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Observational, Real World Study of Osimertinib for Patients with Locally advanced/Metastatic T790M Mutation-Positive An observational, retrospective study conducted among locally advanced or metastatic T790M mutation-positive NSCLC patients progressed after EGFR TKI treatment to evaluate osimertinib effectiveness in a real world settingNSCLC progressed on previous EGFR TKI

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1 Works for me dx.doi.org/10.17504/protocols.io.2qygdxw

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ABSTRACT

EGFR tyrosine kinase inhibitor (TKI) can significantly improve objective response rate (ORR) and prolong progression free survival (PFS) in EGFR mutated locally advanced or metastatic NSCLC patients compared to platinum-based chemotherapy, with less adverse events and higher quality of life (QoL).Osimertinib is an oral, potent, irreversible third-generation EGFR TKI that is selective for EGFR TKI sensitizing mutation and the T790M resistance mutation. Two phase 2 studies(AURA extension, AURA2)have demonstrated encouraging efficacy and tolerable toxicity.However, local data reflecting testing status including testing platform, sample tested, and turnaround time in China is still lacking. The current study will not only assess the effectiveness of osimertinib treatment in a real world setting, but will also help us to understand the real-world testing patterns among T790M mutation positive locally advanced or metastatic NSCLC patients who have progressed after EGFR TKI treatment.

Objectives and Hypotheses:

The objective of this study is to assess osimertinib effectiveness among locally advanced or metastatic T790M mutation positive NSCLC patients who have progressed after EGFR TKI therapy.

The specific study objectives that will be assessed include the following:

Primary Objective

§ To assess the real world effectiveness of osimertinib treatment in locally advanced or metastatic NSCLC patients with a EGFR T790M mutation in terms of response rate (RR)

Secondary Objectives

§ To assess the real world effectiveness of osimertinib treatment in locally advanced or metastatic NSCLC patients with a EGFR T790M mutation in terms of progression free survival (PFS)

§ To describe the pattern of T790M mutation testing, including turnaround time, sample type, testing techniques, EGFR subtype, T790M mutation abundance if tested quantitatively.

§ To assess the real world safety profile of osimertinib

§ To describe the treatment pattern including treatment lines and combination therapy (radiotherapy, surgery, etc.) in a real world setting

EXTERNAL LINK

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THIS PROTOCOL ACCOMPANIES THE FOLLOWING PUBLICATION

Cao Y, Qiu X, Xiao G, Hu H, Lin T (2019) Effectiveness and safety of osimertinib in patients with metastatic EGFR T790M-positive NSCLC: An observational real-world study. PLoS ONE 14(8): e0221575. doi: 10.1371/journal.pone.0221575

1 **Study Timetable and Early Termination of Enrolment and Study**

The end of the study is defined as 'the last visit of the last patient undergoing the study'. Thestudy is expected to start in Quarter 1 2017 and to end by Quarter 3 2017

AstraZeneca reserves the right to terminate the enrolment of the study. Should AstraZeneca decide to discontinue the study prior to what was established in this protocol, the investigator, and relevant authorities should receive written notice describing the reasons why the study was terminated at an earlier date.

2 **Data Collection**

Data will be entered in the web-based data capture (WBDC) system at the Investigator's site. The Investigator (or delegate) will be responsible for entering data into the WBDC system and according to the Investigator Instructions Manual. The Investigator Instructions Manual will also provide the study site with data entry instructions.

Data entered in the WBDC system will be immediately saved to a central database and changes tracked to provide an audit trail. When data have been entered, reviewed and edited, the Investigator will be notified to sign the CRF electronically as per the agreed project process. A copy of the CRF will be archived at the Investigator's site.

3 **Monitoring**

Before the first subject is recruited into the study, the local Marketing Company, MEOR Delivery Director, MEOR Operations Lead or CRO Representative will:

- Establish the adequacy of the facilities and the investigator's capability to appropriately select the sample
- Discuss with the investigator(s) (and other personnel involved with the study) their responsibilities with regards to protocol compliance, and the responsibilities of AstraZeneca or its representatives. This will be documented in an Observational Study Primary Agreement between AstraZeneca/delegate and the investigator.

During the study the local MC representative or delegate can implement different activities to assure compliance with AZ standards of quality. These activities could include but are not limited to:

Contacts with the sites to:

- Provide information and support to the investigator(s)
- Confirm that the research team is complying with the protocol and that data are being accurately recorded in the case report forms (CRFs)
- Ensure that the CRFs are completed properly and with adequate quality.

Monitoring activities for:

- Checking that subjects exist in medical records

The extent and nature of monitoring will be decided during the study planning based on design, complexity, number of subjects, number of sites, etc. Observational Research Center (multi country) /Marketing Company (MC) will give some recommendations that could be locally adapted.

Different signals (e.g., high rejection rate in a site) should be used as potential identification of low protocol compliance by investigators.

If these or any other signal occurs or if the local coordinator is suspicious of a potential non-optimal level of protocol compliance by the site investigator, specific measures should be adopted to evaluate the situation, identify the issue and implement specific action plans to correct the situation.

4 **1.1.1 Patient Informed Consent**

Unless waived by ethic committee, the investigator at each site will ensure that the patient is given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the Non-Interventional Study. Subjects must also be notified that they are free to discontinue from the Non-Interventional Study at any time. The patients should be given the opportunity to ask questions and allowed time to consider the information provided.

Unless waived by ethic committee, the signed and dated patient informed consent must be obtained before any specific procedure for the Non-Interventional Study is performed, including:

· Interview with the investigator

· Fulfil the questionnaires

· CRFs completion.

The Investigator must store the original, signed Patient Informed Consent Form. A copy of the signed Patient Informed Consent Form must be given to the patient.

5 The investigator is responsible for reporting all ADRs, SAEs and AESI specified in the following 6.3.2 Definition of SAE, 6.3.3 definition of AESI section and 6.3.4 definition of ADR section, ensuring that all staff involved in the study is familiar with the content of this section.There is no regional regulation requirement to report AEs to health authority in Macau.

6 All AEs specifically defined in Table 6 study plan will be collected in theeCRF.
For each AE the following variables will be collected as described in section 4.2;
· AE diagnosis/description
· The date when the AE started and stopped
· maximum intensity
· max CTCAE grade
· Whether the AE is serious or not
· Whether the AE is AESI (defined as interstitial lung disease/ pneumonitis-type events, QTc-prolongation events)
· Investigator causality rating against osimertinib (yes or no)
· Action taken with regard to medicinal product
· Outcome
It is important to distinguish between serious and severe AEs. Severity is a measure of intensity whereas seriousness is defined by the criteria in Sections 6.3.2 An AE of severe intensity need not necessarily be considered serious. For example, nausea that persists for several hours may be considered severe nausea, but not a SAE unless it meets one of the criteria shown in Section 6.3.2. On the other hand, a stroke that results in only a limited degree of disability may be considered a mild stroke but would be a SAE if it satisfies one of the criteria shown in Section 6.3.2.

7
The Investigators or other site personnel will inform the appropriate AstraZeneca representatives within one day i.e., immediately but **no later than 24 hours** of when he or she becomes aware of any AE.
The designated AstraZeneca representative works with the Investigator to ensure that all the necessary information is provided to the AstraZeneca Patient Safety data entry site **within 1calendar day** of initial receipt for fatal and life threatening events **and within 5 calendardays** of initial receipt for all other serious ADRs.
For all collected AEs, where important or relevant information is missing, active follow-up is undertaken immediately.
Investigators or other site personnel inform AstraZeneca representatives of any follow-up information within the same timeframe as the original report.
All collected adverse events will be summarised in the final study report.