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Title
Accuracy of a host response test for diagnosis of bacterial and viral infections and prediction of illness severity in Emergency Department patients is not impacted by the patient's immune status

Authors (no more than 10)

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Objectives
Emergency department (ED) patients with suspected infections are common and have diverse diagnoses, severities, and co-morbidities. Specifically, immunocompromised (IC) patients are at high risk for developing severe disease and sepsis. We evaluated the accuracy of the TriVerity™ Acute Infection and Sepsis Test, a 29-mRNA host response test from blood to diagnose bacterial and viral infections and predict illness severity, in IC patients.

Methods
A multicenter, prospective clinical trial (SEPSIS-SHIELD) in EDs across the United States and Europe enrolled adult patients with suspected acute infection or suspected sepsis (NCT04094818). Whole blood was collected in PAXgene® RNA tubes. IC subjects included those with cancer, solid-organ and other transplants, HIV/AIDS, and other immunosuppression (autoimmune, steroids). TriVerity measured the expression of 29 mRNAs on the Myrna™ instrument which reports results via IMX-BVN/SEV-4 classifiers to generate three (bacterial, viral, and illness severity) scores in five discrete interpretation bands (very low, low, moderate, high, very high) in about 30 minutes. Bacterial and Viral score accuracy was evaluated against clinically adjudicated true infection status. Severity score was evaluated against the 7-day need for mechanical ventilation, vasopressors, and/or renal replacement therapy ("ICU-level care"). Sensitivity, specificity, and likelihood ratios (LR) were calculated for each band.
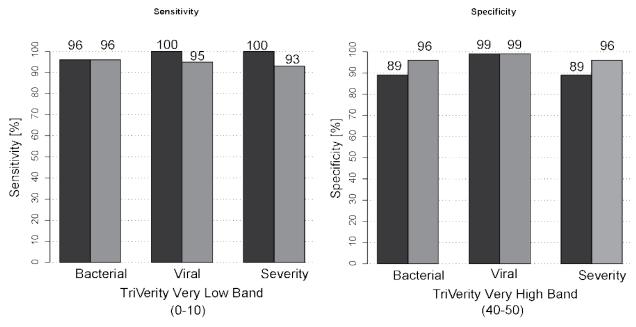
Results/Findings
Of 933 patients enrolled,149 were identified as IC. In an interim analysis, 144 of these IC patients (15%) had available severity endpoints, and 88 (9.4%) patients had available infection status (69 [78%] subjects were adjudicated as bacterial, 8 [9%] as viral, and 11 [13%] as non-infected). For the Very Low bands, the sensitivity of the Bacterial score was 96%; the sensitivity of the Viral score was 100%, and the sensitivity of the Severity score was 100%. The sensitivity of the Very Low bands in immunocompetent (NIC) patients was

similar for the Bacterial (96%) score and lower for the Viral (95%) and Severity (93%) scores. For the Very High bands, the specificity of the Bacterial (89%) score and Severity (89%) were lower than the immunocompetent patients (Bacterial 96%; Severity 96%); while the specificities of the Viral (99%) scores were similar.

Conclusions
The TriVerity test (in development) utilizes host response to aid in the diagnosis of bacterial and viral infections and the prediction of illness severity. Preliminary results indicate the TriVerity test has high diagnostic and prognostic accuracy and is not affected by the patient's immune status.

Figure 1. Sensitivity and Specificity of Bacterial, Viral, and Severity Scores in Immunocompromised (IC) and Immunocompetent (NIC) Patients

IC-dark gray bars; NIC-light gray bars