Abstract 9092: Alectinib activity in ALK+ metastatic non-small cell lung cancer (NSCLC) patients: a national real world analysis (explore ALK, cohort A, GFPC 03-2019)

Authors: Aurélie Swalduz[1], Gaelle Rousseau-Bussac[2], Florian Guisier[3], Hélène Doubre[4], Pierre Fournel[5], Lionel Falchero[6], Laurence Bigay Game[7], Remi Veillon[8], Marie Marcq[9], Charles Ricordel[10], Chantal Decroisette[11], Domitille Dano[12], Grégoire Justeau[13], Stéphanie Martinez[14], Alexis Cortot[15], Hugues Morel[16], Laurent Greillier[17], Renaud Descourt[18]

Affiliations: [1] Léon Bérard Cancer Center, Lyon, France; [2] CHIC Créteil, Créteil; [3] CHU Rouen, Rouen; [4] Hôpital Foch, Suresnes; [5] CHU St Etienne, St Etienne; [6] L'Hôpital Nord-Ouest, Villefranche Sur Saône; [7] CHU Toulouse, Toulouse; [8] CHU Bordeaux, Bordeaux; [9] CHD Vendée, La Roche sur Yon; [10] CHU Rennes, Rennes; [11] CH Annecy-Genevois, Pringy; [12] Institute Paoli Calmette, Marseille; [13] CHU Angers, Angers; [14] Aix-en-Provence Hospital, Aix-en-Provence; [15] CHU Lille, Lille; [16] CHR Orléans, Orléans; [17] Hôpital Nord, Assistance Publique-Hôpitaux de Marseille, Marseille; [18] CHU Morvan, Brest

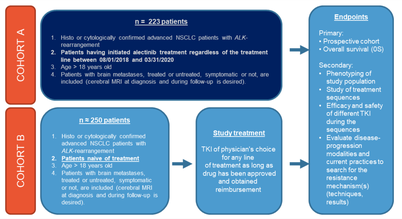
GFPC
Groupe Français de Pneumo-Cancérologie
French Lung Cancer Group

Background and objectives

- **Alectinib is a standard of care option in advanced ALK-rearranged (ALK+)** NSCLC patients, with efficacy established by phase 3 trials, in 1st-line and beyond. In the ALEX trial[1] evaluating alectinib in 1st-line versus crizotinib and including ≥ 50% of Caucasians PS0-2 with 42% of asymptomatic brain metastases, mPFS was 34.9 m and mOS was not reached. In the 2 randomized studies ALUR[2] evaluating alectinib vs chemotherapy post-crizotinib the mPFS was 10.9 m and in ALTA-3[3] comparing brigatinib and alectinib post-crizotinib the mPFS was 19,2 m (95%CI 12.9-NE).
- There are few efficacy data in unselected populations.
- **The objective of this study was to evaluate the efficacy of alectinib in real-world setting.**

Methods

- Explore ALK is a **French, non-interventional, multicenter study** constituted of two parts and including ALK-positive NSCLC patients:
  - Cohort A including patients treated with alectinib since its marketing authorization in France (08/01/2018) until 03/31/2020. All ALK+ advanced NSCLC patients initiating alectinib, whatever the line, during this period were included.
  - Cohort B including patients treated with next-generation ALK inhibitor in 1st line (alectinib, brigatinib or lorlatinib) or other treatment after the 03/31/2020.
- Results presented here are the results of the cohort A.
- Patient characteristics, alectinib duration of treatment (DOT), progression-free survival assessed locally (rwPFS), overall survival (OS) according to the prescription line of alectinib, the presence of brain metastases at alectinib initiation, response rate and tolerance were collected from the medical files.



Results

Baseline patients' characteristics

- 223 patients among 33 centers were included in the cohort A.
- ALK characterization was performed by IHC in 130 (104 were 3+ positive) and by FiSH in 113 patients. Only 5 patients had RNAseq analyses.
- *ALK* fusion partner evaluated in 29 patients was *EML4* for 28 (v1:5; v2:4; v3:4; v5:1; other: 4) and DCTN1 for 1 patient. Only 20 patients had data available regarding c-mutations (3 *KRAS*, 2 *PIK3CA*, 6 *TP53* and 9 others).
- Alectinib was initiated as first-line treatment in 119 patients, 49 patients in second-line treatment and 25, 12 and 18 in 3rd-, 4th- and 5th or more lines respectively.

		N=223
Median age	years (range)	59 (22-101)
Sex female	N (%)	120 (53.8%)
Smoking history	N (%)	
Never		122 (54.7%)
Current		30 (13.4%)
Former		66 (29.6%)
Histology	N (%)	
Adenocarcinoma		212 (95%)
Squamous		4 (1.8%)
Other		7 (3.1%)
Actual stage (n=221)	N (%)	
IIIB		11 (5%)
IV		210 (95%)
PS (n= 193)	N (%)	
0		96 (43.1%)
1		70 (31.4%)
≥2		27 (12.1%)

	N=223
Number of metastatic sites (n=215)	N (%)
1	68 (31,6%)
2	55 (25,6%)
3	33 (15,3%)
≥3	59 (27,4%)
Metastatic sites at diagnosis	
Bones	88 (39,5%)
Lymph nodes	84 (37,7%)
Lung	74 (33,2%)
Pleura	74 (33,2%)
CNS	66 (29,6%)
Liver	46 (20,6%)
Adrenal glands	26 (11,6%)

Alectinib efficacy in first-line (n=119)

In first-line setting, after a median follow-up of 33.7 months (95%CI, 32.2-37.5), the median of rwPFS and DOT were 28.1 (95%CI, 20.7-40.4) and 26.9 (95%CI, 20.2-31.3) months, respectively. The median OS was not reach (NR), the 3-year OS rate was 72.1%. The rwPFS was not significantly different depending on whether or not the patient has brain metastases, 28.1 (95% CI, 14.5-NR) and 30.5 (85% CI, 18.9-40.4) months, respectively. Best responses and intra-cranial responses in evaluable patients are reported in table below.

		N=119
Best response (n, %)		
ORR		**(79%)**
	CR	(21%)
	PR	(58%)
DCR		**(96%)**
mDOR		27.4 (20-NR)
mDOT (median, 95%CI)		26.9 (20.2-31.3)
mPFS (median, 95%CI)		28.1 m (20.7-40.4)
12-months rate		70.7%
24-months rate		49.4%
36-months rate		38.7%
mOS (median, 95%CI)		NR
3-year OS rate		72.1%

	N=39 (%)
Best intra-cranial response	
CR	(26%)
PR	(46%)
SD	(23%)
Non evaluable	9

Figure 1: mPFS in first line

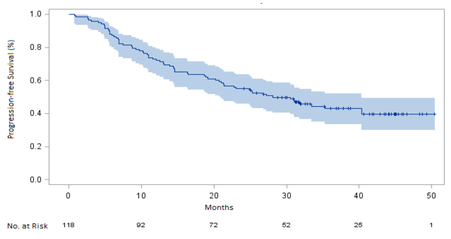
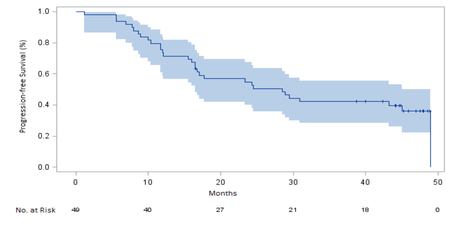


Figure 2: mPFS in second line



Exploration of resistance & perspectives

At the time of progression, 48.1% of patients had a new biopsy (66% of tissue biopsy). Analyses on molecular routine data collected for these cohort A are still on going. Prospective analyses will be performed in BioexALK study including patients of the cohort B of explore ALK who signed a consent for additional analyses on tissue at diagnosis and progressive disease and also on ctDNA at diagnosis, on treatment and at progression.
Data about treatment sequences will also be analyzed.

Alectinib efficacy in second-line and beyond (n=104)

Line of alectinib initiation	Median (95% CI)
2nd (n = 49)	
Duration of treatment	28,9 (17,7-40,6)
rw PFS	28,5 (16,5-49)
pts with cerebral metastasis (n= 23)	*30,9 (17-49)*
pts without cerebral metastasis (n = 26)	*16,8 (9,9-NR)*
OS	NR (NR-NR)
3-year OS rate	70.1%
Duration of first line treatment	
crizotinib (n=37)	*15 (10.4-24)*
others (n=6)	*2.1 (1-3.7)*
3rd (n = 25)	
Duration of treatment	20,6 (17,7-31,2)
rw PFS	19,6 (13,9-31)
OS	NR (36-NR)
3-year OS rate	70.6%
4th (n = 12)	
Duration of treatment	18,7 (1,7-32,7)
rw PFS	17,4 (2,2-22,5)
OS	35,1 (7,8-NR)
≥5th (n = 18)	
Duration of treatment	14,7 (3,1-29,4)
rw PFS	11,7 (3,1-21)
OS	40,1 (7,9-NR)

Tolerance

33% of patients had a grade 3 adverse event, resulting in a temporary interruption of treatment in 7.6% of cases and a permanent discontinuation in 5.9% of cases.

CONCLUSIONS:
In this large real-world, cohort of unselected advanced ALK+ NSCLC pts, alectinib initiated in first-line provides similar efficacy and safety results as obtained in phase III clinical trials.

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@AurelieSwalduz

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