A Study to Help Guide Management Decisions in Patients with Psoriasis and Atopic Dermatitis

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Background

- In the United States, psoriasis affects over 7.5 million people and the prevalence of atopic dermatitis is approximately 24.5 million when considering both adults and children. [1-3]
- The advent of multiple targeted systemic therapies offers additional tools to treat psoriasis and atopic dermatitis for patients with moderate to severe disease. [4-5]
- However, due to the complex pathogenic landscape of these inflammatory diseases, as well as individual genetic and environmental factors, patients respond differently to systemic therapies. [4-5]
- Additionally, there is a subset of difficult-to-diagnose cases that may further contribute to difficulties in therapeutic selection.[8]
- Currently, clinical factors combined with a costly and time-consuming trial-and-error approach are used to determine individual patient response to systemic therapies.[9]
- However, it remains unknown if molecular signatures could improve upon the current clinical approach to determining treatment choice.

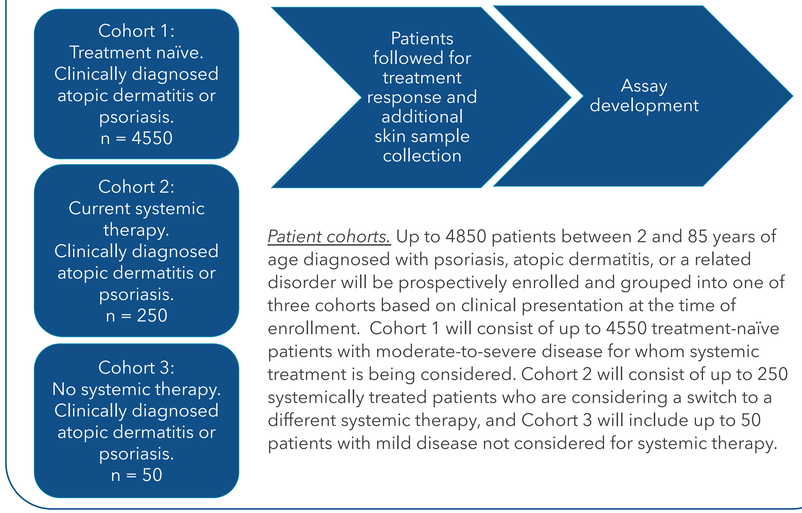
Objective

- To develop and validate one or more gene expression signatures to guide treatment selection in patients with psoriasis, atopic dermatitis, and related conditions.

Study Design

- Here we present the design of an IRB-approved study protocol geared toward developing one or more gene expression profiles for systemic therapy guidance in atopic dermatitis and psoriasis.

Figure 1. Patient Cohorts



Patient cohorts. Up to 4850 patients between 2 and 85 years of age diagnosed with psoriasis, atopic dermatitis, or a related disorder will be prospectively enrolled and grouped into one of three cohorts based on clinical presentation at the time of enrollment. Cohort 1 will consist of up to 4550 treatment-naïve patients with moderate-to-severe disease for whom systemic treatment is being considered. Cohort 2 will consist of up to 250 systemically treated patients who are considering a switch to a different systemic therapy, and Cohort 3 will include up to 50 patients with mild disease not considered for systemic therapy.

Study Design

Table 1. Timeline of Data and Sample Collection Scheduled for Each Visit

Visit #	1	2	3	4	5	6	7	8	9	10	11	Unplanned
Time, months	0 (Enrollment)	1	2	3	6	9	12	18	24	30	36	Any
Cohort 1	x	x	x	x	x	x	x	x	x	x	x	x
Cohort 2	x	x	x	x	x	x	x	x	x	x	x	x
Cohort 3	x						x		x		x	x
Informed consent	x											
Data collection: demographics, medical history, diagnosis and treatment	x											
Data collection: changes in health and/or treatment		x	x	x	x	x	x	x	x	x	x	x
Disease severity scoring (EASI, PASI, vIGA, PGA, BSA)	x	x	x	x	x	x	x	x	x	x	x	x
Patient questionnaires (PIQ, PEST, 4QS, DLQI, CDLQI)	x	x	x	x	x	x	x	x	x	x	x	x
CBI patient questionnaire	x	x	x	x	x	x	x	x	x	x	x	x
Skin sample collected	x	x	x	x	x	x	x	x	x	x	x	x
Diagnostic photography	x											

EASI, eczema area and severity index; PASI, psoriasis area and severity index; vIGA, validated investigator global assessment scale; PGA, physician global assessment; BSA, body surface area; PIQ, patient itch questionnaire; PEST, psoriasis epidemiology screening tool; 4QS, four question screen; (C)DLQI, (children's) dermatology life quality index; CBI, Castle Biosciences Inc.

Data and sample collection. At enrollment, images will be taken to document disease diagnosis and severity. Each patient and enrolling physician will also complete a series of questionnaires documenting disease severity. A noninvasive technique will be used to collect superficial layers of diseased and healthy skin from up to five body regions and samples will be stored in an RNA preserving buffer. Samples will be collected, patients and enrolling physicians will complete follow-up questionnaires, and additional clinical data including systemic treatment type, dose, response, and side effects will be logged in a secure electronic data capture system by study staff during 10 subsequent visits over 3 years for Cohorts 1 and 2 and once a year for 3 years for Cohort 3.

Study Design

Figure 2. Workflow for Assay Development

Test development and validation. RNA from samples will be isolated and unbiased assessment of RNA expression levels using microarray will be performed. Gene targets will be narrowed using machine learning techniques to develop one or more gene signatures that can predict disease clearance and/or failure of systemic treatment.

Conclusion

The development of a test that can identify the likelihood of response to therapy in moderate-to-severe psoriasis and atopic dermatitis may help guide therapeutic choice for patients for whom clinical diagnosis or drug selection may be challenging, thereby decreasing the time and money spent on finding a successful treatment for the patients.

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Disclosures

- ASF is a consultant for Castle Biosciences, Inc. and on the advisory board for Eli Lilly, Sun Pharma, Orthodermatologics, Boehringer Ingelheim, Incyte, Amgen, Galderma, Novartis and Pfizer.
- MSG, APQ, OZ, and KLA are employees and shareholders of Castle Biosciences, Inc.
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