Background: Fibromyalgia (FM) is characterized by debilitating pain that is unresponsive to standard analgesics and the multi-modal approach, including drugs' combination, represents the standard of care. Combination therapeutic strategies also include the integration of drugs and nutraceuticals. Both palmitoylthetanoamide (PEA) and acetyl-L-carnitine (ALC) have demonstrated an effect on chronic widespread pain (CWP).

Objectives: The aim of this study was to evaluate the efficacy of pregabalin (PGB) and duloxetine (DLX) supplemented with palmitoylthetanoamide (PEA) and acetyl-L-carnitine (ALC) in FM patients over a 24-week period.

Methods: After 6 months of stable treatment with DLX+PGB, FM patients were randomized to continue the treatment (Group 1) or to add PEA (600 mg BID)+ALC (500 mg BID) at the ongoing treatment (Group 2). Patients were then followed for 24 weeks. Cumulative disease severity, evaluated using the Widespread Pain Index (WPI), was the primary outcome, the revised Fibromyalgia Impact Questionnaire (FIQR), and the modified Fibromyalgia Assessment Status (FASmod) (second-order outcomes), was calculated every two weeks during the 24-week follow-up and expressed as time-integrated values (AUC).

Results: One hundred and forty-two FM patients started the study (91.5%), 130 completed both steps, respectively 68 patients in Group 1 and 62 in Group 2. After 24 weeks of follow-up after randomization, Group 2 experienced an adjunctive significant improvement in WPI, FIQR (Figure 1), and FASmod, compared to Group 1. Although there was some fluctuation in both Groups throughout the study period, the AUC values of the WPI scores steadily decreased in Group 2 (p=0.048). Group 2 showed better outcomes also in terms of FIQR and FASmod scores' AUC values (p=0.033 and p=0.017, respectively).

Conclusion: This study supports the supplementary value of PEA+ALC in FM patients care and, to best of our knowledge, it is the first study investigating this association treatment.


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All about COVID-19 in Rheumatology

POS0266 CELLULAR IMMUNE RESPONSE PERSISTENCE AFTER COVID-19 MRNA VACCINES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS UNDER RITUXIMAB

Keywords: Rheumatoid arthritis, Vaccination/Immunization, COVID

J. Marin1, P. Bourjoin2, N. Saverna2, C. Cartagena Garcia2, P. Laforgue3, J. Rouzier4, J. M. Busnelli5, N. Balandraud1,3,3 Sainte Marguerite University Hospital: AP-HM, Rheumatology, Marseille, France; 1Immunotech - Beckman Coulter, Global Research Organization, Marseille, France; 2Inserm and Aix Marseille University; UMRS - 1097: Arthrites Autoimmunes, Marseille, France

Background: Humoral response induced by anti-SARS-CoV-2 mRNA vaccine is significantly lower or even absent in patients with inflammatory rheumatic diseases treated with anti-CD20 therapies such as Rituximab (RTX) than in those treated with cytokine therapies (e.g., anti-TNF or anti-IL6) [1]. However, a specific cellular immune response exists 1 or 2 months after vaccination (2, 3). As medications are widely utilized for treatment of non-cancer chronic pain. Among these, pregabalin is a commonly prescribed anticonvulsant, which works by antagonizing L-type calcium channels, decreasing the release of neurotransmitters [2]. Pregabalin use has been associated with reports of congestive heart failure (CHF), including peripheral and pulmonary edema[2,4]. However, the relationship between CHF incidence and pregabalin use among patients at the highest risk of adverse reactions (i.e., senior patients with various co-morbidities) remains unclear.

Objectives: To compare incident CHF among new users of pregabalin versus gabapentin (the active comparator) in Medicare beneficiaries treated for non-cancer chronic pain.

Methods: This was a retrospective cohort study among Medicare beneficiaries aged 65-89 years old with chronic non-cancer pain, without prior history of CHF. We included patients who were newly prescribed users of pregabalin or gabapentin were followed up between 2015-2018. The outcome was incident CHF, ascertained by hospital admissions or emergency room visits with ICD-9 codes and ICD-10 codes in the first position codes. Inverse probability of treatment weighting was used to account for differences between pregabalin and gabapentin users in time-dependent analysis (i.e., Cox proportional-hazards regressions). Covariates used in the propensity scoring were selected based on prior knowledge and literature review, and included categories such as concurrent baseline cardiovascular, neurologic, pain, and psychiatric diagnoses and corresponding medications including opioids and antipsychotics. Non-diagnostic covariates were included, as well as demographics, socioeconomic status, and indicators/metrics of health care utilization.

Results: This study included 17,756 new users of pregabalin and 221,053 new users of gabapentin. The cohort was predominantly female gender (66.7%), and non-Hispanic White (79.9%), with a median age of 73 (IQR: 69-78) years. The most common diagnostic indications for pregabalin and gabapentin were musculoskeletal and back pain. Prior to inverse probability weighting, pregabalin vs gabapentin users had higher daily short-acting opioid morphine equivalent doses (median: 18.0 vs 8.9 mg/d), higher frequency of coxibs (8.6% vs 4.9%), and higher prevalence of diabetic neuropathy (15.9% vs 11.3%) and fibromyalgia (19.9% vs 13.2%). After propensity score weighting, none of the covariates had a standardized difference>=0.10. During 110,439 person-years of follow-up, 1,428 patients developed new CHF. The outcome rate for CHF incidence was 18.67 per 1,000 person-year for pregabalin vs 12.57 per 1,000 person years for gabapentin (adjusted HR 1.48 [95% CI, 1.20-1.81]).

Conclusion: In this retrospective study of Medicare beneficiaries aged 65-89 years with chronic non-cancer pain, new users of pregabalin had higher rates of incident CHF hospitalizations or emergency room visits compared to new users of gabapentin.


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cytotoxic T cells are considered as essential components of the antiviral defense arsenal, and since it is not clear when to do booster shots, analysis of the specific T response over the long term could be a useful decision-making tool.

**Objectives:** This study aims to compare the spike-specific T lymphocytes response in a cohort of Rheumatoid Arthritis (RA) patients under RTX or other therapies (csDMARDs), anti-TNF. Our secondary goal was to assess the retention of this response up to 18 months after the last COVID boost (vaccine or infection).

**Methods:** Patients. Our study cohort included 75 consecutive adult patients with ACPA positive RA, followed at the rheumatology department of Sainte Marguerite Hospital (Marseille, France), prospectively enrolled from April 2022 to October 2022. RA patients fulfilled the 2010 ACR/EULAR criteria for RA and had received at least two doses of SARS-COV-2 mRNA vaccine, whether they had or not a history of COVID.

**Samples.** Heparin-anticoagulated single blood sample was collected for each patient to assess CD19+ cell count, IgG level, and SARS-COV-2 serology. Cellular immune response was assessed by flow cytometry with a previously described procedure [4]. Briefly, 250 µL of whole blood were incubated per condition, including a negative control, Spike peptides from JPT* collection and CEFX peptides (mix of viral peptides) as a positive control. Marker expression was measured with a three-laser 13-color CytoFLEX flow cytometer. T lymphocytes were divided into T4 lymphocytes (LT4) or T8 lymphocytes (LT8) depending on CD8 expression. Finally, CD69, CD154, CD137 and CD107a expressions were monitored to characterize LT4 or LT8 activation.

**Ethics.** All patients gave informed written consent for this study in accordance with Helsinki declaration. Patient data were pseudo-anonymized. Sample collection was approved by the national ethics committee under the number DC-2008-327.

**Results:** Patient characteristics: 51 RA patients were treated with RTX, 24 were treated with csDMARDs or other bDMARDs.

**Humoral response against SARS CoV2:** 30/51 (59%) RA RTX patients versus 13/14 (93%) non RTX patients had a humoral immune response (p = 0.024) with a median titer of 130 BAU/mL versus 688 BAU/mL.

**T cell specific response:** LT4 and LT8 Spike-specific responses were defined by the difference of response between Spike peptides from SARS CoV2 stimulation and no peptides stimulation. The response was divided into quartiles; patients in the upper 3 quartiles were considered to have a specific response. In RA RTX patients, specific LT8 response was shown in 90% of patients versus 42% in non RTX patients (p < 0.0001), and specific LT4 response was shown in 76% of patients versus 75% in non RTX patients (p = 0.42).

**Long term T cell specific response** (Figure 1). RA patients treated with RTX maintained a specific LT4 and LT8 response against Spike peptides with no decrease up to 18 months after the last SARS-COV-2 boost (vaccine dose or COVID 19 infection).

**Conclusion:** Specific LT4 response against Spike peptides was similar in the RTX treated and non-treated RA patients. This was even stronger for the specific LT8 response. The Spike specific T-cell response was maintained in both groups up to 18 months after the last vaccine dose or COVID infection independently to the specific humoral response. This method of analyzing the specific T response against the Spike protein could be used in personalized medicine to decide when revaccination is necessary in a given patient.

**REFERENCES:**


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