COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar

Wednesday, December 8, 2021
4:00pm
2548 NUB or Zoom

"Pharmacokinetic-Pharmacodynamic Analysis using IGA and EASI Models to Predict Efficacy Outcomes in Special Populations with Atopic Dermatitis"

Presented by:

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Abstract: Atopic dermatitis is a chronic, relapsing skin disease characterized by inflammation and pruritis of the skin that affects 10 – 20 percent of children and 5 – 10 percent of adults in the United States. Atopic dermatitis is developed by a combination of epithelial-barrier defects, increased type 2 immune responses (Th2), and environmental factors. For clinical research studies, atopic dermatitis severity is measured using multiple subjective scales. The most prominent assessments are the Eczema Area and Severity Index (EASI) and the Investigator Global Assessment (IGA) – a continuous bounded outcome score assessment and a five-point ordered categorical assessment, respectively. Dupilumab, trade name Dupixent, is a fully human monoclonal antibody that is administered via subcutaneous injection for patients with moderate-to-severe atopic dermatitis. Dupilumab is an interleukin (IL)-4 receptor alpha antagonist that blocks interleukin-4 and interleukin-13 signaling. In the United States, dupilumab is approved for moderate-to-severe atopic dermatitis (6+ years), asthma (12+ years), and chronic rhinosinusitis with nasal polyposis (18+ years). For clinical trials, moderate-to-severe baseline disease severity is defined as an IGA score ≥ 3 and an EASI score ≥ 16, and body surface area (BSA) involvement of $\geq 10\%$. In our project, we will develop pharmacokinetic-pharmacodynamic models for continuous and categorical scaled endpoints using indirect response models. These models will be used to determine efficacy outcomes for special populations (i.e., children) not studied in clinical trials. We hypothesize that children with atopic dermatitis will perform similarly (i.e., exposure-response profiles) to adolescents and adults under corresponding clinical situations using either IGA or EASI endpoints. From this analysis, we hope to make conclusions about exposure-response profiles in similar Th2 immune response indications, particularly with respect to full extrapolation of efficacy based only on concentration data in children.

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