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Feasibility and clinical relevance of *ALK*- and *ROS1*-fusion variant detection using liquid biopsy in advanced NSCLC

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No conflict of interest

ALK- and *ROS1*-fusion detection: from tissue to ctDNA

- Liquid biopsies are an alternative non-invasive approach for molecular characterization of non-small cell lung cancer patients.
  - Routinely validated for tumors harboring EGFR mutations

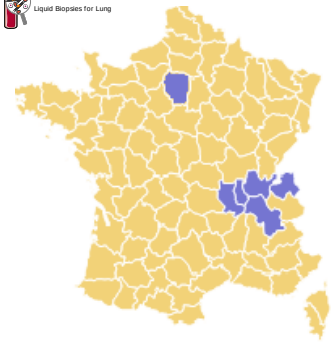
- No validated test for the detection of fusions on plasma cfDNA[1]
  - *ALK*-fusion was reported in small cohorts of patients using FISH in CTCs[2]
  - Two recent studies evaluated the feasibility of *ALK*-fusion detection by NGS in plasma [3,4]

- We report the results of the longitudinal ctDNA profiling of 128 NSCLC patients with either an *ALK*- or a *ROS1*-fusion

[1] MS Tsao et al. *IASLC guidelines*, 2016; [2] Pailler et al. *J Clin Oncol, 2013*; [3] C.McCoach et al. *Clin Cancer Res*, 2018; [4] I. Dagogo-Jack et al, *JCO Precis Oncol,* 2018

1. Enrollment

CENTRE LÉON BERARD
GUSTAVE ROUSSY CANCER CAMPUS GRAND PARIS
LIBIL Liquid Biopsies for Lung



128 advanced NSCLC pts ALK or ROS1 by FISH/IHC

- **101 ALK**
- **27 ROS1**

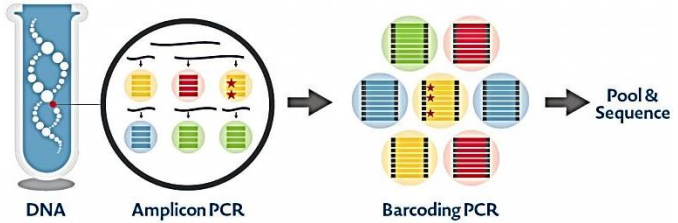
2. Sample Collection

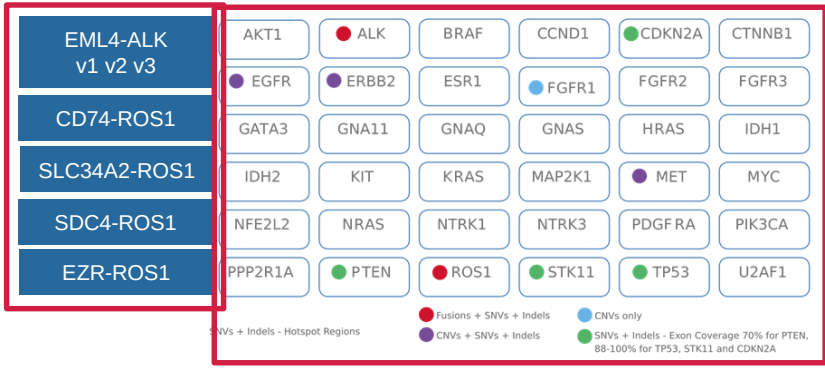
Samples	ALK	ROS1	TOTAL
Diagnosis	25	4	29
Stable disease	106	17	123
Partial and Complete Response	63	20	83
Disease progression	103	15	118
Total	297	56	353

Median sample number per pt: 2 (range: 1-13)

Median follow-up: 8.8months (range: 0-31months)

3. Inivata InVision Sequencing





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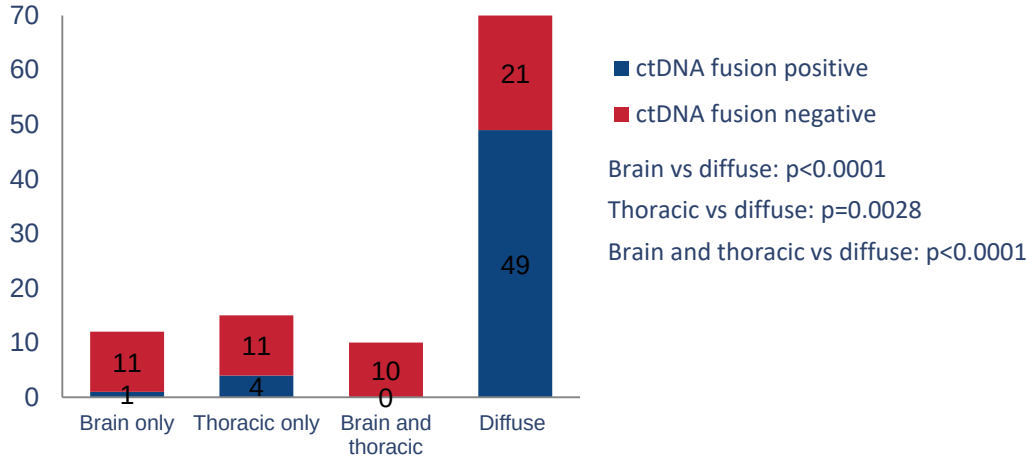
Baseline characteristics

Characteristics		ALK	ROS1
Total		**101**	**27**
Age (Mean (SD))		51.9 (14.1)	54.4 (13.7)
Sex: Female		59 (58.4)	13 (50.0)
Smoking status	Never	57 (57.6)	18 (69.2)
	Former / Current	42 (42.4)	8 (30.8)
Adenocarcinoma		97 (96.0)	25 (96.2)
Stage	I / II / IIIA	7	1
	IIIB / IV	74	21
Brain metastasis at baseline		30 (29.7)	5 (19.2)
FISH (+)		63 (62.4)	19 (70.4)
IHC (+)		80 (76.2)	15 (55.6)
Number of TKI :	1	27 (26.7)	15 (55.6)
	2	42 (41.6)	5 (18.5)
	3 or more	27 (26.8)	2 (7.4)
TKI	Crizotinib	86	18
	Ceritinib	61	2
	Brigatinib	13	0
	Alectinib	7	0
	Lorlatinib	31	8

Detection of fusion in plasma and clinical modifiers

- **At diagnosis (TKI-naïve patients):** ctDNA assay sensitivity was **67% (n=18/27)**[1]
- At progression: ctDNA fusion was detected in 47% of patients (n=47/100)

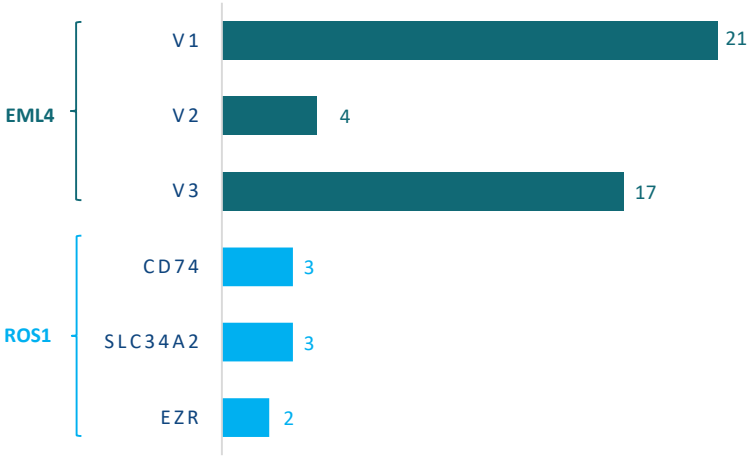
- 86.4% of patients with thoracic and/or cerebral exclusive disease have non detectable ctDNA fusion
- 92.4% of patients with detectable ctDNA fusions had diffuse metastatic disease



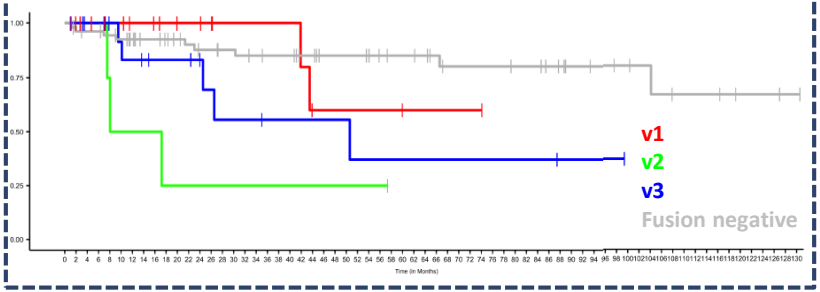
[1] Ortiz-Cuaran S and Swalduz A et al., *Longitudinal circulating-tumor DNA profiling of EGFR-mutated non-small cell lung cancer patients treated with EGFR-tyrosine kinase inhibitors,* AACR 2018

Fusion-variant identification in ctDNA and outcomes

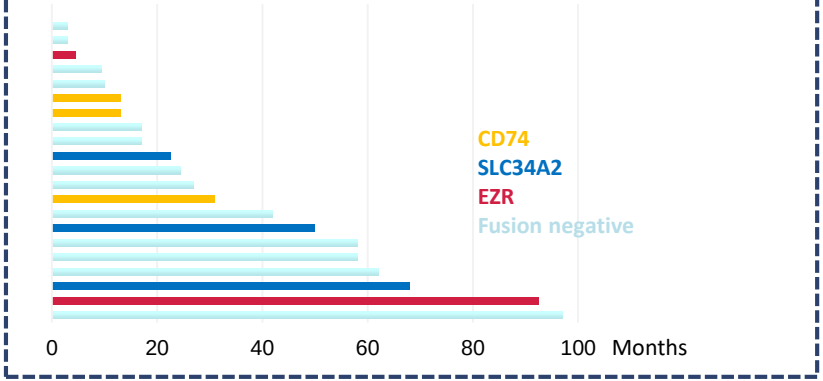
Fusion-variant identification



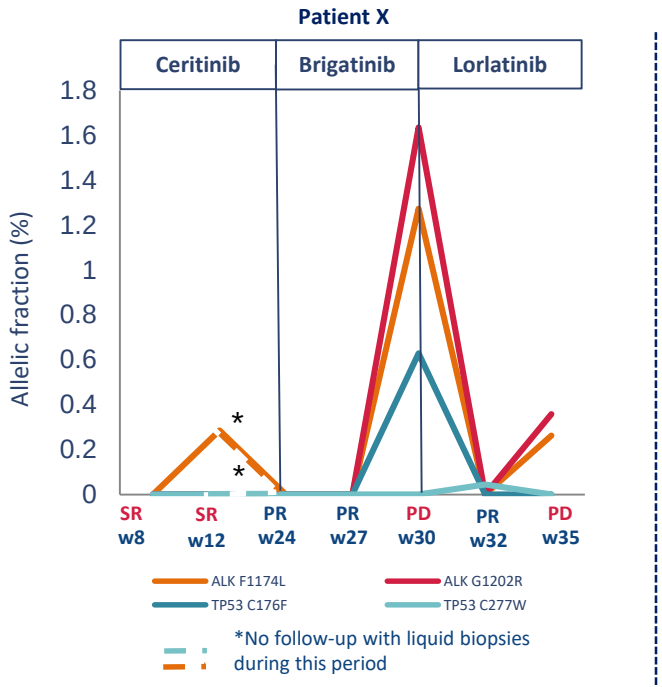
Overall survival according to ALK fusion-variant

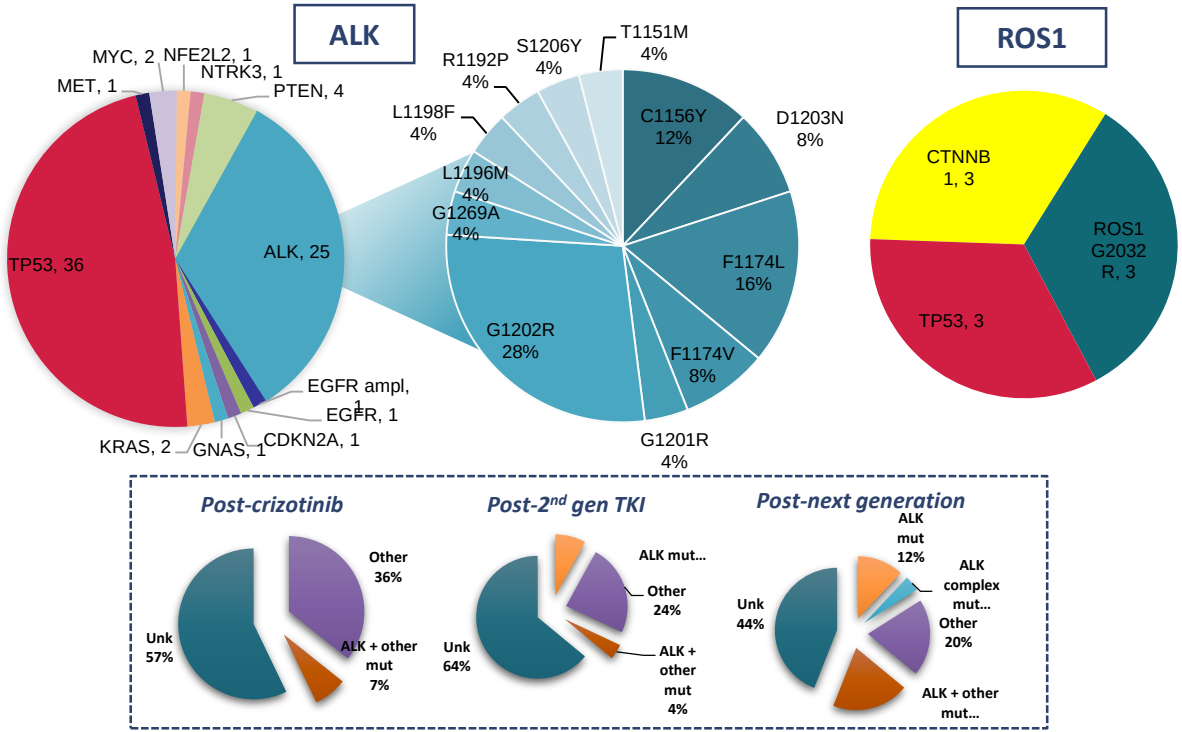


Overall survival according to ROS1 fusion-variant



Monitoring under treatment and characterization of the mutational profile at relapse





Mezquita L* Swalduz A*. *et al,* Poster P1.01-67, presented on September 24th

TAKE HOME MESSAGES

- Tissue remains the gold standard for *ALK*- and *ROS1*-fusion detection.

- Liquid biopsies in patients with tumors harboring fusion allows:
  - Good sensitivity of fusion detection in treatment-naïve patients. However, sensitivity was impacted by metastatic pattern.
  - Identification of the fusion partner which may have an impact on associated-resistance mechanisms and outcomes[1]
  - Good correlation between mutations in ctDNA and response to TKIs, which reinforces the role of liquid biopsies to guide treatment at relapse, avoiding iterative invasive biopsies

- The use of ctDNA NGS for molecular profiling might be a complementary non-invasive tool in the management of NSCLC fusion-positive patients.

[1] Lin JJ et al. *J Clin Oncol,* 2018

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