Model-based meta-analysis of topical treatments for atopic dermatitis: Eczema Area and Severity Index (EASI) as an efficacy endpoint

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Objectives: To analyze percent change from baseline (%CFBL) in EASI of topical therapies for the treatment of atopic dermatitis.

Methods: Sixty-two publications in 1990-2014 that contained topical therapies for atopic dermatitis were selected based on a priori established criteria. EASI together with other efficacy and safety data were extracted to create a database. Thirteen publications that reported EASI %CFBL were included in this analysis. EASI %CFBL at specific time point was summarized using forest plots. EASI %CFBL over time was fitted by the two- and three-parameter Emax models. Possible covariates were evaluated as data permitted. R packages including nlme and metafor were used in data analysis.

Results: EASI %CFBL at treatment week 4 was summarized by treatments and drug classes using forest plots. Treatment effects were observed for some vehicle/placebo treatments and that of active drugs were more pronounced. EASI %CFBL over time was first fit by a simple Emax model with the parameters Emax (the maximal response over time) and EW50 (the time to achieve half of the maximal response). Emax was better estimated as a function of treatment while EW50 a parameter shared by all treatments. Emax estimates varied and reached up to >90% reduction in EASI for some treatments. EW50 was estimated at 0.60 weeks with 95% confidence interval (CI) [0.47, 0.77], indicating an early onset of the treatment effect on EASI. Addition of the Hill parameter in the model did not improve the fitting. The observed and predicted responses over time are given in Figure 1.

Conclusions: The Emax models fit the data well and the model predictions appeared to be consistent with the observed data. The results were used in the planning of clinical program.

Figure 1: Observed and predicted EASI %CFBL by the final 2-parameter Emax model for various treatments. Circles are observed, solid line the predicted, and the dotted lines the 90% CI.