Cancer Drugs Fund

Managed Access Agreement

Nivolumab for previously treated non-squamous non-small-cell lung cancer

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Nivolumab for previously treated non-squamous non-small-cell lung cancer [ID900]

Company name: Bristol-Myers Squibb Company

Primary source of data collection: Ongoing clinical study

Secondary source of data collection: Systemic anti-cancer therapy data set

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Public Health England Agreement Manager	Martine Bomb, Head of Data Projects, National Cancer Registration and Analysis Service
BMS Agreement Manager	Benjamin Hickey, UK General Manager

1 Purpose of data collection arrangement

1.1 The purpose of the agreement is to describe the arrangements and responsibilities for further data collection of nivolumab for lung cancer (non-small-cell, non-squamous, metastatic) after chemotherapy [ID900] (to be updated with TA number after final guidance has been published). A positive recommendation within the context of a managed access agreement 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. The data collection is anticipated to conclude June 2019, when it is expected that 5-year follow-up data will be available from the CheckMate 057 clinical trial.

2.2 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the data collection period

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has ended and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the standard timelines described in the addendum to NICE's methods and processes when appraising cancer technologies.

3 Patient eligibility

3.1 Nivolumab is recommended for use within the Cancer Drugs Fund as an option for treating locally advanced or metastatic PD-L1-positive non-squamous non-small-cell lung cancer in adults after chemotherapy. Key patient eligibility criteria for nivolumab's use in the cancer drugs fund include:

- Patient has a confirmed diagnosis of stage IIIB or IV non-small cell lung cancer (non-squamous)

- Patient has progressed after previously receiving at least 2 cycles of platinum-containing chemotherapy for stage IIIB or IV non-small cell lung cancer and also a targeted treatment if the tumour is EGFR positive or ALK positive

- Patient has a performance status of 0 or 1

- 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 unless received as part of the nivolumab EAMS programme for this indication and meeting all other criteria listed.

- Patient has had PD-L1 testing with an approved and validated test to determine the Tumour Proportion Score

- Patients tumour expresses PD-L1, that is with a tumour proportion score ≥ 1%

- Nivolumab will be administered as monotherapy

- Patient has no symptomatically active brain metastases or leptomeningeal metastases.

- Nivolumab will be stopped at 2 years of treatment or on disease progression or unacceptable toxicity, whichever occurs first.

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3.2   It is estimated that 344 patients will receive nivolumab for previously treated non-squamous non-small-cell lung cancer through the Cancer Drugs Fund during the managed access arrangement.

3.3   It is estimated that the average treatment duration for a patient with non-squamous NSCLC will be 5.8 months.

4   Area(s) of clinical uncertainty

4.1   Based on the evidence provided during the appraisals, the NICE committee noted that nivolumab has a different level of clinical effectiveness according to PD-L1 expression. While the use of nivolumab within the CDF is available only to those with a PD-L1 expression of at least 1%, different PD-L1 expression level will therefore be explored as part of the data collection arrangement. The primary data source will be CheckMate -057 as the protocol for this trial included collecting this data along with other biomarkers at baseline. PD-L1 expression subgroup analyses using the 5-year follow-up data will be undertaken, including cost-effectiveness analysis, and provided to NICE when the guidance is reviewed. These analyses are described in Section 7.

4.2   The long-term overall survival and duration of therapy are the two other key areas of uncertainty identified by the NICE committee. The primary source of data to address these will be the ongoing trial described in section 5.

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5 Source(s) of data collection

Clinical trials

5.1 Data collection from the ongoing clinical trial (CheckMate 057) will be the primary source of data collection. A 5-year data cut from the trial is expected in June 2019. A 7-year data cut from CheckMate 003 will also be available in June 2019 as a supportive source of data. Table 1 provides a brief description of the trial details.

Table 1 Trial description

CheckMate 057 – Phase III (n=574)
Description: Nivolumab vs docetaxel for the treatment of patients with metastatic non-squamous NSCLC with progression on or after platinum-based chemotherapy.
Primary Endpoint: *OS*
Secondary Endpoint: *ORR, PFS, PDL1 as a predictive biomarker for OS, ORR, PROs*

CheckMate 003 – Phase IIb (n=129)
Description: Dose escalation study of nivolumab in subjects with selected advanced or recurrent malignancies. Cohort of patients with squamous and non-squamous NSCLC previously treated received at least one prior systemic therapy, including a platinum-based or taxane-based chemotherapy
Primary Endpoint: *safety and tolerability,*
Secondary Endpoint: *ORR, exploratory OS, exploratory PD-L1 expression*

ORR: Overall Response Rate, OS: Overall Survival, PFS: Progression Free Survival, PROs: Patient Reported Outcomes

SACT

5.2 The Systemic Anti-cancer Therapy (SACT) dataset is a mandated dataset as part of the Health and Social Care Information Standards.

5.3 A test for PD-L1 status will be conducted for every patient commencing treatment. Each patient's PD-L1 status will be captured via NHS England's Blueteq system as part of pre-authorisation for treatment. Blueteq will also capture patients who cannot be tested or those whose tests are inconclusive.

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6   Outcome data

Clinical trials

6.1   The two most pertinent outcomes to be measured are long-term overall survival and duration of treatment. At the end of the data collection period 5-year data will be available from the ongoing CheckMate 057 trial. Sub-group analysis by PD-L1 expression level will be provided by 1%, 5% and 10% expression levels and submitted to NICE when the guidance is reviewed. This will be supplemented by the data collected in SACT.

6.2   Long-term comparator data is not being collected because all patients crossed-over to nivolumab in CheckMate 057 at 2 years.

SACT

6.3   Data collection via SACT will support data collected in the clinical trials. During the managed access agreement period, SACT will collect data on overall survival, duration of therapy and PD-L1 expression (obtained via Blueteq).

7   Data analysis plan

Clinical trials

7.1   At the end of the data collection period 5-year overall survival data from the CheckMate 057 will be used to inform the long-term extrapolation in the cost-effectiveness model along with the 7-year overall survival data from CheckMate 003.

7.2   Sub-group analysis by PD-L1 expression level will also be undertaken by 1%, 5% and 10% expression levels. The sub-group analyses and associated cost-effectiveness estimates will be provided to NICE as part of the evidence submission when the guidance is reviewed.

7.3   Any revisions in the timing of the 5-year data will be communicated with NICE. As discussed, quarterly meetings will be set in order to track the progress of the data collection by Public Health England.

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SACT

7.4   Public Health England will provide a report for NHS England based on data collected via SACT during the data collection period. The report will present de-personalised summary data based on the outcomes identified in section 6.2. The report will be shared with BMS prior to the review of the appraisal.

8   Ownership of the data

8.1   For all clinical trial data listed above, Bristol-Myers Squibb Company will be the owner.

8.2   SACT data is owned by individual patients, Public Health England is the data controller and will conduct analysis of SACT data. BMS will not have access to the SACT patient-level data. Public Health England will produce a report for NHS England at the end of the managed access period. The report will be shared with BMS.

8.3   Blueteq's CDF system data is owned by NHS England.

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   Publication of the analysis results of SACT data collected alongside the primary data source will be planned by Public Health England. BMS will be given access to the report produced for NHS England for the review of the appraisal prior to the planned start of the review.

9.3   Publication of the analysis results of Blueteq's CDF system data collected alongside the primary data source will be planned by NHS England. BMS will be given access to any report produced for the review of the appraisal and the review of the appraisal prior to the planned start of the review.

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Commercial Access Agreement

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

Single technology appraisal (STA)

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Cancer Drugs Fund - Glossary of terms

Term	Explanation
Commercial access agreement	The standard way for pharmaceutical companies to make cancer drugs cost effective for the NHS either when they are recommended by NICE for entry into the Cancer Drugs Fund or if they were a transition drug in July 2016 and undergoing appraisal by NICE as a transition drug for exiting from the Cancer Drugs Fund. Each agreement is approved by NHS England.
Patient access scheme	The standard way for pharmaceutical companies to make cancer drugs cost effective for the NHS when they are routinely commissioned. Each scheme is approved by the Department of Health. Patient access schemes are part of the Pharmaceutical Price Regulation Scheme (2014)
Managed access agreement	A Cancer Drugs Fund managed access agreement consists of two components: · The first is a data collection arrangement, which sets out data that will be collected during the 'managed access' period to resolve clinical uncertainty · The second is a commercial access agreement that determines how much the NHS will pay for the treatment during the managed access period. This is normally a commercial access agreement that is managed by NHS England. However, if appropriate, a Department of Health-approved patient access scheme can also be used.