BrigAlec study – Focus on alectinib efficacy after brigatinib exposure in BrigALK2 study (GFPC 02-2019)

#3830

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Background:

- Brigatinib and alectinib are both next-generation ALK inhibitor (ALKi) and first-line standard of care options in advanced ALK-rearranged NSCLC patients (ALK+ aNSCLC), with efficacy established by phase 3 trials (1;2).
- In the management of ALKi therapeutic sequence, many questions remain about the efficacy of second-generation ALKi in the event of discontinuation due to progression or toxicity of a previous second-generation ALKi.
- The objective of BrigAlec was to describe in a real-world setting the efficacy of alectinib post-brigatinib in patients with advanced NSCLC harboring *ALK* rearrangement, pretreated with at least one ALK inhibitor.

Patients and methods:

- BrigAlec is an ancillary study of BrigALK2 that made a focus on alectinib efficacy after brigatinib treatment, according to post-brigatinib treatment line in BrigALK2.
- BrigALK2, a national non-interventional multicenter study, evaluated brigatinib efficacy in 183 ALK+ aNSCLC patients. pretreated with at least one ALK inhibitor (ALKi), during brigatinib French early access program, from 1st August 2016 to 21st January 2019 (3).
- Patient characteristics, alectinib duration of treatment (DOT) and progression-free survival according to investigators (invPFS), response rate, disease control rate and reasons for discontinuation were collected from the medical files

Results:

- 92 (50,3%) patients received ≥ 1 agent(s) post-brigatinib.
- 30 (16,4%) received alectinib regardless of treatment line post-brigatinib.
- 19 were treated with alectinib immediately after brigatinib (*brigatinib-alectinib sequence*) and 11 following at least one line of treatment (chemotherapy (chemo) or another ALKi: *brigatinib-X-alectinib sequence*). table 1.
- At data cut-off (07/07/2022), median follow-up was 25,5 (95% CI: 10,6-30,5) months.
- Data about mutations of resistance post-brigatinib exposure were very scarce and not usable.

Table 1	N= 30 BrigAlec patients	
Age, med, years	54	
Sex, women	63,3%	
Histology, adenocarcinoma	100%	
Median brigatinib DOT, months	13,6	
Median brigatinib invPFS, months	10,9	
Main post-brigatinib progression site, rate	Brain, 71 % (carcinomatous meningitis, 20%)	
Therapeutic sequences	*Brigatinib-alectinib* N= 19	*Brigatinib-X-alectinib* N= 11
Treatment lines before alectinib, med	4	
TKI before alectinib, med	3	
Reasons for brigatinib discontinuation	Progression: n= 14 Toxicity: n= 5	

- For patients treated according to *brigatinib-alectinib sequence* (table 1):
  - mDOT, minvPFS and mOS were 7,1 (95%IC: 2,1-18,2), 4,8 (95%CI 2,0-12,5) and 27 (95%CI: 12,5-NR) months, respectively, from the start of alectinib.
  - Response and disease control rates were 25% and 60% respectively.
  - Among this subgroup, reasons for discontinuation were toxicity for 5 patients: with a mDOT and minvPFS of 18,2 (95%CI 3,4-21,6) and 12,5 (95%CI: 3,3-17,9) months. 14 patients discontinue brigatinib due to progressive disease, with a mDOT and minvPFS of 5,7 (95%CI: 0,9-10,6) and 3,4 (95%CI 0,9-9,2) months.

- For patients treated according to *brigatinib-X-alectinib sequence* (table 1):
  - mDOT, mPFS and mOS were 11,7 (95%CI: 0,7-21,5), 5,0 (95%CI 0,5-18,8) and 16 (95%CI 2,3-NR) months, respectively, from the start of alectinib.
  - Responses and disease control rates were 10 and 30%, respectively.

Table 2	Patients treated with alectinib post-brigatinib : n= 30			
	Brigatinib-alectinib sequence n= 19			*Brigatinib-X-alectinib sequence* n= 11
	Overall	Brigatinib discontinuation due to toxicity n= 5	Brigatinib discontinuation due to progression n= 14	
mDOT, months	7,1 (2,1-18,2)	18,2 (3,4-21,6)	5,7 (0,9-10,6)	11,7 (0,7-21,5)
mPFS, months	4,8 (2-12,5)	12,5 (3,3-17,9)	3,4 (0,9-9,2)	5,0 (0,5-18,8)
mOS, months	27,0 (12,5-NR)			16 (2,3-NR)
RR, %	25			10
DCR, %	60			30

Conclusion: According to our retrospective real-life study, alectinib after brigatinib treatment remains an option in metastatic *ALK*+ NSCLC, especially if brigatinib is discontinued due to toxicity.

(1) Brigatinib Versus Crizotinib in ALK Inhibitor-Naive Advanced ALK-Positive NSCLC: Final Results of Phase 3 ALTA-1L Trial. Camidge et al. J Thorac Oncol. 2021 Dec;16(12):2091-2108

(2) Updated overall survival and final progression-free survival data for patients with treatment-naive advanced ALK-positive non-small-cell lung cancer in the ALEX study. Mok et al. Ann Oncol. 2020 Aug;31(8):1056-1064.

(3) Brigatinib for Pretreated, ALK-Positive, Advanced Non-Small-Cell Lung Cancers: Long-Term Follow-Up and Focus on Post-Brigatinib Lorlatinib Efficacy in the Multicenter, Real-World BrigALK2 Study. Descourt et al. Cancers (Basel). 2022 Mar 30;14(7):1751

R. Descourt disclosures : Takeda, Roche, BMS, MSD, Astrazeneca.. **Funding**: *Academic grant from Takeda*

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