NICE National Institute for Health and Care Excellence

For public

Fully redacted

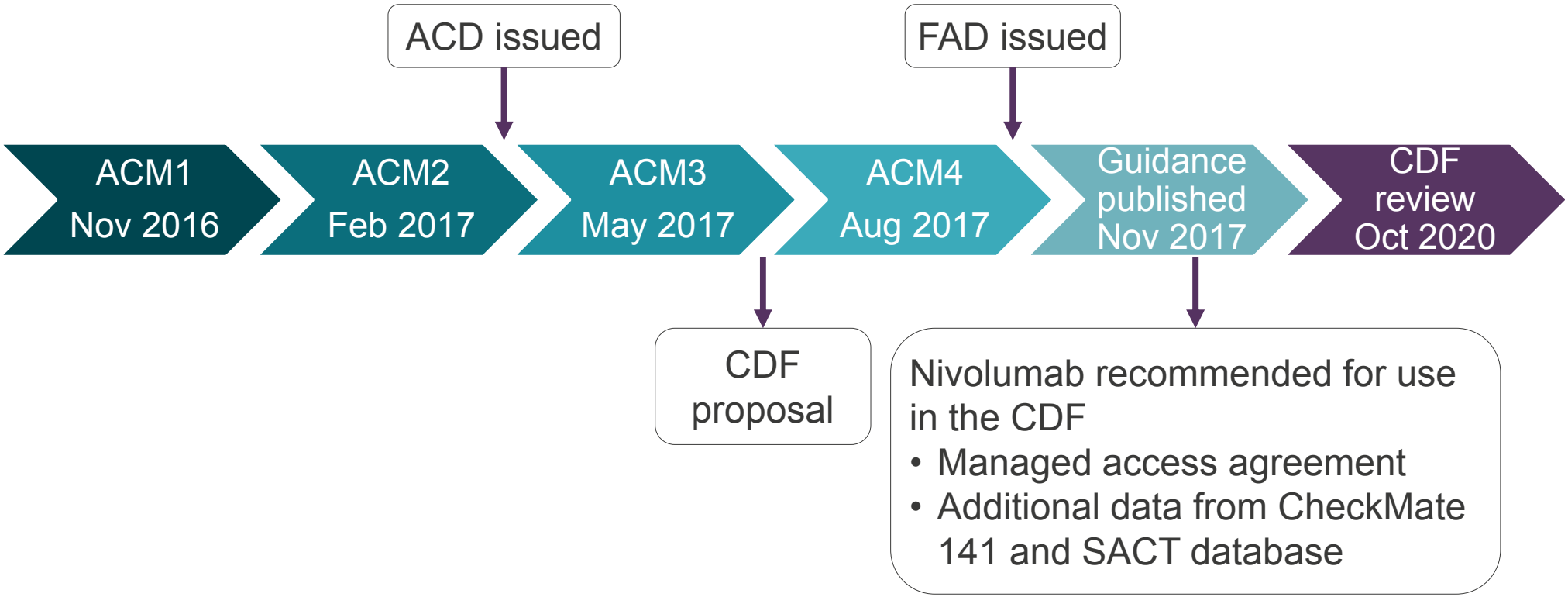
Nivolumab for treating squamous cell carcinoma of the head and neck after platinum-based chemotherapy (CDF review of TA490)

Lead team presentation

Lead team: Rob Hodgson, Guy Makin, Malcolm Oswald
ERG: Kleijnen Systematic Reviews Ltd
Technical team: Lindsay Smith, Nicola Hay, Verena Wolfram, Linda Landells
Company: BMS

CDF review committee meeting 3 December 2020 (virtual)

Summary of original appraisal TA490



Appraisal background

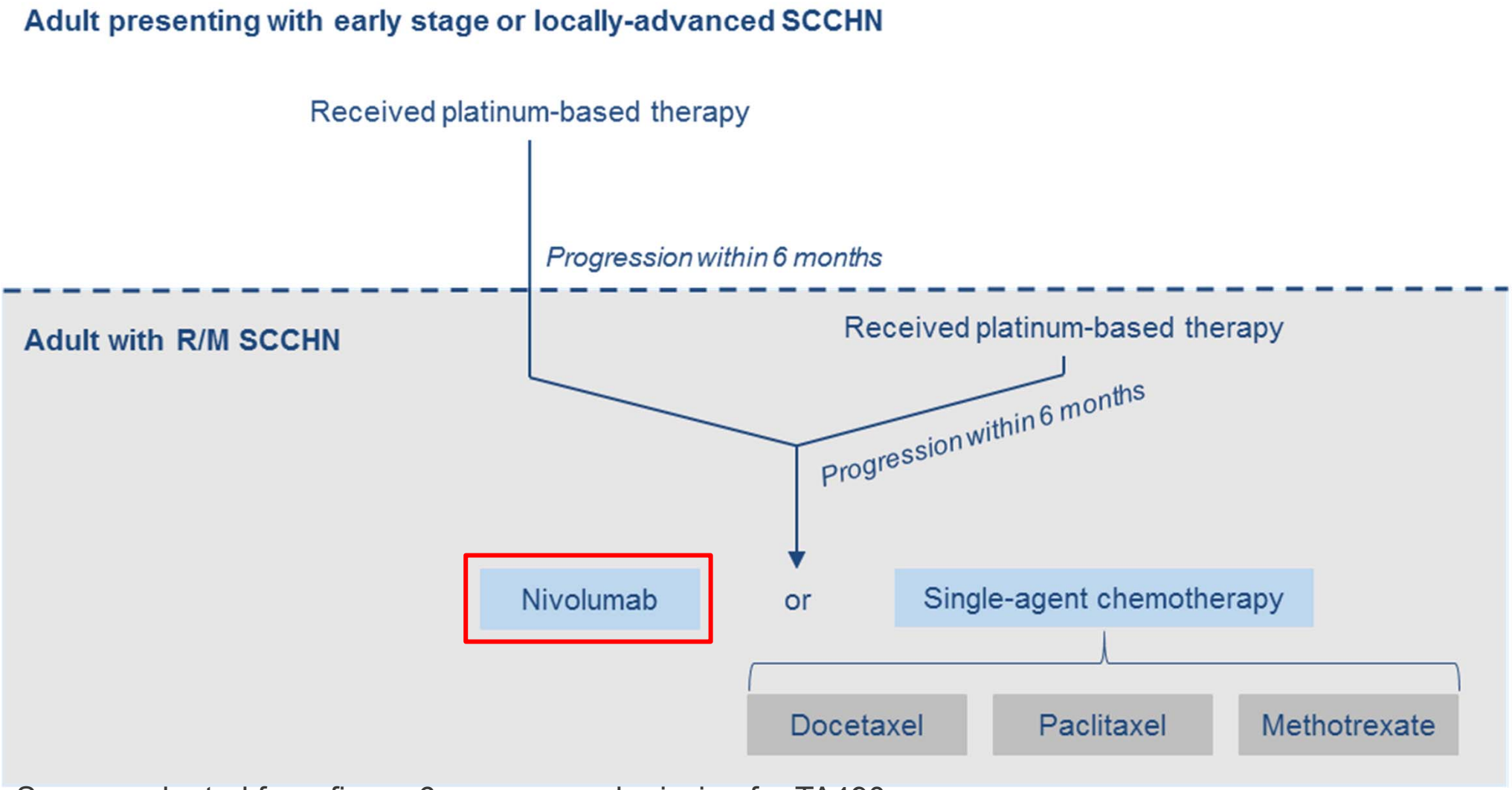
Nivolumab marketing authorisation: treatment of recurrent or metastatic squamous cell cancer of the head and neck in adults progressing on or after platinum-based chemotherapy.

TA490 recommendation: Nivolumab is recommended in the CDF for treating **squamous cell carcinoma of the head and neck**, only if:

- the disease has progressed within 6 months of having chemotherapy
- nivolumab is stopped at 2 years of uninterrupted treatment
- the conditions in the managed access agreement are followed.

	Original appraisal (TA490)	Current CDF review (ID1585)
Population	• Adults with recurrent or metastatic squamous cell head and neck cancer whose disease has progressed within 6 months of platinum-based chemotherapy • PD-L1 ≥1% and PD-L1 subgroups • Docetaxel subgroup was presented	• All-randomised patients (regardless of PD-L1 status) • PD-L1 ≥1% and PD-L1 <1% subgroups also presented • Docetaxel subgroup presented at technical engagement
Comparator	• Docetaxel most relevant comparator • Paclitaxel and methotrexate also considered	• Docetaxel only
Data source	• ITT population • Docetaxel subgroup	• ITT population • Docetaxel subgroup needed
Clinical data	• CheckMate 141 (September 2016)	• CheckMate 141 (Oct 2019) • Systemic anti-cancer therapy (SACT) data from 506 people (to October 2019)

Treatment pathway from TA490



Source: adapted from figure 6 company submission for TA490

- Cetuximab (TA473) and pembrolizumab (TA661) are now recommended for treating recurrent squamous head and neck cell carcinoma in some subgroups

CDF review TA490 - Patient perspective

- **Submissions from The Swallows Head & Neck Cancer Charity and Head and Neck Cancer UK**

	Patient experts comments
Unmet need	• Available treatments are considered good • Treatments that offer a better quality of life (QoL), long term survival, and reduced side effects would be beneficial • There is a need for support during and after treatment
Quality of life	• Refractory or recurrent disease impact all aspects of life including mental wellbeing, social functioning, mobility, work • People might struggle with selfcare, dressing, washing, decision making, eating, drinking, and communicating, there might also be disfigurement • People might be depressed and dealing with suicide thoughts 'Why me' 'Can't go on like this'
Advantages	• Treatment was beneficial but people would have liked more understanding of the outcomes and impact on QoL • Positive impact on QoL but it was less than people hoped
Side effects	• Dry mouth, fatigue
Subgroups	• Younger people might benefit more as they might tolerate the treatment better

CDF review TA490 – Key considerations

Issue	Committee preferred in TA490	Company base case in current CDF review	Technical team judgement ICER impact
Comparator	Docetaxel	Docetaxel	✓ Docetaxel
Data source	• ITT population • Docetaxel subgroup	ITT population	• ITT population • Docetaxel subgroup
OS extrapolation Issue 2	Nivolumab and IC: piecewise with lognormal (20, 36 and 48-week cut-off points)	Nivolumab and IC: piecewise with lognormal (96-week cut-off point)	✓ ▯▯▯ • Nivolumab and IC: piecewise with log-normal (96-week cut-off point) • *Clinical expert validation needed*
PFS extrapolation	Nivolumab and IC: generalised gamma		✓
TTD Issue 3	Nivolumab and IC: generalised gamma	Nivolumab: 2-spline normal IC: [redacted]	✓ ▯▯▯ • Nivolumab: 2-spline normal • IC: [redacted] • *Scenario analyses*

NICE ▯ High ICER impact ▯ Moderate ICER impact ▯ Low ICER impact

CDF review TA490 – Key considerations

	Committee preferred in TA490	Company base case in current CDF review	Technical team judgement ICER impact	
2-year stopping rule **Issue 4**	Considered inappropriate Accepted only as part of CDF	2-year stopping rule	✗	• No stopping rule preferred
Duration of continued treatment effect **Issue 4**	3 years after treatment is stopped (total of 5 years)	Lifetime	✗	• 3 years after treatment is stopped (if stopping rule were applied)
Utility values **Issues 5**	Both treatment-dependent and independent utility values considered	Only treatment-dependent utility values included Time-to-death utility decrements applied	✗	• Both treatment-dependent and independent utility values considered
Dose	Weight-based	Fixed dose in line with SmPC	✓	


High ICER impact


Moderate ICER impact


Low ICER impact

CDF review TA490 – Key clinical evidence

CheckMate 141 has 37 months of additional data

Outcome	TA490		CDF review		
	CheckMate 141 September 2016		CheckMate 141 October 2019		SACT October 2019
	Nivolumab (ITT) (n=240)	IC (ITT) (n=121)	Nivolumab (ITT) (n=240)	IC (ITT) (n=121)	Nivolumab (n=506)
Deaths, n (%)	[redacted]	[redacted]	218 (90.8)	118 (97.5)	335/506 (66.2)
Median OS, months (95% CI)	[redacted]	[redacted]	7.72 (5.68, 8.74)	5.06 (4.04, 6.24)	6.5 (5.6, 7.6)
HR	0.70 (97.73% CI: 0.51, 0.96)		0.69 (95% CI: 0.55, 0.86)		NA
Survival rate, % (95% CI)					
12-month	[redacted]	[redacted]	33.4 (27.5, 39.5)	19.4 (12.9, 26.9)	34 (29, 38)
18-month	[redacted]	[redacted]	22.1 (17.0, 27.6)	8.4 (4.3, 14.3)	NA
24-month	[redacted]	[redacted]	16.8 (12.3, 21.9)	5.9 (2.6, 11.1)	NA
36-month	[redacted]	[redacted]	10.3 (6.8, 14.7)	2.5 (0.7, 6.6)	NA
48-month	[redacted]	[redacted]	8.0 (4.9, 12.0)	1.7 (0.3, 5.4)	NA

Source: Table 5 from company submission, table 3.4 from the ERG report; CI: confidence interval; HR: hazard ratio; IC: investigator choice; NA: not available; OS: overall survival

CDF review TA490
Outstanding issues after technical engagement

No issues were resolved during technical engagement

- **Issue 1:** Generalisability
- **Issue 2:** Extrapolation of overall survival
- **Issue 3:** Time to treatment discontinuation
- **Issue 4:** Stopping rule & treatment effect duration
- **Issue 5:** Utility values
- **Issue 6:** PD-L1 expression subgroups

Issue 1: Generalisability of CheckMate 141 – data source

TA490 Committee conclusion

- **Population** – generalisable; some differences between baseline characteristics of trial population and UK population
- **Comparators** – uncertainty whether comparators in trial were generalisable to clinical practice
- **Most relevant comparator** – docetaxel
- Docetaxel subgroup was presented

Population is generalisable but comparators are uncertain

Company update (CDF review TA1585)

- 1-year survival rate in CheckMate 141 and SACT data set were similar
- Median OS 95% confidence interval overlap for CheckMate 141 and SACT data set
- Docetaxel subgroup not presented because trial was not statistically powered for this

Trial results are generalisable; ITT population appropriate data source

ERG (CDF review TA1585)

- Docetaxel subgroup results should be presented and used in analysis

Docetaxel subgroup most appropriate data source

CDF review technical engagement responses:

- **Company:** provided trial results for docetaxel subgroup
- **ERG:** there is little difference in baseline characteristics of ITT population and docetaxel subgroup

What is the most appropriate data source for assessing nivolumab's clinical- and cost-effectiveness compared with docetaxel? ITT population or docetaxel subgroup?

Issue 1: Generalisability of CheckMate 141

Docetaxel subgroup – people who would have received docetaxel as investigator choice

Outcome	CDF review CheckMate 141 docetaxel subgroup October 2019	
	Nivolumab (n=)	Docetaxel (n=)
Deaths, n (%)	[redacted]	[redacted]
Median OS, months (95% CI)	[redacted]	[redacted]
Survival rate, % (95% CI)		
12-month	[redacted]	[redacted]
18-month	[redacted]	[redacted]
24-month	[redacted]	[redacted]
36-month	[redacted]	[redacted]
48-month	[redacted]	[redacted]

Source: table 2 and table 6 from company response to technical engagement; CI: confidence interval; HR: hazard ratio; OS: overall survival

Comparison of hazard ratios for ITT population and docetaxel subgroup

Population		ITT population		Docetaxel subgroup	
		Nivolumab	IC	Nivolumab	Docetaxel
All patients	n (%)	218/240 (90.8)	118/121 (97.5)	[redacted]	[redacted]
	HR (95% CI; p-value)	0.69 (0.55, 0.86; p<0.001)		[redacted]	

Source: table 9 from company response to technical engagement; CI: confidence interval; HR: hazard ratio; IC: investigator choice; OS: overall survival

Moderate ICER impact

Issue 2: Overall survival extrapolation

TA490 Committee conclusion

- Better OS in the nivolumab arm compared with IC (ITT) at 18-month follow up
- Long-term survival uncertain
- Piecewise method using Kaplan-Meier data followed by parametric distribution seemed appropriate; timepoint to extrapolate from and distribution need exploring

Long-term survival was uncertain

Company update (CDF review TA1585)

- Updated CheckMate 141 results
- Used piecewise method – Kaplan-Meier data followed by log-normal distribution from 96 weeks
- Presented scenario analyses using log-normal and log-logistic extrapolation

Explored different extrapolation methods

ERG and Technical team (CDF review TA1585)

- Agree with company approach
- But like to see external validation

External validation needed

CDF review technical engagement responses:

- **Company**: Acknowledge that fully parametric models may provide plausible alternatives; however state that impact on ICER is minimal

What is the most appropriate method for extrapolating overall survival (OS) data in the ITT population?

Issue 2: Overall survival extrapolation

- Overall survival extrapolation for ITT data

Extrapolation model, years	1	2	3	4	5	10	15	20	25
Nivolumab									
CheckMate 141 (Kaplan-Meier data)	33.4	16.8	10.3	8.0	n/a	n/a	n/a	n/a	n/a
Piecewise, log-normal, 96-week (base-case)	33.4	16.1	10.1	7.3	5.7	2.6	1.5	1.0	0.8
Fully parametric, log-normal	33.6	17.3	10.6	7.2	5.2	1.6	0.7	0.4	0.2
Fully parametric, log-logistic	32.7	16.5	10.5	7.4	5.7	2.4	1.4	1.0	0.7
Investigator's choice (IC)									
CheckMate 141 (Kaplan-Meier data)	19.4	5.9	2.5	1.7	n/a	n/a	n/a	n/a	n/a
Piecewise, log-normal, 96-week (base-case)	19.4	5.6	2.3	1.1	0.6	0.1	0.0	0.0	0.0
Fully parametric, log-normal	18.9	5.5	2.2	1.0	0.6	0.1	0.0	0.0	0.0
Fully parametric, log-logistic	17.6	5.7	2.8	1.7	1.1	0.3	0.2	0.1	0.1

Source: Company's model ("OS" tab); table 4 company's response to technical engagement

Issue 3: Time to treatment discontinuation

TA490 Committee conclusion	Company update (CDF review TA1585)
• No parametric distributions fitted the progression-free survival and TTD data well • Generalised gamma distribution was preferred	• Updated CheckMate 141 results • Used 2-spline normal distribution for nivolumab arm as better statistical and visual fit to data • Used [redacted] for IC arm • Explored SACT data for nivolumab arm
Generalised gamma preferred	Different distributions for the 2 arms

ERG (CDF review TA1585)	Technical team (CDF review TA1585)
• Preferred generalised gamma for both arms • SACT provides real world data	• Agree with company to use different approaches for the 2 arms • SACT shows uncertainty of TTD
Same approach as in TA490	Different distributions for the 2 arms

CDF review technical engagement responses:

- **Company**: justified using different approaches for the 2 arms

What is the most appropriate method for extrapolating time on treatment with (a) nivolumab and (b) comparator (docetaxel)?

Issue 3: Time to treatment discontinuation

- Time to treatment discontinuation extrapolation for ITT data

Extrapolation model	3 months	6 months	12 months	18 months	24 months	36 months	5 years	10 years	20 years
Nivolumab									
CheckMate 141 (Kaplan-Meier data)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
SACT (Kaplan-Meier data)	Not reported	28	17	Not reported	n/a	n/a	n/a	n/a	n/a
2-spline normal model	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Generalised gamma	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Investigator's choice (IC)									
CheckMate 141 (Kaplan-Meier data)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Generalised gamma	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: Company's model ("TTD" tab); TTD: time to treatment discontinuation.

Large ICER impact

Issue 4: Stopping rule and duration of treatment effect

TA490 Committee conclusion

- No stopping rule; stopping rule not applied in trial
- 2-year stopping rule was accepted in the context of the CDF
- OS benefit for up to 3 years after stopping treatment (total of 5 years)

No stopping rule

Company update (CDF review TA1585)

- Maintained 2-year stopping rule; deemed acceptable by clinical expert; was feasible during CDF period
- OS benefit continuous for more than 5 years
- Scenarios – no stopping rule, stopping rule but different treatment effect durations, select people with lasting benefit

2-year stopping rule; long-term treatment effect

ERG (CDF review TA1585)

- No stopping rule
- Benefit for up to 3 years after stopping treatment with or without stopping rule

No stopping rule; diminished effect

Technical team (CDF review TA1585)

- No stopping rule; notes that stopping rules apply for other indications and similar treatments
- Benefit for up to 3 years after stopping treatment with stopping rule

No stopping rule; long-term treatment effect

CDF review technical engagement responses:

- **Company**: stopping rules are accepted for nivolumab in other indications and pembrolizumab for squamous cell carcinoma of head and neck

Is a 2-year stopping rule for nivolumab appropriate?
Is it plausible that nivolumab's treatment benefit continues for a lifetime; with or without stopping rule?

Large ICER impact

Issue 5: Utility values

TA490 Committee conclusion	Company update (CDF review TA1585)
• High uncertainty • Most appropriate utility values were between treatment-dependent and treatment-independent estimates • QoL benefit is not constant	• Use of treatment-dependent utility values • Applied time-to-death disutility decrements in last 3 model cycles • Provided scenario analysis without decrements
High uncertainty	Treatment-dependent utility values with decrements

ERG and technical team (CDF review TA1585)

- 2 base cases using treatment-dependent and treatment-independent utility values
- No decrement as it doesn't address uncertainty
- **ERG** noted that there were alternatives proposed in the ERG report for TA490
- **Technical team** noted that there was no new evidence to support changing TA490's decision

Treatment-dependent and treatment-independent utility values with no decrement

CDF review technical engagement responses:

- **Company:** Previous NICE appraisals accepted time-to-death utility approach (TA319 – ipilimumab for previously untreated advanced melanoma, TA600 – pembrolizumab for untreated metastatic squamous NSCLC, TA384 – nivolumab for advanced melanoma)

Which approach to utility values is most appropriate?

Issue 5: Utility values

- Utility values for ITT data

Utility value	Treatment-dependent		Treatment-independent
	Nivolumab	IC	Both treatment arms
Progressed disease	[redacted]	[redacted]	[redacted]
3 months to death (3rd-to-last model cycle)	[redacted]	[redacted]	[redacted]
Decrement	[redacted]	[redacted][a]	[redacted]
2 months to death (2nd-to-last model cycle)	[redacted]	[redacted]	[redacted]
Decrement	[redacted]	[redacted]	[redacted]
1 month to death (last model cycle)	[redacted]	[redacted]	[redacted]
Decrement	[redacted]	[redacted]	[redacted]

[a] As the time-to-death utility (57–91 days) was greater than the PD utility, no decrement was applied.
Source: Table 15 in company submission; IC: investigator's choice.

Low completion rate after 21 weeks in comparator arm

Large ICER impact

Issue 6: PD-L1 expression subgroups

TA490 Committee conclusion	Company update (CDF review TA1585)
• PD-L1 level might influence outcome; treatment more effective in PD-L1 of 1% and greater	• Trial not powered for subgroup analysis • Nivolumab is effective in both PD-L1 subgroups (PD-L1 <1%, PD-L1 ≥1%)
PD-1L subgroups might be relevant	Nivolumab is effective independent of PD-L1 level

ERG and technical team (CDF review TA1585)

- Significant OS benefit in PD-L1 ≥1% but not PD-L1 <1% subgroup
- However, no significant evidence of a treatment and subgroup interaction for OS (p=0.239)
- Small sample size and wide confidence intervals
- **Technical team:** uncertainty in evidence

Uncertainty in evidence for subgroup

CDF review technical engagement responses:

- **Company:** trial not powered to detect difference between treatment arms in PD-L1 subgroups; all-randomised population should be considered

Does clinical- and cost-effectiveness of nivolumab vary by PD-L1 expression status?

Issue 6: PD-L1 expression subgroups

- Clinical evidence for PD-L1 subgroups of ITT population

Outcome	CDF review			
	CheckMate 141 – October 2019			
	PD-L1 <1%		PD-L1 ≥1%	
	Nivolumab (n=76)	IC (n=40)	Nivolumab (n=96)	IC (n=61)
Deaths (n)	72/76 (94.7)	40/40 (100)	87/96 (90.6)	60/61 (98.4)
Median OS, months (95% CI)	6.51 (4.37, 11.73)	5.45 (3.68, 8.54)	8.15 (6.67, 9.53)	4.60 (3.81 5.78)
HR (95% CI)	0.74 (0.50 to 1.10; p=0.138)		0.54 (0.39 to 0.76; p<0.001)	
Source: tables 8 and 9 company submission				

Additional areas of uncertainty

Issue	Why issue is important	Impact on ICER
Change of dosing schedule	**TA490:** dosing was weight based (3 mg/kg every 2 weeks) **CDF review:** flat dose (240 mg every 2 weeks) in line with updated summary of product characteristics The company assume that this dose will have equivalent clinical effectiveness.	Using weight-based dosing increases company's ICER by +£576 par QALY gained

Cost effectiveness results (deterministic) – nivolumab versus IC in ITT population

Issue	Assumptions used	ICER (change vs. base case) ITT population	
	Company's base-case	£37,236	
	Corrected docetaxel dose intensity error	£37,254	+£18
	Corrected docetaxel dose intensity error & generalized gamma for PFS nivo & IC arms	No change	
1	Use ITT population data	No change	
2a	OS: Kaplan-Meier for 96 weeks + log-normal	No change	
2b	OS: Fully parametric log-normal curve	£41,178	+£3,942
3a	TTD: 2-point spline normal for nivo; [redacted]	No change	
3b	TTD: Generalised gamma for nivo and IC	£39,840	+£2,604
4a	No stopping rule	£49,036	+£11,800
4b	With stopping rule & 5-year OS benefit	£45,039	+£7,803
5	Treatment independent (TI) & treatment dependent (TD) utilities but no time-to-death disutility decrements	TI: £41,557 TD: £35,357	+£4,321 -£1,879

NICE ICERs are calculated by tech team

Cost effectiveness results (deterministic) – nivolumab versus IC in ITT population

Issue	Assumptions used	ICER (change vs. base case) ITT population	
	Company's base-case	£37,236	
	Corrected docetaxel dose intensity error	£37,254	+£18
	Corrected docetaxel dose intensity error & generalized gamma for PFS nivo & IC arms	No change	
1, 2a, 3a, 4a, 5	**Technical team preferences combined (no stopping rule)**	**TI: £54,700** **TD: £46,540**	**+£17,464** **+£9,304**
1, 2a, 3a, 4b, 5	**Technical team preferences combined (with stopping rule & 5-year OS benefit)**	**TI: £50,748** **TD: £42,222**	**+£13,512** **+£4,986**
1, 2a, 3b, 4a, 5	**ERG preferences combined (no stopping rule)**	**TI: £49,233** **TD: £41,888**	**-£11,997** **-£4,652**
1, 2a, 3b, 4b, 5	**ERG preferences combined (with stopping rule & 5-year OS benefit)**	**TI: £54,513** **TD: £45,355**	**-£17,277** **-£8,119**

Cost effectiveness results (probabilistic) – nivolumab versus IC in ITT population

Issue	Assumptions used	ICER (change vs. base case) ITT population
1, 2a, 3a, 4a, 5	Technical team preferences combined (no stopping rule)	TI: £53,134 TD: £45,586
1, 2a, 3a, 4b, 5	Technical team preferences combined (with stopping rule & 5-year OS benefit)	TI: £50,321 TD: £41,549
1, 2a, 3b, 4a, 5	Technical team preferences combined (no stopping rule)	TI: £49,098 TD: £41,943
1, 2a, 3b, 4b, 5	Technical team preferences combined (with stopping rule & 5-year OS benefit)	TI: £55,773 TD: £45,667

ICERs are calculated by tech team

Cost effectiveness results (deterministic) – nivolumab versus IC in PD-L1 subgroups

Issue	Assumptions used	ICER (change vs. base case) PD-L1 <1% subgroup		ICER (change vs. base case) PD-L1 ≥1% subgroup	
	Company's base-case	£46,309		£36,163	
	Corrected docetaxel dose intensity error	£46,339	+£30	£36,174	+£11
0a	PFS: PD-L1 <1% generalised gamma for nivo; [redacted] for IC PD-L1 1≥1% 1 spline hazard for nivo; [redacted] for IC	No change		No change	
0b	PFS: Generalised gamma for nivo & IC arms	£46,140	-£169	£36,205	+£42
1	Use all-randomised trial data	No change		No change	
2a	OS: Kaplan-Meier for 48 weeks + log-normal for nivo, [redacted] for IC	No change		No change	
2b	OS: Kaplan-Meier for 48 weeks + log-normal	£46,520	+£211	£36,285	+£122
2c	OS: Fully parametric log-normal curve	£46,863	+£554	£37,000	+£837
3a	TTD: PD-L <1% [redacted] for nivo & IC; PD-L1 ≥1% 1-spline odds for nivo, [redacted] for IC	No change		No change	
3b	TTD: PD-L <1% 1-spline normal for nivo & IC; PD-L1 ≥1% generalised gamma for nivo & IC	IC: OS below TTD (£45,140)		£38,694	+£2,531

ICERs are calculated by tech team

Cost effectiveness results (deterministic) – nivolumab versus IC in PD-L1 subgroups

Issue	Assumptions used	ICER (change vs. base case) PD-L1 <1% subgroup		ICER (change vs. base case) PD-L1 ≥1% subgroup	
	Company's base-case	£46,309		£36,163	
	Corrected docetaxel dose intensity error	£46,339	+£30	£36,174	+£11
4a	No stopping rule	£50,278	+£3,969	£46,293	+£10,130
4b	With stopping rule & 5-year OS benefit	£52,368	+£6,059	£43,064	+£6,901
5	Treatment independent (TI) & treatment dependent (TD) utilities but no time-to-death disutility decrements	TI: £54,041 TD: £43,181	+£7,732 -£3,128	TI: £38,980 TD: £34,718	+£2,817 -£1,445

NICE ICERs are calculated by tech team

Cost effectiveness results (deterministic) – nivolumab versus IC in PD-L1 subgroups

Issue	Assumptions used	ICER (change vs. base case) PD-L1 <1% subgroup		PD-L1 ≥1% subgroup	
	Company's base-case	£46,309		£36,163	
	Corrected docetaxel dose intensity error	£46,339		£36,174	
0a, 1, 2-4a, 5	Technical team preferences combined (no stopping rule)	TI:£58,634 TD: £46,851	+£12,325 +£542	TI: £49,885 TD: £44,430	+£13,722 +£8,267
0a, 1, 2&3a, 4b, 5	Technical team preferences combined (with stopping rule & 5-year OS benefit)	TI: £61,947 TD: £48,319	+£15,638 +£2,010	TI: £46,493 TD: £40,958	+£10,330 +£4,795
0b, 1, 2&3b, 4a, 5	ERG preferences combined (not stopping rule)	TI: £55,078 TD: £43,820	+£8,769 -£2,489	TI: £49,214 TD: £43,645	+£13,051 +£7,482
0b, 1, 2-4b, 5	ERG preferences combined (with stopping rule & 5-year OS benefit)	TI: £60,607 TD: £47,037	+£14,298 +£728	TI: £50,267 TD: £44,058	+£14,104 +£7,895

NICE ICERs are calculated by tech team

End of life

TA490 Committee conclusion

- **Life expectancy** – median OS 5.1 months in IC arm of trial, 8.16 to 9.84 months based on piecewise log normal model (depending on the time point for extrapolation of the trial data)
- **Life extension** – 4.68 to 6.24 months based on piecewise log-normal model

End-of-life criteria met for ITT population

ERG and technical team (CDF review TA1585)

- No change in OS for the ITT population
- Updated data supports previous conclusion for ITT population

	ITT population		Docetaxel population		PD-L1 <1% ITT subgroup		PD-L1 ≥1% ITT subgroup	
	Nivo	IC	Nivo	Doc	Nivo	IC	Nivo	IC
Median OS (months)	7.72	5.06	[redacted]	[redacted]	6.51	5.45	8.15	4.60
Life extension (months) (based on model)	6.8 to 9.2		6.7		6.3		12	

- Uncertain whether life extending criterion is met for docetaxel population

End-of-life criteria met for ITT population and PD-L1 subgroups BUT there is uncertainty for docetaxel subgroup

Is the end of life criterion 'extension of life' met for the relevant population?

Equality

- Patient expert highlighted equality issues for the treatment because of:
  - religious and cultural concerns
  - language barriers
  - age (to understand the diagnoses and treatment – caregiver might be important)