SAN FRANCISCO 2014

World Transplant Congress

Richard Haynes, DM MRCP on behalf of the 3C Study Collaborative Group
University of Oxford, Oxford, UK

Campath, Calcineurin inhibitor reduction and Chronic allograft nephropathy: the 3C Study

Alemtuzumab-based *versus* basiliximab-based induction therapy in kidney transplantation

I have financial relationship(s) within the last 12 months relevant to my presentation with:
Novartis Pharma (unrestricted grant); Pfizer (unrestricted grant)

I intend to reference unlabeled/unapproved uses of alemtuzumab for induction therapy in kidney transplantation in my presentation.

Background

- Over the last few decades, long-term outcomes after kidney transplantation have not improved[1]
- Chronic calcineurin inhibitor (CNI) nephrotoxicity may contribute to late graft loss[2]
- Reliable large randomized trials needed of strategies to reduce CNI exposure

[1] Meier-Kreische *Am J Transplant* 2004
[2] Nankivell *et al. New Engl J Med* 2003

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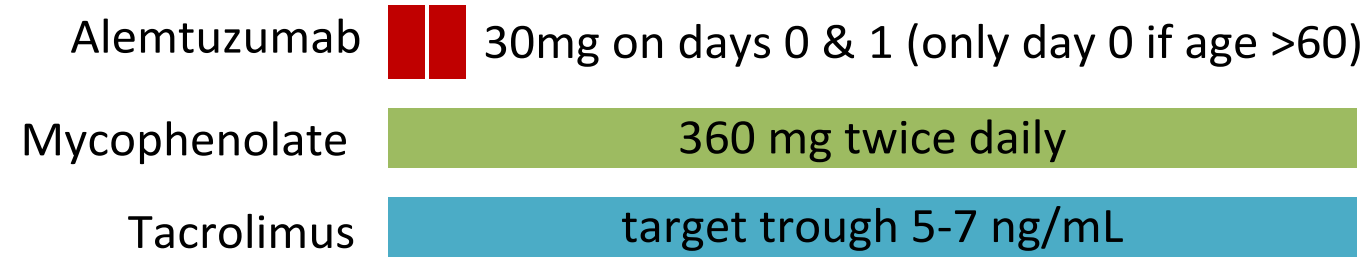
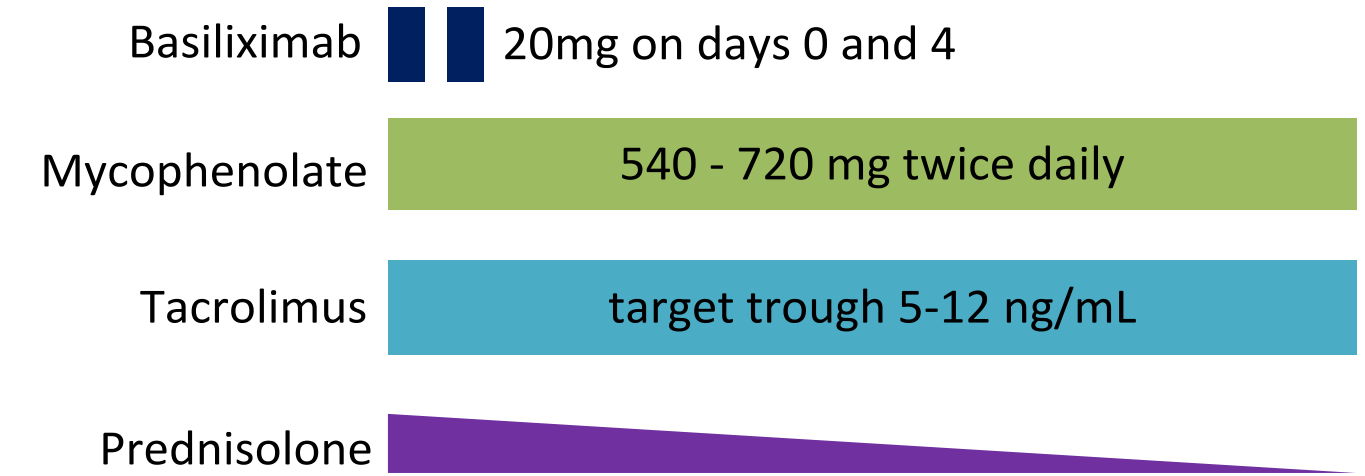
Induction therapy regimens in the 3C Study

Alemtuzumab-based induction therapy



Basiliximab-based induction therapy



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Eligibility criteria

- Inclusion criteria
  - Age ≥18 years
  - Scheduled to receive kidney transplant in next 24 hours

- Exclusion criteria
  - Prior treatment with alemtuzumab
  - History of malignancy in last 5 years
  - Active infection
  - Multi-organ transplants

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Baseline characteristics

	Alemtuzumab n=426	Basiliximab n=426
Age (SD)	51.6 (13.3)	51.3 (13.3)
Male sex (%)	65%	65%
Prior transplant (%)	8%	8%
Mean HLA mismatch A-B-DR	1.0 – 1.0 – 0.7	1.0 – 1.0 – 0.7
Highly sensitized (cRF >85%) (%)	4%	4%
Donor type (%)		
DBD	35%	34%
DCD	37%	37%
Living	28%	29%
Donor age, mean (SD)	48.1 (17.8)	47.8 (19.6)

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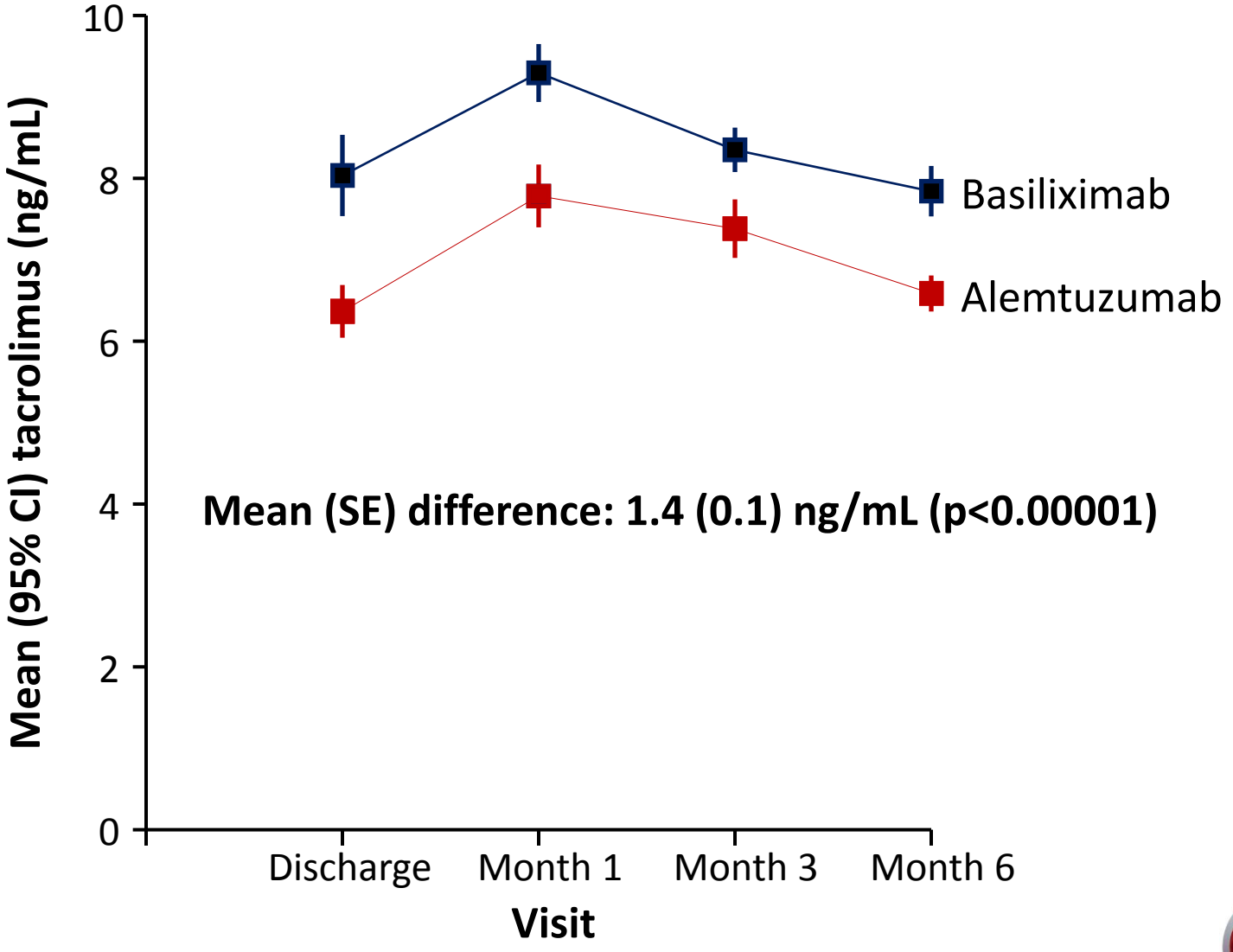
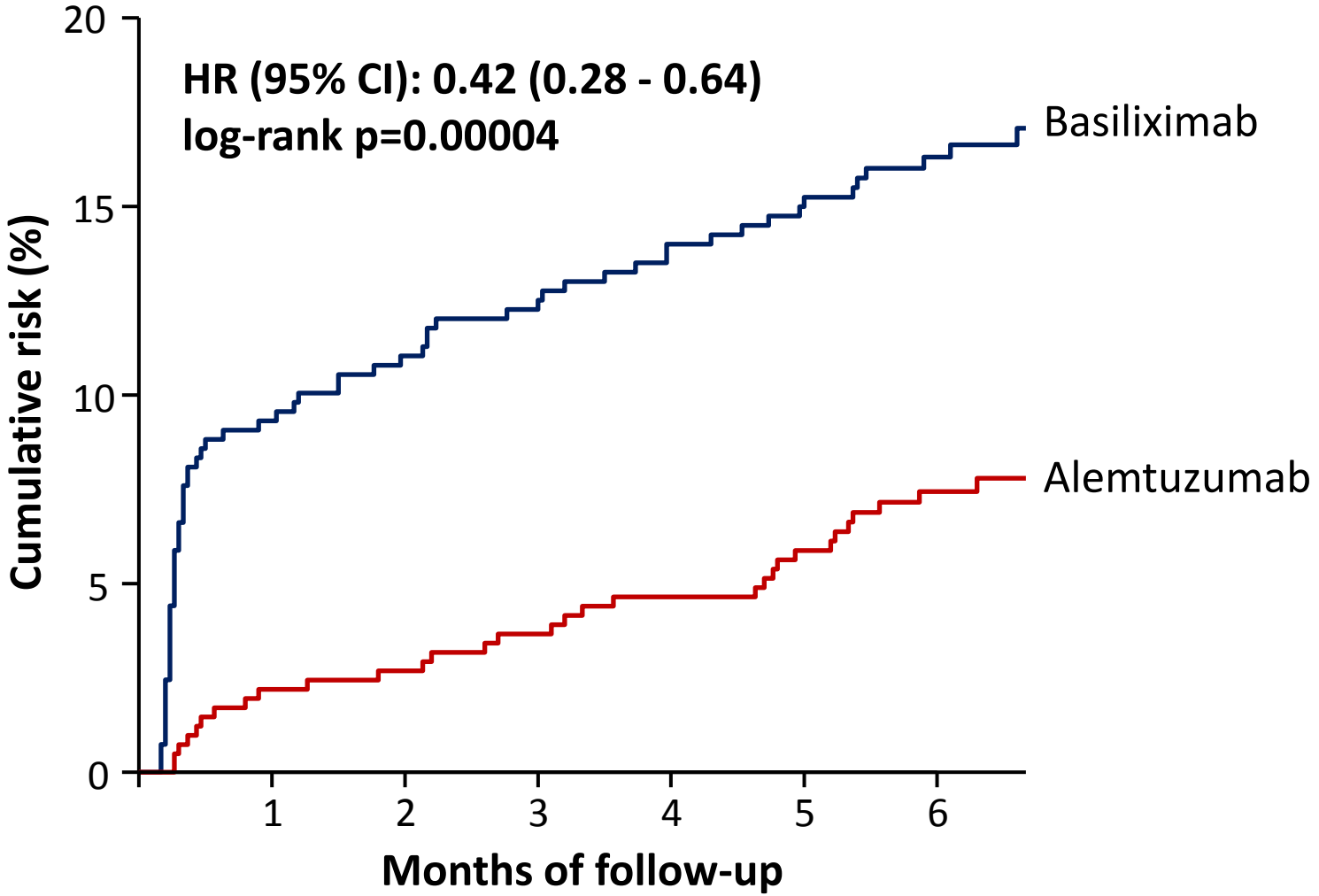
Mean tacrolimus concentration by visit

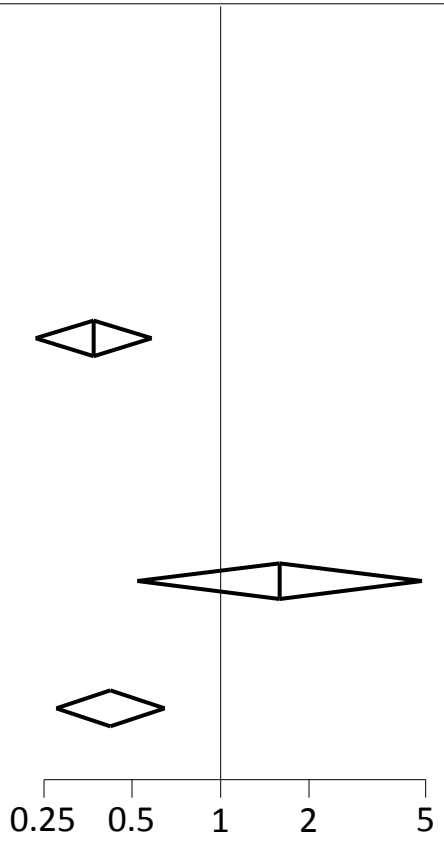


Biopsy-proven acute rejection



BPAR events in the first 6 months, by type

	Number with event: Alemtuzumab-based induction therapy (n=426)	Number with event: Basiliximab-based induction therapy (n=426)	HR (95% CI) p value
Biopsy-proven acute rejection			
Cellular			
Banff I	19 (4.5%)	47 (11.0%)	
Banff II	7 (1.6%)	18 (4.2%)	
Banff III	3 (0.7%)	1 (0.2%)	
Any	**26 (6.1%)**	**65 (15.3%)**	**0.37 (0.23 - 0.58) p<0.00001**
Antibody mediated			
Banff I	6 (1.4%)	1 (0.2%)	
Banff II	3 (0.7%)	4 (0.9%)	
Banff III	1 (0.2%)	1 (0.2%)	
Any	**8 (1.9%)**	**5 (1.2%)**	**1.59 (0.52 - 4.86) p=0.41**
Unknown	0 (0.0%)	1 (0.2%)	
Any	**31 (7.3%)**	**68 (16.0%)**	**0.42 (0.28 - 0.64) p=0.00004**



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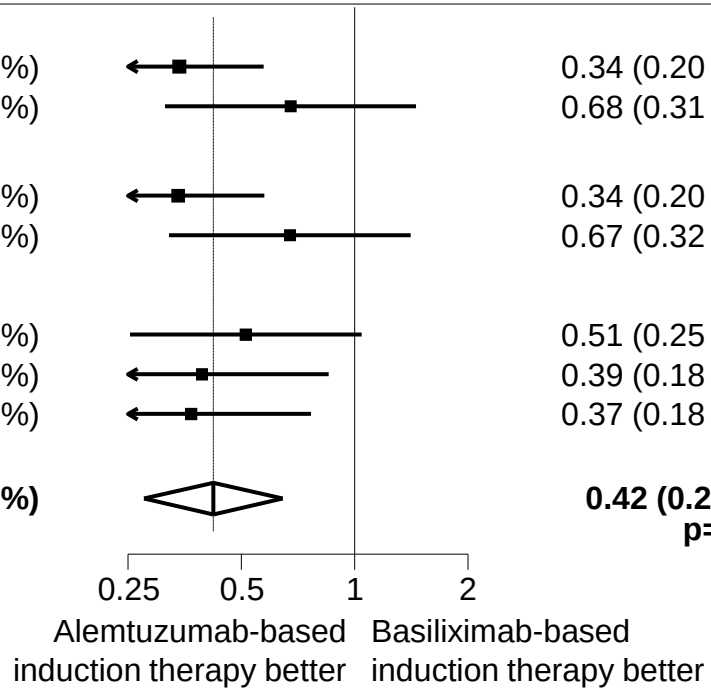
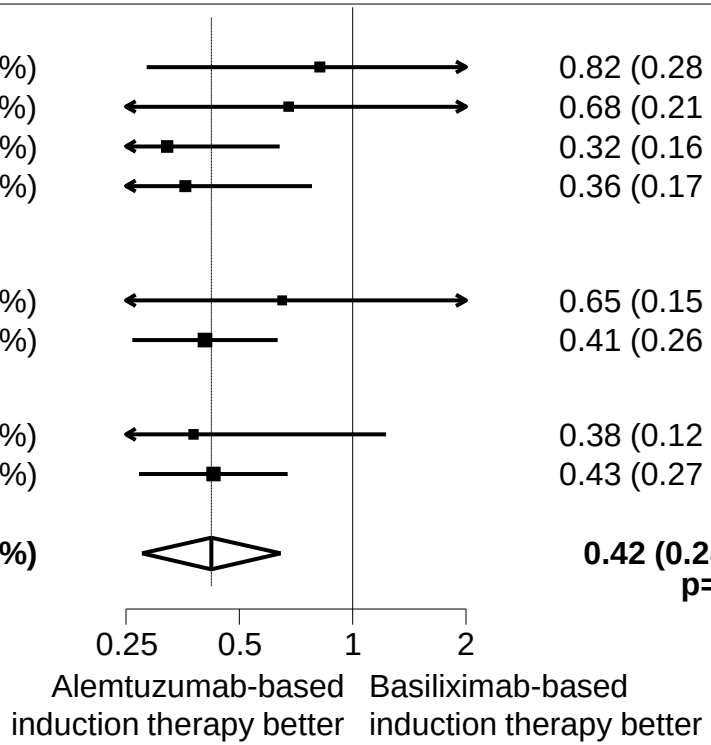
BPAR in first 6 months, by baseline characteristics

	Alemtuzumab-based induction therapy (n=426)	Basiliximab-based induction therapy (n=426)	HR (95% CI)	Heterogeneity trend test
Sex				
Male	20 (7.2%)	52 (18.9%)	0.34 (0.20 - 0.57)	χ^2_1=2.08 (p=0.1)
Female	11 (7.4%)	16 (10.6%)	0.68 (0.31 - 1.46)	
Age (years)				
< 60	19 (6.6%)	51 (17.6%)	0.34 (0.20 - 0.58)	χ^2_1=2.18 (p=0.1)
≥ 60	12 (8.8%)	17 (12.4%)	0.67 (0.32 - 1.41)	
Donor type				
Living	12 (10.0%)	21 (17.1%)	0.51 (0.25 - 1.04)	χ^2_2=0.46 (p=0.8)
DBD	9 (6.1%)	22 (15.2%)	0.39 (0.18 - 0.85)	
DCD	10 (6.3%)	25 (15.8%)	0.37 (0.18 - 0.77)	
Any	**31 (7.3%)**	**68 (16.0%)**	**0.42 (0.28 - 0.64) p=0.00004**	



BPAR in first 6 months, by baseline characteristics

	Alemtuzumab-based induction therapy (n=426)	Basiliximab-based induction therapy (n=426)	HR (95% CI)	Heterogeneity trend test
HLA mismatch				
Tier 1	6 (13.3%)	8 (17.0%)	0.82 (0.28 - 2.36)	
Tier 2	5 (5.3%)	7 (7.4%)	0.68 (0.21 - 2.13)	χ^2_1=2.10
Tier 3	11 (5.6%)	31 (16.1%)	0.32 (0.16 - 0.64)	(p=0.1)
Tier 4	9 (9.9%)	22 (23.9%)	0.36 (0.17 - 0.78)	
Highly sensitised				
Yes	3 (18.8%)	4 (26.7%)	0.65 (0.15 - 2.91)	χ^2_1=0.35
No	28 (6.8%)	64 (15.6%)	0.41 (0.26 - 0.63)	(p=0.6)
Previous transplant				
Yes	4 (11.1%)	9 (26.5%)	0.38 (0.12 - 1.23)	χ^2_1=0.04
No	27 (6.9%)	59 (15.1%)	0.43 (0.27 - 0.67)	(p=0.9)
Any	**31 (7.3%)**	**68 (16.0%)**	**0.42 (0.28 - 0.64) p=0.00004**	



Serious infections in the first 6 months

	Alemtuzumab n=426	Basiliximab n=426	HR (95% CI)	p value
Opportunistic infections				
Cytomegalovirus	39 (9.2%)	43 (10.1%)		
BK	32 (7.5%)	17 (4.0%)		
Fungal	9 (2.1%)	13 (3.1%)		
Other	16 (3.8%)	11 (2.6)		
Any opportunistic infection	**81 (19.0%)**	**78 (18.3%)**	**1.06 (0.78-1.45)**	**0.70**
Other serious infections				
Urinary tract	44 (10.3%)	55 (12.9%)		
Respiratory	22 (5.2%)	22 (5.2%)		
Any other serious infection	**71 (16.7%)**	**83 (19.5%)**	**0.85 (0.62-1.17)**	**0.33**
Any serious infection	**135 (31.7%)**	**136 (31.9%)**	**1.02 (0.80-1.29)**	**0.88**

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Transplant failure and death in the first 6 months

	Alemtuzumab n=426	Basiliximab n=426	HR (95% CI)	p value
Transplant failure				
Primary non-function	2 (0.5%)	0 (0.0%)		
Glomerular disease	2 (0.5%)	1 (0.2%)		
Fibrosis/atrophy	0 (0.0%)	3 (0.7%)		
Medical/surgical condition	7 (1.6%)	8 (1.9%)		
Rejection	5 (1.2%)	1 (0.2%)		
Any transplant failure	**16 (3.8%)**	**13 (3.1%)**	**1.23 (0.59-2.55)**	**0.58**
Death	**11 (2.6%)**	**6 (1.4%)**	**1.79 (0.66-4.83)**	**0.25**

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Conclusions

- 3C is the largest trial of induction therapy in kidney transplantation
- Alemtuzumab-based induction therapy halved the risk of acute rejection in first 6 months
- No overall excess of serious infections with alemtuzumab-based therapy
- Long-term results will provide reliable assessment of this strategy on transplant function and survival

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Acknowledgements

- All participants in the 3C Study
- Local clinical and coordinating centre staff
- Steering Committee
- Data Monitoring Committee
- Funders: NHS Blood and Transplant, Pfizer and Novartis UK

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