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Clinical Study Synopsis for Public Disclosure

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1. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: GIOTRIF®			
Name of active ingredient: Afatinib (L01XE13)			
Report date: 25 Jan 2022	**Study number:** BI 1200.247	**Version/Revision:** 1.0	**Version/Revision date:** NA
Title of study:	A multicentre, cohort study to assess the impact on SYMptom burden and patient health-related quality of Life of afatinib treatment in advanced non-small cell lung cancer in a real world setting in Greece. The 'SYM-Less' study		
Keywords:	Non-small cell lung cancer (NSCLC), afatinib, real-world evidence, health-related quality of life (HRQoL), Average Symptom Burden Index (ASBI) of Lung Cancer Symptom Scale (LCSS)		
Rationale and background:	There is limited real-world evidence of afatinib outcomes in NSCLC patients.		
Research question and objectives:	The study primarily aimed at assessing the impact of afatinib on patient-reported lung cancer-specific symptom burden using the ASBI of the LCSS, after 6 months of therapy. The main secondary objectives included the evaluation of the impact of afatinib on total symptomatic distress, functional activity, and global QoL (using the LCSS), and on the generic HRQoL (using the EQ-5D-3L questionnaire), as well as the assessment of treatment adherence and the description of patterns of afatinib use in terms of treatment modifications, and reasons for these modifications, in a representative sample of EGFR-TKI naïve subjects with locally advanced or metastatic NSCLC in real-life clinical settings in Greece.		
Study design:	Non-interventional, multicentre, prospective study including a minimum 12-month and a maximum 48-month observation period.		
Setting:	The study was conducted in 7 Oncology and Pulmonology hospital centres/clinics in Greece. The 77 eligible patients analysed were enrolled over a 47.5-month recruitment period [from 01 March 2016 (first patient first visit) to 18 February 2020 (last patient first visit)]. The overall study duration until study completion (last patient last visit) was 59.5 months [from 01 March 2016 to 17 February 2021]		
Subjects and study size, including dropouts:	The study eligible population included 77 patients of whom 53 comprised the per protocol set used for the primary objective analysis. Of the patients, 81.8% (63/77) were withdrawn after a median of 10.6 months, mainly due to afatinib treatment discontinuation (73.0%) and loss to follow-up (15.9%).		

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Variables and data sources:	Primary data were collected prospectively during the study visits through patients' interview and patient reported outcomes (LCSS patient scale and EQ-5D-3L) or as performed per standard clinical practice.		
Results:	Eligible patients (all Caucasians; 62.3% females; median age at enrolment 68.4 years; 66.2% suffered from at least one comorbidity) were followed for a median of 12.6 months. All but one of evaluable patients (98.7%; 75/76) had adenocarcinoma. At baseline, 90.9% (70/77) had stage IV [63.6% (49/77) had M1b], with most common metastatic sites being the bones (65.3%; 32/49), and the brain (34.7%; 17/49). Exon 19 deletion (44.2%) and exon 21 L858R (28.6%) were the most common mutations. Of the patients, 74.0% (57/77) had not received any prior systemic treatment for NSCLC. At baseline, 88.3% (68/77) of the patients had ECOG PS 0-1 [59.7% (46/77) had ECOG PS0], whereas the median LCSS total, ASBI, EQ-VAS, and EQ-5D utility index scores were 14.9, 12.3, 80.0, and 0.76, respectively. Of the evaluable patients, 78.9% (60/76) had low baseline symptom burden (ASBI score <25). Afatinib starting dose was 40 mg once-daily for all patients. During the follow-up period, 20.0% (13/65) of the evaluable patients reported missing > 1 afatinib tablet with a total of 194 afatinib tablets missed over the 32,043 planned to be received, resulting in a median adherence ratio of 1.0. In addition, 72.7% (56/77) of the patients permanently discontinued afatinib after a median of 9.3 months mainly due to 'disease progression' (76.8%; 43/56), and 'adverse event other than disease progression' (12.5%; 7/56). Temporary treatment interruptions and dose decreases were reported for 33.8% (26/77) of the patients each, mainly due to 'adverse event/disease progression' in 31.2% (24/77) and 29.9% (23/77) of the patients, respectively. Among patients with two consecutive LCSS-ASBI assessments over the 6 months post-baseline, 24.5% (13/53; 95%CI:12.9%-36.1%) achieved a decrease in baseline ASBI ≥10 in the mean of two consecutive post-baseline assessments (median time to achievement: 2.1 months), whereas 60.4% (32/53; 95%CI:47.2%-73.5%) had a stable and 15.1% (8/53; 95%CI:5.5%-24.7%) a deteriorated symptom burden. Excluding all patients with baseline score <10, unless they had an ≥10 increase in baseline ASBI, the relevant symptom improvement rate increased to 41.9% (13/31; 95%CI:24.6%-59.3%). No statistically significant change from baseline was observed in EQ-VAS or EQ-5D utility index score at any of the post-baseline timepoints except for the 18- and 24-month		

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	timepoints where the median baseline EQ-VAS significantly declined by a median of 2.0 points at both timepoints. At study participation completion, 76.5% (52/68) of patients had retained or improved their baseline ECOG PS. (N)SADR rate excluding disease progression was 71.4% (55/77), including four serious events experienced by three patients. Six patients died during the study observation period for reasons unrelated to afatinib.		
Discussion:	The results of this study provide real-world evidence on the clinical and patient-reported outcomes of treatment with afatinib in routine care settings of Greece. Although almost 8 in 10 patients (~79%) had low symptom burden at baseline as assessed by the LCSS ASBI, in the majority of the evaluable patients baseline symptom burden was maintained (in 6 out of 10) or improved (in 1 out of 4) over the 6-month treatment period. Furthermore, neither ASBI nor LCSS total score showed any statistically significant change from baseline at any of the post-baseline study timepoints examined. Similarly, albeit generic HRQoL was not markedly impaired at baseline, no significant changes were observed at most of the post-baseline timepoints. In regards to ECOG PS, approximately 9 in 10 (88%) patients had PS 0/1 at baseline, yet almost 8 in 10 (~77%) retained or improved their baseline PS at the end of study participation. The above findings were accompanied by high treatment adherence and a predictable and manageable safety/tolerability drug profile.		
Marketing Authorisation Holder(s):	Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 Ingelheim, Germany		
Names and affiliations of principal investigators:	The names and affiliations of the study principal investigators are kept in the trial master file and can be provided upon request.		