The Collaborative Precision Medicine Research Program:

Call for Industry Participation

Notice: This is an English translation of the Chinese announcement. In case of any discrepancy between the English translation and the Chinese version, the Chinese version shall prevail.

Introduction

Precision medicine is a fast-emerging field. Advances in next-generation sequencing and related sequencing technologies have enabled the integration of bioinformatics and big data for personalized medicine optimization. Thus, precision medicine has become the focus of medical development worldwide. The first step in cancer precision medicine involves employing next-generation gene sequencing and collecting patients' clinical information simultaneously, which combines genomic profiles and clinical data, and facilitates the acquisition of knowledge on the most suitable treatments. Precision medicine thereby benefits patients, accelerates the development of medicine and new drugs, and has become a driving force for advances in medicine related industries.

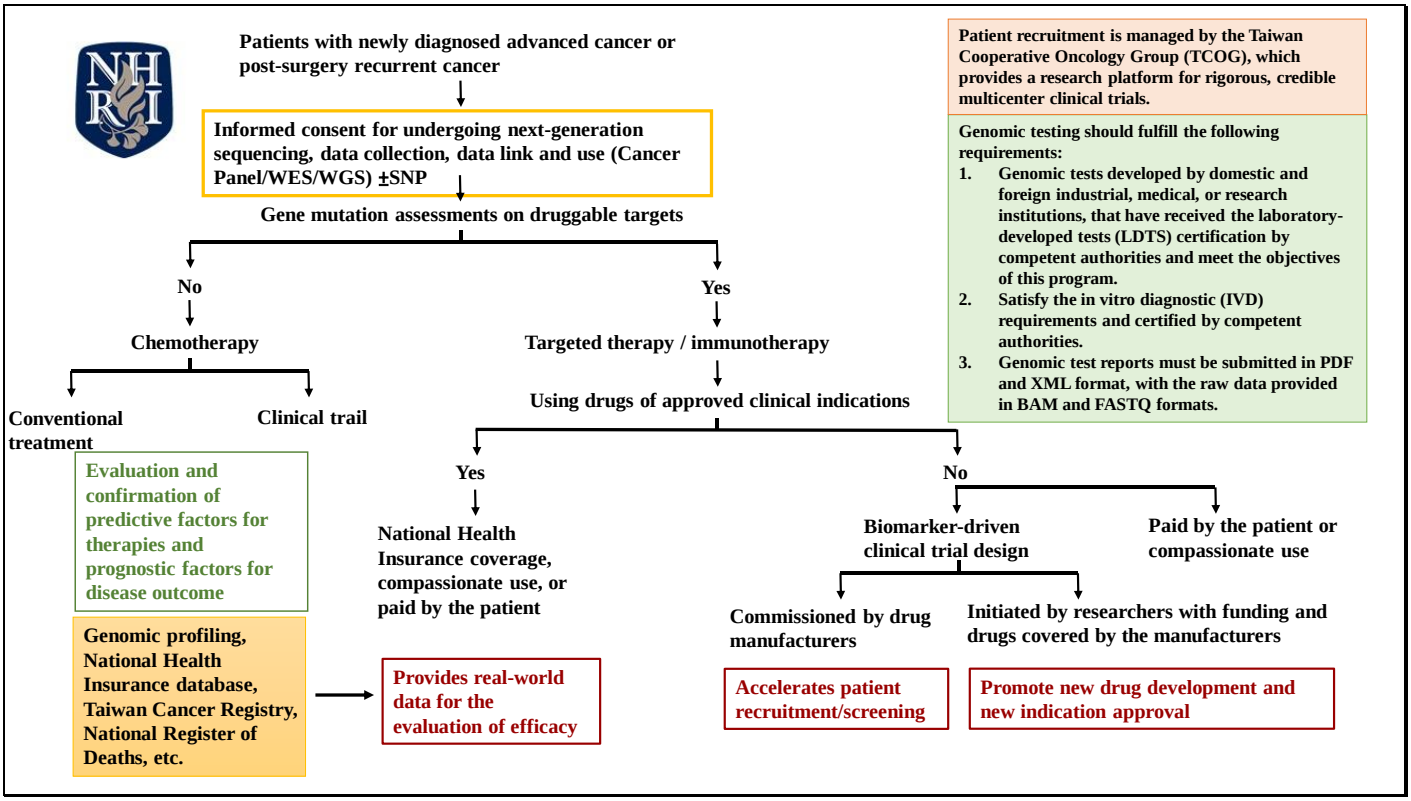
Precision medicine can be applied to new drug discovery, clinical trials, new drug assessments, and post-marketing research, among others, to help establish guidelines for cancer treatment and care. In addition, implementation of precision medicine enhances researches in cancer genetics/clinical epidemiology, drug efficacy, drug safety, drug indications, and pharmacoeconomics. Precision medicine also benefits disease prevention and precision health management. Therefore, establishing real-world data/evidence on precision medicine in the holistic health care network in Taiwan would not only demonstrate the high quality of the national health care system, but also contribute to the establishment of a highly applicable, accurate, and high-quality database. As a result, investments from industrial sector can be brought in, improvements on the allocation and efficiency of medical resource utilization for cancer treatment can be achieved, and therefore benefit our society as a whole.

The Collaborative Precision Medicine Research Program (hereafter "this program") aims to build a high-quality and efficient environment conducive to advances in precision or personalized medicine, clinical research, and related industrial development. By incorporating knowledge and resources from various fields, this program promotes collaboration among industrial, governmental, medical, and research institutions, as well as enhances the integration of genomic and clinical data to establish

big data on health. This program furthers the development of precision medicine-related industries through real-world data/evidence, helping Taiwan's biotechnology industry to become an integral part of the global precision medicine value chain.

Established upon the framework of inter-hospital and multicenter cooperation for clinical trials by the Taiwan Cooperative Oncology Group (TCOG) of the National Health Research Institutes, a clinical trial platform will be constructed through this program to provide consultation services, assist in screening for the most suitable patients and recruiting the most suitable researchers for trial implementation, and reinforce coordination among physicians and hospitals. When patients with druggable gene mutations are identified, approved drugs can be directly used for treatment, whereas unapproved drugs (new indications or off label use) are subjected to clinical trials, in which drugs are provided free of charge by manufacturers with funding either for compassionate use or investigator-initiated trials.

This clinical study platform will prospectively collect data through patient follow-up, including information on drug efficacy and side effects, to serve as a reference for new drug development and the establishment of real-world evidence. The focus of this program is presented in the following figure.



Companies interested in this program may participate by investing their resources in specific projects. Our focus is on major cancers in Taiwan, and we will follow a standardized process for patient recruitment through clinical research platforms (e.g., TCOG). In this public-private partnership alliance program, cancer panel test results

that conform to international next-generation sequencing standards will be provided in real-time as information for further treatment. This allows for a considerable reduction of the costs involved in selecting the few patients with genetic mutations from a substantial large group, of which the cost is relatively large as in individual projects. This clinical study platform will track down treatment efficacy, side effects, and follow-ups, among other elements, then combine the follow-up and outcome information with the genomic profiles of the patients to establish a comprehensive precision medicine database. Furthermore, with informed consent from the patients, this precision medicine database can link other public health-related databases and made available for use to academic and industrial sectors.

As shown in the figure, comprehensive genomic testing (e.g., for cancer) can be the first stage of industrial contribution. Moreover, projects for research on drug indications can be initiated. Herein, an appropriate path for the development of this program is presented. Its foci include both clinical trials for drug indications and the empirical establishment of real-world data/evidence. The research itself can center on drug development, biomarker identification, exploration of the possible LDTS or IVD applications, or the application of health insurance benefits. Collaboration among industrial, governmental, academic, and research institutions facilitates the production of high-quality results along an optimized timeline in each phase of the collaboration program.

As the results of genomic tests will be used for treatments, the genomic tests used in this program must receive LDTS or IVD certification by competent authorities. Genomic test reports must be submitted in PDF/XML format, with the raw data provided in BAM and FASTQ formats.

1. Application requirements

(1) Eligibility

Biotechnology-related companies registered in Taiwan with a concrete plan on collaboration with NHRI in the field of precision medicine.

(2) Content of the letter of intent (LOI)

Applicants must follow the format specified for the LOI (up to seven pages, excluding attachments), which should include the following:

1. Collaborative project title
2. Name of the company and information of the person in charge of the company
3. Study objectives and project abstract
4. Research questions and content
5. Methodology

6. Funding from the company: research funding is broadly defined as the provision of financial support, genetic testing, medications, or a combination of the above.

(3) Other relevant documents

1. Company registration certificate and other supporting documents. A biotechnology company in Taiwan commissioned for participating in this program by a foreign biotechnology company should submit supporting document/certificate of being legitimately authorized.
2. Applicants performing genomic tests must provide LDTS or IVD certifications.

(4) Avoidance of conflicts of interest

All personnel involved in the review process must abide by the principle of avoidance of conflicts of interest.

2. Guidelines for the LOI review

(1) Whether the research objectives of the LOI aligns with the objectives of this program.

(2) The scientific and ethical feasibility of the plan.

(3) Whether the applicant takes adequate and appropriate data protection measures.

3. Application and review process

(1) Application deadline: There are three rounds of application each year, please follow the deadline announced in each round. All applications are reviewed upon submission on a first come, first served basis.

(2) Please submit your LOI to the Center of Biomedical Resources at the National Health Research Institutes. LOIs will be reviewed by an expert panel, and applicants will be invited to give oral presentation on the review meeting.

(3) After passing the reviewing process, the applications will be forwarded to the supervisory committee established by the Ministry of Health and Welfare for approval.

(4) After approval, the implementing agency (i.e., the National Health Research Institutes) will sign agreements with the participating companies to specify the details of the collaboration.

4. Project supervision

This program is overseen by the Ministry of Health and Welfare.

5. Incentive measures

This program will enact the following incentive measures, which are potentially

subject to change depending on the contribution of each participating company.

(1) The Center for Drug Evaluation will offer consultation services to the participating companies. Specifically, for applications using real-world data/evidence in the study design of a clinical trial, free consultation services on the submission process will be provided.

(2) Taiwan Food and Drug Administration (TFDA) will determine the review procedure in advance for projects within this precision medicine collaboration and to members of the precision medicine alliance. This service is based on review mechanisms for new drugs, including the priority mechanism for the review and registration of new drugs developed by the TFDA.

(3) The National Health Insurance Administration will grant priority in the pricing mechanism to the companies which are members of this precision medicine alliance.

6. Others

The ownership of intellectual property rights for research and development results shall be handled following relevant laws and regulations and under mutual agreement.

7. National Health Research Institute contact person

Ms. Lee at the Center of Biomedical Resources by phone (037-206166#33610) or by e-mail: ppp_nhri@nhri.edu.tw.