

Durvalumab for treating limited-stage small-cell lung cancer after chemoradiation [ID5073]

Slides for public –
NoCON

Technology appraisal committee D [12 June 2025]

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Durvalumab for treating limited-stage small-cell lung cancer after chemoradiation [ID5073]

- ✓ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ❑ Summary

Background on limited-stage small-cell lung cancer

- There are 2 main types of lung cancer, small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC)
- SCLC is less common than NSCLC making up around 10 to 15% of lung cancer cases
- Around 2,600 people were diagnosed with SCLC in England in 2022
- SCLC is more aggressive than NSCLC and has a poor prognosis because of its high potential for metastasis
- Most people with SCLC present with distant metastases, but around 30% have limited-stage SCLC (LS-SCLC) where the cancer is contained in a single area that can be treated with radiotherapy (corresponding stages 1-3)
- Based on company estimates, the number of people with LS-SCLC eligible for durvalumab is expected to be around 300 per year
- Symptoms may include persistent cough, shortness of breath, chest pain and weight loss
- LS-SCLC is treated with curative intent

Patient perspectives

Submission from Roy Castle Lung Cancer Foundation

- SCLC is a particularly aggressive type of cancer
- 5-year survival for SCLC (limited and extensive stage disease) is only about 5%
- For people with limited stage SCLC, 5-year survival is thought to range from about 15 to 30%
- There have been few developments in the treatment of SCLC in decades, and outcomes for people having current treatments are poor
- There is a huge unmet need for therapies with better outcomes than those currently available
- Durvalumab has shown significantly longer overall survival and progression-free survival than placebo in people with LS-SCLC

“A diagnosis of SCLC is devastating. Small cell is a particularly aggressive type of cancer, patients often being symptomatic at presentation. This is a rapidly progressive disease and as such, patients should be assessed quickly and systemic anticancer treatment started quickly.”

“Symptoms such as breathlessness, cough and weight loss are difficult to treat, without active anti-cancer therapy. Furthermore, these are symptoms which can be distressing for loved ones to observe.”

Clinical perspectives

Submissions from the British Thoracic Oncology Group (BTOG), Association of Respiratory Nurses (ARN) and clinical expert statements

- LS-SCLC has a poor prognosis – there have been limited advances in treatment and prognosis in over 20 years
- There are no maintenance treatments following chemotherapy and radiotherapy available
- Durvalumab is the first adjuvant immunotherapy in LS-SCLC that has been shown to improve survival
- Durvalumab would improve the pathway by giving people more treatment options and a better chance of long-term survival
- Durvalumab is expected to result in increased healthcare resource use, but it is well tolerated with known and manageable side effects

“if we can halt the progression... and maintain the fitness of these patients... we will not only help these patients live longer, but we will also be improving quality of life by reducing disease burden for a longer period of time.”

“Trial results are highly clinically and statistically significant. This is the first increase in OS as a result of a change in systemic cancer therapy for many years.”

“It is the first step change [in] the way we treat SCLC in the future, and addresses a huge unmet need”.

Equalities

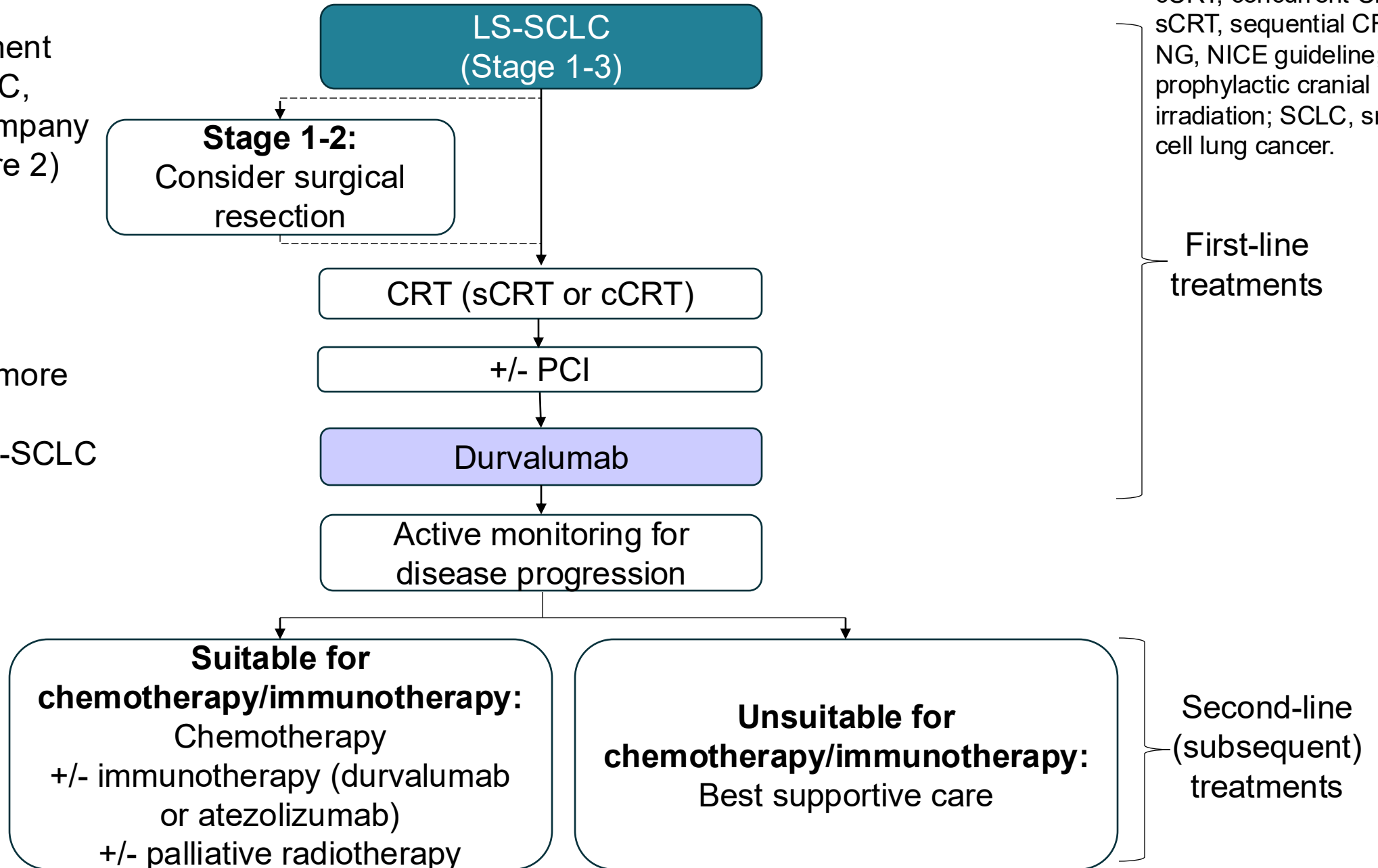
No equalities issues raised at scoping, in submissions or expert statements

Treatment pathway

Figure 1: Treatment pathway for SCLC, adapted from company submission (figure 2) and EAG report

[NG122](#) provides more detail on first-line treatments for LS-SCLC (see [Appendix](#))

Abbreviations:
CRT, chemoradiotherapy;
cCRT, concurrent CRT;
sCRT, sequential CRT;
NG, NICE guideline; PCI,
prophylactic cranial
irradiation; SCLC, small-
cell lung cancer.



Durvalumab (Imfinzi, AstraZeneca)

Marketing authorisation	• MHRA marketing authorisation granted 25 April 2025: • <i>“IMFINZI as monotherapy is indicated for the treatment of adults with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following platinum-based chemoradiation therapy.”</i>
Mechanism of action	• IgG1 kappa monoclonal antibody that selectively blocks the interaction of PD-L1 with receptors PD-1 and CD80
Administration	• 1500 mg (fixed dose) intravenously every 4 weeks until disease progression, intolerable toxicity, or a maximum of 24 months (that is, a 2-year stopping rule)
Price	• List price of £2,466 for a 500 mg vial and £592 for a 120 mg vial (BNF 2025) • There is a commercial arrangement in place

Abbreviations: BNF, British National Formulary; CD80, cluster of differentiation 80; IgG1, Immunoglobulin G1; LS-SCLC, limited-stage small-cell lung cancer; PD-1 programmed cell death protein-1; PD-L1, programmed cell death ligand 1.

Key issues

Key issues	ICER impact
Generalisability of trial data	Unknown
Extrapolation of OS and PFS (and the cure assumption)	Moderate (OS)
	Small (PFS)
	Small (cure assumption)
Treatment effect waning	Large
Resource use	Moderate
Other issues (see Appendix)	ICER impact
Subsequent treatment	Small

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Key clinical trial – ADRIATIC

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	ADRIATIC; NCT03703297 (n=730)
Design	Ongoing, three-arm, double-blind, phase 3, placebo-controlled, RCT
Population	Adults with histologically and/or cytologically documented LS-SCLC (stage 1 to 3) who had previously received four cycles of first-line cCRT, had an ECOG performance status of 0 or 1 and had no disease progression after cCRT
Interventions	• Durvalumab monotherapy with placebo tremelimumab (n=264) ↗ • Durvalumab in combination with tremelimumab (n=200*)
Comparator	Placebo (durvalumab placebo with tremelimumab placebo) (n=266)
Duration	• Median OS follow-up; durvalumab 30.75 months, placebo 28.63 months • Median PFS follow-up; durvalumab 9.07 months, placebo 7.39 months • Data cut-off date: 15 January 2024
Primary outcome	Dual primary efficacy endpoints – OS and PFS
Key secondary outcomes	Adverse effects, health-related quality of life (EQ-5D-5L), time to treatment discontinuation
Locations	19 countries including 1 site in UK

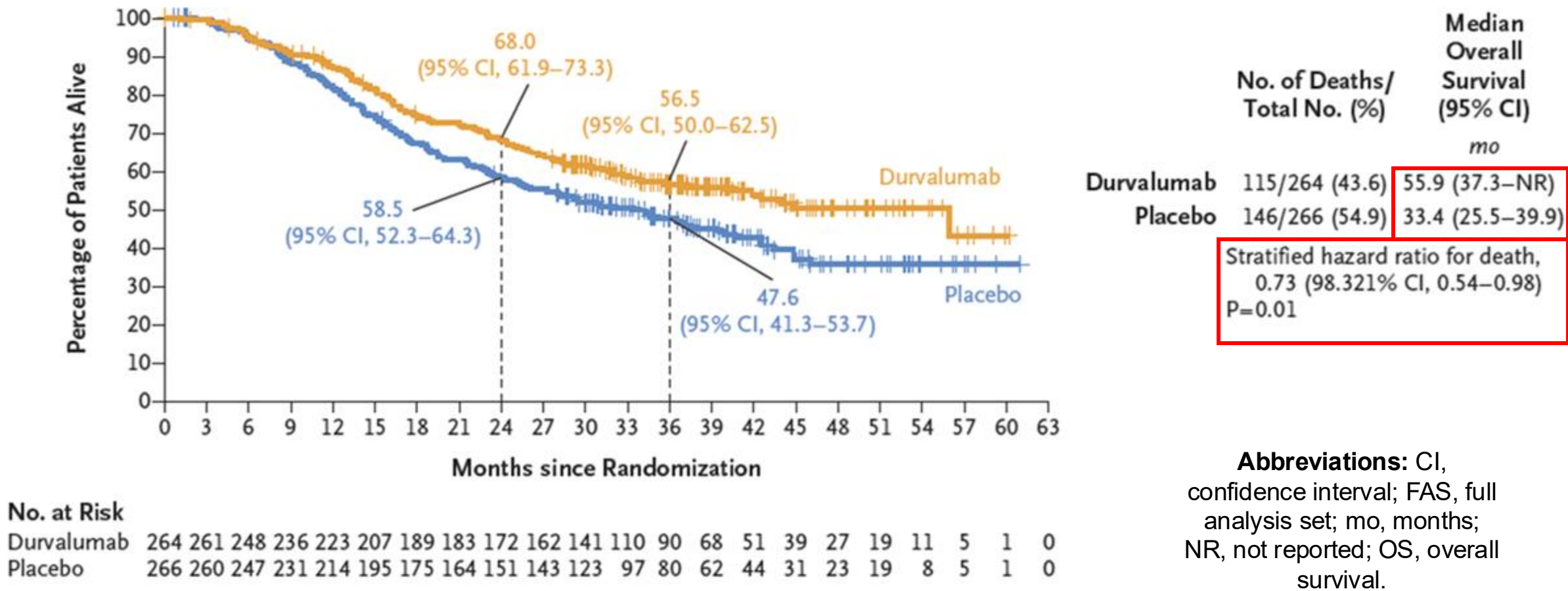
Intervention
being
appraised

EAG: People in the trial received tumour assessments at specified intervals. The EAG considers that this adequately represents active monitoring.

ADRIATIC results – overall survival

There was a statistically significant reduction in the risk of death with durvalumab compared to placebo (hazard ratio: 0.73; 98% CI 0.54 to 0.98)

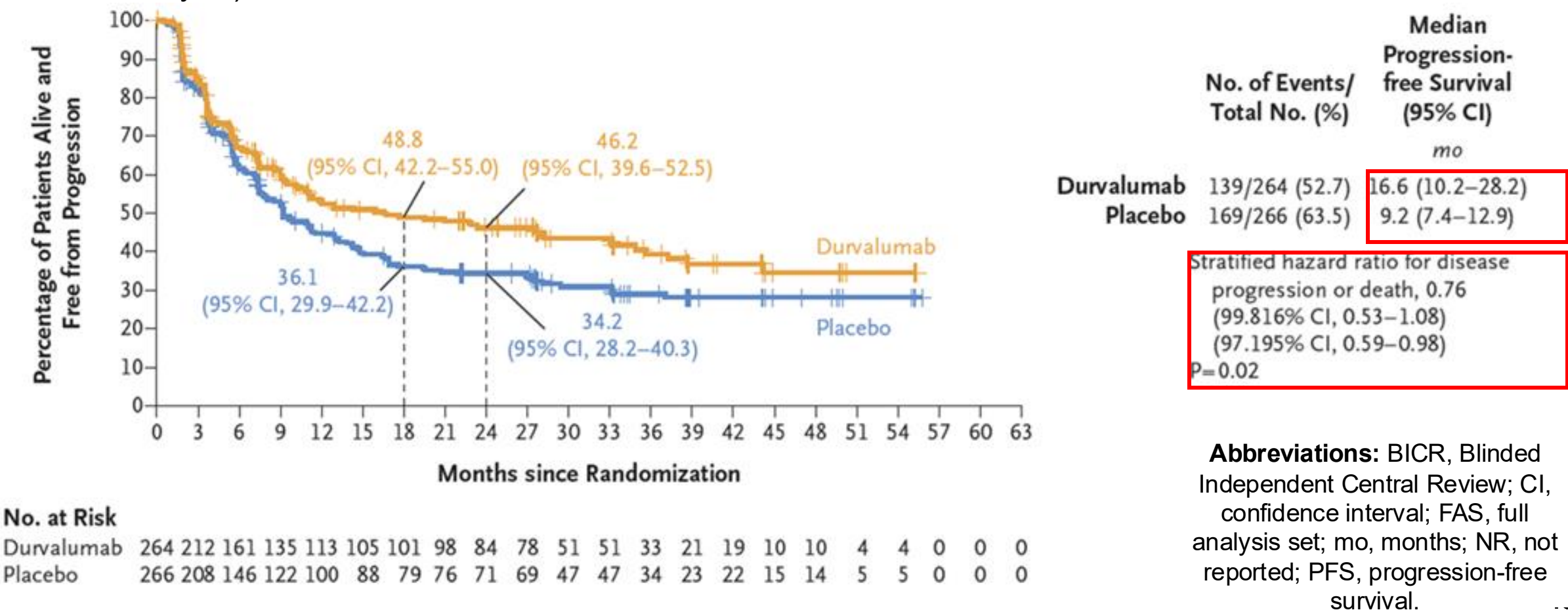
Figure: Kaplan-Meier plot of OS results (FAS population, first interim analysis)



ADRIATIC results – progression-free survival

There was a statistically significant reduction in the risk of progression or death with durvalumab compared to placebo (hazard ratio: 0.76; 97% CI 0.59 to 0.98)

Figure: Kaplan-Meier plot of PFS as assessed by BICR (FAS population, first interim analysis)



Key issue: Generalisability of trial data

Background

- Population in [final scope](#) and marketing authorisation is people with LS-SCLC whose disease has not progressed after CRT
- This includes people who have had concurrent chemotherapy and radiotherapy (cCRT) and sequential chemotherapy and radiotherapy (sCRT)

EAG comments

- No evidence was provided for people whose disease has not progressed after sCRT
- [ADRIATIC trial](#) only included people who had cCRT, people who had sCRT were excluded
- People who have had sCRT are typically less fit and have an ECOG status greater than 1
- It is plausible that people who have previously had sCRT may not benefit as much from treatment, therefore reducing cost-effectiveness
- Highlighted previous appraisals where committee restricted recommendations in line with trial data:
 - In [TA798](#) (durvalumab for NSCLC) – recommendation was restricted to previous cCRT
 - In [TA638](#) (atezolizumab for extensive-stage SCLC) – recommendation restricted to ECOG status 0-1

Key issue: Generalisability of trial data

Company

- Expect people who have had sCRT would still benefit from durvalumab
- Provided data from PACIFIC-6 and PACIFIC-R trials in NSCLC (see [Appendix](#))
- Results from these trials could be extrapolated to support use of durvalumab in SCLC after sCRT

EAG clinical experts

- Results from studies in NSCLC are not considered generalisable to people with SCLC whose disease has not progressed after sCRT
- However, it may be reasonable to assume that people who have had sCRT might still benefit from durvalumab maintenance
- Noted that the population who have sCRT is likely to be small, as most people are expected to have cCRT

Clinical expert statements

- Both experts agreed that most people having CRT for LS-SCLC have cCRT as opposed to sCRT
 - One expert stated that in their institution, 80 to 90% have cCRT, but this may differ in other institutions
- Neither expert aware of any data for adjuvant durvalumab following sCRT
 - In the absence of data suggesting otherwise, experts consider results of ADRIATIC generalisable to the sCRT population

Key issue: Generalisability of trial data

- 
- Are results from ADRIATIC generalisable to people whose disease has not progressed after sCRT? Or should any recommendation be restricted to people whose disease has not progressed after cCRT?
 - ADRIATIC only included people with ECOG status 0 and 1 – is a restriction to the population according to ECOG status appropriate (as per TA638 and TA1041)?
 - Would restricting the recommendation result in any equalities issues?

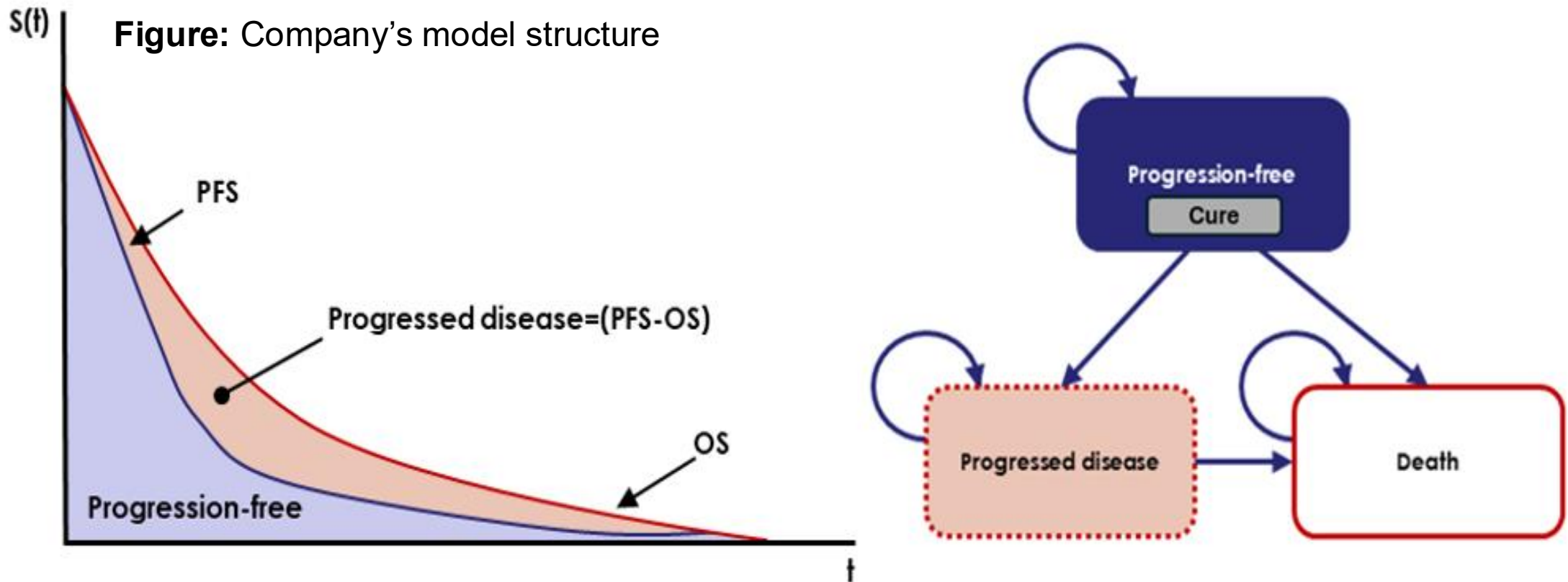
Abbreviations: cCRT, concurrent chemoradiotherapy; ECOG, Eastern Cooperative Oncology Group; ICER, incremental cost-effectiveness ratio; sCRT, sequential chemoradiotherapy.

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Company's model overview

Partitioned survival model with three health states: progression-free, progressed disease, and death



EAG: The three-state partitioned survival model structure is appropriate. It follows the same structure as that used in the previous NICE technology appraisals for lung cancer. The EAG identified no deviations from the reference case.

Key issue: Extrapolation of OS and PFS (and cure assumption)

Company

- Fit a range of standard parametric and spline-based curves to OS and PFS data from ADRIATIC
- Curve selection based on goodness of fit statistics, visual fit to Kaplan–Meier (KM) plots, assessment of hazard function, and (for OS only) a comparison with published literature cohorts. Selected curves:
 - OS – **2-knot spline normal**; PFS – **1-knot spline normal**
- Spline models selected as they accommodate the complex hazard functions seen in ADRIATIC
- Proportional hazards assumed not to hold – models fit independently for each arm (however, same curve was used for both arms)
- PFS capped to ensure it did not exceed OS
- Cure fraction of 90% applied to people who were progression-free at 5 years in both treatment arms

EAG comments

- Alternative models provide a better statistical fit to KM data (see [Appendix](#)). EAG's selected curves:
 - OS – **1-knot spline hazard**; PFS – **generalised gamma**
- Preferred not to apply a cure assumption as this may overestimate survival
 - Spline models already accommodate complex hazard functions
 - People whose SCLC does not relapse within 5 years may still have long-term toxicities due to radiotherapy
- Using EAG's preferred assumptions for PFS curve and cure assumption does not significantly impact the ICER, but OS assumption has a moderate impact – alternative scenarios for all assumptions provided

Key issue: Extrapolation of OS and PFS (and cure assumption)

Figure 1: Company base case

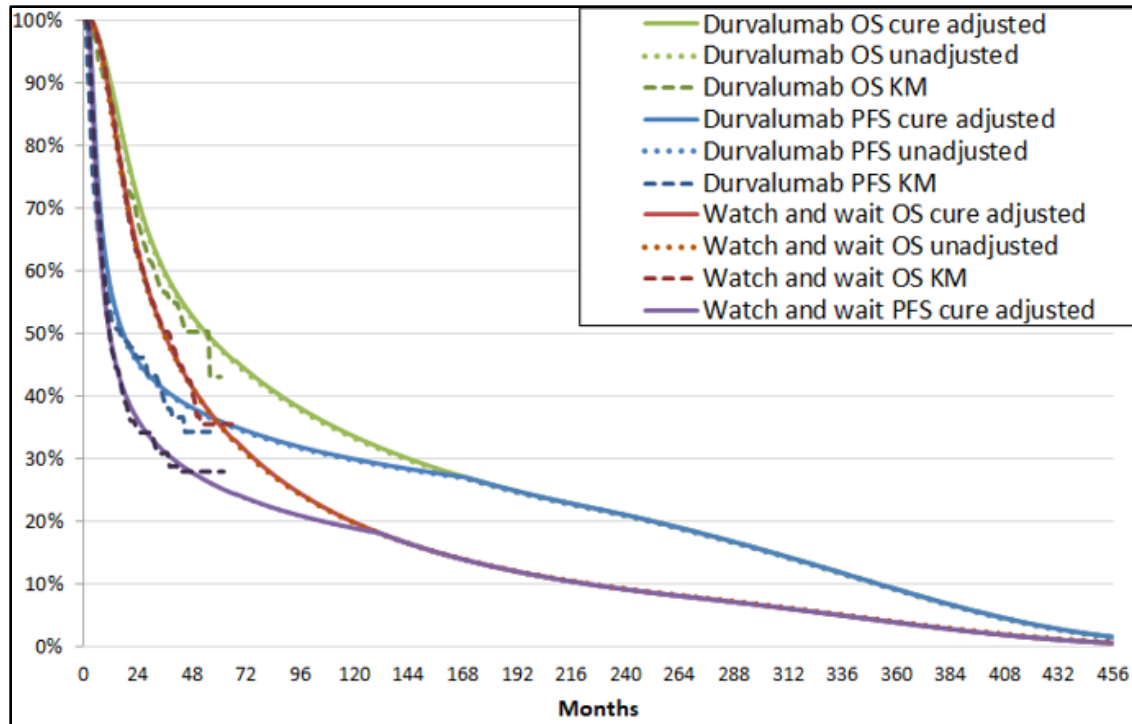
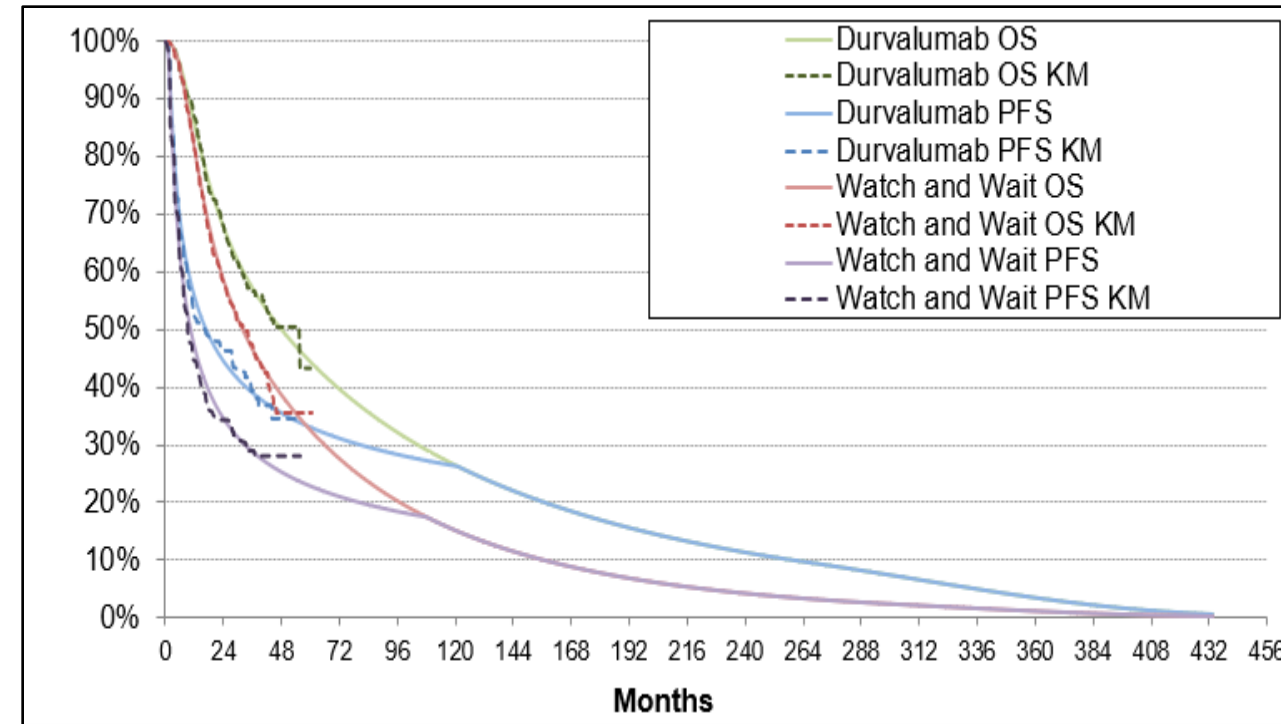


Figure 2: EAG base case



Note: A cure assumption is included in company's base case. The graph above shows the extrapolations with and without the cure assumption (solid and dotted curves). Note that the cure assumption does not have a significant impact on the extrapolations.

Key issue: Extrapolation of OS – company versus EAG base case with external validation from literature cohorts

	1 year	2 years	5 years	10 years	20 years
Walls 2024 (CONVERT*)	77%-82%	52%-57%	32%-34%	23.0%	-
Bogart 2023 (CALGB 3061*)	78%-82%	56%-58%	29%-32%	-	-
Watch and wait OS KM	81.9%	58.5%	35.7%	-	-
Watch and wait OS company base case	81.5%	58.7%	33.1%	18.1%	8.3%
Watch and wait OS EAG base case	81.5%	58.7%	32.6%	15.2%	4.2%
Durvalumab OS KM	87.3%	68.0%	43.1%	-	-
Durvalumab OS company base case	86.3%	67.5%	45.8%	31.7%	19.3%
Durvalumab OS EAG base case	85.7%	67.9%	44.5%	26.6%	11.4%

Note: *CONVERT and CALGB 3061 are trials of concurrent chemoradiotherapy in people with LS-SCLC

Company assumption: 2-knot spline normal

EAG assumption: 1-knot spline hazard (better AIC / BIC ranking)

Key issue: Extrapolation of PFS – company versus EAG base case with external validation from literature cohorts

	1 year	2 years	5 years	10 years	20 years
Walls 2024 (CONVERT*)	55%-59%	37%-39%	28%-30%	19%-24%	-
Bogart 2023 (CALGB 3061*)	54%-54%	36%-36%	24%-25%	-	-
Watch and wait PFS KM	44.6%	34.2%	-	-	-
Watch and wait PFS company base case	45.1%	34.5%	24.5%	18.1%	8.3%
Watch and wait PFS EAG base case	47.1%	34.6%	22.8%	15.2%	4.2%
Durvalumab PFS KM	53.1%	46.2%	-	-	-
Durvalumab PFS company base case	53.6%	44.0%	35.2%	29.2%	19.3%
Durvalumab PFS EAG base case	55.8%	44.6%	33.1%	26.4%	11.4%

Note: *CONVERT and CALGB 3061 are trials of concurrent chemoradiotherapy in people with LS-SCLC

Company assumption: 1-knot spline normal

EAG assumption: generalised gamma (better AIC / BIC ranking)

Key issue: Extrapolation of OS and PFS (and cure assumption)

Clinical experts:

- **Expert 1:** *“I would consider a patient cured from LS-SCLC if they had reached 5 years without relapse. It might also be possible to conclude that, if a patient has reached 4 years without relapse, they are probably cured.”*
- **Expert 2:** *“We normally say that if patients survive for more than 5 years after their initial treatment, it is rare for the cancer to come back, although in my experience I have seen a proportion of patients whose cancer comes back after 5 years.”*

- 
- For **OS**, which extrapolation is appropriate (company's **2-knot spline normal** model, EAG's **1-knot spline hazard** model, or another scenario)?
 - For **PFS**, which extrapolation is appropriate (company's **1-knot spline normal** model, EAG's **generalised gamma** model or another scenario)?
 - Should a cure fraction of 90% for people who are progression-free at 5 years in both treatment arms be applied? Is another cure fraction % or time point appropriate?

Key issue: Treatment effect waning

Company

- As per the marketing authorisation, durvalumab can be used for a maximum of 2 years
- No treatment effect waning applied in company base case – no clinical evidence for this

EAG comments

- There is uncertainty over the company's assumption of no treatment effect waning due to:
 - appraisal committee's conclusions in other appraisals – **presented later in slide deck**
 - the median OS follow-up of durvalumab in the ADRIATIC trial (30.75 months) which may not be long enough to ascertain that there was no treatment effect waning
- In its original report, the EAG implemented treatment effect waning scenarios by assuming durvalumab OS and PFS was equal to 'watch and wait' OS and PFS (equalising curves) – **presented in [Appendix](#)**
- Prior to committee meeting, the EAG provided additional scenarios implementing treatment effect waning by equalising the hazards rather than curves at the following time points:
 - 5 years after starting treatment
 - gradually between 3 and 5 years after starting treatment
- The EAG consider that the updated approach (equalising hazards) results in extrapolations that are more plausible than the EAG's original approach (equalising curves)
- Details of the EAG's preferred approach are **presented on next 2 slides**

Key issue: Treatment effect waning scenarios – equalising hazards

Figure 1: Company base case with EAG scenario using updated approach equalising hazards 5 years after starting treatment

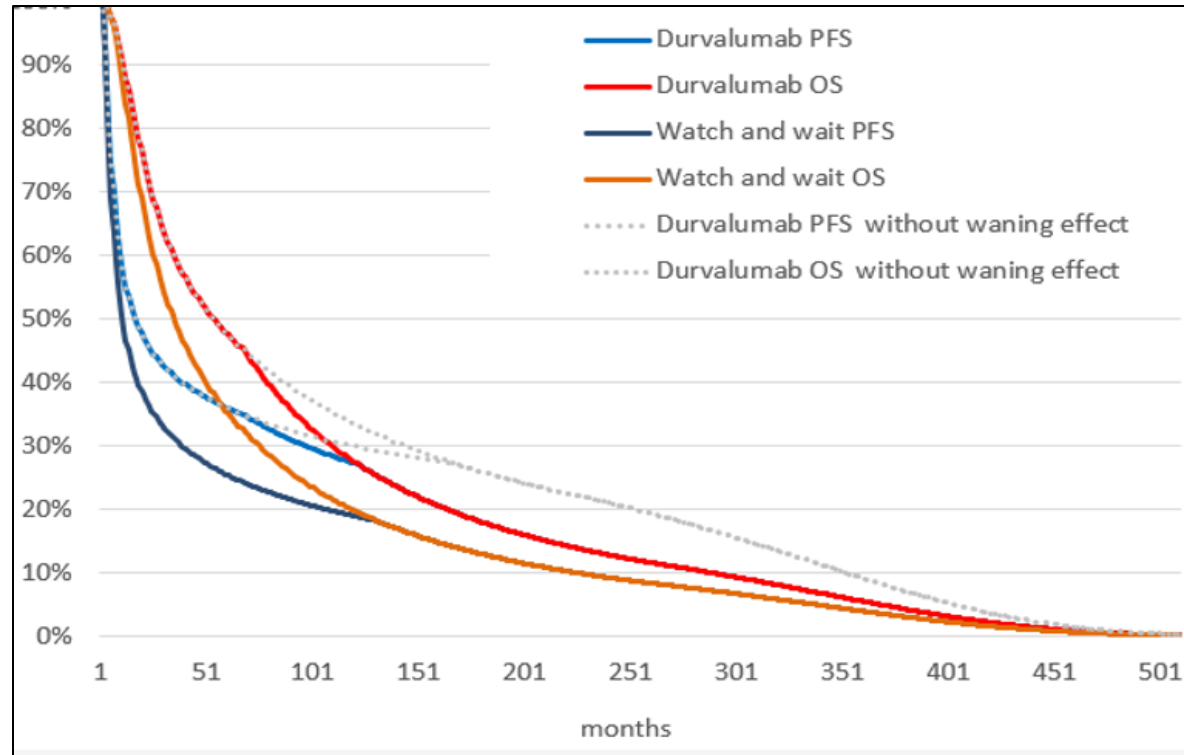
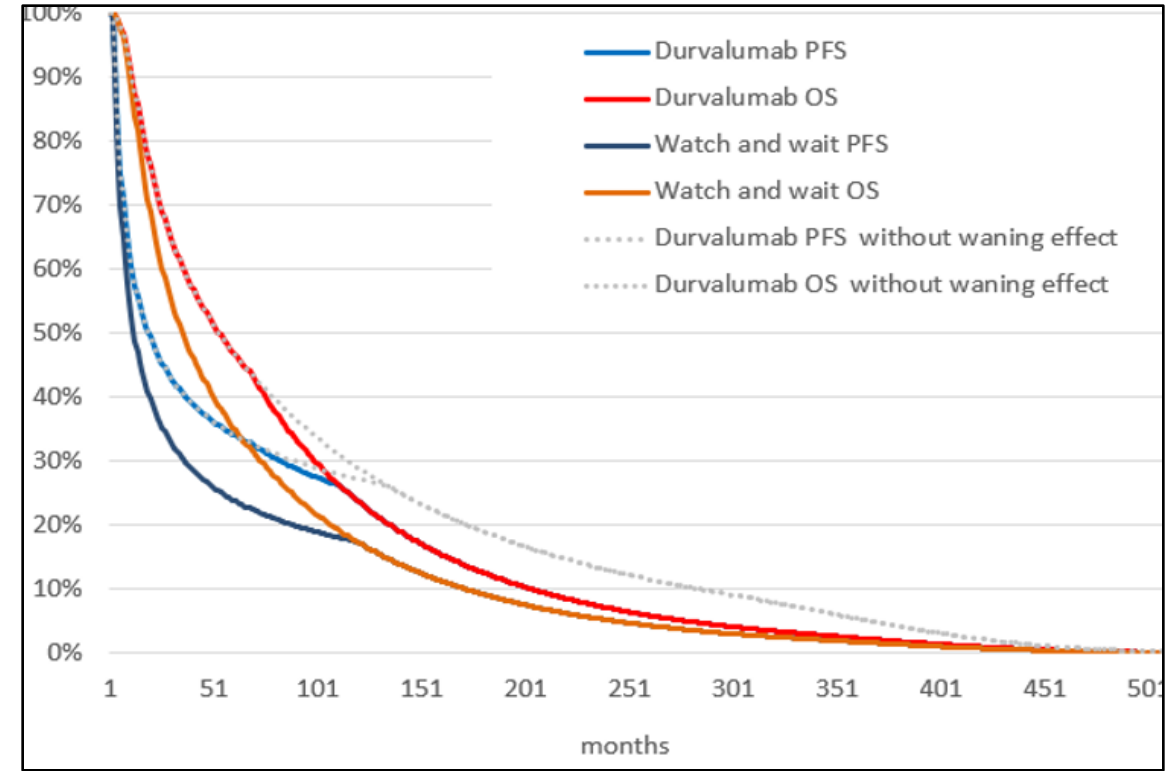


Figure 2: EAG base case with EAG scenario using updated approach equalising hazards 5 years after starting treatment



Key issue: Equalising hazards – corresponding survival estimates

	Curves	Year 1	Year 2	Year 5	Year 10	Year 20
Company base case	Durvalumab OS	86.3%	67.5%	45.8%	31.8%	19.3%
	Watch and wait OS	81.5%	58.7%	33.1%	18.2%	8.3%
	Durvalumab PFS	53.6%	44.0%	35.2%	29.2%	19.3%
	Watch and wait PFS	45.1%	34.5%	24.5%	18.2%	8.3%
+ Treatment effect capped at 60 months	Durvalumab OS	86.3%	67.5%	45.8%	25.3%	11.6%
	Watch and wait OS	81.5%	58.7%	33.1%	18.2%	8.3%
	Durvalumab PFS	53.6%	44.0%	35.2%	25.3%	11.6%
	Watch and wait PFS	45.1%	34.5%	24.5%	18.2%	8.3%
EAG base case	Durvalumab OS	85.7%	67.9%	44.5%	26.7%	11.4%
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	Watch and wait PFS	47.1%	34.6%	22.8%	15.3%	4.2%

By year 10, PFS has been capped by OS; durvalumab OS remains higher than W&W OS

Abbreviations: ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression-free survival; W&W, watch and wait.

Key issue: Treatment effect waning

Table 1: Rationale for including/excluding treatment effect waning in previous technology appraisals

TA	Details	Committee conclusion on treatment effect waning	Rationale
TA184	Topotecan, relapsed SCLC	Not included but not discussed	N/A
TA638	Atezolizumab, extensive-stage SCLC	Committee uncertain about the duration of treatment benefit but 5-year treatment effect scenario considered	Small impact on ICER, not important for decision making. Clinical experts expected less than 1% to be alive at 5 years (later stage disease than this indication)
TA798	Durvalumab NSCLC	Yes – appropriate to consider both 3- and 5-year waning (after starting treatment)	Survival extrapolations only plausible when treatment effect waning applied. <i>(Note that if the curves take into account treatment-effect waning, then may not need to apply separately)</i>
TA1041	Durvalumab, extensive-stage SCLC	Not discussed (cost comparison)	N/A

Key issue: Treatment effect waning

Clinical experts:

- How long would the treatment effect of durvalumab be expected to continue for after stopping treatment?
 - **Expert 1:** *“I am not able to give an accurate estimate of this. It is likely measured in weeks, perhaps up to 2-3 months, but there is no data to reliably inform on a more precise answer.”*
 - **Expert 2:** *“This differs for patients, but certainly in the patients with limited NSCLC, we are seeing the effect persist for years and that may well be the case for this patient group as well.”*

Does the chosen extrapolation implicitly take into account treatment effect waning?

Should treatment effect waning apply? If so:



Are committee satisfied with the EAG's updated approach to exploring treatment effect waning (i.e. equalising hazards rather than curves)?

At what time point after starting treatment should this apply?

Key issue: Resource use – progression free

Background

- Company's resource use was taken from TA798 which is based on the PACIFIC trial data (NSCLC)
- EAG made some adjustments based on clinical expert opinion

Table: Progression-free resource use per year – company vs EAG

Item	Company (TA798)			EAG clinical experts		
	Durv on tx	Durv off tx	w&w	Durv on tx	Durv off tx	w&w
Outpatient oncologist visit: Y1	0	5	5	12	4-6	5
Outpatient oncologist visit: Y2	0	3	3	12	4-6	3
Outpatient oncologist visit: Y3–5	0	2	2	0	2	2
Chest X-ray: Y1	0	2	2	0	0	0
Chest X-ray: Y2	0	0	0	0	0	0
Chest X-ray: Y3–5	0	2	2	0	0	0
CT scan (chest): Y1	6	3	3	4	4	3
CT scan (chest): Y2	6	3	3	4	4	3
CT scan (chest): Y3–5	6	0	0	1	1	1
Blood tests	24	0	0	12	4	0
Cost – year 1	£84	£122	£122	£238	£115	£116
Cost – year 2	£84	£122	£122	£238	£115	£85
Cost – year 3-5	£84	£37	£37	£16	£45	£44

EAG: Assumed more frequent outpatient oncologist visits than the company, particularly whilst on durvalumab treatment

EAG: Most centres use CT scans not chest x-rays

EAG: Assumed different frequencies of CT scans and blood tests to company

Abbreviations: CT, Computed Tomography; durv, durvalumab; ICER, incremental cost-effectiveness ratio; NSCLC, non-small-cell lung cancer; tx, treatment; w&w, watch and wait.

Note: Dark grey shading shows differences between company's and EAG's assumptions.

Key issue: Resource use – progressed

Table: Progressed resource use per year – company vs EAG

Cost Item	Resource per year	
	Company (TA798)	EAG clinical experts
Outpatient oncologist visit	9.61	9-12
Chest X-ray	6.79	0
CT scan (chest)	0.62	6.79
CT scan (other)*	0.36	6.79
ECG	1.04	1.04
Community nurse visit	8.70	8.70
Clinical nurse specialist	12.00	12.00
GP surgery	12.00	12.00
Blood test	0.00	9-12
Cost per year	£373	£511

EAG: Most centres use CT scans not chest x-rays

EAG: Assumed more blood tests than company

Note: Dark grey shading shows differences between company's and EAG's assumptions.



Do committee prefer the company or EAG's estimates of resource use?

Summary of company and EAG base case assumptions

Assumption	Company base case	EAG base case
OS distribution for both arms	2-knot spline normal	1-knot spline hazard – alternative scenarios provided
PFS distribution for both arms	1-knot spline normal	Generalised gamma – alternative scenarios provided
Cure assumption	Yes – 90% cure fraction at 5 years	No – alternative scenarios provided assuming a range of cure fractions and time points
Resource use	TA798 / PACIFIC trial data (NSCLC)	Clinical advice to EAG
Subsequent treatment	ADRIATIC trial + advisory board	ADRIATIC trial only – alternative scenario provided based on clinical advice to EAG
Treatment effect waning	No	No – alternative scenarios provided

Cost-effectiveness results

All ICERs are reported in PART 2 slides
because they include confidential
PAS discounts for subsequent therapies

When the company and EAG base case ICERs are calculated using confidential prices, the company base case is between £20,000 and £30,000 per QALY gained and the EAG base case is above £30,000 per QALY gained

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Other considerations

Managed access

- The committee can make a recommendation with managed access if:
 - the technology cannot be recommended for use because the evidence is too uncertain
 - the technology has the plausible potential to be cost effective at the currently agreed price
 - new evidence that could sufficiently support the case for recommendation is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
 - data could feasibly be collected within a reasonable timeframe (up to a maximum of 5 years) without undue burden.
- The company has not submitted a managed access proposal

Severity modifier

- No QALY weighting for severity applies

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	Small (PFS)
	Small (cure assumption)
Treatment effect waning	Large
Resource use	Moderate
Other issues (see Appendix)	ICER impact
Subsequent treatment	Small