Application of Model-Based Meta-Analysis to Set Benchmarks for New Treatments of Systemic Lupus Erythematosus

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INTRODUCTION

- Systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organ systems and is unpredictable in disease course, with fluctuating disease activity including flares.
- In the past 60 years, there have been only two drugs developed that have been approved by the Food and Drug Administration (FDA) for treatment of SLE, anifrolumab and belimumab.
- In the development of SLE treatment it is important to assess a compound’s efficacy by comparing it to benchmark drug treatments of SLE.
- When evaluating the efficacy of an SLE treatment in a clinical trial, several composite scores using summary-level data, and without any treatment effects on the rate parameter provided adequate fit according to ELPD.

RESULTS

- The SLE literature review identified 25 different studies, 81 different treatment arms, and a total of 16 different drugs of SLE, with the most common being belimumab, anifrolumab, and epratuzumab (Table I).
- The most common endpoints reported were SRI-4, SRI-6, BICLA, and SRI-5.
- Other efficacy outcomes, such as Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) and Lupus Low Disease Activity State (LLDAS), were not widely reported so they were not included as outcomes in model development due to data limitations.
- After exploring model variations, a model with relative change treatment effect and without any treatment effects on the rate parameter provided adequate fit according to ELPD.
- Residual diagnostics of this model were not reflective of any model deficiencies, and VPCs showed alignment between the observed and simulated data; therefore, this model was selected as the final predictive MBMA DTM. (Figure 1)
- Model estimates indicate that for a treatment arm receiving anifrolumab (mg) IV Q4W treatment, the effect at 50% of Emax is achieved at a dose of 259 mg (95% CI = (71, 541)) and for a treatment arm receiving belimumab IV (mg/kg) Q2Wx3+Q4W treatment, the effect at 50% of Emax is achieved at a dose of 0.79 mg/kg (95% CI = (0.33, 1.5)). (Figure 2)

Figure 1: Treatment effect estimates using MBMA SLE DTM

CONCLUSION

- A literature review of randomized clinical trials of drugs for SLE was performed where summary-level data of longitudinal efficacy data, dose regimens, and baseline disease severity was collected for each treatment arm.
- This summary data was used to develop a latent MBMA DTM for the SLE longitudinal efficacy data of SRI and BICLA SLE outcomes.
- The model included a continuous Emax dose effect for the FDA approved SLE treatments anifrolumab and belimumab.
- The final MBMA DTM can be used to predict response rates of SRI and BICLA so they can be used as benchmarks for new treatments of SLE.