

**L0045 A randomised comparison of GeneXpert Ultra MTB/RIF and GeneXpert for the diagnosis of tuberculous meningitis**

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**Background:** Tuberculous meningitis (TBM) is the most severe form of tuberculosis. Current diagnostic tests are insufficiently sensitive for *Mycobacterium tuberculosis* (*Mtb*) detection in cerebrospinal fluid (CSF). Xpert MTB/RIF (Xpert) is valuable in TBM diagnosis, yet a negative test cannot exclude the disease. Xpert MTB/RIF Ultra (Ultra) aims to improve tuberculosis diagnosis and rifampicin resistance identification. Study data describing Ultra in TBM are limited to 23 HIV co-infected individuals, yet the World Health Organisation now recommends Ultra as a replacement for Xpert in all settings. A large prospective randomised study, inclusive of HIV uninfected individuals, is urgently required.

**Materials/methods:** We performed a prospective randomised study comparing the diagnostic performances of Ultra and Xpert for the diagnosis of *Mtb* in CSF. The uniform case definition for TBM was used as a reference standard, with neither Xpert nor Ultra included in this standard. Individuals  $\geq 16$  years old, with TBM or non-TBM brain infection were enrolled at the Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam.

**Results:** 210 patients were consecutively enrolled from October 2017 to February 2019. Diagnostic performances compared against a reference standard of definite, probable plus possible TBM, are displayed.

	<b>Ultra</b> <b>(N=106)</b>	<b>Xpert</b> <b>(N=104)</b>
Positive tests in TBM <sup>#</sup>	24/50	21/51
Sensitivity	48.0%	41.2%
(95% confidence interval)	(34.8-61.5%)	(28.8-54.8%)
Positive tests in non-TBM brain infection <sup>#</sup>	0/45	0/42
Specificity	100%	100%
(95% confidence interval)	(92.1-100%)	(91.6-100%)

<sup>#</sup>Includes only individuals where final diagnosis was known at time of writing

Diagnostic sensitivities of Ultra and Xpert for the detection of *Mtb* in CSF were not significantly different (48.0 vs. 41.2%,  $p=0.62$ ). Sensitivities of Ziehl-Neelsen smear and mycobacterial culture were 74.8 and 51.8%

respectively. In HIV uninfected individuals Ultra showed increased diagnostic sensitivity over Xpert against the same reference standard, and against culture (39.4 vs. 23.5%,  $p=0.26$ ; 83.3 vs. 66.7%,  $p=0.71$ , respectively), however these were also not statistically significant. Rifampicin resistance was detected in 5/24 (20.8%) and 5/21 (23.8%) positive Ultra and Xpert tests, respectively.

**Conclusions:** Ultra was not superior to Xpert for the diagnosis of TBM. Ultra and Xpert specificities were both 100%. A high sensitivity diagnostic test for TBM remains elusive.

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