

C. Mignard⁵, L. Arnold¹², A. Bruno¹⁰, L. Calvet⁹, M. Colombeau¹⁶, J. Corre¹⁷, O. Cuvillier¹¹, B. Eckel²⁰, O. Degout³, A. Gonzalez-Jouhanneau⁸, L. Goetsch⁸, D. Guenet²², J. Iovanna¹⁹, M. Kurasi¹, Ch. Lautrette⁸, F. Le Vacon³, B. Malavaud¹³, Ph. Merle¹⁸, F. Meyer-Losic⁷, F. Praz¹⁵, O. Rosmorduc²³, J.-E. Sarry¹⁷, S. Tabone-Eglinger²¹, I. Treilleux¹⁴, Ph. Vaglio⁴, L.Ysebaert¹³, O. Duchamp⁵

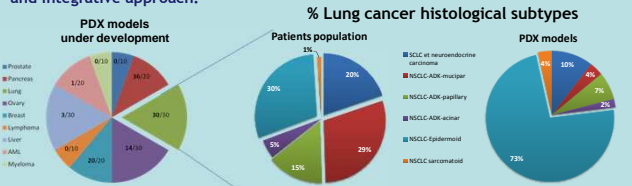
¹Ariana Pharmaceuticals, Paris; ²BIOFORTIS MERIEUX NUTRISCIENCES, Saint-Herblain; ³CTI-BIOTECH, Lyon; ⁴Modul-Bio, Marseille; ⁵Oncoedgen, Dijon; ⁶Oncomedics, Limoges; ⁷Ipsen Innovation, Les Ulis; ⁸Pierre Fabre Research Institut, St-Julien-en-Genevois; ⁹Sanofi, Vitry-sur-Seine; ¹⁰Servier Research Institut, Suresnes; ¹¹CNRS U0509, Toulouse; ¹²Centre Georges François Leclerc, Dijon; ¹³Toulouse Hospital; ¹⁴Centre Léon Bérard, Lyon; ¹⁵INSERM U938, Paris; ¹⁶INSERM U1033, Lyon; ¹⁷INSERM U1037, Toulouse; ¹⁸INSERM U1052, Lyon; ¹⁹INSERM U1068, Marseille; ²⁰INSERM U1111, Lyon; ²¹Fondation Synergie Lyon Cancer, Lyon; ²²Strasbourg University; ²³Pitié-Salpêtrière Hospital, Paris, FRANCE.

What about IMODI

The national IMODI (Innovative MODELS Initiative) consortium includes 25 partners (pharma, SMEs, academic research labs and clinical centers) with the aim of developing more predictive tools to improve the selection of new effective treatments to combat 9 cancer pathologies. These developments include:

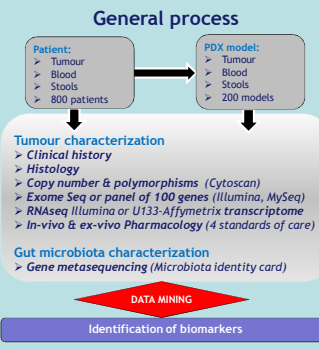
- Collection of *in-vivo* PDX models (procedures were approved by Animal Care Committees, according to ethical guidelines for animal care and handling)^{1,2},
- Collection of *in-vitro* derived cell lines,
- 2D & 3D *ex-vivo* assays,
- In-vivo* humanized models (immune system, liver and tumour stroma),
- Characterization of tumour histology, gene mutations, gene expression, pharmacological responses and gut microbiota,
- Biobanks of tumours, blood, serum and stools (patient specimens were obtained from 7 clinical centers with written informed patient consent for providing surgical tumor samples and for HIV1&2, HTLV1&2, HBV and HCV serological status testing),
- Central database,
- Datamining,

Results on NSCLC lung cancer xenograft developments, molecular and pharmacological characterizations and data analysis are presented as an example of the IMODI holistic and integrative approach.



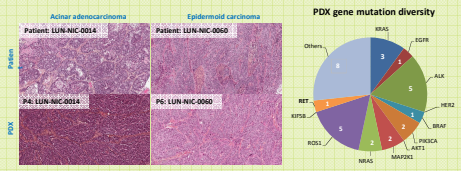
Products & Services

- In-vivo models**: Tissue microarray, Services on in-vivo models
- Ex-vivo assays**: Cancer stem cell lines, Services on cell lines
- In-vitro assays**: Data Mining, Tumour Biomarkers
- Modul-Bio**: Data Base software
- Biofortis**: Stool and serum biobank, Gut microbiome Biomarkers, Services for microbiota analysis



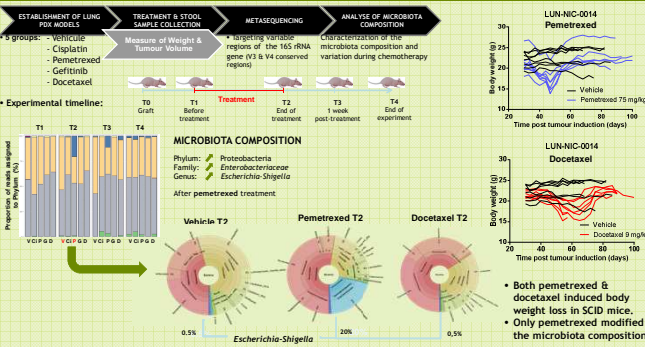
Histology and Genomic Characterization

- Example of a well characterized NSCLC PDX collection
- Highly conserved phenotype and genotype
 - Histological PDX profiles are in concordance with those observed in patient tumours
 - Major molecular subtypes are represented in the NSCLC collection
 - EGFR-mutated models are under development



RESULTS

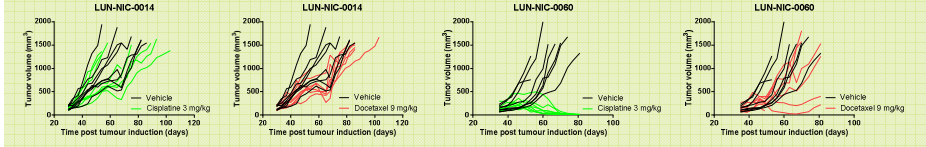
Gut Microbiota Analyses



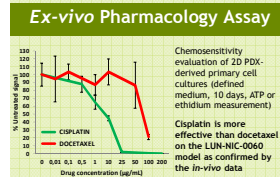
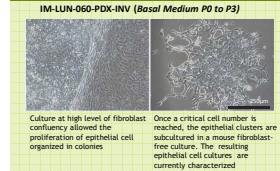
In-vivo Pharmacological Response to Standards of Care

- Significant efficacy of cisplatin and gemcitabine on the LUN-NIC-0060 epidermoid model
- Marginal activity of gefitinib on the LUN-NIC-0014 acinar adenocarcinoma model (EGFR wt, KRAS wt, BRAF wt, ALK wt, ROS1 wt)
- LUN-NIC-0014 PDX resistance to cisplatin and docetaxel correlates with patient outcome (non responsive to cisplatin + docetaxel)

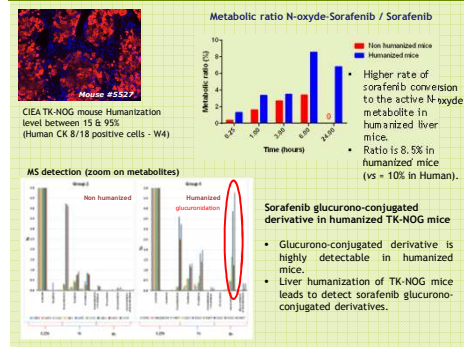
Drugs	ΔT/ΔC (%) (LUN-NIC-0014)	ΔT/ΔC (%) (LUN-NIC-0060)	Activity
Cisplatin 3 mg/kg	64	-4	High antitumor activity (with regression)
Pemetrexed 75 mg/kg	51	Non-tested	Marginal antitumor activity
Gefitinib 100 mg/kg	37	Non-tested	No antitumor activity
Docetaxel 9 mg/kg	59	75	High antitumor activity (with regression)
Gemcitabine 120 mg/kg	Non-tested	-10	Marginal antitumor activity



In-vitro PDX-Derived Cell Line



Liver-Humanized Microenvironnement



Conclusion and perspectives

- IMODI is an operational consortium with the goal to continuously delivering new predictive models in regards to specific clinical needs and diversity.
- All results are available for selection of new therapeutic and diagnostic candidates.
- IMODI has developed ex-vivo models/assays that can accurately predict in-vivo standard of care sensitivity in lung PDX models.
- The effects of chemotherapeutic agents on microbiota composition, and the impact of the microbiota on drug efficacy and toxicity are currently being evaluated.
- IMODI develops a platform of 2nd generation PDX models in mice humanized with human liver to better evaluate the ADME-Tox profile of new compounds.

(1). European Directive 2010/63 and its national transcription "Décret 2013-118 du 1er Février 2013 relatif à la protection des animaux utilisés à des fins scientifiques"; (2). Guidelines for the welfare and use of animals in cancer research, Workman et al., Br J Cancer, 2010; 102(11):1555-1577.