ABSTRACT NUMBER: 701

In Patients with Ankylosing Spondylitis Treated with Adalimumab, Combination Therapy with DMARD, Increase the Serum Level of Adalimumab and Decrease Immunogenicity

José Rosas[1], Francisca Llinares-Tello[2], José Miguel Senabre-Gallego[1], Mariana Marco-Mingot[3], Ana Pons[1], Xavier Barber[4], Gregorio Santos-Soler[1], Esteban Salas-Heredia[1], Catalina Cano[1], Juan Molina[3], Marina Sanchís[4], Mario García-Carrasco[5] and AIRE-MB Group, [1]Rheumatology, Hospital Marina Baixa, Villajoyosa (Alicante), Spain, [2]Laboratory, Hospital Marina Baixa, Villajoyosa, Spain, [3]Laboratory, Hospital Marina Baixa, Villajoyosa (Alicante), Spain, [4]CIO, Universidad Miguel Hernández, Elche, Spain, [5]Systemic Autoimmune Diseases Research Unit, HGR 36-CIBIOR Instituto Mexicano del Seguro Social, Puebla, Mexico

Meeting: 2016 ACR/ARHP Annual Meeting

Date of first publication: September 28, 2016

Keywords: Adalimumab, Ankylosing spondylitis (AS) and anti-TNF therapy, DMARDs

SESSION INFORMATION

Date: Sunday, November 13, 2016

Session Title: Spondylarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment - Poster I: Axial and Peripheral Spondyloarthritis – Clinical Aspects, Imaging and Treatment

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose: In patients with rheumatoid arthritis, methotrexate (MTX), improves the clinical efficacy of anti-TNF (TNFi), among other reasons, for reducing the immunogenicity. However, there are doubts of their benefit in patients with ankylosing spondylitis (AS) The purpuse of this study is to evaluate the influence of combined treatment with DMARD in clinical efficacy in patients with AS treated with adalimumab (ADL).

Methods: Prospective, observational study was done in 62 consecutive patients diagnosed with axial AS, treated with ADL, receiving DMARD, according to clinical practice, at the discretion of the rheumatologist. Epidemiological patient data (age, gender, body mass index), type of concomitant DMARD, EA characteristics (time of evolution of disease, presence of psoriasis or inflammatory bowel disease, HLA-B27), were collected, and information of ADL, too (order of introduction of TNFi treatment and time, and presence of serum anti-ADL antibodies). Clinical response was assessed using the Spanish version of BASDAI and ASDAS-ESR index. Serum concentrations of free ADL (trough level) and anti-ADL antibodies (Ab), were measured using Promonitor-ADL and Promonitor Anti-ADL Ab ELISA kits (Progenika Grifols SA, Spain), as standardised conditions, specified by the manufacturer, cut-off value were >0.024 mg/L for the serum levels of ADL and >3.5 AU/mL for positive anti-ADL Ab. The anti-ADL Ab and ADL serum level were determined by ELISA (Progenika, Grifols SA, Spain). Cut-off level for ADL were <0.004 mg/L and anti-ADL Ab >3.5 AU/mL. Samples was obtained just before subcutaneous (s.c.) injection of ADL (trough level) and was stored at -80 °C until analysis.

Results: Of the 62 patients with axial involvement included, 31 (50%) were women, with a mean age of 46±10.years and a mean BMI of 27.47±4.49. The average time of evolution of the AS was 9.5±9.25 years. HLA-B27 was positive in 74%. DMARD was combined to ADL in 14 (23%) patients (methotrexate: 10, sulfasalazine: 3 and azathioprine 1 patient). In 47 (76%) patients, they were not associated with another extraskeletal manifestation of AS, but 12 (19%) patients had AS associated with inflammatory bowel disease and 3 (5%) patients, with psoriasis. ADL was the first TNFi in 66% of patients. The average duration of treatment with ADL was 1.33±1.44 years (median: 1 year). The average serum level of ADL was 8.62±8.59. In 19 (31%) patients were detected anti-ADL Ab, all of them (100%), in the group of patients not receiving DMARD. When comparing the group of patients treated with ADL combined with DMARD and those without (Table 1), the group treated without DMARD only presented significantly the presence of anti-ADL Ab (40% vs 0%; p <0.0001) and trend to lower serum level ADL (10.82±02.05 mg/L vs 7.59±5.5 mg/L; p=0.064). The group with anti-ADL Ab versus those without anti-ADL Ab, showed levels of ADL almost undetectable (mean: 0.082±0.16 vs 10.32±4.49; p <0.0001) and significant loss of clinical efficacy by BASDAI and ASDAS: mean: 5.53±2.0 vs 3.59±2.0 (p <0.0001) and 3.2±2.1 vs 1.92±0.74 (p = 0.038), respectively.

	DMARD Yes (n: 14/23%)	**DMARD No (n: 48/77%)**	**p**
ADL monitoring, n (%)	34 (31)	79 (69)	
Age (years): mean (SD) Median	48,07 (10.80) 48.5	46.13 (10.75) 45.0	0.56
Male, n (%)	8 (57)	23 (49%)	0.69
BMI (kg/m^2): mean (SD) Median	28.12 (3.89) 28.16	27.18 (4.73) 27.51	0.46
Time of disease evolution (years): mean (SD) Median	7.45 (7.09) 6,25	10.46 (9.87) 5.33	0.22
HLA B27 positive, n (%)	10 (71)	36 (77)	0.69
ADL order of treatment, n (%): First TNFi Second TNFi Third TNFi	8 (57) 4 (29) 2 (14)	33 (70) 14 (26) 3 (4)	0.48 0.90 0.68
Time (years) on ADL: mean (SD) Median	1.67 (1.57) 1.0	1.36 (1.27) 0.91	0.51
ADL serum level, mg/L: mean (SD) mediana	10.82 (5.16) 11.25	7.59 (5.5) 8.34	**0.064**
anti-ADL Ab, AU/L, n (%):	0 (0)	19 (40)	**0.0001**

BASDAI: mean (SD) Median	4.09 (2.14) 4.1	3.98 (2.20) 4.05	0.86
BASFI: mean (SD) Median	3.67 (2.0) 4.05	3.87 (2.40) 3.90	0.75
ASDAS: mean (SD) Median	2.09 (0.62) 2	2.23 (1.40) 2.1	0.60

Conclusion: 1) The prevalence of anti-ADL Ab in AS is 31%. 2) In our cohort, 100% of patients with AS who have immunogenicity, were been treated with ADL in monotherapy. 3) Patients with anti-ADL Ab has ADL levels almost undetectable and loss of efficacy. **Funding**: The study was supported by a research grant from the Spanish Foundation of Rheumatology (2012) and the Association for Research in Rheumatology of Marina Baixa (AIR-MB). Conclusion:

Disclosure: J. Rosas, None; **F. Llinares-Tello**, None; **J. M. Senabre-Gallego**, None; **M. Marco-Mingot**, None; **A. Pons**, None; **X. Barber**, None; **G. Santos-Soler**, None; **E. Salas-Heredia**, None; **C. Cano**, None; **J. Molina**, None; **M. Sanchís**, None; **M. García-Carrasco**, None.

To cite this abstract in AMA style:

Rosas J, Llinares-Tello F, Senabre-Gallego JM, Marco-Mingot M, Pons A, Barber X, Santos-Soler G, Salas-Heredia E, Cano C, Molina J, Sanchís M, García-Carrasco M. In Patients with Ankylosing Spondylitis Treated with Adalimumab, Combination Therapy with DMARD, Increase the Serum Level of Adalimumab and Decrease Immunogenicity [abstract]. *Arthritis Rheumatol.* 2016; 68 (suppl 10). http://acrabstracts.org/abstract/in-patients-with-ankylosing-spondylitis-treated-with-adalimumab-combination-therapy-with-dmard-increase-the-serum-level-of-adalimumab-and-decrease-immunogenicity/. Accessed November 8, 2016.

ACR Meeting Abstracts - http://acrabstracts.org/abstract/in-patients-with-ankylosing-spondylitis-treated-with-adalimumab-combination-therapy-with-dmard-increase-the-serum-level-of-adalimumab-and-decrease-immunogenicity/