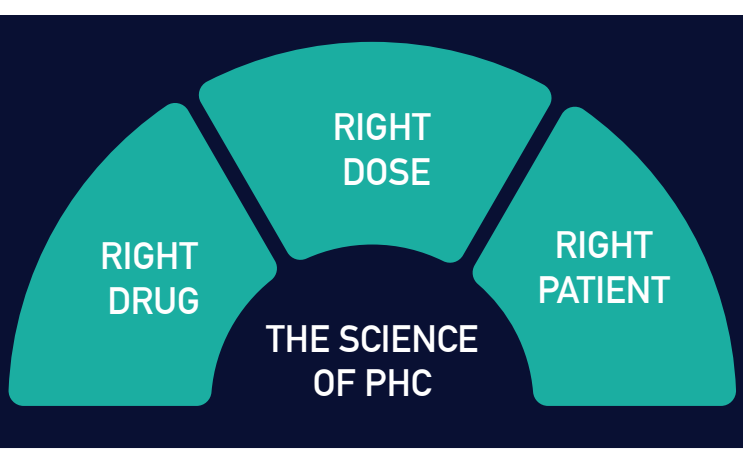

DEVELOPMENT SCIENCES

Immunogenicity

IMMUNOGENICITY PLAYS A KEY ROLE IN UNDERSTANDING THE EFFECTIVENESS AND SAFETY OF MEDICINES. THE IMMUNOGENIC POTENTIAL OF EACH NEW PRODUCT MUST BE CONSIDERED TO AVOID LOSS OF CLINICAL RESPONSE OR ADVERSE EFFECTS SO THAT PATIENTS CAN ULTIMATELY RECEIVE SAFE AND EFFICACIOUS MEDICINES TO TREAT THEIR DISEASE. HOW THE BODY RESPONDS TO MEDICINES IS UNPREDICTABLE SINCE IMMUNE RESPONSES ARE SPECIFIC TO INDIVIDUAL PATIENTS. AN IMMUNE RESPONSE IS DESIRABLE IN VACCINE DEVELOPMENT.

an overview

WHAT IS IT?

Immunogenicity is the body's immune response to a foreign protein that enters a person's body. The responses can be onto itself or immunologicaly related adverse clinical events.

Today, "biologic" drugs provide more treatment options that benefit patients, however even prescribing these newer protein drugs pose challenges to physicians due to a percentage of patients who may have an unwanted immune response to the drugs. That response - called "immunogenicity" or referred to as anti-drug antibodies (ADAs) in clinical development can make the drugs less effective or unsafe for some patients.

The challenge for researchers now is to develop biologic drugs that do not provoke unwanted immune responses, so that more patients can be treated more effectively with these medicines. Understanding individual variations in immune response is an area where scientific insights may help the industry progress in biologic product design.

why it matters

WHERE THIS IS BENEFICIAL

Vaccines: We actively want to provoke immune response. Vaccines work by stimulating the immune system to produce an adaptive immune response against a foreign agent so that the body can protect itself from subsequent infections.

WHERE THIS IS HARMFUL

Biologics: In biologic drugs, immunogenicity can have undesirable consequences. The production of an unwanted immune response directed at a biologic drug can potentially reduce drug levels in the body, compromise therapeutic efficacy, or cause an adverse event.

WHY IT'S AN INDUSTRY CHALLENGE

Currently, it is not possible for physicians to predict which patients may experience an immunogenic response, which makes it challenging to monitor them and prescribe the right treatment. Immune responses and clinical consequences can vary dramatically.

our work

A FEW HIGHLIGHTS OF WHAT WE ARE DOING IN DEVSCI TO HELP SOLVE THE CHALLENGE OF IMMUNOGENICITY:

IMMUNOGENICITY TESTING*

In addition to other focus areas in BioAnalytical Sciences (BAS), we set strategies to study immunogenicity in all of our clinical trials. The BAS group develops methods, oversees data generation and interprets results to assess immunogenicity and determine whether it is affecting the safety and efficacy of our protein therapeutics.

* FDA, EMEA and many other world regulators require that immunogenicity of biotherapeutics be evaluated.

WHERE OUR BAS TEAM GETS INVOLVED:

Throughout the lifecycle of biotherapeutic development, immunogenicity assessments play a key role in ensuring the safety and efficacy of a biologic drug for patients. BAS partners with the research group to identify drug candidates that have a low risk of immunogenicity during molecule selection. When a therapeutic enters development, (non-clinical and clinical trials), BAS helps design the studies, develops methods and generates data to characterize immunogenicity in each study. BAS also leads the interpretation of immunogenicity data in the context of other clinical information, since it can have significant impact on pharmacokinetics (PK), safety and/or efficacy, and affect program development plans.

Late Stage Research

INITIAL RISK BASED ASSESSMENT:

- Partner with Research on efforts to de-risk clinical immunogenicity potentiality during molecule selection

Preclinical Ph I – III Clinical Trials

IMMUNOGENICITY ASSESSMENT:

- Develop immunogenicity testing strategy & mitigation plan
- Develop screening & characterization assays
- Oversee data generato=ion and Interpret the data
- Partner with Process Development to determine monitoring needs for molecule and materials used to generate it during manufacturing

Filing

INTEGRATE DATA INTO ASSESSMENT FOR FILING:

- Submit data into assessment of immunogenicity for BLA:
  - In-study cut points
  - Immunogenicity risk assessment
  - Integrated Summary of Immunogenicity (ISI)
- Interact and respond to Health Authority questions

Post Approval

IMMUNOGENICITY SUPPORT FOR:

- Product line extensions
- Manufacturing process modifications
- Post marketing commitments
- Adverse events in clinic

the future

BAS is in the ideal position to implement reverse translation, for example by monitoring immunogenicity rates from protein therapeutics that are produced by Genentech and by other companies and comparing these to results from in vitro assays, so that we can assess their utility for risk ranking. Although current Health Authority guidance does not require in vitro risk ranking assays, BAS is positioned to be a leader in this field and has the potential to influence Health Authority guidance.

1. Generation and reverse translation of clinical data to enable better molecule selection
2. Monitoring of clinical data and relevant literature
3. Lead the field in use of relevant internal and external data on understanding the immunogenic nature of molecules

LEARN MORE BY VISITING OUR BAS IMMUNOGENICITY RESOURCE PAGE.

Development Sciences