

# **CLINICAL VALIDITY AND UTILITY OF THE PsoriasisDX GENETIC TEST FOR PSORIATIC ARTHRITIS**

This document discusses the clinical validity and utility of the PsoriasisDX Genetic Test for Psoriatic Arthritis (PsA).

## **INTRODUCTION: GENETIC SCREENING**

The goal of genetic screening is to identify subjects for preventive treatment or extended surveillance prior to onset of symptoms; therefore, the sensitivity of the test should be high so most people that eventually will develop the condition will be identified early. Also, a high specificity is desired to increase the efficacy of the screening and minimize the number of subjects that will be treated unnecessarily.

In addition, unlike traditional medical diagnostics, genetic tests may have no immediate clinical benefit, but may have great clinical utility. Accordingly, the National Institute of Health (NIH) commissioned the Task Force of Genetic Testing to expand the definition of clinical utility of genetic tests. The expanded definition takes into account the usefulness of a genetic test for the individual, family, and society as well as the social, economic and health impact on the individual.

## **STATISTICAL ANALYSIS**

We will demonstrate the clinical validity of the PsoriasisDX Genetic Test using standard statistical methods.

We pooled data from two independent peer reviewed and published studies that demonstrated statistical significant association between the genetic variants measured by the PsoriasisDX Genetic Test for PsA and psoriatic arthritis (1,2). The studies examined Jewish Caucasian and Spanish populations. A total of 316 individuals were genotyped, including males and females.

The mean ( $\pm$  SD) age of the PsA patients was  $46 \pm 12.5$  and  $36.4 \pm 15.7$  years for the Spanish and Jewish populations, respectively. The mean age at the presentation of arthritis was  $37 \pm 13.5$  years in the Spanish population and  $41 \pm 15.3$  years in the Jewish population. Age and ethnicity matched control populations were used for comparative analysis in both studies.

The pooled data reported by the studies is presented in the table below:

MICA-A9 Allele	Psoriatic Arthritis	Non-Psoriatic Arthritis	TOTAL
A9+	TP = 78	FP = 53	131
A9-	FN = 55	TN = 130	185
TOTAL	133	183	316

Abbreviations used: T = a positive test result i.e., presence of an A9 allele;  $\sim$ T = a negative test result i.e., absence of an A9 allele; D = a person having the disease i.e., PsA;  $\sim$ D = a person not having the disease i.e., non-PsA; TP = True Positive; FN = False Negative; FP = False Positive; TN = True Negative

Based on the pooled data we calculated the following:

Sensitivity = the probability that a person with psoriatic arthritis will test positive =  $P(T|D) = 59\%$

Specificity = the probability that a person without psoriatic arthritis will test negative =  $P(\sim T|\sim D) = 71\%$

The clinical value of the PsoriasisDX genetic screening test needs to be interpreted in relation to the population prevalence of psoriatic arthritis among psoriasis patients.

We selected a disease (psoriatic arthritis) prevalence =  $P(D) = 40\%$ . This prevalence number is a lifetime estimate cited by Gladman et al. (3); however, the prevalence of PsA may be higher than estimated due to the lack of accepted diagnostic criteria and manifestation of symptoms that are similar to other arthritic condition.

Of particular importance to physicians is the probability that a person will develop psoriatic arthritis if he or she tested positive, as well as the probability that a person will not develop psoriatic arthritis if he or she tested negative.

Applying the Bayes formula to the pooled data we conclude:

Probability that a person that tested positive will develop psoriatic arthritis =  $P(D|T) = 59\%$

Probability that a person that tested negative will not develop psoriatic arthritis =  $P(\sim D|\sim T) = 70\%$

## **CLINICAL VALIDITY**

Using the PsoriasisDX Genetic Test for psoriatic arthritis, a physician can conclude that a patient that tests positive has approximately 60% chance of developing PsA; thus, the patient will likely benefit from early treatment.

Similarly, a physician can conclude that a patient that tests negative has approximately 70% chance of not developing psoriatic arthritis; thus, the patient may be able to avoid costly treatment.

As any screening test is not perfect, the PsoriasisDX genetic screening test may fail to identify some patients that will ultimately develop PsA; therefore, the PsoriasisDX screening test should always be accompanied by appropriate medical diagnostic.

## **CONCLUSION**

In the majority of the patients, PsA symptoms appear at least a decade after the onset of cutaneous psoriasis; therefore, dermatologists have a unique opportunity to practice preventative medicine. The importance of this therapeutic window is underscored by the fact that PsA becomes more severe when left untreated, leaving patients with significant joint damage, functional impairment, and reduced quality of life.

FDA approved medications for the treatment of PsA are most effective at controlling inflammation and arresting joint destruction, but are ineffective at reversing joint damage; therefore, it is important to identify psoriasis patients at high risk for developing PsA prior to the onset of arthritic symptoms.

Current PsA screening techniques identify symptomatic patients after the onset of the inflammatory arthritis. The objective of the PsoriasisDX screening test is to help physicians identify patients with a high risk for developing PsA prior to the onset of symptoms.

Identifying PsA in an earlier or pre-clinical stage will allow treatment to be initiated at a time when intervention has a greater likelihood of succeeding. Early screening combined with tailored treatment will help prevent disease progression and slow joint destruction.

## REFERENCES:

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4. Ackermann, C., et al. Economic burden of psoriatic arthritis. *Pharmacoeconomics*. 2008, 26 (2): 121-129.