



RACP Foundation Research Awards

PROGRESS REPORT

Project / Program Title	A novel clinician-reported treatment response measure in systemic lupuserythematosus (TRM-SLE)	
Name	Dr Kathryn Connelly	
Award Received	2020 RACP NHMRC CRB Blackburn Top-Up Scholarship	
Report Date	14/01/2021 – Year 1	
Funding Period	Start Date:	February 2020
	Finish Date:	January 2023

PROJECT SUMMARY

Systemic lupus erythematosus (SLE, lupus) is a chronic autoimmune disease that typically affects young women. Current treatments are unable to adequately control disease with acceptable toxicity in many patients, resulting in irreversible organ damage, poor quality of life and reduced life expectancy compared to the general population. Despite recognition of the need for new treatments in SLE, only one new drug has been approved for SLE in over 50 years, with many promising treatments failing in clinical trials. It is widely acknowledged that the inadequacy of current measures of treatment response used in SLE clinical trials has been a major contributor to these trial failures, and there is an urgent need for new instruments that better determine whether or not a new treatment is effective. This project aims to address this area of unmet need by undertaking steps towards the development and initial validation of a new measure of treatment response for use in SLE clinical trials.

PROJECT AIMS / OBJECTIVES

The overarching aim of this project is to develop and validate a new clinician-reported outcome measure for SLE, designed specifically to capture clinically important changes in SLE disease activity in response to therapy, and to be implemented as a primary outcome measure in lupus clinical trials for regulatory approval of novel therapies. The goals/projects outlined in Part 1 will form the bulk of my PhD project.

Part 1: Development of the novel treatment response measure

- 1a. To perform an extensive literature review to characterise the research problem and inform the approach to developing and validating a new treatment response measure
- 1b. To investigate the role of laboratory parameters in treatment response using an existing lupus cohort, to inform the inclusion of laboratory variables in the novel treatment response measure
- 1c. To undertake multi-stage consensus methods informed by existing literature and trial data resulting in the development of a preliminary treatment response measures

Part 2: Validation of the novel treatment response measures

- 2a. To evaluate the new measure in existing clinical trial datasets to determine discriminatory capacity and compare performance to existing trial endpoints

- 2b. To compare the new measure against clinician judgment of response and existing response using paper-based cases
- 2c. To evaluate the associations of the new measure with clinically important long-term outcomes in a longitudinal validation study

SIGNIFICANCE AND OUTCOMES

There is a major unmet need for new therapies in lupus to improve patient outcomes. In order for new treatments to become available and successfully utilised, an accurate means of determining treatment response in clinical trials is vital. Current trial endpoints in SLE are widely recognised to be suboptimal, and the development and validation of a new treatment response measure is a top research priority. This project in its entirety will span several years and completion of the development phase is on track to be completed within the tenure of my PhD. Using a rigorous data-driven and expert-consensus informed process, it is anticipated that this work will result in a well-designed and empirically validated treatment response measure that can be employed in clinical trials, improving identification of effective therapies and facilitating their regulatory approval so they may become available to patients in need of new therapeutic options

PUBLICATIONS / PRESENTATIONS

Systemic lupus erythematosus: a clinical update.

Submitted for publication in the Internal Medical Journal (IMJ)

Clinician-reported outcome measures in lupus trials: a problem worth solving

Manuscript in preparation for submission

Longitudinal improvement in abnormal laboratory tests are associated with clinical outcomes in patients with active SLE

Manuscript in preparation for submission

Conference abstracts to be submitted in early 2021.

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