Cancer Drugs Fund

Managed Access Agreement

Pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel for untreated metastatic squamous non-small-cell lung cancer [ID1306]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer [ID1306]

Company name: Merck Sharp & Dohme Ltd. (MSD)

Primary source of data collection: KEYNOTE- 407 ongoing clinical study

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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 Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer [ID1306]. 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. The data collection period is anticipated to conclude June 2019 (see Section 5.1). The process for exiting the Cancer Drugs Fund will begin at this point and the review of the NICE guidance will start.

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

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.

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

2.4 Any changes to the terms or duration of any part of the managed access agreement must be approved by NICE and NHS England as co-signatories to the agreement.

2.5 If data collection is anticipated to conclude earlier than the timelines stated in the managed access agreement, for example due to earlier than anticipated reporting of an ongoing clinical trial:

- Where capacity allows NICE will endeavour to reschedule the CDF 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 outcomes will no longer provide meaningful data).

2.6 If data collection from an ongoing clinical trial is anticipated to be delayed, please note:

- NICE and NHS England should be informed immediately as co-signatories to the agreement
- Unless a strong compelling rationale is provided, the CDF guidance review will proceed according to the original timelines outlined in the MAA.
- Resource/capacity issues will not be accepted as reasons for delaying the associated CDF guidance review.
- It may not be possible to amend the date of the final SACT or real-world data report, in which case it will be available before the Clinical Study report is completed.

3 Patient eligibility

3.1 Pembrolizumab in combination with carboplatin and paclitaxel has been recommended for use in the Cancer Drugs Fund for treating adults for untreated metastatic squamous non-small-cell lung cancer in line with the entire population covered by the marketing authorization.

3.2 Key patient eligibility criteria for the use of Pembrolizumab in combination with carboplatin and paclitaxel in the Cancer Drugs Fund include

- a histologically- or cytologically-confirmed diagnosis of stage IIIB or stage IIIC or stage IV squamous non-small cell lung cancer
- PD-L1 testing with an approved and validated test to determine the Tumour Proportion Score (TPS)
- **either** the patient has a PD-L1 TPS of 0-49% **or** has a PD-L1 TPS of 50-100% **and** requires an urgent clinical response (e.g. impending major airway obstruction) so as to justify the use of the combination of pembrolizumab, carboplatin and paclitaxel rather than pembrolizumab monotherapy **and** this issue has been fully discussed with the patient
- patient has not received previous cytotoxic chemotherapy for advanced /metastatic disease.
    - completion of treatment for earlier stage disease with chemotherapy with or without radiotherapy as part of neoadjuvant/concurrent/adjuvant therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of recurrent locally advanced or metastatic disease
- commence treatment with a maximum of 4 3-weekly cycles of the combination of pembrolizumab (200mg), carboplatin (AUC 6mg/ml/min) and paclitaxel (200mg/m²)

  - during the combination phase, 3-weekly dosing of pembrolizumab 200mg must be used (i.e. not 6-weekly dosing of pembrolizumab 400mg)

- after completion of the combination of pembrolizumab, carboplatin and paclitaxel and in the absence of disease progression, continued treatment with 3-weekly cycles of pembrolizumab monotherapy 200mg (or if the patient is stable and well, 6-weekly cycles of pembrolizumab monotherapy 400mg) will continue until **whichever of the following occurs first:**

  - loss of clinical benefit or unacceptable toxicity or withdrawal of patient consent, or

  - maximum treatment duration of 2 years (or 35 3-weekly cycles of pembrolizumab including the initial 4 induction cycles of treatment or its equivalent if 6-weekly pembrolizumab monotherapy dosing is used)

- patient is fit for the combination of pembrolizumab, carboplatin (AUC 6mg/ml/min) and paclitaxel (200mg/m²) **and** has an ECOG performance status score of 0 or 1

- no symptomatically active brain metastases or leptomeningeal metastases

- 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

- a formal medical review as to whether treatment with the combination of pembrolizumab, carboplatin and paclitaxel should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment

- treatment breaks of up to 12 weeks beyond the expected cycle length are allowed but solely to allow any immune toxicities to settle

3.3 The maximum number of patients who could have pembrolizumab combination therapy from availability through to data collection end would be 405 in 2019 and 590 in 2020. It is not expected that pembrolizumab combination therapy would have 100% uptake.

3.4 The maximum treatment duration (time on treatment per patient) is 2 years. The estimated average treatment duration within the Cancer Drugs Fund during the managed access agreement period is under 2 years, given the anticipated length of the agreement period. The overall survival rate, reported in IA2 for 12 months was 65.2% in the pembrolizumab combination arm. Median OS at IA2 was 15.9 months.

4 Area(s) of clinical uncertainty

4.1 The key clinical uncertainties identified by the appraisal committee were as follows:

- Overall survival of pembrolizumab combination therapy versus standard care for the intention to treat population and by PD-L1 TPS subgroups.
- Overall survival in the comparator arms, particularly the magnitude of subsequent immunotherapy benefits and whether the technology meets NICE's end of life criteria for patients with a short life expectancy.

5 Source(s) of data collection

Clinical trial

5.1 The primary source of data collection during the managed access arrangement period will be the ongoing clinical study KEYNOTE-407, as described below:

KEYNOTE-407 (NCT02775435); an ongoing, worldwide, randomized, placebo-controlled with active treatment, parallel-group, multi-site, double-

blind trial of pembrolizumab combined with carboplatin-paclitaxel/nab-paclitaxel chemotherapy in untreated subjects with metastatic squamous NSCLC.

Other data

5.2 Data will be collected via Public Health England's routine population-wide datasets, including the Systematic Anti-Cancer Therapy (SACT) dataset. This collection will not support data collected in the clinical trial as it was determined that no meaningful data would be captured during the period of data collection.

6 Outcome data

Clinical trial

6.1 The outcome data that will be collected during the data collection arrangement is described below:

Data on overall survival will be collected at the final analysis of the KEYNOTE-407 clinical trial. This will provide overall survival data for the comparison of pembrolizumab in combination with carboplatin-paclitaxel/nab-paclitaxel chemotherapy vs carboplatin-paclitaxel/nab-paclitaxel chemotherapy in the ITT population and across PD-L1 subgroups (TPS <1%, TPS 1-49% and TPS ≥50%).

Data will be collected in the final analysis on the proportion of patients in the standard of care arm who received subsequent immunotherapy and the OS in this arm of the trial in the ITT population and across PD-L1 subgroups (TPS <1%, TPS 1-49% and TPS ≥50%).

Other data, including SACT

6.2 Outcome data will be available for carboplatin-paclitaxel/nab-paclitaxel chemotherapy from KEYNOTE-407.

6.3 Data will be collected via Public Health England's routine population-wide datasets, including the SACT dataset. This collection will not support data collected in the clinical trial as it was determined that no meaningful data would be captured during the period of data collection.

7 Data analysis plan

Clinical trials

7.1 The details and timeframe of the data analyses are as follows:

KEYNOTE-407: The point at which final OS is conducted is event driven and is scheduled when approximately 361 death events have occurred. Based on current projections the final analysis is estimated for June 2019.

8 Ownership of the data

8.1 The data being collected from KEYNOTE-407 belongs to MSD. The data collection is being managed under the KEYNOTE-407 clinical trial protocol.

9 Publication

9.1 The details/authorship of any proposed publications arising from the KEYNOTE-407 will be planned with the publication of the final study results.

10 Data protection

10.1 The terms of clause 7 (data protection) of the managed access agreement, as apply between NHS England and MSD, 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.