

**PROJECT**

**Use and validation of biomarkers  
in cancer clinical trials**

*proposed by*

*International Drug Development Institute (IDDI)*

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**BACKGROUND**

“Biomarkers” play an increasing role in the development of new cancer treatments. A biomarker is defined as “a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention”. Biomarkers can be broadly categorized as follows:

- as prognostic factors to predict the outcome of individual patients in terms of a clinical endpoint
- as predictive factors to predict the effect of treatments in groups of patients
- as surrogates for clinical endpoints of interest

They can be used for a variety of purposes:

- to select the patients for entry in clinical trials
- to stratify the patients at entry in clinical trials
- to replace the clinical endpoint in the evaluation of the effects of new treatments
- to guide treatment decisions in order to improve the therapeutic index of new treatments

The clinical literature is replete with examples of the use of biomarkers, but in many cases these have not been properly validated, resulting in a large number of false claims, inappropriate trial designs, and ultimately sub-optimal patient management. The aim of this project is to clarify the

situation by identifying minimal methodological requirements for the identification, use and validation of biomarkers in cancer research.

## **PROJECT DESCRIPTION**

This project will consist of

1. reviewing the literature on the use of biomarkers in cancer clinical trials;
2. reviewing the literature on the validation of prognostic, predictive and surrogate biomarker validation;
3. writing up a summary paper to describe the findings;
4. (if time allows) developing trial designs appropriate for biomarker identification and validation.

## **PRE-REQUISITES**

No particular theoretical background is needed for the project. The student should have a broad interest in clinical trial methodology, in cancer biology and in drug development. Excellent proficiency in English is a must.

## **LOCATION & SUPERVISION**

The project can be carried out anywhere, providing the students can plan regular visits to the offices of IDDI in Ottignies Louvain-la-Neuve. The project will be supervised by Marc Buyse and Linda Danielson at IDDI. .

## **REFERENCES**

1. Biomarkers Definition Working Group. Clin Pharmacol Ther 69:89, 2001.
2. Mandrekar SJ, Grothey A, Goetz MP, Sargent DJ. Clinical trial designs for prospective validation of biomarkers. Am J Pharmacogenomics. 5:317-25, 2005.
3. Sargent D, Allegra C. Issues in clinical trial design for tumor marker studies. J Clin Oncol 29:222-30, 2002.