Managed Access Agreement

Osimertinib for treating metastatic EGFR and T790M mutation-positive non-small-cell lung cancer

Cancer Drugs Fund Data Collection Arrangement

Osimertinib for locally advanced or metastatic, EGFR and T790M mutation positive non-small cell lung cancer

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TAGRISSO (osimertinib) Data Collection Arrangement

1. Objective

This document sets out the data collection arrangement, which forms part of the agreement between NHSE and AstraZeneca regarding entry into the Cancer Drugs Fund for osimertinib for the treatment of patients with EGFR T790M mutation positive NSCLC following progression on a 1st generation EGFR-TKI.

2. Key Clinical Uncertainties to be addressed

A. Extrapolation of overall survival: The greatest area of uncertainty in the company base-case model is the extrapolation of OS data for patients treated with osimertinib. This is the result of the maturity of the currently available evidence from the AURAext/AURA2 studies.

B. Generalisability to UK clinical practice: During the Appraisal Committee meetings, a discussion took place regarding the generalisability of the results of the AURA clinical trials to UK clinical practice due to potential differences in treatment patterns and baseline characteristics.

3. Data collection sources

A. Ongoing clinical trials: Results from the ongoing studies evaluating osimertinib in the licensed indication will become available over the next 24 months as summarised below and will answer the majority of clinical uncertainties to be addressed.

AURA3 RCT	AURA Phase 2 (AURAext/AURA2)
Primary Analysis (PFS & secondary endpoints) *DCO April 2016* Results to be published at WCLC in December with parallel manuscript publication planned. A topline summary of these results has been shared confidentially with NICE/NHSE.	[redacted]
[redacted]	[redacted]
[redacted]	
Final (third) OS analysis [redacted] Event driven but based on current HE modelling not before mid-2018	

B. SACT dataset collection

The SACT database mandated by NHS England will, in addition to the data from the ongoing studies, be used to provide further information on real world treatment patterns with osimertinib in the UK and provide a secondary source of information next to the results of the confirmatory AURA3 RCT. The key area of interest is duration of treatment.

4. CDF Inclusion Criteria

NHS England and AstraZeneca have agreed the below outlined eligibility criteria for patients to commence treatment with osimertinib:

All of the 9 criteria below must be met:

- *Application made by and first cycle of systemic anti-cancer therapy to be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy*
- *Histologically or cytologically documented NSCLC that carries an EGFR and a T790M mutation*
- *Locally advanced or metastatic NSCLC*
- *Radiological documentation of disease progression following 1st line EGFR TKI treatment with only one TKI and without any further systemic anti-cancer treatment*
- *Treatment with no more than one prior line of treatment for advanced NSCLC*
- *No prior chemotherapy unless any prior neoadjuvant or adjuvant chemotherapy had been completed at least 6 months prior to starting 1st line EGFR treatment*
- *Performance status of 0 or 1*
- *At time of starting osimertinib, the patient must be fit enough to have potentially started platinum-based doublet chemotherapy*
- *Documented expected start date of osimertinib treatment*

5. Proposal for duration of CDF Agreement

AstraZeneca proposes that the trigger for a re-evaluation by NICE should be based on the final overall survival analysis from the confirmatory AURA3 RCT. This analysis will be performed when the OS data are [redacted] This final OS analysis from AURA3 will be supported by AURA ext/2 and IMPRESS final OS data to understand long-term survival profiles and the need to adjust for crossover confounding. Also, supportive data from UK practice with CUP/EAMS patients and CDF patients will be used to demonstrate generalizability and treatment duration in a UK setting.

Based on current economic modelling, the time from estimated final OS data analysis of the AURA 3 trial is anticipated to occur in mid-2018. AstraZeneca therefore proposes for osimertinib to be available through the CDF for a period of up to 30 months (October 2016 to March 2019). The time from mid 2018 to March 2019 is designed to cover possible delays in the final events that trigger the final OS analysis (due to slower death rate than planned by the study protocol), documentation preparation and final NICE technology appraisal. AZ proposes that the time osimertinib is reimbursed through the Cancer Drugs fund will end at time of baseline commissioning funding (if there is a positive recommendation when the guidance is reviewed) or March 2019 whichever occurs earlier.

AstraZeneca will keep NHS England updated on the estimated timelines of these final analyses (commercial in confidence) as well as interim analyses from both the AURA3 and AURA Phase2 studies becoming available in the meantime.

A summary of anticipated further analyses to become available in the next 24 months is provided above. It should be noted that percent maturity for the AURA3 programme is estimated across both arms whereas the percent for AURA Phase 2 applies to osimertinib only.

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