Background: When a targeted marketed therapy exists in a molecularly defined subgroup of patients
Risk of a wide off-label use of the drug

Objectives: 1) Promote a secured access for all patients with an advanced refractory malignancy and no therapeutic alternative through an academic phase II clinical trial
- One trial for each targeted treatment selected
- Withdrawal or high toxicity or inefficacy in a predefined number of patients with the same tumor type
- Lack of efficacy to inform pharmaceutical firms for drug development decision making

2) Ensuring equity of access to innovation
- Provide nationwide molecular tumor diagnosis for all patients through the beta testing molecular cancer centers
- Where the hospital institution status (public, private, hospital...)
- Perform high-quality tests
- Hematopathologists, solid tumors

France organization of the 28 molecular centers for personalized medicine

Partnerships between acute hospitals laboratories in the Cancer Network (TUTHYREF
- Hemopathies program
- TUTHYREF, Saint-Côme, Grenoble, France

AcSé program

Background:
- Crizotinib is registered for treating ALK and ROS1-translocated lung cancer. Crizotinib is also a NTRK inhibitor.
- Crizotinib activity in MET amplified (+) tumors was explored within the French National Cancer Institute (INCa) AcSé program.
- This included access to tumor molecular diagnoses and an exploratory multi tumor 2-stage phase II clinical trial.

Main objective:
- Identification of subsets of patients that may benefit from treatment

Population: Patients > 1 year
- Advanced disease harboring a genomic alteration in a crizotinib target-
- Patients not eligible for any other active academic or industry trial targeting the same alteration.

Treatment plan
- Treatment pursued until progression, unacceptable toxicity, undercurrent conditions, physician decision or patient refusal

Efficacy
- Disease response assessed every 8 weeks with CT and/or PET
- Sample size estimation: 500 pts.
- Sample size: 18 patients included (including 17 children).
- Median age: 58 years old (1-92)

Statistical design
- Main endpoint: objective response (CR, PR) after 2 cycles. May also be changed to the best response for cohorts that are displaying a low enough PFS or OS; or if access to RBC 1.1 criteria in patients onto the trial are not reached.

Conclusion
- Since start study, crizotinib was registered for ROS+ stage I NSCLC (2015).
- Crizotinib showed activity in pediatric and adults malignancies with ALK, ROS1 and MET alterations.

The AcSé program provided a secured national access to both biomarker testing and treatment for children and adolescents with life threatening malignancies.

Acknowledgments
- Prospective INSERM clinical trial (GT2015-00467) at the French AcSé program (Département de Biologie AcSé).
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- The research was conducted in accordance with the principles of the Declaration of Helsinki and the Good Clinical Practice.

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Type of Research: Cross sectional research

Focus on Non-Small Cell Lung Cancers

MET amplification NSCLC

RESULTS

Biomarkers testing
- MET amplification in NSCLC (Gustave Roussy Cancer Campus, Villejuif, FR)

Efficacy
- Level of MET amplification: not predictive of response in 2 cycles of crizotinib

Survival Probability
- OS
- PFS
- Median PFS: 1.6 months with a 50% (95% CI: 1.6, 8.8 months)
- Median OS: 17.2 months with a 50% (95% CI: 11.3, 35 months)

Crizotinib activity in MET amplified (+) tumors was explored within the French National Cancer Institute (INCa) AcSé program.

Determining malignancies.

PI : Gilles VASSAL / NCT02034981

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