CARDIOVASCULAR OUTCOMES IN ANCA-VASCULITIS PATIENTS

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INTRODUCTION

- **Granulomatosis with polyangiitis (GPA), (Wegener's), and microscopic polyangiitis (MPA) are subgroups of antineutrophil cytoplasm antibodies (ANCA)-associated vasculitis (AAV)**
- **After the first year of diagnosis cardiovascular disease is the major cause of death, with an odds-ratio of 6.7 compared to the general population.**
- **B cell depletion has been associated with protection against atherosclerosis**
- **The standard treatments for vasculitis are changing with increasing use of rituximab (RTX) (anti-CD20 monoclonal antibody) in place of cyclophosphamide (CYC).**

OBJECTIVES and METHODS

Single center retrospective review of **307 patients** diagnosed with AAV and treated at **Addenbrooke´s** Hospital **, Cambridge (UK)** between **1979 y 2011.**

MAIN

Identify predictors for CVE (cardiovascular event) and death

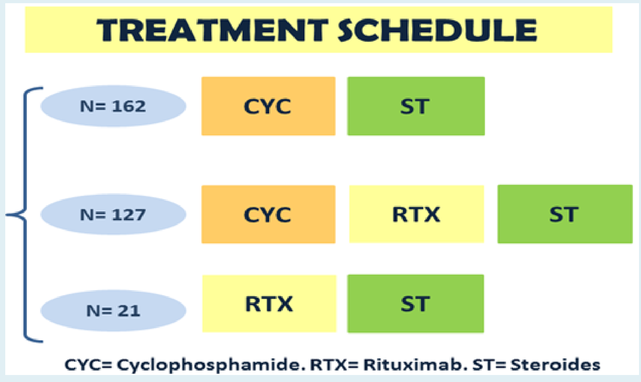
SECONDARY

The association of vasculitis therapies with CVE or death

Primary end-point was:

1. CVE (Acute coronary syndrome, new onset angina, Peripheral vascular disease, stroke or transient ischaemic attack)
2. Death

TREATMENT SCHEDULE



RESULTS

BASELINE CHARACTERISTIC

Main diagnosis:	
•GPA	134 (43.7%)
•MPA	177 (56.3%)
Age (years)	53.0 ± 17.2
Male Gender n (%)	143 (46.6%)
BMI (kg/m²)	27.12 ± 6.11
DM (yes) (%)	12.0%
•Treatment:	
- Diet	20%
- Oral	48%
- Insulin	28%
- Both	4%
HYPERTENSION (Yes) (%)	47.8%
Mean Number antihypertensive drugs (n)	0.8 ± 1.04
DYSLIPIDAEMIA (Yes) (%)	19.8 %
Smoke	
- Current	16.9 %
- Former	23.9 %
Family history of CVE	11%
Prior CVE (Yes) (%)	8.27%
- Acute coronary syndrome	3.4%
- Stroke	2.4%
- Symptomatic PVD	1.7%
- New onset Angina	2%
Follow up (years)	6.05 ± 5.26

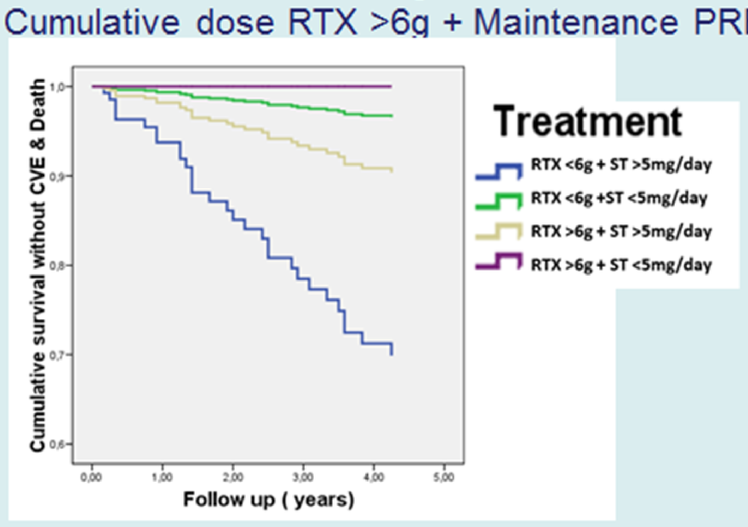
Cox regression analyses of survival to CVE/death

	MULTIVARIATE		
	HR	95% CI	P †
Main diagnosis (MPA)	0.246	0.02-3.094	0.278
ANCA status at diagnosis			
•MPO	1.005	0.999-1.012	0.111
•PR3	0.97	0.995 – 0.99	**0.029***
Age	0.939	0.847-1.041	0.231
Prior CVE	5.3	1.015-27.69	**0.048***
PRED maintenance (>5 mg/day)	169.6	1.18-24200	**0.004***
Cumulative Cyc (>10g)	15.98	0.005-0.83	**0.036***
Cumulative RTX (>6g)	11.54	0.052- 22.48	0.374
ESRD	5.584	0.205- 152.1	0.308
eGFR at end follow up	0.961	0.902-1.024	0.223
Hb at end follow up	0.417	0.262-0.987	**0.039***
CRP at end follow up	1.017	0.988-1.047	0.257

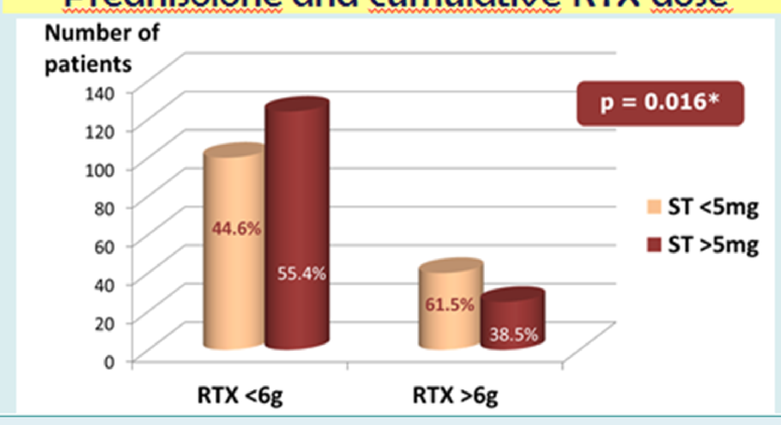
MPA= Microscopic Polyangiitis.
CYC= Cyclophosphamide.
RTX= Rituximab.
PRED= prednisolone.
ESRD= end stage renal disease.
eGFR= estimated glomerular filtration rate.
Hb= hemoglobin.
CPR = C - reactive protein.

Kaplan-Meier survival curves for time to CVE/death in 4 groups of patients:

Cumulative dose RTX <6g + Maintenance PRED dose > 5mg/day
Cumulative dose RTX <6g + Maintenance PRED dose < 5mg/day
Cumulative dose RTX >6g + Maintenance PRED dose > 5mg/day
Cumulative dose RTX >6g + Maintenance PRED dose < 5mg/day (P < 0.001 by log rank test).



Relationship between maintenance Prednisolone and cumulative RTX dose



CONCLUSIONS

- **CVE/death risk in AAV patients is especially high within the first 1 and 5 years of diagnosis.**
- **Prior CVE, negative PR3-ANCA at onset and lower hemoglobin at the end of follow-up were associated with increased cardiovascular risk.**
- **Aggressive immunosuppressive treatment of AAV at onset and avoidance of high long-term prednisolone dosage was associated with a protective effect against atherosclerosis.**
- **Rituximab therapy was associated with a steroid-sparing effect.**