



## EPAAC WP8 Pilot Project 1 “European cancer research coordination in early phase clinical research”

### Update

#### Objectives of PP1

The purpose of PP1 is to design and fund state-of-the-art biomarker-driven phases I/II academic clinical trials on investigational drugs so as to accelerate the development of new treatments or new therapeutic use of existing treatments. This project endeavors to spur access to innovative molecules for patients in the framework of early-phase academic trials.

PP1 is modeled from the French national CLIP<sup>2</sup> program and the UK Alliance program.

The development of this pilot case comprises the following main steps:

- 1) The grant of designation, in each participating European countries, of centres of excellence in early phase clinical research, with access to molecular biology infrastructures;
- 2) The constitution of a European network with the above designated expert centres to allow potential clinical trial designs to be discussed and developed jointly;
- 3) The development of relationship with the pharmaceutical industries to gain access to innovative therapeutics.

It is expected that the proposed above organisational framework will help integrate clinical research and biology into the decisional process and facilitate the evolution of stratified medicine in Europe.

PP1 will focus on new applications of original compounds in rare cancers or outside the company's own development plan, including novel combination therapies.

In terms of coordination pathway, PP1 is about combining and/or expanding innovative national programs that have proven track records.

#### Main achievements & steps with regard PP1 developments

- Research Forum (Brussels, July 2012): agreement across the participants that the two suggested pilot coordination areas (early phase clinical research and outcome research) should be pursued, and that prevention and public health research, another highly relevant and important area, should be prioritized for another pilot coordination project
- Follow-up workshop (Paris, October 2012): discussion among leading research funding organizations about the proposed coordination modalities. An overview of the French CLIP<sup>2</sup> programme, the UK Alliance programme and various other national initiatives was provided. The program's steps and pre-requisites (designation of expert centres, funding models, etc.) were reviewed in light of existing European initiatives. Participants agree that PP1 should focus on new therapies for unmet medical needs, where collaboration is essential to reach critical mass of patients. The idea of opening up existing national networks to collaboration with other countries across Europe was viewed as particularly

attractive. It was decided that at its outset, PP1 should assess the feasibility of linking the UK and French programmes.



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- Follow-up meeting (Valencia, April 2013): a detailed review of both the CLIP<sup>2</sup> and the Alliance program' steps was done during the meeting by the lead organizations of both programs. The designation phase of the expert centers was not considered at this stage, since the purpose is to use the existing organizational framework as they are and coordinate the programs, not to harmonize their procedures. It appears feasible, despite some discrepancies in the respective process, to coordinate both programs and launch joint calls for transnational multi-center studies across the UK and French networks. Alternative coordination options were suggested like opening pre-selected studies submitted by the UK centres in the Alliance program to the French CLIP<sup>2</sup> cooperation and vice versa. It was decided to exchange key paperwork related to both programs (MoU, agreements, and call documents) and that INCa would be invited to attend the next Alliance's joint steering committee in May 2013.
- INCa's representative attended the NCRN/ECMC/AstraZeneca Alliance Symposium (May 2013, London): this annual symposium represents an important milestone of the Alliance program. Preselected clinical studies projects are presented by the investigators in front of the evaluation panel (with pharmaceutical and ECMC/NCRN committee's representatives).
- Presentation of PP1 at the TRANSCAN meetings (Athens, June 2013): the state of PP1 development was presented in front of the TRANSCAN members in June 2013.

Representatives of the Dutch cancer society confirmed their interest to join PP1 and a meeting was planned between INCa and the Dutch Cancer Society in July to share detailed information on the CLIP<sup>2</sup> program and its potential expansion in Netherland.

- Bilateral meeting organised between INCa and the Dutch Cancer society (Paris, July 2013): representatives from the Dutch Cancer Society came to INCa to review in detail the CLIP<sup>2</sup> program steps and discuss how to join PP1. The meeting was followed by an exchange of key CLIP<sup>2</sup> program documents, including criteria used for the designation of expert centres.
- Presentation of PP1 during working meetings with pharmaceutical leaders by INCa: Inca has explored the potential interest of various pharmaceutical companies, already involved in the CLIP<sup>2</sup> program, for a CLIP<sup>2</sup>-like program at European level. In particular, the following laboratories have expressed their potential interest: Novartis, Pfizer, Astra Zeneca, Roche. Some of them attended and actively participated to the Research Forum and follow-up meetings organised in the frame of EPAAC WP8.
- Research workshop (Madrid, September 2013): discussion among leading research funding organizations about the proposed coordination modalities. 3 complementary options have arisen from the discussion, which will be pursued in parallel. See below for full report.

### Next steps (beyond EPAAC)

- INCa will continue to pursue both development paths : 1) combination of CLIP<sup>2</sup> and Alliance programs and 2) expansion of CLIP<sup>2</sup> program with the countries that have expressed an interest (Italy and Netherland) to show the feasibility of PP1
- A meeting is planned with representative of the Italian ministry of health in December, with a specific focus on PP1 and PP2

- With regard the combination of the CLIP<sup>2</sup> and Alliance program, the next steps relate to the launch of a joint call for collaborative proposals across both networks, targeting rare cancer tumors (sarcoma) or rare molecular subtypes, with Astra Zeneca portfolio of therapeutic agents. Astra Zeneca is currently involved in both programs and has expressed a strong interest for PP1.
- INCa will explore the interest of pharmaceutical companies involved in the CLIP<sup>2</sup> program and already aware of PP1 to open their molecule portfolio for cross company combination studies (current combination studies are done with chemotherapy or RT)
- INCa will explore the feasibility to introduce an amendment in its current CLIP<sup>2</sup> agreements with pharmaceutical companies to include the participation of other European centers of excellence. May not be feasible before 2015, after the designation of eligible centres based on quality control and data management. Netherland has already expressed its interest to join a CLIP<sup>2</sup>-like program. Same with Italy. Spanish centers of excellence could be included in the program with private funding.
- INCa will work with the Italian Ministry of Health and the Dutch Cancer Society towards the above goal.
- INCa will organize a workshop in 2014 with potential expert centers and funders in IT and NL to develop a join program

## Future

- To run the pilot with few countries & show the feasibility and added value of the network
- To work with IMI2 as a platform to get access to cross company libraries of molecules & perform cross company combination studies of targeted molecules.
- To advance on molecular profiling of relapsing tumors or on mechanisms of resistance to treatments

## Annex1

### Research Workshop, 13th September 2013 Instituto de Salud Carlos III, Madrid Meeting report

#### Attendees:

Christine BERLING, INCa, France  
Béatrice BUSSIERE, INCa, France  
Antoine ITALIANO, Institut Bergonié-Bordeaux, France  
Philippe CASSIER, Centre Léon Bérard-Lyon, France  
Eric ANGEVIN, Institut Gustave Roussy-Villejuif, France  
Wouter EIJGELAAR, KWF Kankerbestrijding, Netherlands  
Clare SHAW, NCRN, United Kingdom  
Robert WILLIAMS, ECMC, CR UK, United Kingdom  
Miguel QUINTELA-FANDIÑO, CNIO, Spain  
Antonio LÓPEZ, CNIO, Spain

#### PP1 breakout session agenda and presentations

**9:45 Update on Pilot Project 1 and objectives of the day**

Christine Berling (INCa, France)

**10:05 Short presentation of France CLIP<sup>2</sup> program/status of the partnership & molecule portfolio**

Béatrice Bussière (INCa, France)

**10:20 Short presentation of UK Alliance program**

Clare Shaw / Robert Williams (NCRN/CR UK; ECMC, UK)

**10:35 General discussion/similarities and discrepancies of the respective programs**

Main points addressed:

- Combination on rare diseases: as phase 1 studies usually require few participating sites, EU collaboration has added value on rare disease, when number of patients in a particular country is not sufficient. Study on CTC (circulating tumor cells), characterization of circulating DNA, biomarkers studies: this kind of study is not possible for one site, need of a network with few clinical sites.
- PK studies need to be centralized: how standardize the process, is a centralized procedure needed? At a national level?
- Phase I or later stage studies
- Sponsorship of studies across Europe (IGR confirms capabilities)
- View of Astra Zeneca which is currently involved in the two programs
- How to keep coordination & review as simple as possible

- Strong interest for brokering cross company combination studies (currently studies involve targeted compound in combination with chemotherapy or RT)

**11:00 Coffee break**

**11:15 Presentation by each of the French CLIP<sup>2</sup> center representative (with a particular focus of their area of expertise, the current studies under the CLIP<sup>2</sup> program and their vision of the UK/French coordination)**

Eric Angevin (Institut Gustave Roussy, France)  
 Philippe Cassier (Centre Léon Bérard, France)  
 Antoine Italiano (Institut Bergonié, France)

**11:45 Discussion & first recommendations for linking both programs**

Main points addressed:

- Getting access to molecule portfolio is the key issue in most studies/ added value of the network
- Should aim at studies on molecular profiling of relapsing tumors or on mechanisms of resistance to targeted therapies with large portfolio of molecules (molecular profiling of patients/ would help select the best class of compounds)
- May need to have disease specific trial to identify the resistance mechanism
- 2014 : renewal of the designation of the CLIP<sup>2</sup> centers
- 2015 : renewal of the designation of the NCRN centres

Recommendations for the combination of the CLIP<sup>2</sup> and Alliance program:

- To open a call for proposals across both networks
- Indication : a rare cancer tumor (sarcoma, where links exist already) or rare molecular subtypes
- Need to involve a translational program
- To approach Astra Zeneca (Astra Zeneca is currently involved in both programs and has expressed a strong interest for PP1) – UK representatives to speak to AZ during the Alliance next steering committee of October

**12:45 Lunch**

**14:15 Short presentation of the Dutch KWF Kankerbestrijding**

Wouter EIJGELAAR (KWFK, NL)

**14:30 General discussion & potential collaboration**

Main points addressed:

- Currently no government funded cancer research program/ Funding can be done by the Dutch Cancer Society
- should be ready in 2015 once the evaluation of capacities of the Dutch clinical trials groups is finished
- Issue is to set up the quality control & data management procedures
- most interested to connect to the existing french CLIP<sup>2</sup> Program/ joint proposal could be developed by the NL & FR centers
- Large phase I centers in NL located in the 8 university medical sites

**14:50 Short presentation of the Centro Nacional de Investigaciones Oncológicas**

Miguel Quintela-Fandiño (CNIO, Spain)

Antonio López (CNIO, Spain)

**15:05 General discussion & potential collaboration**

Main points addressed:

- The CNIO is a structure that performs translational research, it is organized in different units, these units have connections with clinical research units of hospitals to perform clinical trials. CNIO is often the sponsor.
- CNIO is partially funded by the government with 20 M€/year, projects are funded by pharmas or public calls. They have units where they perform drug development.
- CNIO was ranked among the top 10 cancer research institutes in 2009

**15:30 End of PP1 breakout session**

**Conclusions and action plan:**

- 1) To open a joint call for collaborative proposals across both UK and France networks on rare disease (sarcoma) or rare molecular subtype. Collaborative proposals between the UK and the FR sites would be required. Need to approach Astra Zeneca (UK will take this action during the next Alliance steering committee.
- 2) Inca should explore the interest of pharmaceutical companies already involved in the CLIP<sup>2</sup> program to open their molecule portfolio for cross company combination studies
- 3) Introduce an amendment to the current CLIP<sup>2</sup> agreements to include the participation of centers from NL and Spain. May not be feasible before 2015, after the designation of eligible centres based on quality control and data management.