

# CO-MEDICATION WITH STEROIDS IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER BIOLOGIC AGENTS

SOFIA RAMIRO, RAQUEL ROQUE, FILIPE VINAGRE, PEDRO GONÇALVES, ANA  
CORDEIRO, VIVIANA TAVARES, J. CANAS DA SILVA, M. JOSÉ SANTOS

RHEUMATOLOGY DEPARTMENT, HOSPITAL GARCIA DE ORTA,  
ALMADA, PORTUGAL

# Background

- Steroids have an important role in early RA:
  - ▣ Anti-inflammatory and disease-modifying properties<sup>1-6</sup>
  - ▣ EULAR recommendations: steroids provide benefit at low to moderately high doses in addition to DMARDs<sup>1</sup>
- But...important adverse events with corticotherapy<sup>7,8</sup>:
  - ▣ Long-term therapy and cumulative dose
  - ▣ Infections (biologic agents)<sup>9-11</sup>
  - ▣ EULAR recommendations: steroids for initial short-term treatment, but should be tapered as rapidly as clinically feasible<sup>1</sup>
- Timely prescription of DMARDs → ↓ chronic corticotherapy?

<sup>1</sup> Smolen 2010 ARD; <sup>2</sup> van Everdingen 2002 Ann Intern Med; <sup>3</sup> Kirwan 1995 N Engl J Med; <sup>4</sup> van Tuyl 2010 ARD; <sup>5</sup> Jacobs 2006 A&R; <sup>6</sup> Verstappen 2010 ARD; <sup>7</sup> Da Silva 2006 ARD; <sup>8</sup> Hoes 2007 ARD; <sup>9</sup> Salliot 2007 Rheumatology; <sup>10</sup> Greemberg 2010 ARD; <sup>11</sup> Strangfeld 2009 JAMA

# Objectives



1. To evaluate the intake of steroids among patients with RA after starting a biologic DMARD
2. To identify factors associated with therapy with steroids
3. To identify factors associated with the steroids dosage

# Methods

- ❑ Population: patients with RA under biological therapy, followed at Hospital Garcia de Orta, Almada, since 2000, and included in the national registry – Reuma.pt
- ❑ Demographic and clinical data – disease activity, biological therapy, DMARDs, steroids
- ❑ Frequency of steroids intake and dosages in prednisolone equivalents at the onset of biologics and at last visit
- ❑ Comparison between patients with and without corticotherapy at last visit (t-test and  $X^2$ )
- ❑ Identification of factors associated with the current intake of steroids the steroids dosage (logistic and linear regression, respectively, uni- and multivariable)

# Results

- ❑ 123 patients
- ❑ Therapy with steroids:
  - ❑ Onset of first biologic:
    - ✓ 94 patients (76%)
    - ✓ Average dosage:  $6.4 \pm 4.4$  mg/day (prednisolone equivalents)
  - ❑ Last visit:
    - ✓ 66 patients (54%)
    - ✓ Average dosage:  $5.2 \pm 2.0$  mg/day (prednisolone equivalents)
    - ✓ 10 (8%) were on deflazacort, 30 (24%) on prednisolone and 26 (21%) on prednisone
  - ❑ Time period between baseline and last visit:  $4.4 \pm 2.2$  years

# Results – comparison between groups

	Without steroids (n = 57) Mean $\pm$ SD or %	With steroids (n = 66) Mean $\pm$ SD or %	P-value*
Age (years)	56.63 $\pm$ 12.60	57.25 $\pm$ 13.58	0.80
Female gender (%)	87.7	85.0	0.65
BMI (kg/m <sup>2</sup> )	27.64 $\pm$ 5.42	27.71 $\pm$ 5.20	0.94
Disease duration (years)	11.65 $\pm$ 8.13	11.67 $\pm$ 7.89	0.99
<b>DAS28 (4v) – last visit</b>	<b>3.34 <math>\pm</math> 1.09</b>	<b>3.99 <math>\pm</math> 1.27</b>	<b>0.00*</b>
DAS28 (4v) – onset of biologic	5.56 $\pm$ 1.10	5.88 $\pm$ 1.24	0.15
Delta DAS28	2.26 $\pm$ 1.40	1.81 $\pm$ 1.37	0.10
HAQ (0-3)	0.79 $\pm$ 0.81	1.12 $\pm$ 0.55	0.06
Swollen joints (0-28)	1.11 $\pm$ 2.05	1.78 $\pm$ 2.50	0.12
<b>Tender joints (0-28)</b>	<b>2.17 <math>\pm</math> 3.32</b>	<b>3.84 <math>\pm</math> 4.90</b>	<b>0.03*</b>
<b>VAS patient's global evaluation (0-100)</b>	<b>26.57 <math>\pm</math> 20.22</b>	<b>38.23 <math>\pm</math> 20.23</b>	<b>0.00*</b>
<b>VAS pain (0-100)</b>	<b>26.67 <math>\pm</math> 19.20</b>	<b>35.98 <math>\pm</math> 20.05</b>	<b>0.01*</b>
ESR (mm/h)	30.82 $\pm$ 17.62	38.75 $\pm$ 26.35	0.06
<b>Rheumatoid factor positivity(%)</b>	<b>58.9%</b>	<b>72.7%</b>	<b>0.02*</b>
Exposure to biologics (years)	4.66 $\pm$ 2.54	3.95 $\pm$ 3.08	0.17
<b>Duration of last biologic (days)</b>	<b>1178.86 <math>\pm</math> 855.97</b>	<b>826.78 <math>\pm</math> 840.01</b>	<b>0.02*</b>
Total number of biologics	1.61 $\pm$ 0.77	1.80 $\pm$ 1.07	0.26
Number of concomitant DMARDs	1.07 $\pm$ 0.46	1.23 $\pm$ 0.63	0.11
Metotrexato concomitante (%)	87.7%	80.3%	0.27
Concomitant methotrexate dosage (mg/week)	16.20 $\pm$ 3.40	17.55 $\pm$ 3.84	0.06

\* Statistically significant (p < 0.05)

# Results - factors associated with steroids intake

	Univariable analysis OR (CI 95%)	Multivariable analysis adjusted for age and gender OR (CI 95%)
<b>Patient's global assessment (0-100)</b>	<b>1.03 (1.01 ; 1.05)</b>	<b>1.04 (1.02 – 1.07)</b>
<b>Concomitant methotrexate dosage (mg/week)</b>	<b>1.11 (0.99 – 1.24)</b>	<b>1.14 (1.00 - 1.30)</b>
Gender (female vs male)	0.78 (0.28 – 2.21)	0.76 (0.18 – 3.12)
Age (years)	1.00 (0.98 – 1.03)	0.99 (0.97 – 1.03)
Tender joints (0-28)	1.11 (1.00 ; 1.23)	¥
Duration of last biologic (days)	0.99 (0.99 – 0.99)	¥
DAS28	1.61 (1.14; 2.27)	**
VAS pain (0-100)	1.03 (1.00-1.05)	¥
HAQ (0-3)	2.04 (0.98 – 4.25)	¥
ESR (mm/h)	1.02 (1.00 – 1.03)	¥
Exposure to biologics (years)	0.92 (0.81 – 1.04)	¥
Number of concomitant DMARDs	1.69 (0.87 – 3.31)	¥
Swollen joints (0-28)	1.14 (0.96 – 1.36)	¥

OR – odds ratio; CI – confidence interval; \*\* variable not included in the multivariable analysis, due to the inclusion of the individual components; ¥ variables that were not selected during multivariable regression analysis ( $p \geq 0.05$ )

# Results - factors associated with steroids dosage

	Univariable analysis $\beta$ (CI 95%)	Multivariable analysis adjusted for age and gender $\beta$ (CI 95%)
<b>Duration of last biologic (days)</b>	<b>-0.00 (-0.00 ; 0.00)</b>	<b>-0.00 (-0.00; -0.00)</b>
<b>BMI (kg/m<sup>2</sup>)</b>	<b>0.08 (-0.02 ; 0.17)</b>	<b>0.11 (0.01; 0.20)</b>
<b>Disease duration (years)</b>	<b>0.06 (0.00 ; 0.12)</b>	<b>0.11 (0.05; 0.18)</b>
Gender (female vs male)	0.27 (-1.08 ; 1.61)	-1.00 (-2.42; 0.42)
Age (years)	-0.02 (-0.05 ; 0.02)	-0.02 (-0.06; 0.02)
HAQ (0-3)	0.86 (-0.25 ; 1.96)	¥
Total number of biologics	0.41 (-0.03 ; 0.85)	¥
Rheumatoid factor positivity	-0.77 (-1.57 ; 0.03)	¥

¥ variables that were not selected during multivariable regression analysis ( $p \geq 0.05$ )



# Conclusions

- With the introduction of biologic agents, 20% of the patients stopped steroids and the others had its dosage reduced.
- Still, half of the patients were maintained on steroids.
- Higher dosage of MTX and a worse patient's global assessment were associated to a higher chance of intake of steroids
- A higher retention on the current biologic was associated with a lower dosage of steroids, while higher disease duration and BMI were associated with a higher dosage of steroids
- A stricter inflammatory control is warranted in order to enable the reduction of chronic and prolonged corticotherapy.

World Congress on Debates & Consensus in Bone, Muscle & Joint Diseases  
Barcelona, 19-22 January 2012