Outcomes of patients treated with tocilizumab or abatacept as steroid-sparing agents with giant cell arteritis

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Background: Giant cell arteritis (GCA) is a common form of systemic vasculitis. The current mainstay of GCA management is glucocorticoid (GC) therapy. Recently, at least 2 biological therapies [tocilizumab (TCZ) and abatacept (ABA)] have been proven to be effective in the management of GCA in randomized controlled trials. Nevertheless, their use as steroid sparing agents might need further investigation.

Objectives: We aimed to investigate the steroid-sparing effect of biological therapies, namely TCZ and ABA, in a cohort of GCA patients when compared to standard GC treatment.

Methods: We retrospectively collected data from GCA patients who attended the S.G. Bosco Hospital, Turin, Italy, who were treated with TCZ, both intravenous (IV) and subcutaneous (SC), and/or ABA SC (8 mg/kg/mo, 162 mg/week, and 125 mg/week respectively). Therapies were prescribed as first line agents or as second line when patients were refractory/intolerant/contraindicated to standard immunosuppressive therapies. Complete response to the treatment was defined as a clinical and serological remission after 12 months of therapy; partial response was defined as clinical or serological remission after 12 months of therapy; partial response defined as ≥50% reduction in prednisone dose. Complete response to the treatment was defined as a clinical and serological remission after 12 months of therapy; partial response was defined as clinical or serological remission after 12 months of therapy. After 12 months of therapy, 100% of patients in GCA groups, both IV and SC, showed a complete response to the treatment. Among the ABA group, 86% experienced a response (36% complete response and 50% partial response). After 12 months of therapy, 100% of patients in GCA groups, both IV and SC, showed a complete response to the treatment. Among the ABA group, 86% experienced a response (36% complete response and 50% partial response). Mean baseline CRP (mg/dl) 1.9±2.3, mean CRP after 12 months of therapy 0.3±0.2; mean baseline ESR (mm/h) 58.1±25.6, mean ESR after 12 months 9.5±4.2; TCZ SC group: mean baseline CRP 4.5±3.8, mean CRP after 12 months 0.2±0.2; mean baseline ESR 51.9±27, mean ESR after 12 months 6.5±6.6. When compared to standard GC regimen [1], in patients treated with TCZ, both IV and SC, we estimated a median steroid-sparing effect quantifiable in 30 mg/week in the first month and an overall steroid-sparing effect of 15 mg/week when assessed in 12 months.

Conclusion: This retrospective study confirms the efficacy of biological therapies in the management of GCA. Besides, in our experience TCZ allowed a significant reduction of GCs use, especially in the first month of therapy, when compared to standard GCs based regimens.

REFERENCE:

Disclosure of Interests: None declared


Severity and response to induction therapy in new and relapsing ANCA associated vasculitis patients – real world practice data

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Background: ANCA-associated vasculitis (AAV) presents clinically with variable severity of disease and current clinical guidelines give varying advice on initial treatment to induce remission. Achieving remission quickly is important to gain disease control and avoid cumulative organ damage from treatment related adverse events. This study examined real world practice of AAV treatment in Europe to understand the AAV severity spectrum and the response to therapy over 12 months.

Methods: 929 incident and 268 relapsing EU AAV patients receiving care from 399 physicians were studied. Patients were referred between 2014-17 and data collected retrospectively at baseline and 1, 3, 6 and 12 months following induction therapy. Birmingham Vasculitis Activity Score (BVAS) was collected in only 12% of patients and severity was defined as mild (localized disease with no systemic symptoms), moderate (Mod, systemic disease with lung and/or kidney involvement) or systemic (rapidly progressive systemic disease with lung and/or kidney involvement). AAV disease severity varied in both incident (mild 12.2%, moderate 54.3%, severe 33.6%) and relapsing (9.7, 64.6 and 25.7) patients at start of treatment. Comorbidity at time of event.

Results: This retrospective study included 33 GCA patients (mean age 74 (range 85-57), females 63%, mean follow-up from GCA diagnosis 4.4 years (range 85-57), females 63%, mean follow-up from GCA diagnosis 4.4 (range 85-57), females 63%, mean follow-up from GCA diagnosis 12 months 25.7 months). Table 1 describes the characteristics of the GCA patients included in the study.

Abstract THU0315 – Table 1

<table>
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<th>Total number of patients</th>
<th>%</th>
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Demographic characteristics

- Female/Male: 22/12
- Age (years, mean, SD): 73.6±8.7

Clinical characteristics at the onset of GCA

- Fever: 12 (36.4)
- Fatigue: 18 (54.5)
- Headache: 28 (84.8)
- Scalp tenderness: 8 (24.2)
- Jaw claudication: 15 (45.4)
- Vision loss: 16 (48.5)
- PRN (mg): 11 (33.3)

Diabetes prevalence: 27/32 (84.4)

PET positivity: 12/29 (41.4)

ECG abnormality in 30/31 (97)

GC therapy

- previous methyldiphenylciclohexane therapy: 7 (21.2)
- Oral prednisone: 33 (100)
- Dose of oral prednisone (mg/day): 49.7±15.1

Previous immunosuppressive therapy

- Methotrexate: 11 (33.3)
- Mean dose of methylprednisolone (mg/day): 15.6±15.7
- Mycophenolate: 6 (18.1)
- Mean dose of methylprednisolone (mg/day): 2.2±0.4

Table 1: Characteristics of the patients included in the study

1 month 3 months 6 months 12 months

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<th>Mild</th>
<th>Mod</th>
<th>Severe</th>
<th>Mild</th>
<th>Mod</th>
<th>Severe</th>
<th>Mild</th>
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<th>Mild</th>
<th>Mod</th>
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<tr>
<td>Full</td>
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<td>13.5</td>
<td>59.4</td>
<td>47.2</td>
<td>28.7</td>
<td>82.6</td>
<td>45.0</td>
<td>82.8</td>
<td>70.7</td>
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</tr>
<tr>
<td>Partial</td>
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<td>67.9</td>
<td>38.4</td>
<td>48.8</td>
<td>56.8</td>
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<td>No</td>
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<td>4.9</td>
<td>18.6</td>
<td>2.2</td>
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<td>14.5</td>
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induction therapy was more common in severe patients (71.8% of patients having at least one comorbidity) compared to mild patients (55.1%). Since BVAS was not measured routinely, clinical response was categorized as full (no vasculitis activity and GC taper on track), partial (reduction in vasculitis activity and major organ damage arrested) and no response (no improvement in vasculitis). Clinical response is presented below (% patients) for combination of incident and relapsing patients demonstrating that response varied with many patients having slow and/or incomplete response. Response varied by severity of the disease when induction therapy commenced.

Conclusion: Incident and relapsing AAV patients have variable disease severity at the time of induction therapy. Response to induction therapy is with few exceptions better in patients with milder AAV but overall many patients are slow to respond or have only a partial response to current induction therapy.

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Disclosure of Interests: Peter Rutherford Employee of: Vifor Pharma, Dieter Götte Employee of: Vifor Pharma


THU0316

PROTEINASE-3 REGULATING MICRO-RNA IN GRANULOMATOSIS WITH POLYANGIITIS

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Background: Dysregulated miRNA expression profiles have been described in diverse chronic inflammatory diseases. We previously did a microarray screening of 847 miRNAs in nasal tissue from GPA patients and we found a disease associated alteration of miRNA expression compared to healthy controls (HC) and chronic rhinosinusitis (CRS).

Objectives: In order to identify new miRNA targets of potential pathophysiological relevance in GPA, we validated dysregulated miRNAs by qPCR

Results: In an independent validation cohort (tissue and sera from 14 GPA-patients, 10 disease controls: CRS and Crohn’s/CD) 12 miRNAs were examined by qPCR. Validated and computational miRNA targets were identified by mirDIP algorithms. The inhibitory capacity of miRNAs on Proteinase-3 (PRTN3) was estimated by a dual-luciferase reporter system (Promega®). The 3’UTR-PRTN3 sequence was cloned and inserted into the pmirGlo vector and co-transfected with the hsa-mirna mimics (Dharmacon®) into HeLa cells. As a second method, the effect of miR-184 transfection on the endogenous PRTN3 expression in the human myeloid leukemia cell line HL-60 was estimated by western blot.

Results: Microarray screening revealed alterations of 24 miRNAs in GPA nasal tissue compared to HC and CRS. qPCR confirmed dysregulation of 6 tissue related miRNAs also in GPA sera. Compared to CD 4 miRNAs (miR-10b, -99a/100, -125b, -532–5p) were down regulated in GPA tissue. The miRNA with the highest expression level in nasal tissue from GPA was miR-184. miR-184 along with miR-708 and miR-214-5p were also predicted to target PRTN3 by the mirDIP algorithm. The dual-luciferase reporter assay revealed a significant reduction of PRTN3 expression by miR-184, while these effects could not be observed for miR-708 or miR-214-5p. The transfection of miR-184 into HL-60 cells resulted in a dose-dependent knockdown of PRTN3 expression as detected by Western blot.

Conclusion: Characteristic miRNA signatures in GPA, CRS and CD suggest distinct pathophysiological mechanisms. It indicates at a local miRNA dysregulation in inflamed GPA tissue with a corresponding serum signature that might serve as novel biomarkers. To our knowledge this is the first analysis that attempts to correlate GPA-associated miRNA expression patterns in tissue with serum. Moreover, this is the first description of a miRNA (miR-184) that potentially regulates the expression of the GPA autoantigen PRTN3.

REFERENCES:


THU0317

IDENTIFICATION OF ENDOTHELIAL PROTEIN C RECEPTOR AND SCAVENGER RECEPTOR CLASS B TYPE 1 AS MAJOR AUTOANTIGENS IN TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) affects the aorta and its major branches. It has been recognized that high numbers of patients with TAK possessed antiendothelial cell antibodies (AECA), which have potential to induce vascular lesion. However, their major target antigens remain unclear. The target antigens of AECA are plasma membrane proteins, and traditional methods to identify autoantigens do not differentiate between cell-surface molecules and intracellular molecules. To overcome this problem, we have developed an expression cloning system to identify cell-surface antigens: serological identification system for autoantigens using a retrovector and flow cytometry (SARS)1,2. Because there

Abstract THU0316 – Figure 1.

Fig 1. Dual-luciferase reporter assay showing a decrease in luciferase activity when faced to the 3’UTR of PRTN3 and co-transfected with microRNA-184 mimic. No reduction can be observed for the negative control (mock-transfected). The 3’UTR of AKT2 was used as a positive control, since it is a validated target of miR-184. Effects of miR-184 targeting the reporter was compared to co-transfected reporter with cel-miR-67 (negative mimic). Data represent 3 independent experiments with triplicate measurements. P<0.01; **P<0.001; ns = not significant; error bars display standard deviation.