Orbitopathie Basedowienne et RITUXIMAB

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Randomized Controlled Trial of Rituximab in Patients With Graves' Orbitopathy

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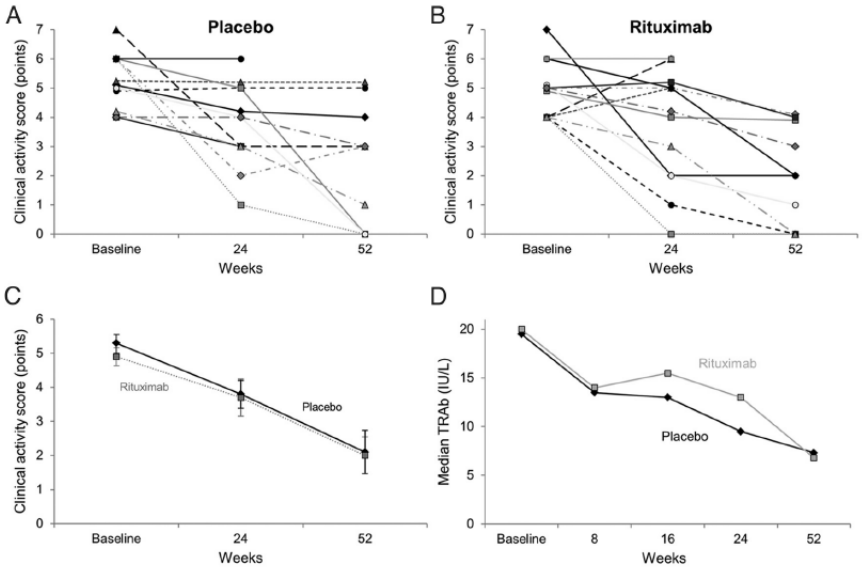
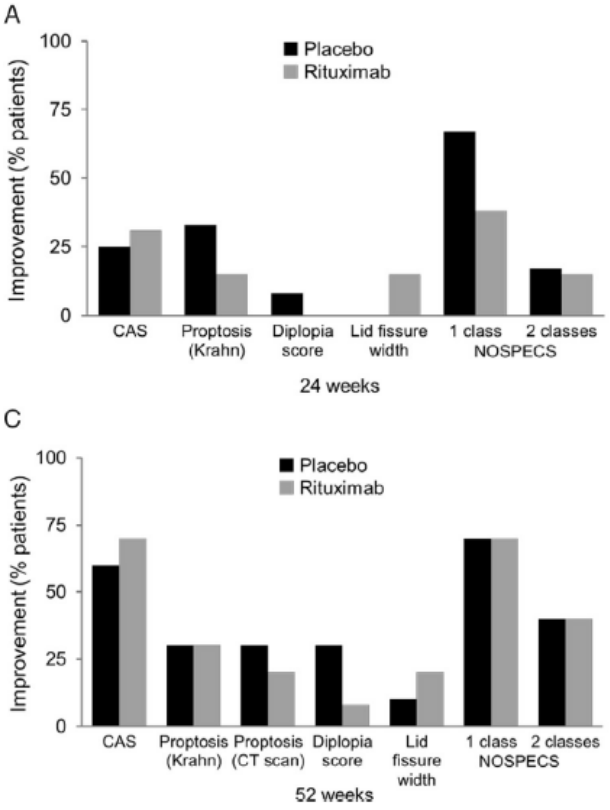


Figure 2. Change in CAS and TRAb levels over the course of the study showing individual patient data for (A) CAS - placebo group; (B) CAS - rituximab-treated group; (C) mean CAS ± SD for each group; and (D) median TRAb levels for each group. Patients who discontinued the trial prior to week 52 were evaluated before discontinuation and those data were carried forward to either 24 weeks (for the 5 patients who discontinued prior to or at week 24) or 52 weeks (for the single patient discontinued from the trial after 24 weeks) as the final evaluation for that patient. There were no significant differences in mean CAS or TRAb levels between the study groups at any time point.



RTX 1g répété 15 jours + tard

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- Durée évolution OB: 299 j (253–595) 9,8 m pour placebo; 373 j (240–1080) 12,2 m pour RTX
  2 placebo et 4 RTX > 2ans
- CAS : 5,3 +/- 1 pour placebo et 4,9 +/- 0,7 pour RTX

- 24/25 patients évolutifs au début de l'étude; 1 RTX stable, mais actif et modérément sévère
- 10 patients (4 RTX et 6 placebo) ont eu GC avec fin > 1,5 mois et tous aggravation à arrêt GC

- score de diplopie subjectif (échelle Gorman)

- Critères exclusion: DON, décompression

- 59 patients éligibles:
  - Propositions: protocole, GC IV, surveillance rapprochée
  - 25 Ok pour protocole
  - Refus: peur des ES, RTX hors protocole
  - Objectif: 30

Efficacy of B-Cell Targeted Therapy With Rituximab in Patients With Active Moderate to Severe Graves' Orbitopathy: A Randomized Controlled Study

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- Durée évolution OB: 4,6 +/- 2,6 mois pour GC; 4,5 +/- 2,9 mois pour RTX
- CAS : 4,7 +/- 0,7 pour GC et 4,4 +/- 0,7 pour RTX

- 32 patients évolutifs au début de l'étude
- 6 patients (3 GC, 3 RTX) ont eu GC avec fin > 3 mois

- score de diplopie subjectif (échelle Gorman): NS + motilité oculaire objective: S
  - 5 non diplopes dans chaque groupe

- 2 décompressions groupe GC: DON, ulcère cornée

- 32patients éligibles:
  - Proposition: protocole
  - 32 Ok pour protocole; 1 refus secondaire bras RTX
  - Objectif: 60, arrêt prématuré car récidives groupe GC et pas de récidive groupe RTX

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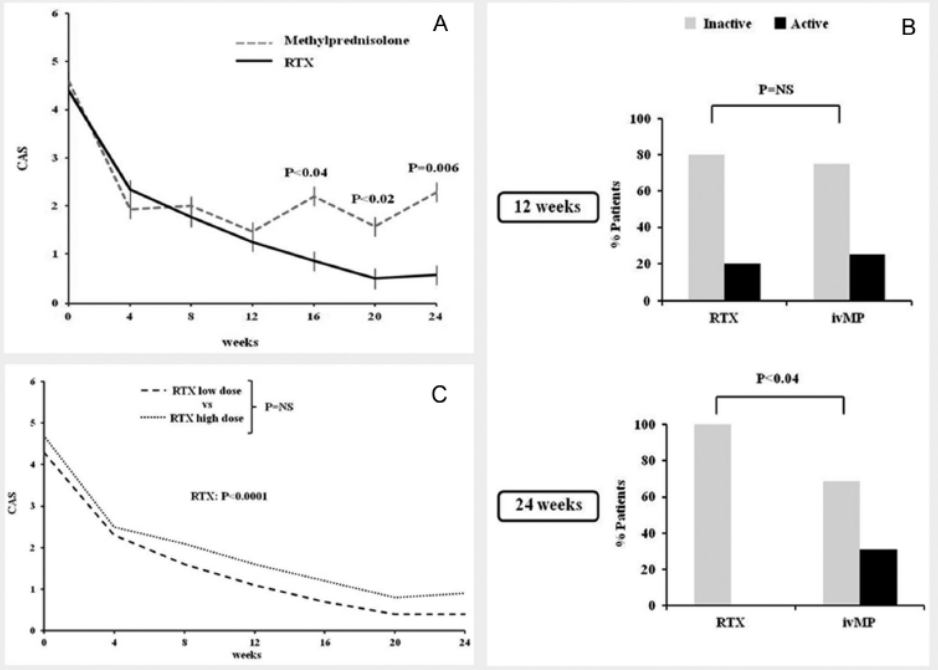
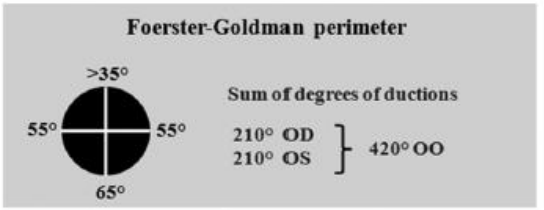


Figure 3. Analysis of the primary end point of the study. A, Changes of the CAS in patients treated with either ivMP or RTX from baseline up to 24 weeks of follow-up (Wilcoxon). B, Outcome of the primary end point of the study after ivMP and RTX at 12 and 24 weeks (Fisher exact test). C, Changes of the CAS after a high dose (2000 mg) of low-dose (500 mg) RTX from baseline up to 24 weeks of follow-up (Mann-Whitney).

RTX 1g répété 15 jours + tard puis 500 mg 1x

A



B

Weeks	0	24	52
IVMP	OD 179.2±8.6 OS 177.3±8.7	OD 178.6±6.7 OS 178.6±7.3	OD 188.2±7.0 OS 192.5±6.8
RTX	OD 187.0±5.8 OS 186.7±6.2	OD 197.3±5.6 OS 191.7±6.5	OD 196.1±5.0 OS 196.4±5.8
P value		OD = 0.019 OS = ns	OD = 0.014 OS = 0.026

Figure 2. Motility assessment in patients with GO after treatment with either ivMP or RTX. A, Calculation of the TMS by assessment of the degrees of ductions by the Foerster-Goldman perimeter. B, Outcome of TMS at 24 and 52 weeks after ivMP and RTX in both the right (OD) and the left (OS) eye (Wilcoxon).

Échelle Gorman NS

Expérience Nantaise du RTX

- RCP pathologies orbitaires depuis 2009
- RTX depuis 2012
- n=10+1 (Étude rétrospective)
  - 6 patients
    - 5R+/6
    - S2 à M6
  - 1 patient: 1 œil puis l'autre
    - 2R+/2
  - 3 en cours

Méthodologie

- 3 formes d'OB
  - Inflammatoire: CAS
  - Musculaire: diplopie/ Lancaster
  - Neuro/compression: AV, CV, FO
- Gluco dépendance/ résistance
  - GD: aggravation à l'arrêt GC
  - GR: aggravation sous GC
  - Protocole GC IV hebdomadaire: 500 mg x6 + 250 mg x6
- IRM orbitaire
  - Inflammation
  - Épaisseur muscles

Résultats

Nom Pr	sexe	âge	Tabac	TT	Forme OB	GD/ GR	Poso RTX	R	DO	RTE
ROB Fa	F	38	+	+	I	GD 4,5 g Récidive M1 4,25 = 8,75g	1gx2	R+ S6		
DEV Sa	F	34	+	+	I N(M3)	GR 5,5g	1gx2	R+ (I) M3	M2	
MOR Ro	F	42	- (6 mois)	+	I M	GR 7,5g	1gx2	R-		M6 +
MOR Ma	F	65	+ Sevrage précoce	+	I M N(M3)	GD (I+M) 7 + 4,5 = 11,5 g GR	1gx2	R+ (I) M4	M-3 OD M-1 OG	
ROU Fl	H	40	+	+	OD:M I(M3) N(M3) OG: I M N (M4)	GR 7g	330 mg + 1g	R+ (I N) M6 OG (VLMB OD)	M-1 et M3 OD	
ROT Sy	F	60	+	-	I M N	GR 2,5g	RTX 1gx2	R+ (I N) S6	M0	
LEP So OG	F	43	+	+	M	GR 7g	RTX 1gx2	R+ S2		
LEP So OD	F	44	+	+	M	GR 4,5g	RTX 1gx2	R+ M3		

Notre proposition

- Travail collaboratif national
  - Français
  - Multi centrique
- Etude rétrospective
  - Critères inclusion: tout patient traité par RTX pour OB en France avec suivi d'au moins 3 mois
  - Observationnelle
    - Qui: 1°/ 2° intention? GR/GD? I/M/N? délai par rapport aux 1° symptômes?
    - Comment?
    - Résultats?
  - Comparaison R+ vs R-
- A terme :
  - Publications et communications
  - Proposition PHRC: étude prospective randomisée de l'efficacité du RITUXIMAB sur une population ciblée en 1° intention vs GC
    - Critère secondaire: évaluation médico économique

TEM Gi	F	69 a	Tabac –	TT?	M I (M1)	GD 7,5 g (I mieux mais M=)	RTX 1g x2	?		
HER An	F	68 a	Tabac?		I M N	GR 2,5g	RTX 1g x2	?	DO (même temps)	
BRU Is	F	45 a	Tabac+		M	GR 4,5 (amélioration) + 3 (stable)	RTX 1g x2	?		