For public observers – fully redacted

NICE National Institute for Health and Care Excellence

Pembrolizumab with platinum-based chemotherapy for untreated advanced oesophageal cancer

Lead team presentation

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Company: MSD

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Disease overview – oesophageal or gastroesophageal junction cancer

- Oesophageal cancer can occur at any point in the oesophagus (gullet)
- Gastroesophageal junction (GOJ) cancer occurs at the point the oesophagus joins the stomach
- Squamous cell carcinoma mostly occurs in the upper oesophagus and accounts for ~1/3 of UK cases
- Adenocarcinoma mostly occurs in the lower oesophagus and accounts for ~2/3 of UK cases
- 7,569 new cases of oesophageal cancer diagnosed in England, in 2017
- Around 40% of oesophageal cancers develop in people aged 75 and over
- Incidence is higher in men

Pembrolizumab (KEYTRUDA)

Mechanism of action	Anti-programmed cell death 1 (PD-1) antibody; blocks interaction with PD-L1 and PD-L2 ligands and reactivates T-cell anti-tumour activity
Marketing authorisation	Indicated for first-line treatment of locally advanced unresectable or metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma in adults whose tumours express PD L1 with a CPS ≥ 10, in combination with platinum and fluoropyrimidine based chemotherapy
Administration & dose	Pembrolizumab: IV, 200mg every 3 weeks, for 35 cycles (approximately 2 years) or until progression Plus platinum and fluoropyrimidine based chemotherapy: IV, 800 mg/m^2 per day on days 1 to 5, every 3 weeks
List price	£2,630 per 100 mg vial £5,260 per single administration Confidential PAS discount also in place

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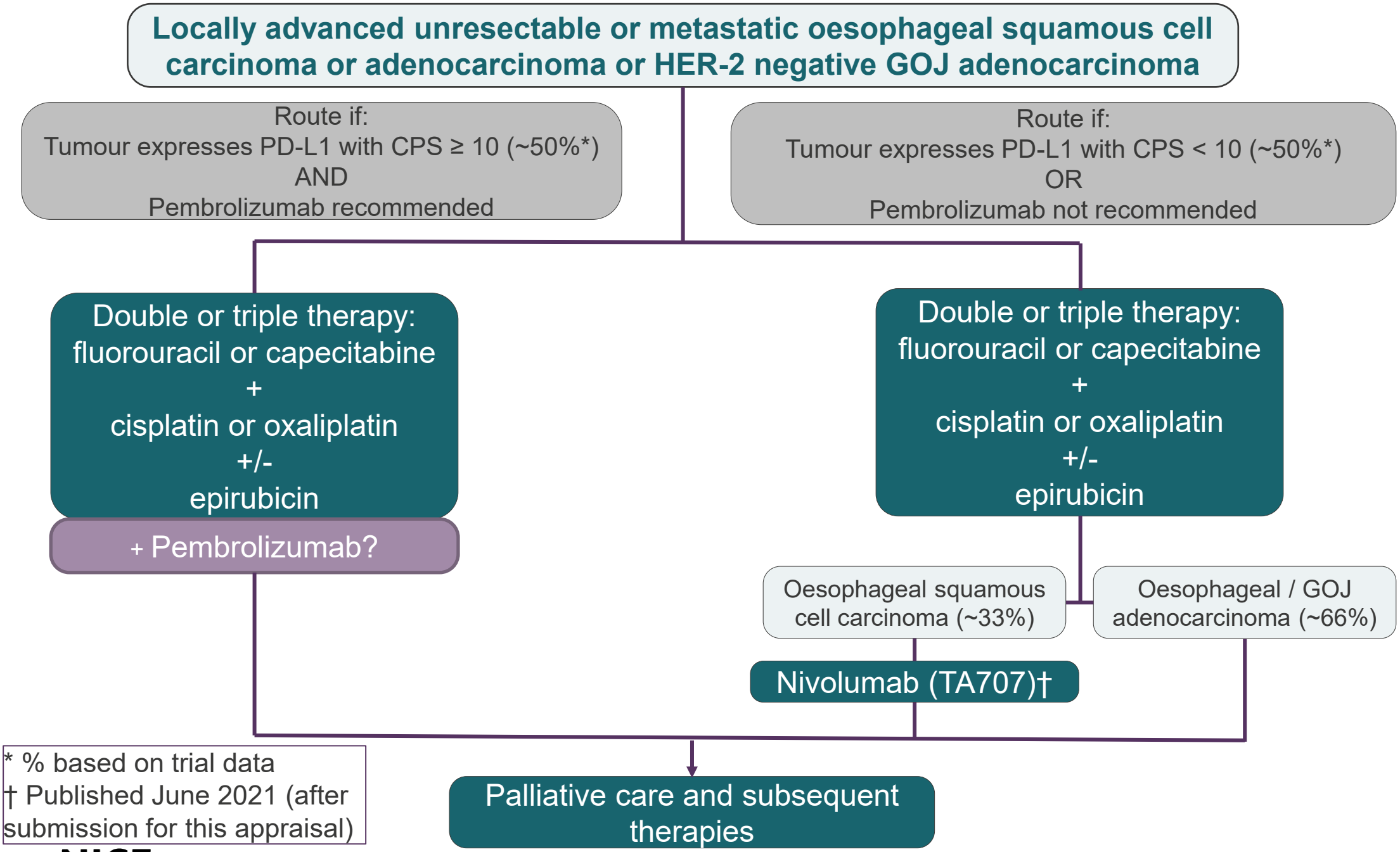
PD-L: programmed cell death-ligand, HER-2: human epidermal growth factor receptor 2, CPS: combined positive score, IV: intravenous, PAS: patient access scheme

Treatment pathway



HER-2: human epidermal growth factor receptor 2, GOJ: gastroesophageal junction, PD-L1: programmed death-ligand 1, CPS: combined positive score

Clinical issues: histology

- **Is any difference between adenocarcinoma and squamous cell carcinoma (prognosis or treatment response) relevant if treatment is limited to people with CPS ≥10?**
  - The proportion of trial participants with squamous cell carcinoma and adenocarcinoma is different to UK practice
  - Only the population with a CPS ≥ 10 from the trial is relevant for decision making (analysis of approx. 50% of trial participants)
- **What is the significance of HER-2 status in gastroesophageal junction cancer?**
  - HER-2 positive tumours not included in marketing authorisation, but unclear if included in the trial

Further clinical issues

- **Generalisability:** is the trial generalisable based on geography and histology?
- **Comparator:** what is current standard of care – double or triple therapy?
- Previous introduction of a monoclonal antibody in addition to chemotherapy resulted in use of trial chemotherapy regimen rather than standard of care as combination. If recommended, what is the most appropriate platinum and fluoropyrimidine based chemotherapy for use in combination with pembrolizumab?
- If recommended, would pembrolizumab in combination with chemotherapy first-line be preferable to nivolumab second-line, for people with oesophageal squamous cell carcinoma?
- Are there any potential issues with implementing PD-L1 and CPS assessments in practice? Company has included cost of PD-L1 testing in its model.

Decision problem

Expected indication was amended at technical engagement, to include only tumours expressing PD-L1 with a CPS ≥ 10 (~50% of trial population)

	Scope	Company model (post-technical engagement)
Population	Adults with untreated, unresectable locally advanced or metastatic oesophageal cancer or gastroesophageal junction adenocarcinoma	Adults with untreated, unresectable locally advanced or metastatic oesophageal cancer or gastroesophageal junction adenocarcinoma **whose tumours express PD L1 with a CPS ≥ 10**
Intervention	Pembrolizumab with platinum-based chemotherapy	Pembrolizumab with cisplatin plus fluorouracil
Comparators	Platinum-based chemotherapy without pembrolizumab, such as: •double treatment with fluorouracil or capecitabine plus cisplatin or oxaliplatin •triple treatment with fluorouracil or capecitabine plus cisplatin or oxaliplatin and epirubicin	• Cisplatin plus fluorouracil (referred to as standard of care) • Blended chemotherapy (double and triple therapy based on UK market share)
Outcomes	•Overall survival •Progression-free survival •Response rate •Adverse effects of treatment •Health-related quality of life	As scope except response rates not included

CPS: combined positive score

Patient perspectives: living with the condition

Submissions received from Guts UK and Heartburn Cancer UK

- Swallowing problems can be severe and people may be unable to swallow their own saliva, leading to pain, reflux and indigestion
- Fatigue and weight loss are major symptoms
- Symptoms and treatment side effects have wide impact on quality of life, impacting relationships and affecting social experiences such as sharing meals with family
- Quality of life depends on the individual's functional fitness and nutritional status, ability to eat, use of a feeding tube and family support
- Oesophageal and GOJ cancer are difficult to diagnose at an early stage and are deemed less survivable cancers

GOJ: gastroesophageal junction

Patient perspectives: treatment options

Current treatment:

- Challenging to experience and treatment is not always effective
- Treatment schedule constantly interrupts normal life

Pembrolizumab:

- New treatments for oesophageal cancer are needed
- Oesophageal and GOJ cancer are life limiting conditions – pembrolizumab may help people living with these cancers to participate and enjoy time with family and provide valuable additional time
- Immunotherapy shows promise for some people, although it does not impact on current chemotherapy schedule as it is given with chemotherapy
- Aware there may be additional side effects to current therapy
- Pembrolizumab offers another option where there are currently few available

GOJ: gastroesophageal junction

Pivotal trial: KEYNOTE-590

Trial design	Ongoing, phase III, randomised, double-blind, placebo-controlled trial	
Population	People with locally advanced unresectable or metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus or advanced/metastatic Siewert type 1 adenocarcinoma of the GOJ • ECOG score of 0 or 1	
Intervention / comparator	Pembrolizumab + cisplatin + fluorouracil (n=373)	Placebo + cisplatin + fluorouracil (n=376)
Proportion of arm CPS≥ 10	49.9% (n=186)	52.4% (n=197)
Outcomes	**Primary** • Overall survival • Progression free survival	**Secondary** • Objective response rate • Adverse effects of treatment • Health-related quality of life
Stratification factors	• Geographic region • Histology • ECOG performance score	• Disease status • Age category • Sex

Is proportion of CPS≥ 10 population (~50%) representative of NHS clinical practice?

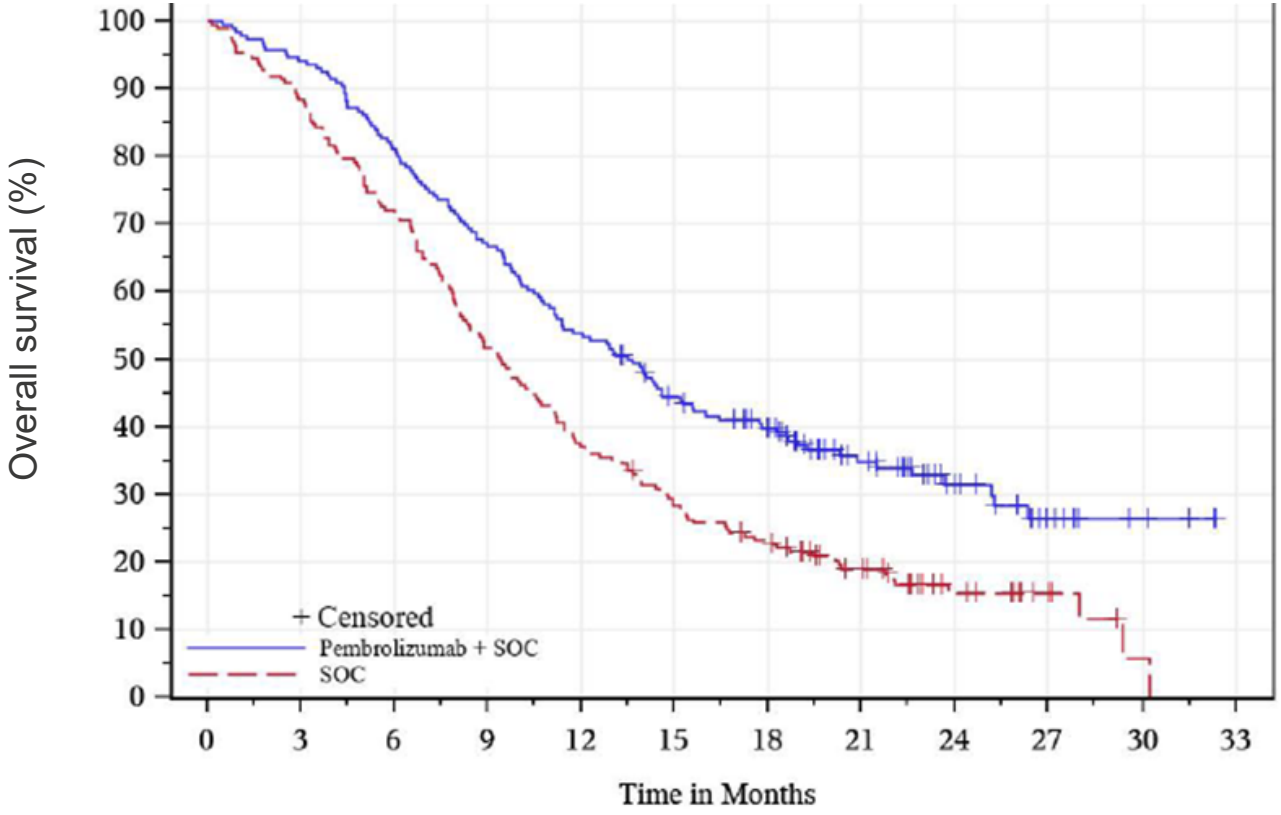
ECOG: Eastern cooperative group, GOJ: gastroesophageal junction, CPS: combined positive score

KEYNOTE-590 - overall survival

PD-L1 biomarker-positive (CPS ≥10)

	Pembrolizumab + Chemotherapy (n=186)	SOC (n=197)
Median OS, months (95% CI)	13.5 (11.1, 15.6)	9.4 (8.0, 10.7)
Number of events (%)	[redacted]	[redacted]
Hazard Ratio (95% CI) Pembrolizumab + Chemotherapy vs SOC	0.62 (0.49, 0.78) p<0.001	

OS rate at X Months (95% CI)	Pembrolizumab + Chemotherapy (n=186)	SOC (n=197)
3 Months	[redacted]	[redacted]
12 Months	[redacted]	[redacted]
24 Months	[redacted]	[redacted]



Number of Subjects at Risk

Pembrolizumab + SOC	186	175	151	125	100	79	66	40	23	10	4	0
SOC	197	174	142	102	73	55	42	28	13	6	1	0

SOC: standard of care, OS: overall survival, CI: confidence intervals

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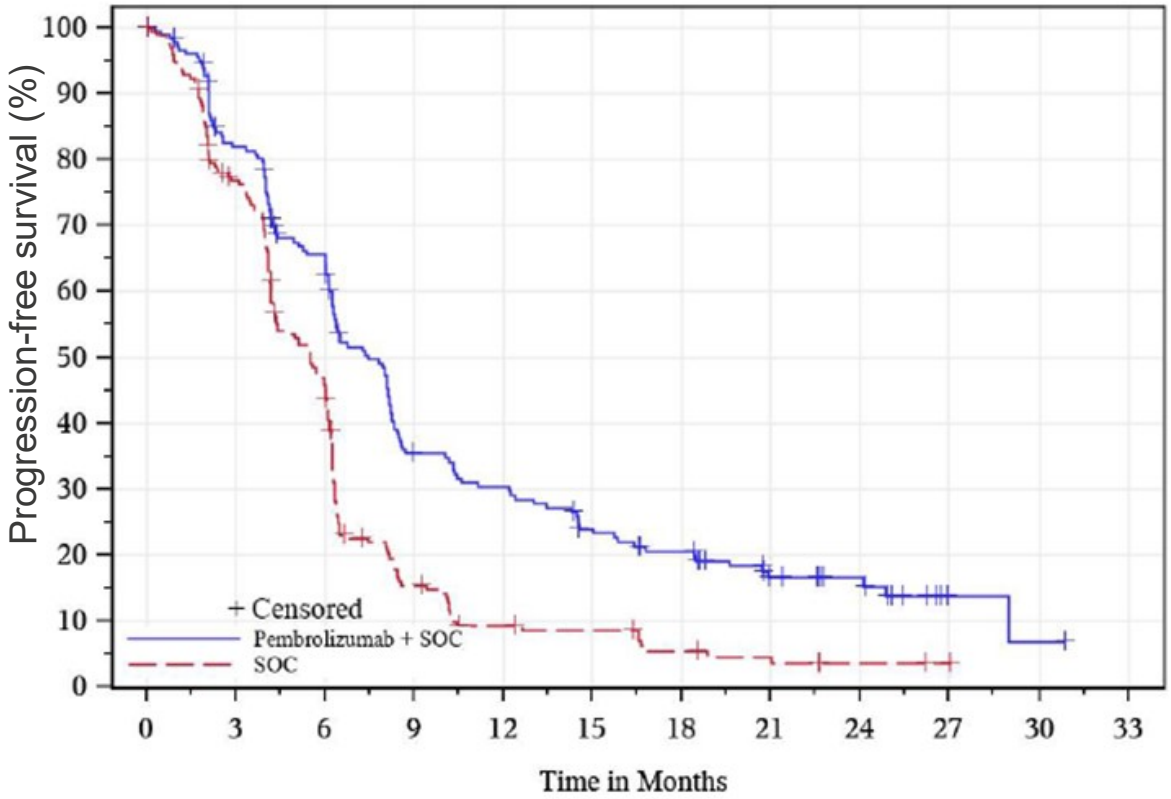
KEYNOTE-590 – progression-free survival

PD-L1 biomarker-positive (CPS ≥10)

PFS based on investigator assessment

	Pembrolizumab + Chemotherapy (n=186)	SOC (n=197)
Median PFS, months (95% CI)	7.5 (6.2, 8.2)	5.5 (4.3, 6.0)
Number of events (%)	[redacted]	[redacted]
Hazard Ratio (95% CI) Pembrolizumab + Chemotherapy vs SOC	0.51 (0.41, 0.65) p<0.0001	

PFS rate at X Months (95% CI)	Pembrolizumab + Chemotherapy (n=186)	SOC (n=197)
3 Months	[redacted]	[redacted]
12 Months	[redacted]	[redacted]
18 Months	[redacted]	[redacted]



SOC: Standard of care, PFS: progression free survival, CI: confidence intervals

Number of Subjects at Risk

Pembrolizumab + SOC	186	143	109	56	48	36	29	17	12	2	1	0
SOC	197	145	85	26	14	12	7	5	2	1	0	0

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Clinical evidence may not be generalisable to the UK population (1)

Background:

- 54.8% of KEYNOTE-590 CPS≥10 population were from Asia
- Model uses population characteristics from European participants, but effectiveness inputs from global population
- 56.1% of KEYNOTE-590 CPS ≥10 population had squamous cell carcinoma
  - In UK, oesophageal cancer is 1/3 squamous cell carcinoma, 2/3 adenocarcinoma
- Unclear what proportion of GOJ adenocarcinoma patients (12.1% of ITT population) in KEYNOTE-590 were HER-2 negative, in line with the marketing authorisation

ERG:

- Differences between Asian and Rest Of World (ROW) population may lead to differences in outcome
- Relative benefit of pembrolizumab greater in Asian than ROW population; estimates of OS and PFS may be over estimate for UK
- Overrepresentation of squamous cell carcinoma may impact generalisability

Clinical expert comments:

- Treatment regimens similar in Europe, US and Asia – use international treatment guidelines
- Histology composition is not relevant to efficacy if population is restricted to CPS≥10

CPS: combined positive score, GOJ: gastroesophageal junction, ITT: intention to treat, OS: overall survival, PFS: progression-free survival, HR: hazard ratio, CI: confidence interval

Clinical evidence may not be generalisable to the UK population (2)

Company comments:

- KEYNOTE-590 baseline characteristics are comparable with UK clinical practice
- Treatment regimens are similar between Asia and ROW - many Asian countries follow ESMO guidelines
- Nivolumab for oesophageal squamous cell carcinoma appraisal (TA707) committee accepted evidence from a population where 96% had Asian family background

Ad-hoc analysis of overall survival in CPS≥10 population: Europe and ROW

HR (95% CI)	OS
European region (n=57)	[redacted]
ROW (n=326)	[redacted]

- KEYNOTE-590 showed positive OS regardless of tumour histology (smaller sample size in European region leads to greater uncertainty)
- Treatment doesn't change based on histology
- Unmet need in both squamous cell carcinoma and adenocarcinoma

Is KEYNOTE-590 generalisable to clinical practice in the NHS?

ESMO: European Society for Medical Oncology, HR: hazard ratio, OS: overall survival, CI: confidence interval, ROW: rest of the world

Uncertainty around appropriate comparator

Background:
- NICE clinical guideline recommends double or triple treatment
- Scope includes double and triple treatments
- Company assumes equivalent efficacy between double and triple regimens
  - Uses comparator arm of KEYNOTE-590 (cisplatin + fluorouracil) in the model

ERG:
- All relevant scope comparators, including triple treatments should be considered – can be achieved using data from gastric cancer studies

Company comments:
- Using gastric cancer studies for indirect treatment comparisons is inappropriate

Clinical expert comments:
- Triple regimens are not recommended by international guidelines
- Recent trial in gastric cancer demonstrated double regimens are more favourable than triple
- Assuming clinical equivalence of double and triple treatments is reasonable

Is double therapy the most relevant comparator?

NMA: network meta-analyses, GOJ: gastroesophageal junction, OS: overall survival, PFS: progression-free survival, HR: hazard ratio

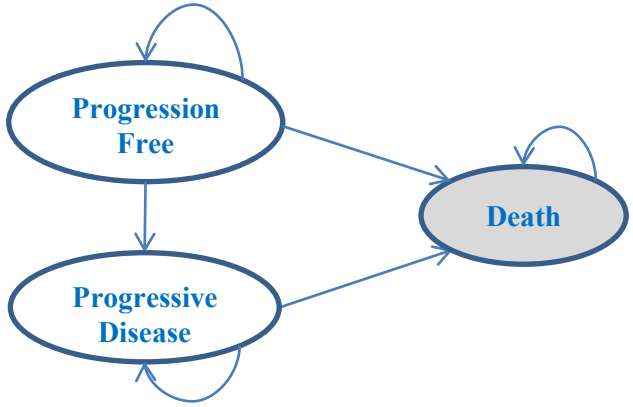
Clinical issues

- Is the trial generalisable based on geography and histology (considering CPS ≥ 10 restriction, squamous cell carcinoma and adenocarcinoma population distribution and HER-2 status)?
- What is current standard of care – double or triple therapy?
- Previous introduction of a monoclonal antibody in addition to chemotherapy resulted in use of trial chemotherapy regimen rather than standard of care as combination. If recommended, what is the most appropriate platinum and fluoropyrimidine based chemotherapy for use in combination with pembrolizumab?
- If recommended, would pembrolizumab in combination with chemotherapy first-line be preferable to nivolumab second-line, for people with oesophageal squamous cell carcinoma?
- Are there any potential issues with implementing PDL1 and CPS assessments in practice? Company has included cost of PDL1 testing in its model

Key cost effectiveness issues

- **Is end of life criteria met?**
- **Which model for estimating overall survival does the committee prefer?** ***(Key model driver)***
  - Company base case - log-logistic piecewise, 40-week cut off
  - ERG base case - log-logistic piecewise, 40-week cut off + treatment waning
  - ERG scenario – log-logistic fully parametric *(greatest impact on ICER)*
- **Which method of utility estimation is most appropriate?**
  - Company base case - time-of-survival (ToS) utilities
  - ERG base case - progression-based utilities
- **Which assumption for incorporating nivolumab is most appropriate?**
  - Company base case – incorporates nivolumab costs based on % receiving subsequent PDL1 inhibitors in KEYNOTE-590
  - ERG scenario - incorporates nivolumab costs and efficacy based on % receiving any subsequent treatment in KEYNOTE-590
- **Which treatment is currently used in clinical practice and which would be likely to be used in combination with pembrolizumab?**
  - Company base case - as per KEYNOTE-590 (cisplatin and fluorouracil)
  - ERG scenario - oxaliplatin + capecitabine with pembrolizumab and as comparator

Company's economic model



Model type	3-state partitioned survival model: • progression-free • progressed-disease • death
Time horizon	30 years*
Model cycle	1 week
Discount rates	3.5%
Population	KEYNOTE-590 CPS≥10 population†
Intervention	Pembrolizumab plus cisplatin and fluorouracil
Comparators	a) Cisplatin and fluorouracil *(base case)* b) Blended comparator, using UK market share of chemotherapy options†
Utility values	KEYNOTE-590 EQ-5D data; time-of-survival utility model
Subsequent treatments	Nivolumab costs included based on distribution of PDL1 inhibitors given as subsequent treatments in KEYNOTE-590†
Treatment waning	Not applied
PD-L1 testing costs	Included

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*updated at clarification
†updated at technical engagement

Company and ERG preferred assumptions

	Company base case assumption	ERG base case assumption
Overall survival	KEYNOTE-590 KM 40-week cut off + log-logistic extrapolation	Same as company + treating waning *ERG note that all scenarios presented for OS are plausible*
Progression-free survival	KEYNOTE-590 KM 10-week cut off + log-logistic extrapolation	Same as company with 37-week cut off
Utility values	Time-of-survival utilities	Progression-based utilities
Treatment waning	Treatment waning not included	Includes treatment waning between 5 to 7 years
Comparator	a) Cisplatin and fluorouracil b) Blended comparator, using UK market share of all chemotherapy options	Cisplatin and fluorouracil
Half cycle correction	Included	Removed
Administration costs	Based on outpatient setting	Based on day case setting
Stopping rules	Included to cap treatment costs according to trial protocol in addition to ToT KM data	Not included *ERG note not required as included in ToT data*
Subsequent treatments	• Includes costs of nivolumab for PDL1 inhibitors in model • Excluded subsequent treatments received by <5% of patients	• Includes nivolumab as company does • Redistributed subsequent treatments to account for all treatments received in KEYNOTE-590
PD-L1 testing	Included	Included

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KM: Kaplan Meier, OS: overall survival, ToT: time on treatment

Model driver

End of life – PD-L1 CPS ≥ 10 population

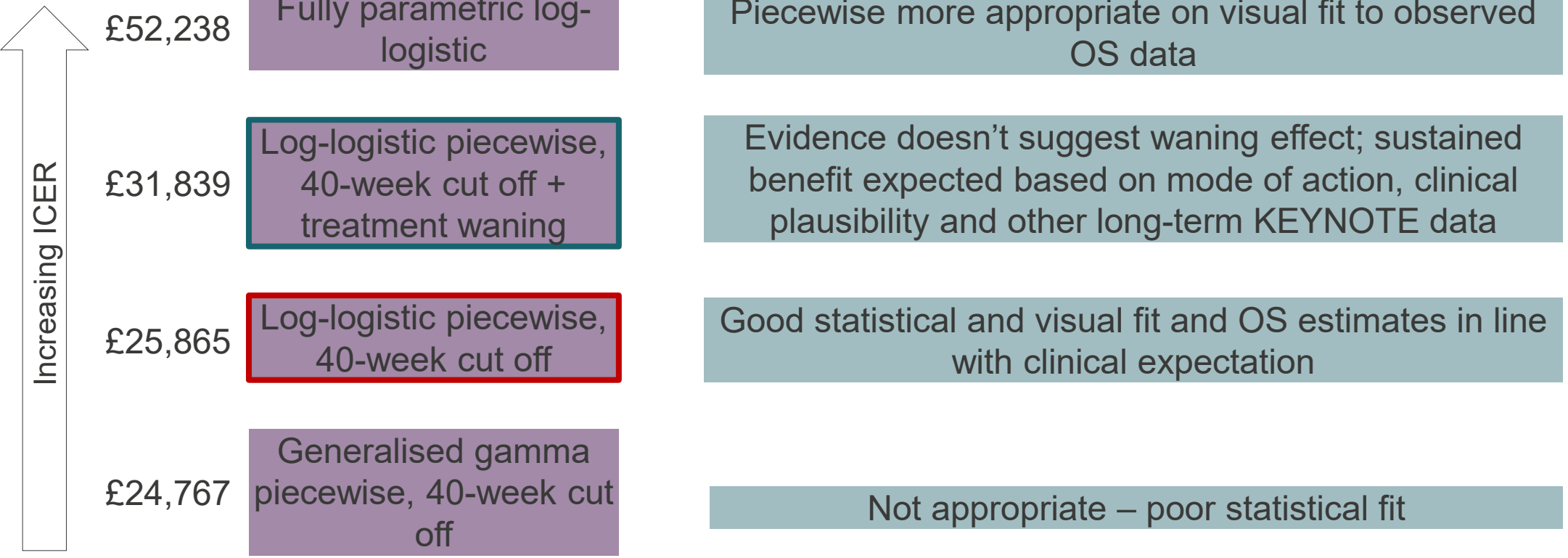
Criterion	Evidence	Criterion met?
The treatment is indicated for patients with a short life expectancy *(normally less than 24 months)*	KEYNOTE-590 median overall survival in standard of care arm = 9.4 months	Yes
Evidence to indicate that the treatment has the prospect of offering an extension to life *(normally of a mean value of at least an additional 3 months compared with current NHS treatment)*	KEYNOTE-590 increase in median overall survival = 4.1 months Company model increase in mean overall survival = 13.9 months	Yes

Have end of life criteria been met?

Estimated overall survival (1)

Background:

- Company base case used log-logistic piecewise model with KEYNOTE-590 KM data and 40-week cut off
- ERG explored scenarios to show impact on ICER of different OS estimates
- Clinical advice to ERG that all four are clinically plausible



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KM: Kaplan-Meier

Estimated overall survival (2)

ERG:

- Consider all approaches are plausible
- Chose base case as it is the mid-range estimate of all plausible scenarios based on clinical opinion
- 5 to 7 year treatment waning applied as benefit could be maintained, but unlikely to be indefinite
- Company's choice of 40-week cut point is not appropriately justified (based on cut-point used for ITT population)
- Company base case estimates [redacted] alive at 10 years, and [redacted] alive at 20 years; ERG's base case estimates [redacted] of people alive at 10 years and [redacted] alive at 20 years

Clinical expert comments:

- Chemotherapy with pembrolizumab is likely to have a long term benefit
- People alive at 2 years may be in remission and may not progress in the future
- The magnitude of improved survival seen with pembrolizumab has not been observed in oesophageal cancer before

Which model for estimating overall survival does the committee prefer?

OS: overall survival, ITT: intention to treat

The use of time-to-death utilities (referred to as time-of-survival [ToS] utilities) (1)

Background:

- Company base case uses time-of-survival (ToS) utility model
- ToS generates utility values using groupings of utility observations based on how close they were reported to OS time
- Company note:
  - ToS utilities appropriate in a rapidly progressing cancer, where people deteriorate quickly as they approach death
  - EQ-5D data were collected at 30-day post-treatment discontinuation which does not truly represent the progressed state – ToS utilities avoids this issue

ERG:

- ToS utility values higher than expected compared to general population; company capped utilities to equal general population
- Average ToS and progression-based utilities varied notably
- Concerns over face validity of relatively high utility values from KEYNOTE-590, regardless of approach used
- ERG prefer progression-based utilities (least optimistic option)
- Progression-based approach more often (but not always) used for evaluations of cancer therapies which use a 3-state partitioned survival model

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ToS: time-of-survival, OS: overall survival

The use of time-to-death utilities (referred to as time-of-survival [ToS] utilities)(2)

Company comments:

- ERG's approach using average utilities over lifetime misrepresents average utility observed by majority from the start of treatment
- Difference in average progression-based and ToS utilities minimal when the model is restricted to 1 year
- ERG approach penalises a therapy that extends length of life
- Interaction model also presented to address over-estimation of QoL (used in scenario analysis)

CPS ≥10 population*	ToS	Progression-based	ToS and progression-based interaction model
Average utilities over 1 year	[redacted]	[redacted]	[redacted]
Average utilities over lifetime	[redacted]	[redacted]	[redacted]

*ERG calculated average utilities based on CPS ≥10 population

ERG comments:

- Both ToS approaches show greater utility values than progression-based approach
- Using 1-year timepoint doesn't fully represent the true average utilities
- More people predicted to live at least an additional year than there are progression-free patients in years 2 to 10 of the model – explains why the average utility is higher for ToS vs progression approach, as there are people included who have progressed disease and life expectancy > 1 year
- Disagrees that approach penalises treatment that extends life

The use of time-to-death utilities (referred to as time-of-survival [ToS] utilities) (3)

ERG comments on interaction model:

- Cannot fully critique company's interaction model due to limited information
- Unclear if interaction model is based on ITT or CPS ≥10 population

	ToS	Progression-based	ToS and progression-based interaction model	
			Progression-free	Progressed
≥360 days	[redacted]	-	[redacted]	[redacted]
180 to 360 days	[redacted]	-	[redacted]	[redacted]
90 to 180 days	[redacted]	-	[redacted]	[redacted]
30 to 90 days	[redacted]	-	[redacted]	[redacted]
0 to 30 days	[redacted]	-	[redacted]	[redacted]
Progression-free	-	[redacted]	-	-
Progressed	-	[redacted]	-	-

- **Is it plausible that time-of-survival utilities in people with life expectancy >1 year are equal to the general population?**
- **Which method of utility estimation is most appropriate?**

Nivolumab as subsequent treatment

Background:

- Nivolumab is recommended for unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after fluoropyrimidine and platinum-based therapy (TA707, published June 2021)
- Following publication of TA707 and in response to Technical Engagement, company costed nivolumab as a subsequent treatment based on PD-L1 inhibitor use in KEYNOTE-590:
  - [redacted] and [redacted] of KEYNOTE-590 CPS ≥10 population received PD-L1 inhibitor after pembrolizumab in combination with chemotherapy or after chemotherapy alone, respectively
  - PD-L1 inhibitors costed as nivolumab assuming 44 weeks duration (as per trial protocol)

ERG:

- Agree company's approach is suitable, to include nivolumab without making efficacy assumptions
- Trial included some re-treatment with PD-L1 inhibitor – not generalisable to UK practice
- More people may receive nivolumab than in KEYNOTE-590
- ERG scenario analysis incorporates nivolumab costs and adjusts efficacy:
  - [redacted] of KEYNOTE-590 CPS ≥10 population had at least 1 subsequent treatment
  - scenario analysis assumes [redacted] of patients received nivolumab after chemotherapy with no nivolumab use after pembrolizumab
  - efficacy impact included by adjusting comparator arm to apply hazard seen in pembrolizumab plus chemotherapy arm, applied at the average time when patients would receive subsequent treatment (mean PFS of chemotherapy arm)

Which assumption for incorporating nivolumab is most appropriate?

The double therapy used in the economic model may not reflect clinical practice in the UK

Background:
- Company base case compares pembrolizumab plus cisplatin and fluorouracil with cisplatin and fluorouracil as in KEYNOTE-590
- Company also presented analysis comparing pembrolizumab plus cisplatin and fluorouracil with blended chemotherapy based on UK market shares

ERG:
- Scenario analysis uses oxaliplatin + capecitabine with pembrolizumab as intervention and alone as comparator - accounts for differences in costs but not effectiveness

Company comments:
- Agree with ERG approach of exploring additional scenarios
- ERGs scenario has negligible impact on ICER

Clinical expert comments:
- Significant variability in practice - oxaliplatin is slowly replacing cisplatin but both still used
- Fluorouracil is required when swallowing is not possible
- Efficacy for all regimens is similar

Which treatment is used in clinical practice in the NHS, and which would be likely to be used in combination with pembrolizumab?

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SOC: Standard of care, OS: Overall survival, CI: confidence intervals

Cost-effectiveness results including PAS for pembrolizumab

		Costs (£)	QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Company base case (deterministic)	Pembrolizumab + cisplatin + fluorouracil	[redacted]	[redacted]	26,296	0.92	28,651
	Cisplatin + fluorouracil	[redacted]	[redacted]			
Company base case (probabilistic)	Pembrolizumab + cisplatin + fluorouracil	[redacted]	[redacted]	26,213	0.92	28,564
	Cisplatin + fluorouracil	[redacted]	[redacted]			
ERG base case (deterministic)	Pembrolizumab + cisplatin + fluorouracil	[redacted]	[redacted]	26,192	0.76	34,330
	Cisplatin + fluorouracil	[redacted]	[redacted]			

Note: results with PAS prices for subsequent treatments are presented in part 2

Scenario analysis: ERG and company

Source	Scenario	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Company	Company base case (vs cisplatin + fluorouracil)	26,296	0.92	28,651
Company	Company base case (vs blended comparator)	26,393	0.92	28,757
	Overall survival			
ERG	Single log-logistic parametric model	26,001	0.50	52,238
ERG	Treatment waning between 5 to 7 years*	26,234	0.82	31,839
Company	Piecewise 40-week cut off + log-logistic	26,368	1.02	25,865
ERG	Piecewise 40-week cut off + generalised gamma	26,404	1.07	24,767
	Progression-free survival			
Company	Piecewise 37-week cut off + log-logistic distribution*	26,744	0.92	29,140
	Utility values			
Company	ToS + progression-based interaction	26,296	0.89	29,539
ERG	Progression-based utilities*	26,296	0.82	31,963
	Nivolumab as subsequent treatment			
ERG	Nivolumab included using ERG efficacy adjustment	4,980	0.66	7,528

*ERG's preferred assumption

Key cost effectiveness issues

- **Is end of life criteria met?**
- **Which model for estimating overall survival does the committee prefer?** ***(Key model driver)***
  - Company base case - log-logistic piecewise, 40-week cut off
  - ERG base case - log-logistic piecewise, 40-week cut off + treatment waning
  - ERG scenario – log-logistic fully parametric *(greatest impact on ICER)*
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  - Company base case - as per KEYNOTE-590 (cisplatin and fluorouracil)
  - ERG scenario - oxaliplatin + capecitabine with pembrolizumab and as comparator

Back up slides

Additional scenarios

Source	Scenario	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
	Utility values			
ERG	Reduce magnitude by 10%	26,296	0.85	30,978
ERG	Apply published values	26,296	0.74	35,772
	Stopping rules			
Company	Turning off stopping rules*	26,732	0.92	29,127
	Adjusting for triple treatment efficacy			
ERG	Triple efficacy using UK expected market share	26,243	0.83	31,447
ERG	Triple efficacy using fluorouracil + cisplatin + epirubicin	25,712	0.65	39,478
ERG	Triple efficacy using fluorouracil + oxaliplatin + epirubicin	25,752	0.65	39,540
ERG	Triple efficacy using capecitabine + oxaliplatin + epirubicin	25,643	0.65	39,359
ERG	Triple efficacy using capecitabine + cisplatin + epirubicin	25,675	0.65	39,421
	Changing double treatment as chemotherapy + in combination with pembrolizumab			
ERG	Pembrolizumab in combination with capecitabine plus oxaliplatin versus capecitabine plus oxaliplatin	26,756	0.92	29,152

*ERG preferred assumption