MBMA SubSIG: a collaborative initiative for promoting model-based meta-analysis and its application in drug development

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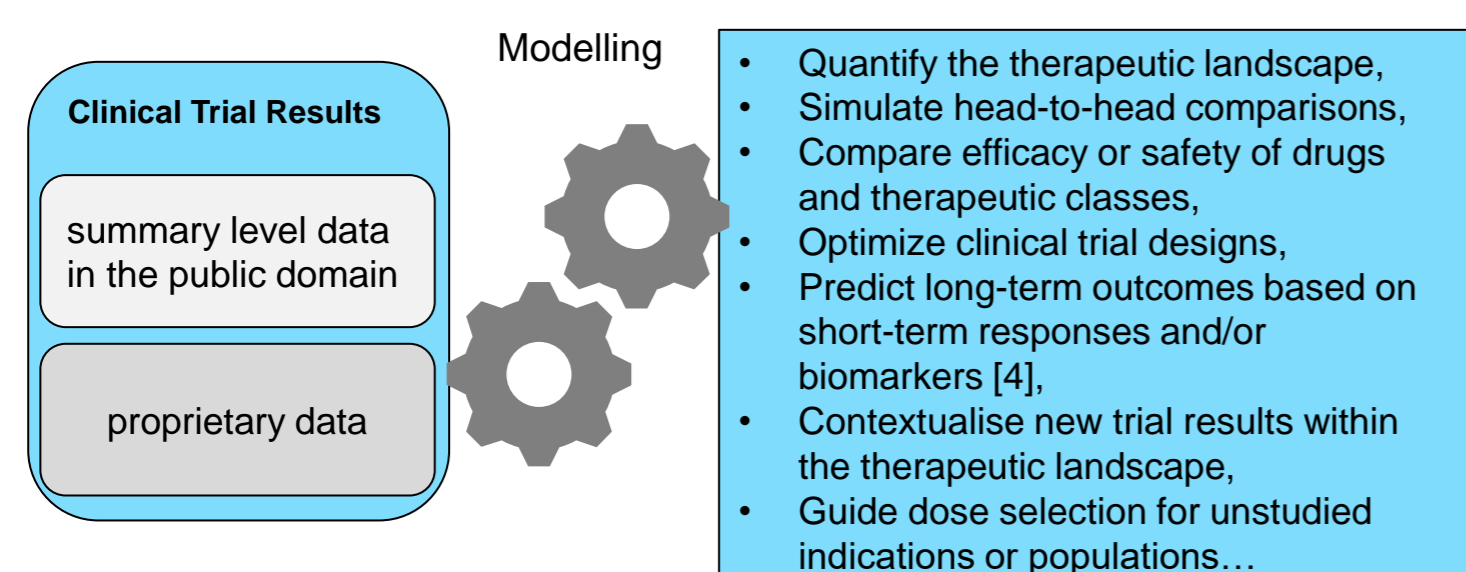
Background

Model-based meta-analysis (MBMA) is a method to integrate data from multiple studies using mathematical models to quantitatively describe the effect of treatment, time, and patient population characteristics on the trial outcomes.

- Sheiner and Steimer [1] first used the term model-based meta-analysis in 2000 to described a population analysis of individual data from multiple trials [2].
- Mandema et al 2005 [3]: MBMA to predict comparative efficacy between two drugs at doses that had not been directly compared in a head-to-head study, including longitudinal response data.
- Exponential number of MBMA articles publications since 2010 (134 publications, 32 in 2021 alone)

MBMA is a powerful tool for integrating prior knowledge to inform and de-risk drug development decisions.

Figure 1. MBMA scoping in Drug Development

Modelling

Clinical Trial Results
- summary level data in the public domain
- proprietary data

- Quantify the therapeutic landscape,
- Simulate head-to-head comparisons,
- Compare efficacy or safety of drugs and therapeutic classes,
- Optimize clinical trial designs,
- Predict long-term outcomes based on short-term responses and/or biomarkers [4],
- Contextualise new trial results within the therapeutic landscape,
- Guide dose selection for unstudied indications or populations…

In response to the increasing attention to this methodology, and because this topic offers a unique opportunity for the collaboration between Pharmacometricians and Biostatisticians, the ISoP-ASA Statistics and Pharmacometrics Special Interest Group (SxP SIG) [5] sponsored the creation of the MBMA Special Interest Sub-Group (MBMA SubSIG) at the end of 2019.

Our mission

To promote model-based meta-analysis and its application in drug development, to raise awareness and interest, and to support the education of others in MBMA.

The Team

The SubSIG is composed of:
- **a core team:** nine members from pharmaceutical companies, consulting companies, and regulatory agencies - responsible for the achievement of the SubSIG workstream goals.
- **an advisory team:** senior members from pharmaceutical and consulting companies - provides strategic support and leadership.

Chairs
Marion Bouillon-Pichault [BMS] &
Matt Zierhut [Certara]

Core Team
Phyllis Chan [Genentech],
Yaming Hang [Takeda],
Rana Jreich [Sanofi],
Junshan Qiu [CDER, FDA],
Clemence Rigaux [Sanofi],
Monica Simeoni [GSK],
Chandni R. Valiathan [Janssen],
Jian Zhou [Bristol-Myers Squibb],
Hao Zhu [CDER, FDA].

Advisory Team
Jonathan French [Metrum]
Jaap Mandema [Certara]
Jose Pinheiro [Janssen]
Jeff Sachs [Merck]
Bernard Sebastien [Sanofi]
Kevin Sweeney [Pfizer]

Workstream Goals

1. **Raising awareness and building a community of practice**
2. **Identifying training opportunities for MBMA**
3. **Establishing best practices in MBMA**
4. **Broadening the scope of MBMA beyond PMx/Statistics**

Our activities

- **Regular meetings** to advance on the different workstream activities.
For example within workstream 1) the objective *to create and grow an active MBMA community* has fostered:
- the creation of **LinkedIn group** [7] (Figure 2 left panel).
- including the design of a template for **LinkedIn posts** (Figure 2 right panel).
- the collation of literature material which will constitute a **repository for impactful MBMA examples.**
While the *objective to Raise awareness and promote MBMA* will be pursued
- organizing **Webinars** – e.g. "Introduction to MBMA" 26 January, 2021 [6].
- by **conference** attendance and feed-back (PAGE, ASCPT, ACoP).

Figure 2. LinkedIn Webpage and post example

Model–Based Meta–Analysis (MBMA)
Listed group
17 members

Accept Invitation

About this group
We are a group MBMA enthusiasts, sharing information about the application of Model-Based Meta-Analysis in the pharmaceutical industry. This community provides…

See all

Connections in this group

Marion Bouillon–Pichault, Chandni Valiathan, and 1 other person you know are in this group

See all

Characterizing exposure dependent adverse events for immune check point inhibitors in oncology

80 Clinical trials used in model based meta-analysis

Number of patients included in analysis 2345

PD-1 and CTLA-4 therapies analyzed in monotherapy and combination

https://link.springer.com/article/10.1007/s11095-022-03201-5#Sec6
#aggregateddata #pooledsafetyanalysis
#immunecheckpointinhibitor #MBMA
Tag: Phyllis Chan, Kirill Peskov, Xuyang Song

Scientific discussion, relevant literature and MBMA impact cases will be available soon at this website!

Topics will include
- Handling of missing data in MBMA
- Fully parametric & non-parametric placebo models
- Network meta-analysis & MBMA …

Conclusions

The MBMA SubSIG is a **collaborative effort to promote MBMA** and interdisciplinary communication in drug development, leveraging the experiences of a broader community. The MBMA SubSIG is keen to learn from individual users of this methodology, and **participation is open to all who are interested**.

Please send any questions to: MBMAsig@gmail.com.

References

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[3] Mandema JW, Cox E, Alderman J. Therapeutic benefit of eletriptan compared to sumatriptan for the acute relief of migraine pain—results of a model-based meta-analysis that accounts for encapsulation. Cephalalgia 25, 715– 725 (2005). (https://doi.org/10.1111/j.1468-2982.2004.00939.x)
[4] Leil TA, Lu Y, Bouillon-Pichault M, Wong R, Nowak M. Model-based meta-analysis compares DAS28 rheumatoid arthritis treatment effects and suggests an expedited trial design for early clinical development. Clin Pharmacol Ther. 2021; 109: 517- 527. (https://doi.org/10.1002/cpt.2023)
[5] Statistics and Pharmacometrics (SxP) SIG (go-isop.org)
[6] https://youtu.be/bf7_-cNjydQ
[7] https://www.linkedin.com/groups/12564166/

Acknowledgments