



University of Exeter

Medical School



PenTAG

# Treatments for renal cell carcinoma [ID6186]: A Pathways Pilot Appraisal

## Appendix Q: Economic results

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**List of abbreviations**

Abs	absolute
AE	Adverse Event
ASCO	American Society Of Clinical Oncology
AUC	Area Under The Curve
BSC	Best Supportive Care
cabo	cabozantinib
CDF	Cancer Drugs Fund
CE	Cost Effectiveness
DSU	Decision Support Unit
EAG	External Assessment Group
EOL	End Of Life
evero	everolimus
fav	favourable
FP	Fractional Polynomial
Gen	general
HFS	Hand Foot Syndrome
HR	Hazard Ratio
HRQL	Health-Related Quality of Life
ICER	Incremental Cost-Effectiveness Ratio
int	intermediate
IO	Immune-Oncology
IPD	Individual Patient Data
ipi	ipilimumab
IV	Intravenous
KM	Kaplan-Meier
lenv	lenvatinib
LY	Life Year(s)
LYG	Life Year(s) Gained
MRU	Medical Resource Use
NICE	National Institute For Health And Care Excellence
nivo	nivolumab
NMA	Network Meta-Analysis
OS	Overall Survival
PAS	Patient Access Scheme
pazo	pazopanib
PD	Progressed Disease
pem	pembrolizumab

PFS	Progression Free Survival
PH	Proportional Hazards
Pop	population
PPS	Post Progression Survival
Prop	proportional
QALY	Quality Adjusted Life Year(s)
QC	Quality check
RCC	Renal cell carcinoma
RDI	Relative Dosing Intensity
RWE	Real World Evidence
SF	shortfall
SOC	Standard of care
sun	sunitinib
TA	Technology appraisal
tivo	tivozanib
TKI	Tyrosine Kinase Inhibitor
TTD	Time To Discontinuation
TTP	Time To Progression
UK	United Kingdom
vs	versus

## **Appendix Q. Economic evidence**

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This document contains automated reporting from R. Confidentiality marking needs to be applied separately.





**Appendix R. Results of Model Run in R Scenario name: Base case**

Date and time run: Fri Aug 23 12:57:34 2024

**Table 1:** Base-case results (ordered in increasing cost)

Technologies	Costs (£)	LYG	QALYs	Inc. Costs	Inc. LYG	Inc. QALYs	ICER cabo + nivo vs comparator	ICER incremental
<b>Risk population: All risk</b>								
Sunitinib	£77,050	2.78	1.68	£0	0.00	0.00	£336158	£0
Pazopanib	£80,399	2.84	1.71	£3,349	0.06	0.03	£347366	£119516
Tivozanib	£100,005	2.76	1.67				£291017	(dominated)
Cabozantinib plus nivolumab	£268,539	3.71	2.25	£188,140	0.88	0.54		£347366
<b>Risk population: Favourable risk</b>								
Sunitinib	£81,665	3.68	2.22	£0	0.00	0.00	£465558	£0
Pazopanib	£86,100	3.73	2.24	£4,435	0.06	0.03	£484904	£156257
Tivozanib	£116,790	3.66	2.21				£385004	(dominated)
Cabozantinib plus nivolumab	£306,115	4.52	2.70	£220,016	0.78	0.45		£484904
<b>Risk population: Intermediate / poor risk</b>								



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<b>Technologies</b>	<b>Costs (£)</b>	<b>LYG</b>	<b>QALYs</b>	<b>Inc. Costs</b>	<b>Inc. LYG</b>	<b>Inc. QALYs</b>	<b>ICER cabo + nivo vs comparator</b>	<b>ICER incremental</b>
Sunitinib	£74,884	2.45	1.47	£0	0.00	0.00	£312114	£0
Pazopanib	£77,793	2.50	1.50	£2,909	0.05	0.03	£323708	£104944
Tivozanib	£92,997	2.43	1.47				£272605	(dominated)
Cabozantinib	£121,724	2.57	1.51				£238820	(ext dominated)
Nivolumab plus ipilimumab	£165,014	2.72	1.67				£223146	(ext dominated)
Lenvatinib plus pembrolizumab	£221,773	3.25	2.01	£143,980	0.75	0.51	Cabo+nivo dominated	£281970
Cabozantinib plus nivolumab	£238,117	3.30	2.00					(dominated)

Abbreviations: ICER, incremental cost-effectiveness ratio; LYG, life-years gained; QALY, quality-adjusted life-year



**R.1. Qualification for the severity modifier****Table 2:** Application of the severity modifier to the base case

<b>Risk group</b>	<b>SOC QALYs</b>	<b>Gen pop QALYs</b>	<b>Abs SF</b>	<b>Prop SF</b>	<b>Modifier</b>	<b>Treatment considered SOC</b>
All	1.712	10.382	8.670	0.835	1.0	Pazopanib
Fav	2.244	10.382	8.138	0.784	1.0	Pazopanib
Int/poor	2.013	10.382	8.369	0.806	1.0	Lenvatinib plus pembrolizumab
Int/poor	1.502	10.382	8.879	0.855	1.2	Pazopanib
Int/poor	1.510	10.382	8.872	0.855	1.2	Cabozantinib

Abbreviations: Abs, absolute; Fav, favourable; Gen, general; Int, intermediate; pop, population; Prop, proportional; QALYs, quality adjusted life years; SF, shortfall; SOC, standard of care

**R.2. Breakdowns by health state and cost category****Table 3:** Summary of LY gain by health state (all risk, cabo+nivo vs next best non-dominated comparator: Pazopanib)

<b>Health state</b>	<b>LY Cabozantinib plus nivolumab (X)</b>	<b>LY Pazopanib (Y)</b>	<b>Increment</b>	<b>Absolute increment</b>	<b>% absolute increment</b>
1L: off treatment	0.109	0.115	-0.006	0.006	0%
1L: on treatment	1.945	1.144	0.801	0.801	50%
2L: off treatment	0.288	0.158	0.130	0.130	8%
2L: on treatment	0.843	0.541	0.302	0.302	19%
3L: off treatment	0.026	0.109	-0.083	0.083	5%
3L: on treatment	0.142	0.365	-0.223	0.223	14%
4L: off treatment	0.001	0.009	-0.007	0.007	0%
4L: on treatment	0.007	0.054	-0.048	0.048	3%
BSC	0.353	0.341	0.011	0.011	1%
Death	0.000	0.000	0.000	0.000	0%
<b>Total</b>	<b>3.715</b>	<b>2.837</b>	<b>0.878</b>	<b>1.611</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; BSC, best supportive care; LY, life years; vs, versus

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers

**Table 4:** Summary of LY gain by health state (favourable risk, cabo+nivo vs next best non-dominated comparator: Pazopanib)

Health state	LY Cabozantinib plus nivolumab (X)	LY Pazopanib (Y)	Increment	Absolute increment	% absolute increment
1L: off treatment	0.274	0.266	0.008	0.008	1%
1L: on treatment	2.582	1.828	0.753	0.753	49%
2L: off treatment	0.288	0.164	0.124	0.124	8%
2L: on treatment	0.844	0.562	0.282	0.282	18%
3L: off treatment	0.026	0.113	-0.087	0.087	6%
3L: on treatment	0.142	0.379	-0.237	0.237	15%
4L: off treatment	0.001	0.009	-0.008	0.008	1%
4L: on treatment	0.007	0.056	-0.050	0.050	3%
BSC	0.353	0.355	-0.001	0.001	0%
Death	0.000	0.000	0.000	0.000	0%
<b>Total</b>	<b>4.517</b>	<b>3.733</b>	<b>0.784</b>	<b>1.549</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; BSC, best supportive care; LY, life years; vs, versus

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers

**Table 5:** Summary of LY gain by health state (intermediate / poor risk, cabo+nivo vs next best non-dominated comparator: Lenvatinib plus pembrolizumab)

Health state	LY Cabozantinib plus nivolumab (X)	LY Lenvatinib plus pembrolizumab (Y)	Increment	Absolute increment	% absolute increment
1L: off treatment	0.076	0.058	0.017	0.017	3%
1L: on treatment	1.572	1.704	-0.133	0.133	24%
2L: off treatment	0.287	0.204	0.083	0.083	15%
2L: on treatment	0.840	0.636	0.204	0.204	37%
3L: off treatment	0.026	0.041	-0.015	0.015	3%
3L: on treatment	0.142	0.184	-0.042	0.042	8%
4L: off treatment	0.001	0.009	-0.008	0.008	1%
4L: on treatment	0.007	0.055	-0.048	0.048	9%
BSC	0.352	0.355	-0.004	0.004	1%
Death	0.000	0.000	0.000	0.000	0%
<b>Total</b>	<b>3.302</b>	<b>3.247</b>	<b>0.055</b>	<b>0.555</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; BSC, best supportive care; LY, life years; vs, versus

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers

**Table 6:** Summary of QALY gain by health state (all risk, cabo+nivo vs next best non-dominated comparator: Pazopanib)

Health state	QALY Cabozantinib plus nivolumab (X)	QALY Pazopanib (Y)	Increment	Absolute increment	% absolute increment
1L: off treatment	0.074	0.079	-0.005	0.005	1%
1L: on treatment	1.333	0.798	0.535	0.535	59%
2L: off treatment	0.130	0.082	0.048	0.048	5%
2L: on treatment	0.462	0.325	0.137	0.137	15%
3L: off treatment	0.013	0.048	-0.035	0.035	4%
3L: on treatment	0.071	0.188	-0.117	0.117	13%
4L: off treatment	0.001	0.004	-0.003	0.003	0%
4L: on treatment	0.003	0.024	-0.020	0.020	2%
BSC	0.166	0.164	0.003	0.003	0%
Death	0.000	0.000	0.000	0.000	0%
<b>Total</b>	<b>2.254</b>	<b>1.712</b>	<b>0.542</b>	<b>0.904</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; BSC, best supportive care; LY, life years; vs, versus

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers

**Table 7:** Summary of QALY gain by health state (favourable risk, cabo+nivo vs next best non-dominated comparator: Pazopanib)

Health state	QALY Cabozantinib plus nivolumab (X)	QALY Pazopanib (Y)	Increment	Absolute increment	% absolute increment
1L: off treatment	0.177	0.175	0.002	0.002	0%
1L: on treatment	1.688	1.222	0.465	0.465	57%
2L: off treatment	0.128	0.083	0.045	0.045	5%
2L: on treatment	0.454	0.329	0.125	0.125	15%
3L: off treatment	0.013	0.049	-0.036	0.036	4%
3L: on treatment	0.070	0.191	-0.121	0.121	15%
4L: off treatment	0.001	0.004	-0.004	0.004	0%
4L: on treatment	0.003	0.024	-0.021	0.021	3%
BSC	0.164	0.166	-0.002	0.002	0%
Death	0.000	0.000	0.000	0.000	0%
<b>Total</b>	<b>2.697</b>	<b>2.244</b>	<b>0.454</b>	<b>0.821</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; BSC, best supportive care; LY, life years; vs, versus

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers



**Table 8:** Summary of QALY gain by health state (intermediate / poor risk, cabo+nivo vs next best non-dominated comparator: Lenvatinib plus pembrolizumab)

Health state	QALY Cabozantinib plus nivolumab (X)	QALY Lenvatinib plus pembrolizumab (Y)	Increment	Absolute increment	% absolute increment
1L: off treatment	0.052	0.040	0.012	0.012	4%
1L: on treatment	1.091	1.191	-0.100	0.100	33%
2L: off treatment	0.131	0.100	0.032	0.032	11%
2L: on treatment	0.467	0.368	0.098	0.098	33%
3L: off treatment	0.014	0.020	-0.006	0.006	2%
3L: on treatment	0.071	0.094	-0.023	0.023	8%
4L: off treatment	0.001	0.004	-0.004	0.004	1%
4L: on treatment	0.003	0.025	-0.022	0.022	7%
BSC	0.168	0.170	-0.002	0.002	1%
Death	0.000	0.000	0.000	0.000	0%
<b>Total</b>	<b>1.998</b>	<b>2.013</b>	<b>-0.015</b>	<b>0.298</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; BSC, best supportive care; LY, life years; vs, versus

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers



**Table 9:** Summary of costs by health state

Technologies	1L costs			Subsequent treatment			MRU			Total cost
	Drug cost	Admin cost	AE cost	Drug cost	Admin cost	AE cost	1L	Subsequent treatment	EOL cost	
<b>Risk population: All risk</b>										
Sunitinib	£4,555	£294	£604	£45,047	£906	£692	£2,628	£14,362	£7,962	£77,050
Pazopanib	£6,481	£324	£512	£46,503	£893	£688	£2,628	£14,422	£7,949	£80,399
Tivozanib	£27,787	£336	£408	£44,922	£971	£660	£2,628	£14,328	£7,966	£100,005
Cabozantinib plus nivolumab	£201,969	£3,566	£1,127	£35,969	£271	£920	£4,088	£12,897	£7,732	£268,539
<b>Risk population: Favourable risk</b>										
Sunitinib	£6,887	£349	£604	£45,797	£921	£704	£4,058	£14,602	£7,743	£81,665
Pazopanib	£9,859	£395	£512	£47,276	£908	£699	£4,058	£14,662	£7,730	£86,100
Tivozanib	£42,269	£413	£408	£45,670	£987	£671	£4,058	£14,567	£7,747	£116,790
Cabozantinib plus nivolumab	£238,967	£3,804	£1,127	£35,434	£267	£907	£5,354	£12,707	£7,549	£306,115
<b>Risk population: Intermediate / poor risk</b>										
Sunitinib	£3,627	£272	£604	£44,491	£895	£684	£2,080	£14,185	£8,048	£74,884
Pazopanib	£5,137	£296	£512	£45,929	£882	£679	£2,080	£14,244	£8,035	£77,793
Tivozanib	£22,024	£305	£408	£44,367	£959	£652	£2,080	£14,151	£8,052	£92,997

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Technologies	1L costs			Subsequent treatment			MRU			Total cost
	Drug cost	Admin cost	AE cost	Drug cost	Admin cost	AE cost	1L	Subsequent treatment	EOL cost	
Cabozantinib	£48,330	£292	£732	£46,183	£1,073	£698	£2,080	£14,314	£8,024	£121,724
Nivolumab plus ipilimumab	£107,171	£4,254	£335	£30,114	£229	£634	£2,931	£11,366	£7,981	£165,014
Lenvatinib plus pembrolizumab	£156,566	£2,753	£1,062	£34,897	£275	£879	£3,606	£13,902	£7,834	£221,773
Cabozantinib plus nivolumab	£172,139	£3,209	£1,127	£36,244	£273	£927	£3,368	£12,995	£7,836	£238,117

Abbreviations: admin, administration; AE, adverse event; EOL, end of life; MRU, medical resource use

**Table 10:** Summary of predicted resource use by category of cost (all risk, cabo+nivo vs next best non-dominated comparator: Pazopanib)

<b>Item</b>	<b>Cost Cabozantinib plus nivolumab (X)</b>	<b>Cost Pazopanib (Y)</b>	<b>Increment</b>	<b>Absolute increment</b>	<b>% absolute increment</b>
Drug acquisition cost (1L)	£201,969	£6,481	£195,487	£195,487	91%
Admin cost (1L)	£3,566	£324	£3,242	£3,242	2%
AE cost (1L)	£1,127	£512	£615	£615	0%
Drug acquisition cost (2L+)	£35,969	£46,503	£-10,534	£10,534	5%
Admin cost (2L+)	£271	£893	£-622	£622	0%
AE cost (2L+)	£920	£688	£233	£233	0%
MRU 1L	£4,088	£2,628	£1,460	£1,460	1%
MRU 2L+	£12,897	£14,422	£-1,525	£1,525	1%
EOL	£7,732	£7,949	£-217	£217	0%
<b>Total</b>	<b>£268,539</b>	<b>£80,399</b>	<b>£188,140</b>	<b>£213,936</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 2L+, 2nd line-plus; admin, administration; AE, adverse event; EOL, end of life; MRU, medical resource use

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers

**Table 11:** Summary of predicted resource use by category of cost (favourable risk, cabo+nivo vs next best non-dominated comparator: Pazopanib)

Item	Cost Cabozantinib plus nivolumab (X)	Cost Pazopanib (Y)	Increment	Absolute increment	% absolute increment
Drug acquisition cost (1L)	£238,967	£9,859	£229,108	£229,108	92%
Admin cost (1L)	£3,804	£395	£3,409	£3,409	1%
AE cost (1L)	£1,127	£512	£615	£615	0%
Drug acquisition cost (2L+)	£35,434	£47,276	£-11,842	£11,842	5%
Admin cost (2L+)	£267	£908	£-641	£641	0%
AE cost (2L+)	£907	£699	£208	£208	0%
MRU 1L	£5,354	£4,058	£1,296	£1,296	1%
MRU 2L+	£12,707	£14,662	£-1,956	£1,956	1%
EOL	£7,549	£7,730	£-181	£181	0%
<b>Total</b>	<b>£306,115</b>	<b>£86,100</b>	<b>£220,016</b>	<b>£249,255</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 2L+, 2nd line-plus; admin, administration; AE, adverse event; EOL, end of life; MRU, medical resource use

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers

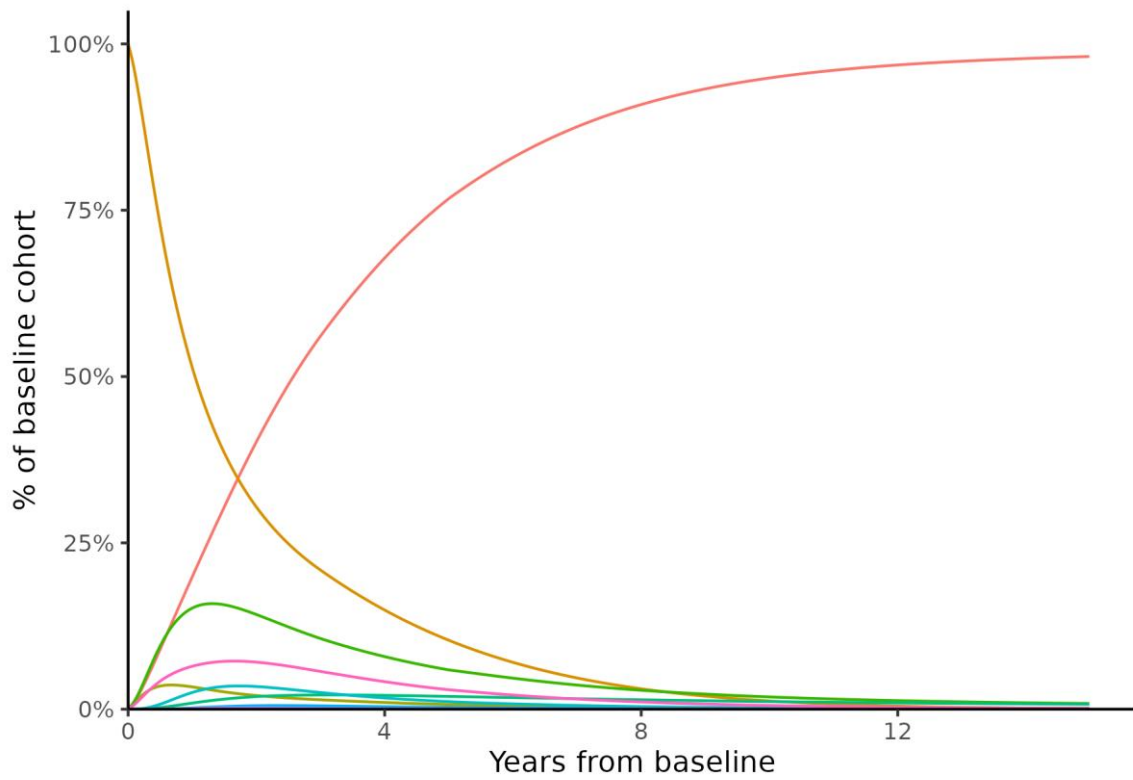
**Table 12:** Summary of predicted resource use by category of cost (intermediate / poor risk, cabo+nivo vs next best non-dominated comparator: Lenvatinib plus pembrolizumab)

Item	Cost Cabozantinib plus nivolumab (X)	Cost Lenvatinib plus pembrolizumab (Y)	Increment	Absolute increment	% absolute increment
Drug acquisition cost (1L)	£172,139	£156,566	£15,573	£15,573	84%
Admin cost (1L)	£3,209	£2,753	£455	£455	2%
AE cost (1L)	£1,127	£1,062	£65	£65	0%
Drug acquisition cost (2L+)	£36,244	£34,897	£1,348	£1,348	7%
Admin cost (2L+)	£273	£275	£-2	£2	0%
AE cost (2L+)	£927	£879	£48	£48	0%
MRU 1L	£3,368	£3,606	£-238	£238	1%
MRU 2L+	£12,995	£13,902	£-907	£907	5%
EOL	£7,836	£7,834	£2	£2	0%
<b>Total</b>	<b>£238,117</b>	<b>£221,773</b>	<b>£16,345</b>	<b>£18,638</b>	<b>100%</b>

Abbreviations: 1L, 1st line; 2L, 2nd line; 2L+, 2nd line-plus; admin, administration; AE, adverse event; EOL, end of life; MRU, medical resource use

Discrepancies in sums due to rounding errors: totals shown are calculated on unrounded numbers

**Figure 1:** Markov trace: All risk, Cabozantinib plus nivolumab

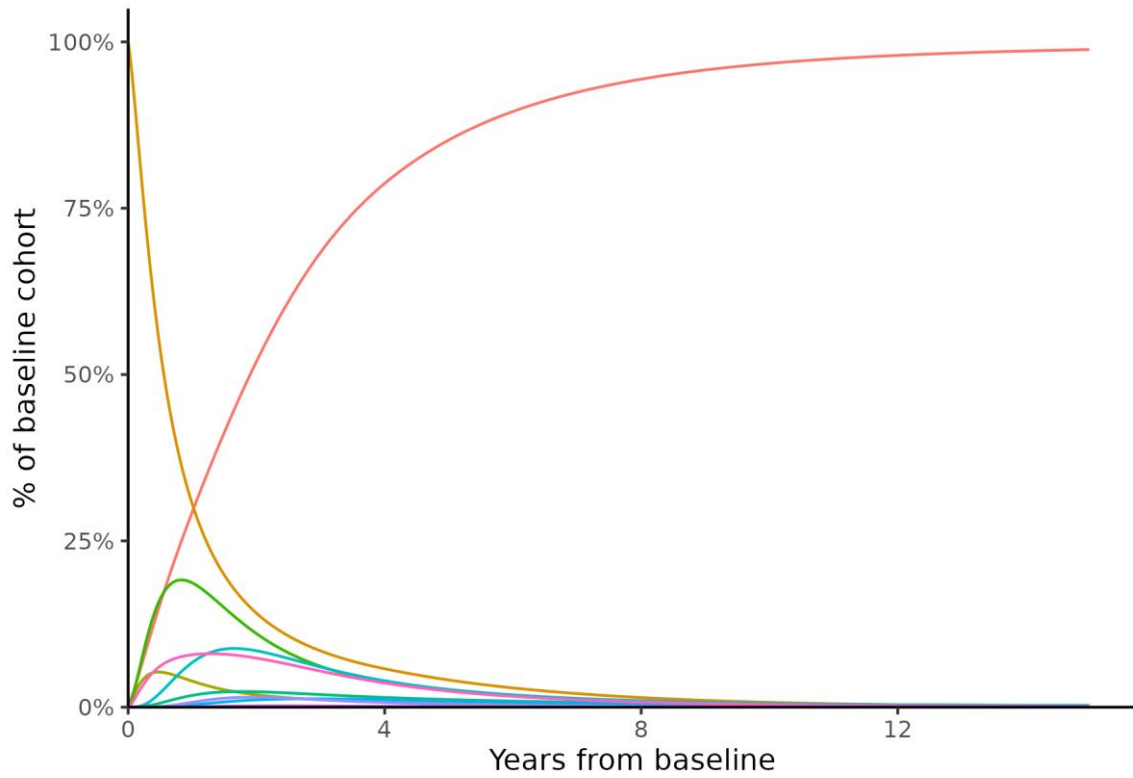


lead                    — L1 (off treatment)   — L2 (off treatment)   — L3 (off treatment)   — L4  
.1 (on treatment)   — L2 (on treatment)   — L3 (on treatment)   — L4 (on treatment)   — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line



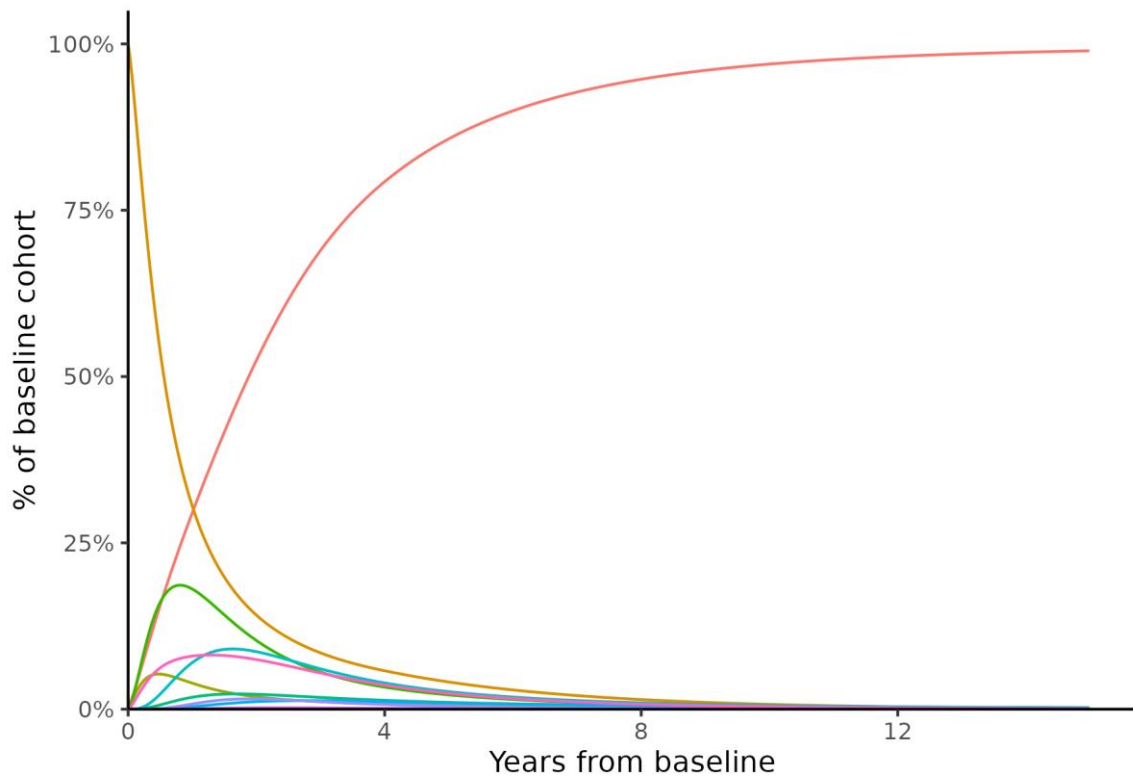
**Figure 2:** Markov trace: All risk, Pazopanib



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

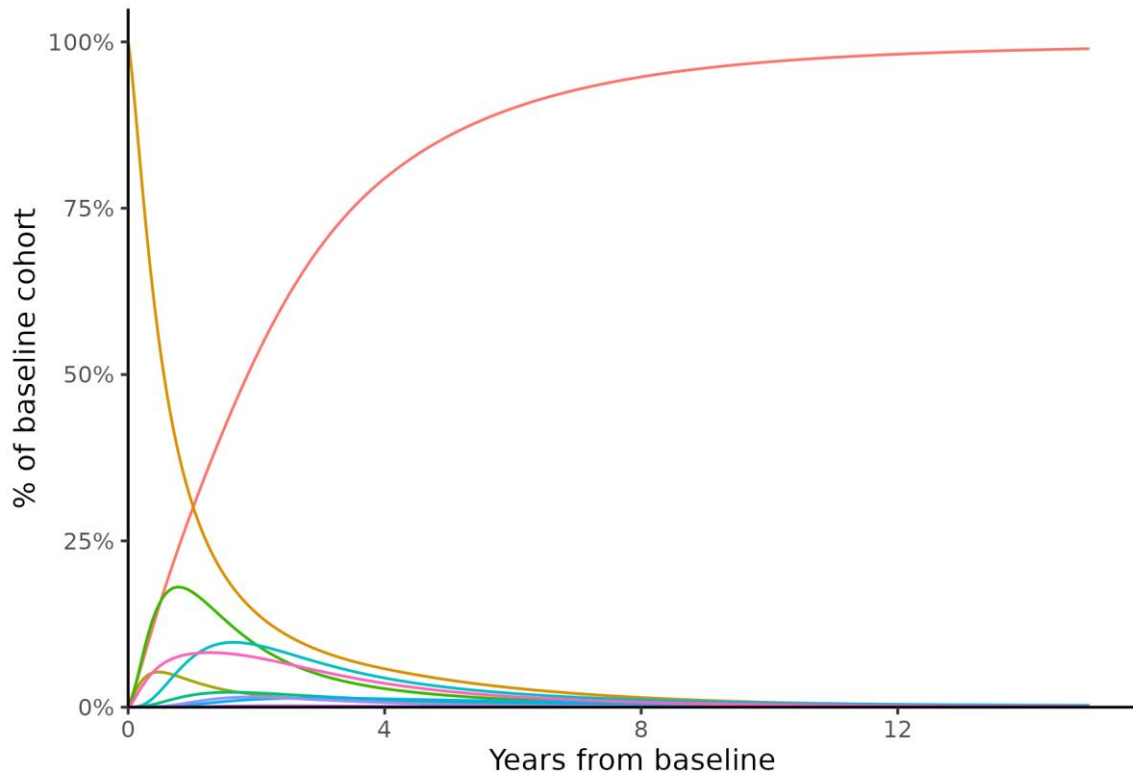
**Figure 3:** Markov trace: All risk, Sunitinib



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

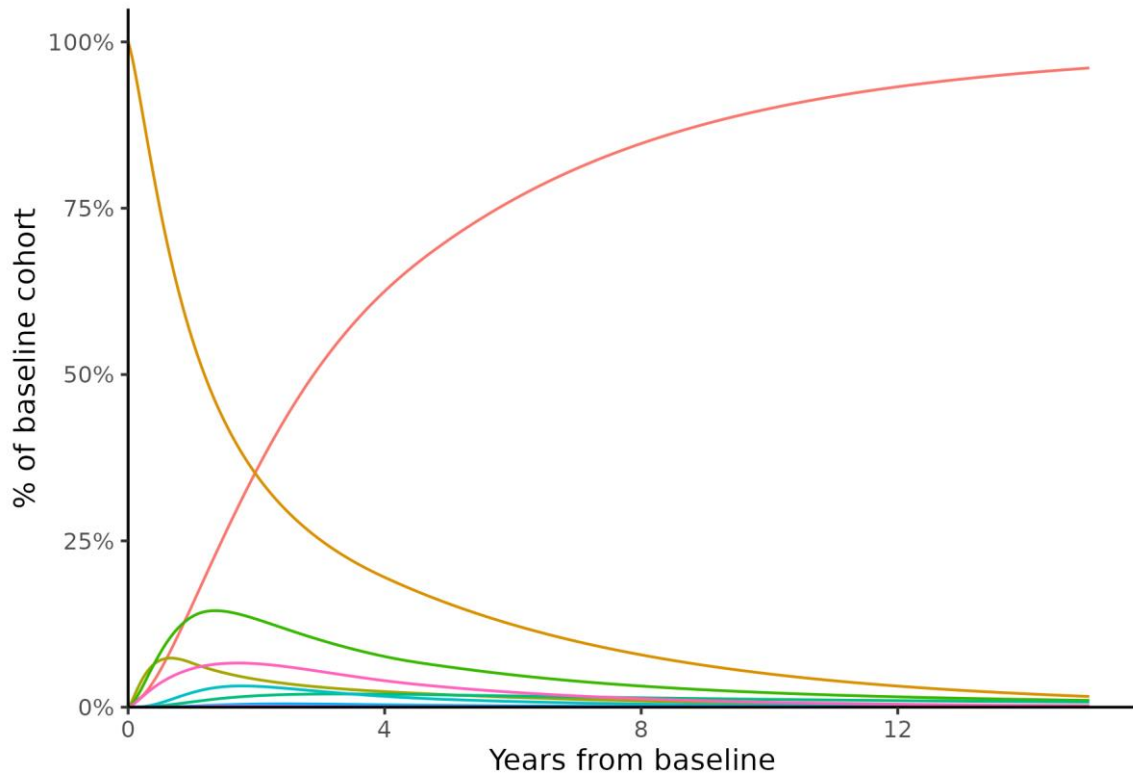
**Figure 4:** Markov trace: All risk, Tivozanib



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

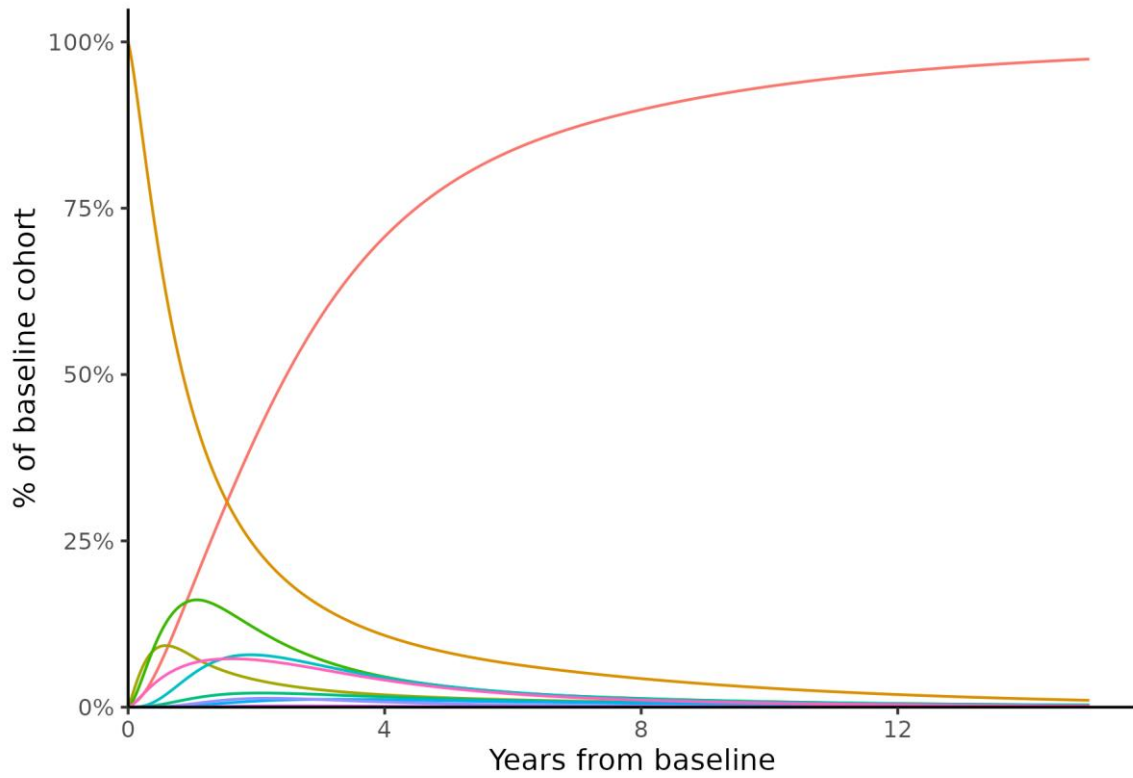
**Figure 5:** Markov trace: Favourable risk, Cabozantinib plus nivolumab



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

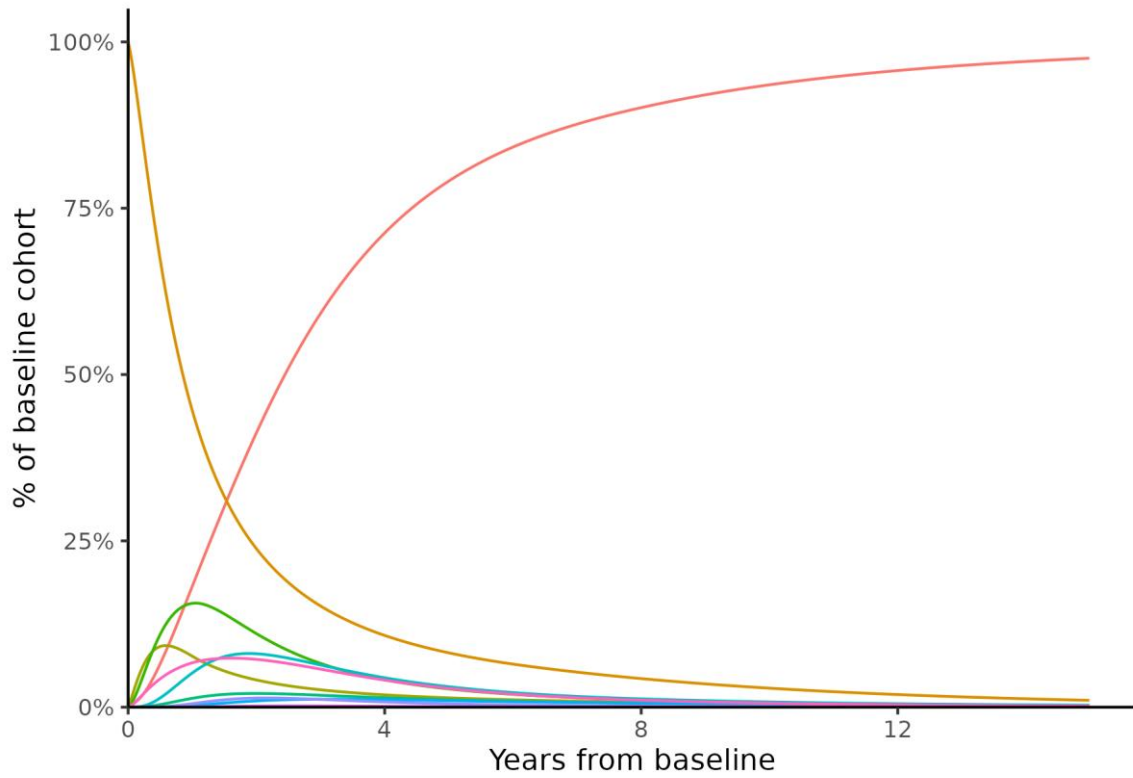
**Figure 6:** Markov trace: Favourable risk, Pazopanib



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

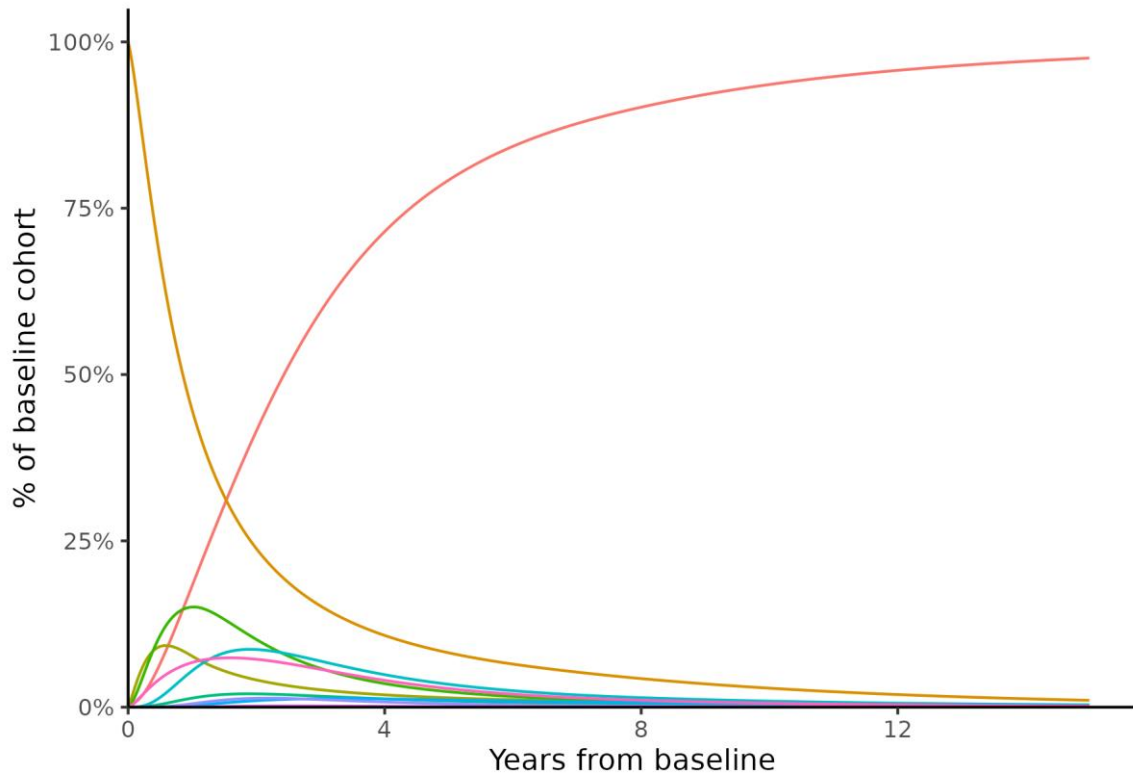
**Figure 7:** Markov trace: Favourable risk, Sunitinib



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

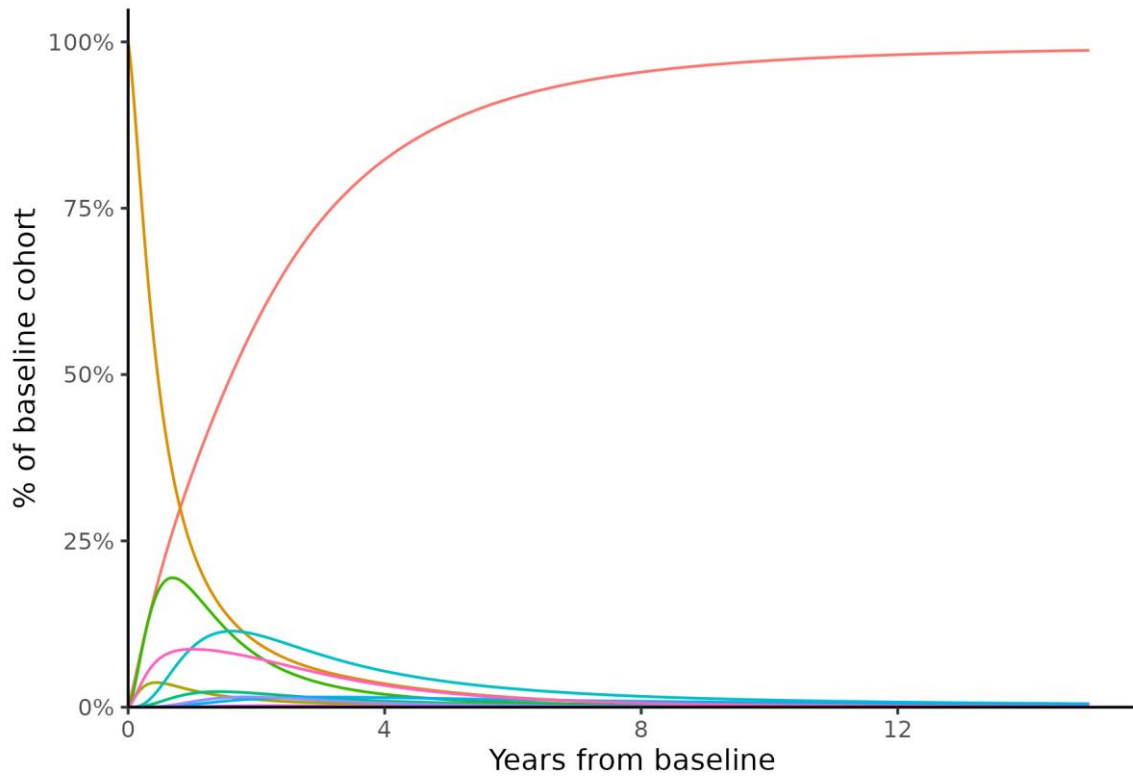
**Figure 8:** Markov trace: Favourable risk, Tivozanib



lead                    L1 (off treatment)    L2 (off treatment)    L3 (off treatment)    L4  
.1 (on treatment)    L2 (on treatment)    L3 (on treatment)    L4 (on treatment)    L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

**Figure 9:** Markov trace: Intermediate / poor risk, Cabozantinib

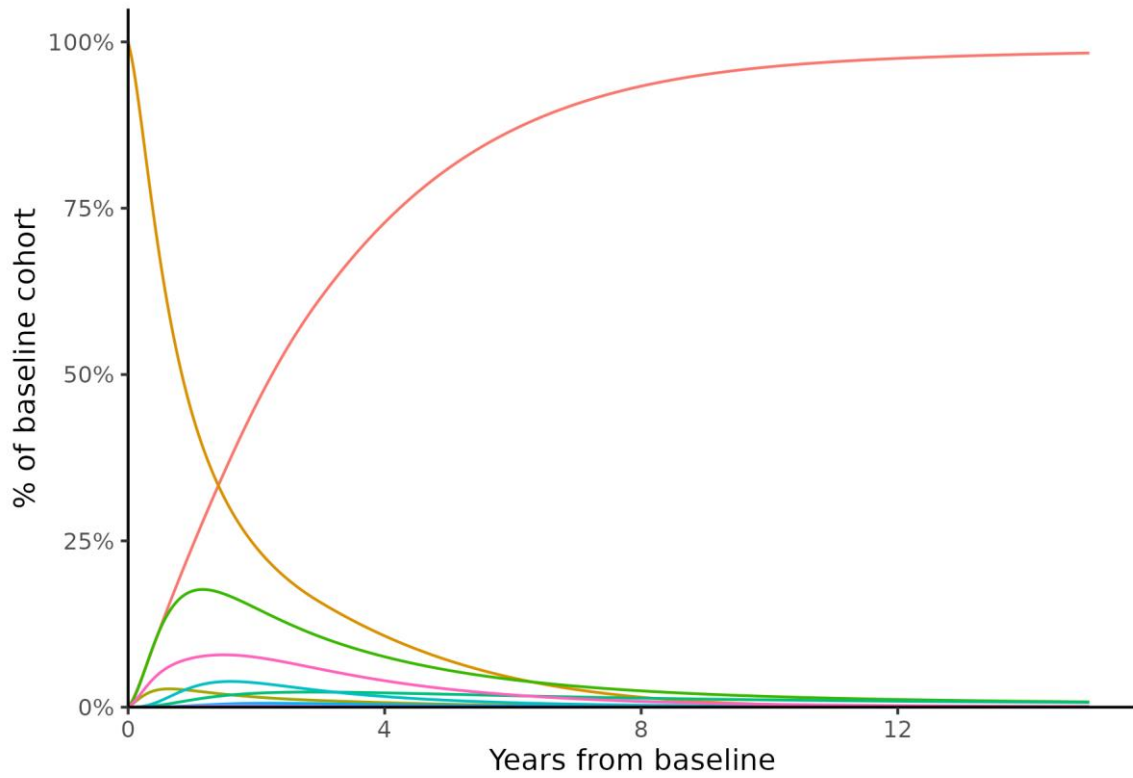


lead                    L1 (off treatment)    L2 (off treatment)    L3 (off treatment)    L4  
.1 (on treatment)    L2 (on treatment)    L3 (on treatment)    L4 (on treatment)    L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line



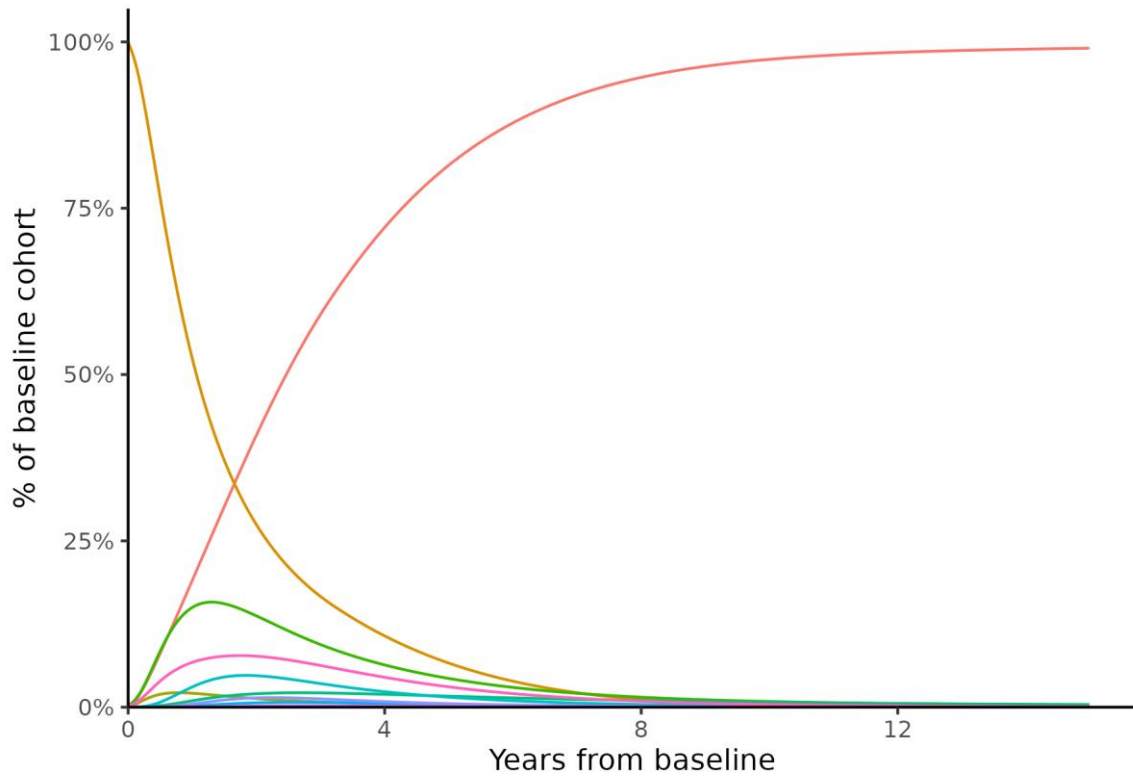
**Figure 10:** Markov trace: Intermediate / poor risk, Cabozantinib plus nivolumab



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

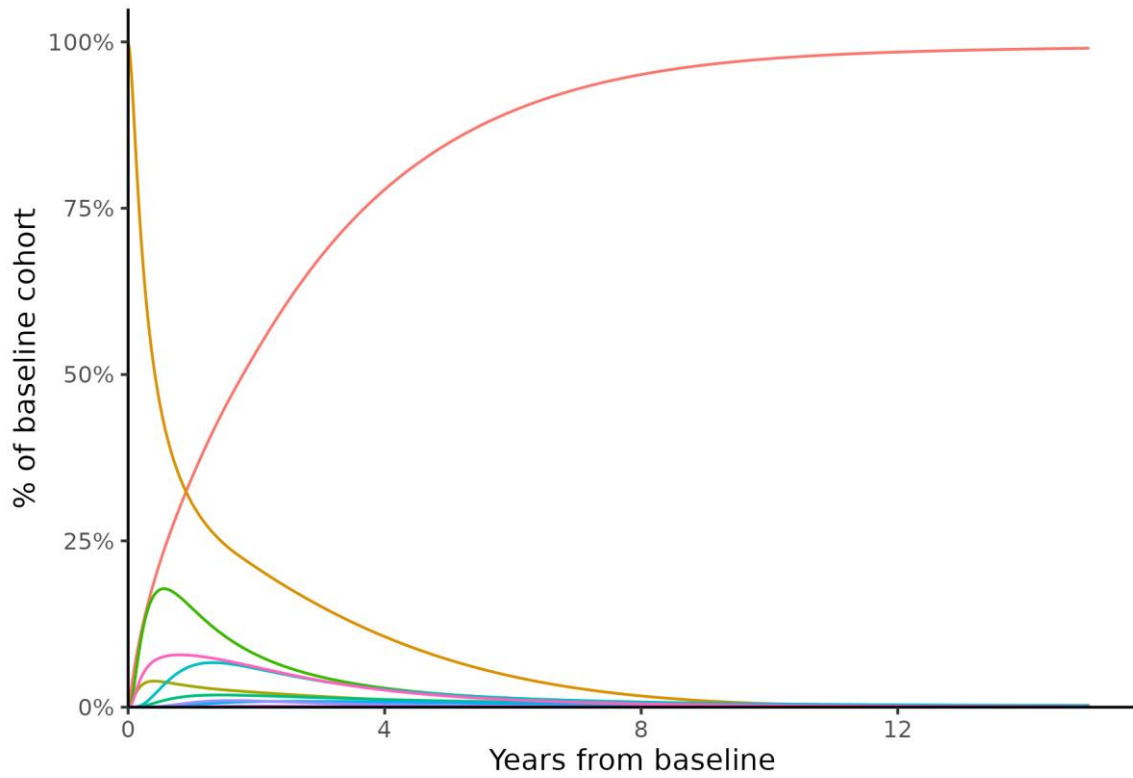
**Figure 11:** Markov trace: Intermediate / poor risk, Lenvatinib plus pembrolizumab



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

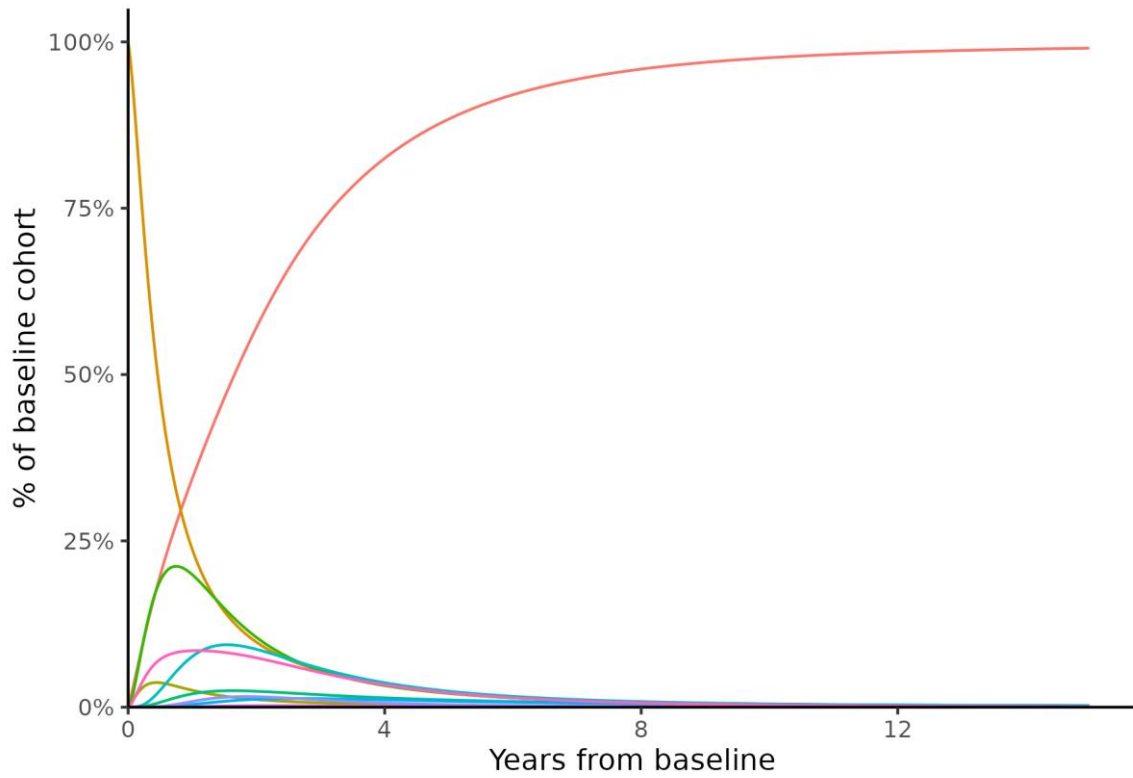
**Figure 12:** Markov trace: Intermediate / poor risk, Nivolumab plus ipilimumab



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

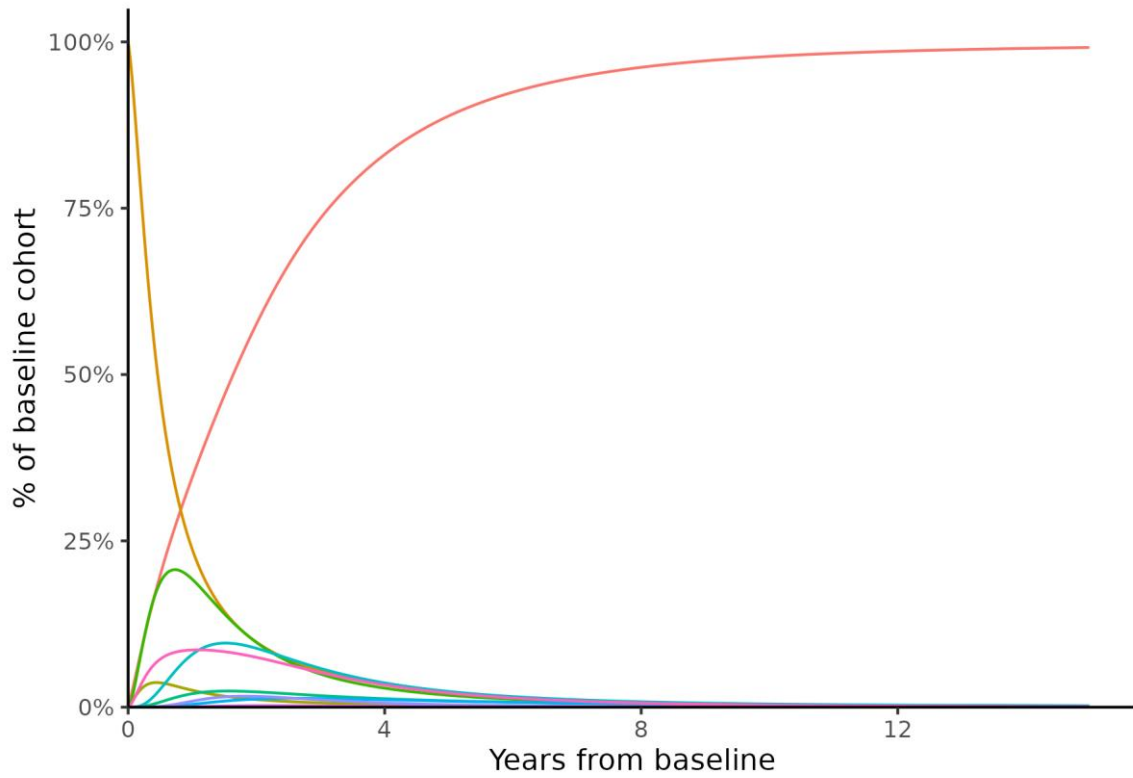
**Figure 13:** Markov trace: Intermediate / poor risk, Pazopanib



lead                    — L1 (off treatment)    — L2 (off treatment)    — L3 (off treatment)    — L4  
.1 (on treatment)    — L2 (on treatment)    — L3 (on treatment)    — L4 (on treatment)    — L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

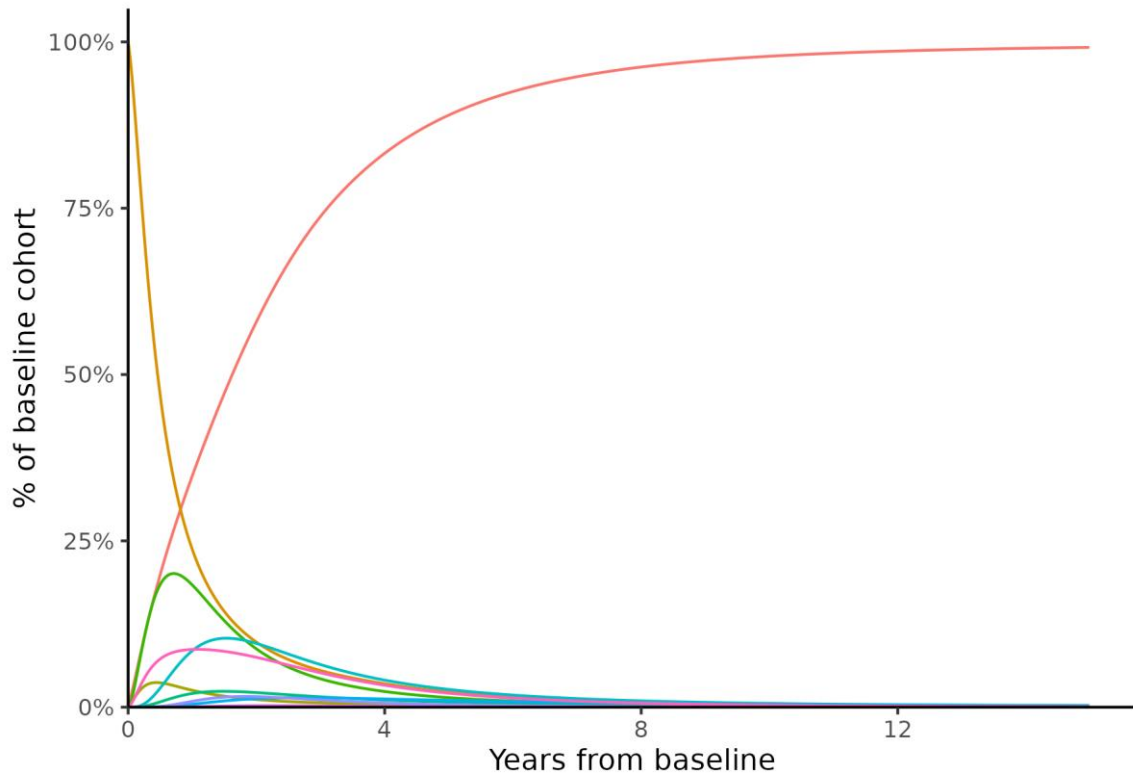
**Figure 14:** Markov trace: Intermediate / poor risk, Sunitinib



lead                    L1 (off treatment)    L2 (off treatment)    L3 (off treatment)    L4  
.1 (on treatment)    L2 (on treatment)    L3 (on treatment)    L4 (on treatment)    L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

**Figure 15:** Markov trace: Intermediate / poor risk, Tivozanib



lead                    L1 (off treatment)    L2 (off treatment)    L3 (off treatment)    L4  
.1 (on treatment)    L2 (on treatment)    L3 (on treatment)    L4 (on treatment)    L5

Abbreviations: L1, 1st line; L2, 2nd line; L3, 3rd line; L4, 4th line; L5, 5th line

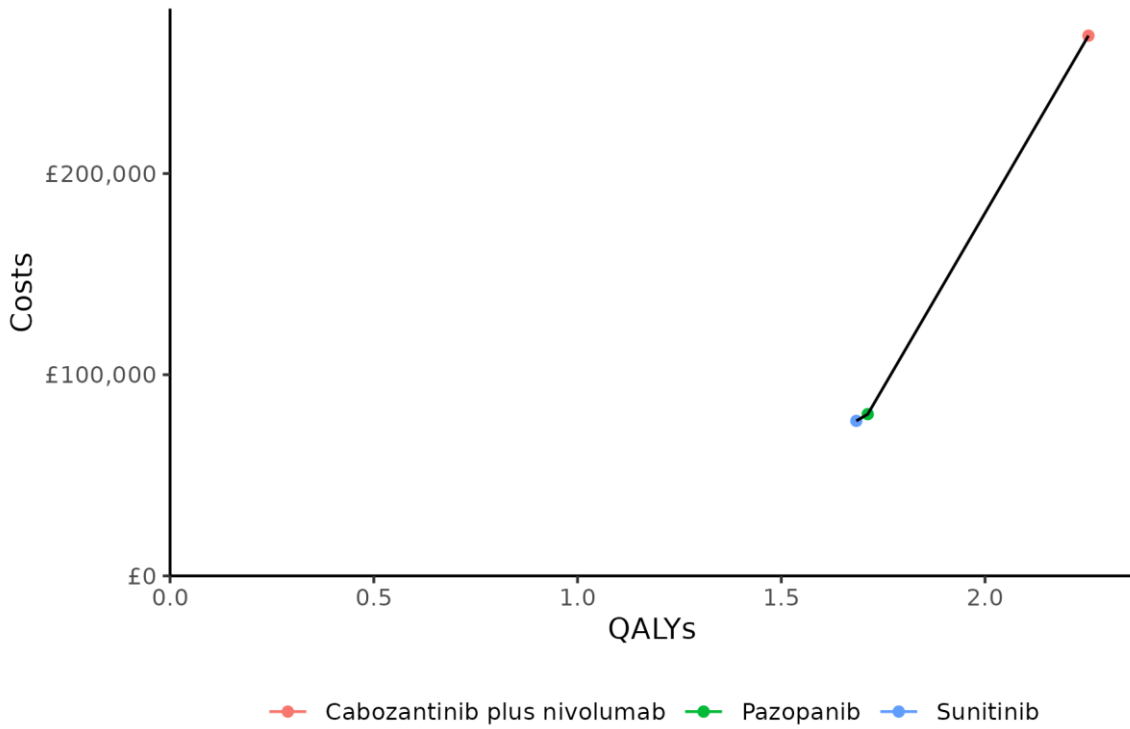


### **R.3. Cost-effectiveness acceptability frontiers**

Cost-effectiveness acceptability frontiers are presented for all non-dominated treatments for each of the risk groups

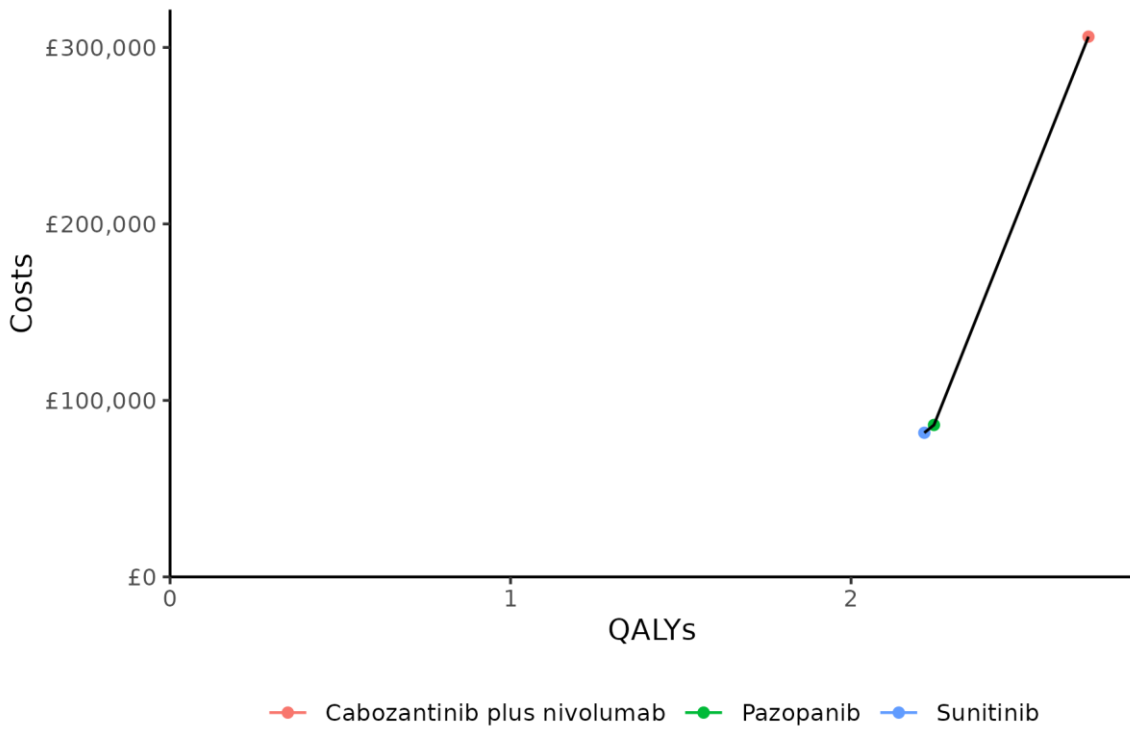


**Figure 16:** Cost-effectiveness acceptability frontier – all risk



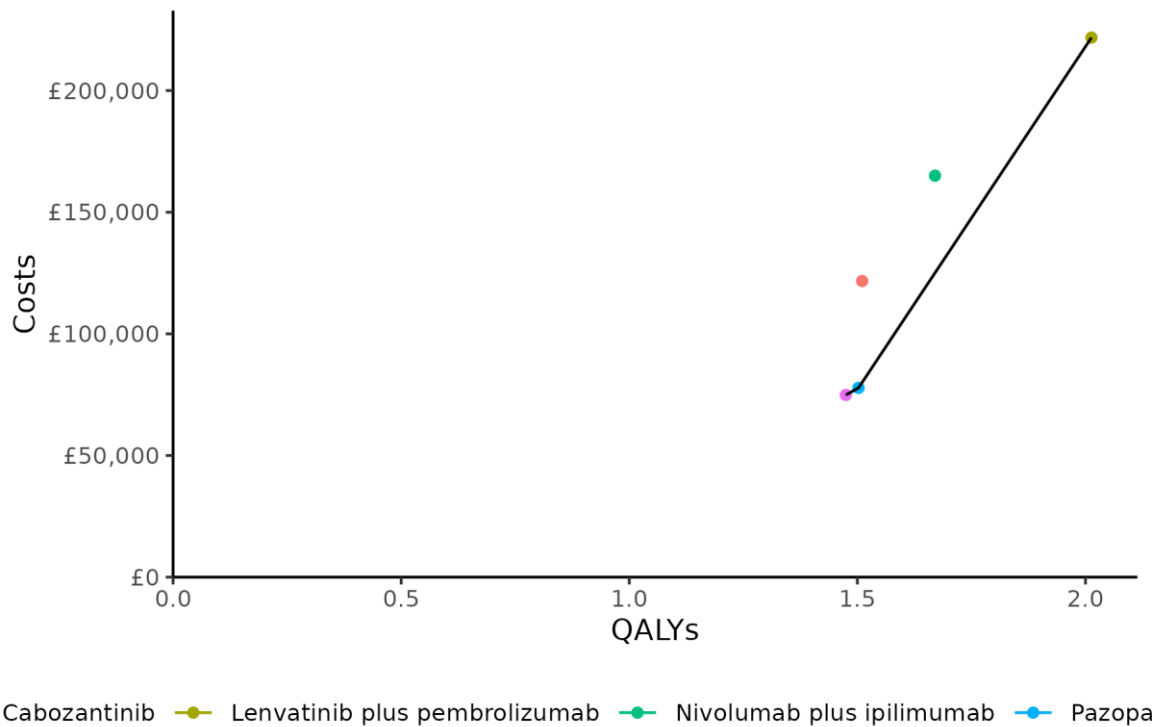
Abbreviations: QALYs, quality-adjusted life-years

**Figure 17:** Cost-effectiveness acceptability frontier – favourable risk



Abbreviations: QALYs, quality-adjusted life-years

**Figure 18:** Cost-effectiveness acceptability frontier – intermediate / poor risk



Abbreviations: QALYs, quality-adjusted life-years

## Appendix S. Scenario analysis style tables

**Table 13:** Scenario analysis - all risk

<b>Scenario</b>	<b>Next best comparator*</b>	<b>Incremental costs</b>	<b>Incremental QALYs</b>	<b>ICER (£/QALY)</b>
Base case	Pazopanib	£188,140	0.542	£347,366

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; AEs, adverse events; AUC, area under the curve; axi, axitinib; BSC, best supportive care; evero, everolimus; FP, fractional polynomial; ICER, incremental cost-effectiveness ratio; IO, immune-oncology; IV, intravenous; KM, Kaplan-Meier; OS, overall survival; PD, progressed disease; PFS, progression free survival; PH, proportional hazards; PPS, post-progression survival; QALYs, quality adjusted life years; RDI, relative dosing intensity; RWE, real world evidence; tivo, tivozanib; TKI, tyrosine kinase inhibitor; TTD, time to discontinuation; TTP, time to progression

\*Next best comparator defined as next most efficient non-dominated comparator.

**Table 14:** Scenario analysis - favourable risk

<b>Scenario</b>	<b>Next best comparator*</b>	<b>Incremental costs</b>	<b>Incremental QALYs</b>	<b>ICER (£/QALY)</b>
Base case	Pazopanib	£220,016	0.454	£484,904

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; AEs, adverse events; AUC, area under the curve; axi, axitinib; BSC, best supportive care; evero, everolimus; FP, fractional polynomial; ICER, incremental cost-effectiveness ratio; IO, immune-oncology; IV, intravenous; KM, Kaplan-Meier; OS, overall survival; PD, progressed disease; PFS, progression free survival; PH, proportional hazards; PPS, post-progression survival; QALYs, quality adjusted life years; RDI, relative dosing intensity; RWE, real world evidence; tivo, tivozanib; TKI, tyrosine kinase inhibitor; TTD, time to discontinuation; TTP, time to progression

\*Next best comparator defined as next most efficient non-dominated comparator.

**Table 15:** Scenario analysis - intermediate / poor risk

<b>Scenario</b>	<b>Next best comparator*</b>	<b>Incremental costs</b>	<b>Incremental QALYs</b>	<b>ICER (£/QALY)</b>
Base case	Lenvatinib plus pembrolizumab	£0	0.000	Cabo+nivo dominated

Abbreviations: 1L, 1st line; 2L, 2nd line; 3L, 3rd line; 4L, 4th line; AEs, adverse events; AUC, area under the curve; axi, axitinib; BSC, best supportive care; evero, everolimus; FP, fractional polynomial; ICER, incremental cost-effectiveness ratio; IO, immune-oncology; IV, intravenous; KM, Kaplan-Meier; OS, overall survival; PD, progressed disease; PFS, progression free survival; PH, proportional hazards; PPS, post-progression survival; QALYs, quality adjusted life years; RDI, relative dosing intensity; RWE, real world evidence; tivo, tivozanib; TKI, tyrosine kinase inhibitor; TTD, time to discontinuation; TTP, time to progression

\*Next best comparator defined as next most efficient non-dominated comparator.

**Table 16:** Scenario analysis pairwise comparison table

<b>Technologies</b>	<b>Costs (£)</b>	<b>QALYs</b>	<b>LYG</b>	<b>Inc. Costs</b>	<b>Inc. QALYs</b>	<b>Inc. LYG</b>	<b>ICER cabo + nivo vs comparator</b>
<b>Risk population: All risk</b>							
Cabozantinib plus nivolumab	£268,539	2.25	3.71				
Pazopanib	£80,399	1.71	2.84	£188,140	0.54	0.88	£347366
Tivozanib	£100,005	1.67	2.76	£168,534	0.58	0.95	£291017
Sunitinib	£77,050	1.68	2.78	£191,489	0.57	0.93	£336158
<b>Risk population: Favourable risk</b>							
Cabozantinib plus nivolumab	£306,115	2.70	4.52				
Pazopanib	£86,100	2.24	3.73	£220,016	0.45	0.78	£484904
Tivozanib	£116,790	2.21	3.66	£189,325	0.49	0.86	£385004
Sunitinib	£81,665	2.22	3.68	£224,451	0.48	0.84	£465558
<b>Risk population: Intermediate / poor risk</b>							
Cabozantinib plus nivolumab	£238,117	2.00	3.30				
Nivolumab plus ipilimumab	£165,014	1.67	2.72	£73,104	0.33	0.59	£223146
Lenvatinib plus pembrolizumab	£221,773	2.01	3.25	£16,345	-0.02	0.06	Cabo+nivo dominated
Pazopanib	£77,793	1.50	2.50	£160,325	0.50	0.80	£323708
Tivozanib	£92,997	1.47	2.43	£145,120	0.53	0.87	£272605

Treatments for renal cell carcinoma [ID6186]: pathways pilot appraisal

Assessment report: Appendix Q

<b>Technologies</b>	<b>Costs (£)</b>	<b>QALYs</b>	<b>LYG</b>	<b>Inc. Costs</b>	<b>Inc. QALYs</b>	<b>Inc. LYG</b>	<b>ICER cabo + nivo vs comparator</b>
Sunitinib	£74,884	1.47	2.45	£163,233	0.52	0.86	£312114
Cabozantinib	£121,724	1.51	2.57	£116,393	0.49	0.73	£238820

Abbreviations: ICER, incremental cost-effectiveness ratio; inc. incremental; LYG, life-years gained; QALY, quality-adjusted life-year

