Comparison of Three Commercial Assays for the Quantitation of BK Virus in Renal Transplant Patients.

Neisha J eoffreyes

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Cairns, Australia
• Polyoma virus family
  • BK & JC (1971)
  • WU, KI & Merkel (2007-8)
  • TSPyV, HPyV6, HPyV7, HPyV9 & MWPyV (2010-13)

• BK & JC
  • Acquired during childhood (50 – 80%)
  • Sub-clinical or mild respiratory infection
  • Latent infection
  • Reactivation in immunocompromised host
BK Virus in Renal Transplant Patients

- BK virus reactivates in urogenital tissues
  - Haemorrhagic cystitis in BMT patients
  - BK virus associated nephropathy (BKVAN) in renal transplant patients

- BKVAN occurs in 1-10% of transplant recipients
- Premature graft loss in 15 - 80% affected patients
- BKVAN rates are increasing
Quantitative Detection of BK virus

- BKVAN traditionally detected by biopsy
- Routine monitoring using quantitative BK virus PCR
- > 10,000 copies/mL BK virus
- Variability between assays
- Treatment and reduced immunosuppression
- Ongoing weekly / fortnightly monitoring
- Better outcomes
Commercial Assays - Affigene

- Affigene BKV trender – Cepheid (CE-IVD)
- Real time PCR
- Blood and serum
- Sensitivity 464 cps/mL
- Quantitative range $10^3 – 10^8$ cps/mL
- No X-reaction with JC or SV-40
- Simple & quick
- Very expensive, delay in reporting
Commercial Assays - artus

- *artus* BK Virus PCR kit – Qiagen (CE)
- Real time PCR
- Plasma & urine
- Sensitivity 26.7 cps/mL plasma
- Quantitative range $50-10^7$ cps/mL
- No X reaction with JC or SV40
- Simple set up/ longer analysis
- More cost effective, concurrent runs
Commercial Assays - IAM

- Iam BKV with LIASON IAM analyser – DiaSorin (CE)
- Loop-mediated isothermal amplification (LAMP)
- Plasma & Urine
- Sensitivity 450 cps/mL plasma; 540 cps/mL urine
- Quantitative range $10^4 - 10^{10}$ cps/mL
- No X-reaction with JC or SV40
- Simple set up and analysis
- Most cost effective
Study Design

141 samples

artus BKV → In-house qualitative polyomavirus PCR → Positive → Affigene BKV trender → BK/JC specific PCR

Iam BKV

Discrepant

Nick Rismanto
St Vincents Hospital
Results

- 141 samples
  - 129 clinical (118 plasma, 2 CSF, 9 urine)
  - 12 QAP (results pending)

- 47/129 positive on at least one test (37%)
- 22 positive all assays – similar quantitative level
- Results do not correlate
Correlation

Artus
IAM
Affigene

CIDM
Centre for Infectious Diseases & Microbiology
Public Health

NSW Government Health Pathology
Discrepant results

• 7 positive polyomavirus / neg BK quantitative - JC virus

• 5 False Negative Results - below LOD
  • *lam* 5/5 neg (4/5 rpt); *artus* 3/5 neg (2/5 rpt); Affigene 1/5 neg (0/5 rpt)

• *artus*
  • 3 False Negative results (rpt pos)
  • 7 False Positive results (5 rpt neg, 2 insuff)
  • 2 Inhibited (1 neg on rpt)
  • 1 Cross reaction with JC virus (urine)
Genotype coverage

- 6 BKV genotypes
- Genotype I most common in US
- All assays theoretical coverage
  - Affigene – reduced sensitivity in types III & IV
- Reports of reduced sensitivity to genotype IV

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Future

• No longer offer polyomavirus qualitative assay

• *Iam* BKV (DiaSorin) twice weekly on plasma & urine

• Genotypes of low positive samples

• Prevalence study of BK genotypes in Australian population

• Possible introduction of a genotyping assay for all new patients with alternative monitoring
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DiaSorin