MATCH-R, Development of preclinical models from patients with acquired resistance to targeted therapy

Ludovic Bigot

Gustave Roussy Institute, France

Abstract

Advances in molecular oncology and cancer genetics in the last 15 years have defined many of the key driving oncogenes in human cancer. Despite these successes it is now apparent that tumor cells adapt and develop acquired resistance to these targeted inhibitors so that disease progresses within a 5-7 months. At Gustave Roussy, we have opened a prospective clinical trial, MATCH-R (NCT02517892): is a prospective single-institution trial aiming to identify mechanisms of resistance to targeted agents and immunotherapy in patients with advanced cancer (NCT02517892). Patients was enrolled to MATCH-R study before initiated a therapy and then they achieved an initial partial or complete response or stability of disease for at least 6 months are included upon disease progression. Extensive molecular profiling with panel next-generation sequencing, whole exome sequencing (WES) and RNA sequencing (RNAseq) is performed on tumor samples. In the same time, we develop preclinical models (Patient derived xenograft, organoids, and Notes: cell lines) at the stage of acquired resistance. These models will be used to improve our knowledge on the mechanisms underlying resistance to treatment and to develop new therapeutic strategy set up for the patient. As November 2019, 200 tumor biopsies were taken from patients to develop 70 PDX models, 20 organoids and 30 cell lines to develop preclinical research at Gustave Roussy. We carry our efforts on androgen therapy for prostate cancer, ALK/EGFR inhibitor for lung cancer and FGFR inhibitors for bladder and cholangiocarcinoma.

Biography

In 2005 Ludovic Bigot obtained a Master degree in genetics at Paris 7 university. He joined different research team, Saint-Antoine hospital (Paris), Gustave Roussy Institute (Villejuif) and Institute Cancer Research (London). These experiences gave him the opportunity to develop an expertise in oncology, in particularity on preclinical models as PDX models and organoids. In 2014, he returned at Gustave Roussy as Project manager and his mission is development of preclinical models (PDX and organoids) from MATCH-R trials (biopsies collected at the stage of acquired resistance).
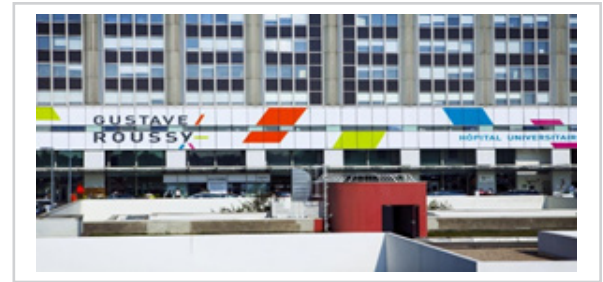
Publications

1. Ludovic Bigot, Gonzalo Recondo, Laura Mezquita, Francesco Facchinetti, David Planchard, Anas Gazzah, Ahsan Z Rizvi, Olivier Deas, Dariya Samofalova (2019) Diverse Resistance Mechanisms to the Third-Generation ALK Inhibitor Lorlatinib in ALK-Rearranged Lung Cancer, Clinical Cancer Research

2. Ludovic Bigot, Valérie Boige, Caroline Mollevi, Sophie Gourgou, David Azria, Jean-François Seitz (2019) Impact of single nucleotide polymorphisms in DNA repair pathway genes on response to chemoradiotherapy in rectal cancer patients: results from ACCORD-12/PRODIGE-2 phase III Trial, International Journal of Cancer

3. L Bigot, Olivier Deas, Guillaume Lang, Fabrice Andre, Luc Friboulet (2018) 31PMATCH-R development of preclinical models from patient with acquired resistance to targeted therapy, Annals of Oncology

4. L Bigot, Olivier Deas, Guillaume Lang, Fabrice Andre, Luc Friboulet (2018) Development of preclinical models to accelerate the identification of next generation treatments for patients with acquired resistance to targeted therapies, Cancer Research

5. Ludovic Bigot, Dora Sabino, Isabelle Martins, Mélanie Polrot, Salima Benbarche, Sylvie Souquère, Michel Ducreux, David Malka (2018) Tumour spheres with inverted polarity drive the formation of peritoneal metastases in patients with hypermethylated colorectal carcinomas, Nature Cell Biology

17th International Conference on Oncology Nursing and Cancer Care
Edinburgh, Scotland | March 04-5, 2020