Figure 1

Disclosure of Interests: None declared

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FRI0041 INCIDENCE AND TREND OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN. (TREND-AR STUDY)

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Background: Treatment with biological agents is recognized as a potential risk factor for the development of Progressive Multifocal Leukoencephalopathy (PML), a rare and often fatal demyelinating disease of the CNS caused by John Cunningham Virus infection.

Objectives: Analyze the incidence and trend of hospital admissions for PML in patients with RA, in Spain, during the period between 1999 and 2015.

Methods: Population study based on the analysis of a national administrative database that includes a Minimum Basic Data Set (MBDS) of the income of patients with RA (ICD 9 714). Period: January 1, 1999, to December 31, 2015. The cases of PML were identified due to the presence in the primary and secondary diagnosis of the codes ICD 9 046.0 to 046.9. The population at risk was estimated through the population census of the National Institute of Statistics, with an estimated prevalence

of RA of 0.5% in both sexes (0.2% in men and 0.8% in women). Crude and adjusted rates were calculated at national level. The trend was analyzed using Generalized Linear Models (MLG) using the variable year as the analysis variable.

Results: Of the total of 338,343 hospital admissions in patients with RA during the 17 years of the study period, only 14 cases (0.004%) of PML were recorded, nine (64.3%) were women and 5 (35.7%) men. The mean age was 69.5 years (SD 16.8); 74.56 (SD14.8) in women and 60 (SD18.1) in men (p = 0.145). Five patients (35.7%) died during admission (2 women and 3 men) (p = 0.266). The average of the Charlson index was 2.21 (SD 1.7); 3 (SD 2.5) in women and 1.78 (SD 1.1) in men (p = 0.227).

The crude incidence rate of PML was 0.54/100,000 inhabitants * year, 0.85/100,000 inhabitants * year in men and 0.37/100,000 inhabitants * year in women. The Relative Risk male: female was 2.34. The gross rate of PML increased from 0.32/105 * year in the period 1999-2002, to 0.74 between 2011 and 2015, both in women (from 0.19 in the period 1999-2002 to 0.52 from 2011 to 2015) as well as men (from 0.82 in the period 1999-2002 to 1.64 during 2011-2015). It is estimated that this increase is of 19.7% per year.

Conclusion: In Spain, between 1999 and 2015, there has been an increase in the incidence rate of PML in patients with RA. We estimate an annual increase of 19.7%.

Disclosure of Interests: None declared

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FRI0042 CERTOLIZUMAB PEGOL EFFECTIVENESS IN WOMEN OF CHILDBEARING AGE WITH RHEUMATOID ARTHRITIS: RETROSPECTIVE ANALYSIS OF AN INTERNATIONAL MULTICENTRE COHORT

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Background: Even though certolizumab pegol (CZP) has been licensed for the treatment of rheumatoid arthritis (RA) a long time ago, observational data in real-life settings are still lacking. Moreover, recent data on the lack of transplacental passage (1) make CZP particularly appealing for the treatment of RA women with a desire of pregnancy.

Objectives: To evaluate in a real-life international cohort the frequency of use, the clinical response, and the retention rate of CZP in RA women of childbearing age.

Methods: Data were retrospectively extracted from the Italian LORHEN and the Romanian Registry of Rheumatic Diseases (RRBR) registries, which include all RA patients treated with CZP between December 2010 and October 2018. The analysis was limited to women who received CZP as first-line biologic agent. The study population was stratified according to childbearing age (18-49 versus >49 years). The 6-, 12- and 24-month clinical response was evaluated as the proportion of patients achieving Disease Activity Score 28 (DAS28) remission and compared between the subgroups by a chi-squared test. The 5-year retention rate was calculated by the Kaplan-Meier method and compared between the subgroups by log-rank test.

Results: The whole cohort included 630 RA patients treated with CZP. According to the inclusion criteria, the study population consisted of 308 female RA patients (mean [± standard deviation, SD] age 54.2±12.1 years; mean disease duration 8.7±8.4 years; baseline DAS28 5.25±1.72, positive anti-citrullinated peptide antibody 161/254 [63.4%], positive rheumatoid factor 213/297 [71.7%]). Apart from mean age (39.6±6.6 vs 60.8±7.2, respectively; p<0.001), no other significant differences in baseline characteristics between the childbearing (n=97, 31.5%) and non-childbearing age (n=211, 68.5%) groups were observed. In the overall population, DAS28 remission was achieved by 29.9%, 42.1%, and 39.7% of patients at 6, 12, and 24 months, respectively. This proportion was significantly higher in childbearing compared with non-childbearing women at each timepoint (39.4% vs 25.4, p=0.02 at 6 months; 52.8% vs 37%, p=0.014 at 12 months; 52% vs 34.2%, p=0.014 at 24 months). The overall 5-year retention rate was 37.1%, with a higher (but not statistically significant) persistence in the childbearing versus non-childbearing subgroup (55.1%

vs 33.4%, $p=0.177$). In the whole cohort the most frequent reason for withdrawal was inefficacy (60.9%), whereas only 10.9% of patients discontinued the drug because of adverse events.

Conclusion: In our real-life data, CZP showed a high remission rate with a good safety profile and high persistence on treatment over 5 years. These findings were even more favorable during the childbearing age, supporting the use of CZP in RA women with a desire for pregnancy.

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FRI0043

CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS ADMITTED TO AN INTENSIVE CARE UNIT IN SPAIN SINCE 2005–2015. TREND-AR STUDY

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Objectives: To analyse the clinical features of patients with Rheumatoid Arthritis (RA) that were admitted to an Intensive Care Unit (ICU) from January 2005 to December 2015.

Methods: A retrospective observational populational study was conducted analysing the national database that includes the Minimum Basic Data Sets (MBDSs) of admissions of RA patients to an ICU during the 2005–2015 period. Demographic characteristics, length of stay, clinical course, outcome and the MBDS codes for the main reason of admission were recorded. The cases were detected by the presence of their CIE-9 codes in the primary or secondary diagnoses. Statistical analysis was performed with Stata 15.0 software.

Results: During the 11 years of the study, a total of 2719 RA patients required 2806 admissions to an ICU. Average age was 69.7 ± 10.8 years and women constituted 58.5% of the cases. 30% of the patients admitted to an ICU had required ≥ 3 previous admissions and 11% required readmission within the next 30 days. Average Charlson index was 2.33 ± 1.4 . Average length of stay was 9.3 ± 14 days and 64.2% died in the ICU during hospitalization. The main causes of hospitalization were cardiovascular events (45.7%), lung diseases (16%) and infections (10%). In the univariate analysis mortality was significantly increased in patients presenting infections (90%), lung disease (89%), severe hepatopathy defined by ascites and/or encephalopathy and/or gastrointestinal bleeding (88%), nephropathy/kidney disease (73%) and a higher Charlson index (2.4 vs 2.2). Multivariate analysis showed that mortality was increased among patients presenting respiratory complications and infections.

Conclusion: The most frequent hospitalization causes for patients with Rheumatoid Arthritis in Spain between 2005 and 2015 were cardiovascular, pulmonary and infectious diseases. RA patients that were admitted to the ICU showed an increased mortality. This increased mortality was mainly found in patients presenting respiratory or infectious conditions.

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FRI0044

RISK FACTORS FOR CORONARY ARTERY ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease leading to significant increase in cardiovascular morbidity and mortality. Development of coronary artery diseases (CAD) in RA patients (pts) is associated with the accumulation of traditional risk factors and immunological disorders. Coronary angiography (CAG) is the gold standard to identify coronary artery atherosclerosis (CAA).

Objectives: To identify CAA predictors and determine CAA detection rates in RA pts with suspected CAD.

Methods: Examination of 77 RA pts with suspected CAD, male/female 28/48, mean age 59 [53;64] years, with a long history of the disease (10[6;20] years), who were seropositive for IgM rheumatoid factor (RF) (82%) and anti-cyclic citrullinated peptide (ACCP) (58%), with moderate to high clinical disease activity DAS 28 4.2[3.2;5.3]. CAG was performed in all pts. CAA risk factors in RA pts were identified by the multiple linear stepwise regression analysis.

Results: Out of 77 RA pts CAA was detected in 52 (68%) (male/female 25/27 (group I)), while intact coronary arteries (CA) were found in 25 (32%) (male/female 3/22 (group II)) pts. Both groups were comparable in terms of age, disease duration and RA activity (DAS 28 score). Males prevailed in Group I: 48% vs 3% in Group II ($p<0.05$). Group I pts included more smokers than Group II (44% vs 8%, $p<0.05$). Other traditional risk factors were equally represented in both groups: arterial hypertension - 87% and 84%, dyslipidemia - 75% and 64%, diabetes mellitus - 15% and 8%, physical inactivity - 58% and 42%, obesity - 29% and 28% pts in Groups I and II, respectively. Serum HDL cholesterol (HDL-C) concentrations were lower (1.3[1.0;1.4] mmol/l) and triglyceride (1.5[1.1;2.0] mmol/l) levels were higher in Group I vs Group II (1.6[1.2;1.9] and 1.2[0.9;1.5] mmol/l), $p<0.01$. Concentration of total cholesterol and LDL-C were similar in pts from both Groups. Both Groups showed similar atherosclerotic plaques detection rates in carotid arteries (19/12%). Variety of administered drugs (disease-modifying antirheumatic drugs, biological drugs and oral glucocorticoids) and therapeutic regimens were also comparable in Groups I and II. Multiple linear regression analysis indicates close association of CAA with pts' age (unstandardized coefficient $B=0.017$, 95% confidence interval (95% CI) [0.004-0.030], $p=0.011$), smoking ($B=0.246$, 95% CI [0.055-0.437], $p=0.013$), HDL-C ($B=-0.325$, 95% CI [-0.557-(-0.095)], $p=0.0073$), atherosclerotic plaques in carotid arteries ($B=0.549$, 95% CI [0.120-0.901], $p=0.003$) and ACCP ($B=0.309$, 95% CI [0.028-0.589], $p=0.03$), coefficient of multiple determination (R^2) = 0.6. Subsequent ROC analysis confirmed the diagnostic value of HDL-C and CAA in RA pts. HDL-C levels below 1.32 mmol/l can be considered as a prognostic factor of CAA presence in RA pts with 68% sensitivity and 65% specificity (area under the curve is 0.711; 95% CI 0.580-0.842; $p=0.04$).

Table 1. Values of analyzed parameters predictive of CAA according to the multiple linear stepwise regression analysis.

Variable	Unstandardized coefficient			P
	B	- 95% CI	- 95% CI	
Age	0,017	0,004	0,030	0,011
Smoking	0,246	0,055	0,437	0,013
HDL-C	-0,325	-0,557	-0,095	0,007
Carotid artery plaques	0,549	0,120	0,901	0,003
ACCP-positivity	0,309	0,028	0,589	0,03

CI – confidence interval

Conclusion: Male gender, low HDL-C levels, plaques in carotid arteries, and ACCP-positivity are associated with increased CAA risk in RA pts. Low HDL-C level can be considered as CAA predictor in RA pts.

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