RACP
Specialists. Together
EDUCATE ADVOCATE INNOVATE

RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		Clinical Evaluation of Osteoarthritis (OA) Biomarkers for Regulatory Qualification: the Foundation for the National Institute of Health Biomarkers OA Consortium (PROGRESS OA).
Name		Dr Leticia Deveza
Award Received		2020 RACP Australian Rheumatology Association & D.E.V Starr Research Establishment Fellowship
Report Date		27/05/2021
Funding Period	Start Date:	01/05/2019
	Finish Date:	30/12/2020

PROJECT SUMMARY

The lack of tools for early diagnosis and measures to predict disease progression in osteoarthritis (OA) continues to be a major hurdle in drug development, and there are currently no validated clinical biomarker endpoints for OA. The results of this project will provide a set of qualified biomarker tools that will impact clinical trial design by decreasing the number of patients needed, and decreasing the time and costs needed for OA drug development. The Biomarkers Consortium's PROGRESS OA - Clinical Evaluation and Qualification of Osteoarthritis Biomarkers Project is the second phase of a two-stage strategy to address the most fundamental obstacles to the development of new treatments for OA. This project will validate the highest performing biomarkers from the Phase I OA Biomarkers Consortium Project, which was completed in 2015.

PROJECT AIMS / OBJECTIVES

The goal of this proposal is to pursue formal Food and Drug Administration (FDA) and European Medicines Agency (EMA) qualification of osteoarthritis (OA) biomarkers for two distinct contexts of use:

A) Validation of the ability of a baseline set of plain radiographic measures, MRI measures and biochemical markers to predict likelihood of disease progression for qualification as prognostic markers with which to enrich OA trials for progressors.

B) Assess short-term change (baseline to 6 and 12 months) of a set of plain radiographic measures, MRI measures and biochemical markers to predict the likelihood of disease progression for qualification as prognostic markers to facilitate early identification of subjects likely to progress without treatment. This will be pursued by deploying novel biomarker measures in placebo-treated participants from extant clinical trials to determine if they have greater prognostic ability than the existing gold standard of radiographic joint space width (JSW).

The core hypothesis for this study is that single and/or combinatorial biochemical and imaging (MRI and novel bone measures on radiograph) biomarkers will have better prognostic validity than the

existing reference standard biomarker, radiographic joint space width, for disease progression in knee OA.

Progress during 2020: We have started with data acquisition and have completed all radiograph reads. MRI reads and biochemical marker measurements are underway. We have been working with a team of statisticians from several parts of world and have refined the statistical analysis plan for the project. We have submitted a qualification package to the FDA and are awaiting for feedback with delays due to the COVID pandemic.

SIGNIFICANCE AND OUTCOMES

Only around 1 in 10 participants in osteoarthritis (OA) clinical trials investigating disease-modifying therapies experience disease progression over the course of the trial despite not receiving any treatment. In addition, the only currently approved tool to assess the effect of an intervention in trials is the joint space width measured on plain x-rays, which has inherent shortcomings such as limited responsiveness to change over time. The lack of tools to predict disease progression in OA continues to be a major hurdle in drug development, and there are currently no validated clinical biomarker endpoints for OA. This project will improve clinical trial design by providing a set of qualified biomarker tools that will reduce the number of participants needed and reduce the time and costs needed for OA drug development, increasing the probability that a new candidate treatment will successfully perform in trials. The acceptance of these biomarkers for use in drug development will pave the way for improved clinical trials and treatments for patients with knee OA.

The results of the project are critical to establishing biomarkers that can be effectively used to develop new disease-modifying regimens for OA and creating an environment that encourages drug and device companies to invest in developing new therapies in this field. Without this, the development of new treatments in OA is likely to continue to be minimal. The potential public health benefit of this project is substantial, as it will address several of the most fundamental obstacles to the development of new treatments for OA, a disease that presents a large and growing global health burden.

PUBLICATIONS / PRESENTATIONS

In addition to making progress in the conduct of the Phase 2 Biomarkers study, we have published the final results of the Phase 1 of this work.

Hunter DJ, Deveza LA, Collins JE, Losina E, Nevitt MC, Roemer FW, Guermazi A, Bowes

MA, Dam EB, Eckstein F, Lynch JA, Katz JN, Kwoh CK, Hoffmann S, Kraus VB. Multivariable modeling of biomarker data from the phase 1 Foundation for the NIH Osteoarthritis Biomarkers Consortium. Arthritis Care Res (Hoboken). 2021 Jan 9. doi: 10.1002/acr.24557. Epub ahead of print. PMID: 33421361.

ACKNOWLEDGEMENTS

RACP Foundation has been acknowledged in the following publication which is part of this project:

Hunter DJ, Deveza LA, Collins JE, Losina E, Nevitt MC, Roemer FW, Guermazi A, Bowes MA, Dam EB, Eckstein F, Lynch JA, Katz JN, Kwoh CK, Hoffmann S, Kraus VB. Multivariable modeling of biomarker data from the phase 1 Foundation for the NIH Osteoarthritis Biomarkers Consortium. Arthritis Care Res (Hoboken). 2021 Jan 9. doi: 10.1002/acr.24557. Epub ahead of print. PMID: 33421361.

Leticia Deveza is funded by the Royal Australasian College of Physicians and Australian

Rheumatology Association & D.E.V Starr Research Establishment Fellowship.