TITLE: Comparative effectiveness of systemic psoriasis therapeutics; Inflammatory Biomarker Response

ABSTRACT: Aggressive treatment with anti-inflammatory therapeutics is controversial as to improvement of cardiovascular disease (CVD) risk. Meta analyses of psoriasis patients treated with methotrexate have demonstrated improvement, whereas other analyses have suggested that systemic therapies trend toward an increased risk of myocardial infarction. We propose to perform a prospective longitudinal observational pilot study of the behavior of established (plasma/serum) and investigative (cellular) biomarkers that are associated with increased risk of CVD events. The biomarkers will be measured during and after one year of a continuous intensive therapy algorithm using standard-of-care systemic agents designed to achieve >75% psoriasis. Change in the level of clinical response, serum biomarkers including highly sensitive C reactive protein (hsCRP), myeloperoxidase (MPO), adiponectin and resistin will be monitored during treatment. In addition to plasma/serum biomarkers, we will also assess novel cellular biomarkers including the circulating percentage of circulating Intermediate-Mon-2 (CD14++CD16+) monocytes, monocyte Tissue Factor (CD142) expression, and circulating Myeloid Derived Suppressor Cells (MDSCs). To complement blood biomarkers, we propose to use imaging modalities to directly image and quantitate carotid artery intimal medial thickness (CIMT) and arterial inflammation by positron emission tomography (PET) with magnetic resonance (PET/MR) at baseline and 12 months of therapy. The final endpoint of the proposed study will be a ranking of the examined biomarkers based upon an integrated assessment of biomarker behavior over time. Our specific aims are to: 1.) Determine whether plasma biomarkers associated with atherosclerotic and metabolic syndrome risk (hsCRP, resistin, MPO, adiponectin) change following treatment with systemic therapies for psoriasis, 2.) Determine whether inflammatory monocytic cells (CD14++CD16+, CD142highCD14+, MDSCs) change following treatment with systemic therapies for psoriasis, 3.) Determine whether carotid artery intimal thickness (CIMT) and/or coronary PET/MR-visualized-arterial inflammation change following one year of treatment with systemic therapies for psoriasis and determine if change in arterial inflammation correlates with biomarker change, 4.) Determine whether changes in psoriasis severity correlate with biomarker change and 5.) Determine biomarker ranking for likelihood of performance in a large scale study of comparative effectiveness on CVD biomarkers with the goal of performing a power analysis for such a study using the top performing biomarkers.

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