Retrospective review of biologic and targeted-synthetic disease modifying anti-rheumatic drugs in individuals with Down syndrome

Nicole Boswell, MD, Ipsit Shah, Tasya Rakasiwi, Chenin Ryan, Alan Vu MD, Diana Zarowin, Catherine Reilly, Alice Lin, Jordan Lamb, Eun Jae Kim, Madeline Hlobik, Vincent Hou, Sadaf Hussain MD, Katherine Marks MD, Elena Harwyluk MD, Colleen Cotton MD, James Treat MD, Emily Gurnee MD, Irene Lara-Corrales MD, Jillian Rork MD, Kristen E Holland MD

Department of Dermatology, Dartmouth Health, Manchester, NH, USA; Geisel Medical School, Hanover, NH, USA; Department of Dermatology, Medical College of Wisconsin, Milwaukee, WI, USA; Albert Einstein College of Medicine, Bronx, NY, USA; Georgetown University School of Medicine, Washington, DC, USA; University of Pittsburg School of Medicine, Pittsburg, PA, USA; Harvard Medical School, Boston, MA, USA; Division of Dermatology, Children's National Hospital, Washington, DC, USA; Department of Dermatology, University of Pittsburgh Medical Center, Wexford, PA, USA; Dermatology Program, Boston Children's Hospital, Boston, MA, USA Department of Dermatology, Massachusetts General Hospital, Boston, MA, USA; Section of Dermatology, Children's Hospital of Philadelphia, Philadelphia, PA, USA; Department of Dermatology, Children's Hospital Colorado, Aurora, CO, USA; Division of Dermatology, The Hospital for Sick Children, Toronto, Ontario, CAN

Background

- Down syndrome (DS) is the most common chromosomal condition diagnosed in the United States and is associated with various dermatologic conditions including hidradenitis suppurativa (HS), psoriasis, and alopecia areata. [1-5]
- Patients with DS have an increased risk of respiratory infections, with higher rates of pneumonia and higher rates of hospitalization. In addition, they are at increased risk for leukemia.
- As the inherent health risks associated with DS may be exacerbated by biologic use, it is important to understand the subsequent effects of biologics in those with DS not only to prevent adverse events, but also to avoid undertreatment of conditions due to lack of data.
- DS patients are often excluded from clinical trials leading to a paucity of data on the safety of biologics and other DMARDs in those with DS. [6-9]

Key Objective

Explore the use of biologic therapy and other DMARDs in patients with Down syndrome with a focus on safety.

Methods

Patients with an ICD-9/ICD-10 diagnosis of DS (758.0/Q90.9) with an outpatient dermatology visit between January 2006 and December 2021 who were prescribed a medication of interest were eligible for this retrospective chart review. Data was stored in Dartmouth Hitchcock Health REDCap database. The data collected was then analyzed for frequency and prevalence of biologics used and adverse events that occurred during treatment.

Results

- 86 patients from 9 institutions have been included to date. Demographics are included in Table 1. 66 (77%) had one medication, 9 (10%) had 2 medications, 6 (7%) had 3 medications, 3 (3%) had 4 medications, and 2 (2%) had 5 medications resulting in a total of 124 medication courses. Medications used and diseases treated are outlined in Figures 1 and 2.
- At time of chart review, patients were still on treatment in 64/124 (52%) of the medication courses reviewed, with an average treatment duration of 3.5 years, SD = 3.0, median = 2.3, range = 0.08 to 13.5 years.
- Of the 60/124 (48%) treatment episodes that were discontinued, insufficient effect was the most common reason for stopping treatment (31/60, 52%) across all diseases (Figure 6).
- The most common infections were upper respiratory infection (26/96, 20%), otitis media (17/96, 14%) , and skin infection (17/96, 14%).
- There were 7 hospitalizations for infection: 2 SARS-CoV-2, 2 pneumonia, 1 URI, and 1 otitis media.
- Infection resulted in discontinuation of the medication in only 5 cases.
- No hematologic malignancy or death from a medication complication was identified during or after treatment courses reviewed.

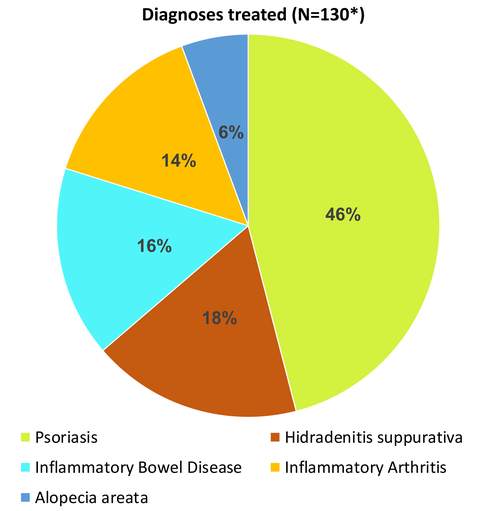


Figure 1: Diagnoses treated in our patient population

*More than one diagnosis was treated in some cases

	N(%) = 86
Age at Time of 1st Medication	15.5 [2 – 56]
Sex at Birth	
Female	43 (50%)
Male	43 (50%)
Race	
White	65 (76%)
Black or African American	8 (9%)
Asian	4 (5%)
American Indian or Alaska Native	1 (1%)
Multiracial	1 (1%)
Unknown/Does not specify	7 (8%)
Ethnicity	
Hispanic/Latino/a/x	8 (9%)
Non-Hispanic/Latino/a/x	78 (91%)

Table 1: Demographics of our patients

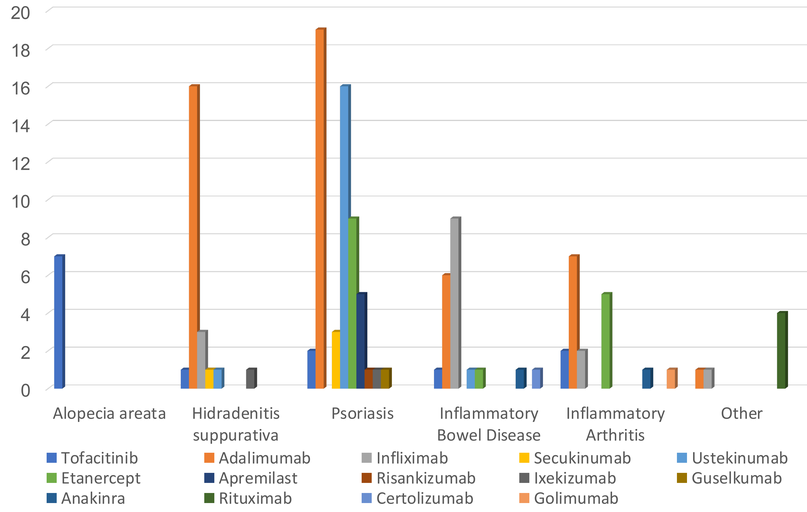
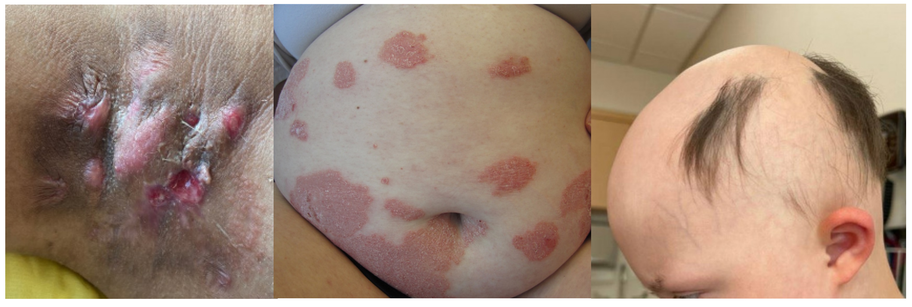


Figure 2: Biologics Used for Each Associated Disease



Figures 3-5: Hidradenitis suppurativa, psoriasis, and alopecia areata pictured.

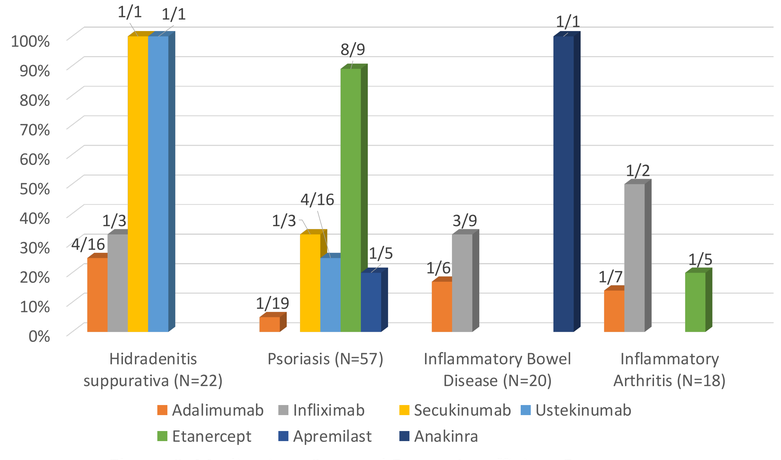


Figure 6: Medications Stopped Due to Insufficient Response

Adverse Events (AE) that Led to Treatment Discontinuation (N=21)		N (%)
Infection during course of treatment	Lower tract respiratory infection	2 (10%)
	Upper airway respiratory infection	1 (5%)
	Skin infection	1 (5%)
	Otitis Media	1 (5%)
Allergy	Allergic Reaction, unspecified	4 (19%)
Gastrointestinal	Abdominal Pain	1 (5%)
	Diarrhea	2 (10%)
Paradoxical flare of inflammatory condition	Paradoxical flare of inflammatory condition that is being treated	4 (19%)
	Paradoxical flare of separate inflammatory condition	2 (10%)
Psychiatric Condition	Other (Behavior changes/manic episodes, and aggressive behavior, swearing, self-harm)	2 (10%)
Other AE	Worsening hypogammaglobulinemia	1 (5%)

Table 2: Adverse events that led to treatment discontinuation

Discussion

- The rate of hospitalization or medication discontinuation due to infection was low (Table 2).
- Results of this study suggest that the use of biologics in DS patients does not place them at higher risk for more severe infection despite their baseline predisposition.
- While treatment durations were limited in this review, no patients were diagnosed with a hematologic malignancy following biologic use despite concerns for baseline risk.
- Although the overall number of reported adverse events and adverse effects were low, future studies are needed to further characterize the definitive safety of biologics in patients with DS.
- Further evidence of safety of biologic therapy in DS patients may help to assuage fears surrounding use of these medications and promote better care for these patients.

Sources