NICE National Institute for Health and Care Excellence

NICE guidance

Durvalumab for treating limited-stage small-cell lung cancer after platinum-based chemoradiotherapy

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendation

1.1 Durvalumab can be used, within its marketing authorisation, as an option to treat limited-stage small-cell lung cancer that has not progressed after platinum-based chemoradiotherapy in adults. Durvalumab can only be used if the company provides it according to the commercial arrangement.

What this means in practice

Durvalumab must be funded in the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. Durvalumab must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that durvalumab provides benefits and value for money, so it can be used routinely across the NHS in this population.

NICE has also produced tools and resources to support the implementation of this guidance.

Why the committee made this recommendation

Usual treatment for limited-stage small-cell lung cancer that has not progressed after platinum-based chemoradiotherapy is active monitoring (regular outpatient appointments and scans).

Clinical trial evidence shows that durvalumab increases how long people have before their condition gets worse and how long they live compared with active monitoring.

The cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. So, durvalumab can be used.

2 Information about durvalumab

Marketing authorisation indication

2.1 Durvalumab (Imfinzi, AstraZeneca) is indicated as monotherapy for 'the treatment of adults with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following platinum-based chemoradiation therapy.'

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for durvalumab.

Price

2.3 The list price is £592 for a 120-mg vial and £2,466 for a 500-mg vial (excluding VAT; BNF online accessed June 2025).

2.4 The company has a commercial arrangement. This makes durvalumab available to the NHS with a discount. The size of the discount is commercial in confidence.

Carbon Reduction Plan

2.5 For information, the Carbon Reduction Plan for UK carbon emissions is published on AstraZeneca's webpage on sustainability.

3 Committee discussion

The evaluation committee considered evidence submitted by AstraZeneca, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of condition

3.1 Small-cell lung cancer (SCLC) is an aggressive type of lung cancer that grows rapidly and spreads quickly to other areas of the body. In most people diagnosed with SCLC, the cancer has already spread (metastasised). But in about 30% of people, the cancer is contained in a single area that can be treated with radiotherapy. This is known as limited-stage SCLC (LS-SCLC). The patient organisation's submission explained that a diagnosis of SCLC is devastating. People are often symptomatic at presentation and symptoms such as breathlessness, coughing up blood, hoarseness, chest pain and weight loss are distressing for both people with SCLC and their families. The patient organisation explained that SCLC is a rapidly progressing disease with a poor prognosis. The professional organisations' submissions explained there have been limited advances in the treatment of LS-SCLC for over 20 years, and there are no maintenance treatments available after chemotherapy and radiotherapy. People with the condition and healthcare professionals would welcome more options early in the treatment pathway because of the poor prognosis. The committee agreed there is an unmet need for new and effective treatments for LS-SCLC, particularly earlier in the treatment pathway.

Clinical management

Treatment pathway

3.2 NICE's guideline on diagnosis and management of lung cancer provides

recommendations for the first-line treatment of LS-SCLC. These include 4 to 6 cycles of platinum-based combination chemotherapy alongside radiotherapy, known as concurrent chemoradiotherapy (cCRT). People who are too unwell to have cCRT may have radiotherapy after chemotherapy, known as sequential chemoradiotherapy (sCRT). Surgery may also be an option for some people with early (stage 1 to 2) SCLC, but surgery is not possible for most people with LS-SCLC. Prophylactic cranial irradiation (radiotherapy to prevent or reduce the risk of cancer cells spreading to the brain) may also be used after chemotherapy and radiotherapy. After first-line treatments, people are actively monitored for cancer recurrence. This involves outpatient appointments and regular imaging (scans). Durvalumab is positioned as an addition to active monitoring when the cancer has not progressed after platinum-based chemoradiotherapy. So, the comparator is active monitoring alone. If the cancer recurs after first-line treatment, second-line treatment options include further treatment with a chemotherapy regimen, with or without an immunotherapy such as atezolizumab (see NICE's technology appraisal guidance on atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer) or durvalumab (see NICE's technology appraisal guidance on durvalumab with etoposide and either carboplatin or cisplatin for untreated extensive-stage small-cell lung cancer). Palliative radiotherapy may also be offered.

Clinical effectiveness

Data sources

3.3 The clinical evidence for durvalumab in LS-SCLC came from ADRIATIC, a double-blind, phase 3, placebo-controlled trial. ADRIATIC compared durvalumab monotherapy and placebo in people with stage 1 to 3 LS-SCLC who had had 4 cycles of first-line cCRT without disease progression and had an Eastern Cooperative Oncology Group status of 0 or 1. At the January 2024 data cut-off, median overall survival was 55.9 months for durvalumab and 33.4 months for placebo (stratified hazard ratio [HR] 0.73, 98% confidence interval [CI] 0.54 to 0.98). Median progression-free survival was 16.6 months for durvalumab and 9.2 months for placebo (stratified HR 0.76, 97% CI 0.59 to 0.98). The EAG noted that all people in the trial had tumour assessments at specified intervals and

considered that this adequately represented active monitoring. The EAG's clinical experts advised that the improvement in median overall survival seen with durvalumab is clinically meaningful. The committee concluded that the trial data showed that durvalumab improves overall and progression-free survival compared with placebo.

Generalisability

3.4 The population in NICE's final scope and the marketing authorisation is people with LS-SCLC that has not progressed after chemoradiotherapy. This includes people who have had either cCRT or sCRT. The EAG noted that no evidence was provided by the company for SCLC that has not progressed after sCRT because ADRIATIC only included people who had cCRT. The EAG noted that people who have had sCRT may not benefit as much from treatment because they have a larger disease burden. But one of the clinical experts at the committee meeting explained that ADRIATIC is broadly representative of people with LS-SCLC who would be seen in clinical practice, because very few people have sCRT for LS-SCLC. This is because LS-SCLC is a rare diagnosis, and most centres offer cCRT rather than sCRT. So, the clinical expert advised it is reasonable to extrapolate results of ADRIATIC to people who have had sCRT. They explained there is no biological rationale to suggest that people with sCRT would not also benefit from treatment with durvalumab. The committee concluded that ADRIATIC is broadly generalisable to people expected to have durvalumab in clinical practice.

Economic model

Company's modelling approach

3.5 The company's economic model was a partitioned survival model with 3 health states: progression-free, progressed disease and death. Health state occupancy over time was informed directly by ADRIATIC overall survival and progression-free survival extrapolations (see section 3.6). All people entered the model in the progression-free health state, and could transition to progressed disease or

death. Patients in the progressed-disease health state were also at risk of transitioning to death. The EAG advised that the company's model structure is appropriate and follows the same structure used in previous NICE technology appraisals for lung cancer treatments. The committee agreed the company's model was acceptable for decision making and the modelling and analyses had been done to a good standard.

Survival extrapolations

3.6 The company fit a range of standard parametric and spline models to survival data from ADRIATIC. The company explained that spline models were selected because they accommodated the complex hazard functions seen in the ADRIATIC data. The company selected the 2-knot spline normal model for extrapolation of overall survival, and the 1-knot spline normal model for progression-free survival. The same model was selected for both treatment arms, but models were fit independently for each arm because the proportional hazards assumption was not assumed to hold. The company also applied a cure fraction of 90% to people who were progression-free 5 years after starting treatment in both arms. The EAG noted that alternative models provided a better statistical fit to data from ADRIATIC. The EAG preferred to use the 1-knot spline hazard model for overall survival, and the generalised gamma model for progression-free survival. The EAG preferred not to apply a cure fraction separately, because it noted that its spline model already accommodated the complex hazard function seen in the trial data. It also noted that people whose cancer does not relapse after 5 years may still have long-term toxicity from radiotherapy. The clinical experts explained that after 5 years without progression the chance of the cancer coming back is very low, but it can in rare cases. The committee noted that most people having durvalumab for LS-SCLC would not have had surgical resection, and durvalumab would be used as a maintenance treatment. So, most people would still be living with cancer after initial treatment. The clinical experts considered the 10-year survival estimates from the EAG's and company's extrapolations and advised that both are plausible, but uncertain. The committee noted that the choice of progression-free survival curve had minimal impact on the incremental cost-effectiveness ratio (ICER), but choice of overall-survival curve did have an impact. Removing the cure fraction had minimal impact on the ICER. Although both the company's and EAG's extrapolations for overall survival were plausible,

the EAG's extrapolation for durvalumab appeared to be a better visual fit to the Kaplan–Meier data. As with the treatment effect waning assumption (see section 3.7), the committee agreed that the EAG's extrapolations were able to capture the hazards at the end of observed follow-up period without the need for any further adjustments. So, the committee preferred the EAG's base case that used the 1-knot spline hazard model for overall survival and the generalised gamma model for progression-free survival, without a cure assumption applied.

Treatment effect waning

3.7 According to the marketing authorisation, durvalumab should be stopped on disease progression, unacceptable toxicity or after 24 months (2 years). The company's model did not include treatment effect waning. The company stated there was no evidence to support this. The EAG noted that the median overall survival follow-up period in ADRIATIC for durvalumab (30.75 months) may not have been long enough to rule out treatment effect waning, which may occur far beyond the end of trial follow up. So, the EAG explored several scenarios to explore the impact of including treatment effect waning. It explained that the most plausible of these involved equalising the hazards in both arms. It presented scenarios equalising the hazards between arms immediately at 5 years after starting treatment and gradually between 3 and 5 years after starting treatment. The EAG explained that although there is no evidence for treatment effect waning there is uncertainty about the biological plausibility that after treatment is stopped, it still has an impact on the disease. The clinical experts explained that immunotherapies can have a sustained benefit, which continues for some time after stopping treatment. They explained the difficulties in predicting survival at 10 or 20 years, including how treatment effect waning may influence these estimates. The committee noted that applying treatment effect waning had a large impact on the ICER particularly in the EAG's base case, which applied waning to the full cohort because a cure assumption was not applied. The committee agreed that the decision to apply treatment effect waning should be based on evidence specific to this evaluation, including the follow-up data available and the selected survival extrapolations. The committee decided that, given the fixed treatment duration of 2 years, the overall-survival follow-up duration in ADRIATIC was sufficient despite the EAG's concerns. It noted that the trial data already appeared to capture some increase in hazards after people

stopped treatment at 2 years and that spline models were flexible enough to capture the trajectory of the observed data. The committee agreed that some people have durable responses to immunotherapies that are maintained after treatment is stopped. It noted that this can be seen more clearly when immunotherapies are used in early-stage cancers. Rates of relapse may increase after durvalumab is stopped, but the extent to which this occurs should already be captured in the observed data and the survival extrapolations. So, the committee concluded that it preferred to use the available data and not apply an additional adjustment for treatment effect waning.

Costs

Resource use

3.8 The company's estimates for resource use were taken from NICE's technology appraisal guidance on durvalumab for maintenance treatment of unresectable non-small-cell lung cancer after platinum-based chemoradiation. This was based on data from the PACIFIC trial. The EAG made the following adjustments to the company's estimates based on clinical expert opinion:

- including outpatient oncologist visits during durvalumab treatment
- including CT scans instead of chest X-rays
- assuming a higher number of blood tests for people with progressed disease.

The total resource-use cost per year in the EAG's base case was higher than in the company's base case, mainly driven by the frequency of outpatient visits. During the committee meeting, the company explained it had not included costs for outpatient visits during durvalumab treatment because it considered this to be double counting. The company assumed that the cost for these visits would be captured by the administration costs already applied. The clinical experts explained that people having durvalumab would see an oncologist separately to having durvalumab administered, so the cost of oncologist visits should be included in addition to the cost of administration. They also explained that CT scans rather than chest X-rays

would be used, because chest X-rays are not used for ongoing monitoring. They advised that monitoring after progression was more likely to be in line with the EAG's higher estimates because people may go on to have subsequent treatments. The committee concluded that the EAG's estimates of resource use were more aligned with expected resource use in clinical practice.

Subsequent treatment

3.9 The company's model only included the costs for subsequent (second-line) treatments. The company stated this was because the effects were already captured by post-progression survival data from ADRIATIC. The types and proportions of subsequent treatments in the company's base case were based on ADRIATIC data, adjusted based on clinical expert input at an advisory board. The EAG's clinical experts advised that subsequent treatment choice depends on how quickly the cancer relapses. The EAG explored estimates based on clinical expert opinion as a scenario. But in its base case, the EAG preferred to use unadjusted subsequent treatment data from ADRIATIC to align costs and effects. The committee noted the very small impact of this on the cost-effectiveness estimates and agreed that the EAG's preferred approach of aligning costs and effects was appropriate.

Cost-effectiveness estimates

3.10 Because of confidential discounts for durvalumab and subsequent treatments the exact ICERs are confidential and cannot be reported here. The committee's preferred assumptions aligned with the EAG's base case and included:

- estimating overall survival using the 1-knot spline hazard extrapolation (see section 3.6)
- estimating progression-free survival using the generalised gamma extrapolation (see section 3.6)
- no cure assumption (see section 3.6)

- no treatment effect waning (see section 3.7)
- resource use based on the EAG's clinical experts' estimates (see section 3.8)
- unadjusted subsequent treatments as used in ADRIATIC (see section 3.9).

Acceptable ICER

3.11 NICE's manual on health technology evaluations notes that, above a most plausible ICER of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits.

The committee considered that, if approved, durvalumab would be the first treatment available in this indication and address an unmet need. It noted that the consequences of decision error if durvalumab was recommended were low, based on the small number of people expected to be eligible for treatment in clinical practice. It also noted that the length of follow up in the trial reduces the uncertainty about the duration of treatment benefit after stopping durvalumab, but the size and duration of the long-term benefits are still uncertain. So, the committee concluded that an acceptable ICER would be around or slightly above the middle of the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

Other factors

Equality

3.12 The committee did not identify any equality issues that may arise from its recommendation.

Uncaptured benefits

3.13 The committee considered whether there were any uncaptured benefits of durvalumab. It did not identify additional benefits not captured in the economic modelling. So, the committee concluded that all additional benefits of durvalumab had already been taken into account.

Conclusion

3.14 Clinical trial evidence shows that durvalumab increases how long people have before their condition gets worse and how long people live compared with active monitoring. The cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. So, durvalumab can be used.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has limited-stage small-cell lung cancer and the healthcare professional responsible for their care thinks that durvalumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Megan John
Chair, technology appraisal committee D

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Anna Willis
Technical lead

Albany Chandler
Technical adviser

Kate Moore

Project manager

Ross Dent
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