

# The use of antiviral prophylaxis following corneal grafts

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On behalf of the UK Transplant Ocular Tissue Advisory Group

## Background

- Prophylactic antiviral medications are used in the management of Herpes Simplex Virus (HSV) related keratitis.
- However, there are very limited data available on their effect on corneal graft survival.
- Following the introduction of new national data collection forms in April 1999, there are now sufficient data to investigate this effect.

## Data

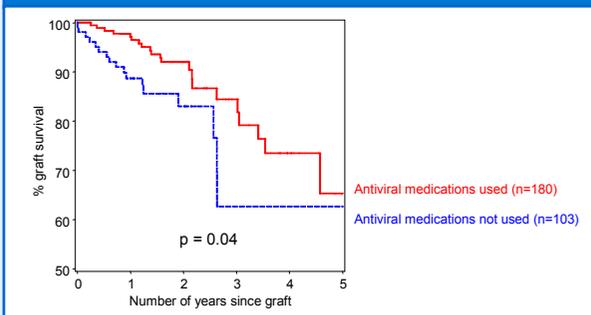
- There were 326 first Penetrating Keratoplasty (PKP) performed between April 1999 and October 2003 where the graft was required due to a viral infection.
- Of these 326 grafts, 283 (87%) had reported follow-up outcomes of graft survival.
- No data are available on the specifics of the type of viral infection. It is likely however, that a large proportion of patients within this category are HSV related.

## Methods

- Kaplan-Meier survival curves were used to illustrate effects.
- Cox regression analysis considered the influence of:
  - Pre-operative factors
  - Post-operative antiviral prophylaxis
  - Time to first rejection episode
- This was modified to a Piecewise Cox Model to allow for non-proportional hazards.
- Time dependent covariates were used to model post-operative factors.

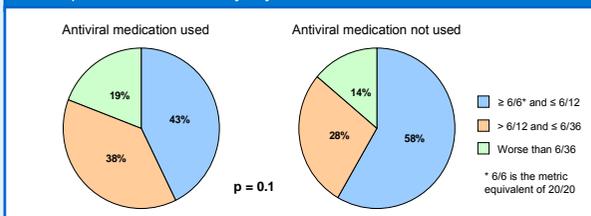
## Results

### Five year graft survival, by use of antiviral medication



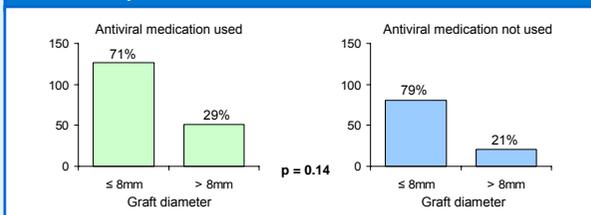
- Antiviral medication was used post-operatively in 180 (64%) of the 283 corneal grafts included in this study. Patients receiving antiviral medication had better graft survival than those who did not receive them.

### Pre-operative visual acuity, by use of antiviral medication



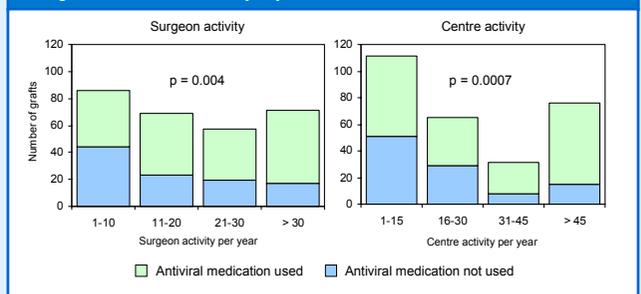
- Patients receiving post-operative antiviral medication generally had worse pre-operative visual acuity than patients who did not receive them.

### Graft size, by use of antiviral medication



- There was a larger percentage of grafts that were greater than 8mm in diameter among patients who received antiviral medication.

### Surgeon and centre activity, by use of antiviral medication



- Antiviral medications were more frequently used by surgeons who performed larger numbers of grafts per year. This effect was even stronger when considering centre activity.

### Relative risk of graft failure at five years

Factor	Level	RR	95% CI	p
Superficial vascularisation	< 1 year	1.0	-	
	None	1.1	0.4 - 3.6	0.81
	1-2 years	1.0	-	
	None	5.5	1.3 - 22.6	0.02
	2-3 years	1.0	-	
> 3 years	None	29.6	5.1 - 172	0.0002
	1 or more	1.0	-	
	None	23.6	3.0 - 186	0.003
Inflammation at time of graft	No	1.0	-	
	Yes	3.0	1.5 - 6.1	0.003
Graft size	≤ 8mm	1.0	-	
	> 8mm	2.8	1.4 - 5.9	0.006
Antiviral medication	Yes	1.0	-	
	No	3.5	1.7 - 7.5	0.001
Rejection episodes	None	1.0	-	
	One or more	7.2	3.2 - 16.3	< 0.0001

- Of the pre-operative factors considered, superficial corneal vascularisation, graft size and whether or not the eye was inflamed at the time of the graft were all found to affect graft survival.

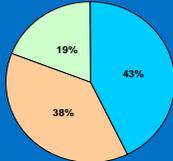
- There was also a statistically significant association between graft survival and the use of prophylactic antiviral medications (p=0.001). Grafts where patients did not receive antiviral medications post-operatively were 3.5 times more likely to have failed at 5 years, when compared with patients who did receive them.

- Patients who experienced one or more immunological rejection episode also had an increased risk of graft failure.

## Summary

- The use of post-operative antiviral prophylaxis improved graft survival, even when taking account of other factors that may affect graft survival.
- Therefore, it would appear that the use of antiviral prophylaxis should be seriously considered in the post-operative period following corneal grafts for HSV.
- However, as there are no data on the specifics of the type of viral infection, perhaps a prospective study could be undertaken. This would also enable additional data to be collected on the type and duration of medication.

Antiviral medication used



- 6/12 or better
- > 6/12 and <= 6/36
- > 6/12 and <= 6/36

6/12 or better  
Worse than 6/36  
> 6/12 and <= 6/36