NICE National Institute for Health and Care Excellence

Pembrolizumab for adjuvant treatment of renal cell carcinoma [ID3810]

Lead team presentation

Technology appraisal committee B [12/05/2022]

Chair: Dr. Charles Crawley

Lead team: Prof Nicky Welton, Tony Wootton

Evidence review group: BMJ-TAG

Technical team: Henry Edwards, Rufaro Kausi, Susan O'Connell

Company: Merck Sharp & Dohme (MSD)

© NICE 2021. All rights reserved. Subject to notice of rights. The content in this publication is owned by multiple parties and may not be re-used without the permission of the relevant copyright owner.

Key issues

Key: Large impact  Small/moderate impact  Unknown impact 

No.	Issue	Resolved?	ICER impact
1	DFS and OS data from the KEYNOTE-564 trial are immature which adds uncertainty to the evidence and economic modelling.	No – for discussion	
2	Long term risk of relapse	No – for discussion	
3	Transitions from the disease-free health state (Joint or separate fitting of Exponential & Gompertz extrapolation)	No – for discussion	
4	IA versus BICR assessment from KEYNOTE-564	No – for discussion	
5	Is the technology eligible for the Cancer Drug Fund (CDF)?	No – for discussion	
6	Treatment regimen and resource use for pembrolizumab	Resolved during technical engagement	

Abbreviations: BICR, blinded independent central review; DFS, disease free survival; IA, Investigator assessed; OS, overall survival

Background and decision problem

Disease background

Causes and epidemiology

- Renal cell carcinoma (RCC) originates in the lining of the kidney tubule (smallest tubes in the nephrons)
- RCC is the **most common type of kidney cancer (>80% of cases)** with the highest rate in people over 85 years of age as incidence rate increases with age
- **Diagnosis and classification**
- ~ 11,000 new cases of kidney cancer in England in 2017
- ~ 2/3 diagnosed without evidence of metastatic disease

Symptoms and prognosis

- Symptoms can include blood in urine, persistent pain in lower back or side, extreme tiredness, loss of appetite, persistent hypertension and night sweats
- Surgery is performed with curative intent and more than 50% of people diagnosed with Kidney cancer in England between 2013 and 2017 survive their cancer for 10 years or more.

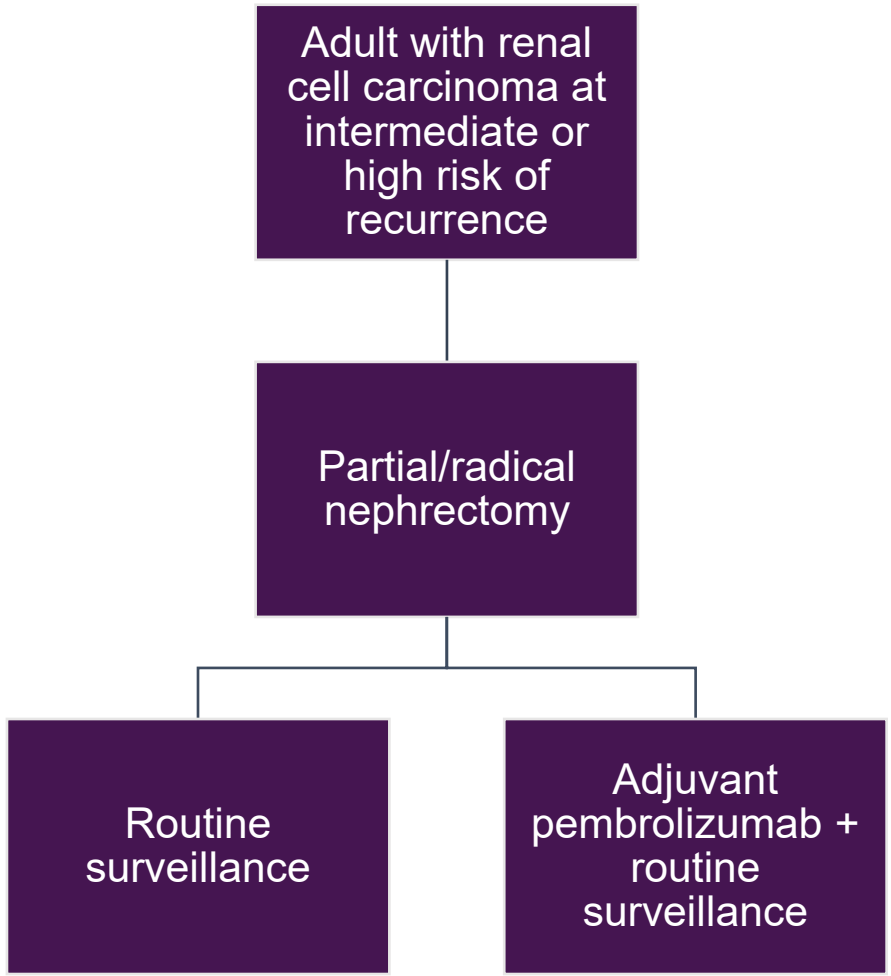
Pembrolizumab (KEYTRUDA, MSD)

Marketing authorisation	• Pembrolizumab as monotherapy is indicated for the adjuvant treatment of adults with renal cell carcinoma at intermediate or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.
Mechanism of action	• Pembrolizumab is a monoclonal antibody (mAB) of the IgG4/kappa isotype designed to exert a dual ligand blockade of the PD-1 pathway by directly blocking the interaction between PD-1 and its associated ligands, PD-L1 and PD-L2 which appear on the antigen-presenting or tumour cells.
Administration	• Monotherapy 200mg every 3 weeks (Q3W) up to 17 cycles or 400mg every 6 weeks (Q6W).
Price	• £2,630 per 100mg vial. • £89,420 per patient for 17 cycles (12 months of treatment) • Confidential patient access scheme

Abbreviations: MHRA, Medicines and Healthcare products regulatory agency

Treatment pathway

The company's proposed positioning of pembrolizumab in the NICE pathway is as adjuvant therapy following partial or complete nephrectomy.



Decision problem is in line with the scope

	Final scope	Evidence used in the model
Population	People with renal cell carcinoma (RCC) who have had nephrectomy	Adjuvant treatment of adults with renal cell carcinoma at intermediate or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions. Narrower than scope but aligned with MA and key clinical trial
Intervention	Pembrolizumab	In line with scope SmPC: pembrolizumab administered until disease recurrence, unacceptable toxicity, or for a duration of up to one year Clinical advice that proposed duration of treatment is reasonable and in line with current UK practice.
Comparators	Established clinical management without pembrolizumab	In line with scope
Outcomes	Overall survival Disease-free survival Adverse effects of treatment Health-related quality of life	In line with scope

Abbreviations: SmPC, Summary of product characteristics

Patient and Clinical expert perspectives

Renal cell carcinoma

- Biomarkers for treatment of RCC are yet to be identified, process of elimination to find effective treatments
- Most patients with metastatic RCC face disease progression → worsening of symptoms, such as severe pain, fatigue, and shortness-of-breath.
- After surgery patients feel abandoned, emotionally low, and anxious about the cancer returning.

Current treatment

- Current treatments have significant toxicity and aide effects
  - extreme fatigue, night sweats, rashes, chronic diarrhoea, severe mouth ulcers, nausea, hypertension, muscle and joint pain → severely affect quality of life

New treatment options

- Unmet need for effective adjuvant treatments
  - would help prevent disease spread and metastases, especially more aggressive and rare types
- New treatment options for RCC are therefore very welcome

Without an adjuvant treatment, some patients will go on to develop metastatic RCC, sometimes months or even years after surgery. Metastatic RCC is a devastating disease and is currently incurable

Planning is the worse problem – you can't plan to do anything.

I never know from day to day how I am going to feel, which side effect I will be suffering from and how ill it will make me

Clinical effectiveness

NICE National Institute for Health and Care Excellence

KEYNOTE-564

Phase 3 randomised, double-blind, placebo controlled clinical trial

Used in company model

Patients
- ≥18 years
- Advanced or metastatic RCC with clear cell component
- Intermediate or high risk of recurrence
- Treatment-naive
- ECOG performance status 0 or 1
- Nephrectomy>=4 weeks prior to screening
- No brain, chest, abdomen or pelvis tumours

Pembrolizumab (n=488
200mg iv Q3 x 17 cycles
(1 year)

Treat to until disease recurrence or until discontinuation

Placebo (n=496)
(incl. routine surveillance)
200mg iv Q3 x 17 cycles

Endpoints*

1°
- Disease Free Survival

2°
- Overall Survival
- DRSS 1 & 2 (investigator assessed)
- EFS assessed by BICR
- Adverse Effects
- HRQoL

Median duration XXX months

Intermediate-high risk: pathologic tumour stage T2 (pT2) with Grade 4 or sarcomatoid; pT3, any grade without nodal involvement (N0) or distant metastases (M0)
High risk: any pT4, any grade N0 and M0, any pathologic tumour stage, any grade with nodal involvement and M0.

ERG
Clinical experts consider the population characteristics to be generalisable to those undergoing nephrectomy for RCC in England.
NB. Baseline characteristic in backup slides

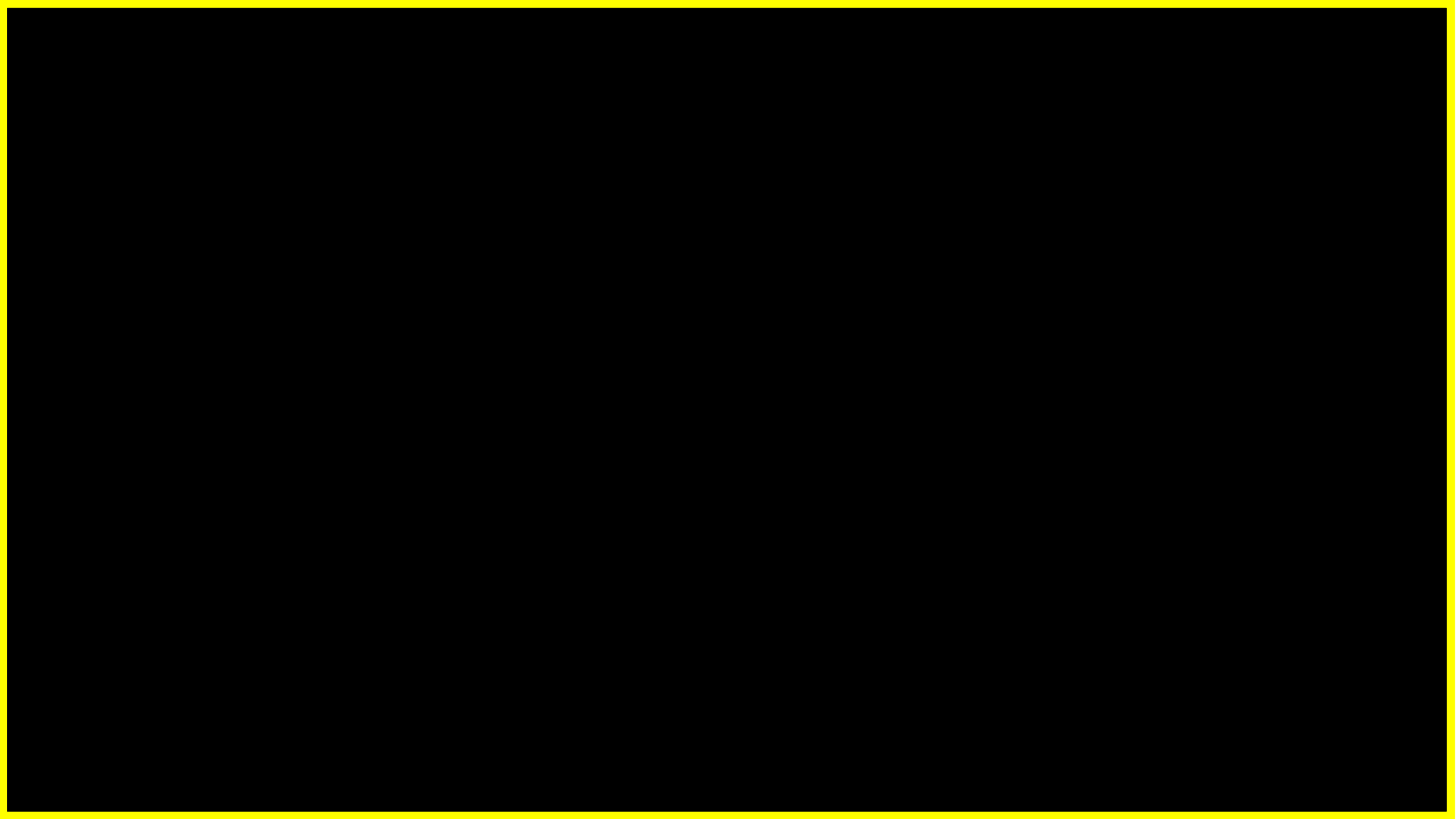
Abbreviations: DRSS, disease recurrence-specific survival; BICR, blinded independent central review; IA, investigator assessed EFS, event free survival, RCC, renal cell carcinoma; SoC, Standard of Care

Disease Free Survival from KEYNOTE-564

Intent to Treat Population	Pembrolizumab (N=496)	Placebo (N=498)
Number of Events (%)	XXXX	XXXX
Death without recurrence	XXXX	XXXX
Disease Recurrence	XXXX	XXXX
Number of Censored (%)	XXXX	XXXX
Last Tumour Assessment Showing No Disease Recurrence	XXXX	XXXX
No Post-Baseline Disease Status Assessment	XXX	XXX
Kaplan-Meier Estimates (months)	XXXX	XXXX
Median (95% CI)	XXXX	XXXX
[Q1, Q3]	XXX	XXX
vs Placebo		XXXX
Hazard Ratio (95% CI)		XXXX
p-value		XXXXXXX

Disease Free Survival Kaplan Meier Curve

Database Cutoff date:
14JUN2021



Overall Survival From KEYNOTE-564

Intent to Treat Population	Pembrolizumab (N=496)	Placebo (N=498)
Number of Events (%)	XXXXXXX	XXXXXXX
Kaplan-Meier Estimates (months) Median (95% CI) [Q1, Q3]	XXXXXXX	XXXXXXX
vs Placebo Hazard Ratio (95% CI), p value		XXXXXXX
OS Rate at month 12 (%) (95% CI)	XXXXXXX	XXXXXXX
OS Rate at month 18 (%) (95% CI)	XXXXXXX	XXXXXXX
OS Rate at month 24 (%) (95% CI)	XXXXXXX	XXXXXXX

The company reports that mortality was reduced with pembrolizumab compared to placebo

Overall Survival Kaplan Meier Curve

Database Cutoff date:
14JUN2021

Key issue 1: Immaturity of the data

DFS and OS data from the KEYNOTE-564 trial are immature which adds uncertainty to the evidence and economic modelling

Will further data collection add certainty to the clinical evidence and economic modelling? Is further data collection feasible?

Background

- DFS and OS results from KEYNOTE-564 are immature XXXXXXXXXXXXXXXXXXXXXX
  - Inform the transitions in the model → subject to increased uncertainty

Company

- Company agreed that the data are immature
  - Possible candidate for the CDF which would allow additional data collection
  - Final analysis for DFS is anticipated to be available in 2024

Clinical expert

- Further data collection should be feasible

Abbreviations: DF, disease free; DFS, disease free survival; LR, local recurrence; OS overall survival

Key issue 4: IA versus BICR assessment from KEYNOTE-564

Does IA or BICR assessment provide more a more robust estimate of treatment effect?

ERG comments

- In KEYNOTE-564, the primary outcome is investigator assessed DFS and in the model the data informing the transitions from DF health state are based on this.
- The results of the IA and BICR analyses of DFS are expected to be similar. It is unclear what caused the numerical differences between the IA and BICR analyses in KEYNOTE-564.
- The ERG considers that DFS assessment by BICR is less likely to be affected by detection bias and therefore more robust.
- The ERG considers that the two sets of analyses are equally plausible with no compelling reason to favour one over the other. For committee to make the most informed decision, the ERG considers it important that the cost effectiveness results based on both analyses are considered

Abbreviations: BICR, blinded independent central review; ERG, Evidence Review Group; IA, investigator assessed; HR, hazard ratio

Key issue 4: IA versus BICR assessment from KEYNOTE-564

Company

- The company considers the results to be consistent with substantial overlap in the confidence intervals: IA [redacted] versus BICR HR of [redacted]
- The company considers that IA DFS data is more generalisable to NHS as clinicians would determine the recurrence of disease based on local review of diagnostic imaging and that discrepancies between the results are not statistically meaningful.
- NICE has previously made positive recommendations for adjuvant cancer treatment based on investigator assessed outcomes of disease/recurrence/relapse-free survival as the primary endpoint.

Clinical expert considers

- BICR assessment is more methodologically robust
- Investigator assessed DFS to be appropriate and reflective of UK clinical trial practice.
- KEYNOTE-564 is a blinded trial which so there shouldn't be any bias in the assessment

Abbreviations: BICR, blinded independent central review; DFS, disease free survival

Adverse events

Are adverse events (AE) XXXXXXXX between the two groups?

The most frequently reported AEs at the latest data cut-off were XXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX for those receiving pembrolizumab, and XXXXXXXXXX for those receiving placebo.

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	**488**		**496**	
with toxicity grade 3-5 adverse events	XX	XX	XX	XX
with toxicity grade 3-5 drug-related adverse events	XX	XX	XX	XX
with serious adverse events	XX	XX	XX	XX
with serious drug-related adverse events	XX	XX	XX	XX
who died	XX	XX	XX	XX
who died due to a drug-related adverse event	XX	XX	XX	XX
discontinued drug due to an adverse event	XX	XX	XX	XX
discontinued drug due to a drug-related adverse event	XX	XX	XX	XX
discontinued drug due to a serious adverse event	XX	XX	XX	XX
discontinued drug due to a serious drug-related adverse event	XX	XX	XX	XX

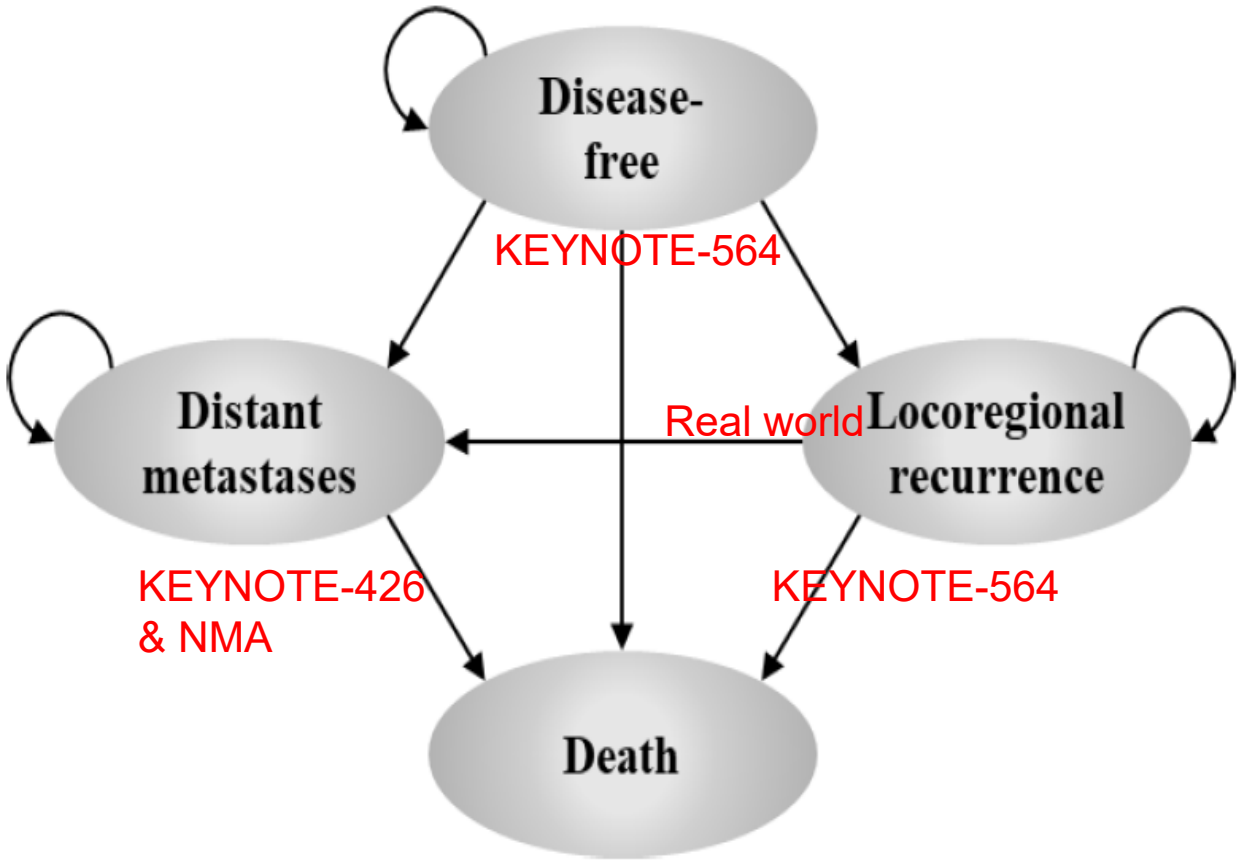
Abbreviations: AE, adverse event; AEOSI, adverse event of special interest, SAE, serious adverse event

Cost effectiveness

NICE National Institute for Health and Care Excellence

Company's model structure

Markov model with 41 year time horizon, 1 week cycle length



Locoregional recurrence	• **Disease at the primary site or nearby lymph nodes** • 22% receive salvage surgery
Distant metastases	• **Cancer spread from primary site to secondary/distant organ/lymph nodes)** • Receive 1st line treatments for (aRCC) • 21% receive salvage surgery • Costs of 2nd line aRCC treatments are included

ERG

- Consider the model structure to be appropriate
- Previously accepted in TA553 (pembrolizumab for adjuvant treatment of melanoma with high risk of recurrence)

Health state transitions

Health state transition	Informed by	
DF to LR	KEYNOTE-564 - time to LR failure (4 years)	Exponential model – Company: PH model with time-varying treatment effect (one HR for up to 1 year and HR for year 2 onwards)
DF to DM	KEYNOTE-564 - time to DM failure (4 years)	Extrapolated using Gompertz - Company: PH model with time-varying treatment effect (one HR for up to 1 year and HR for year 2 onwards)
DF to death	KEYNOTE-564 - time to death (4 years)	Extrapolated using exponential - Maximum of estimated KEYNOTE-564 probability and general population all-cause mortality.
LR to DM	US SEER Medicare database - time to event	Extrapolated using an exponential model. No on-going efficacy of adjuvant treatment assumed after recurrence.
LR to death	Assumed = DF to death for routine surveillance	Maximum of estimated KEYNOTE-564 probability and general population all-cause mortality.
DM to death	OS and PFS from KEYNOTE-426 and a published network meta-analysis of first-line aRCC treatments.	

Abbreviations: aRCC, advanced renal cell carcinoma; DF, disease free; DM, distant metastases; HR, hazard ratio; LR, locoregional recurrence; NMA, network meta-analysis; OS, overall survival; PH, proportional hazards; SEER, Surveillance, Epidemiology and End Results.

Economic model inputs

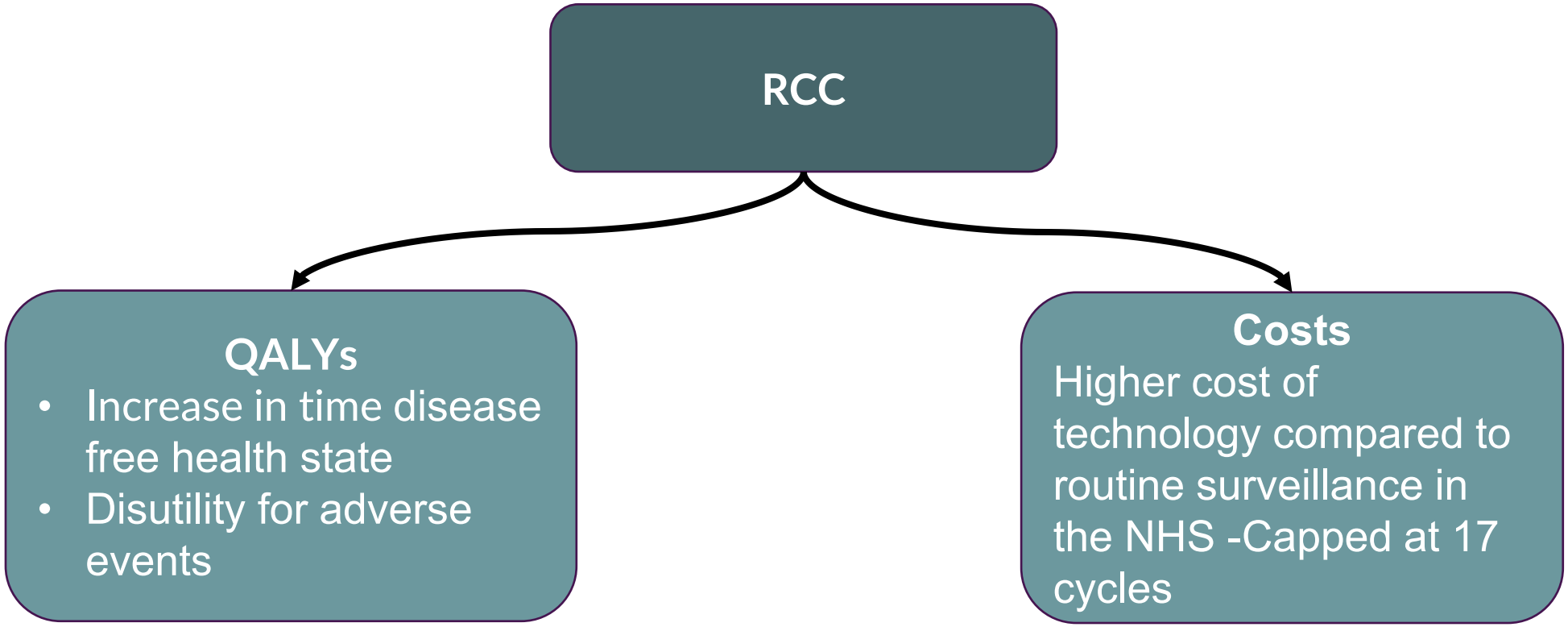
Input	Assumption and evidence source
Baseline characteristics	Patients in the KEYNOTE-564 and KEYNOTE-426 are representative of the UK population. Baseline characteristics in KEYNOTE-564 were balanced in both groups.
Intervention efficacy	DFS from KEYNOTE-564, pembrolizumab arm
Comparator efficacy	DFS from KEYNOTE-564, standard care arm
Utilities	Derived from • EQ-5D-5L data from the KEYNOTE-564 trial for the disease free and locoregional recurrence health state (mapped to EQ-5D-3L) • EQ-5D-3L data from KEYNOTE-426 for the distant metastases health state
Costs	NHS reference costs, BNF and published literature are used as appropriate
Resource use	NHS reference costs, BNF and published literature are used as appropriate
Discounting	3.5% for costs and health effects

The ERG considers the modelled population, intervention and comparators are in line with the NICE final scope. The model structure allows important differences in costs and QALYs to be captured.

NICE

Abbreviations: BNF, British National Formulary; DFS, disease free survival; QALY, Quality adjusted life year

Where do the QALY and cost differences come from in the model?



Key model drivers are:
- Transitions from DF → LR, and DF → DM
- Utility values in DF, L and DM

Abbreviations: DF, disease free; DM, distant metastases; LR, locoregional recurrence; QALY, quality adjusted life year; RCC, renal cell carcinoma

Utility values

	Utility value	Durational difference in arms?	comment
Disease free	0.868 (Keynote-564)	Longer DFS for Pembrolizumab	Pembrolizumab is modelled as having greater overall life years, with greater duration in the disease free health state.
Locoregional recurrence	0.839 (Keynote-564)	Shorter for Pembrolizumab	
Distant metastases (pre-progression)	0.803 (Keynote-426)	Shorter for Pembrolizumab	
Distant metastases (post-progression)	0.772 (Keynote-426)	Shorter for Pembrolizumab	
Disutility due to adverse events	Greater QALY loss for Pembrolizumab due to more adverse events	N/A	Small impact
Age related disutility	Same in both arms	Greater for Pembrolizumab due to overall survival	Small impact

Abbreviations: QALY, quality-adjusted life year;

Key issue 2: Long term risk of relapse

Is it reasonable to consider that pembrolizumab treated patients would demonstrate the same pattern in relapse as routine surveillance patients

ERG

- Aim of treatment is to remove any residual microscopic disease after resection and reduce risk of relapse and progression to metastatic disease
- Pembrolizumab is given for a maximum of 17 cycles (1 year) – outcomes are extrapolated over a lifetime horizon
  - substantial uncertainty around the long-term duration of effect.
- ERG explored scenario - assumed that the risk of relapse was equal to that seen in routine surveillance data
  - explored at 4, 7 and 10 years
  - analysis at 4 years almost doubled the ERG base case ICER (slightly reduced for longer durations)

Abbreviations: ERG, Evidence Review Group

Key issue 2: Long term risk of relapse

Company

- ERG waning assumption as an abrupt change in the risk of recurrence is implausible
  - For that reason, treatment effect waning is considered implausible in the adjuvant setting where patients have received surgery with curative intent prior to therapy
- No evidence of treatment effect waning in the metastatic setting in multiple indications for which there is long-term data for pembrolizumab
- The plausibility of changes in treatment effect over time is best informed by log-cumulative hazard plots for transitions from the disease free health state.
  - the plots are parallel for the routine surveillance and pembrolizumab arms indicating a maintenance of relative efficacy.
- The clinical trial data shows that there is a difference in risk of relapse between the two treatment arms.
- ERG scenario analysis (4-, 7- or 10-years) not supported by the trial data from KEYNOTE-564

Clinical expert noted

- Early indications are findings from KEYNOTE-564 are likely to be maintained
- An estimated 30% of patients go on to have long-term durable remission
- Agrees with company position – the longer someone remains disease free the lower the risk of recurrence

Key issue 3: Transitions from the disease-free health state *(Joint or separate fitting of Exponential & Gompertz extrapolation)*

Is fitting separate curves to Pembrolizumab and placebo (Approach 1) more robust than a jointly fitted curve and use of a hazard ratio (Approach 3) ?

- Patient-level data from KEYNOTE-564 was used to estimate time to DFS failure (locoregional recurrence, distant metastases or death).
    - The company considered each failure as a competing risk, such that for a specific DFS failure, the two competing failure types (distant metastases and death) were treated as censoring events
- Once KEYNOTE-564 time-to-event data using competing risk censoring was obtained, the company followed a parametric multistate modelling approach to estimate cause-specific hazards of each transition from the DF health state over time

Key issue 3: Transitions from the disease-free health state *(Joint or separate fitting of Exponential & Gompertz extrapolation)*

The company explored the following three approaches to select appropriate standard parametric models to estimate cause-specific hazards for DF to LR and DF to DM transitions:

Approach 1: standard parametric models fitted independently to pembrolizumab and placebo data from KEYNOTE-564.

Approach 2: standard proportional hazards (PH) parametric models (exponential, Weibull and Gompertz) jointly fitted to pembrolizumab and placebo data from KEYNOTE-564 with a time-constant hazard ratio (HR) for pembrolizumab versus placebo applied (PH model).

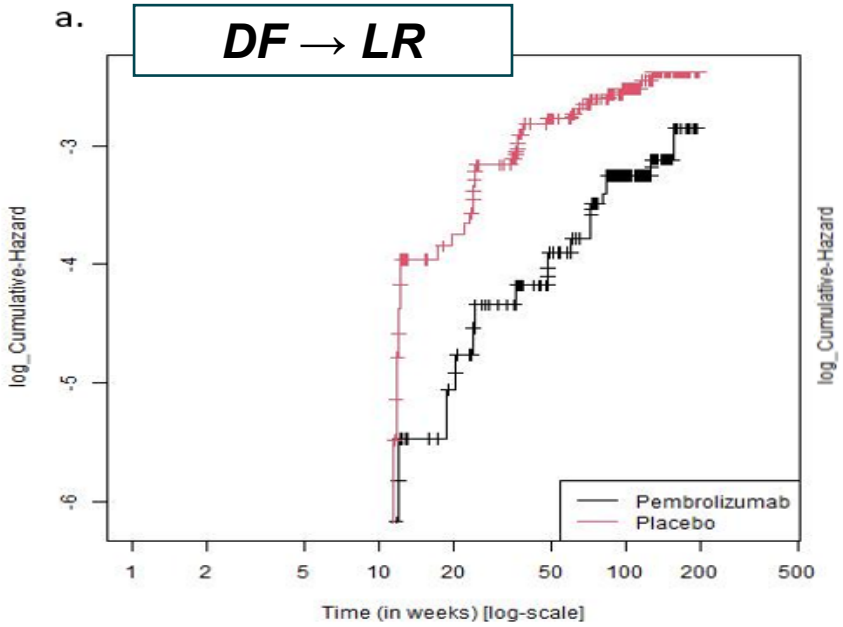
Approach 3: standard PH parametric models (exponential, Weibull and Gompertz) jointly fitted to pembrolizumab and placebo data from KEYNOTE-564 with a HR for pembrolizumab versus placebo applied to year one and another HR applied for year two onwards (time-varying PH model).

Abbreviations: aRCC, advanced renal cell carcinoma; DF, disease free; DM, distant metastases; HR, hazard ratio; LR, locoregional recurrence; NMA, network meta-analysis; OS, overall survival; PH, proportional hazards; SEER, Surveillance, Epidemiology and End Results.

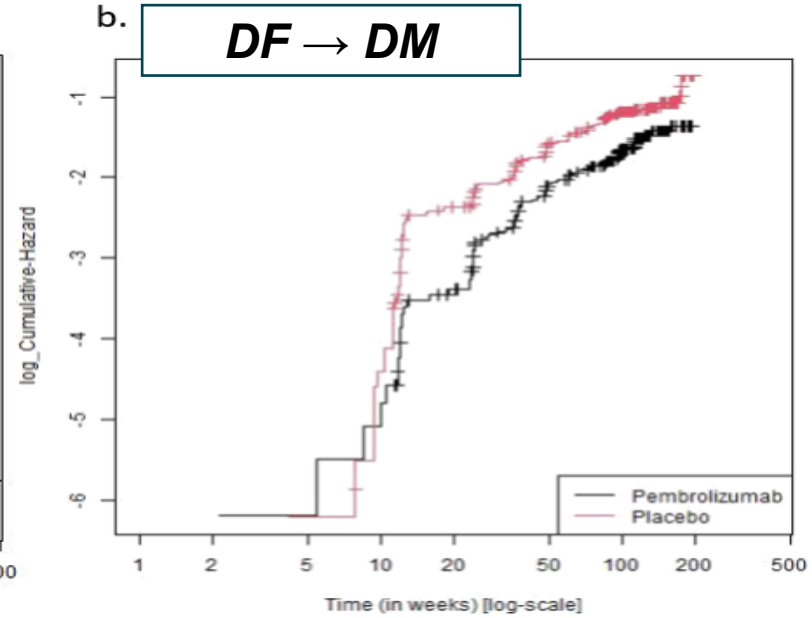
Key issue 3: Transitions from the disease-free health state

Log-cumulative hazards plots (LCH) of the hazard of a DFS event

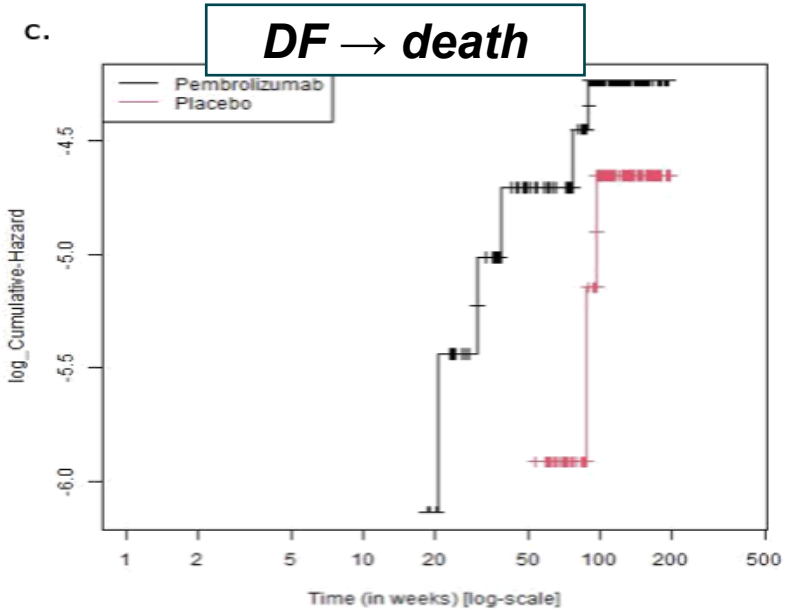
a. ***DF → LR***



b. ***DF → DM***



c. ***DF → death***



Abbreviations:
DF, disease free
DM, distant metastases
LR, locoregional recurrence

Key issue 3: Transitions from the disease-free health state
(Joint or separate fitting of Exponential & Gompertz extrapolation)

Company: External validation against long-term published data suggests Approach #3 (jointly fitted curve) to be the most appropriate of estimating long-term transition probabilities from DF.

Approach #1 is likely to underestimate the benefit of adjuvant pembrolizumab

ERG comments: As patient level data is available for both Pembrolizumab and placebo arms, the ERG considers fitting independent models to each treatment arm (Company Approach #1) a more robust method for extrapolation of the cause-specific time-to-event data used in the model.

Other considerations: The ERG cautions that even though Approach #1 is more robust, it is still informed by immature data and subject to substantial uncertainty.

Approach 3 (Company base case), placebo arm only

External and predictive validations of long-term DFS in the routine surveillance arm using base-case assumptions for transitions from DF state

Approach 3 (Company base case), pembrolizumab

External and predictive validations of long-term DFS in the pembrolizumab arm versus active treatment arms in previous trials of adjuvant therapy (statistically significant DFS benefit observed only in S-TRAC)

Approach 3 (Company base case)

Base-case modelled DFS over the lifetime time horizon (data cut-off: 14-JUN-2021)

Comparison of Approach 1 and 3

Disease-free predictions of base case and scenario parametric models

Approach/ source	Parametric model combination	Disease-free survival by year				
		1 year	3 years	5 years	10 years	30 years
Placebo						
Company base case – Approach 3	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX
ERG preferred – Approach 1	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX
S-TRAC (observed)	-	78%	60%	51%	-	-
SEER data (observed)	-	80%	59%	48%	33%	-
SEER data (extrapolated)	Lognormal (DFS and OS)	82%	59%	47%	31%	12%
Pembrolizumab						
Company base case – Approach 3	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX
ERG preferred – Approach 1	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX

Abbreviations: DF, disease-free; DM, distant metastases; LR, locoregional recurrence.

Comparison of Approach 1 and 3

Overall survival predictions of base case and scenario parametric models

Approach/ source	Parametric model combination	Overall survival by year				
		1 year	3 years	5 years	10 years	30 years
Placebo						
Company base case – Approach 3	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX
ERG preferred – Approach 1	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX
S-TRAC (observed)	-	99%	91%	82%	-	-
SEER data (observed)	-	98%	82%	68%	48%	-
SEER data (extrapolated)	Lognormal (DFS and OS)	97%	82%	69%	45%	10%
Pembrolizumab						
Company base case – Approach 3	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX
ERG preferred – Approach 1	Exponential (DF → LR) and Gompertz (DF → DM)	XX	XX	XX	XX	XX

Abbreviations: DF, disease-free; DM, distant metastases; LR, locoregional recurrence.

Company and ERG base case assumptions

Assumption	Company base case	ERG base case	Impact
Survival extrapolations	Joint fitting for the placebo, with a hazard ratio applied for Pembrolizumab (approach 3)	Independently fitted to both placebo and Pembrolizumab data (approach 1)	Large
Long term risk of relapse	Extrapolation curves remain separated, as modelled	No change but explored in scenario	Large
IA versus BICR assessment	IA used in base case	IA used in base case, BICR approximation explored as a scenario	Large
Oral Administration Costs	Included	Excluded	Small
Truncation to the ToT curve for Pembrolizumab	Included	Excluded	Small
Pembrolizumab RDI	Included	Excluded	Small
Subsequent treatment market share estimates	Included	Alternative guided by expert opinion used	Small

Abbreviations: BICR, blinded independent central review; ERG, Evidence Review Group; IA, investigator assessment; RDI, relative dose intensity; ToT, time on treatment

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS discounts

Other considerations

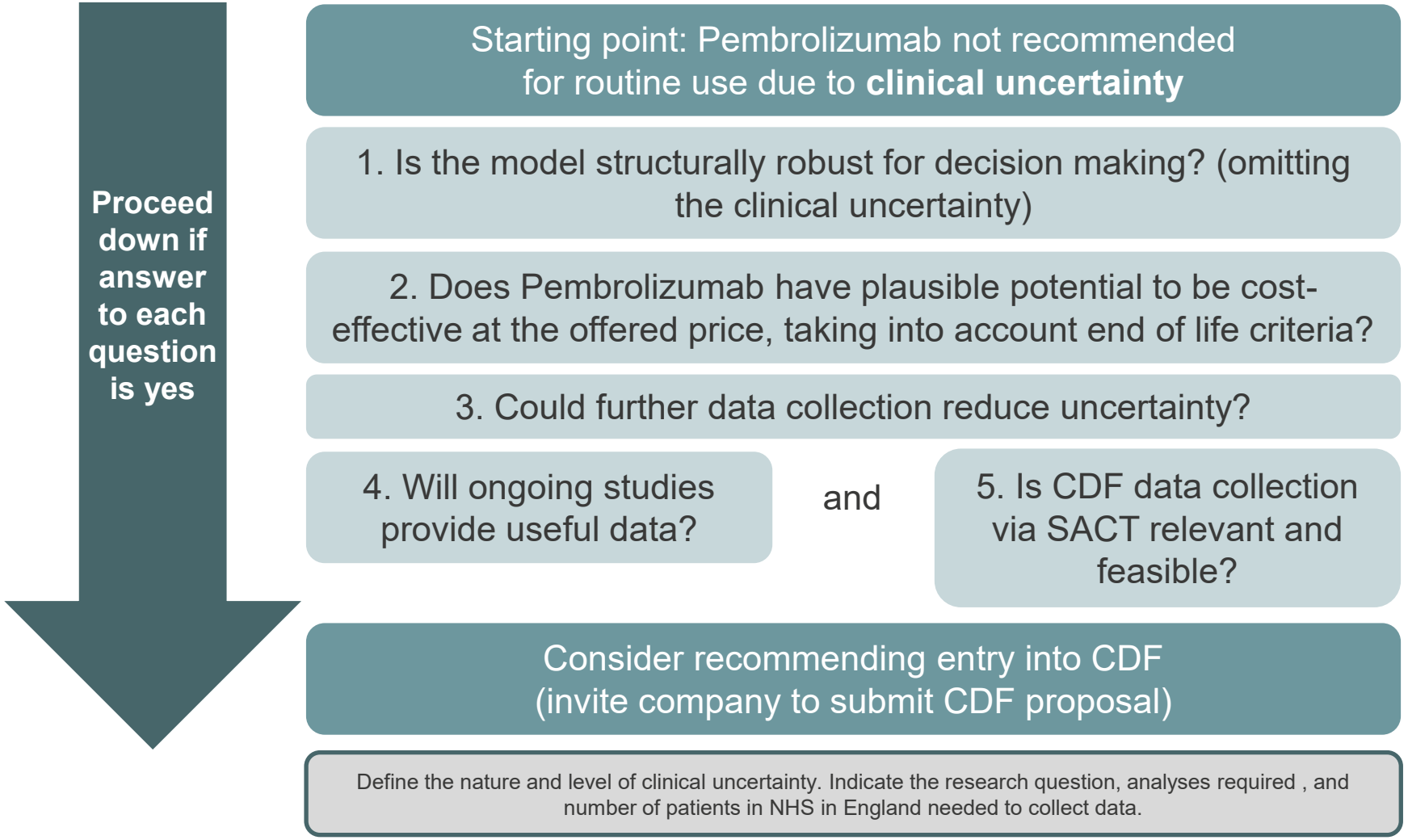
Equality considerations

- Use of Pembrolizumab is not expected to raise any equalities issues

Innovations described by the company

- Currently no NICE recommended active adjuvant therapy for RCC post-nephrectomy
- Pembrolizumab offers a durable and well tolerated adjuvant treatment option for patients RCC post-nephrectomy
- option to administer Q6W, which would substantially decrease the logistical and administrative burden on the health system compared to Q3W administration, as well as decreasing the burden on patients who need to travel to cancer treatment centres for each administration

Does the Committee consider Pembrolizumab to be eligible for the CDF



NICE

Abbreviations: CDF, Cancer Drug Fund

NICE National Institute for Health and Care Excellence

Thank you.

© NICE [insert year]. All rights reserved. Subject to Notice of rights.

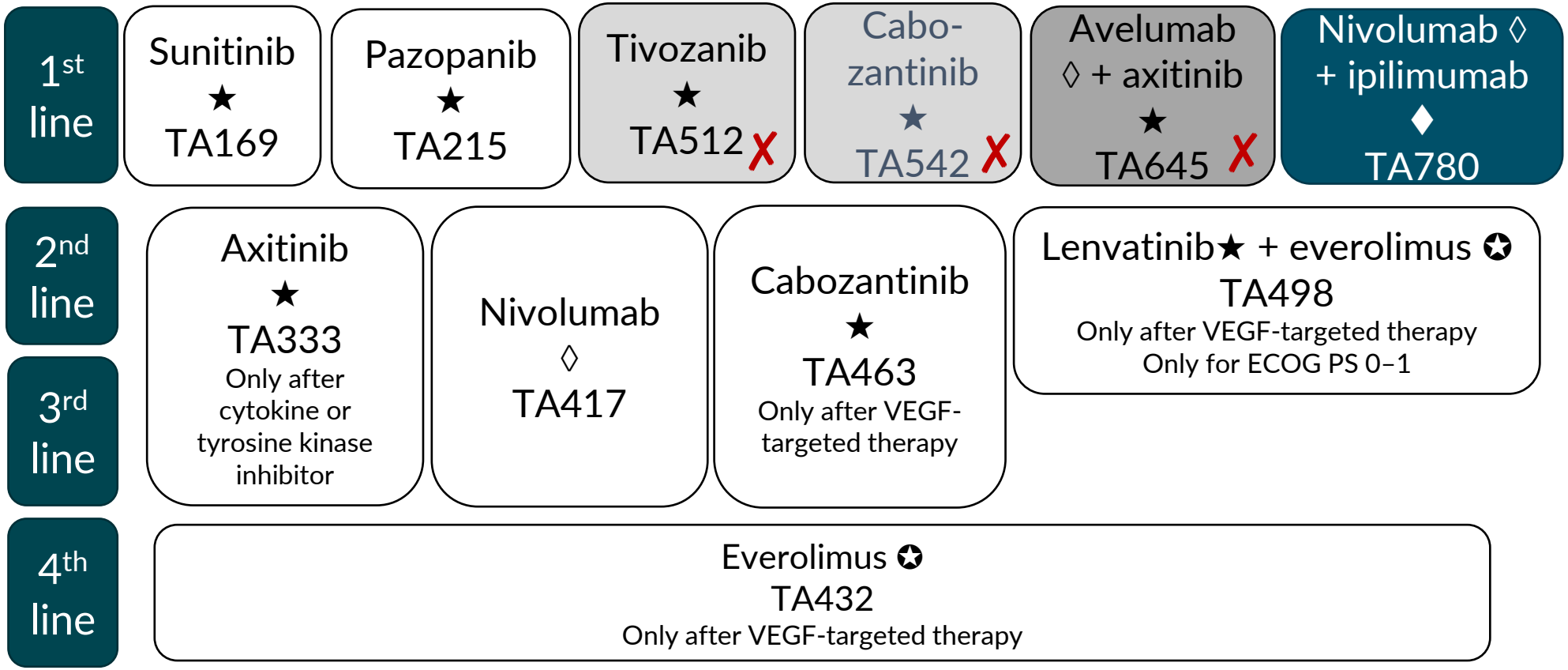
Clinical trial 1 baseline characteristics

Characteristic	Intervention (n=496)	Comparator (n=498)
Sex (male : female) %	70 : 30	72% : 28
Age (mean, SD)	58.3 years (10.6)	58.6 years (11.0)
Geographic region of enrolling site %	North America: 26.8 European Union: 37.9 Rest of World: 35.3	North America: 25.1 European Union: 37.6 Rest of World: 37.3
ECOG Performance Scale (0 : 1) %	84.9 : 15.1	85.5 : 14.5
Type of nephrectomy (partial : radical) %	7.5 : 92.5	7.6 : 92.4
Lymph node stage (N0 : N1) %	93.8 : 6.3	93.8 : 6.2
Metastatic Staging (M0 : M1 NED) %	94.2 : 5.8	94.2 : 5.8
RCC Risk Category %	M0-Intermediate High Risk: 85.1 M0-High Risk: 8.1 M0-Others: 1.0 M1-NED: 5.8	M0-Intermediate High Risk: 86.9 M0-High Risk: 7.2 M0-Others: 0.0 M1-NED: 5.8

ERG clinical experts consider the population characteristics to be generalisable to those undergoing nephrectomy for RCC in England.

Treatment pathway from TA780

Intermediate-/poor-risk



✗ *= not a comparator in TA581 or in TA7801*

Note: Nivolumab is 2nd + 3rd line option

Key: ECOG PS, Eastern Cooperative Oncology Group performance status; VEGF, vascular endothelial growth factor ★: oral tyrosine kinase inhibitors (TKI); ✪: oral mammalian target of rapamycin (mTOR) inhibitor; ◊: anti-programmed death 1 (PD-1) inhibitor; ♦: anti-CTLA-4 inhibitor