

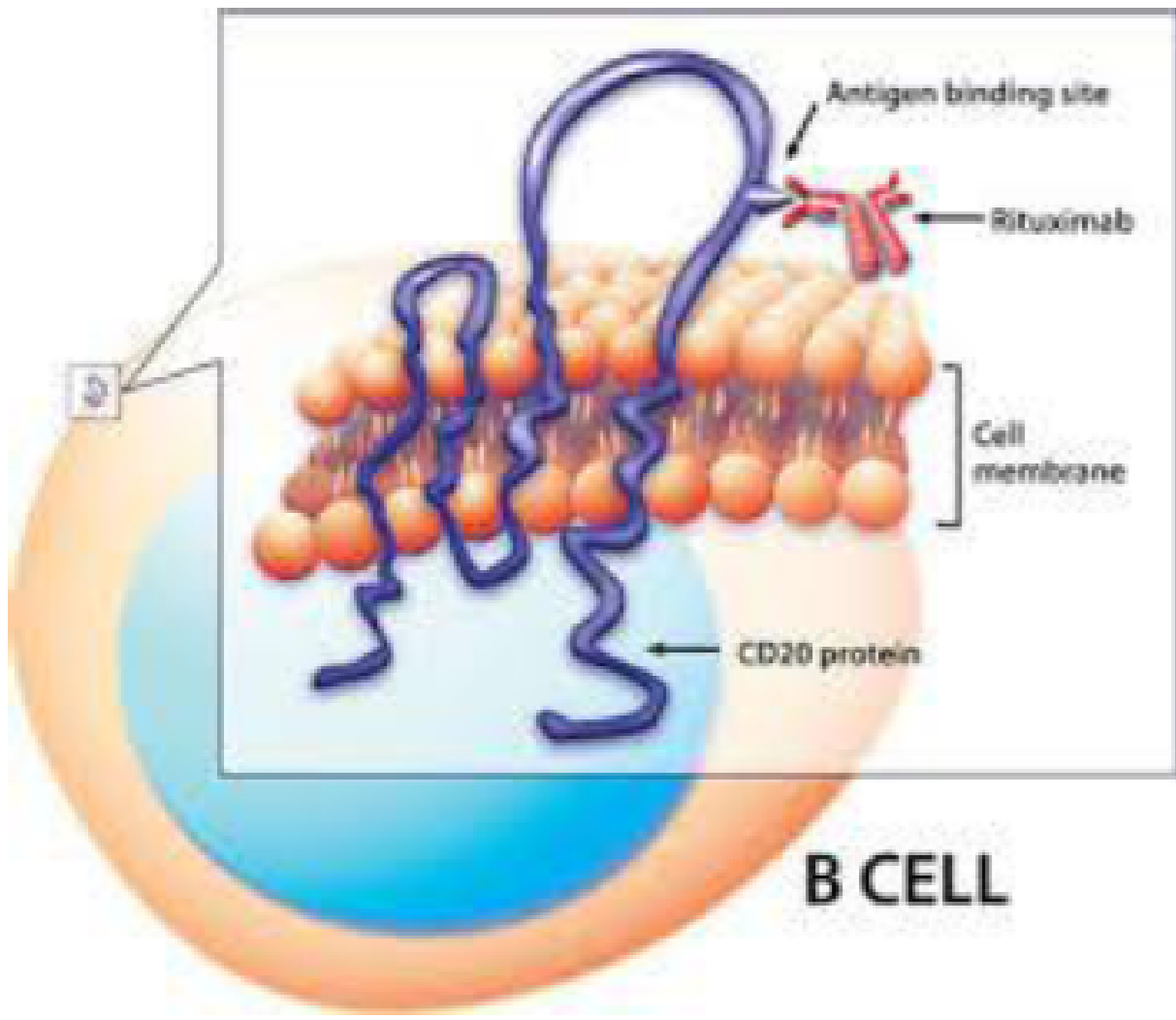
EFFECT OF A VERY LOW DOSE OF RITUXIMAB ON ACTIVE MODERATE-SEVERE GRAVES' ORBITOPATHY (GO): AN INTERIM STUDY REPORT (EUDRACT 2012-001980-53)

Vannucchi G, Campi I, Covelli D, Currò N, Dazzi D, Avignone S, Sina C, Guastella C, Pignataro L, Salvi M

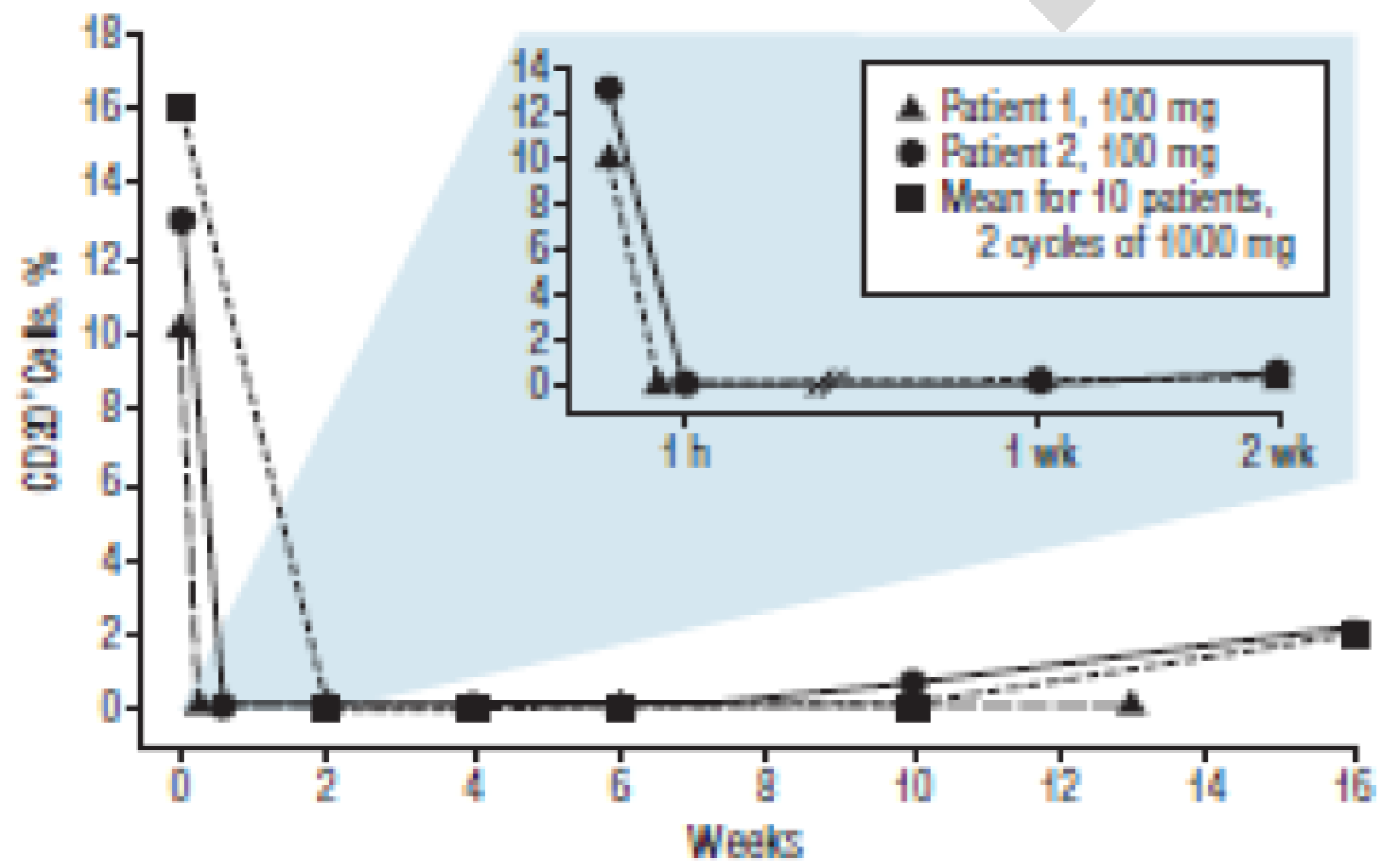
Department of Medical Sciences, Endocrine Unit, Ophthalmology, Neuroradiology Otolaryngology, Fondazione IRCCS Cà Granda, Milan, Internal Medicine, Ospedale di Fidenza, Fidenza, Italy

INTRODUCTION

Rituximab (RTX) is a monoclonal antibody which binds CD20 antigen and induces B cell depletion.



Study	N. of patients treated	RTX dose	CAS before therapy	CAS after therapy (16 wks)	Severity after RTX (response)	N. of patients with side effects	GO relapse
Salvi <i>et al.</i> 2006-07	9	1g twice	4.7	1.8	all improved	3 (minor)	no
El Fassi <i>et al.</i> 2006	2	375 mg/m ² for 4 wk	5.5	1.5	all improved	1 (minor)	no
Khanna <i>et al.</i> 2010	6	1g twice	5.5	1.3	all improved	2 (minor) 1 (major, cardiac death)	no
Silkiss <i>et al.</i> 2010	12	1g twice	5.5	1.9	all improved	none	no
Krassas <i>et al.</i> 2010	1	1g twice	7	7	worsened	n.r.	yes
Madaschi <i>et al.</i> 2010	1	1g twice	5	0	improved	no	no
Salvi <i>et al.</i> 2012	3	100 mg single dose	5.3	1.6	all improved	2 (major but transient)	no
Mitchell <i>et al.</i> 2013	9	500 mg or 1g twice	6.5	3	6 pts. improved 3 pts. Unchanged	4 (minor)	no
Salvi <i>et al.</i> 2015	16	1g twice and then 500 mg single dose	4.4	0.9	All improved	13 (2 major, 1 minor)	no
Stan <i>et al.</i> 2015	13	1g twice	4.9	3.7	5 pts improved	11 (5 major, 6 minor)	no

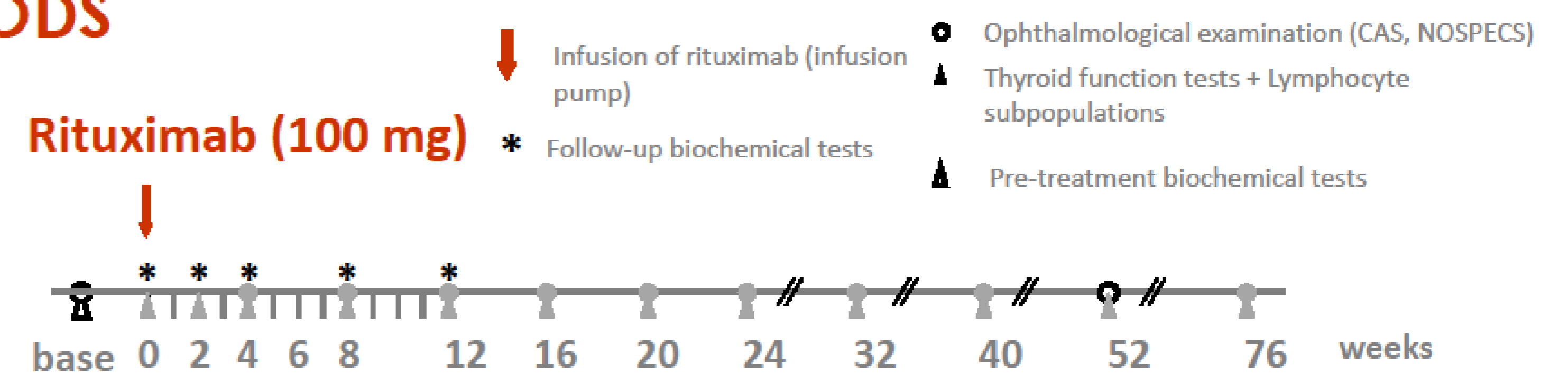


10 patients enrolled (+4 compassionate use of RTX)
 -7 patients previously treated with i.v. steroids and either non responsive or with disease relapse
 -7 patients newly diagnosed GO

AIM:

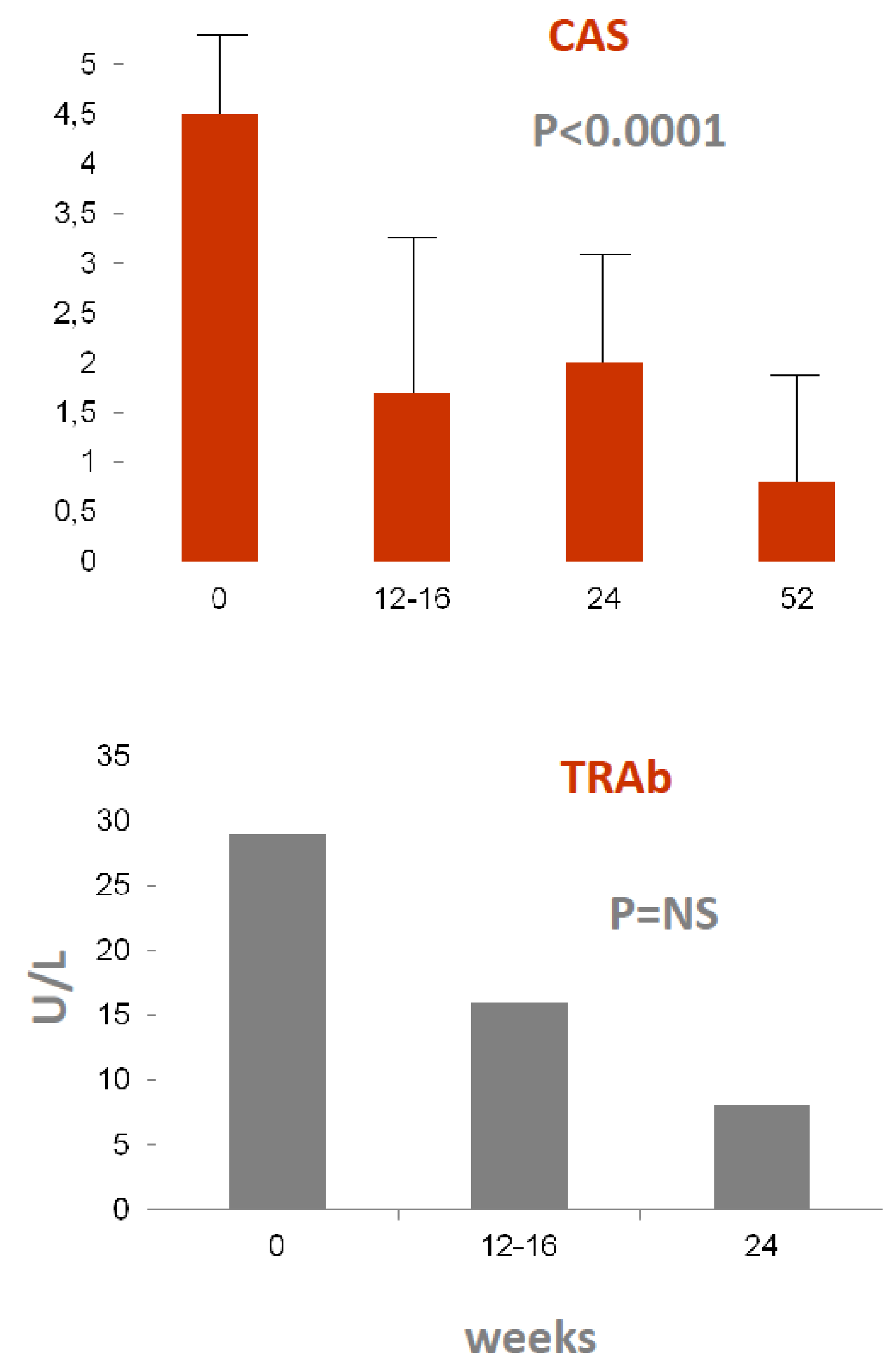
To evaluate the effect of a very low dose RTX moderate-severe active GO

PATIENTS & METHODS



PRIMARY ENDPOINT: decrease of clinical activity score (CAS) of 2 points or CAS ≤ 3

Patients	GO duration	CAS				FOLLOW-UP
		Months	Weeks			
		0	12-16	24	52	
#1	8.8	4	1			
#2	4.2	4	2	2	1	
#3	1.9	6	1			
#4	1	4	2 (8 w)	-	-	Surgical decompression at 11 weeks for congestion
#5	7.6	5	0			
#6	8	4	0			
#7	3.3	4	2	1	1	
#8	4.7	4	0			
#9	10.3	4	2	-	-	Surgical decompression at 20 weeks for subclinical DON
#10	1.1	4	2	4	0	
#11	1.5	4	3	0 (20 w)		
#12	1.8	7	5	2	3	
#13	0.5	4	5	-	-	Surgical decompression at 12 weeks for subclinical DON in OS
#14	4.6	5	3	1	0	
Mean ±SD	4.2±3.2	4.5±0.9	1.7±1.6	2±1	1±1.2	



SUMMARY

1. A single low dose of RTX (100 mg) was effective in inactivating GO in 12/14 patients (85.7%) with a short disease duration (4.2 - 3.3 months). None of these patients required further immunosuppression (at the present time of follow-up).
2. 7/14 (50%) patients had either recurrent or resistant GO after a previous course of i.v. steroids.
3. Two patients did not respond to RTX treatment and developed DON treated with surgical orbital decompression. In one patient DON was likely subclinical at the time of treatment (#9). In another patient (#13) steroid-resistant DON had previously developed in the contralateral eye.
4. Patient #4 underwent elective surgical orbital decompression after rapid disease inactivation (8 weeks) due to disfiguring proptosis.

In conclusion, this study confirms the effectiveness of monotherapy with one single dose of RTX, even in a minute dose, in active moderate-severe GO of short duration, in the absence of signs of subclinical or overt DON.