

# Diagnosis and management of BK polyoma virus in UHW

Should we be screening for BK in UHW?

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## Introduction

### **BK polyoma virus (BKPyN)**

- Occurs in up to 10 % kidney allograft recipients
- Reported incidence of allograft failure: 15 to 50 % of affected individuals

### **Diagnosis**

- Asymptomatic
- Unexplained rise in creatinine
- BK DNA PCR  $> 1 \times 10^7$  urine
- BK DNA PCR  $> 1 \times 10^4$  blood

## Introduction

### Treatment

- Reduction in immunosuppression (increasing risk of acute rejection)
- Ciprofloxacin/Leflunomide/Cidofovir/Immunoglobulins (no clear guidelines)

## Introduction

### BK polyoma virus (BKPyV)

- **Disease process:**

Detection in urine → detection in blood → rise in creatinine

## Introduction

### Guidelines (KDIGO 2009):

#### **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 ( $10^7$  copies/l). (2D)

## Objective of audit

- BK nephropathy can lead to transplant dysfunction and failure
- KDIGO recommends screening in first year
- In UHW currently:
  - Except ABO incompatible, BK testing individual clinical decision
- Therefore, how has BK been diagnosed and managed in UHW?
- Would screening improve our management of BK?

## Aims and Methods

**Aims:** Retrospective analysis of BK diagnosis and management

**Period:** January 2006- July 2017

### **Data collection:**

- BK diagnosis list
- Computer systems: Resulting Reporting, Pharmacy

# Results



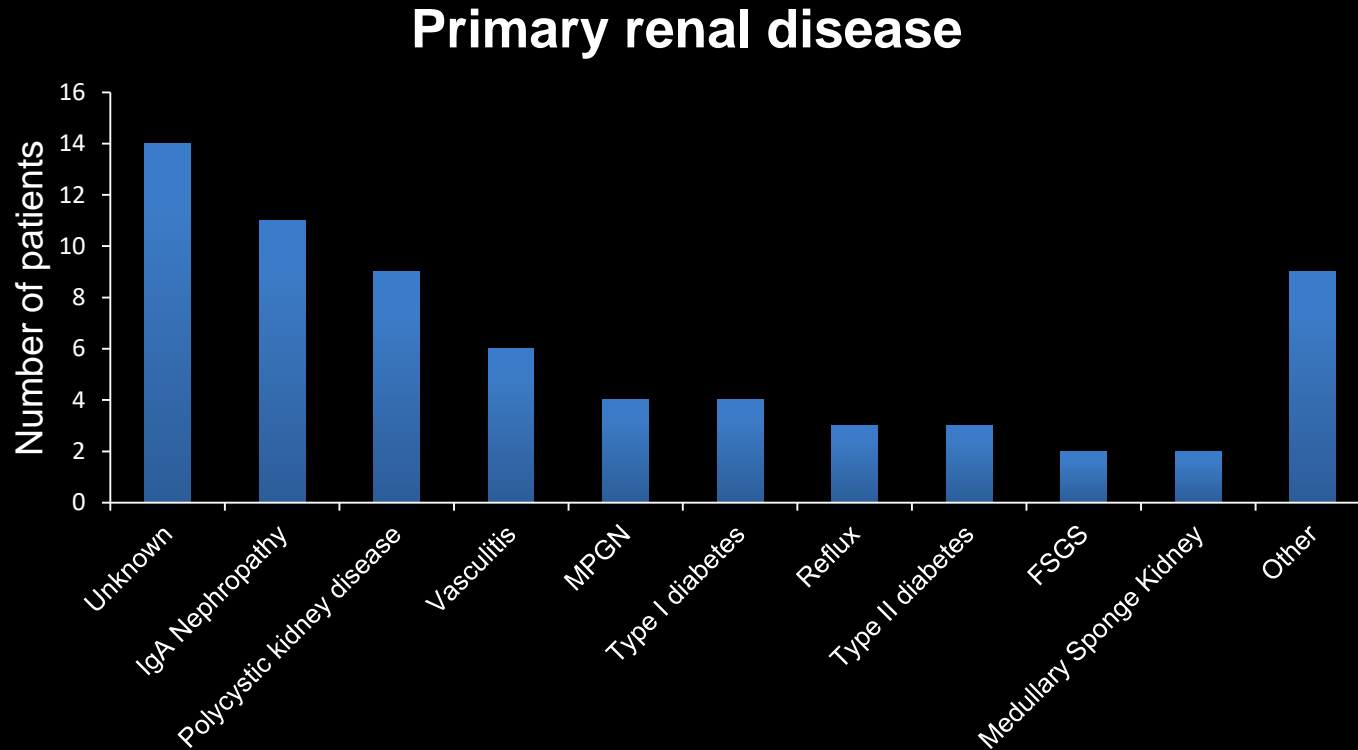
# Results

## Baseline characteristics

- Number of patients: 67
- Male:Female ratio: 41: 26
- Mean age of patient: 48 (range 18-79)
- Previous transplants: 11 patients one or more previous transplants

# Results

## Baseline characteristics



Other: tubulointerstitial nephritis, hypertension, hypertensive nephrocalcinosis, ischaemic nephropathy, renal dysplasia, BK + CIN from lung transplant, obstructive uropathy, collagen nephropathy, Alports

# Results

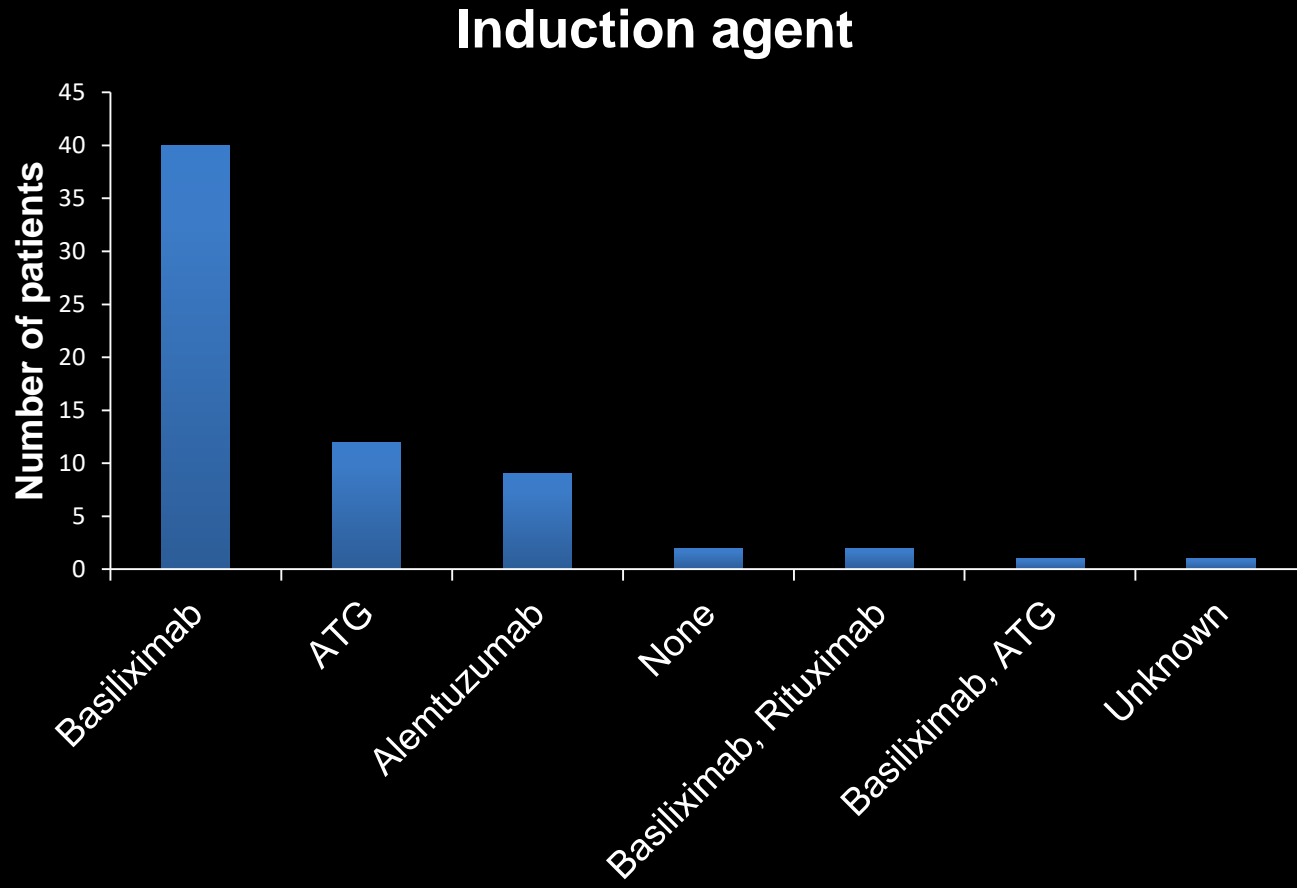
## Baseline characteristics

### Type of transplant

- Live 28 patients
- DBD 26 patients
- DCD 13 patients

# Results

## Baseline characteristics



## Results

### **Baseline characteristics**

#### **Initial maintenance therapy**

- MMF, tacrolimus, prednisolone: 58 patients
- MMF, tacrolimus: 8 patients
- Ciclosporin, azathioprine, prednisolone: 1 patient

#### **Duration of prednisolone treatment**

- Greater than one year: 44 patients
- Less than one year: 13 patients

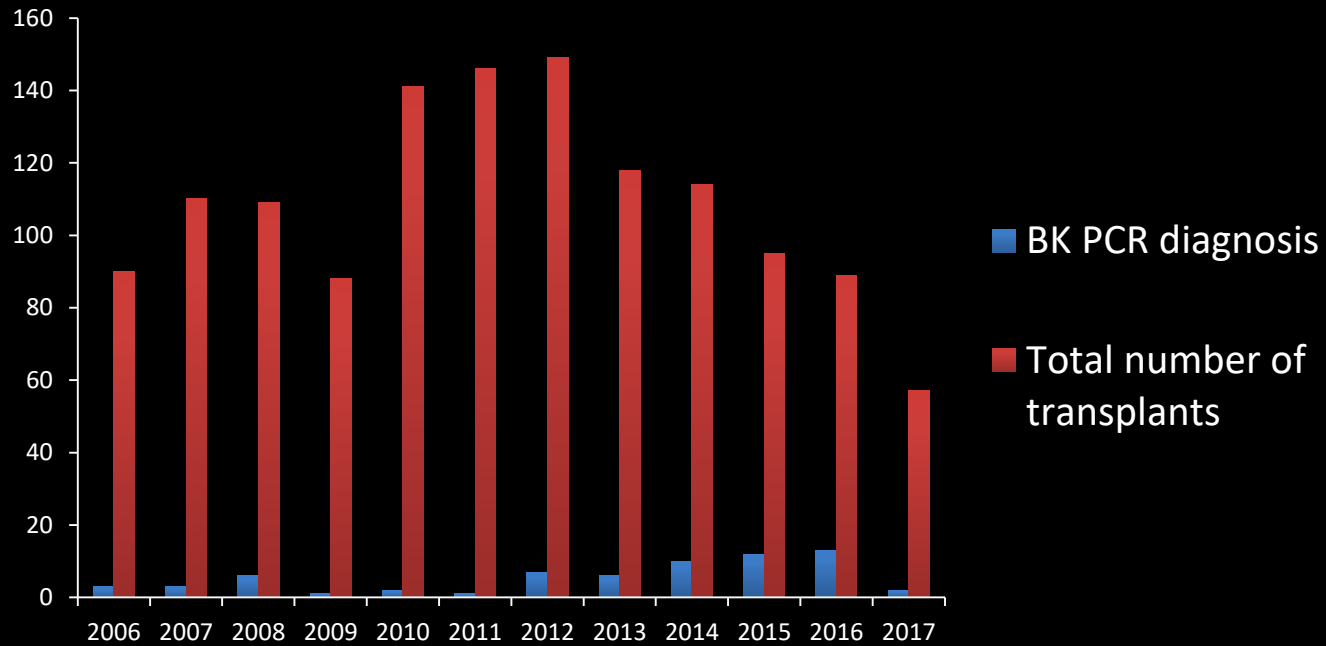
## Results

### **BK diagnosis**

- Positive BK serum: 66 patients
- BK positive biopsy: 23 patients
- BK negative biopsy: 18 patients
- No biopsy: 26 patients

# Results

## Incidence of BK PCR detected (January 2006-August 2017)

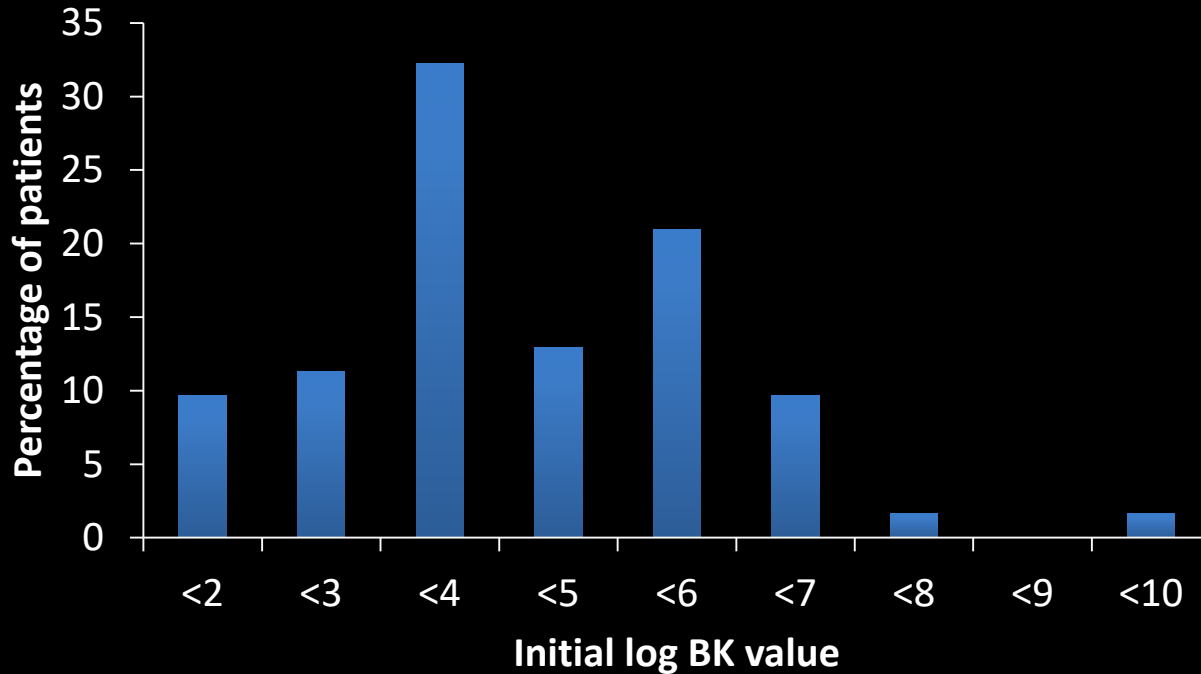


Incidence of BK PCR detected: 5%

Variability in diagnosis rate

# Results

## Log BK PCR value at diagnosis





## Results

Time to diagnosis:

All 67 patients:

- Median time from transplant to BK diagnosis: 7.2 months (1.4 to 87.6)
- 47/67 diagnosed within 1 year of transplant
- 12/67 diagnosed between 1-2 years of transplant
- 8/67 diagnosed >2 years after transplant

## Results

Time to diagnosis:

Initial log BK PCR value > 4:

- Median time from transplant to BK diagnosis: 5.1 months (2.3 to 33.1)

**Treatment**

## Results

- **Treatment – change in tacrolimus dose**

	Pre BK diagnosis	Post BK diagnosis
Mean	8.2 +/- 1.2	7.3 +/- 1.4
Median	8.2	7.5

Tacrolimus range:

- After ATG: 5-8 (long term)
- After Alemtuzumab: 5-8 (long term)
- After Basiliximab: 6-9 (first 3 months), 5-8 (long term)

## Results

- Treatment – change in MMF dose
- Functioning transplants

MMF dose	Percentage of significant log BK at diagnosis ( <u>&gt; 4</u> )	Median log BK value	Last follow-up value, % BK not detected (serum)	ACR after BK diagnosis
No change	6.7% (1/15)	2.82	93.3%	20.0%
Reduced	71.4% (15/21)	4.66	38.0%	9.5%
Stopped	58.3% (7/12)	5.37	33.4%	16.7%

## Results

- Treatment – change in MMF dose
- Failed transplants

MMF dose	Percentage of significant log BK at diagnosis ( <u>&gt; 4</u> )	Median log BK value	ACR after BK diagnosis
No change	0% (0/6)	2.71	50%
Reduced	100% (2/2)	5.89	100%
Stopped	60% (3/5)	4.95	60%

## Results

- **Treatment – change in MMF dose**
- **Functioning and failed transplants**

<b>MMF dose</b>	<b>ACR after BK diagnosis</b>
No change	28.6%
Reduced	8.7%
Stopped	29.4%

## Results

- Treatment

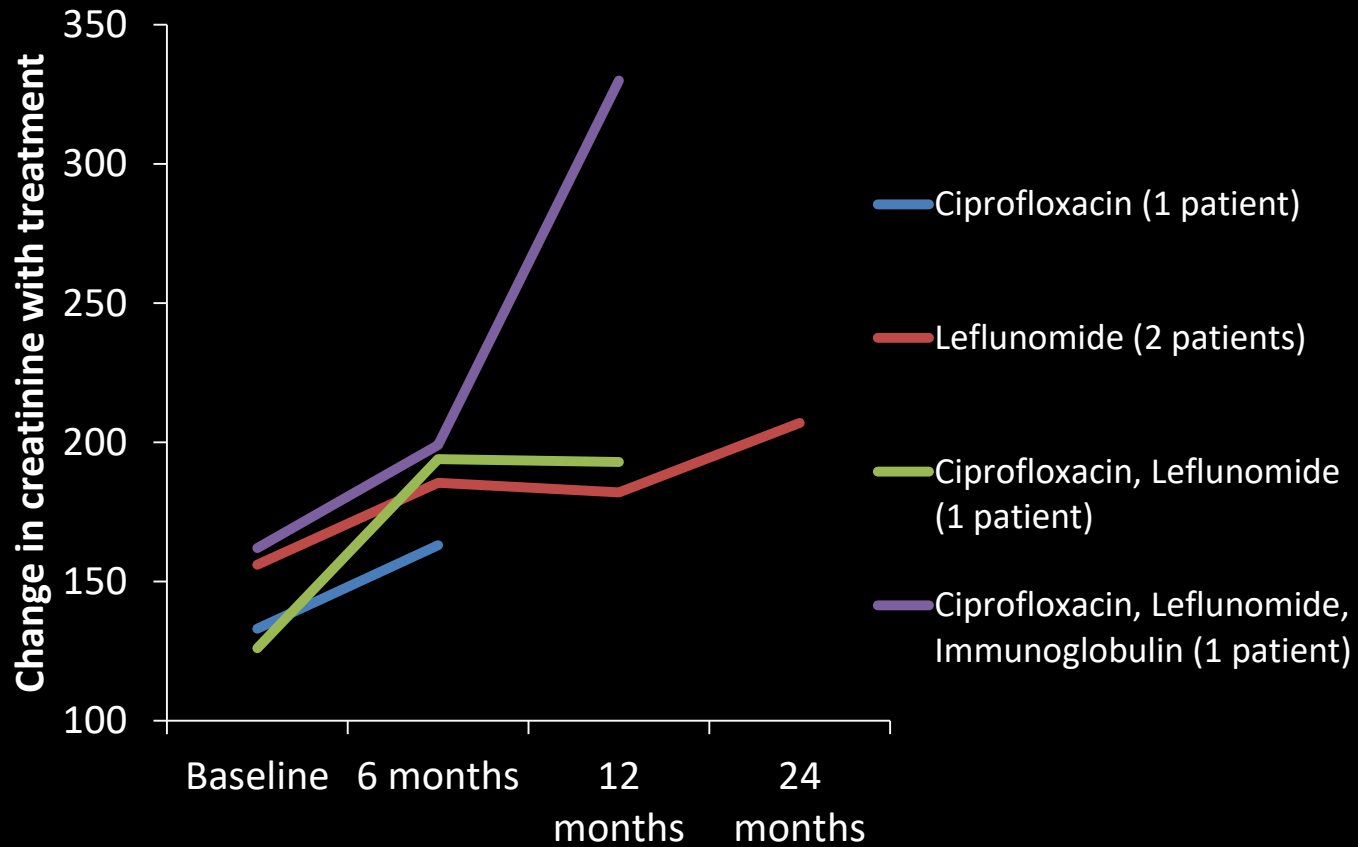
### **Patients who received specific treatments**

- Five patients in total
- 4 patients had BK present on biopsy
- 1 patient received prolonged course of Ciprofloxacin
- 2 patient received prolonged course of Leflunomide
- 1 patient received prolonged course of Leflunomide and Ciprofloxacin
- 1 patient received prolonged course of Leflunomide, Ciprofloxacin and Immunoglobulins



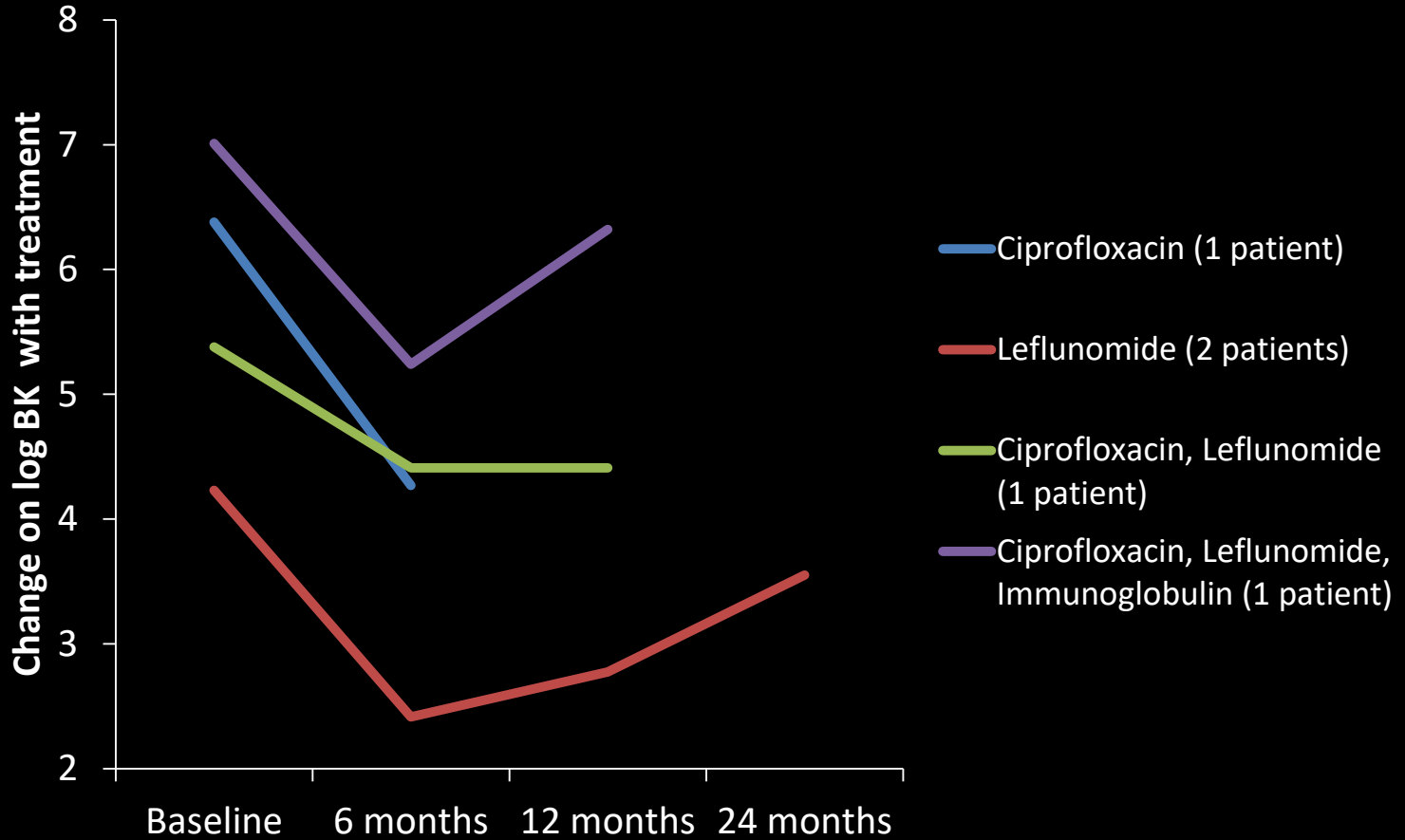
# Results

- Treatment



# Results

- Treatment



## Results

### **End of audit:**

- 50 functioning grafts
- 13 failed grafts
- 4 patients died with functioning grafts

## Results

### Failed graft

- 13 total failed grafts:
  - 7 with acute or chronic rejection
  - 3 recurrence of primary disease
  - 1 chronic allograft nephropathy
  - 1 BK and ACR
  - 1 unknown
- (4 patients died with functioning grafts)

## Results

- Univariate analysis

	Graft lost n=13	Graft survived n=54	p-value
Creat at BK diagnosis	268	156	0.01
Log PCR mean	4.05	4.07	NS
h/o acute rejection	7 (54%)	18 (33%)	0.34
Median time from Tx to BK	7.7	6.2	NS
Median follow-up time from BK	33	34	NS

- Multivariate analysis: creatinine at diagnosis found to be significant for predicting graft failure

# Conclusions

## Conclusions

- Incidence of BK similar to reported in the literature
- Significant number of patients remain on prednisolone after 1 year
- Yearly variability in diagnostic rate
- Median of significant BK PCR result within first 6 months after transplant
- Increased incidence of ACR when MMF stopped
- No clear evidence to suggest novel treatments are of benefit (potentially delay graft loss)

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## Evidence for screening

- Variable incidence of BK (physician dependent)
- Higher log value, increased likelihood MMF stopped with increased level of rejection observed
- Higher initial creatinine significant risk of graft failure
- Evidence change in MMF clears virus
- KDIGO recommends 6 time points throughout first year – initially screen around 6 month time point