DAYZERO DIAGNOSTICS

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**Abstract Summary**

# Direct-from-Blood Predictive AST from Clinical Samples

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**Background**

Current antimicrobial susceptibility testing (AST) methods rely on slow culture-based phenotyping, while faster marker-based molecular diagnostics lack breadth of coverage. We report interim results from a first-of-its-kind clinical study demonstrating rapid and comprehensive predictive AST for a broad panel of antibiotics directly from clinical blood samples, without culture. The method leverages a proprietary process for ultra high enrichment (UHE) of microbial DNA directly from blood with near complete genome recovery, sequencing (WGS), and predictive AST machine learning algorithm.

**Methods**

Blood samples were collected from patients with suspicion of bacteremia at 4 Boston hospitals 7/2023-3/2024 in 2 observational studies. Samples were processed with the Day Zero Diagnostics (DZD) UHE process, sequenced on an Oxford Nanopore Technologies sequencer, and analyzed by DZD's predictive AST algorithm. Categorical predictions (S/I/R) were compared to phenotypic AST derived from matched hospital blood cultures to calculate categorical agreement (CA), and very major, major, and minor error rates (vME, ME, mE). We report predictive AST accuracy for 13/16 patient samples that passed data QC, for 65 high-confidence models and an additional panel of 70 R&D stage models.

**Results**

The high-confidence predictions achieved an aggregate CA of 92.3% and vME/ME rates of 0.0%/2.6%. The extended panel including R&D stage models had a CA of 88.2% and vME/ME rates of 3.6%/2.0%. This panel produced predictions for all on-panel species encountered in the study: 3 gram-positive (S. aureus, S. agalactiae, S. pyogenes) and 3 gram-negative (E. coli, K. pneumoniae, P. aeruginosa). It provided predictions for >88% of all drugs tested by the hospitals, including 100% coverage for E. coli and P. aeruginosa. The algorithm demonstrated high accuracy for many clinically important combinations, such as S. aureus/oxacillin, P. aeruginosa/ciprofloxacin, and K. pneumoniae/cefepime (all with CA=100%).

**Conclusion**

To our knowledge, this is the first clinical study demonstrating direct-from-blood, broad-panel predictive AST, demonstrating the promise of rapid and comprehensive AST determination.