Cancer Drugs Fund

Managed Access Agreement

Crizotinib for treating ROS1-positive advanced non-small-cell lung cancer

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Crizotinib for treating ROS1-positive advanced non-small-cell lung cancer [ID1098]

Company name: Pfizer Ltd

Primary source of data collection: **Public Health England routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy dataset (SACT)**

Secondary source of data collection: PROFILE 1001 and Ox-Onc clinical studies

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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 crizotinib for treating ROS1-positive advanced non-small-cell lung cancer [ID1098] (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 period is anticipated to conclude following a period of up to 5 years (April 2023). Annual reviews will take place at years 2, 3 and 4 to consider whether sufficient data has been collected and if continued data collection is necessary. If it is unanimously agreed by the signatories that sufficient data has been collected to resolve the uncertainties identified, the data collection period will be brought to an

end. Once the data collection period has concluded the process for exiting the Cancer Drugs Fund will begin and the review of the NICE guidance will start. Following receipt of the final report by Public Health England, it is anticipated that Pfizer Ltd will be in a position to submit new evidence to NICE in approximately a 6 month period if sufficient data has been collected.

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.

3 Patient eligibility

3.1 Crizotinib has been recommended for use within the Cancer Drugs Fund for the treatment of adults with ROS1-positive advanced non-small cell lung cancer (NSCLC). The recommendation encompasses patients who have or have not previously received cytotoxic chemotherapy for locally advanced or metastatic non-small cell lung cancer.

3.2 ROS1-positive NSCLC status should normally be established prior to initiation of crizotinib therapy. NHS England has a strong preference for ROS1-positive patients to be treated with crizotinib as 1st line therapy for advanced NSCLC but recognises that some patients have had to be treated with chemotherapy for urgent clinical reasons before the ROS1 result is known. Assessment of ROS1 status should be performed by laboratories with demonstrated proficiency in the specific technology being utilised. An accurate and validated assay for ROS1 is necessary for the selection of patients for treatment with crizotinib.

3.3 Key patient eligibility criteria and conditions for the use of crizotinib in the Cancer Drugs Fund include:

- Patient has a histologically or cytologically confirmed diagnosis of stage IIIB or stage IV non-squamous non-small cell lung cancer with a

confirmed ROS1 gene rearrangement as demonstrated by an accurate and validated assay

- Patient has not previously received ROS1-targeted therapy
- Patient has received no previous cytotoxic chemotherapy for locally advanced or metastatic non-small cell lung cancer OR has been previously treated with cytotoxic chemotherapy for locally advanced or metastatic disease

  Note: NHS England has a strong preference for ROS1-positive patients to be treated with crizotinib as 1st line therapy for locally advanced/metastatic NSCLC though recognises that some patients have had to be treated with chemotherapy for urgent clinical reasons before the ROS1 result is known
- Crizotinib will be used only as single-agent therapy
- Patient has an ECOG performance status of 0, 1 or 2
- Patient either has no brain metastases or, if the patient has brain metastases, the patient is symptomatically stable prior to starting crizotinib
- Treatment will continue until loss of clinical benefit or excessive toxicity or patient choice to discontinue treatment, whichever is the soonest
- Treatment breaks of up to 6 weeks are allowed but solely to allow toxicities to settle
- Crizotinib will be otherwise used as set out in its Summary of Product Characteristics (SPC)

3.4 As of May 2018 crizotinib is available through a compassionate access scheme. This scheme is likely to close once access via the CDF is available

to patients. The cohort of patient receiving access via this scheme will not be captured by the data collection outlined in this arrangement.

3.5 Approximately 80 ALK-positive patients were treated per year (2014 and 2015 CDF reports) with crizotinib. Due to the lower incidence of ROS1-positive NSCLC, it is therefore estimated that approximately 40 patients per year will be diagnosed with ROS1-positive advanced non-small cell lung cancer (NSCLC) and treated with crizotinib within the Cancer Drugs Fund.[1] This estimate is based on ROS1 testing being set up and being readily available.

3.6 The estimated treatment duration of crizotinib, per patient, within the Cancer Drugs Fund is estimated to be 23 months, based on the median treatment duration from the PROFILE 1001 study, which was conducted in patients with ROS-1 positive advanced NSCLC. The median overall survival from PROFILE 1001 was not reached at the data cut-off date The OxOnc study reported a median overall survival of 32.5 months. The median duration of follow-up was 25 months, which is expected to be the minimum expected overall survival for patients with ROS1-positive NSCLC treated with crizotinib.

4 Area(s) of clinical uncertainty

4.1 The Appraisal Committee identified the following areas of clinical uncertainty:

- Due to the single-arm study design of PROFILE 1001, there is a lack of data comparing crizotinib with ‘standard care’ in ROS1-positive disease, which makes any assessment of relative effectiveness challenging.

- Uncertainty was noted as to whether the documented similarities between ALK-positive and ROS1- positive advanced NSCLC will hold true as more patients with ROS1- positive advanced NSCLC are identified.

- There is also uncertainty in the post-progression survival estimates, and therefore overall survival estimates, due to high rates of crossover from

chemotherapy to crizotinib in the PROFILE 1007 and PROFILE 1014 trials (used as a proxy for ROS1).

5 Source(s) of data collection

SACT dataset

5.1 The primary source of data collection during the managed access arrangement period will be data collated by Public Health England including SACT.

5.2 Public Health England identifies, collects, collates, quality-assures and analyses large population-level datasets for specific diseases and conditions, including cancer. These datasets include the SACT dataset, which is a mandated dataset as part of the Health and Social Care Information Standards. Public Health England will use the routinely-captured data collected during the period of the data collection arrangement to provide analyses as defined in sections 6.3 and 7.3

Blueteq database

5.3 NHS England's Blueteq database captures the CDF population. NHS England shares Blueteq data with Public Health England for the CDF evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

Other data

5.4 Additional data will be collected through the ongoing PROFILE 1001 clinical trial, a single-arm study across 8 sites in the US, Australia and South Korea. The final analysis of PROFILE1001 is due to be performed after the last patient last visit and will follow the analysis plan outlined in the trial protocol (due approximately by [redacted]). It is noted that this reporting date falls outside of the anticipated period of data collection. Therefore data will only be presented from PROFILE 10001 if interim analysis is available. The outcomes for PROFILE 1001 are outlined in 6.1.

5.5 Additional data will be collected through the ongoing OxOnc clinical trial. The final analysis of OxOnc is due to be performed after the last patient last visit

and will follow the analysis plan outlined in the trial protocol (due approximately by [redacted]). OxOnc is a phase 2, single-arm study in east Asian patients (n=127) with ROS1-positive, ALK-negative locally advanced or metastatic NSCLC with ≤3 lines of prior chemotherapy.

6 Outcome data

SACT

6.1 No data will be collected for the comparators.

6.2 Data will be collected via Public Health England's routine population-wide datasets, including the SACT dataset. This collection will support data collected in the clinical trial. During the managed access agreement period, Public Health England will collect data to provide information on:

- Age (broad age bands)
- Performance status at the start of regimen
- Sex
- Outcome summary – the reason a patient stopped treatment
- Treatment duration
- Overall survival
- Previous treatments – before crizotinib if data is available

Clinical trial, PROFILE 1001

6.3 The following outcomes are planned to be collected in the ongoing PROFILE1001 clinical trial in ROS1-positive NSCLC patients (any update to these will be communicated to NICE and CDF):

- Objective response rate
- Progression-free survival
- Overall survival
- Time to response
- Duration of response
- Disease control rate
- Time to progression
- Time to treatment failure
- Safety outcomes

Clinical trial, OxOnc

6.4 The following outcomes are planned to be collected in the ongoing OxOnc clinical trial in ROS1-positive NSCLC patients (any update to these will be communicated to NICE and CDF):

- Objective response rate
- Progression-free survival
- Overall survival
- Time to response
- Duration of response
- Disease control rate
- Time to progression
- Safety outcomes
- Quality of life

The collection of overall survival in both clinical trials will help to reduce the uncertainty around the clinical effectiveness of crizotinib in ROS1 NSCLC. When median overall survival is met, this can be compared to the median overall survival associated with chemotherapy in the proxy ALK-positive populations to get an indication of the comparative efficacy of crizotinib over chemotherapy.

7 Data analysis plan

SACT

7.1 At the end of the data collection period Public Health England will provide a final report for NHS England based on routinely collected population-wide data, including that collected via SACT. The report will present depersonalised summary data, including the total number of patients starting treatment, overall survival and treatment duration. The cohort of interest will be identified from Blueteq using those eligibility criteria. The total number of patients starting treatment will be determined by implementation of and access to ROS-1 testing. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with Pfizer Ltd in advance of the planned review of guidance.

7.2 Completeness of SACT dataset reporting will be shared with NHS England and the Pfizer Ltd on a quarterly basis. Public Health England will provide summary results for time on treatment and survival to NHS England and to Pfizer Ltd on an annual basis, to check the continuing validity of the period of the data collection arrangement.

Clinical trials

PROFILE 1001

7.3 From the clinical study report, the efficacy analyses can be conducted for subpopulations, for example, according to: the number of previous antitumor treatments for advanced/metastatic disease (0, ≥1), type of prior treatment for advanced/metastatic disease, ECOG performance status (0, 1), age

group (<65 years, ≥65 years), gender, and race group (Asian, non-Asian). There will be no interim analyses during the data collection period.

OxOnc

7.4 The final analysis on the outcomes outlined in section 6.4 will be performed as per the trial protocol.

8 Ownership of the data

8.1 For all clinical trial data listed above, Pfizer Ltd will be the owner.

8.2 The data analysed by Public Health England is derived from patient-level information collected by the NHS, as part of the care and support of cancer patients. The data is collated, maintained, quality-assured and analysed by the National Cancer Registration and Analysis Service, which is part of Public Health England. Access to the data was facilitated by the Public Health England Office for Data Release. Pfizer Ltd will not have access to the Public Health England patient data, but will receive de-personalised summary data, with appropriate controls in place to cover this. Public Health England will provide a report to NHS England and Pfizer Ltd at the end of the managed access period.

8.3 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 Public Health England, have been established with NHS Trusts and NHS England.

8.4 Blueteq's CDF system data is owned by NHS England. NHS England is responsible for implementing Blueteq data collection and generally for analysis of these data. NHS England, however, shares Blueteq data with Public Health England for CDF evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

9 Publication

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

9.2 Publication of the analysis results of data collected by Public Health England, including through SACT and the data from Blueteq's CDF system, will be planned and implemented by Public Health England.

10 References

1. Scheffler M, Schultheis A, Teixido C, et al. ROS1 rearrangements in lung adenocarcinoma: prognostic impact, therapeutic options and genetic variability. Oncotarget 2015;6:10577-85.

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.