Managed Access Agreement

Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection [ID3835]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection [ID3835]

Company name: AstraZeneca UK Limited

Primary source of data collection: Ongoing clinical study - ADAURA

Secondary source of data collection: NHS Digital routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy data set

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AstraZeneca Agreement Manager	Carla Fisher, Market Access Team Lead

1 Purpose of data collection arrangement

1.1 The purpose of the agreement is to describe the arrangements and responsibilities for further data collection for osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (ID3835) (to be updated with TA number after final guidance has been published). A positive recommendation within the context of a managed access agreement (MAA) has been decided by the appraisal committee.

2 Commencement and period of agreement

2.1 This data collection arrangement shall take effect on publication of the managed access agreement.

2.2 Estimated dates for data collection, reporting and submission for CDF guidance review are:

End of data collection (primary source)	H1 2023
Data available for development of company submission	Q3 2023
Anticipated company submission to NICE for Cancer Drugs Fund review	January 2024

2.3 AstraZeneca anticipate the results from the additional data collected during the Cancer Drugs Fund period will be incorporated into an evidence submission and the updated economic model by January 2024.

2.4 AstraZeneca acknowledge their responsibility to adhere as closely as possible to the timelines presented in this document.

2.5 NICE will, as far as is practicable, schedule a Cancer Drugs Fund review into the technology appraisal work programme to align with the estimated dates for the end of data collection. The review will use the process and methods in place at the time the invitation to participate in the guidance review is issued, which will be no earlier than 4 weeks prior to the anticipated company submission date. For further details of the expected timelines for the Cancer Drugs Fund guidance review see 6.27 of the technology appraisal process guide.

2.6 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the end of data collection and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the Cancer Drugs Fund guidance review timelines described in NICE's guide to the processes of technology appraisal.

2.7 The company is responsible for paying all associated charges for a Cancer Drugs Fund review. Further information is available on the NICE website.

2.8 The company must inform NICE and NHS England and NHS Improvement in writing of any anticipated changes to the estimated dates for data collection at the earliest opportunity.

2.9 Any changes to the terms or duration of any part of the data collection arrangement must be approved by NICE and NHS England and NHS Improvement.

2.10 If data collection is anticipated to conclude earlier than the estimated dates for data collection, for example due to earlier than anticipated reporting of an ongoing clinical trial, the company should note:

- Where capacity allows, NICE will explore options to reschedule the Cancer Drugs Fund guidance review date to align with the earlier reporting timelines.
- It may be necessary to amend the content of the final SACT or real-world data report (for example if planned outputs will no longer provide meaningful data).

2.11 If data collection is anticipated to conclude later than the estimated dates for data collection, the company should note:

- The company must submit a written request to NICE and NHS England and NHS Improvement, with details of the extension requested, including an explanation of the factors contributing to the request.
- It may be necessary for the company to mitigate the impact of any delay, and reduce any risks of further delays.
- In the event of an extension, it may not be possible to amend the date of the final SACT or real-world data report, although NICE will explore options with NHS Digital to provide data over the extended period.

2.12 AstraZeneca acknowledge their responsibility to provide an evidence submission for this technology to NICE under all circumstances following a period of managed access.

2.13 In the event that AstraZeneca do not make a submission to NICE for the purpose of updating the guidance, NICE and NHS England and NHS Improvement will require the company agree to submit the clinical evidence collected during the managed access period, and to participate in an engagement meeting convened by NICE with attendance from NHS England and NHS Improvement, patient and professional group stakeholders, with the company presenting the clinical evidence collected during the managed access period and an explanation of the decision to proceed with withdrawal of the guidance.

2.14 NICE and NHS England and NHS Improvement may consider the data collection agreement no longer valid, and withdraw the technology from the Cancer Drugs Fund for the following, non-exhaustive, grounds:

- The primary sources of data are delayed, without reasonable justification.

- The primary sources of data are unlikely to report outcome data that could resolve the uncertainties identified by the technology appraisal committee.
- Amendments are made to the marketing authorisation.

3 Patient eligibility

3.1 Key patient eligibility criteria for the use of adjuvant osimertinib in the Cancer Drugs Fund include:

- application is being made by the first cycle of systemic anti-cancer therapy with adjuvant osimertinib prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
- the patient has histologically documented non-small cell lung cancer (NSCLC).
- the patient has undergone a complete resection of the NSCLC with all surgical margins negative for tumour.
- the pathological stage determined on the patient's surgical NSCLC specimen is a stage IB or IIA or IIB or IIIA tumour according to the UICC/AJCC TNM 8th edition.
- the patient's NSCLC has been documented on the tumour specimen (biopsy or surgical specimen) as exhibiting either an epidermal growth factor (EGFR) exon 19 deletion (Ex19del) or an exon 21 (L858R) substitution mutation, whether alone or in combination with other EGFR mutations.

- the patient did not receive any pre-operative systemic therapy (cytotoxic chemotherapy, immunotherapy, EGFR-targeted tyrosine kinase inhibitors) for the NSCLC.
- the patient did not receive any pre-operative or post-operative radiation therapy for the NSCLC.
- no more than 10 weeks have elapsed since surgery if the patient did not receive adjuvant chemotherapy or no more than 26 weeks have elapsed since surgery if the patient was treated with adjuvant cytotoxic chemotherapy after surgery for the NSCLC.
- the patient has had no prior treatment with an EGFR inhibitor.
- the patient has an ECOG performance status (PS) of 0 or 1.
- the patient does not have brain metastases on CT or MR imaging of the brain done either before surgery or prior to this application.
- the patient will be treated with osimertinib for whichever is the sooner of: disease progression or unacceptable toxicity or withdrawal of patient consent or for a total treatment duration of 3 calendar years.
- a formal medical review as to how osimertinib is being tolerated and whether treatment with osimertinib should continue or not will be scheduled to occur at least by the end of the second 4-weekly cycle of treatment.
- when a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.

- osimertinib will be used as set out in its Summary of Product Characteristics (SPC).

3.2 An early access programme was put in place in May 2021 to enable patients access to osimertinib in order to bridge the gap between MHRA decision and final NICE decision[redacted]. As of October 2021, [redacted] eligible patients have been enrolled in-line with the Blueteq criteria.

3.3 The estimated patient numbers per year for this technology within the Cancer Drugs Fund are:

As estimated by the company	[redacted]patients in Year 1[redacted]patients in Year 2[redacted]patients in Year 3
As estimated by NICE Resource Impact Assessment team	Year 1: 279 Year 2: 558 Year 3: 558

Patient safety

3.4 The company and NHSE&I have the responsibility to monitor the safety profile of the technology and must provide an overview of any new or updated safety concerns to NICE. If any new safety concerns are confirmed, NICE and NHSE&I will take steps, as appropriate, to mitigate the risk including but not limited to updating the eligibility criteria or recommending that the managed access agreement be suspended.

4 Area(s) of clinical uncertainty

4.1 The appraisal committee identified the following key areas of uncertainty during the course of the appraisal process:

1. what extent a benefit in disease-free survival translates into a benefit in overall survival
2. the extent of the cure proportion, and the cure time point
3. the impact of the 3-year stopping rule
4. the proportion of patients that would be retreated with osimertinib.

4.2 The committee expect further data collection will allow for a new model (mixture-cure model if data allows) to be presented as a scenario analysis when the guidance is updated.

4.3 The committee concluded that further data collection within the Cancer Drugs Fund could resolve these uncertainties. For further details of the committee's discussion see section 3 of the Final Appraisal Document.

4.4 The committee considered data collected from the ongoing ADAURA RCT, due to complete in January 2023, would sufficiently resolve the majority of these uncertainties. The committee were aware that SACT data collection was unlikely to provide meaningful data on the proportion of patients that would be retreated with osimertinib in clinical practice in a reasonable timeframe. The committee considered this was acceptable as this assumption made no significant difference to the cost effectiveness estimates.

5 Sources of data collection

Primary and secondary sources of data collection

Primary source(s)	○ Ongoing clinical study - ADAURA
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHS England and NHS Improvement's Blueteq data

Description of sources

5.1 ADAURA (NCT02511106) is a Phase III, randomised, double-blinded, placebo-controlled, multicentre study to examine the efficacy and safety of osimertinib as an adjuvant therapy to complete resection in adult patients with stage IB–IIIA EGFRm-positive NSCLC.

5.2 NHS England and NHS Improvement's Blueteq database captures the Cancer Drugs Fund population. NHS England and NHS Improvement shares Blueteq data with NHS Digital for the Cancer Drugs Fund evaluation purposes. The lawfulness of this processing is covered under article 6(1) e of the United Kingdom General Data Protection Regulations (GDPR) (processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller). NHS Digital, through the National Disease Registration Service, does have statutory authority to process confidential patient information (without prior patient consent) afforded through the National Disease Registries (NDRS) Directions 2021 issued to it by the Secretary of State for Health and Social Care, and has issued the NDRS Data Provision Notice under section 259 of the Health and Social Care Act 2012 regarding collection of the Blueteq data from NHS England and NHS Improvement.

5.3 The Systemic Anti-Cancer Therapy (SACT) dataset, is a mandated dataset as part of the Health and Social Care Information Standards. NHS Digital is responsible for the collection, collation, quality-assurance and analysis of this dataset.

6 Outcome data

Clinical trial

6.1 Outcomes expected from ADAURA clinical trial

- Final DFS analysis (Stage II-IIIa). [redacted] *(247 events)* [redacted]

- Exploratory OS analysis – Stage II-IIIA. [redacted] *(94 deaths) expected 2023*
- Proportion of patients that are re-treated with osimertinib (following successful completion of 3 years of adjuvant osimertinib)
- Longer follow up data and impact of the 3 year stopping rule. *It is expected that at time of final OS data analysis* [redacted].

The committee concluded that even though the overall survival data may still be immature, the trial would provide a longer follow-up for disease-free survival. This should provide more evidence on the impact of the 3-year stopping rule, the most appropriate cure time point, and the extent of the cure proportion.

Other data, including SACT

6.2 NHS Digital will collect the following outcomes through SACT unless it is determined by the SACT Operational Group that no meaningful data will be captured during the period of data collection:

- Number of patients starting treatment
- Baseline patient characteristics, including gender, age and performance status
- Treatment duration
- Overall survival

6.3 NHS England and NHS Improvement's Blueteq system will collect the following outcomes:

- Number of applications to start treatment

7 Data analysis plan

Clinical trials

7.1 Final DFS analysis (Stage II-IIIa) as per the analysis plan outlined in the ADAURA clinical study protocol.

- Event driven – 247 events [redacted]
- [redacted]
- 63% of the DFS events expected in the planned final analysis (156/247 DFS events) had already occurred in DCO1 Jan 2020, which reported 2 years earlier than planned.

7.2 Exploratory OS analysis – Stage II-IIIA as per the analysis plan outlined in the ADAURA clinical study protocol.

- Event driven – 94 deaths [redacted]
- Expected 2023

Other data

7.3 At the end of the data collection period NHS Digital will provide a final report for NHS England and NHS Improvement which provide analyses based on NHS England and NHS Improvement's Blueteq data and routinely collected population-wide data, including that collected via SACT. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with the company in advance of the planned review of guidance. Where SACT is a secondary source of data, availability of the final SACT report will be aligned to the availability of data from the primary source. The end of SACT data collection will be 8 months prior to

the availability of the final SACT report to allow for NHS trusts to upload SACT data, data cleaning, and report production.

8 Ownership of the data

8.1 For all clinical trial data listed above, AstraZeneca will be the data owner

8.2 This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHS Digital.

8.3 The company will not have access to the NHS Digital patient data, but will receive de-personalised summary data, with appropriate governance controls in place.

8.4 The SACT dataset is a mandated dataset as part of the Health and Social Care Information Standards. All necessary governance arrangements through SACT, and other datasets brought together by NHS Digital, have been established with NHS Trusts and NHS England and NHS Improvement.

8.5 Blueteq's Cancer Drugs Fund system data is owned by NHS England and NHS Improvement. NHS England and NHS Improvement is responsible for implementing Blueteq data collection and generally for the analysis of these data. NHS England and NHS Improvement, however, shares Blueteq data with NHS Digital for Cancer Drugs Fund evaluation purposes. The lawfulness of this processing is covered under article 6(1)e of the United Kingdom General Data Protection Regulations (UK GDPR) (processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller). NHS Digital, through the National Disease Registration Service, does have statutory

authority to process confidential patient information (without prior patient consent) afforded through the National Disease Registries (NDRS) Directions 2021 issued to it by the Secretary of State for Health and Social Care. The lawfulness of NHS Digital's processing is covered under article 6(1)(c) of the UK GDPR – processing is necessary for compliance with a legal obligation to which the controller is subject (the NDRS Directions).

9 Publication

9.1 The details/authorship of any proposed publications arising from these studies will be planned with the publication of the final study results.

9.2 NHS Digital will produce a final report which includes analysis of data collected through SACT and from NHS England and NHS Improvement's Blueteq system. This report will be provided to NHS England and NHS Improvement and the company at the end of the managed access period. The final report will form part of NHS England and NHS Improvement's submission to the Cancer Drugs Fund guidance review, and will therefore be publicly available at the conclusion of the guidance review.

9.3 NHS Digital will produce interim reports, which will be shared with NHS England and NHS Improvement, NICE and the company at regular intervals during the data collection period. These reports will be used to determine whether real-world data collection is proceeding as anticipated, and will not form part of the guidance review.

9.4 Publications of any data from the NHS Digital reports is not permitted until after the date of publication of the NICE committee papers (on the NICE website) following the first NICE guidance review committee meeting.

9.5 The contribution of all relevant individuals must be acknowledged in any publications regarding the data collection or analyses generated from the

data collection arrangement. Authors will need to contact the NICE Managed Access Team for the full list of relevant individuals.

10 Data protection

10.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHS England and NHS Improvement and AstraZeneca, shall also apply between the parties to this data collection arrangement in relation to the performance of their obligations under this data collection arrangement

11 Equality considerations

11.1 Do you think there are any equality issues raised in data collection?

☐ Yes ☒ No

Commercial Access Agreement

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The contents of this document have been redacted as they are confidential

- A glossary of terms relating to managed access agreements in the Cancer Drugs Fund is available here.