Dermatology:

Atopic Dermatitis

Dupilumab in Atopic Dermatitis

- Evaluate the [optimal] utilization of dupilumab for the treatment of AD within the evolving therapeutic landscape including dose modification
- Real world AD patient / disease characteristics, burden of AD and comorbid conditions
- Dupilumab use patterns, effectiveness, and other attributes in real-world setting
- Special populations (e.g., skin of color, mild to moderate AD, H&F)
- Studies to measure the effect of dupilumab on AD symptoms and other important disease domains that are insufficiently characterized (sleep, pain, mental health, sensory processing, executive function, etc.)
- New mechanistic insights into dupilumab MOA, including effect on important inflammation markers in lesional and non-lesional skin not studied previously
- Effect of dupilumab in AD patients with comorbid type 2 inflammatory diseases (e.g. AD with comorbid asthma ± allergic rhinitis ± food allergy, etc.)
- Effect of early AD treatment with dupilumab on the development of type 2 comorbidities, atopic march and disease modifying aspects in general
- Dupilumab in the context of COVID-19 pandemic
- Effectiveness of dupilumab across different phenotypes and endotype

New Disease Areas

- Other dermatologic diseases have been added to the New Indication Plans for additional New Disease Area Scope (refer to NDIs AoI).

Disease State

- AD time course (natural history)
- New mechanistic insights into AD pathophysiology, including the identification of distinct phenotypes and endotypes

Epidemiology

- Prevalence of AD by gender, age group, age of onset, associated comorbidities, special populations
- Treatment patterns throughout the course of AD

Mechanistic

- Further understand the AD mechanism of disease, or dupilumab mechanism of action in relevant pathobiological contexts
- Pathobiology of IL4R alpha in chronic itch
- IL-4/13 signaling in fibrosis and skin remodeling

New Dermatology Indications

Other Dermatological Diseases – prurigo nodularis, chronic spontaneous urticaria, chronic cold-induced urticaria, chronic pruritus of unknown origin, bullous pemphigoid.

Patient population

- Epidemiology
- Natural history including disease progression
- Burden and unmet needs including limitations of current therapies

Pathogenesis

- Pathogenesis including the role of IL-4 and/or IL-13 and mechanisms of itch and neuropathy
- Barrier disruption and tissue remodeling
- Characteristics of lesional and non-lesional skin

Clinical practice

- Diagnosis and assessment including biomarkers and imaging
- Disease endotypes
- Comorbidities including Type 2
- Special populations including skin of color

Other Dermatologic Diseases beyond the diseases listed above, where existing data suggest that IL-4 and/or IL-13 may play a central role.

- Effect of dupilumab

NOTE: prior to submission via the ISS portal, proposals must undergo preliminary review to evaluate regulatory/patent risk and ensure there is no overlap with ongoing initiatives.

- *Respiratory:*

Asthma

Establishing criteria for disease modification in asthma
Mechanism of Action (MOA)

- FeNO as prognostic/predictive biomarker
- Identifying novel response biomarkers
- Phenotyping/endotyping response
- Airway hyperresponsiveness
- Understanding mechanism of peripheral eosinophilia after dupilumab initiation
- Understanding the role of type 2 inflammation as driver of acute exacerbation
- Role of dupilumab as disease modifying drug
- Long term prevention of lung function decline
- Understanding remission on therapy
- Understand the role of type 2 inflammation on airway smooth muscle contractility, airway barrier function and viral-medicated exacerbations

Observational Studies

- Understanding burden of disease
- Real world effectiveness
- Understanding disease severity criteria

Comparative Data

- Efficacy in patients who switch biologics
- Indirect treatment comparisons among subpopulations
- OCS burden

Special Populations

- Asthmatics with smoking history
- Obesity
- Exercise induced asthma
- Efficacy in diverse populations
- Efficacy in underrepresented populations

Pediatric Asthma

Mechanistic

- Airway Hyper Responsiveness
- Airway remodelling/Lung function decline
- Understanding peripheral eosinophilia
- Understanding and characterizing the role of T2 inflammation in driving disease
- Predictive T2 biomarkers for exacerbations, lung function, lung function decline
- Lung function "trajectory" along the ages
- Impact on growth and development

Observational Studies

- Characterization of pediatric asthma population (biomarkers, lung function, OCS use.)
- Burden of disease (patients and caregivers)
- Burden of OCS and impact on growth
- Impact on inhaled therapy uses

Comparative Data *(direct or indirect)*

RWE effectiveness

Special Populations

- Allergic subtypes based on total/specific IgE and other type 2 biomarkers
- Underrepresented populations
- Associated atopic conditions
- Corticosteroids burst users
- Impaired lung function
- Switch from previous biologic

Chronic Rhinosinusitis with Nasal Polyps

Mechanism of Action

- Loss of sense of smell in CRSwNP and its diagnostic and prognostic value

- Role of Type 2 cytokines on CRSwNP development & progression
- Disease control, remission and /or modification in CRSwNP
- Prevention of nasal polyp regrowth and relationship to surgery
- relationship between Type 2 inflammation and symptoms
- Sinus opacification in CRSwNP and predictive value of reducing opacification
- Role of Type 2 inflammation (cytokines such as IL4, IL13) on nasal polyp formation (e.g., epithelial barrier function, mucus production), and loss off sense of smell
- Understanding neuroinflammatory pathways and potential impact of dupilumab
- Dupilumab impact on improving sleep, smell and taste in patients with CRSwNP
- Dupilumab efficacy/effectiveness on long term outcomes such as surgery, oral steroid usage reduction

Pathophysiology

- Role of IL-4 and IL-13 in de novo polyp formation
- Chronic Rhinosinusitis without Nasal Polyps (CRSsNP) phenotypes

Observational Studies

- Prevalence of sleep disorders, depression, anxiety in patients with CRSwNP
- Burden of Disease prevalence of type-2 inflammation in CRSwNP (esp. in Asia)
- Development of simple patient tools to detect smell loss in CRSwNP
- Burden of surgery and systemic steroids in patients with CRSwNP

Comparative Data

- Indirect treatment comparison of dupilumab with other biologics
- Biologic switch data

Special Populations

- Age 65+
- Underserved populations

COPD

- Epidemiology/Distribution of COPD (esp. in moderate-severe pts)
- Predictive biomarkers
- Characterizing COPD patients through Endotyping/phenotyping
- Drivers of disease in non-smoking related disease (pollution, genetics, etc) & response
- Natural progression of disease
- Cardiovascular comorbidities
- Understand the role of Type 2 inflammation in COPD
- Effect of dupilumab on disease modification, airway remodeling, prevention of lung function decline
- Effect of dupilumab on mucus plugging
- Viral infections in COPD
- Reduction of concomitant OCS, ICS, rescue treatment, antibiotics
- Patient-centric endpoints (ex. quality of life, sleep, depression, exercise tolerance, hospitalization, ER visits, mortality)

Gastroenterology

EoE

- Advance understanding of the complex pathophysiology of EoE (barrier dysfunction, adaptive and innate immunity, inflammatory cells, remodeling and fibrosis)
- Elucidate endotype / phenotype heterogeneity in EoE
- Explore predictive biomarkers of EoE disease progression
- Investigate advantages and limitations of standard of care therapy
- Identify predictive biomarkers of steroid refractory patients
- Describe epidemiology and treatment patterns of EoE patients
- Establish disease burden while on SoC, sequence of treatment, dilation and emergency intervention requirements