SESSION PROPOSAL 9

BENEFIT-RISK ASSESSMENT IN CLINICAL TRIALS WITH INDIVIDUAL PATIENT NEEDS IN MIND

Shahrul Mt-Isa, Biostatistics and Research Decision Sciences (BARDS), MSD

Description of Session:

Introduction: This session focuses on the recent developments, challenges, and opportunities in medicine in clinical trials. In the era of pandemic when time is precious, and resources are scarce, the use of statistical methods when characterizing individualized benefit-risk balance may help to better elucidate delicate benefit-risk balance between health technologies, and to clarify priorities.

Background: It is known that benefits and risks are multidimensional, and these can vary between patients receiving the same treatment. Often the population-level benefit-risk balance is sufficient and acceptable in regulatory decision-making, but in some cases, it is not ideal. When thinking about how individual clinical trial subject respond to treatment, there may be occasions when, albeit rare, that some subjects may benefit without any adverse effect, and vice versa. A population-level benefit-risk analysis would miss this nuance without a rigorous assessment that considers the benefit-risk balance at the individual level.

Statistical uncertainty, among others, also plays a key role in the confidence to determine the true patient outcome and their benefit-risk balance. Therefore, whilst deterministic analysis may dominate the field of benefit-risk assessment, accounting for uncertainty is also a crucial aspect when it comes to making informed treatment decisions.

In this session, our panel of prominent experts will discuss the merits and challenges of development and implementation of statistical methodologies in this complex but important area. With a growing number of initiatives and resources, such as, from the US Food and Drug Administration (FDA), European Medicines Agency (EMA), the Council for International Organizations of Medical Sciences (CIOMS), Innovative Medicines Initiative (IMI), American Statistical Association (ASA), and the European Federation of Statisticians in the Pharmaceutical Companies (EFSPI), our session would contribute to the active discussions and debates on this topic.

Talk 1: Prof Pocock will present a novel method to assess individual patient's benefit-risk trade-off with some examples of application using clinical trials data. Multivariable predictive models for efficacy and safety outcomes are used to quantify the absolute treatment effects on benefit and harm for any individual patient's profile, therefore facilitating clinical judgement as to which patients have (and not have) a favorable benefit-risk trade-off.

Talk 2: Prof Ashby will continue the session with key foci on the multidimensional aspects of benefit-risk assessment and the importance of addressing and managing uncertainty. The Bayesian statistics paradigm provides the natural framework here, and subsequently makes elegant probabilistic statement.

Discussions and Dialogues: Prof Rockhold and Dr Baumgartner will then provide commentary and extend the dialogues on these emerging methodologies in clinical trials and precision medicine, and the preparedness of sponsors, regulators, and the scientific community to welcome them; as well the transparency they bring to the benefit-risk assessments, especially when patient perspectives and/or preferences may alter the optimal treatment decision.

Target audience: The topic would be of particular interest to clinicians, pharmaceutical companies, sponsors, regulatory agencies, health technology assessment bodies, payers, and academic researchers in this area.

Disclaimers: The views and opinions presented in this session are of the speakers only, and do not represent their institutions / companies or the views of the pharmaceutical industry.

Contributors:
Ruth Owen, London School of Hygiene and Tropical Medicine, London, United Kingdom
Prof Deborah Ashby, Imperial College London, London, United Kingdom

Prof Frank Rockhold, Duke University, Durham NC, USA
Dr Richard Baumgartner, Merck & Co., Kenilworth NJ, USA