Report from the COMBINE Expert Workshop: Recurring problems and mitigation strategies in the development of monoclonal antibodies (mAbs) against AMR pathogens

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BACKGROUND

Monoclonal antibodies (mAbs) represent a promising strategy to treat or prevent antimicrobial resistance (AMR) infections, especially those caused by ESCAPE pathogens (E. faecium, S. aureus, C. difficile, A. baumannii, P. aeruginosa, and Enterobacteriaceae). However, only one mAb (bezlotoxumab) is currently licensed for use against the ESCAPE pathogens. One of the aims of the COMBINE project, part of the IMI AMR Accelerator, is to identify and overcome bottlenecks in the preclinical and clinical development of mAbs against AMR.

METHODS

The Paul-Ehrlich-Institut, on behalf of COMBINE, organized a virtual expert workshop to discuss recurring problems and mitigation strategies in the development of mAbs against AMR pathogens (8th and 9th of June, 2022). Twenty-four experts from industry, academia, public health and regulatory bodies (20 of whom not affiliated to COMBINE) contributed to the workshop. The sessions fostered cross-pathogen learning exchanges at preclinical, translational and clinical level. Upon registration, attendees were invited to express their preferences for topics of the panel discussions via an online survey.

RESULTS

All experts noted that mAbs have distinct development challenges when used for either therapeutic or prophylactic treatments. The preclinical experts discussed different approaches in the design of mAb targets, directly targeting the bacteria or targeting the virulence factors to preserve the immune response against bacteria, and emphasized that robust (efficacy) data from animal models should be collected prior to starting clinical testing. The necessity for further research in Immunoglobulin M mAb and administration of mAbs through inhalation to treat lung infections were discussed. In the translational session, the experts discussed physiologically-based pharmacokinetic models and how to integrate various variables (e.g. degree of inflammation, tissue distribution, bacterial growth or other clinically relevant markers) into these models.

The lively discussions about drug development in humans integrated clinical, statistical, and operational perspectives and learnings from COVID-19 trials. The experts concurred that the selection of the primary endpoint, the identification of the right patient population, and the availability of rapid diagnostics are critical aspects for future studies. Potential solutions to increase efficiency of clinical trials (e.g. adaptive trials, clinical trial networks, meta-analyses of smaller trials) were debated.

CONCLUSIONS

The workshop provided an open discussion forum to identify and prioritise challenges and propose mitigation strategies for future mAbs development. The hypotheses generated in the workshop will guide future COMBINE work.

About COMBINE

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About the Innovative Medicine Initiative

About the Innovative Medicine Initiative The Innovative Medicines Initiative (IMI) is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients. IMI supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe. IMI is a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations, EFPIA.

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