BrigALK2 study: a multicentric real-world study evaluating brigatinib in ALK positive advanced pretreated non-small-cell lung cancers: long-term follow-up, with focus on lorlatinib efficacy after brigatinib.

#2920P

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Background:

- Brigatinib is a next-generation ALK inhibitor (ALKi), initially developed in ALK+ non-small-cell lung cancer (NSCLC) pretreated with crizotinib. Based on ALTA-1L results (1), Brigatinib was approved in Europe in April 2020 for patients with treatment-naïve advanced ALK-positive NSCLC
- In France, brigatinib was available through an early access program (EAP) from 1st August 2016 to 21st January 2019 for patients with ALK-positive NSCLC refractory to crizotinib and ceritinib. This program closed following the European approval of brigatinib post-crizotinib.
- BrigALK study analyzed ALK-positive advanced NSCLC patients enrolled in the brigatinib French EAP. First published results after 104 patients were enrolled demonstrated the efficacy of brigatinib in a cohort of pretreated advanced ALK+ NSCLC (2).

Patients and methods:

- BrigALK study (GFPC 07-2017) was a national non-interventional study that retrospectively included advanced ALK+ NSCLC pretreated with at least one ALKi during brigatinib EAP (up to January 1st, 2019). Primary endpoint was investigator-assessed progression-free survival (invPFS).
- **BrigALK2** study covered the entire EAP period and was an update of abstract 1392P presented at ESMO 2020 with a longer follow-up and a focus on lorlatinib efficacy after brigatinib.

Inclusion criteria

- advanced NSCLC
- FISH a/o IHC ALK positive
- > 18 years old
- previous treatment with at least one ALK inhibitor

Treatment

Brigatinib 180 mg/day with a 7-days lead–in at 90 mg/day

Objectives

Primary: median investigator-assessed PFS from brigatinib initiation (minvPFS)

Secondary: Overall response Rate (ORR), Overall Survival (OS) from brigatinib initiation and from NSCLC diagnosis, duration of treatment (DoT), subsequent lines post-brigatinib.

Results:

- 183 patients were included from 66 GFPC-affiliated or associated centres in France between August 1st, 2016, and January 21st, 2019.
- At the time of data cut-off (01/02/2021):
  - median duration of follow-up was 40.5 months (range: 38.4-42.4)
  - 21 patients (11,5%) were still on treatment.
- Before brigatinib:
  - Patients received a median of 3 lines (range 1-6) and were preteated with a median number of 2 ALKi (crizotinib: 91.8%, ceritinib: 85.3%, alectinib: 9.2%).
  - The most frequent sequences were 2 (mainly, crizotinib-ceritinib. N= 36 (19.5%)) or 3 lines (mainly, chemotherapy-crizotinib-ceritinib. N= 49 (26.6%)).
  - 129 patients (70.1%) were treated with prior chemotherapy before brigatinib.
- Brigatinib therapy:
  - 14 patients (8,2%) received brigatinib in 2nd line, 44 (23,9%) in 3rd line, 74 (40,2%) in 4th line and 51 (27,7%) in 5th line.
  - 175 patients (95,6%) received brigatinib at 180 mg/day with a 7-days lead–in of 90 mg/j. 37 (20.1%) patients underwent dose adjustments without definitive interruption due to intolerance or patient request and 19 (10.3%) had a permanent discontinuation due to adverse events or patient wishes.

Table 1: Baseline characteristics at brigatinib initiation

	N= 183 (%)
Date of NSCLC diagnosis before 2015	94 (51.1)
Age, years	60 +/- 12.7
Gender male/female n(%)	74 (40.4) / 109 (59.6)
Smoking active/former/non n(%)	15 (8.1), 56 (30.4), 104 (56.5)
Stage 4, n(%)	180 (97.8)
ECOG PS 0 / 1, n(%)	92 (50%)
≥ 3 metastatic sites, n(%)	121 (67.6%)
Brain metastases, n(%)	131 (71.1)

Table 2: Efficacy of brigatinib

	N= 183 (ITT)
Median follow-up, months (95%CI)	40.5 (38.4-42.4)
Median invPFS, months (95%CI)	**7.3 (5.9-9.6)**
mDoT, months (95%CI)	
Overall population	**7.3 (5.8-9.4)**
1 ALKi before brigatinib (n= 22)	12.9 (3.8-25.2)
2 ALKi before brigatinib (n= 146)	7.4 (5.6-9.9)
3 ALKi before brigatinib (n= 15)	4.9 (1.7-9.3)
mOS from brigatinib start, months (95%CI)	
Overall population	**20.3 (15.6-27.6)**
1 ALKi before brigatinib (n= 22)	33.0 (9.7-NR)
2 ALKi before brigatinib (n= 146)	20.3 (15.7-28.7)
3 ALKi before brigatinib (n= 15)	18.1 (3.3-24.5)
ORR, n(%)	75 (44.3)
Disease control rate, n (%)	125 (74.2)

Therapy post-brigatinib. Focus on lorlatinib

- 106 (57.6%) patients received at least one subsequent therapy after brigatinib. Clinical data could be obtained for 92 (86,8%) of them.
- 68 (64.1%) patients were treated with lorlatinib post-brigatinib: most patients (n= 51, 75%) received lorlatinib immediately after brigatinib. 17 patients were treated with lorlatinib after the sequential administration of another second-generation ALKi + chemotherapy (figure 1).
- Time from advanced NSCLC diagnosis and lorlatinib start was 52.8 months (43.2-60.3).

Figure 1: therapeutic sequences after brigatinib

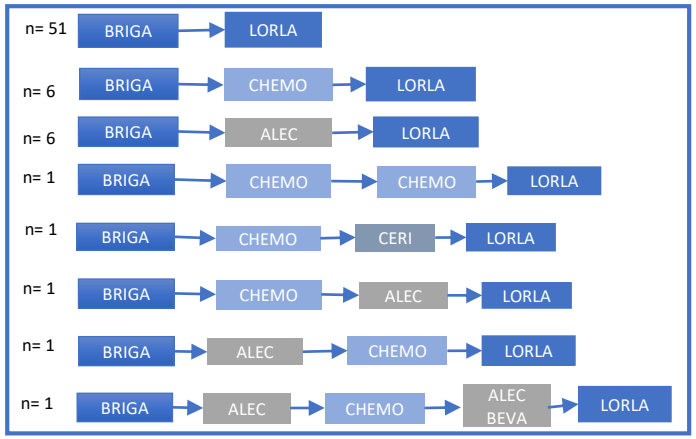

Table 3: Lorlatinib post-brigatinib

	N= 68
mFollow-up, months	29.9 (25.7-33.1)
mDoT, months	**5.3 (3.7-8.7)**
mOS from lorlatinib start	**14.1 (10.3-19.2)**

Conclusion: The analysis of the EAP confirms the effectiveness of brigatinib in a cohort of heavily pretreated ALK-positive aNSCLC patients and the activity of subsequent ALKi after brigatinib.

(1) Camidge DR, Kim HR, Ahn MJ, et al. Brigatinib versus Crizotinib in Advanced ALK Inhibitor-Naive ALK-Positive Non-Small Cell Lung Cancer: Second Interim Analysis of the Phase III ALTA-1L Trial. J Clin Oncol. 2020 Nov 1;38(31):3592-3603.

(2) Descourt R, Perol M, Rousseau-Bussac G et al. Brigatinib in patients with ALK-positive advanced non-small-cell lung cancer pretreated with sequential ALK inhibitors: A multicentric real-world study (BRIGALK study). Lung Cancer. 2019 Oct;136:109-114.

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