The accuracy of the Xpert-MTB-HR Prototype was evaluated against Xpert MTB/RIF, which is the most likely confirmatory assay in high-burden, resource-limited settings, and parallel against a comprehensive microbiological reference standard (CMRS) consisting of multiple cultures.

Of 201 patients included, 67 were culture-positive for Mycobacterium tuberculosis. With Xpert MTB/RIF as diagnostic reference, AUC for the Xpert-MTB-HR Prototype was 0.94 (95% CI 0.91-0.96). With the CMRS as reference, AUC was 0.89 (95% CI 0.83-0.94) for the Xpert-MTB-HR Prototype with a specificity of 55.9% (CI 47.2-64.1) at 91% sensitivity. Considering Xpert-MTB-HR Prototype as a triage test (at nearest upper value of sensitivity to 90%), the corresponding specificity was 55.9% (CI 47.2-64.1).

Comparing Xpert MTB/RIF as a confirmatory test, Xpert-MTB-HR Prototype specificity was 85.9% (CI 79.3-85.7). Considering Xpert-MTB-HR Prototype as a stand-alone diagnostic test at a specificity near 95%, the test achieved a sensitivity of 65.7% (CI 53.7-75.9).

CPR performed similarly in the triage use-case against the CMRS but substantially poorer against Xpert MTB/RIF as reference standard and in a diagnostic use-case.

Discussion

- To achieve global end TB goals, Cepheid's novel Xpert-MTB-HR Prototype may make an important contribution for patients whose disease can be difficult to diagnose due to their limited ability of producing a sputum sample, including HIV-positive patients and children.
- This trial supports the technical feasibility of the Sweeney et al. 3-gene signature as a non-sputum triage test for Cepheid's GeneXpert platform.
- Performance was demonstrated in a cohort of HIV positive patients and implicates a potential benefit for other patient groups where a non-sputum sample is favorable.

Given that we tested an early prototype of the cartridge, further improvements in its diagnostic performance are conceivable with refinements in its development.

Conclusion

This is the first accuracy trial of a novel blood-based host-marker assay, here we show the value of the Xpert-MTB-HR Prototype for diagnosis of TB in a vulnerable and very difficult to diagnose population living with HIV.

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