IDDI

PASSION. SCIENCE. EXPERIENCE.

STATISTICAL VALIDATION OF BIOMARKERS AND IVDS

GAIN TIME AND EFFICIENCY THROUGH A FASTER VALIDATION

LONG-STANDING EXPERIENCE IN IDENTIFYING AND VALIDATING SINGLE BIOMARKERS, BIOMARKER PROFILES, AND IVDS

- **50+ TRIALS IN ONCOLOGY, AD AND OTHERS**
- **60+ PUBLICATIONS**

EXPERT SKILLS IN STATISTICAL BIOMARKER AND IVD VALIDATION

LEVERAGE OUR STATISTICAL METHODS TO IDENTIFY AND VALIDATE (ANALYTICAL AND CLINICAL VALIDATION) YOUR SINGLE BIOMARKERS, BIOMARKER PROFILES AND IVDS.

ANALYTICAL VALIDATION OF AN IVD

- For different aspects of assay performance:
  - Precision, limit of detection, and linearity
  - According to ISO standards and CLSI (formerly NCCLS) guidelines
  - For different assay types: single/multiplex, Micro arrays, mass-spectrometry, ELISA, RT-PCR,...

CLINICAL VALIDATION OF A BIOMARKER OR IVD

- Advanced statistical methodology to:
  - Construct biomarker profiles or indices
  - Validate biomarkers in the absence of a Gold Standard
  - Increase efficiency and reduce costs of clinical validation studies by taking development data into account

VALIDATION OF A GENETIC SIGNATURE FOR WOMEN WITH NODE-NEGATIVE BREAST CANCER

A 70-gene signature was shown in a single institution to have prognostic value in patients with node-negative breast cancer. The purpose of this study was to validate this signature in independent patient samples. Hazard ratios were estimated to compare prognosis for high versus low risk groups. The models were stratified by a clinic-pathological risk group to verify if the gene signature adds independent prognostic information to clinic-pathological risk factor.

IDDI PROJECTS IN STATISTICAL VALIDATION OF BIOMARKERS AND DIAGNOSTICS/IVD & CLINICAL VALIDATION OF GENE SIGNATURES AND PROTEIN EXPRESSION ANALYSES

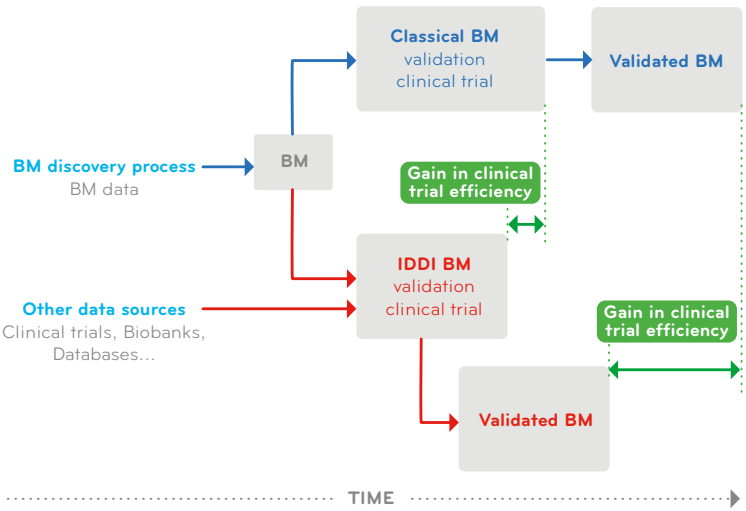
IDDI has experience in the challenging statistical issues that characterize the identification and validation of biomarkers of diagnostic utility, prognostic and/or predictive ability, and those that can potentially be used as surrogate endpoints in clinical trials. Here some examples:

- **DIAGNOSTIC BIOMARKERS:**
  Allow for classifying patients with and without a condition or disease of interest, thus being useful for screening, diagnosis, and correct ascertainment of cases.
  - Validation of a diagnostic biomarker signature for early detection of a rare oxygen deficiency in newborn infants.
  - Clinical validation for an innovative epigenetic-based diagnostic kit for the detection of thyroid cancer.
  - Validation of a companion diagnostic in colorectal cancer: validation of the predictive character of an oncology biomarker. Study designs were provided in accordance with FDA's pre-market approval studies (PMA) process.

- **PROGNOSTIC BIOMARKERS:**
  Biomarkers associated with outcomes regardless of treatment type, thus being useful to create prognostic scores and classify patients in clinical practice.
  - Study carried out in parallel with a randomized controlled trial to identify prognostic biomarkers for disease recurrence.
  - Independent validation of genomic grade
  - Independent validation of gene signatures

- **PREDICTIVE BIOMARKERS:**
  Biomarkers associated with benefit from specific treatments, thus allowing for patient selection and application of precision medicine.
  - Companion diagnostics measure predictive biomarkers
  - Development of a procedure for selection of genes with expression levels exhibiting monotonic dose-response pattern, as markers of treatment response.
  - Study of the predictive value of baseline parameters for clinical, radiological and/or health economic parameters in a study of an innovative cell therapy
  - Validation, in a randomized clinical trial, of the predictive effect of a biomarker(e.g.: her2-neu) on the clinical benefit of a treatment (e.g. trastuzumab)
  - Meta-analysis to validate the predictive effect of topo-II amplification on the clinical benefit of a treatment

- **SURROGATE BIOMARKERS:**
  Aim at replacing a clinical endpoint in clinical trials carried out to evaluate the effect of a specific treatment.
  - Validation of circulating tumor cells as a surrogate endpoint for survival in patients with
  - metastatic castrate-resistant prostate cancer Investigation, through simulations, of potential biomarkers such as bone mineral density and bio-imaging parameters for bone fractures in
  - women with osteoporosis Investigation of prostate specific antigen (PSA) as a biomarker in patients with advanced prostate cancer



OUR EXPERTISE CAN HELP YOU DEVELOP PROGNOSTIC, PREDICTIVE, SURROGATE BIOMARKERS AND DIAGNOSTICS.

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