PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	An international observational atopic dermatitis cohort to follow natural history and treatment course: TARGET-DERM AD study design and rationale
AUTHORS	Abuabara, Katrina; Silverberg, Jonathan I.; Simpson, Eric L.; Paller, Amy S.; Eichenfield, Lawrence; Bissonnette, Robert; Krueger, James; Harris, John; Dalfonso, Laura; Watkins, Stephanie; Crawford, Julie; Thaçi, D.; Guttman-Yassky, Emma

VERSION 1 – REVIEW

REVIEWER	Ryoji Tanei Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology Japan
REVIEW RETURNED	22-May-2020

GENERAL COMMENTS	I think this paper presented by the authors of Abuabara K, et al, "Protocol for an observational atopic dermatitis cohort: TARGET-DERM AD study design and rationale," represents a groundbreaking research plan. This long-term observational study is sure to bring new progress to medical care and research of atopic dermatitis (AD), with significant benefits for patients with AD, their families, and clinicians involved in the clinical practice of AD. Clinicians and researchers who, like me, are interested in the pathophysiology of AD would look forward to announcing their research results. However, achieving that may require the extraordinary intelligence of the authors and the enormous effort of the participants and the project team. The results of the TARGET DERM AD cohort will be expected to establish a new strategy for the management of AD as a lifelong immune-mediated inflammatory skin condition characterized by eczema and dermatitis. This will be a great job.

REVIEWER	Droitcourt C University of Rennes Department of Dermatology Rennes, France
REVIEW RETURNED	06-Jul-2020

GENERAL COMMENTS	Thank you for giving me the opportunity to review this paper. Additional data on the use and the safety of immunosuppressive drugs for atopic dermatitis with long-term endpoints are an important issue. - Page 4 lines 12 to 16: What about the AD patients seen in primary care and for whom topical treatments are prescribed? Are the AD patients seen in the community clinical centers? Your

	objective is to understand how treatments are used in clinical practice in tertiary centres or to include a large spectrum of AD forms also seen in primary and secondary cares? Please clarify - Page 4 line 56 and page 5 lines 3 -4 I suggest you say these studies provide additional and complementary information to the clinical trials on the use of AD treatment. Furthermore, clinical trials rarely include long-term endpoints - Page 4 lines 50 to 52: Yes. Some pragmatic studies describing the use of systemic treatments have been however published both in adults and children and using the “drug survival”, a comprehensive outcome covering effectiveness and safety particularly informative in the assessment of these treatments. - Page 8 lines 54-55 Page 9 lines 3 to 6: I would suggest giving more details on the sample calculation in the manuscript. In the section methods and analysis: I would suggest doing a separated chapter on the outcomes - In the section discussion I would like to mention the other DA registry/cohort initiatives for example in Europe

VERSION 1 – AUTHOR RESPONSE

Reviewers' Reports:

Reviewer: 1
Reviewer Name: Ryoji Tanei
Institution and Country: Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology, Japan
Please state any competing interests or state ‘None declared’: None

I think this paper presented by the authors of Abuabara K, et al, "Protocol for an observational atopic dermatitis cohort: TARGET-DERM AD study design and rationale," represents a groundbreaking research plan. This long-term observational study is sure to bring new progress to medical care and research of atopic dermatitis (AD), with significant benefits for patients with AD, their families, and clinicians involved in the clinical practice of AD. Clinicians and researchers who, like me, are interested in the pathophysiology of AD would look forward to announcing their research results. However, achieving that may require the extraordinary intelligence of the authors and the enormous effort of the participants and the project team. The results of the TARGET DERM AD cohort will be expected to establish a new strategy for the management of AD as a lifelong immune-mediated inflammatory skin condition characterized by eczema and dermatitis. This will be a great job.

We appreciate the encouraging comments.

Reviewer: 2
Reviewer Name: Droitcourt C
Institution and Country: University of Rennes, Department of Dermatology, Rennes, France
Please state any competing interests or state ‘None declared’: None declared

Thank you for giving me the opportunity to review this paper. Additional data on the use and the safety of immunosuppressive drugs for atopic dermatitis with long-term endpoints are an important issue.

1. Page 4 lines 12 to 16: What about the AD patients seen in primary care and for whom topical treatments are prescribed? Are the AD patients seen in the community clinical centers? Your objective is to understand how treatments are used in clinical practice in tertiary centres or to include a large spectrum of AD forms also seen in primary and secondary cares? Please clarify

We plan to enroll patients in both academic and community settings. We added a sentence in the Methods/Study design section to further clarify: “Adult and pediatric patients of all ages will be enrolled from up to 100 dermatology practices, including both academic practices affiliated with a University health system and community-based or private practice clinical centers.”

2. Page 4 line 56 and page 5 lines 3 -4. I suggest you say these studies provide additional and complementary information to the clinical trials on the use of AD treatment. Furthermore, clinical trials rarely include long-term endpoints

We agree and added to the background section to further clarify this point: “Pragmatic, real-world studies that capture long-term variability in atopic dermatitis disease activity and management can provide complementary data to clinical trials.”

3. Page 4 lines 50 to 52: Yes. Some pragmatic studies describing the use of systemic treatments have been however published both in adults and children and using the “drug survival”, a comprehensive outcome covering effectiveness and safety particularly informative in the assessment of these treatments.
Please see comment above.

4. Page 8 lines 54-55 Page 9 lines 3 to 6: I would suggest giving more details on the sample calculation in the manuscript.

We appreciate the desire for additional detail on sample size, but as described in the manuscript, the sample size was chosen for logistical reasons and additional post-hoc sample size calculations are unlikely to be helpful [PMID: 3155238].

5. In the section methods and analysis: I would suggest doing a separated chapter on the outcomes. In the section discussion I would like to mention the other DA registry/cohort initiatives for example in Europe

Thank you for these recommendations, in the methods we have added a sub-section heading for outcomes, and in the discussion we added the following sentence: “TARGET-DERM AD fills an important niche; although other atopic dermatitis registries exist, these are largely focused on the impacts of specific treatments (PEER and APPLE)11,12, genetic markers for susceptibility (Atopic Dermatitis Research Network),13 or systemic treatments (TREAT).14”

VERSION 2 – REVIEW

REVIEWER	DROITCOURT C Department of Dermatology, University Hospital of Rennes, France
REVIEW RETURNED	07-Sep-2020

GENERAL COMMENTS	Thank you for your responses and this work. I have no additional comments

VERSION 2 – AUTHOR RESPONSE

1. Can you please clarify/ revise the following in the abstract? “There have been no Ethics Committee reviews.” We consider IRBs and Ethics committees to be inter-changeable terms so it is unclear what this means.

This was a misunderstanding; there have been no additional Ethics Committee reviews beyond the IRB approvals listed in part 2.

2. In the abstract you say: “site-specific IRB approvals are obtained prior to patient enrollment where required.” Can you please provide a list of all site-specific IRBs that have approved this study, along with their approval reference numbers? You can include this as a supplementary information file and refer to this in the ethics and dissemination section.

We will include this as a supplementary file (also listed below):

Copernicus Group IRB – IRB20182865

Program for Protection of Human Subjects (PPHS) -HS#: 19-00448; GCO#1: 19-0952

Ann & Robert H. Lurie Children's Hospital of Chicago Institutional Review Board IRB 2019-2675

Northwestern University IRB STU00209616/IRBSITE00000400

Oregon Health and Science University IRB - STUDY00020054

University at Buffalo Institutional Review Board - STUDY00003546

University of Massachusetts Medical School Institutional Review Board - H00011641

Trustees of Dartmouth College Committee for the Protection of Human Subjects STUDY00031709

University of California, San Diego-Human Research Protections Program - Project 191025

University of Utah Institutional Review Board - 00126873

Western Institutional Review Board - IRB20182865

Mayo Clinic Institutional Review Board - 9-005338

We would not usually publish study protocols until ethics (or IRB) approval has been obtained from all participating centres. Please can you clarify when you will have received IRB approval from all participating sites?

Again, apologies for the misunderstanding – our IRB approvals have all been obtained (listed above).