LAB NEWS

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CMV Viral Load: Roche assay to replace lab-developed test

Since 2006, the Virology laboratory has offered a laboratory developed CMV viral load test, which has performed very well both for our patients and in international studies (1, 2). Recently, Roche COBAS Ampliprep/COBAS TaqMan CMV Real-time PCR test became the first CMV viral load test to be approved by the FDA for clinical diagnosis (3-6). The Virology Laboratory has successfully used Roche viral load tests for HIV, HCV and HBV for many years and will implement the Roche CMV viral load assay at the end of July, in part due to increased regulatory pressure to use FDA approved tests when available.

Advantages of using the FDA approved Roche CMV test: 1) Results are reported in International Units (IU) to improve correlation across methods and laboratories; 2) the use of a standardized commercial assay will allow comparisons between centers; 3) the Roche assay has rapidly become the single most commonly used CMV viral load test in the U.S.; 4) the test is automated to reduce human error; 5) clinical trials can now establish cut-offs for pre-emptive treatment that can be applied across institutions.

Disadvantages of the Roche CMV test: 1) The test is less flexible, cannot be done on weekends or holidays, and is not amenable to emergency requests; 2) the test takes longer to perform so results will be reported later in the day than previously; 3) the Roche test is only approved for plasma; 4) the Roche test is much more expensive; 5) the Roche assay quantitative values in IU/mL are 10-fold lower than the previously reported values in copies/mL; 6) there are currently no established Roche CMV PCR cut-off values for pre-emptive therapy in different patient groups.

Sample requirements: Submit two (2) lavender top tubes. The Roche CMV quantitative PCR is performed only on plasma.
Test Availability: Once a day, Monday through Friday. Samples must be received in Virology by noon for results by 6 PM.
Assay Performance characteristics: Limit of detection (LOD), 95% confidence interval: 91 IU/mL. Linear range: 137-9,100,000 UI/mL. Positive results below the linear range will be reported as "Detected", "<137 IU/mL".
Interpretive Comments on Report are as follows: All positive results do not require anti-viral therapy. Trends are more important than absolute numbers. The CMV DNA cut-off values for initiating pre-emptive therapy in patients without symptoms varies depending on the assay used, the risk factors for CMV disease and the type and degree of immunosuppression.
Note: On July 28, 2015, the FDA-approved Roche assay, reported in IU/mL, replaced the YNHH lab-developed CMV quantitative PCR, reported in copies/mL. Roche IU/mL values are expected to be 5-10 fold lower than the prior lab-developed test reported in copies/mL. Clinical trials using the Roche assay to determine cut-off values for pre-emptive therapy for CMV have not yet been reported.

Other sample types: The qualitative lab-developed CMV PCR will be performed for other sample types. In critical situations, the CMV qualitative PCR can be performed for a preliminary result on plasma on weekends and holidays when the Roche test is unavailable.

References

1. Li H, et al. Measurement of human cytomegalovirus loads by quantitative real-time PCR for monitoring clinical intervention in transplant recipients. J Clin Microbiol. 2003 41(1):187-91.
2. Pang XL, et al. Interlaboratory comparison of cytomegalovirus viral load assays. Am J Transplant. 2009 9(2):258-68.
3. Babady NE, et al. Monitoring of cytomegalovirus viral loads by two molecular assays in whole-blood and plasma samples from hematopoietic stem cell transplant recipients. J Clin Microbiol. 2015 53(4):1252-7
4. Mannonen L, et al. Comparison of two quantitative real-time CMV-PCR tests calibrated against the 1st WHO international standard for viral load monitoring of renal transplant patients. J Med Virol. 2014 86(4):576-84
5. Pritt BS, et al. Conversion to the COBAS AmpliPrep/COBAS TaqMan CMV Test for management of CMV disease in transplant recipients. Diagn Microbiol Infect Dis. 2013 75(4):440-2.
6. Hirsch HH, et al. An international multicenter performance analysis of cytomegalovirus load tests. Clin Infect Dis. 2013 56(3):367-73

Prepared by Marie L. Landry, M.D. For questions, contact the Clinical Virology Laboratory at 688-3524.