Managed Access Agreement

Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer [TA823]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer (TA823)

Company name: Roche

Primary source of data collection: Ongoing clinical study – IMpower010

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

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Company Agreement Manager	Siobhán Browne, Health Economics, Reimbursement and Outcomes Chapter 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 atezolizumab for adjuvant treatment of resected non-small-cell lung cancer [TA823]. 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 a guidance update are:

End of data collection (primary source)	[redacted]
Data available for development of company submission	[redacted]
Anticipated company submission to NICE for a guidance update	December 2024

2.3 Roche anticipates that 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 containing final DFS data from IMpower010, most recent cost and background mortality data, by March 2024.

2.4 A NICE guidance update following a period of data collection is the primary mechanism that will for exiting a MAA.

2.5 The NICE guidance update will follow the process and methods applicable to guidance updates that are in place at the time the invitation to participate in the guidance update is issued to the company. These may be different from the process and methods applicable to guidance updates when atezolizumab as an option for treating adjuvant treatment of resected non-small-cell lung cancer was recommended with managed access and/or entered into the MAA.

2.6 Roche acknowledges their responsibility to adhere as closely as possible to the timelines presented in this document.

2.7 NICE will, as far as is practicable, schedule the guidance update into the technology appraisal work programme to align with the estimated dates for the end of data collection.

2.8 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 guidance update follows the standard timelines.

2.9 The company is responsible for paying all associated charges for a guidance update. Further information is available on the NICE website.

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

2.11 Any changes to the terms or duration of any part of the data collection arrangement must be approved by NICE and NHSE.

2.12 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 guidance update 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).

2.13 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 NHSE, 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.

2.14 Roche acknowledges its responsibility to provide an evidence submission for this technology to NICE under all circumstances following a period of managed access.

2.15 In the event that Roche does not make a submission to NICE for the purpose of updating the guidance, NICE and NHSE 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 NHSE, 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.

2.16 NICE and NHSE may consider the data collection agreement no longer valid, and withdraw the technology from the Cancer Drugs Fund on 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 atezolizumab for treating adjuvant treatment of resected non-small-cell lung cancer in the Cancer Drugs Fund are listed below. It is important to note that TNM staging criteria have been updated from the Union for International Cancer Control/American Joint Committee on Cancer (AJCC/UICC) 7th edition (as used in the trial and the marketing authorisation) to the 8th edition and thus NHS England uses the 8th edition TNM stage criteria for the same disease characteristics evident in the TNM 7th edition.

- The application is being made by and the first cycle of systemic anti-cancer therapy with adjuvant atezolizumab will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
- The prescribing clinician is fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies, hepatitis and skin toxicity.
- The patient has a histologically documented diagnosis of non-small cell lung cancer (NSCLC).
- The patient's NSCLC has been documented as exhibiting PD-L1 expression on ≥50% of tumour cells as determined by an approved and validated PD-L1 assay.
- Whether the patient has a NSCLC harbouring an actionable mutation or not has been documented (mutations being EGFR 19 or 21, EGFR exon 20, ALK, ROS1, RET, MET14, KRAS G12C).

- The patient had M0 disease prior to surgery and has undergone a complete resection of the primary NSCLC with all surgical margins negative for tumour i.e. a R0 resection has taken place.
- The pathological TNM stage determined on this patient's surgical NSCLC specimen was a stage IIB or IIIA or N2 only IIIB tumour according to the UICC/AJCC TNM 8th edition.
- The patient commenced adjuvant platinum-based chemotherapy within 12 weeks of resection of the NSCLC.
- The patient has received a maximum of 4 cycles of adjuvant platinum-based chemotherapy.
- The patient has been radiologically re-staged after completion of adjuvant chemotherapy and continues to have no evidence of residual or metastatic disease.
- No more than 12 weeks have elapsed since the start of the last cycle of adjuvant platinum-based chemotherapy.
- The patient has not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody.
- The patient has an ECOG performance status (PS) of 0 or 1.
- Atezolizumab will be stopped at whichever of the following events occurs first: disease progression or unacceptable toxicity or withdrawal of patient consent or on completion of 1 year in total duration of treatment with atezolizumab (i.e. after a maximum of 13 x 4-weekly cycles or its equivalent if 2-weekly or 3-weekly dosing is used).
- A formal medical review as to how atezolizumab is being tolerated and whether treatment with atezolizumab should continue or not will be scheduled to occur at least by the end of the second month of treatment.

- When a treatment break of more than 3 months beyond the expected 2- or 3- or 4-weekly cycle length is needed, the clinician will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of Covid-19.
- Atezolizumab will be otherwise used as set out in its Summary of Product Characteristics (SPC).

3.2 A post-project Orbis free of charge (FoC) scheme was put in place in February 2022 to bridge the gap between MHRA approval and final NICE decision. As of July 2022, [redacted] were enrolled. These early access patients will be included in the NHS Digital report.

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 and [redacted] patients in year 3
As estimated by NICE Resource Impact Assessment team	471 patients in year 1, 707 patients in year 2 and 942 patients in year 3

4 Patient safety

4.1 The company and NHSE 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 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.

5 Area(s) of clinical uncertainty

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

1. Immature data from IMpower010 including disease-free survival and overall survival
2. To what extent disease-free survival improves overall survival
3. The cure assumption used in the submission and the ERG's different assumptions

5.2 The committee expect further data collection will allow for an updated model to be presented when the guidance is updated.

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

6 Sources of data collection

Primary and secondary sources of data collection

Primary source(s)	○ Ongoing clinical trial– IMpower010
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHSE's Blueteq data

Description of sources

6.1 IMpower010 (NCT02486718) a Phase III, global, multicenter, open-label, randomized study to compare the efficacy and safety of atezolizumab for the adjuvant treatment of patients with stage IB (tumours ≥ 4 cm) – IIIA

NSCLC (per the AJCC/UICC staging system, 7th edition) following resection and adjuvant chemotherapy.

6.2 NHSE's Blueteq database captures the Cancer Drugs Fund population. NHSE 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 NHSE.

6.3 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.

7 Outcome data

Clinical trial

7.1 Outcomes expected from IMpower010 clinical trial

[redacted]

[redacted]

The committee expects that further data collection will enable a more robust model to be explored for the guidance update at the end of the period of managed access.

Other data, including SACT

7.2 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 band and performance status at the start of regimen
- Treatment duration
- Overall survival

7.3 NHSE's Blueteq system will collect the following outcomes:

- Number of applications to start treatment
- PD-L1 expression of resected lung cancers
- Presence of otherwise of actionable mutations
- TNM staging information (8th edition)
- Number of cycles of adjuvant chemotherapy administered

8 Data analysis plan

Clinical trials

8.1 Final DFS analysis (PD-L1 ≥1% Stage II-IIIA population) as outlined in the statistical analysis plan in the IMpower010 clinical study protocol.

[redacted]

8.2 Second OS IA analysis (ITT, Stage IB-IIIA population) as outlined in the statistical analysis plan in the IMpower010 clinical study protocol.

[redacted]

Other data

8.4 At the end of the data collection period NHS Digital will provide a final report for NHSE which provide analyses based on NHSE'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 guidance update. 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.

9 Ownership of the data

9.1 For all clinical trial data listed above, Roche will be the owner

9.2 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. 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.

9.3 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 NHSE.

9.4 Blueteq's Cancer Drugs Fund system data is owned by NHSE. NHSE is responsible for implementing Blueteq data collection and generally for the analysis of these data. NHSE, 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).

10 Publication

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

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

10.3 NHS Digital will produce interim reports, which will be shared with NHSE, 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 update.

10.4 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 update committee meeting.

10.5 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.

11 Data protection

11.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHSE and Roche, shall also apply between the parties to this data collection arrangement in relation to the performance of their obligations under this data collection arrangement

12 Equality considerations

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

☐ Yes ☒ No