Non-clinical Immunogenicity Risk Assessment (NCIRA)

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on behalf of the NCIRA working goup members

AAPS Therapeutic Product Immunogenicity Update

Vibha Jawa

Chair TPI Community

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EIP European Immunogenicity Platform

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Key Deliverables

- An evaluated position on the limits of ex vivo and in vivo assays to assess antigenicity of biotherapeutics, cell and gene therapies
- An evaluated position on the utility of pre-clinical/non-clinical assays to inform critical quality attributes such as contaminations, host cell proteins, aggregation, glycosylation, deamidation, etc.
- Proposal for best assay combinations to more robustly inform drug design, development, lead selection and risk assessment
- Increase understanding of the drivers of immunogenicity – innate response, antigen processing & presentation, T & B cell epitopes, immune regulation & immune modulation

Working group activities

- Regular monthly conference calls, since January bi-weekly
- F2F meetings at EIP symposium (2019 and 2020)
- In 2020, additional F2F meeting mid-year
- Current main activity is drafting the manuscript on

Assay format diversity in Pre-clinical Immunogenicity risk assessment: Towards a possible harmonization of antigenicity assays

Problem statement

- Various pre-clinical evaluation tools (*in silico*, *ex vivo* and *in vivo*) are commonly used to assess immunogenicity risk (e.g. ADA).
- Challenges: inappropriate predictions, pharmacology of drug leading to false positives or negatives, HLA diversity, specific $CD4^+$ T cell frequency, assay sensitivity etc.
- Robust, consistent and, where feasible, standardized approaches and methods are required to better inform and mitigate risk.

Aim

- Terminology
- Presentation of methods, assay principles and examples of use
  - Antigen presentation
  - T cell assays
  - B cell assays
  - *In vivo* models
- Description of drawbacks and difficulties in comparison of various method addressing the same part of immune response
- Importance of relevant controls
- What can we ”predict” and more importantly, what we can’t “predict”
- What be done when qualifying assays
- Workflow example – which, when, what?
- Timing vs quality vs timelines

Status

- Extensive debate on scope and content of manuscript
  - Knowledge and experience sharing
  - Is harmonization of methods feasible and reasonable?
  - To which level of recommendations can we go in the manuscript?
- Significant collection of information gathered:
  Draft manuscript (not all sections completed) with more than 11.000 words compiled
- Potential journals for publication identified and editors' interest confirmed

Future perspectives

- Priority: complete manuscript!
- Start discussion on new topics:
  - Path to standardization of assay controls?
  - Cell & Gene therapies
    - Vectors
    - Novel nucleic acid formats
    - Transgene immunogenicity
    - Translatability of animal models
    - Gene editing
  - Antigenicity assessment for synthetic peptides to enable abbreviated new drug application (ANDA)
  - Artificial intelligence and reverse translation in the context of immunogenicity
- Workshop on immunogenicity risk assessment in EU and US
- Outreach to AAPS, BIO, IQ, IMI-ARDAT and other organizations

Do you have questions or suggestions?

Do you want to join the EIP working group?

Contact

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or anybody you know from the working group

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Thank you

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