IMPROVE RELIABILITY AND EFFICIENCY OF BIOMARKER DEVELOPMENT

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HEAD OF BIOANALYTICAL AND BIOMARKER DEVELOPMENT

ALEXION PHARMACEUTICALS

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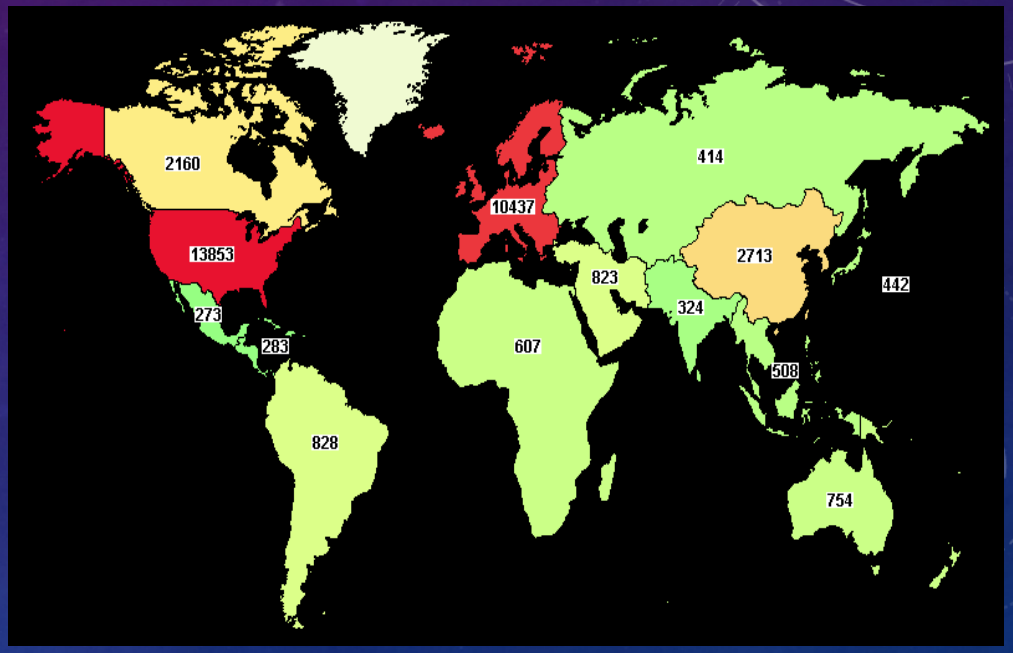
BIOMARKER

- A biomarker can be a gene, a gene mutation, protein, other molecule or clinical measurement that indicates a given disease state. Biomarkers can be diagnostics (telling us of the presence of a given disease), prognostic (telling us of the outcome for a patient with a particular disease) and predictive (telling us of the response of an individual to a given therapy). The latter has led to the rise of so-called personalized or precision medicine.



THE CURRENT BIOMARKER DEVELOPMENT IS PRONE TO FAILURES

- Facts: 80-90% of all biomarker populations for the last 20 years have not and cannot be reproduced. The vast majority of clinically useful cancer biomarkers were discovered in early days
  - Carcinoembryonic antigen – CEA; Prostate-specific antigen –PSA; Carbohydrate antigen 125 -CA125
  - EGFR/KRAS Mutation; PD-L1; Her-2
- Despite massive investments of resources, the biomarker business has added very little to everyday clinical medicine so far
  - Repeated failure in biomarker development for diagnostic and predictive purpose
    - Reported a 85% failure rate
  - An evaluation of the indications and contraindications of all drugs considered by the European Medicines Agency (EMA) and published in 883 European public assessment reports and pending decisions found mentions of only 37 predictive biomarkers for 41 drugs

WHY DO MOST BIOMARKERS FAIL?

- Biomarker study are not designed properly – connecting the dots?
- False discovery - the original performance claims could not be independently reproduced in subsequent validation studies.
    - Methodology issue; Inaccurate claim and error in statistical assessment; Fraudulent publications
- A very large number of candidate biomarkers have been discovered and have been confirmed by reliable methods to provide diagnostic, prognostic or predictive information in certain groups of patients. Unfortunately, this information could not be translated into action for better patient management and outcomes.
    - Tumor suppressor p53; Urokinase plasminogen activator/plasminogen activator inhibitor 1 (uPA/PAI 1)
    - microRNA and C-creative Protein
    - Some genetic test companies have long promoted tests that have limited validity and questionable or clearly no clinical use
- This cocktail of poor methods, selective publication, selective and incomplete reporting, aggravated by “spin” in titles, abstracts, and conclusions, is responsible for a considerable amount of waste in the biomarker discovery

HOW TO IMPROVE RELIABILITY AND EFFICIENCY OF BIOMARKER?

- Method validation
  - Method analytical performance
  - Clinical performance
    - False negative <10%; False positive <10%
    - Sufficient statistical power , CLSI guidelines
- Clinical Translation
  - Identify clinical scenarios for which the markers could still help, in combination with other clinical or biomarker data - umbrella reviews
- Evaluation
  - Increasingly healthcare payers will only be prepared to cover the investments and other costs of biomarker-based assays and technologies
  - Two regulatory pathways in the US: CLIA regulatory strategy or FDA regulatory strategy

FUTURE PERSPECTIVES

- We need to adopt a more strategic and holistic approach to the use of biomarkers if we are to deliver precision medicine that is truly targeted and predictive.
- The future lies in advancing high-throughput technologies in the lab and combining it with artificial intelligence and machine learning to overlay regularly measured biomarker profiles with patient metadata.
- The new trend could drive the evolution of biomarker and drug development- ultimately leading to huge benefits for patients and the healthcare industry around the world.