Antithymocyte globulin use for treatment of biopsy confirmed acute rejection is associated with prolonged renal allograft survival

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Evaluation with missing data

Webfigure 1 shows that the hazard ratio for OKT3 vs ATG useage and 95 % confidence intervals are nearly the same, when missing data are replaced by the median of the respective group.

Red lines indicated with "m" in the model name represent the models computed with data missing, black lines (without indication in model name) represent the hazard ratio and 95 % confidence interval when missing data are replaced.
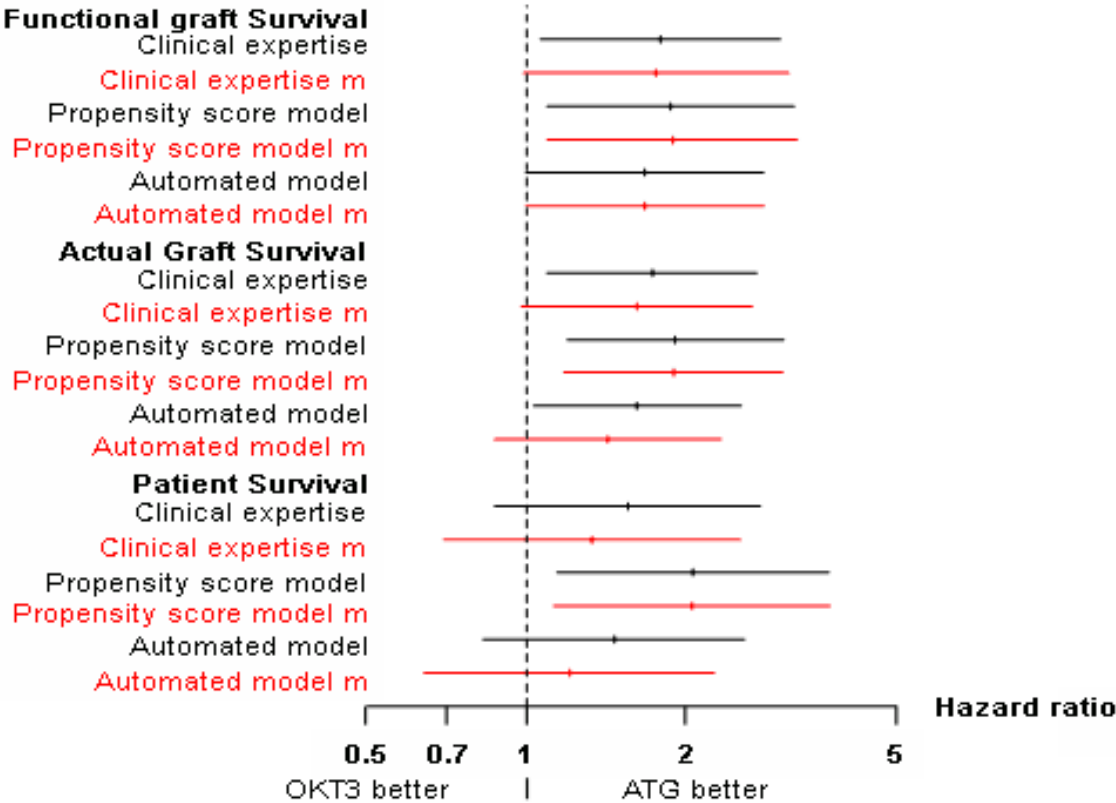
Variables used in propensity score model

Webtable 1 lists the variables wich are used in the logistic regression for computing the propensity score of ATG use.

Variable	Type of variable	Meaning of variable
obs_n_DiabetesID_1	binary	Diabetes Type 1
obs_n_diabetesid_2	binary	Diabetes Type 2
obs_vascid1	binary	cerebrovascular disease
obs_vascid2	binary	periphervascular disease
obs_khk	binary	cardiovascular disease
obs_cmp	binary	heart insufficiency and other heart disease
obs_pu1a	binary	proteinuria 500 – 3500 mg/d
obs_pu2a	binary	proteinuria >3500 mg/d
obs_MAP	continuous	mean arterial pressure
obs_bloodpressidneu	discret	number of antihypertensive drugs
obs_n0_oraleDM	binary	oral antidiabetics
obs_n0_Insulin	binary	insulin
obs_ImmId1	discret	Immunsuppression ID: steroid + AZA + CsA steroid + MMF + CsA steroid free else
obs_DonorAge	continuous	donor age
obs_PRA	continuous	panel receactive antibody
obs_DGF	binary	delayed graft function
obs_can	binary	chronic allograft nephropathy
obs_cholest	continuous	laboratory (annually) cholesterin
obs_hb	continuous	laboratory (annually) haemoglobin
obs_gfr	continuous	calculated glomerular filtration rate (MDRD)
obs_mmsum	discrete	HLA mismatch sum
obs_banffmax	discrete	Banff score

For variables which were missing the value of the "miss-" variable were set to 1

miss_vascid1	binary	
miss_khk	binary	
miss_pu1a	binary	
miss_MAP	binary	
miss_DGF	binary	
miss_cholest	binary	
miss_hb	binary	
miss_gfr	binary	
rawscore_adj	continuous	Score computed from the time weighted pattern of missing values

Confounders which change hazard ratio more than 10 percent

Webtables 2a to 2c list the modification of hazard ratio for OKT3 vs. ATG usage in the automated model, which is calculated as a bivariable model.

Webtable 2a
Functional graft survival

Confounder	Modification of crude HR (%)	Modification of adjusted HR (%)
donorage	-6.1461	.
Banff	3.6465	.
HLA mismatch sum	0.2055	.
PRA	-2.3206	.
Number of transplantation	1.5947	.
Year of transplantation	19.6485	-19.6485

Webtable 2b
Actuale graft survival

Confounder	Modification of crude HR (%)	Modification of adjusted HR (%)
donorage	-4.3402	.
Banff	1.7480	.
HLA mismatch sum	-0.0240	.
PRA	-1.6355	.
Number of transplantation	0.1328	.
Year of transplantation	17.6827	-17.6827

Webtable 2c
Patient survival

Confounder	Modification of crude HR (%)	Modification of adjusted HR (%)
donorage	-2.5159	.
Banff	-0.3497	.
HLA mismatch sum	-0.0459	.
PRA	0.4267	.
Number of transplantation	-0.7300	.
Year of transplantation	21.6072	-21.6072

Schoenfeld residuals

Functional graft survival

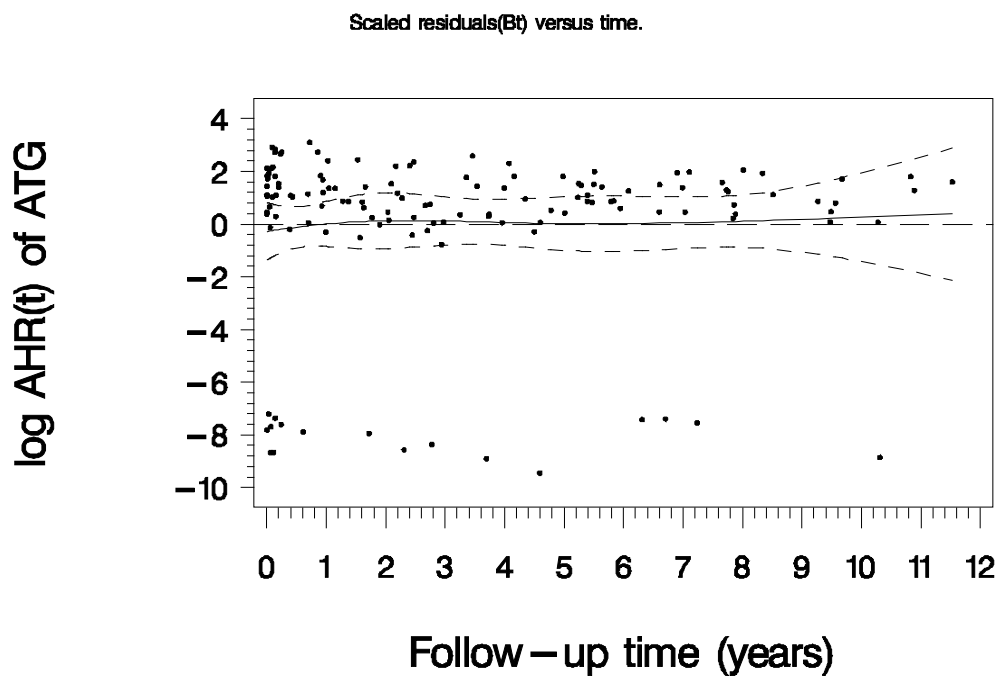Webtable 3
Correlation matrix of the variables with followup time and rank of followup time.
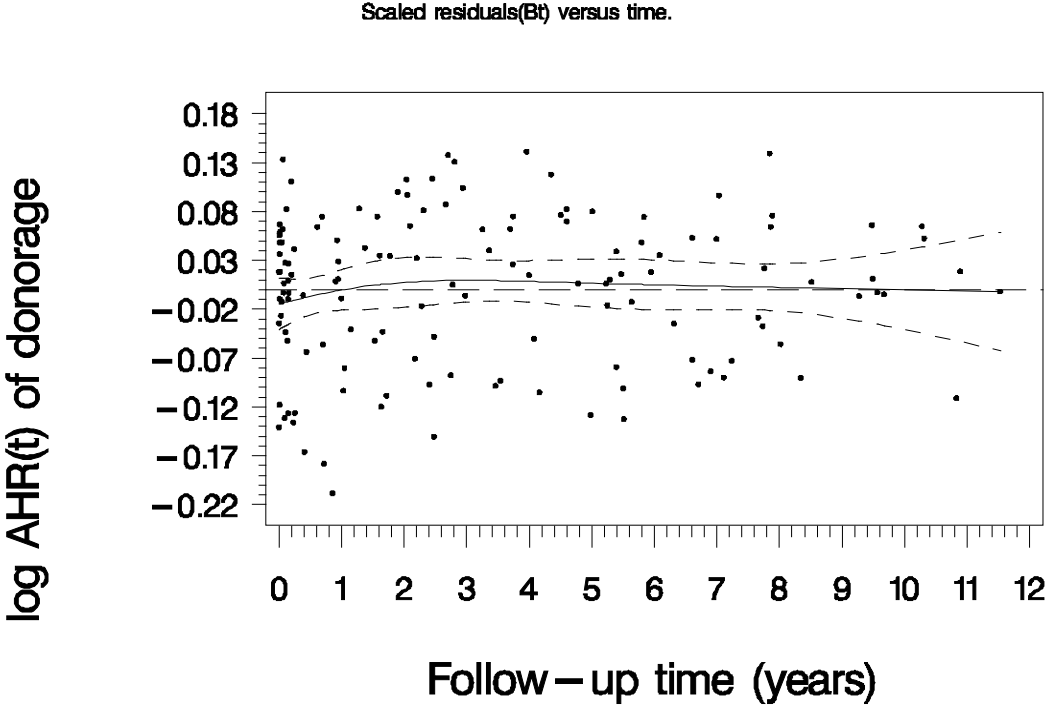
Pearson Correlation Coefficients, N = 136 Prob > |r| under H0: Rho=0		
	Follow-up time	**Rank of follow-up time**
ATG	0.05003 0.5630	0.05373 0.5344
donorage	0.04384 0.6123	0.04590 0.5957
Banff score	0.05047 0.5595	0.04863 0.5740
HLA mismatch sum	0.05382 0.5337	0.02978 0.7308
PRA	0.00264 0.9756	0.04445 0.6073
Number of transplantation	-0.07689 0.3736	-0.10996 0.2025
Year of transplantation	0.05003 0.5630	0.05373 0.5344

Webfigure 2a
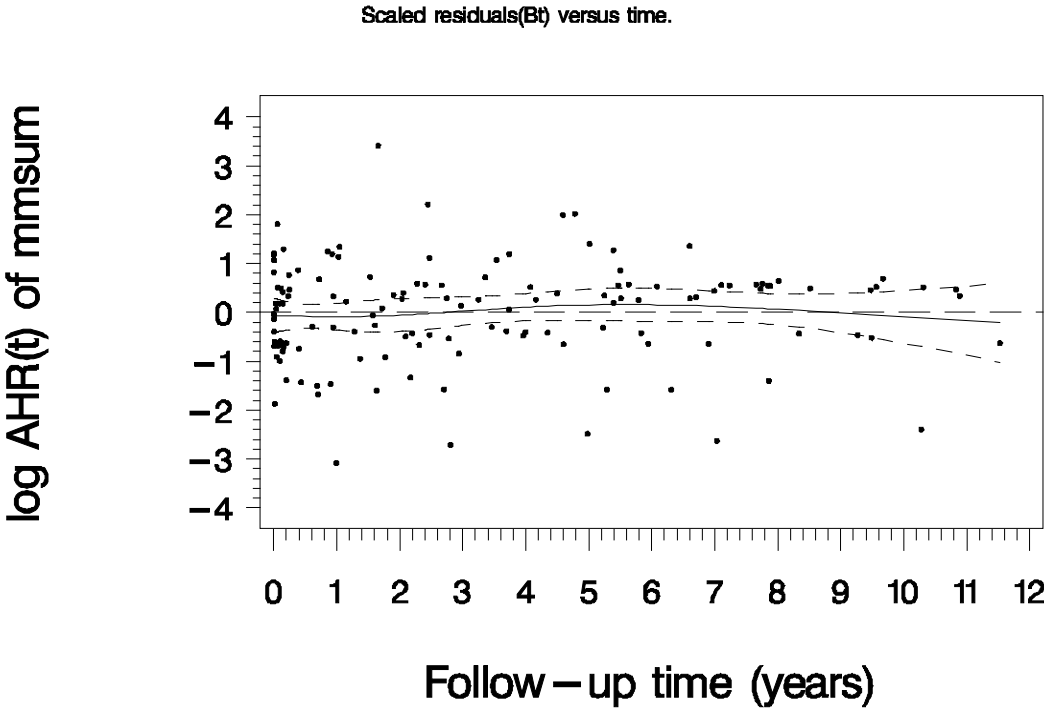Schoenfeld residuals of OKT vs. ATG use

Scaled residuals(Bt) versus time.

Webfigure 2b
Schoenfeld residuals of donorage

Scaled residuals(Bt) versus time.

log AHR(t) of donorage

Follow-up time (years)

Webfigure 2c
Schoenfeld residuals of Banff score

Scaled residuals(Bt) versus time.

log AHR(t) of banffmax

Follow-up time (years)
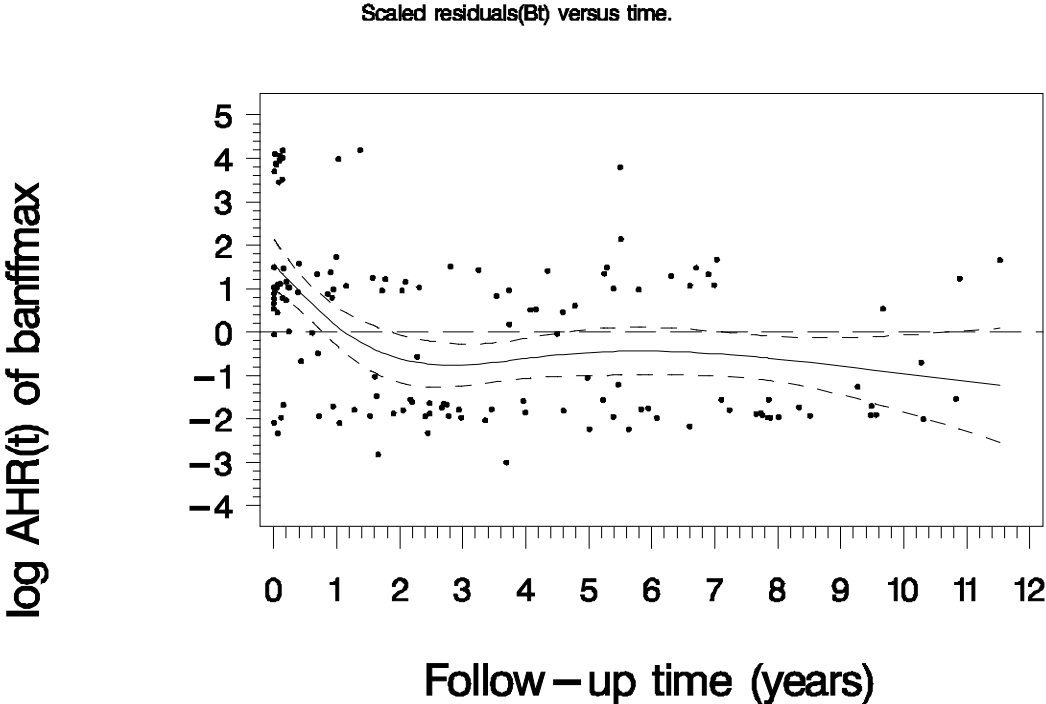
Webfigure 2d
Schoenfeld residuals of HLA mismatch sum

Scaled residuals(Bt) versus time.

Follow−up time (years)

Webfigure 2e
Schoenfeld residuals of PRA

Scaled residuals(Bt) versus time.

Follow−up time (years)
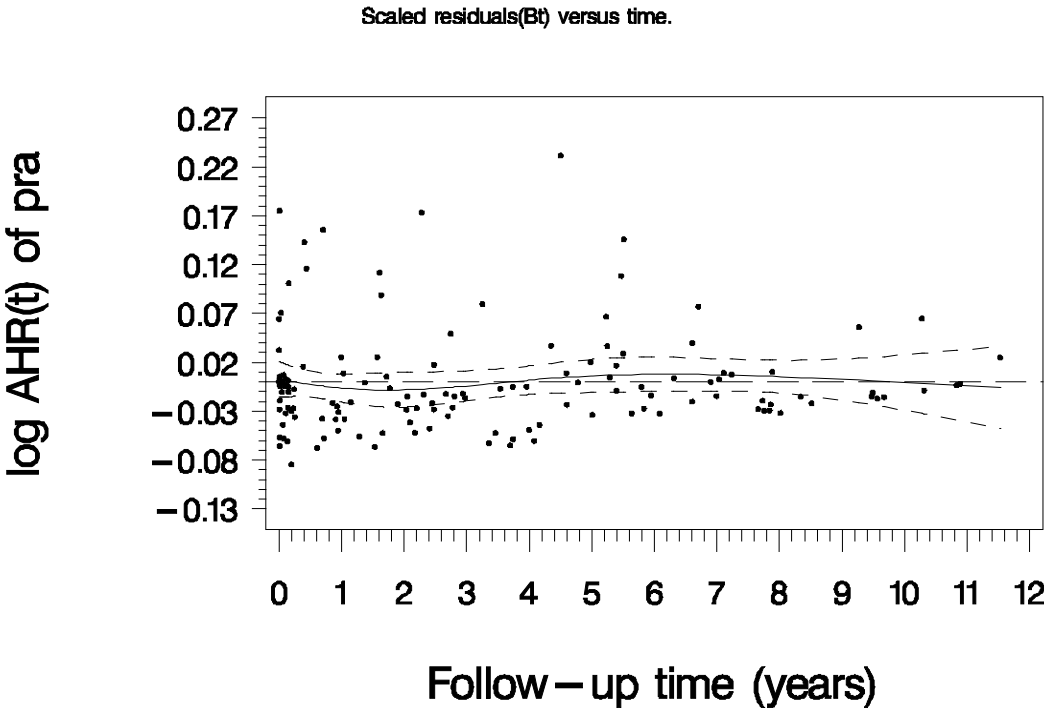
Webfigure 2f
Schoenfeld residuals of number of transplantation

Scaled residuals(Bt) versus time.
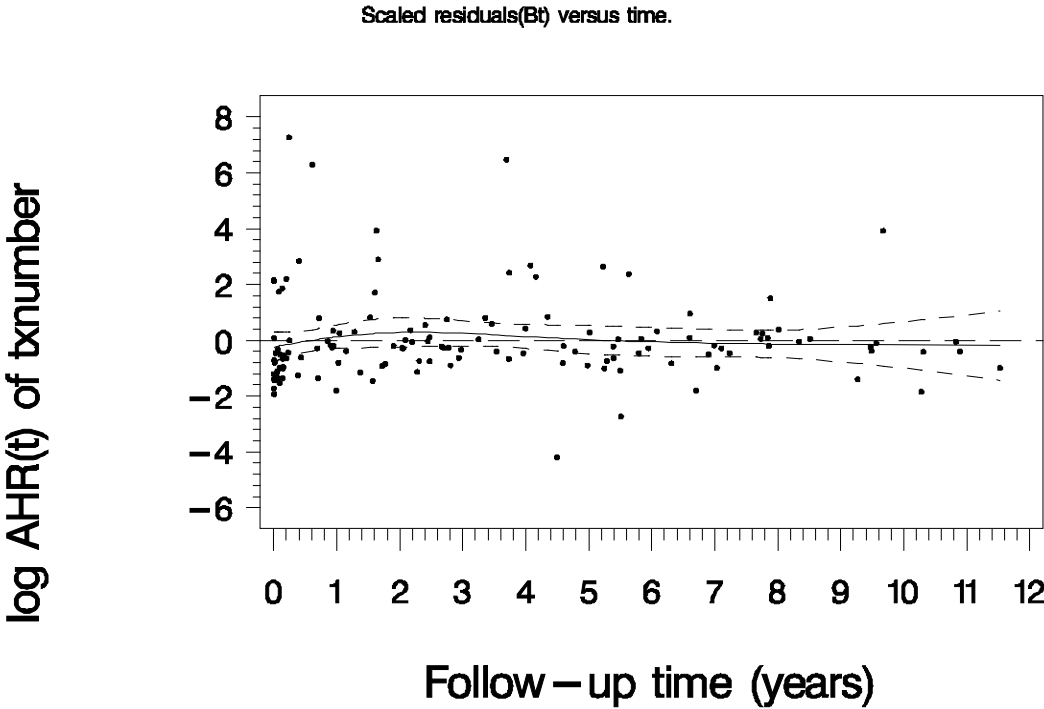
Webfigure 2g
Schoenfeld residuals of year of transplantation

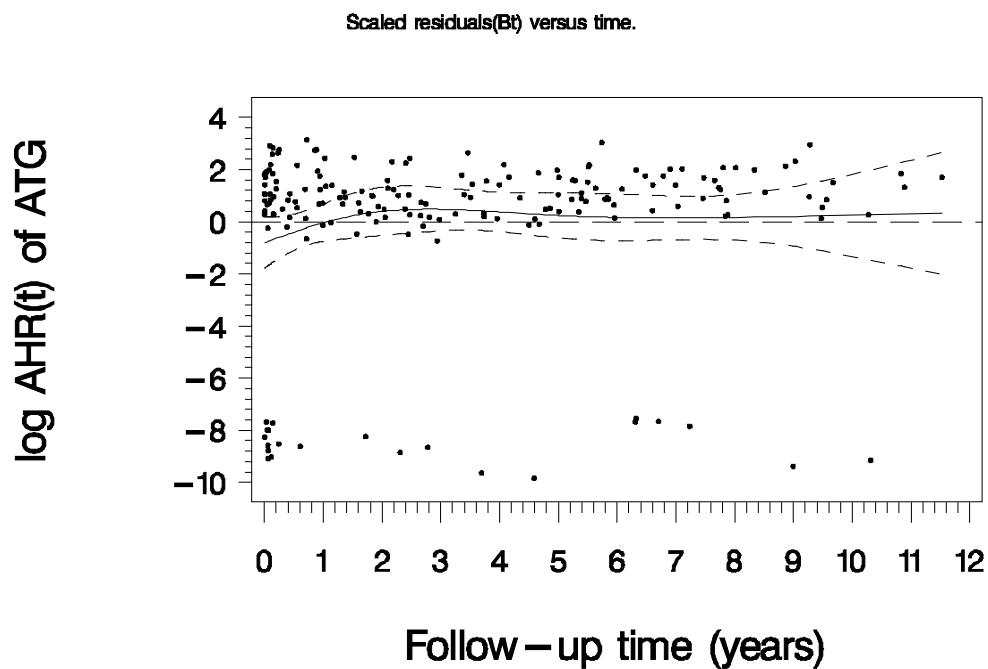Scaled residuals(Bt) versus time.
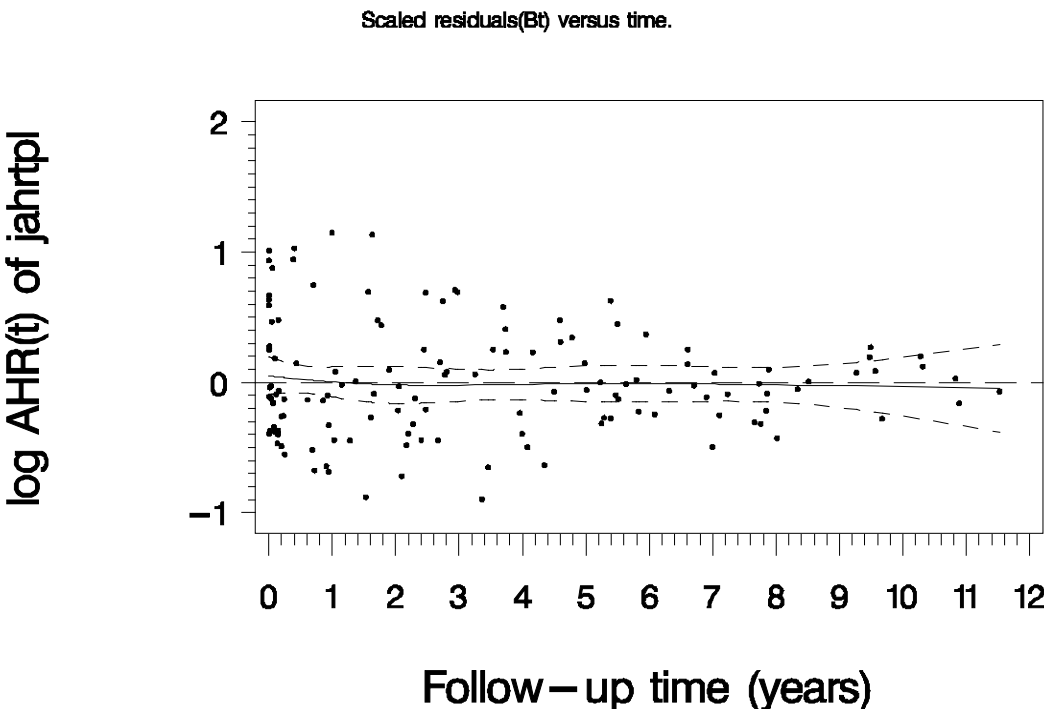
Actual graft survival

Webtable 4
Correlation matrix of the variables with followup time and rank of followup time.

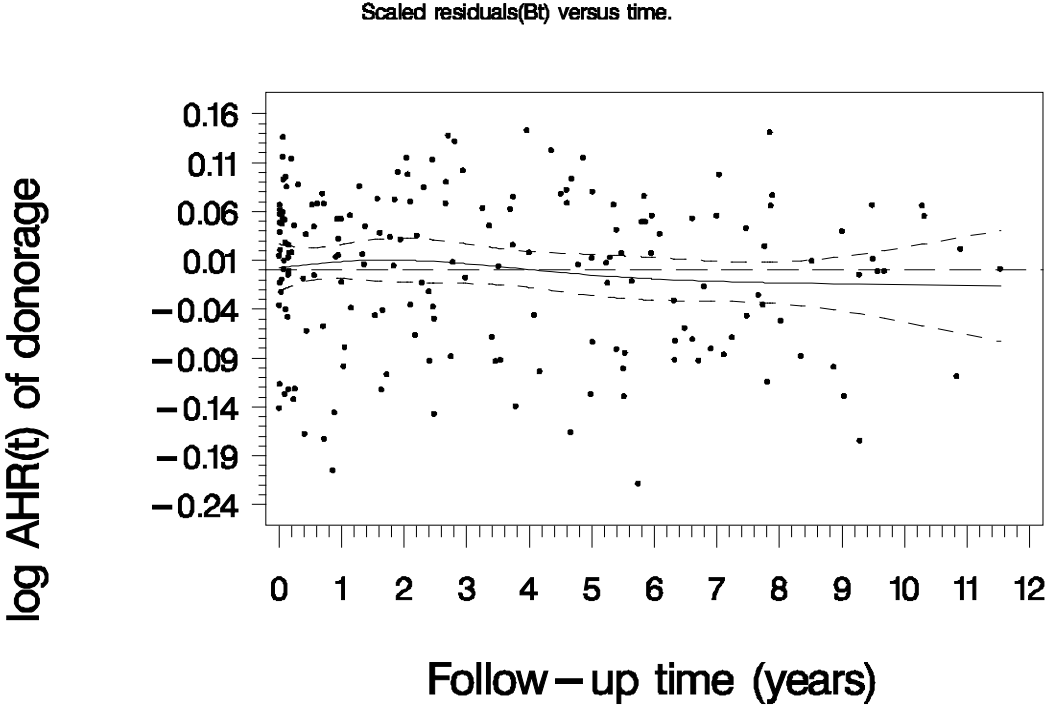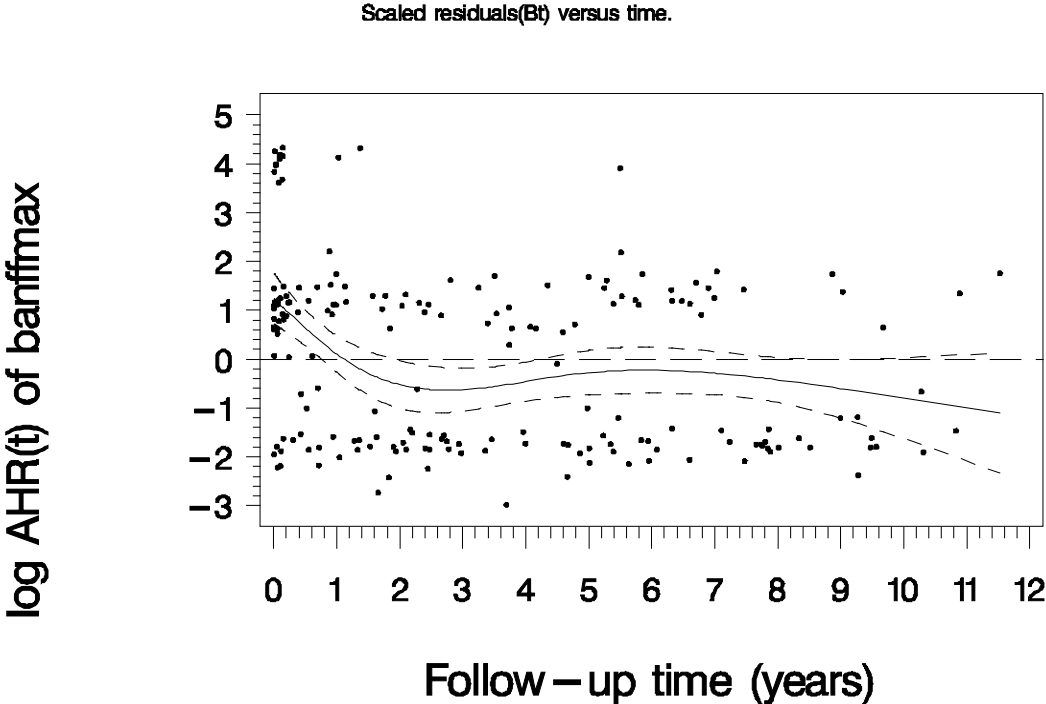| Pearson Correlation Coefficients, N = 184 Prob > |r| under H0: Rho=0		
	Follow-up time	**Rank of follow-up time**
ATG	0.07797 0.2928	0.10686 0.1488
donorage	-0.09451 0.2019	-0.09283 0.2101
Banff score	-0.26228 0.0003	-0.31098 <.0001
HLA mismatch sum	-0.00175 0.9812	0.00021 0.9977
PRA	0.05353 0.4705	0.03429 0.6440
Number of transplantation	-0.00406 0.9564	0.02405 0.7459
Year of transplantation	-0.01500 0.8399	-0.02944 0.6915

Webfigure 3a
Schoenfeld residuals of OKT vs. ATG use

Scaled residuals(Bt) versus time.

Webfigure 3b
Schoenfeld residuals of donorage

Scaled residuals(Bt) versus time.

log AHR(t) of donorage

Follow−up time (years)

Webfigure 3c
Schoenfeld residuals of Banff score

Scaled residuals(Bt) versus time.

log AHR(t) of banffmax

Follow−up time (years)

Webfigure 3d
Schoenfeld residuals of HLA mismatch sum

Scaled residuals(Bt) versus time.

log AHR(t) of mmsum

Follow – up time (years)
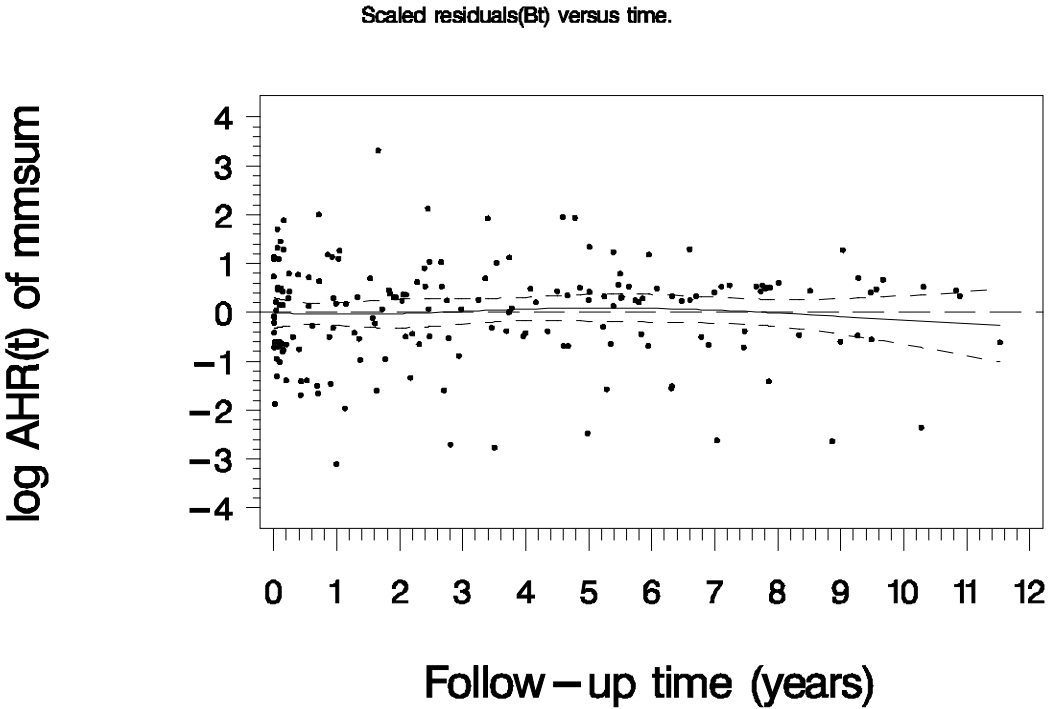
Webfigure 3e
Schoenfeld residuals of PRA

Scaled residuals(Bt) versus time.

log AHR(t) of pra

Follow – up time (years)
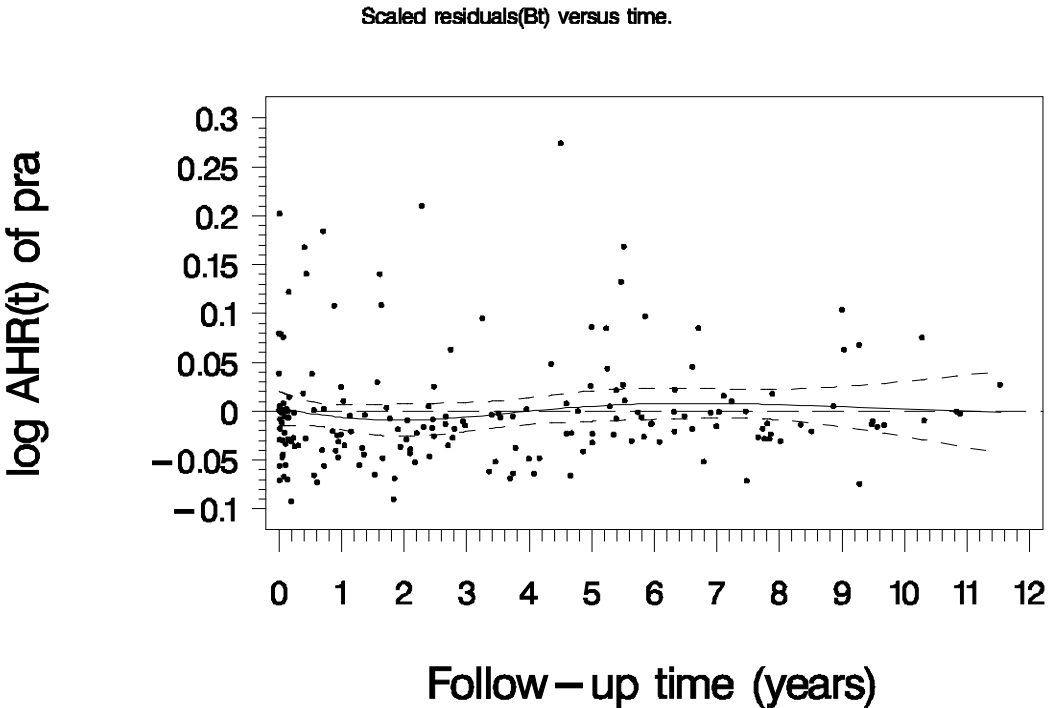
Webfigure 3f
Schoenfeld residuals of number of transplantation

Scaled residuals(Bt) versus time.
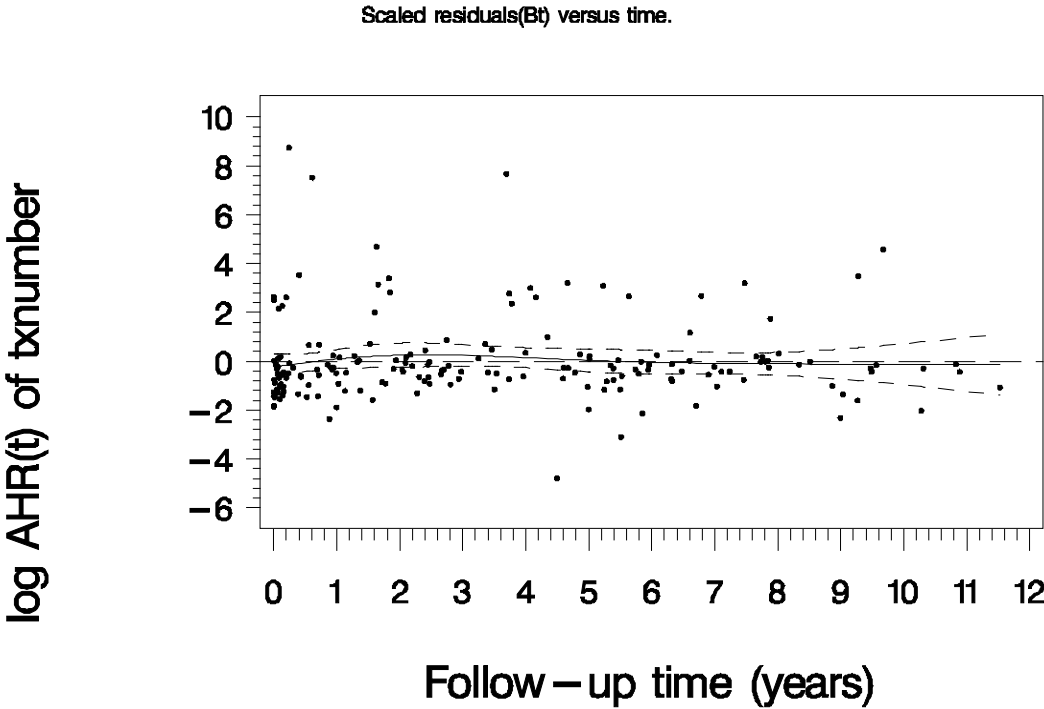
Webfigure 3g
Schoenfeld residuals of year of transplantation

Scaled residuals(Bt) versus time.
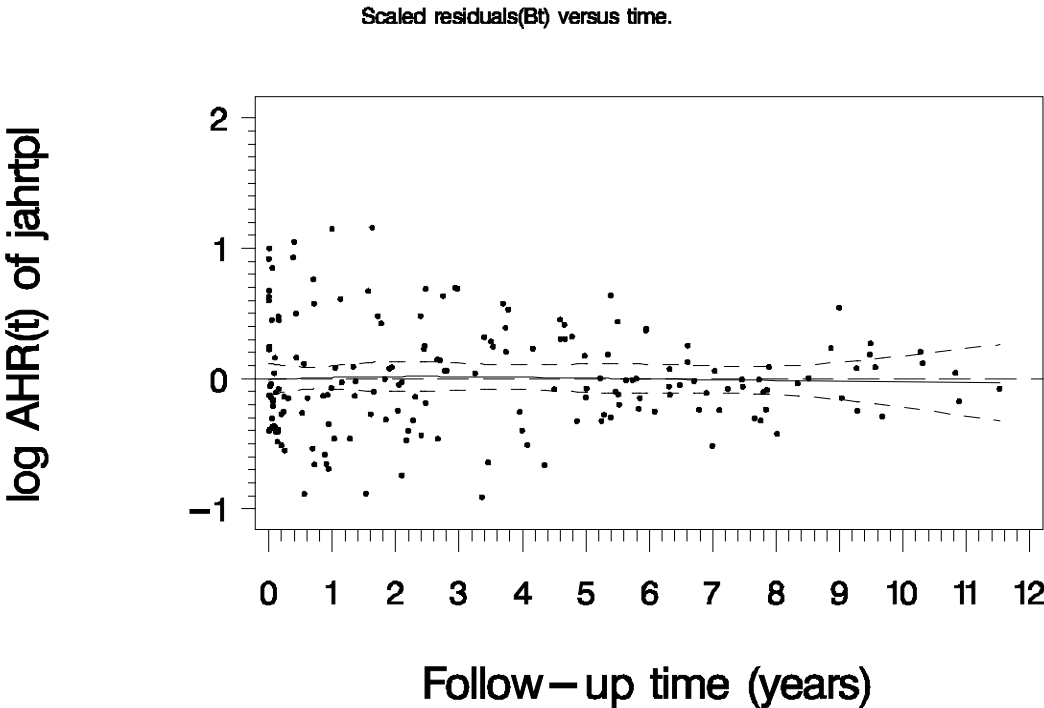
Patient survival

Webtable 5
Correlation matrix of the variables with followup time and rank of followup time.

Pearson Correlation Coefficients, N = 105 Prob > |r| under H0: Rho=0		
	Follow-up time	**Rank of follow-up time**
ATG	0.05311 0.5905	0.06081 0.5377
donorage	-0.27636 0.0043	-0.26935 0.0055
Banff score	-0.06406 0.5162	-0.06196 0.5301
HLA mismatch sum	-0.04134 0.6755	-0.06268 0.5253
PRA	0.08202 0.4055	0.08109 0.4109
Number of transplantation	0.03926 0.6909	0.03824 0.6985
Year of transplantation	-0.04159 0.6735	-0.03711 0.7070

Webfigure 4a
Schoenfeld residuals of OKT vs. ATG use

Scaled residuals(Bt) versus time.

Webfigure 4b
Schoenfeld residuals of donorage

Scaled residuals(Bt) versus time.

Webfigure 4c
Schoenfeld residuals of Banff score

Scaled residuals(Bt) versus time.
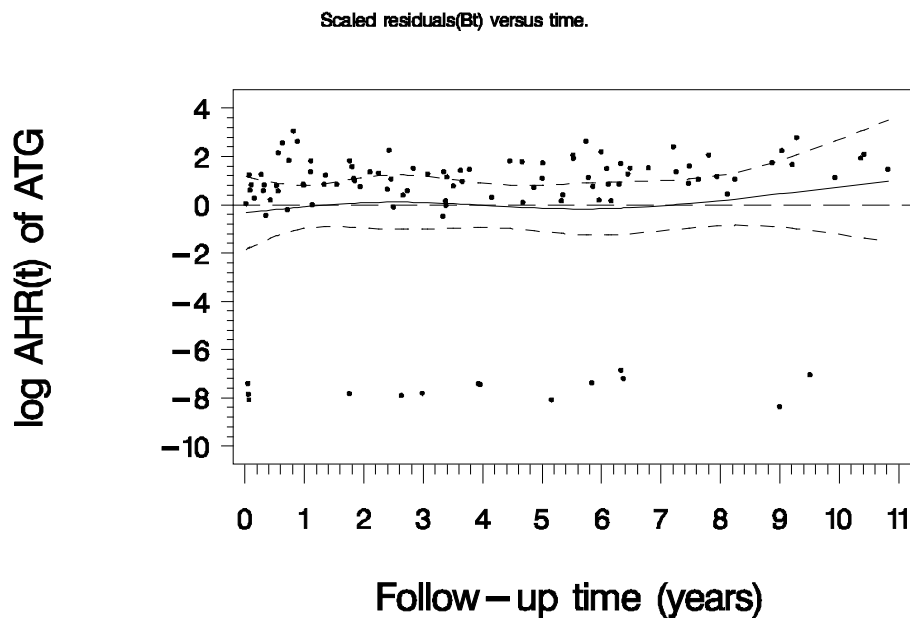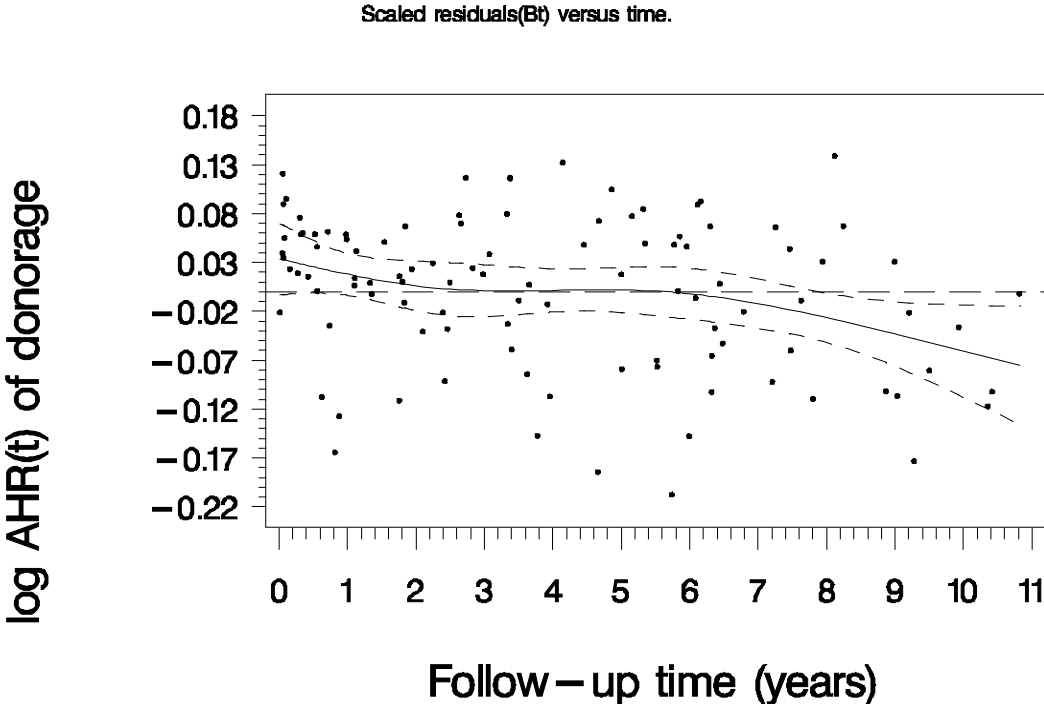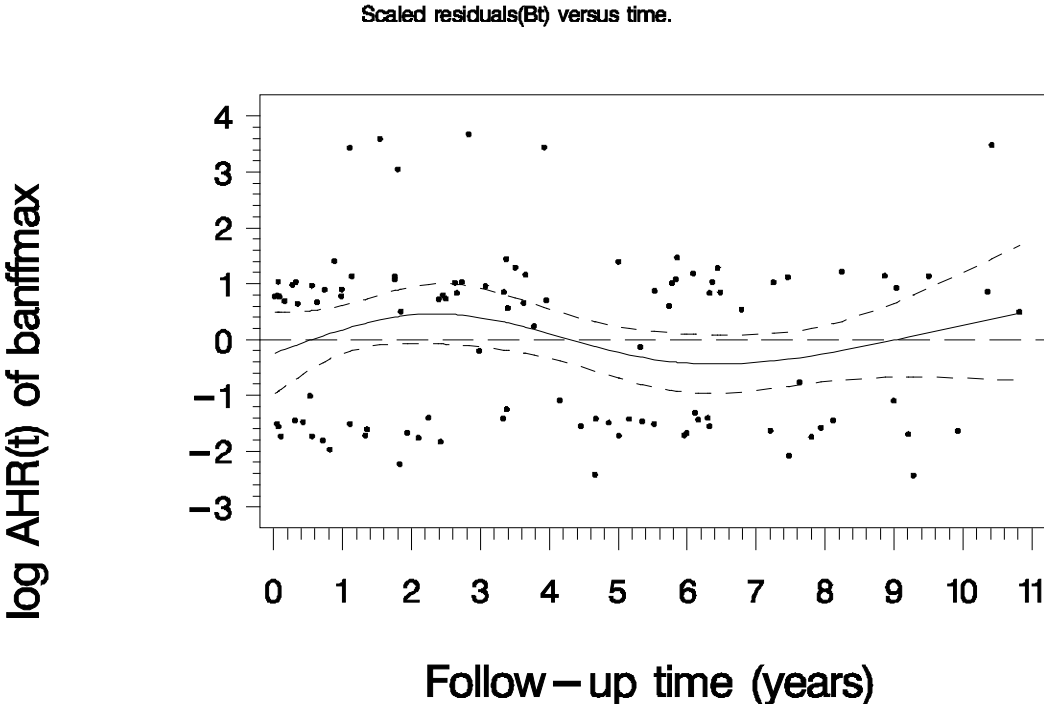
Webfigure 4d
Schoenfeld residuals of HLA mismatch sum

Scaled residuals(Bt) versus time.

Follow−up time (years)
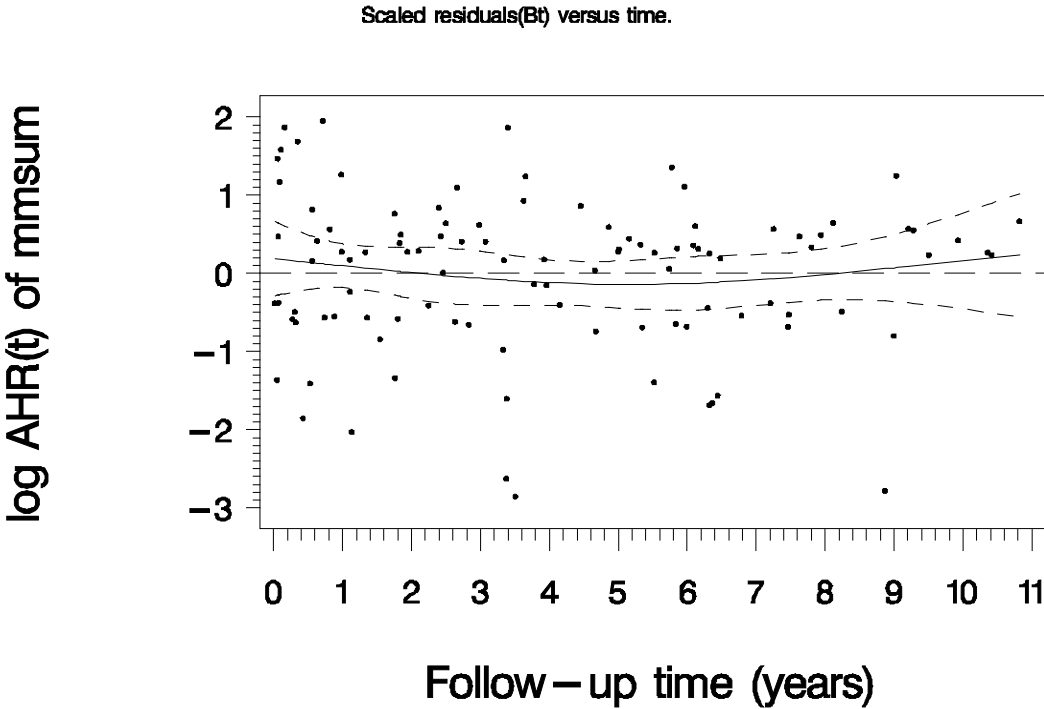
Webfigure 4e
Schoenfeld residuals of PRA

Scaled residuals(Bt) versus time.

Follow−up time (years)
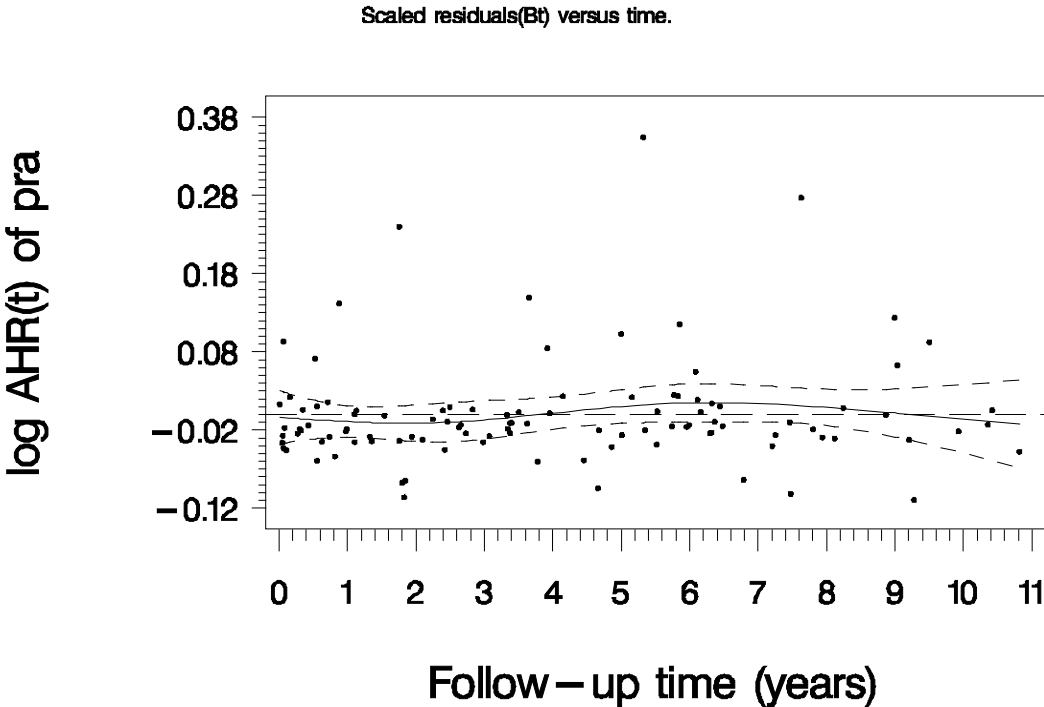
Webfigure 4f
Schoenfeld residuals of number of transplantation

Scaled residuals(Bt) versus time.
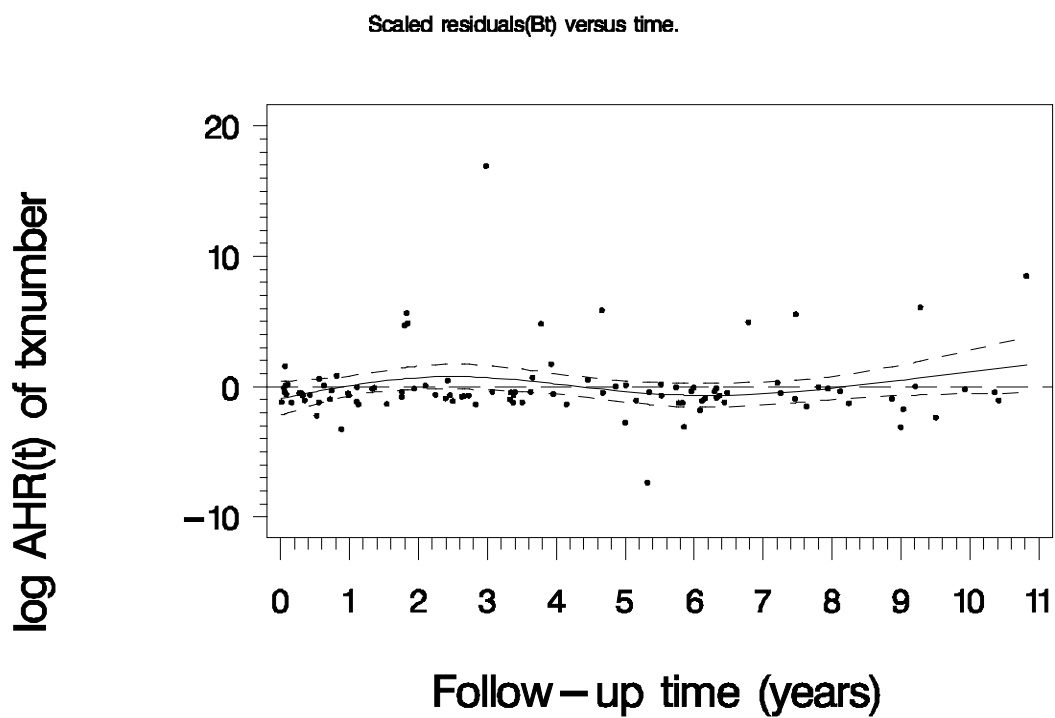
Webfigure 4g
Schoenfeld residuals of year of transplantation

Scaled residuals(Bt) versus time.
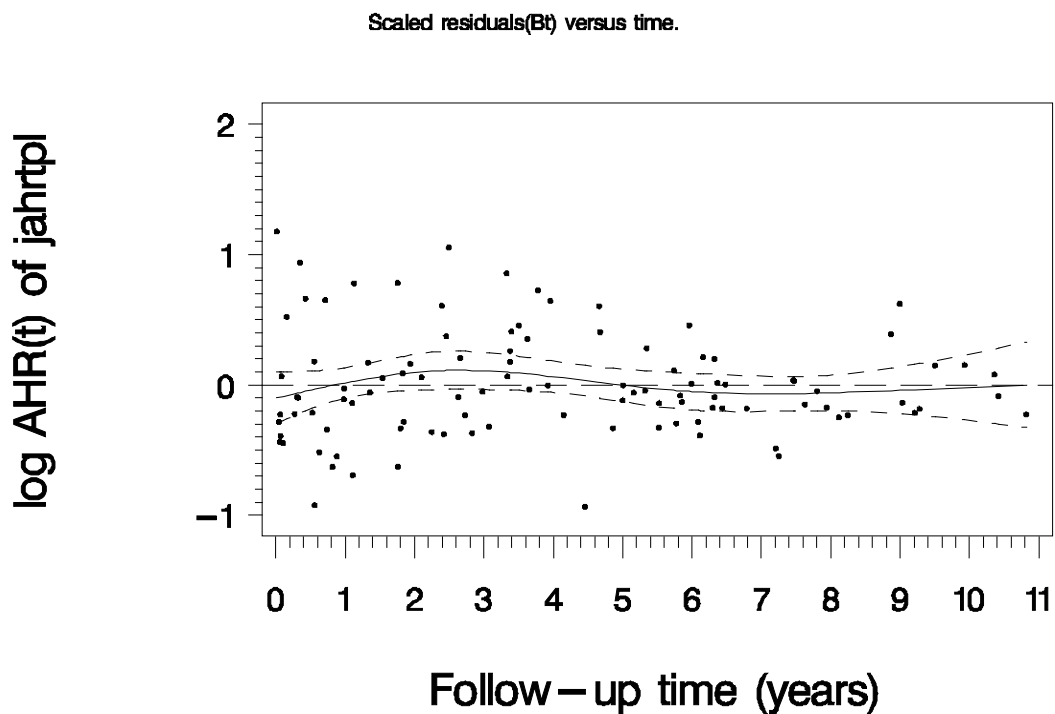
Analyses with first transplantation only

The following analyses include only patients who experienced a BCAR during the first renal allograft.

Functional graft survival

Webtable 6
Associations between OKT3 use and functional graft loss using different model-building strategies

Parameter	Hazard Ratio	95 % confidence interval		p-value
Propensity score model				
OKT3 vs. ATG usage	1.56	0.84	2.88	0.157
Automated model				
OKT3 vs. ATG usage	1.28	0.69	2.35	0.434
Year of transplantation	0.88	0.82	0.95	<0.001
Clinical expertise				
OKT3 vs. ATG usage	1.33	0.71	2.48	0.370
Donor age	1.01	1.00	1.03	0.084
BANFF 2 vs. 1	1.26	0.84	1.90	0.263
BANFF 3 vs. 1	3.48	1.74	6.93	<0.001
HLA mismatch	0.99	0.83	1.18	0.949
PRA	1.01	0.99	1.02	0.565
Year of transplantation	0.87	0.80	0.94	<0.001

Actual graft survival

Webtable 7
Associations between OKT3 use and actual graft loss using different model-building strategies

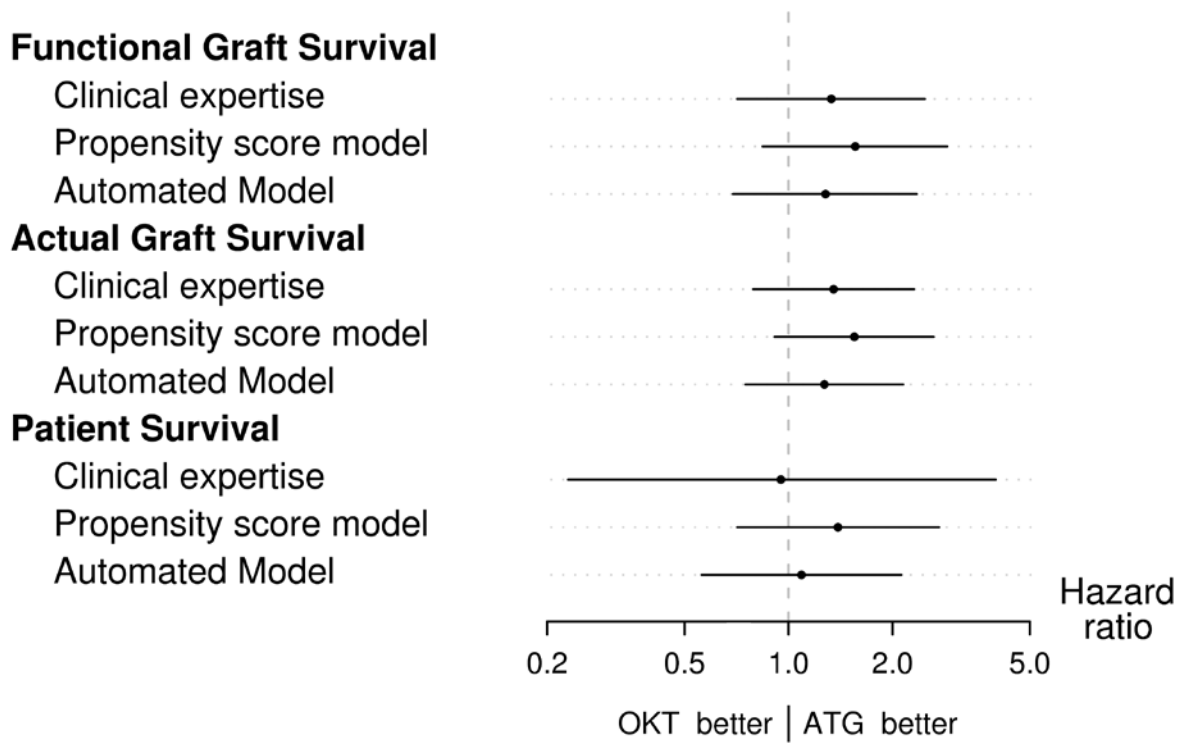| Parameter	Hazard Ratio	95 % confidence interval		p-value
Propensity score model				
OKT3 vs. ATG usage	1.55	0.91	2.63	0.110
Automated model				
OKT3 vs. ATG usage	1.27	0.75	2.15	0.382
Year of transplantation	0.90	0.84	0.95	<0.001
Clinical expertise				
OKT3 vs. ATG usage	1.35	0.79	2.31	0.277
Donor age	1.01	1.00	1.02	0.049
BANFF 2 vs. 1	1.34	0.95	1.88	0.098
BANFF 3 vs. 1	2.55	1.30	4.99	0.006
HLA mismatch	1.02	0.88	1.18	0.817
PRA	1.01	0.99	1.02	0.302
Year of transplantation	0.88	0.83	0.94	<0.001

Patient survival

Webtable 8
Associations between OKT3 use and patient mortality using different model-building strategies

Parameter	Hazard Ratio	95 % confidence interval		p-value
Propensity score model				
OKT3 vs. ATG usage	1.39	0.71	2.73	0.342
Automated model				
OKT3 vs. ATG usage	1.09	0.56	2.12	0.805
Year of transplantation	0.87	0.81	0.95	<0.001
Clinical expertise				
OKT3 vs. ATG usage	0.95	0.23	3.98	0.944
Donor age	1.02	1.00	1.04	0.073
BANFF 2 vs. 1	1.59	0.86	2.94	0.139
BANFF 3 vs. 1	2.67	0.61	11.73	0.195
HLA mismatch	1.09	0.84	1.42	0.509
PRA	0.97	0.90	1.05	0.480
Year of transplantation	0.76	0.68	0.85	<0.001

Summary

Webfigure 5
Forest plot of hazard ratios for OKT3 use as shown in the webtables 6 - 8. The hazard ratios remained virtually unchanged compared to the overall analyses that included also retransplanted subjects. As expected, due to a lower number of patients and thus outcomes, the 95% CI are wider.

Analyses with first transplantation and BCAR in first three months

The following analyses include only patients who experienced a BCAR during the first three months after implantation of the first renal allograft.

Functional graft survival

Webtable 9
Associations between OKT3 use and functional graft loss using different model-building strategies

Parameter	Hazard Ratio	95 % confidence interval		p-value
Propensity score model				
OKT3 vs. ATG usage	1.61	0.80	3.25	0.182
Automated model				
OKT3 vs. ATG usage	1.39	0.69	2.78	0.358
Year of transplantation	0.91	0.83	0.99	0.029
Clinical expertise				
OKT3 vs. ATG usage	1.51	0.84	2.72	0.344
Donor age	1.01	1.00	1.03	0.050
BANFF 2 vs. 1	1.29	0.89	1.87	0.482
BANFF 3 vs. 1	2.63	1.33	5.20	<0.001
HLA mismatch	1.02	0.86	1.19	0.997
PRA	1.01	1.00	1.03	0.165
Year of transplantation	0.90	0.83	0.99	0.029

Actual graft survival

Webtable 10
Associations between OKT3 use and actual graft loss using different model-building strategies

Parameter	Hazard Ratio	95 % confidence interval		p-value
Propensity score model				
OKT3 vs. ATG usage	1.73	0.96	3.11	0.068
Automated model				
OKT3 vs. ATG usage	1.43	0.80	2.56	0.225
Year of transplantation	0.92	0.86	0.99	0.020
Clinical expertise				
OKT3 vs. ATG usage	1.51	0.84	2.72	0.173
Donor age	1.01	1.00	1.03	0.027
BANFF 2 vs. 1	1.29	0.89	1.87	0.179
BANFF 3 vs. 1	2.63	1.33	5.20	0.006
HLA mismatch	1.02	0.86	1.19	0.848
PRA	1.01	1.00	1.03	0.116
Year of transplantation	0.91	0.84	0.98	0.013

Patient survival

Webtable 11
Associations between OKT3 use and patient mortality using different model-building strategies

Parameter	Hazard Ratio	95 % confidence interval		p-value
Propensity score model				
OKT3 vs. ATG usage	1.81	0.85	3.87	0.122
Automated model				
OKT3 vs. ATG usage	1.42	0.67	3.01	0.359
Donor age	1.02	1.01	1.04	0.010
Year of transplantation	0.88	0.80	0.97	0.008
Clinical expertise				
OKT3 vs. ATG usage	1.06	0.25	4.57	0.937
Donor age	1.03	1.00	1.05	0.034
BANFF 2 vs. 1	1.67	0.85	3.27	0.136
BANFF 3 vs. 1	2.86	0.64	12.78	0.170
HLA mismatch	1.09	0.82	1.44	0.546
PRA	0.98	0.86	1.12	0.787
Year of transplantation	0.77	0.66	0.90	<0.001

Summary

Webfigure 6
Forest plot of hazard ratios for OKT3 use as shown in the webtables 9 - 11. The hazard ratios remained virtually unchanged compared to the overall analyses that included also retransplanted subjects, as well as the analysis with first allografts only but BCAR at any time after transplantation.