	\$ 201,510.97
Cost of avelumab and axitinib (\$ per cycle)	\$ 15,173.47	\$ (241,205.22)	\$ (256,378.70)
Cost of adverse effects (pembrolizumab and axitinib, \$)	\$ (113,234.23)	\$ (112,797.52)	\$ 436.72
Cost of adverse effects (avelumab and axitinib, \$)	\$ (112,759.63)	\$ (113,272.12)	\$ (512.50)
Cost of visits (pembrolizumab and axitinib, \$)	\$ (116,352.17)	\$ (109,679.58)	\$ 6,672.58
Cost of visits (avelumab and axitinib, \$)	\$ (109,113.62)	\$ (116,918.13)	\$ (7,804.52)
$\lambda$ of pembrolizumab and axitinib (progression)	\$ (50,513.23)	\$ (165,220.83)	\$ (114,707.60)
$\lambda$ of avelumab and axitinib (progression)	\$ (196,522.36)	\$ (45,896.16)	\$ 150,626.21
$\gamma$ of pembrolizumab and axitinib (progression)	\$ 101,007.41	\$ (273,924.68)	\$ (374,932.09)
$\gamma$ of avelumab and axitinib (progression)	\$ (366,304.04)	\$ 63,906.93	\$ 430,210.97
$\lambda$ of pembrolizumab and axitinib (survival)	\$ (64,342.26)	\$ (210,393.38)	\$ (146,051.12)
$\lambda$ of avelumab and axitinib (survival)	\$ (236,554.08)	\$ (65,707.30)	\$ 170,846.77
$\gamma$ of pembrolizumab and axitinib (survival)	\$ (13,848.94)	\$ 276,968.56	\$ 290,817.50
$\gamma$ of avelumab and axitinib (survival)	\$ 202,140.69	\$ 2,021.94	\$ (200,118.76)
Utility of pembrolizumab and axitinib	\$ (133,641.54)	\$ (97,905.55)	\$ 35,735.99
Utility of avelumab and axitinib	\$ (100,703.30)	\$ (128,758.66)	\$ (28,055.35)
Utility of 2nd line Tx	\$ (121,252.57)	\$ (105,827.03)	\$ 15,425.54
Cost of 2nd line Tx (after pembrolizumab and axitinib, \$)	\$ (119,069.35)	\$ (106,962.40)	\$ 12,106.95
Cost of 2nd line Tx (after avelumab and axitinib, \$)	\$ (112,396.95)	\$ (113,634.80)	\$ (1,237.85)
Discount rate	\$ (113,014.71)	\$ (113,017.05)	\$ (2.34)