THE EFFECT OF DIMETHYL FUMARATE ON IMMUNE PHENOTYPES

Myles Lewis1,3

CD20low, CD38 -) and plasmablasts (PBs) (CD27 +, CD20 low, CD38 +).

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Disclosure of Interests: Luigi Vanvitelli: None declared, Jing yao Leong: None declared, Sotiria Manou-Stathopoulou: None declared, Katriona Goldmann: None declared, Debasish Pyne: None declared, Francesco Ciccia: None declared, Costantino Pitizals: None declared.

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Background: The pathogenesis of large vessel vasculitis (LVV) such as Takayasu arteritis (TAK) and giant cell arteritis (GCA) consists of the immune abnormalities including the interaction between vascular dendritic cells, macrophages and T cells. It is reported that genetic polymorphisms in the immune-modulating cytokine genes such as IL6 and IL12B are associated with LVV. However, little is known about pathological immune cell subsets targeted by immunosuppressants and/or molecular-target therapy such as IL-6 blockade.

Objectives: The aim of this study was to assess the relationship between the phenotype of peripheral immune cells with clinical manifestations and responsiveness to the treatment in patients with LVV.

Methods: Peripheral blood mononuclear cells were obtained from 22 patients with active LVV (TAK 7, GCA 15) and 19 healthy donors (HD). All patients were treated with high dose glucocorticoid (GC). The study included the patients treated with immunosuppressive agents such as azathioprine and methotrexate (n=8) or with anti-IL-6 receptor antibody tocilizumab (n=7).

Results: The proportion of CD3+CD4+CCR6+HLA-DR+ activated Th17 cells and CD3+CD4+CXCR5+ICOS+CD38+ activated Tfh cells in patients with TAK and that of activated Th17 cells and CD3+CD4+CD27+CD122+ Treg cells in patients with GCA. The frequency of activated Th17 cells showed positive correlation and that of CD4+CCR4+CD25+CD127+ T regulatory (Treg) cells showed negative correlation with disease activity scores such as Indian Takayasu Activity Index (ITAS)2010 (2) and ITAS.A (CRP) in both TAK and GCA. The immunosuppressive therapy improved the disease activity in all patients. The frequency of activated Th17 cells was reduced by 24-week treatment with high dose GC and immunosuppressants in TAK and GCA. However, the frequency of Th17 cells was not changed by those treatments. Of note, tocilizumab decreased the proportion of activated Th17 cells and increased the proportion of Treg cells in both TAK and GCA.

Conclusion: The results indicated that the abnormal T cell differentiation correlated with disease activity of LVV. Although T cell activation was improved, Th17 cell activation was not changed by the conventional immunosuppressive agents. By contrast, tocilizumab reduced Th17 cells and increased Treg cells, indicating that IL-6 blockade may correct the impaired balance of Th17 and Treg cells in patients with LVV.
REFERENCE


CIRCULATING CD3+CD31+CXCR4+ T CELLS IN RHEUMATOID ARTHRITIS PATIENTS: CORRELATION WITH RETINAL MICROCIRCULATORY DAMAGE AND POTENTIAL EFFECT OF ABATACTErapy

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Background: T-cells play a role in pathogenesis of rheumatoid arthritis and in its cardiovascular (CV) comorbidities [1]. CD3+CD31+CXCR4+ T-cells may be involved in damaged endothelium repair [2]. The percentage of these cells in the peripheral blood was reported to be lower in RA than in healthy controls, as an effect of disease activity rather than of traditional CV risk factors [3]. Abatacept (ABA), a T-cell co-stimulation blocker, is approved for the treatment of RA. In addition to its effect on disease activity, it may have a CV protective action [4].

Objectives: To evaluate CD3+CD31+CXCR4+ T-cells in a cohort of RA patients in correlation with disease activity, CV parameters, and the potential effect of ABA therapy.

Methods: Thirty-one RA patients (median [IQR] 70.0-62.0 years, baseline C-reactive protein (CRP)-DAS28=43.5), body mass index (BMI)=21.7-28.6 kg/m2, rheumatoid factor (RF) positive 55%, anti-citrullinated peptide antibody negative (ACPA) positive 78%, were enrolled. Thirteen patients were evaluated before and after 6 months of ABA therapy. Among them, in 5 patients without known CV risk factors (history of arterial hypertension, diabetes, hypercholesterolemia, previous CV events and smoking), a morphological evaluation of retinal arterioles was performed by adaptive optics, a validated technique quantifying microvascular damage, and a possible beneficial effect of ABA on the microcirculation in RA patients.

REFERENCE


Acknowledgement: Bristol-Myers-Squibb Italy provided an unrestricted research grant for the study conduct.

Disclosure of Interests: Silvia Piantoni: None declared, Francesca Regola: None declared, Stefano Caletti: None declared, Rajesh Kumar: None declared, Cecilia Nalli: None declared, Chiara Bazzani: None declared, Claudia Rossini: None declared, Damiano Rizzoni: None declared, Angela Tincani: None declared, Paolo Airò: None declared, Carolina De Ciucies: None declared, Damiano Rizzoni: None declared, Angelo Tinacci: Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lilly, Janssen, Cellgenie, Novartis, Paolo Airò: None declared DOI: 10.1136/annrheumdis-2019-eular.665

PERIPHERAL BLOOD REGULATORY T-LYMPHOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE AND AFTER ALFACALCIDOL THERAPY

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Background: The identification of regulatory T cells (Treg) changed the Th1/Th2 dichotomy response in the pathogenesis of autoimmune diseases. Treg suppresses various autoreactive responses and maintain auto-tolerance in the immune system. The vitamin D receptor is widely expressed in immune cells, including monocytes, macrophages, dendritic cells, NK cells, and T and B lymphocytes, and plays an important role in the regulation of the immune system, and in the modulation of immunologically mediated diseases. Alfacalcidol, a synthetic analogue of hormone D, used in the prevention and treatment of osteoporosis, but the last results indicate its potential therapeutic effects in autoimmune diseases.

Objectives: Assess the presence of regulatory T cells in patients with active rheumatoid arthritis (RA)patients before and after 12 weeks of 2 mcg of alfacalcidol administration daily, and in healthy controls.

Methods: The study included 16 patients with RA, both sexes, with active disease (DAS 28 (SE)- 3.2, despite therapy with LMTBs for at least a month and 20 healthy volunteers (the same distribution of sex and age) - a control group of healthy subjects. In addition to their regular LMTB therapy, patients with RA received daily alfacalcidol (2mcg/day) for 12 weeks. Phenotypic characterization of peripheral blood lymphocytes was performed by direct and indirect immunofluorescence technique using the BD FACS Aria III flow cytometer. Descriptive and analytical statistics were used in data analysis.

Results: A small percentage of activated Treg cells [HLA-DR + compared to total T-lymphocytes] in the peripheral blood of patients with active RA was detected in the Treg lymphocytes in relation to the control group of healthy subjects, which is close to the statistical significance level (4.76% versus 6.5% = 0.07). In contrast, the percentage of total Treg cells (Treg versus total CD4 +) was slightly higher in patients compared to the controls.


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