Test Definition: PBKQN

BKV DNA Detect/Quant, P

Overview

Useful For

Detection and serial monitoring of BV virus-associated nephropathy in kidney transplant recipients using plasma specimens

Detection and serial monitoring of BV virus-associated hemorrhagic cystitis in organ transplant recipients

Highlights

This assay detects and quantifies the level of BK virus (BKV) DNA present in the plasma of kidney transplant recipients who are at risk of developing BKV-associated nephropathy leading to decreasing renal function and eventual renal failure. The assay is calibrated to the First World Health Organization International Standard for BKV DNA.

Method Name

Real-Time Polymerase Chain Reaction (RT-PCR)

NY State Available

Yes

Specimen

Specimen Type

Plasma EDTA

Shipping Instructions

1. Ship specimen frozen on dry ice only.

2. If shipment will be delayed for more than 24 hours, freeze plasma at -20 to -80 degrees C (up to 84 days) until shipment on dry ice.

Specimen Required

Supplies: Aliquot Tube, 5 mL (T465)

Collection Container/Tube: Lavender top (EDTA)

Submission Container/Tube: Plastic vial

Specimen Volume: 1.5 mL

Collection Instructions:

1. Centrifuge blood collection tube per manufacturer's instructions (eg, centrifuge within 2 hours of collection for BD Vacutainer tubes).

2. Aliquot plasma into plastic vial.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-General Request (T239)

-Microbiology Test Request (T244)

-Renal Diagnostics Test Request (T830)

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK

Specimen Minimum Volume

0.5 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen (preferred)	84 days	
	Refrigerated	6 days	

Clinical & Interpretive

Clinical Information

BK virus (BKV) is a circular, double-stranded DNA virus with an approximately 5 kilobase-size genome in the polyomavirus family, of which 13 members of the family are known, including the JC virus (JCV) and SV40. BKV shares about 75% of its DNA sequence with JCV. Nearly 80% of the adult population worldwide have antibodies to both viruses, indicating previous infection or exposure to these viruses.

Initial infection with BKV is usually acquired in childhood, mostly asymptomatic or manifesting as a mild flu-like illness.

After primary infection, BKV establishes latency in the kidney and bladder of the infected individual. In the setting of immunosuppression, the virus reactivates and begins to replicate, triggering renal tubular cell lysis and viruria. As the reactivation progresses, the virus multiplies and crosses into the bloodstream, causing viremia and invading the kidney graft. In patients with kidney transplants, reactivation of BKV typically reaches peak incidence at 3 months posttransplantation with BK viral replication in the kidney graft, causing BKV-associated nephropathy (BKVAN), which manifests as kidney dysfunction that may result in eventual loss of the transplanted kidney. Reactivation of BKV in the bladder can lead to hemorrhagic cystitis. Currently, there are no FDA-approved antiviral agents or treatments for BKVAN or BKV-associated hemorrhagic cystitis, and the main treatment is to decrease the immunosuppression, with the risk of acute rejection of the kidney graft.

After BK reactivation, the virus is first detectable in the urine, with viremia developing several weeks later. Quantitative BKV DNA in the plasma is the most widely used and preferred test for the laboratory diagnosis of BKVAN and BKV-associated hemorrhagic cystitis, as BKV viremia has higher positive predictive value (50%-60%) than BKV viruria for the diagnosis of BKVAN. Serial monitoring of BKV DNA level in plasma is recommended to guide optimal immunosuppressant dosing regimen. In those with BKVAN, clearance of BK viremia is a sign of resolution of the nephropathy.

Reference Values

Undetected

Interpretation

The quantification range of this assay is 22 to 100,000,000 IU/mL (1.34 log to 8.00 log IU/mL), with a limit of detection (95% detection rate) at 22 IU/mL.

An "Undetected" test result indicates the absence of BK virus (BKV) DNA in the plasma.

A test result of "<22 IU/mL (<1.34 log IU/mL)" indicates that BKV DNA is detected in the plasma, but the assay cannot accurately quantify the BKV DNA present below this level.

A quantitative value (reported in IU/mL and log IU/mL) indicates the level of BKV DNA (ie, viral load) present in the plasma.

A test result of ">100,000,000 IU/mL (>8.00 log IU/mL)" indicates that BKV DNA level present in plasma is above 100,000,000 IU/mL (8.00 log IU/mL), and the assay cannot accurately quantify BKV DNA present above this level.

An "Inconclusive" result indicates that the presence or absence of BKV DNA in the plasma specimen could not be determined with certainty after repeat testing in the laboratory, possibly due to polymerase chain reaction inhibition or presence of interfering substance. Submission of a new specimen for testing is recommended if clinically indicated.

Cautions

On average, quantitative BK virus (BKV) DNA results in plasma tested with this assay can be up to 1.4-fold (about 0.15 log IU/mL) higher than those generated from the previous laboratory-developed BKV DNA quantification assay performed at Mayo Clinic Laboratories, due to differences in the specimen extraction method and design in the amplification primers and probes for the viral target sequences.

A single "Undetected" test result does not necessarily rule out the presence BKV infection or reactivation. Serial measurement (eg, once weekly) of BKV DNA in plasma is recommended to determine the BKV replication status in a given transplant recipient.

Clinical Reference

1. Bechert CJ, Schnadig VJ, Payne DA, Dong J: Monitoring of BK viral load in renal allograft recipients by real time PCR assays. Am J Clin Pathol. 2010 Feb;133(2):242-250. doi: 10.1309/AJCP63VDFCKCRUUL

2. Hirsch HH, Randhawa P, AST Infectious Diseases Community of Practice: BK polyomavirus in solid organ transplantation. Am J Transplant. 2013 Mar;13 Suppl 4:179-188. doi: 10.1111/ajt.12110

3. Hirsch HH, Randhawa PS, AST Infectious Diseases Community of Practice: BK polyomavirus in solid organ transplantation-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13528. doi: 10.1111/ctr.13528

4. Muhsin SA, Wojciechowski D: BK virus in transplant recipients: current perspectives. Transplant Research and Risk Management. 2019:11:47-58. doi: 10.2147/TRRM.S188021

Performance

Method Description

The cobas BK virus (BKV) assay is an FDA-approved, in vitro nucleic acid amplification test for the quantification of BKV DNA in human EDTA-plasma using either the cobas 6800 or 8800 system for fully automated viral nucleic acid extraction (generic silica-based capture technique) and automated amplification and detection of the viral RNA. This dual-target polymerase chain reaction (PCR) assay amplifies 2 highly-conserved target regions within the BKV genome (small t-antigen and VP2 regions) for real-time detection and quantification by 2 target-specific TaqMan probes. A non-BKV armored DNA quantitation standard (DNA-QS) is introduced into each specimen during sample preparation to serve as internal control for nucleic acid extraction and PCR amplification and detection processes. Fluorescent reporter

dye-labeled TaqMan probes hybridized to the complementary BKV target sequences and DNA-QS sequence undergo hydrolysis during PCR amplification step to generate fluorescent signal detected in 3 different dye channels. Concentration of the BKV DNA in a patient's plasma sample is determined by a ratio of the intensity of the fluorescent dye from the cleaved BKV target sequence probes to that of the DNA-QS target probe detected throughout the PCR process.(Package insert: cobas BKV-Quantitative nucleic acid test for use on the cobas 6800/8800 Systems. Roche Molecular Systems; Doc rev 2.0, 02/2021)

PDF Report

No

Specimen Retention Time

30 days

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

87799

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PBKQN	BKV DNA Detect/Quant, P	32284-2

Result ID	Reporting Name	LOINC®
614567	BKV DNA Detect/Quant, P	32284-2