Paper #29

Prospective, Multicenter, Adjudicator-Blinded Clinical Trial of the Alpha-Defensin Lateral Flow Test for Periprosthetic Infection

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Introduction: The purpose of this study was to evaluate the diagnostic performance of the alpha-defensin (AD) lateral-flow test for periprosthetic joint infection (PJI) for FDA submission, and secondarily to compare the AD lateral flow test to the AD laboratory-based test for PJI.

Methods: A prospective, multicenter, adjudicator-blinded clinical trial (NCT02868736) was designed as required by the FDA for consideration of a de novo diagnostic device. The trial design included 2 arms: 1) a prospective cohort of patients prior to anticipated revision hip or knee arthroplasty (N=305), and 2) a laboratory-derived fresh synovial fluid sample cohort of subjects meeting Musculoskeletal Infection Society (MSIS) criteria for PJI (N=65). The 2013 MSIS criteria were utilized as the gold standard for subject classification, with each subject independently adjudicated by a panel of three expert adult arthroplasty surgeons blinded to study results. Adjudication of the combined cohorts yielded 122 MSIS positive and 248 MSIS negative patients.

Results: The AD lateral flow test for PJI demonstrated a sensitivity of 94.3% (95% CI: 88.5-97.7%) and specificity of 94.8% (95% CI: 91.2-97.2%) in the combined cohorts. In the prospective cohort alone, the AD lateral flow test had a sensitivity of 89.7% (95% CI:78.8-96.1%) and specificity of 94.8% (95% CI:91.2-97.2%). The exclusion of 17 samples with a red blood cell count >1,000,000 cells/ul in this cohort yielded a sensitivity of 94.4% (95% CI:84.6-98.8%). There was no statistically significant impact of prior antibiotic treatment, other medication treatment, underlying systemic inflammatory diagnoses or culture positivity. The sensitivity and specificity of the AD lateral flow test (94.3 and 94.8%) in combined cohorts did not demonstrate a statistically significant difference from the AD laboratory-based test (92.7 and 97.6%; both $p>0.05$).

Conclusions: This study demonstrates that the AD lateral flow test for PJI has excellent performance in diagnosing PJI, similar to the laboratory-based test for AD. It is now the first FDA-authorized diagnostic test to aid in detecting PJI.