

### THU0340 ADRENAL INSUFFICIENCY DURING GLUCOCORTICOID TREATMENT IN PATIENTS WITH POLYMYALGIA RHEUMATICA OR GIANT CELL ARTERITIS

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**Background:** Adrenal insufficiency secondary to long-term systemic glucocorticoid treatment is a well-recognized problem. However, the extent and prevalence of this phenomenon has not been thoroughly explored.

**Objectives:** To investigate the prevalence of adrenal insufficiency in patients with polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) during treatment with low doses of prednisolone (<10mg/day) assessed by the adrenal response to a 250 microgram Synacthen<sup>®</sup> test. To explore whether potential adrenal insufficiency was associated with duration of steroid treatment.

**Methods:** Outpatients were examined when prednisolone doses were between 2.5 and 10 mg/day for >6 months. Adrenal function was evaluated after a 48-hour pause of prednisolone, using a 250 µg Synacthen<sup>®</sup> (ACTH) test where plasma cortisol levels were measured at baseline and 30 minutes after Synacthen injection. Adrenal insufficiency was defined as plasma cortisol <420 nmol/l after 30 minutes according to the validated Roche Elecsys<sup>®</sup>Cortisol II assay. Accumulated doses of prednisolone for the individual patients were calculated. A multiple regression analysis was used to test for an association between the plasma cortisol after 30 minutes and the accumulated dose of prednisolone.

**Results:** Forty-eight patients (35 women) completed the Synacthen<sup>®</sup> test. Seven (14.6%) patients exhibited adrenal insufficiency. Median age was 74 years (Range: 57–89 years). Median accumulated dose was 3.402 mg (Range: 820–21.200mg). Median plasma cortisol after 30 minutes was 562 nmol/l (Range: 92–989 nmol/l). In patients with adrenal insufficiency, median plasma cortisol was 122 nmol/l (Range: 56–275 nmol/l) at baseline and 207 (Range: 92–420 nmol/l) after 30 minutes. In patients without adrenal insufficiency, median plasma cortisol was 359 (Range: 9–710 nmol/l) at baseline and 584 nmol/l (Range: 429–989 nmol/l) after 30 minutes. Accumulated doses of prednisolone did not differ in patients with and without adrenal insufficiency (p=0.49). Plasma cortisol after 30 minutes was not associated with accumulated dose of prednisolone (estimate -0.01, 95% CI: -0.02 to 5.39, p=0.06), when adjusting for sex and age.

**Conclusions:** Iatrogenic adrenal insufficiency was prevalent among patients with PMR or GCA treated with low dose prednisolone. Adrenal function was not associated with the accumulated dose of prednisolone, or the duration of steroid treatment. A Synacthen<sup>®</sup> test is a valuable tool to evaluate the adrenal function, when steroid treatment is tapered in these patients. Latent symptoms of adrenal insufficiency may explain why some patients are reluctant to discontinue steroid treatment even after the inflammatory condition has gone into remission.

**Disclosure of Interest:** None declared

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### THU0341 FLT3 LIGAND CONCENTRATIONS ARE ELEVATED IN ANCA-ASSOCIATED VASCULITIDES (AAV) AND ARE INFLUENCED BY IMMUNOSUPPRESSIVE THERAPY

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**Background:** The cytokine Flt3 ligand is an important cofactor for early hematopoiesis by mainly driving the development of lymphoid and early B-cell precursors. In the periphery functions of Flt3 are more pleiotropic involving the differentiation of regulatory T-cells, dendritic cells as well as peripheral B-cells. Besides its well-known roles in hematological disorders and as an indicator of bone marrow (BM) output capacity, the possible involvement of FLT3 ligand in autoimmune disorders was only discovered recently.

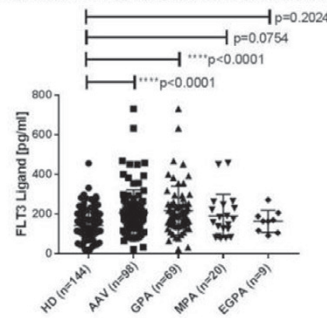
**Objectives:** Our primary aim was to analyze if FLT3 ligand serum concentrations are affected in AAV patients. Secondary aims were to correlate the FLT3 ligand serum concentrations with clinical and laboratory parameters. And, since FLT3 ligand concentrations are elevated in different states of bone marrow failure, we also wanted to evaluate FLT3 ligand as a marker for treatment related BM toxicity in AAV patients.

**Methods:** We performed a cross sectional study using a sandwich ELISA to determine FLT3 ligand concentrations in the serum of 98 well characterized AAV patients (69 GPA, 20 MPA and 9 EGPA) and 144 healthy controls (HC). Statistical evaluation was done using Mann-Whitney or unpaired, two-tailed Student's t-test.

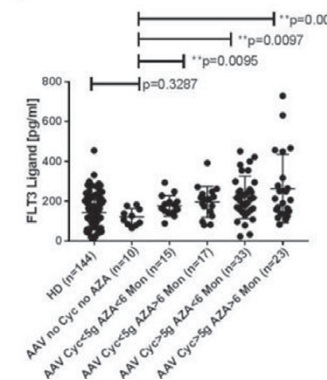
**Results:** In patients with AAV, FLT3 ligand concentrations were significantly elevated (207 pg/ml +/- 116.2 in AAV versus 142.5 pg/ml +/- 65.98 in HC; p<0.0001). Disease specific analysis revealed significantly elevated FLT3 ligand concentrations in GPA (217.6 pg/ml +/- 123; p<0.0001), but no significant differences for MPA and EGPA when compared to HC. FLT3 ligand concentrations did not correlate to serological or clinical markers of disease activity, however, overall disease activity was low in the studied cohort. To assess the influences of treatment regimen on FLT3 ligand concentrations, we focused our analysis on treatment histories of cyclophosphamide (CYC) and azathioprine (AZA) and grouped the patient cohort according to the cumulative CYC dose (< or >5g

and/or duration of AZA therapy (< or >6 months). AZA and CYC naïve patients (n=10) showed FLT3 concentrations comparable to HC (121 pg/ml +/- 42.3), but in patients with low dose CYC and short term AZA therapy FLT3 concentrations were significantly higher (176.6 pg/ml +/- 51.6), both compared to treatment naïve patients and HC (p=0.0095 vs. AZA/CYC naïve, p=0.0105 vs HC). Intensified treatment was associated with even further increased concentrations of FLT3 ligand with highest concentrations found in patients treated with >5g CYC cumulative dose or AZA treatment for >6 months (263.4 pg/ml +/- 172.6; p=0.0024 vs. AZA/CYC naïve, p<0.0001 vs HC).

#### Elevated FLT3 serum concentrations in ANCA-associated vasculitides



#### FLT3 ligand serum concentrations are influenced by therapy



**Conclusions:** Flt3 ligand concentrations are elevated in patients with AAV, especially in patients with GPA. The elevation more likely reflects the therapeutic regimen and history than disease activity as we could show that patients with more intensive treatment including both CYC and AZA show higher FLT3 ligand serum levels when compared to patients with less intense therapy.

#### References:

- [1] Ramos Ml et al. FMS-related tyrosine kinase 3 ligand (Flt3L)/CD135 axis in rheumatoid arthritis. *Arthritis Res Ther.* 2013; 15:R209.
- [2] Giri N et al. Immune status of patients with inherited bone marrow failure syndromes. *Am J Hematol.* 2015; 90:702–8.

**Disclosure of Interest:** None declared

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### THU0342 UTILIZING “REAL LIFE” DATA IN ORDER TO EVALUATE THE ASSOCIATION BETWEEN GIANT CELL ARTERITIS AND AUTOIMMUNE THYROID DISEASE

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**Background:** In 1977, How et al.<sup>1</sup> described the case of a simultaneous presentation of giant cell arteritis (GCA) and hypothyroidism. In the following decades, numerous studies have attempted to determine whether a significant interaction exists between GCA and autoimmune thyroid dysfunction, with conflicting results<sup>2–5</sup>.

**Objectives:** To evaluate whether a genuine association exists between GCA and autoimmune thyroid disease.

**Methods:** Utilizing the medical database of Clalit Health Services, we compared the proportion of autoimmune thyroid disease between patients with GCA and age- and gender-matched controls in a cross-sectional study. Univariate analysis was performed using Chi-square and student t-test and a multivariate analysis was performed using a logistic regression model.

**Results:** 5,663 GCA patients and 23,308 age- and gender-matched controls were