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Personally identifiable information (PII) within this document is either removed or redacted (i.e., specific content is masked irreversibly from view with a black bar) to protect personal privacy. Personally identifiable information includes:

- All named persons associated with the study
- Patient identifiers within text, tables, or figures
- By-patient data listings

Anonymized patient data may be made available subject to an approved research proposal submitted. Information which is considered intellectual property or company confidential was also redacted.

1.0 ABSTRACT

Title

A Cohort Study to Describe the Occurrence of Early-Onset Pulmonary Events in Patients with Anaplastic Lymphoma Kinase-Positive Advanced Non-Small Cell Lung Cancer Treated with Brigatinib: A Post-Authorisation Safety Study

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Safety Pharmacoepidemiology

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Keywords

anaplastic lymphoma kinase-positive, non-small cell lung cancer, early-onset pulmonary events, brigatinib, post-authorisation safety study

Rationale and Background

At the request of European Medicines Agency, this post-authorisation safety study was undertaken to provide real-world evidence for the characterization of the occurrence of early-onset pulmonary events (EOPEs) in the European Union (EU) setting and the effectiveness of the brigatinib (Alunbrig) Patient Alert Card (PAC) among anaplastic lymphoma kinase-positive (ALK+) advanced non-small cell lung cancer (NSCLC) patients treated with brigatinib in Europe.

Research Question and Objectives

The primary objective of this study was to describe the occurrence of EOPEs in ALK+ advanced NSCLC patients treated with brigatinib in real-world practice.

The secondary objectives were:

To describe EOPE risk factors.

To assess the effectiveness of the PAC as a risk minimization measure.

Study Design

This was a non-interventional, observational study of ALK+ advanced NSCLC patients treated with brigatinib in real-world practice. Patients participated in the study for up to 42 days following brigatinib treatment initiation.

Pulmonary events occurring between Day 1 to Day 14 post brigatinib treatment initiation were considered as adverse events of special interest (AESI). Their occurrence could be reported at any time during the study period. An independent adjudication committee has

reviewed all reported pulmonary events to determine, if they meet protocol-defined endpoint of EOPEs.

The receipt, understanding, and use of the PAC was assessed via a phone-based interview that took place 30 days after brigatinib treatment initiation.

Setting

This study was conducted in 10 countries: Austria, Denmark, Finland, France, Germany, Ireland, Italy, the Netherlands, Norway, and the United Kingdom. Patients were recruited only after their healthcare professional/patient decided to proceed with brigatinib.

Subjects and Study Size, Including Dropouts

The study included patients aged 18 years or older, diagnosed with ALK+ advanced NSCLC, and initiating brigatinib monotherapy as per the recommended indication.

This study planned to enroll 120 patients initiating treatment with brigatinib. Patient recruitment continued until 19 February 2024 as required in the protocol, since the number of confirmed EOPEs in this study was fewer than 8.

Variables and Data Sources

Patient demographics,

ALK+ NSCLC characteristics,

Clinical management and medical/medication history,

Vital signs,

Smoking status and alcohol use,

Treatment exposure of brigatinib,

EOPE, and

PAC questionnaire: (1) Receipt, (2) Understanding, and (3) Utilization of Alunbrig PAC by the patients.

Results

Out of 100 patients screened, 98 patients were enrolled in the study. Half of the enrolled patients were female (n=49, 50.0%), and 60 (61.2%) were under the age of 65 years. Eighty (88.9%) patients had Stage IV NSCLC at study entry. During the entire study period, the predominant dose pattern was starting with 90 mg daily dose and then transitioning to 180 mg daily (n=77, 78.6%).

There were no confirmed EOPEs in the study. Of the 98 patients enrolled, 11 pulmonary events defined as AESIs were reported. These events were evaluated by an independent adjudication committee, which did not confirm these events as EOPEs.

Of the 98 patients enrolled, 37 (37.8%) patients agreed to participate in the PAC interview. Of the 37 responders, 23 (62.2%) received the PAC, 21 (56.8%) confirmed that they read the PAC, while 5 (13.5%) showed better understanding of the PAC. There were differences observed in the understanding of the PAC among different age groups, which was evident in the question regarding the potential for fever during brigatinib treatment. Only 2 (13.3%) out of 15 patients aged ≥65 years provided a correct response, while 10 (45.5%) out of 22 patients aged <65 years correctly answered the question, suggesting patient aged 65 and older (target population for lung cancer) were less likely to answer these questions correctly.

Discussion

All AESIs in the study were evaluated by the external adjudication committee using a rigorous set of criteria to determine if these events were confirmed EOPEs. None of the 11 AESIs in the study were confirmed as EOPEs by the adjudication committee. The study demonstrated high relative dose intensity indicating that patients were given the recommended dose, and lack of confirmed EOPE was not attributable to underdosing.

The assessment of the PAC effectiveness did not meet the threshold of 75% per the study protocol. Participation in the PAC questionnaire interview was not mandatory, and more than half of the patients in the study declined to participate.

There were no confirmed EOPEs or new safety concerns identified in the study.

Marketing Authorization Holder(s)

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Not applicable.