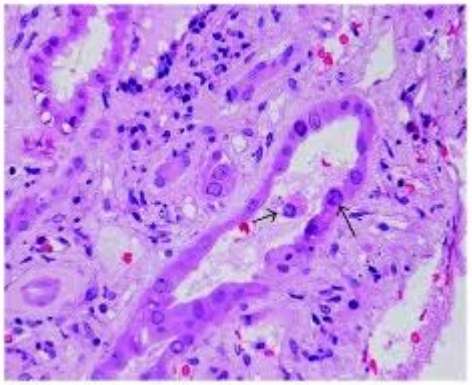
Böbrek transplantasyonunda geç dönem enfeksiyöz komplikasyonların yönetimi



Dr. İsmail Dursun
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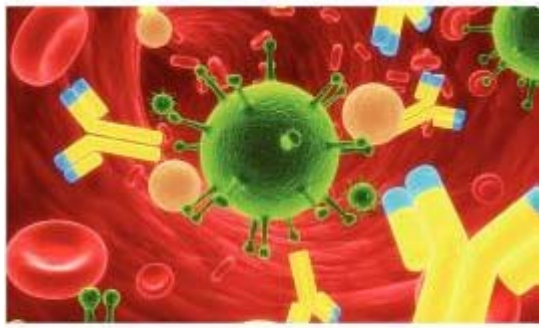
Tıp Fakültesi
Çocuk Nefroloji
Kliniği



Frederic P. Miller, Agnes F. Vandome, John McBrewster (Ed.)

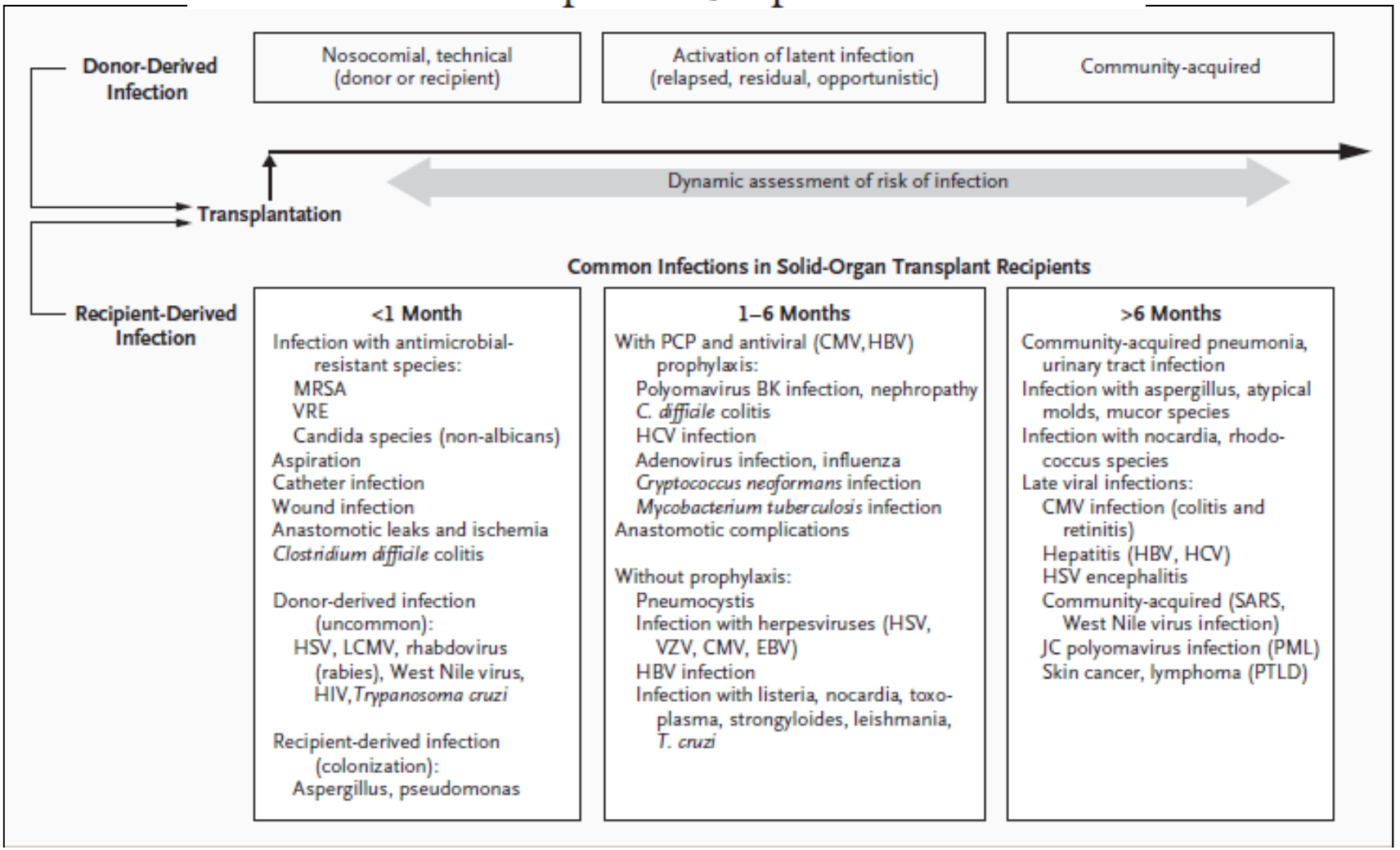
BK virus

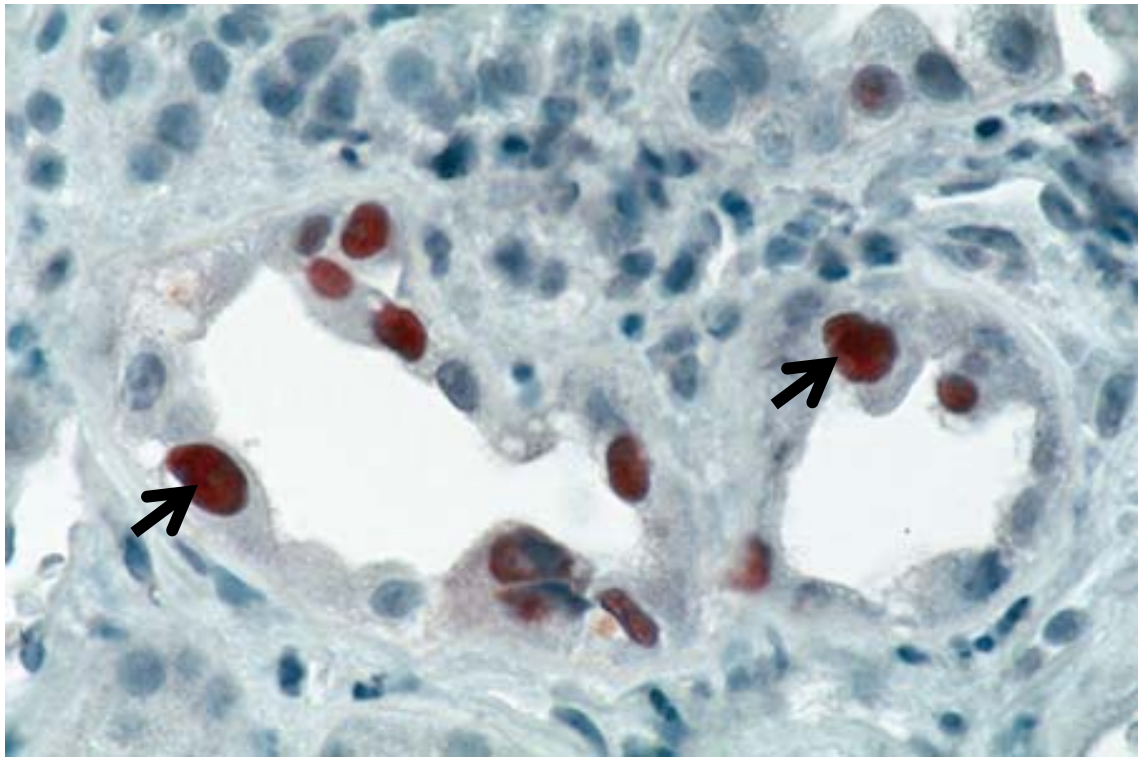
The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

MEDICAL PROGRESS

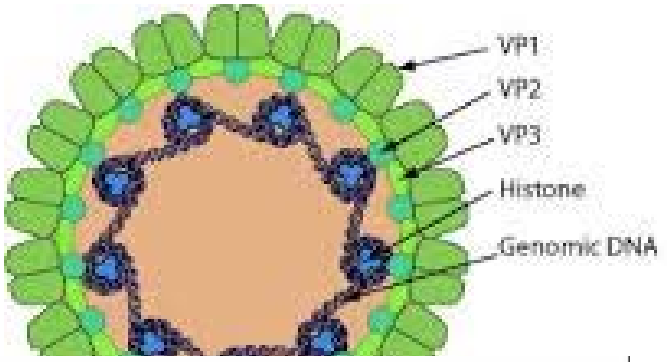
Infection in Solid-Organ Transplant Recipients





BK VİRÜS NEFROPATİSİ

Mikrobiyolojik özellikler



mother and the baby are presented in fig. 2. No rubella antibody was detected in the IgM fraction.

Discussion

In these three cases a significant rise in rubella-antibody titre was detected in pregnant women who were exposed to children with rubella early in pregnancy but had no history of clinical reactions after exposure.

The first question posed by a significant rise in titre is what type of antibody response it represents: a primary response during a subclinical infection, or a secondary response in a naturally immune subject? In case 1 the answer was obvious as rubella immunity was checked some months before the beginning of the pregnancy. This is unusual, however; and very often (as in cases 2 and 3) the first serum sample is taken after exposure, and in some cases the time of the exposure is not clearly defined. For these reasons analysis of serum fractions obtained after sucrose density-gradient ultracentrifugation has been recommended.[2,3] The results obtained in the three patients clearly show that the specific rise of rubella H.I. antibody was only in

NEW HUMAN PAPOVAVIRUS (B.K.) ISOLATED FROM URINE AFTER RENAL TRANSPLANTATION

SYLVIA D. GARDNER ANNE M. FIELD
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DULCIE V. COLEMAN B. HULME
Department of Histopathology and Cytology and Medical Unit, St. Mary's Hospital, London W.2

Summary The isolation of a new papovavirus from the urine of a renal allograft recipient with ureteric obstruction is described. Virus particles were observed in the cells lining the ureter by electron microscopy, and high, rising antibody titres to the virus were demonstrated in the patient's serum. This virus is not identical with any of the previously described members of the polyoma subgroup and has provisionally been named B.K. virus after the patient.

Introduction

Virüri	İdrarda BK virüsün sayıca artması
Viremi	Serumda veya plazmada BK virüsün sayıca artması
BKV Nefropati	Serum kreatininde artma ve renal parankimin virüs ile enfekte edilmesi, tubulointerstisyel nefrit

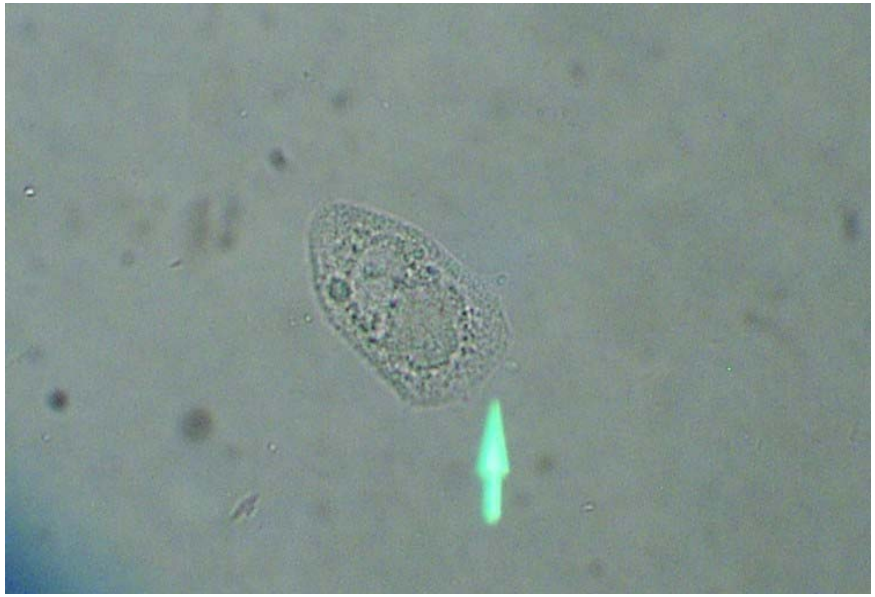
Am J Transplant 6:262–274

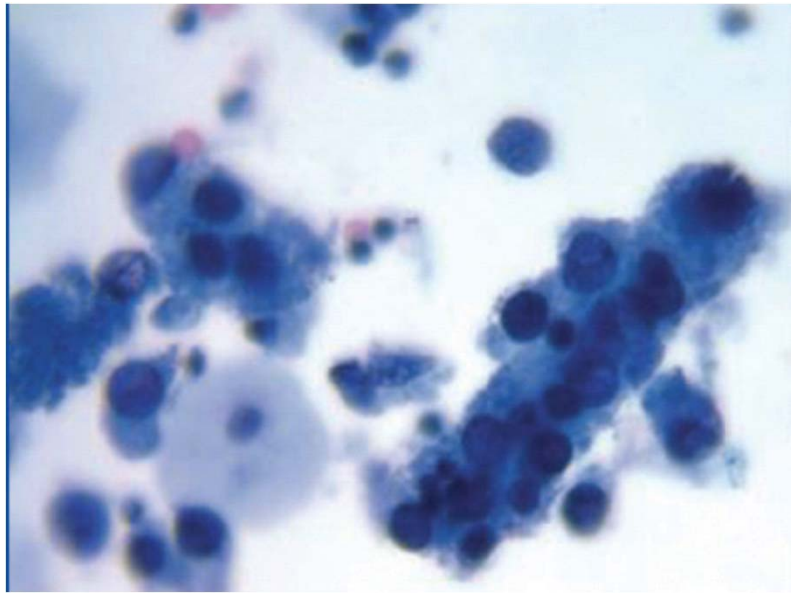
Polyomavirus infeksiyonu

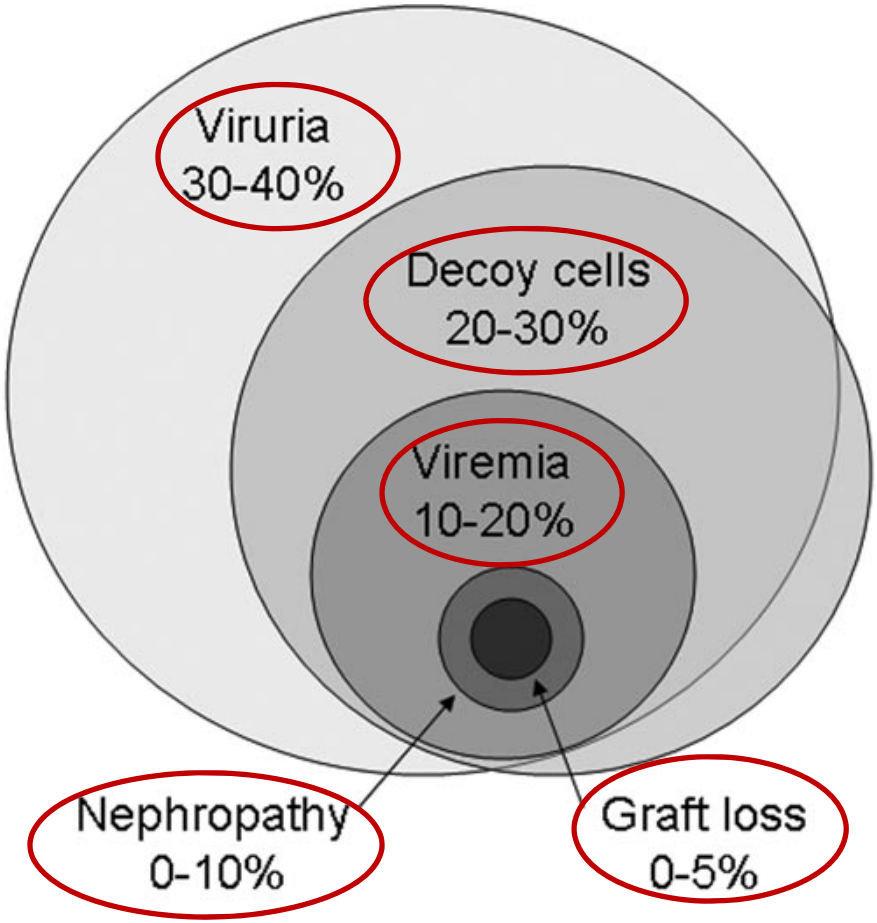
- 10 yaşında sero pozitiflik %65-90
- Asemptomatik
- Üroepitelyal hücrelerde latent kalır
- İmmuno-supresyon ile reaktivasyon
- Sayıca arttığında idrarda “decoy” hücreleri

Transplantation Reviews 2008;22:241–51

DECOY CELLS







*Rare cases of nephropathy without viremia or viremia without viruria may occur

Clin J Am Soc Nephrol 2: S36–S46, 2007

BK Virus Nephropathy in Pediatric Renal Transplant Recipients: An Analysis of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) Registry

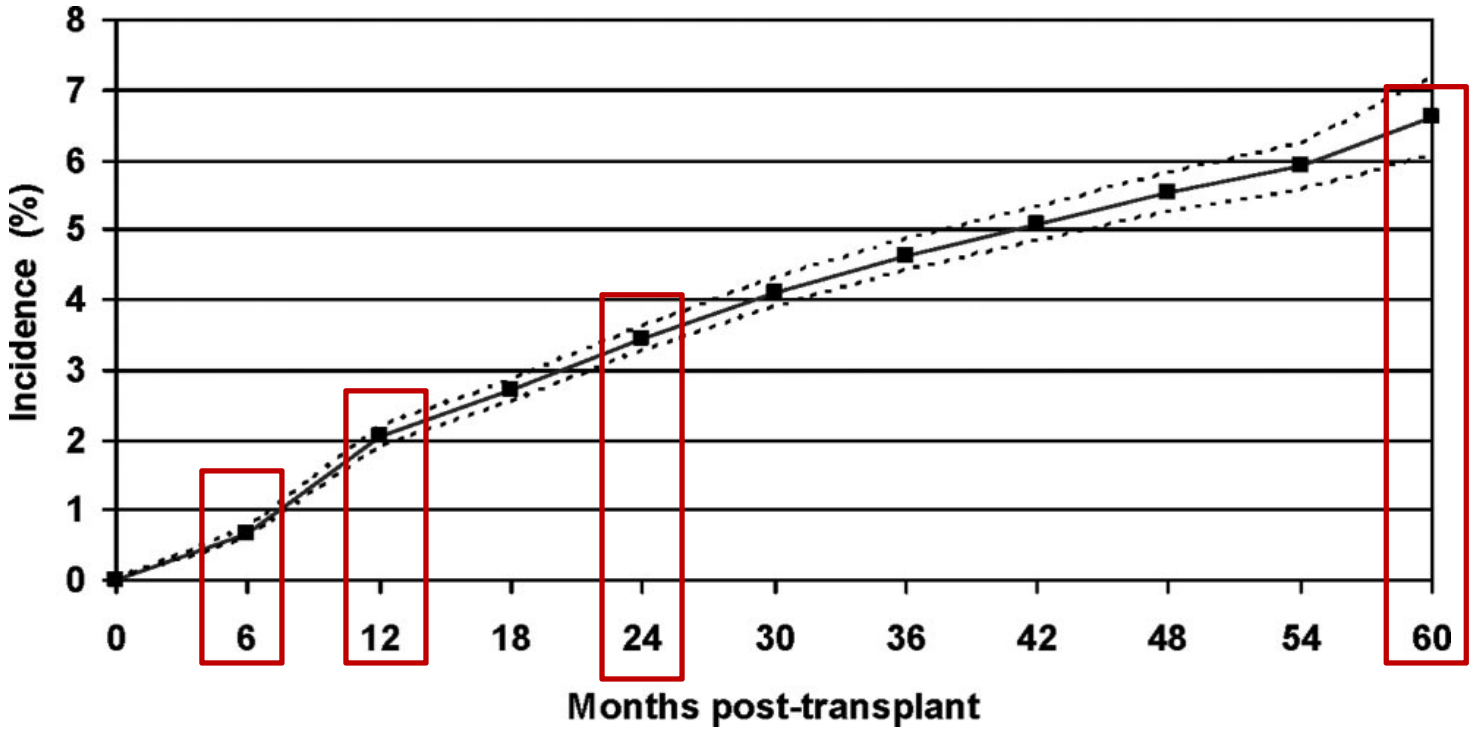
Post transplant 10.ayda hastaların % 4.6-6 ‘sında nefropati saptanmış

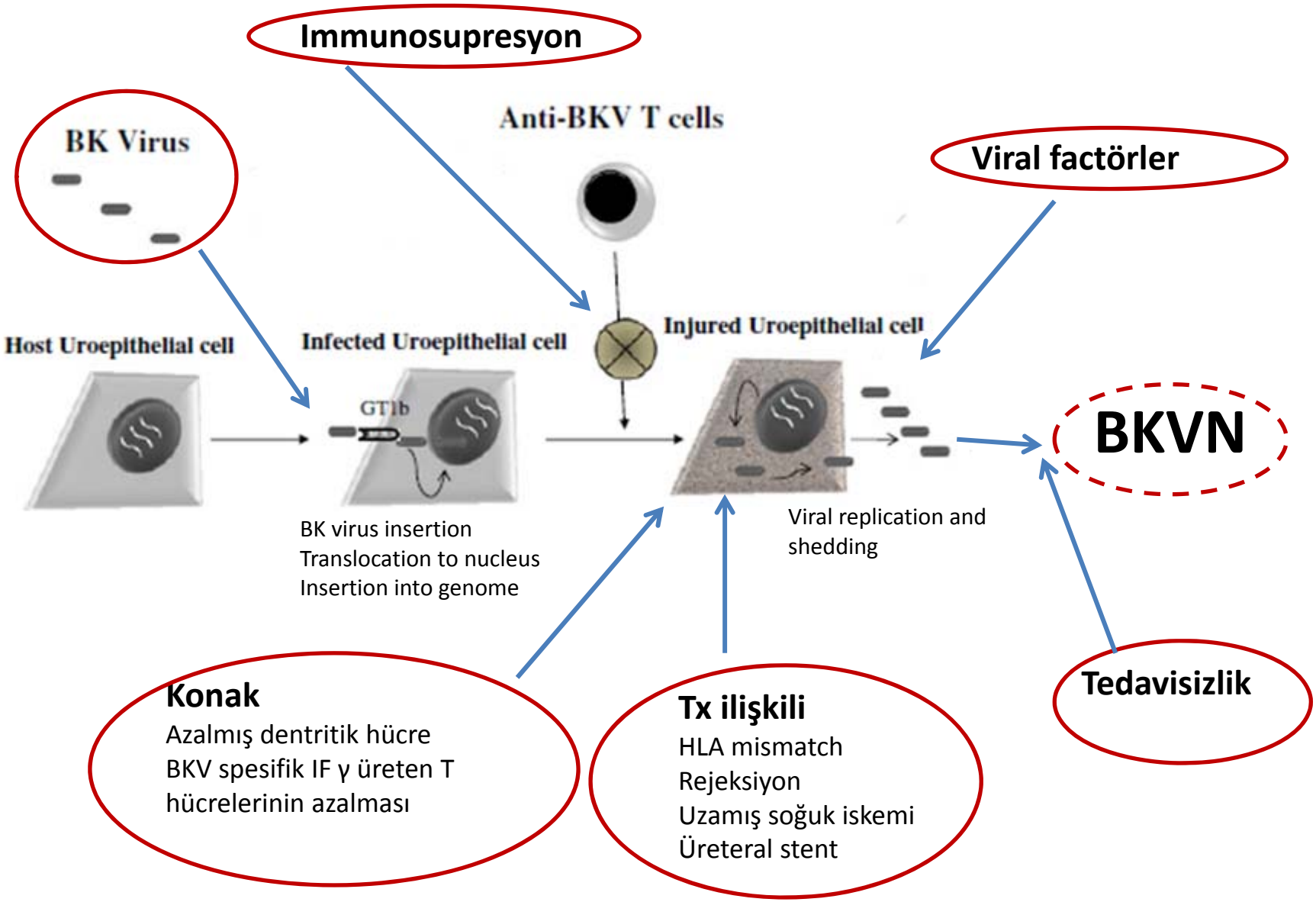
Clin J Am Soc Nephrol 2: 1037-1042, 2007, N Engl J Med 2002;347:488-96

An OPTN Analysis of National Registry Data on Treatment of BK Virus Allograft Nephropathy in the United States

Vikas R. Dharnidharka,[1,4] Wida S. Cherikh,[2] and Kevin C. Abbott[3]

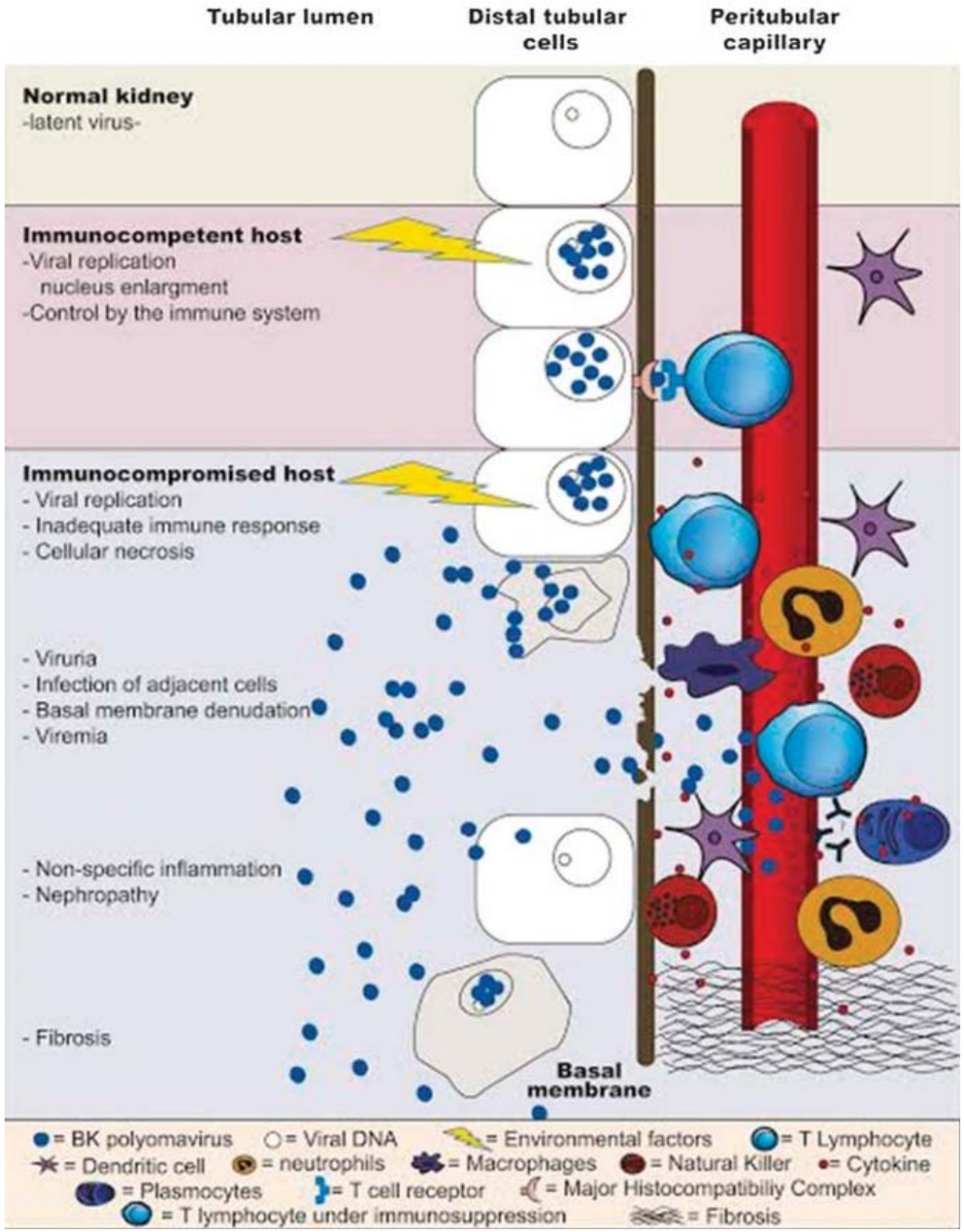
Transplantation 2009;87: 1019–1026





Pediatr Nephrol (2011) 26:1763–1774

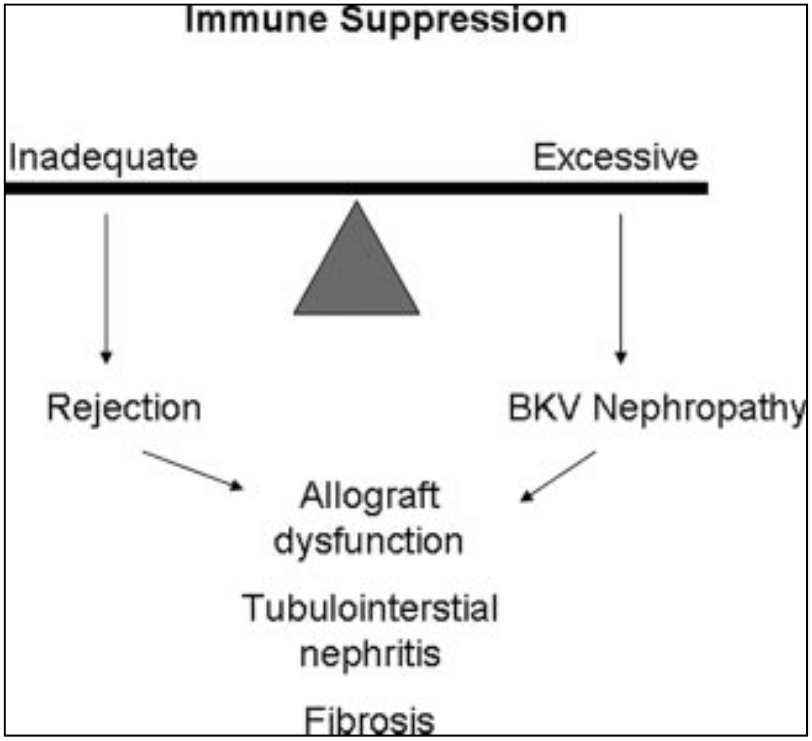
PATOFİZYOLOJİ



Transplantation 2016;100: 2276–2287

Risk faktörleri

- Yoğun immunosupresyon



Clin J Am Soc Nephrol 2: S36–S46, 2007

BK Virus Nephropathy in Pediatric Renal Transplant Recipients: An Analysis of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) Registry

Table 3. Multivariate logistic analysis of risk factors for BKVN[a]

Factor	Comparison Group	Reference Group	OR	95% CI	*P*
HLA-DR	0 mismatches	2 mismatches	7.31	2.58 to 20.71	0.0002
overall $P < 0.0001$	1 mismatches		0.89	0.31 to 2.56	0.8351
Induction therapy	Monoclonal	None	1.64	0.57 to 4.72	0.3638
overall $P = 0.0007$	Polyclonal		11.04	2.94 to 41.52	0.0004

Clin J Am Soc Nephrol 2: 1037-1042, 2007

Ureteral Stents: A Novel Risk Factor for Polyomavirus Nephropathy

Abraham Thomas,[1] Lesia K. Dropulic,[2] M. Hafizur Rahman,[1,3] and Duvuru Geetha[1,4]

TABLE 1. Distribution of cases and controls, according to baseline characteristics

	Cases, n=20	Controls, n=46	*P* value
Age (years) (mean±SD)	51.2 (14.8)	51.3 (12.5)	NS
Males (%)	80	50	0.02
Race			
White (%)	60	67.4	NS
Black (%)	35	30.4	NS
Other (%)	5	2.2	
Deceased donor transplant (%)	70	41.3	0.03
Average HLA mismatch (%)	95	82.6	NS
Average CIT (hours) (mean±SD)	22.8 (8.2)	27.9 (9.5)	NS
History of diabetes (%)	30	41.3	NS
Stent placed (%)	75	34.8	0.003
Delayed graft function (%)	45	17.4	0.02
History of acute rejection (%)	40	43.5	NS
History of urinary obstruction (%)	15	10.9	NS
Average MMF dose (g) (mean±SD)	1.8 (0.4)	1.9 (0.6)	NS
Average prednisone dose (mg) (mean±SD)	11.1 (5.7)	13.1 (6.2)	NS
Average tacrolimus level (ng/ml) (mean±SD)	10.4 (2.9)	9.6 (3.4)	NS
CMV infection donor-recipient (%)			
Negative-negative	26.3	21.7	NS
Negative-positive	10.5	30.4	NS
Positive-negative	31.6	15.2	NS
Positive-positive	31.6	32.6	NS
Exposure to antilymphocyte antibodies (%)	40	15.2	0.03
Exposure to solumedrol pulses (%)	50	41.3	NS

Transplantation 2007;84: 433–436

Ureteral Stents: A Novel Risk Factor for Polyomavirus Nephropathy

Abraham Thomas,[1] Lesia K. Dropulic,[2] M. Hafizur Rahman,[1,3] and Duvuru Geetha[1,4]

TABLE 2. Unadjusted and adjusted odds ratios from logistic regression models

Variables	Univariate model		Multivariate model			
	Odds ratio	*P* value	Odds ratio	*P* value	95% CI	
Stent placed	5.63	0.00	4.71	0.03	1.22	18.18
Age	1.00	0.98	1.01	0.77	0.96	1.06
Male (ref: female)	4.00	0.03	3.70	0.07	0.89	15.38
Deceased donor transplant (ref: live donor)	3.32	0.04	1.22	0.80	0.27	5.55
Delayed graft function	3.89	0.02	2.59	0.22	0.56	11.93
Mean tacrolimus	1.08	0.35	1.18	0.17	0.93	1.49
Exposure to antibodies	3.71	0.03	1.41	0.64	0.32	6.15

Transplantation 2007;84: 433–436

American Journal of Transplantation 2004; 4: 2109–2117
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2004.00629.x

Polyomavirus Nephropathy in Pediatric Kidney Transplant Recipients

Table 1: Patient characteristics of cohort

	All n = 173 (%)	BKVN n = 6 (%)	No BKVN n = 167 (%)	p Value
Median age (range)	12 (2–20)	10.5 (3–16)	12.4 (2–20)	0.3
Male gender	111 (64)	6 (100)	105 (61)	0.09
Transplant type				
Cadaver	64 (37)	2 (33)	62 (37)	0.6
Living	109 (63)	4 (67)	105 (63)	
Induction therapy				
OKT3/ATG/ALG	33 (19)	2 (33)	31 (19)	0.3
IL-2 receptor antagonist	64 (37)	4 (67)	60 (36)	
Primary immunosuppression				
Cyclosporine	148 (86)	6 (100)	148 (86)	0.6
MMF	72 (42)	5 (83)	67 (10)	0.08
Tacrolimus	25 (14)	0	25 (15)	0.6
Sirolimus	13 (8)	1 (17)	12 (7)	0.4
BKV recipient serostatus				
Recipient negative	9*	5 (83)	4 (25)	0.02
Recipient seropositive	13*	1 (17)	12 (75)	
Acute rejection	82 (47)	4 (67)	78 (47)	0.5

*A total of 22 patients were included in the analysis of BKV serostatus.

The genetic predisposition of natural killer cell to BK virus–associated nephropathy in renal transplant patients

Table 1 | Clinical and demographical characteristics of the study patients

Patient characteristics	BKVAN group ($N=48$)	Control group ($N=110$)	P-value
Age (yr), median (range)	59 (31–76)	61 (32–84)	NS
IS initial, n (%)			
Tac or CsA + MMF or AZA + Pred	48 (100%)	91 (83%)	<0.001
Tac or CsA + none + Pred	0 (0%)	19 (17%)	

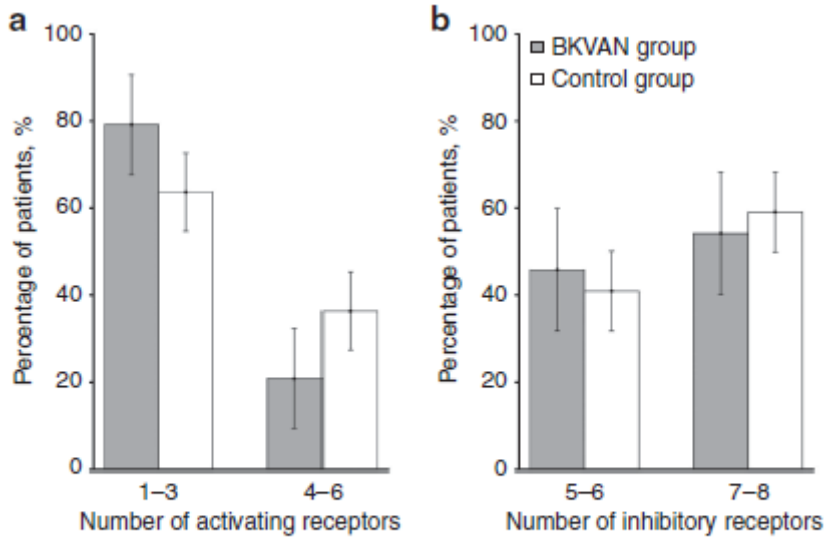


Figure 1 | Low amount of activating killer-cell immunoglobulin-like receptors (*KIR*) genes is associated with BK virus-associated nephropathy (BKVAN).

Kidney International (2013) 84, 359–365

Tanı

Tests	Findings	Comments
Urine cytology	Presence of decoy cells	Seen in 40-60% of transplant recipients, good screening test, positive predictive value around 20%
Viremia (plasma BKV DNA)	Copies >7000 per ml of plasma	Seen in 10-20% of transplant recipients, good screening test, positive predictive value around 60%
Viruria (urinary BKV DNA)	Copies 100-fold higher than plasma values	Seen in 30-40% of transplant recipients, good screening test, positive predictive value around 40%
Urinary BKV mRNA (active viral replication)	Copies diagnostic of BKVN	To be confirmed in other studies, research tool
BKV DNA in renal tissue	Detection of BKV DNA in renal biopsy tissue	Negative predictive value 100%, positive predictive value around 70%
Renal histology	Inflammatory changes with viral cytopathic effects, positive immunoperoxidase reaction with SV40 stain, predominant CD20-positive lymphocytic infiltrates	Gold standard, invasive procedure, focal lesions, chronic state with minimal viral cytopathic effects, mimics acute rejection
Serum BKV-specific antibodies	Diagnostic levels of IgM and IgG?	Seen in 80-90% of general population
BKV-specific antibodies and BKV DNA	Diagnostic levels of BKV-specific antibodies IgM, IgG and BKV DNA?	Research tool
T-cell immunity	Diagnostic measurement?	Research tool

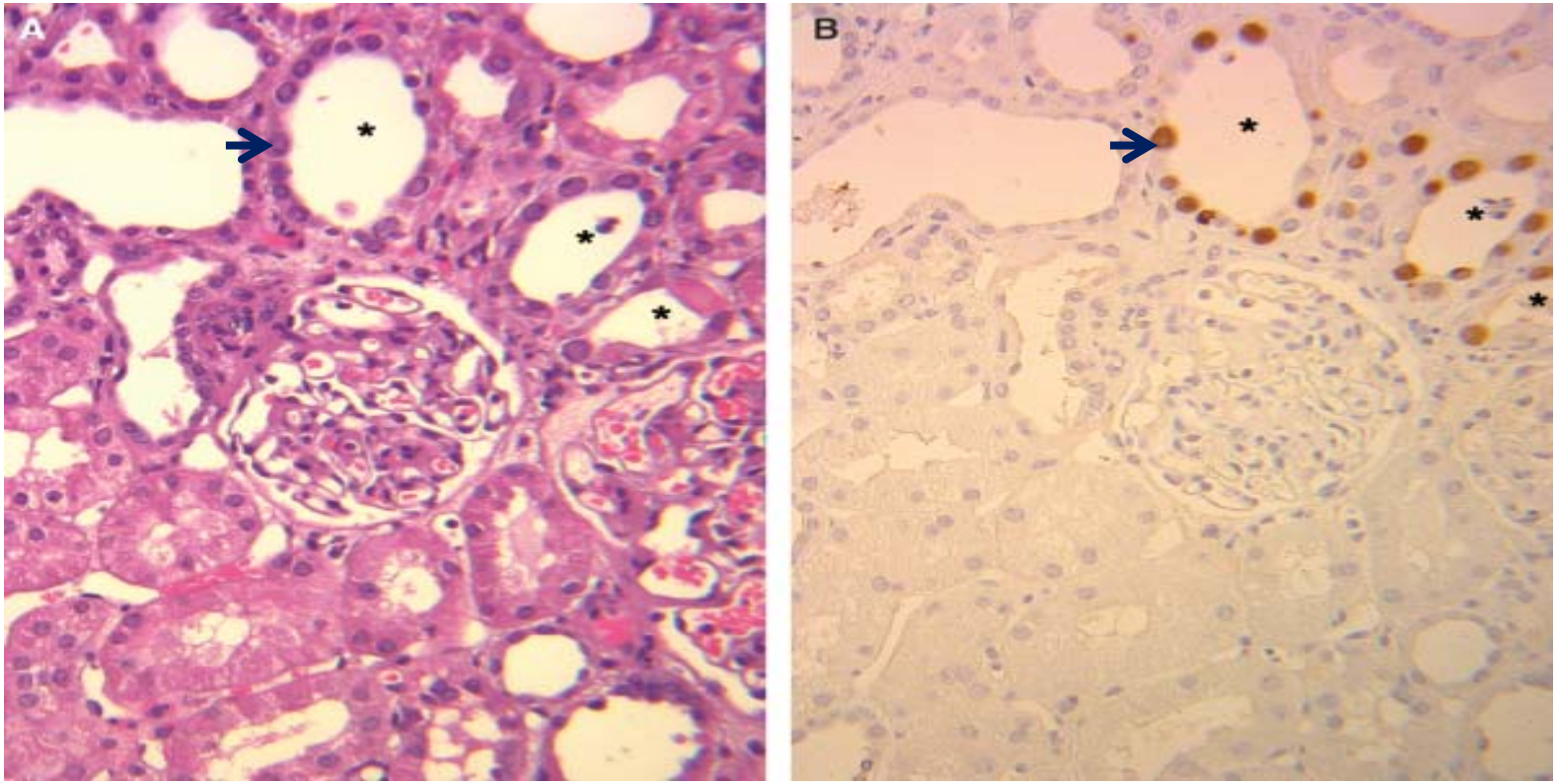
Kidney International (2006) 69, 655–662

Histopatoloji

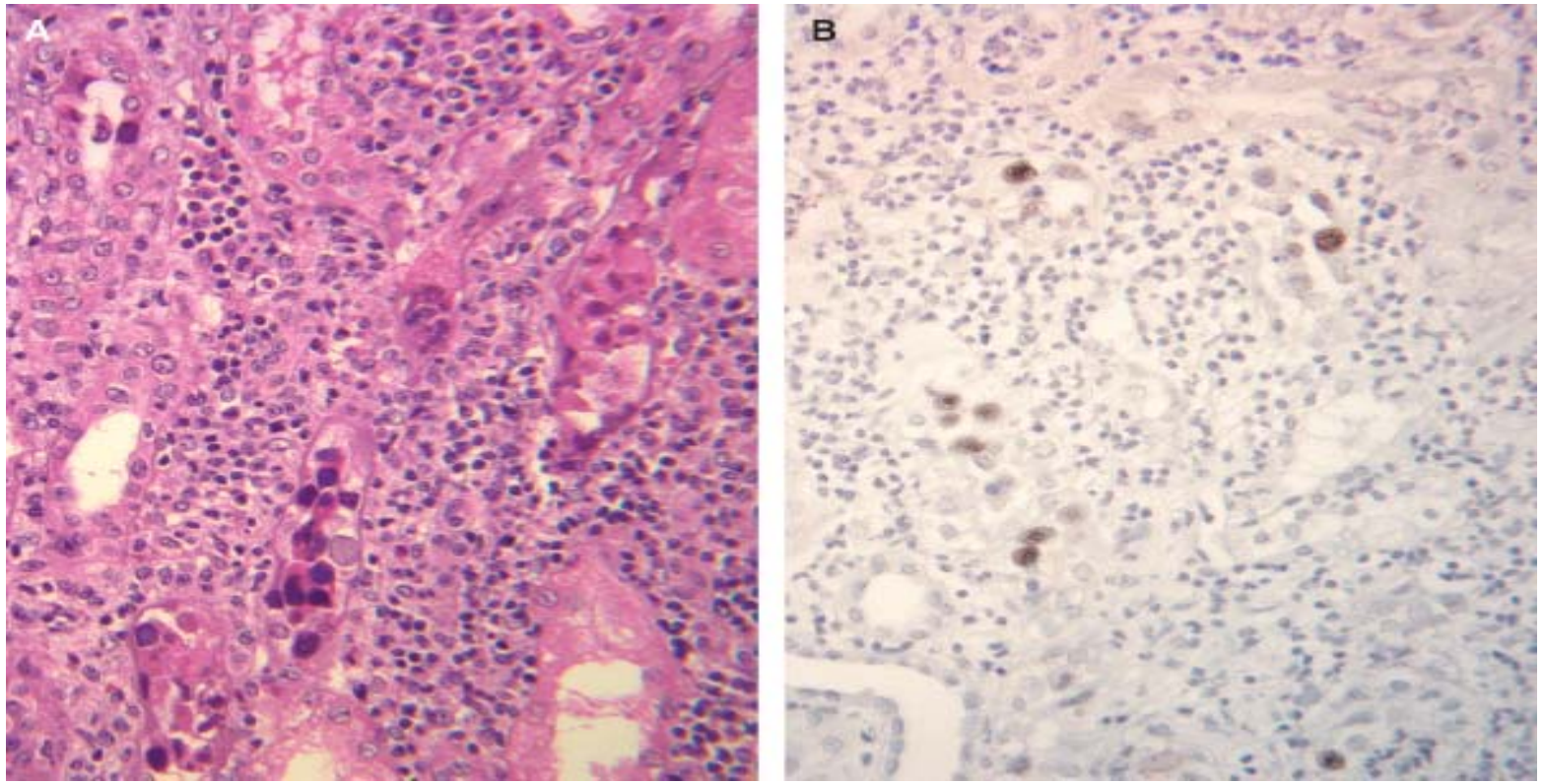
Pattern	Description	Extent of biopsy core	Graft function	Risk of graft loss
PyVAN-A				
Viral cytopathic changes	Mild	≤25%	Mostly baseline	<10%
Interstitial inflammation	Minimal	≤10%		
Tubular atrophy	Minimal	≤10%		
Interstitial fibrosis	Minimal	≤10%		
PyVAN-B*				
Viral cytopathic changes	Variable	11 – >50%	Mostly impaired	50%
Interstitial inflammation	Significant	11 – >50%		
Tubular atrophy	Moderate	<50%		
Interstitial fibrosis	Moderate	<50%		
PyVAN-B1				
Interstitial inflammation	Moderate	11–25%	Slightly above baseline	25%
PyVAN-B2				
Interstitial inflammation	Significant	26–50%	Significantly impaired	50%
PyVAN-B3				
Interstitial inflammation	Extensive	>50%	Significantly impaired	75%
PyVAN-C				
Viral cytopathic changes	Variable	Variable	Significantly impaired progressive failure	>80%
Interstitial inflammation	Variable	Variable		
Tubular atrophy	Extensive	>50%		
Interstitial fibrosis	Extensive	>50%		

American Journal of Transplantation 2013; 13: 179–188

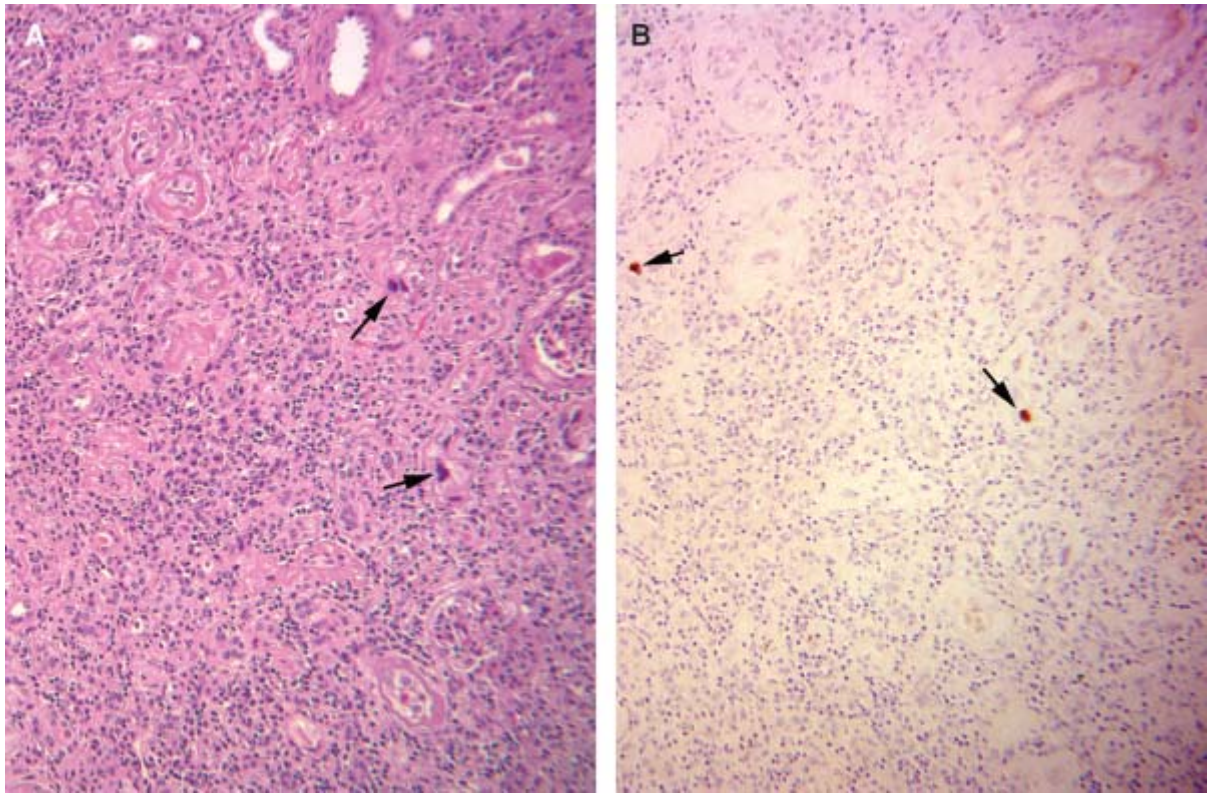
Pattern A

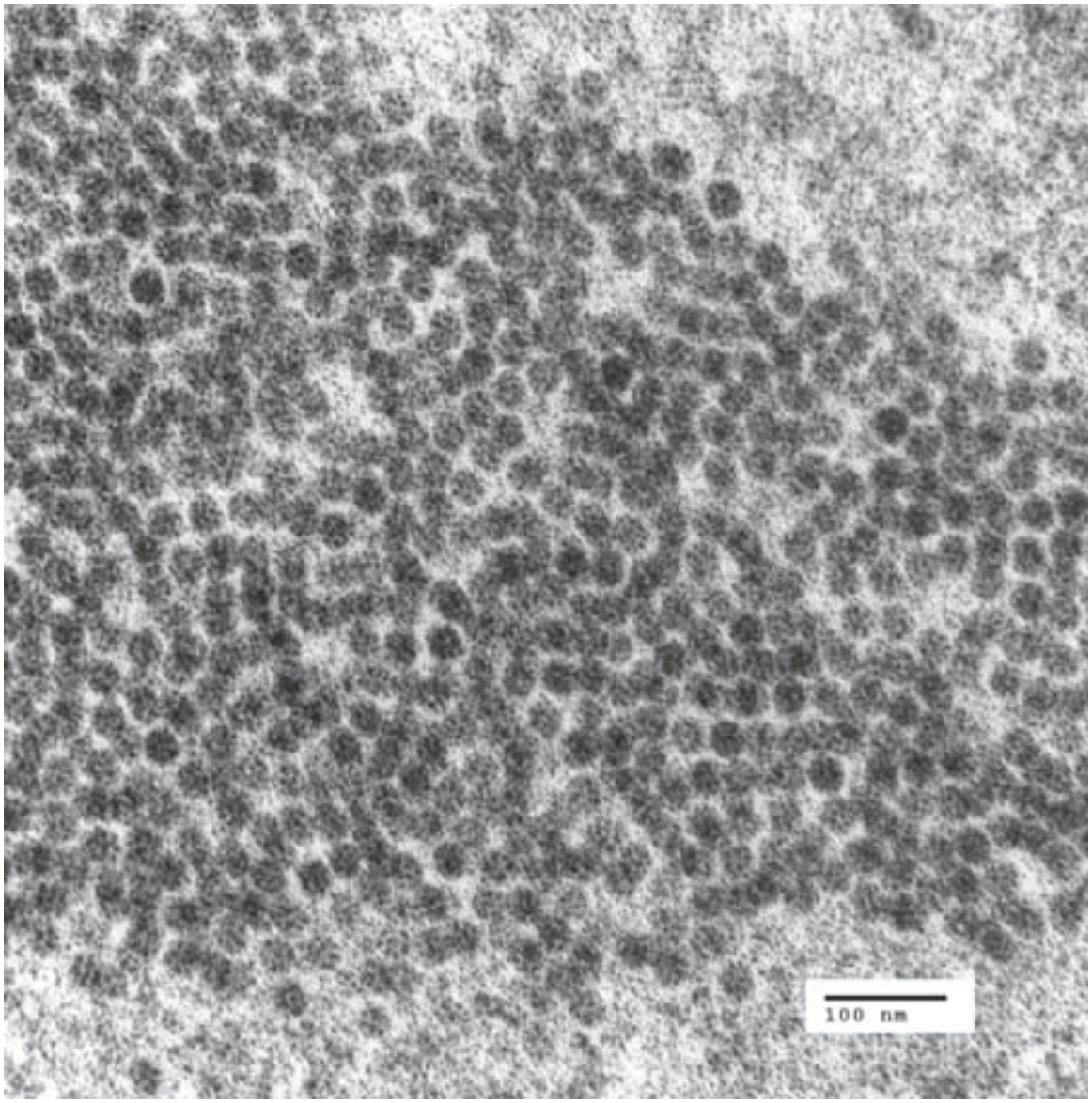


Pattern B



Pattern C-End stage




100 nm

ÖNLEME VE TEDAVİ

Evaluation of Fluoroquinolones for the Prevention of BK Viremia after Renal Transplantation

- Group 1Trimetopri-SMX 6-12 ay profilaksi
- Group 2: Kinolon

Table 3. BKV-related outcomes

	Group I (n = 160)	Group II (n = 25)	p
BK viremia at 1 year (±1 month)	36 (22.5%)	1 (4%)	0.03
BK viremia at any time point	40 (25%)	1 (4%)	0.02
Continued viremia after therapeutic intervention(s)	20 (50%) (n = 40)	0 (0%) (n = 1)	ns
BKVN	14 (35%) (n = 40)	1 (100%) (n = 1)	<0.0001
Serum creatinine at 12 months (mg/dl; mean ± SD)	1.8 ± 0.9 (n = 138)	1.6 ± 0.6 (n = 20)	ns
Allograft loss secondary to BKV	4 (10%) (n = 40)	0 (0%) (n = 1)	ns

ns, not significant.

Clin J Am Soc Nephrol 5: 1298–1304, 2010.

Ciprofloxacin Prophylaxis in Kidney Transplant Recipients Reduces BK Virus Infection at 3 Months But Not at 1 Year

TABLE 3. Estimated risk based on incidence rates for the development of BK viremia and viruria after transplantation

	Group 1 estimated risk	Group 2 estimated risk	Risk difference	95% CI	*P* value
Month 3					
Viremia	0.161	0.065	0.096	0.007–0.184	0.0378
Viruria	0.303	0.146	0.157	0.043–0.271	0.0067
Month 6					
Viremia	0.238	0.161	0.077	−0.039 to 0.192	0.1982
Viruria	0.361	0.230	0.131	0.002–0.261	0.0549
Month 9					
Viremia	0.263	0.217	0.046	−0.082 to 0.175	0.4782
Viruria	0.395	0.323	0.072	−0.069 to 0.214	0.3470
Month 12					
Viremia	0.297	0.261	0.036	−0.101 to 0.174	0.6061
Viruria	0.437	0.389	0.048	−0.099 to 0.197	0.5363

Group 1: TMP/SMX

Group 2: SMZ/TMP + Ciprofloxacin (1 month)

Transplantation. 2012 Dec 15;94(11):1117-23

Humar et al. Trials 2013, 14:185
http://www.trialsjournal.com/content/14/1/185

TRIALS

STUDY PROTOCOL Open Access

Quinolone prophylaxis for the prevention of BK virus infection in kidney transplantation: study protocol for a randomized controlled trial

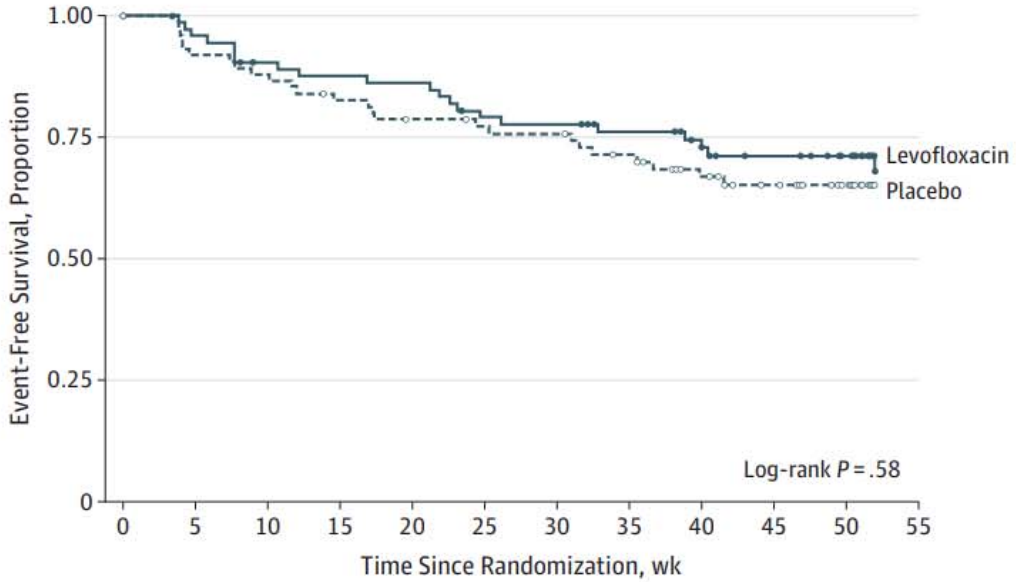
Atul Humar[1†], John Gill[2†], Olwyn Johnston[3], Dean Fergusson[4], Andrew A House[5], Louise Lebel[6], Sandra Cockfield[1], S Joseph Kim[7], Jeff Zaltzman[8], Marcelo Cantarovich[9], Martin Karpinski[10], Tim Ramsay[6] and Greg A Knoll[11*]

Abstract

Background: BK virus infection has emerged as a major complication in kidney transplantation leading to a significant reduction in graft survival. There are currently no proven strategies to prevent or treat BK virus infection. Quinolone antibiotics, such as levofloxacin, have demonstrated activity against BK virus. We hypothesize that administration of a quinolone antibiotic, when given early post-transplantation, will prevent the establishment of BK viral replication in the urine and thus prevent systemic BK virus infection.

Methods/design: The aim of this pilot trial is to assess the efficacy, safety and feasibility of a 3-month course of levofloxacin in the kidney transplant population. This is a multicenter, randomized, double-blind, placebo-controlled trial with two parallel arms conducted in 11 Canadian kidney transplant centers. A total of 154

Figure 2. Time to First Episode of Viruria



No. at risk						
Levofloxacin	76	64	61	54	45	33
Placebo	78	66	57	54	41	27

Circles indicate when data were censored. There was no significant difference in time to first viruria between patients randomized to levofloxacin vs placebo.

KDIGO Recommendations in Chapter 13: Viral Diseases

13.1: BK POLYOMA VIRUS

13.1.1: We suggest screening all KTRs for BKV with quantitative plasma NAT (2C) at least:

- monthly for the first 3-6 months after transplantation (2D);
- then every 3 months until the end of the first post-transplant year (2D);
- whenever there is an unexplained rise in serum creatinine (2D);
- and after treatment for acute rejection. (2D)

13.1.2: We suggest reducing immunosuppressive medications when BKV plasma NAT is **persistently greater than 10 000 copies/mL (107 copies/L). (2D)**

Intervention	Suggested Dose
Cidofovir	0.25-1.0 mg/kg IV biweekly for 8 wk without probenecid, prehydration recommended
Leflunomide	100 mg loading dose × 3 days, 20-60 mg/d, goal leflunomide trough 50-100 ng/mL (consider lower trough goals of 20-40 ng/mL given hemolysis risk, see text)
IVIg	1-2 g/kg IV × 1-2 doses or 150 mg/kg IV biweekly for 8 wk
Fluoroquinolones	Ciproflaxacin, 500 mg/d, duration dependent on virological response

American Journal of Kidney Diseases 2009: pp 131-142

BK Virus Nephropathy in Pediatric Renal Transplant Recipients: An Analysis of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) Registry

- Ortalama 10. ayda nefropati saptanmış
- % 84 olguda immunosupresyon azaltılmış
- % 24 olguda Cidofovir
- %8 Leflunomid
- %20 IVIG
- %32 olguda antiviral tedavi sırasında rejeksiyon
- %24 greft yetersizliği

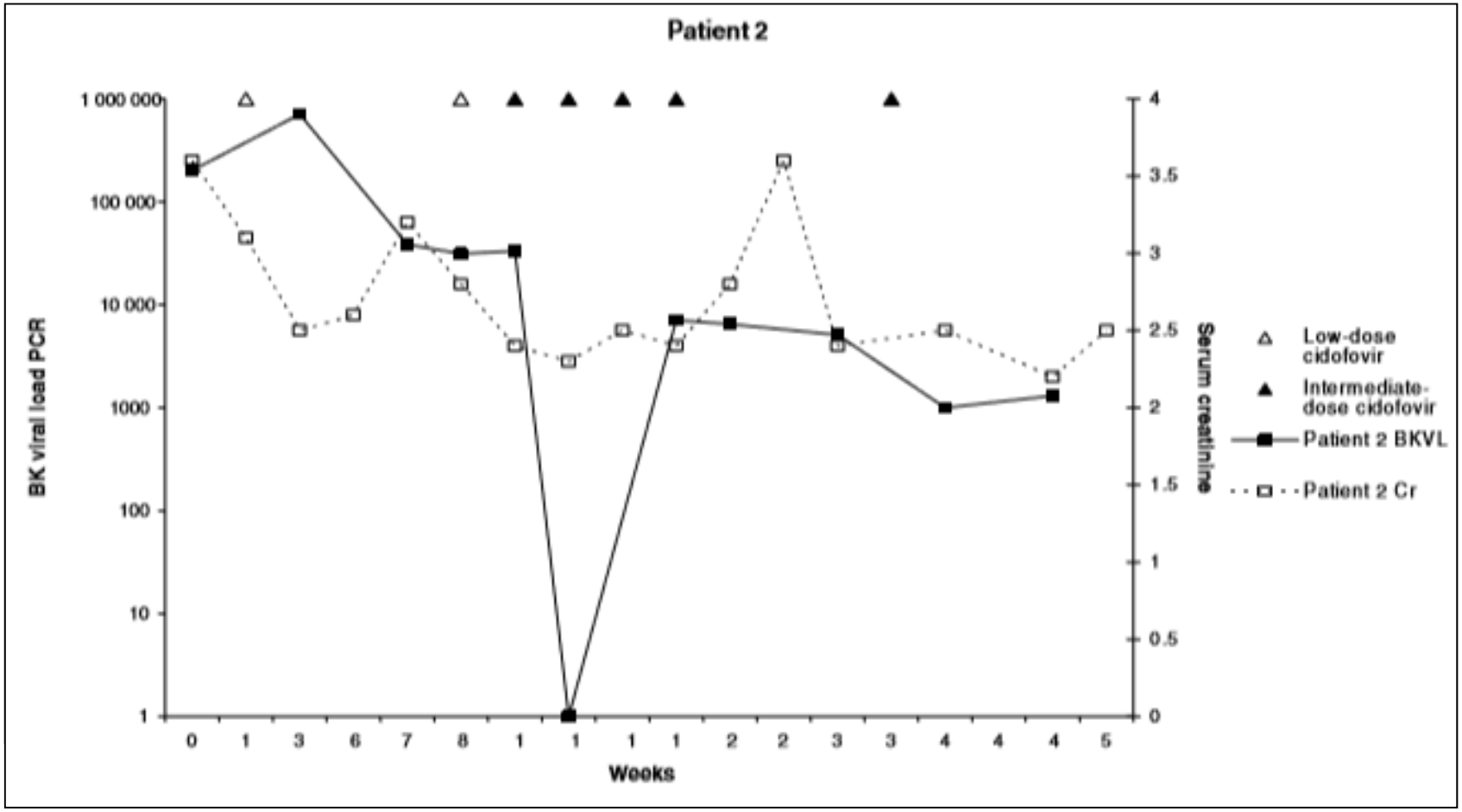
Clin J Am Soc Nephrol 2: 1037-1042, 2007

Pediatric study			
Brennan et al. 2005 [45]	MMF or Aza stopped	22/23 (95%)	No BKVN
N=200, of whom 23 (11.5%) had viremia at 1-year	If viremia still present 4 weeks later, then CNI target levels reduced		No graft loss
			No rebound AR
Bressollette-Bodin et al. 2005 [20]	None	25/30 (83.3%)	No BKVN at time of viremia. No progression to BKVN by 1 year post-transplant
N=104, of whom 30 (29%) had viremia			
Hymes et al. 2006 [13] N=122, of whom 20 (16%) had viremia	MMF/SRL 50% reduction Tacrolimus level lower target of 3-5 ng/ml	4/20 (20%) resolved with reduced immunosuppression	8 had BKVN at viremia, 7/8 received cidofovir
		13 patients still viremic at last follow-up	3 had AR at presentation
			No graft loss but 4 with impaired graft function
Pediatric study			
Almeras et al. 2008 [85] N= 123, 13 (10.5%) with at least viremia	CNI 25% reduction MMF 50% reduction	8/11 (73%)	2/13 patients had BKVN already at viremia, 1/11 of progressed to BKVN AR rate 23% after immunosuppression reduction
Bennett et al. 2010 [86]	MMF stopped at any positive plasma viral load	20/22 (91%)	No BKVN at viremia
N=144, of whom 22 (15.2%) had viremia		1 case each needed additional leflunomide or IVIG	No progression to BKVN, no graft loss AR rate 36% (8/22) after immunosuppression reduction

Pediatr Transplantation 2006: 10: 32–37

Pediatric Transplantation
DOI: 10.1111/j.1399-3046.2005.00391.x

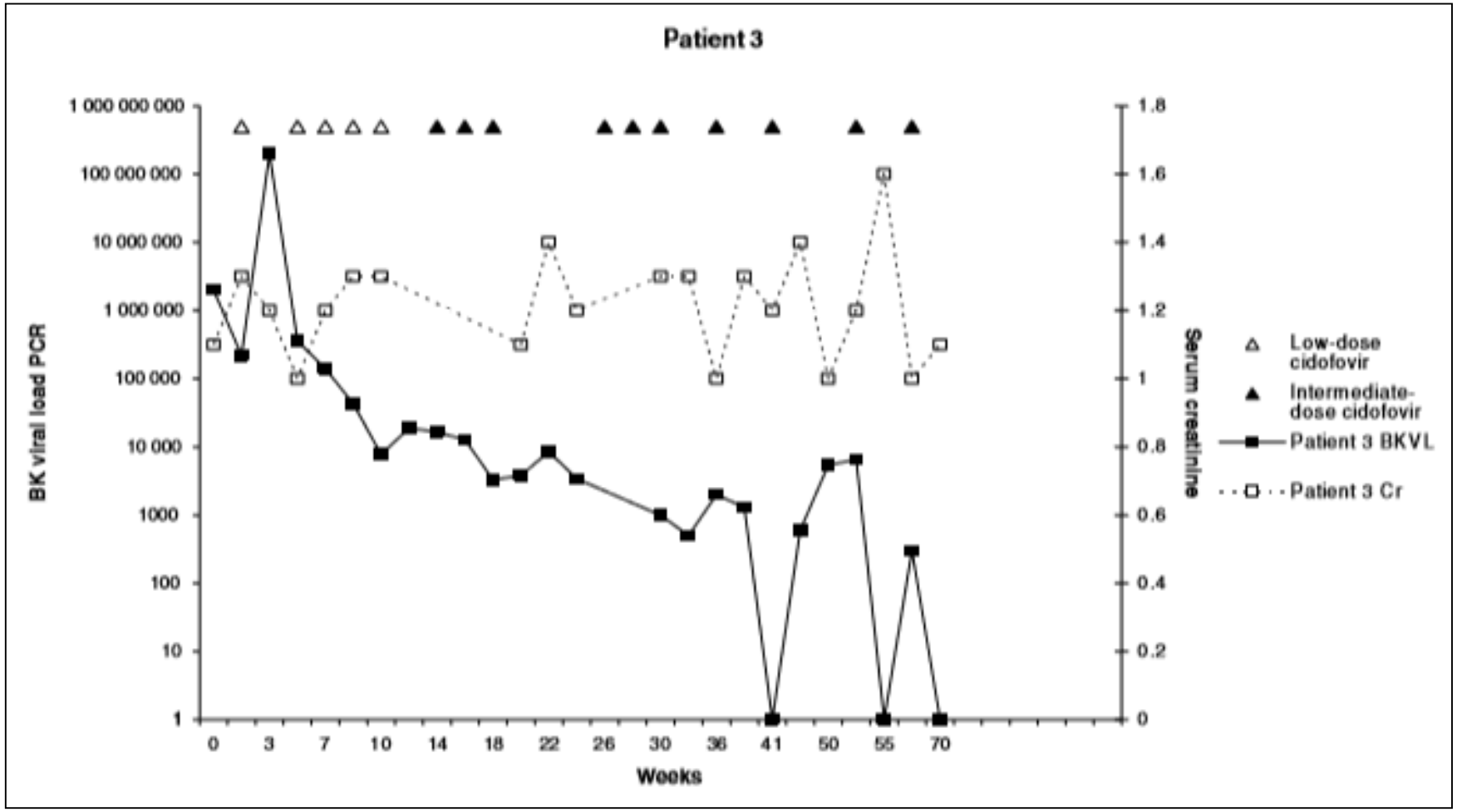
Intermediate-dose cidofovir without probenecid in the treatment of BK virus allograft nephropathy



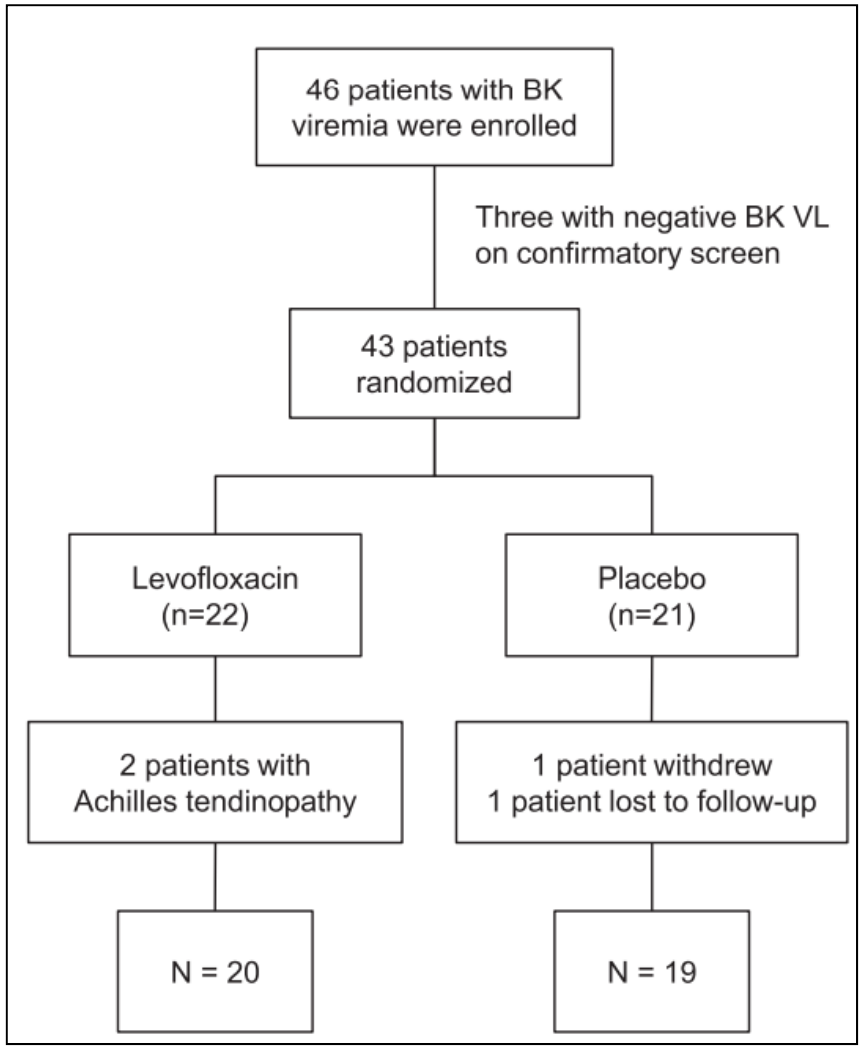
Pediatr Transplantation 2006: 10: 32–37

Pediatric Transplantation
DOI: 10.1111/j.1399-3046.2005.00391.x

Intermediate-dose cidofovir without probenecid in the treatment of BK virus allograft nephropathy



Efficacy of Levofloxacin in the Treatment of BK Viremia: A Multicenter, Double-Blinded, Randomized, Placebo-Controlled Trial



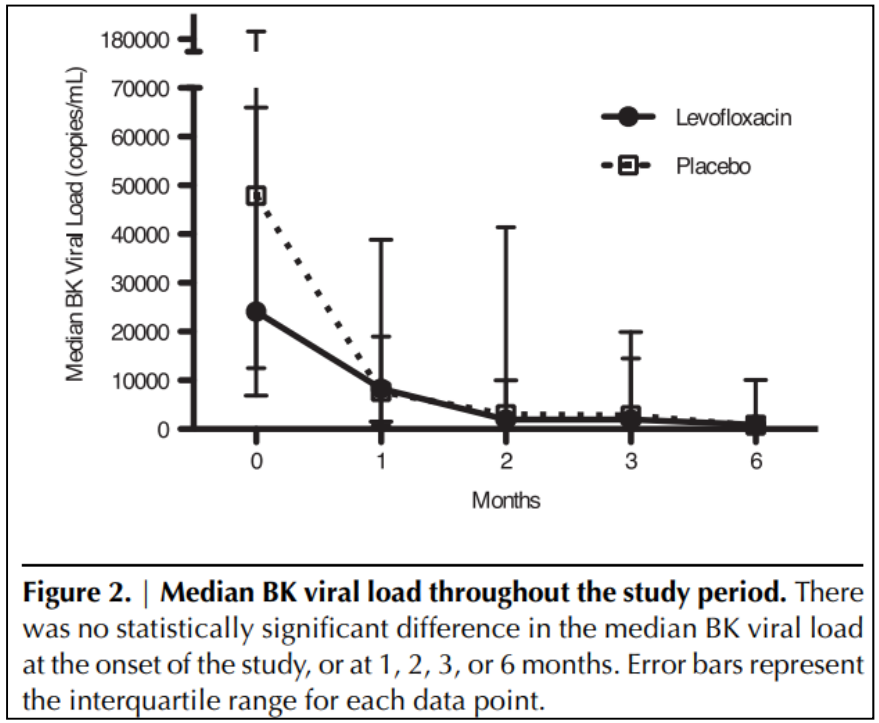
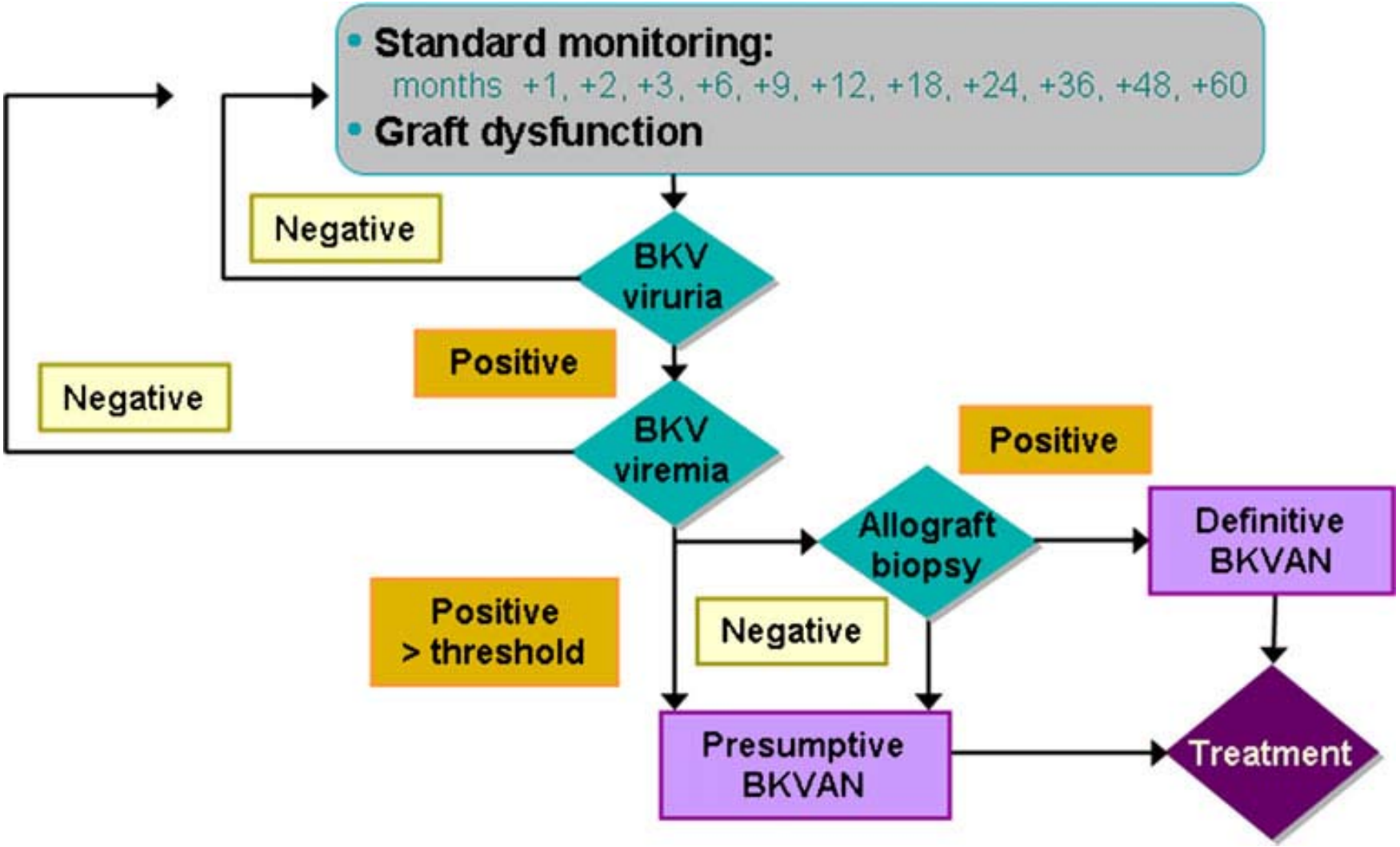


Figure 2. | **Median BK viral load throughout the study period.** There was no statistically significant difference in the median BK viral load at the onset of the study, or at 1, 2, 3, or 6 months. Error bars represent the interquartile range for each data point.

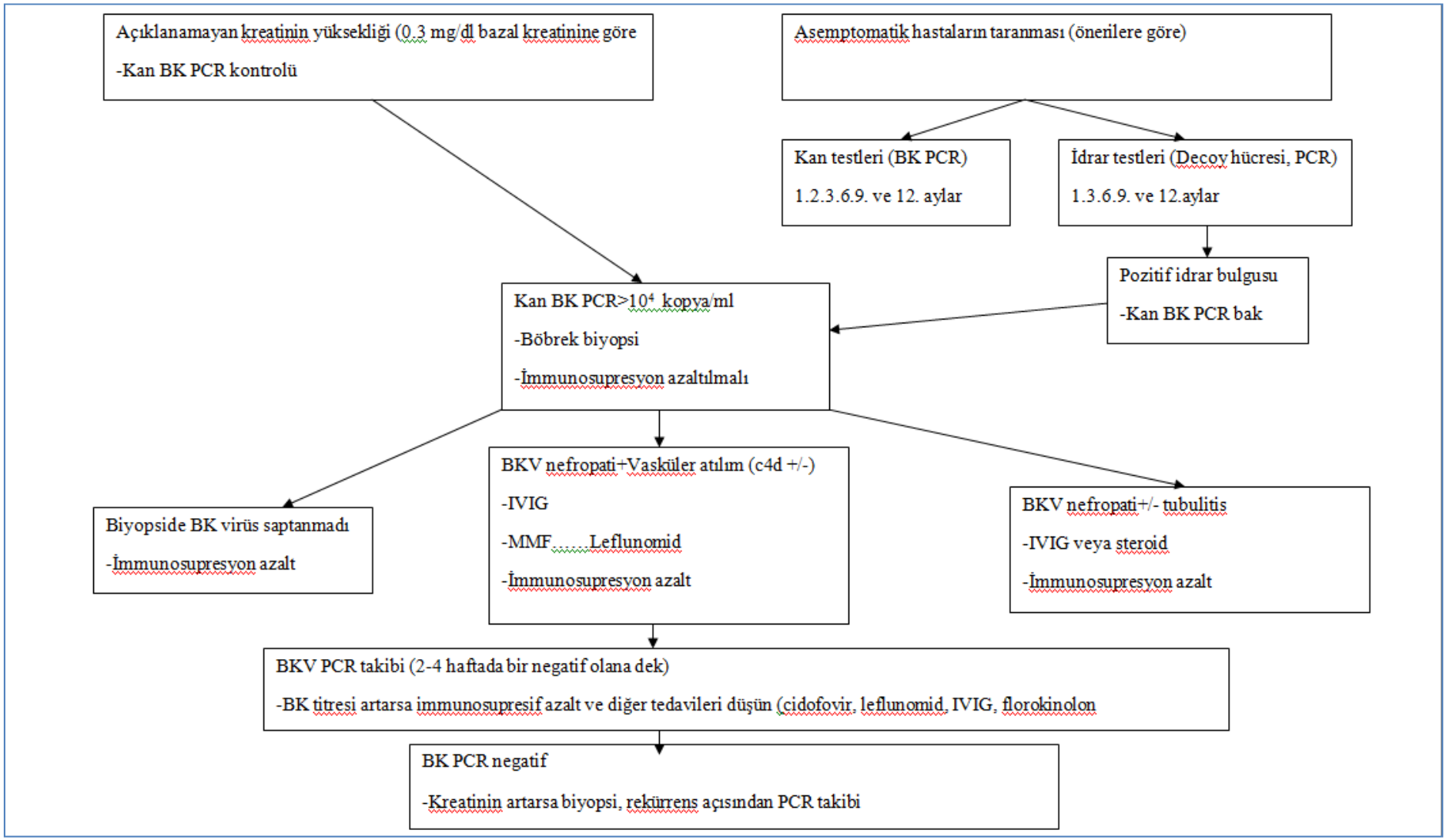
Clin J Am Soc Nephrol 9: 583–589, 2014

BK nefropati takibi



Pediatr Nephrol (2012) 27:705–717

BK nefropati tedavi ve izlem algoritması



American Journal of Kidney Diseases, 2009;1:131-142

Böbrek nakli hastalarında CMV enfeksiyonu

- Herpes virüs
- Profilaksi almayanlarda ilk 3 ay sık
- CMV enfeksiyonu: CMV replikasyonu var, klinik yok
- CMV hastalığı: Klinik yakınma/bulgu+CMV replikasyonu

  -CMV sendromu: Ateş+/-kırgınlık, lökopeni/trombositopeni

  -Doku invaziv CMV hastalığı: Organlara/sistemlere ait spesifik semptomların olması (myokardit, pnömoni, hepatit, ishal vb.)

CMV risk faktörleri

- CMV IgG (+) vericiden CMV IgG (-) alıcıya nakil
- Yoğun immunosupresyon
- Rejeksiyon
- Konak (yaş ve sitopeni varlığı)
- Soğuk iskemi süresi
- ATG kullanımı (özellikle rejeksiyon tedavisinde)
- MMF kullanımı
- TLR2/4 polimorfizmi
- MBL eksikliği
- Kemokin ve sitokin defektleri

Infect Dis Clin N Am 27 (2013) 317–342

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Clinical Utility of Viral Load in Management of Cytomegalovirus Infection after Solid Organ Transplantation

Raymund R. Razonable,[a] Randall T. Hayden[b]

- Klinik önemi bilinen titre ile ilgili net veri yok
- CMV PCR>2000 IUs/ml olduğunda hasta yakından izlenmeli
- CMV PCR>9120 IUs/ml…..CMV sendromu
- CMV PCR>20893 IUs/ml…..invaziv CMV hastalığı ile ilişkili

Klinik bulgular ve komplikasyonlar

Table 2
Direct and indirect effects of CMV in SOT recipients

Direct Effects	Indirect Effects
CMV syndrome	Acute allograft rejection
Tissue-invasive CMV disease	Chronic allograft rejection
Gastrointestinal disease	Bronchiolitis obliterans
Pneumonitis	Transplant vasculopathy
Hepatitis	Tubulointerstitial fibrosis
Central nervous system disease	Opportunistic and other infections
Retinitis	Fungal superinfection
Nephritis	Nocardiosis
Pancreatitis	Bacterial superinfection
Myocarditis	Epstein-Barr virus and posttransplant lymphoproliferative disorder
Others (any organ may be involved)	Hepatitis C recurrence
Mortality	Other viruses (HHV-6, HHV-7)
	New-onset diabetes mellitus
	Thrombosis
	Mortality

Böbrek naklinde CMV gelişimini engellemek için stratejiler

Risk Category	Recommendation/Options
D+/R–	Antiviral prophylaxis is preferred Drugs: valganciclovir is preferred (caution in liver recipients[a]); alternative agents are oral ganciclovir and IV ganciclovir; valacyclovir is an alternative agent for kidney recipients; some centers add adjunctive CMV Ig. Duration: 3–6 mo Preemptive therapy is an option but less preferred. Weekly CMV PCR or pp65 antigenemia for 12 wk after
	recipients[a]); oral ganciclovir and IV ganciclovir are alternative drugs; valacyclovir is an option for kidney recipients Duration: 3 mo Preemptive therapy. Weekly CMV PCR or pp65 antigenemia for 12 wk after transplantation, and if a positive CMV threshold is reached, treat with (1) valganciclovir 900 mg by mouth twice daily, or (2) ganciclovir 5 mg/kg IV every 12 h until negative test

Alıcı ve verici IgG negatif olan olgularda kan transfüzyonu CMV dönörden ve lökosit filtresi ile verildiği sürece profilaksiye gerek yok

Am J Transplant 2013 13 93-106

CMV önlenmesi ve tedavisinde kullanılan ilaçlar

Table 5
Antiviral drugs for CMV prevention and treatment

Drug	Preemptive Therapy and Treatment of CMV Disease	Antiviral Prophylaxis	Comments on Use and Toxicity
Valganciclovir	900 mg by mouth twice daily	900 mg by mouth once daily	Ease of administration Leukopenia
Oral ganciclovir	Not recommended	1 g by mouth 3 times daily	Low oral bioavailability High pill burden Leukopenia Risk of resistance
IV ganciclovir	5 mg/kg IV every 12 h	5 mg/kg IV once daily	IV access Leukopenia
Valacyclovir	Not recommended	2 g by mouth 4 times daily	Kidney transplant recipients only Not recommended for heart, liver, pancreas, lung, intestinal, and composite tissue transplant recipients High pill burden Neurologic adverse effects
Foscarnet	60 mg/kg IV every 8 h (or 90 mg/kg every 12 h) Not recommended for preemptive therapy	Not recommended	Second-line agent for treatment Highly nephrotoxic Treatment of UL97-mutant ganciclovir-resistant CMV
Cidofovir	5 mg/kg once weekly × 2 then every 2 wk thereafter Not recommended for preemptive therapy	Not recommended	Third-line agent Highly nephrotoxic Treatment of UL97-mutant ganciclovir-resistant CMV

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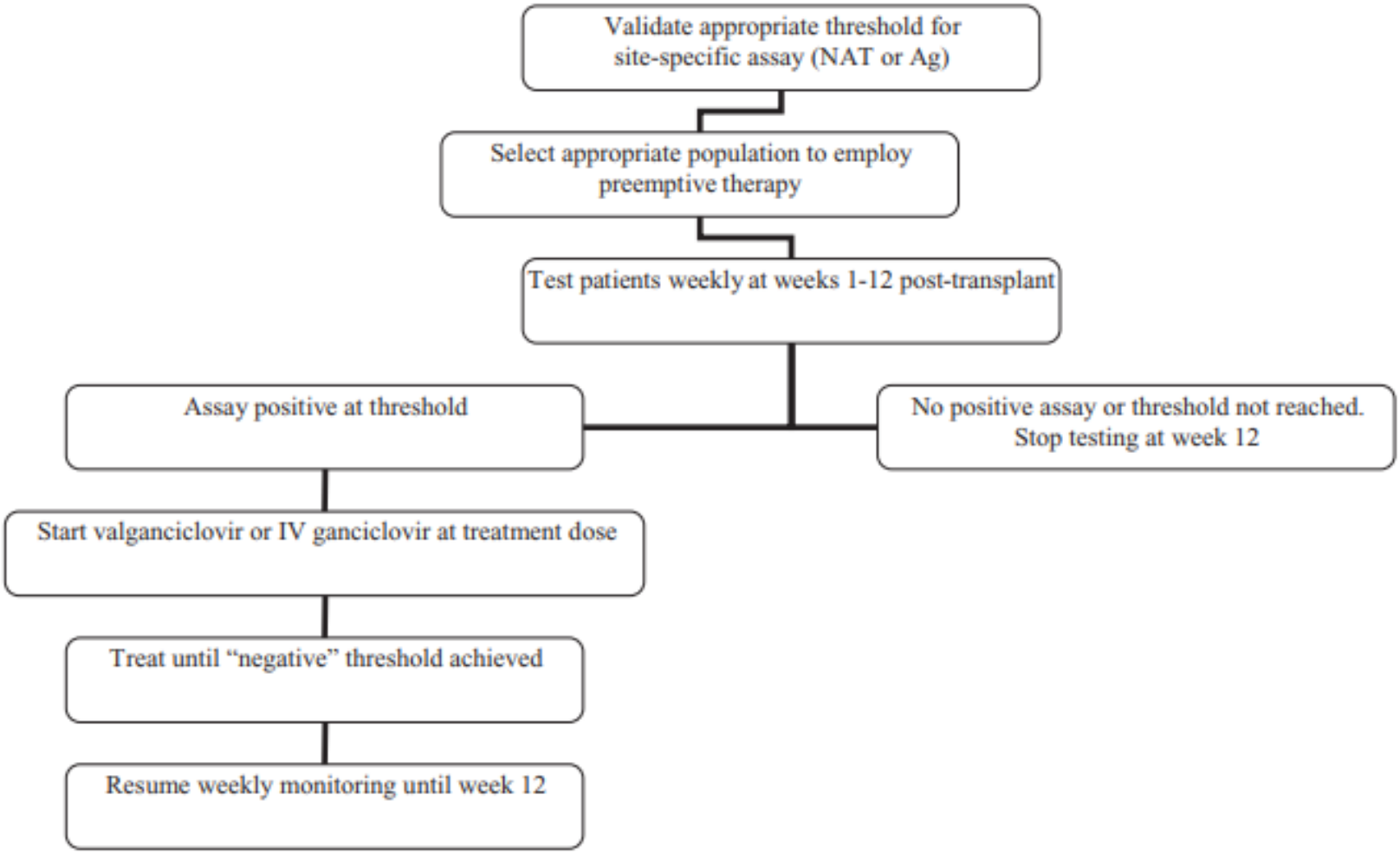
Wiley Periodicals Inc.

doi: 10.1111/ajt.12103

Special Article

Cytomegalovirus in Solid Organ Transplantation



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