Figure 1. Heatmap based clustering analysis of serum miRNA expression

Figure 2. STRING Protein networks of gene targets of DE miRNAs

b/c, -378a, -423, -3184; $p_{adj} < 10^{-10}$), whereas 60 miRNAs were decreased (e.g. miRNA-128, -937, -30c, -328, -26a, $p_{adj} < 0.005$), thereby representing the IgAV-associated serum miRNA signature. The miRor platform identified 426 protein-coding genes as targets of the 54 DE miRNAs ($\log_2$ fold change $\geq |1|$, $p_{adj} < 0.01$). As analyzed by STRING, these miRNA target genes were enriched in distinct molecular networks and biological pathways, including "Phosphoproteins (FDR 7.4×10^{-5})", "Alternative splicing" (FDR 2.8×10^{-4}), "Regulation of actin cytoskeleton" (FDR 0.008), "Proteoglycans in cancer" (FDR 0.009) and "Fc gamma receptor dependent phagocytosis" (FDR 0.01) (Figure 2). Additionally, miRNA gene targets formed three distinct molecular clusters, specifically "Chemokines and their receptors", "Ubiquitination process" and "Vesicle, endocytosis, lysosomes and their trafficking" (Figure 2). This suggests that the altered miRNAs in IgAV regulate diverse cellular functions, reflecting or contributing to the key aspects of disease pathogenesis.

Conclusion: Here we report for the first time an IgAV-associated serum miRNA signature. The altered miRNAs clearly discriminate IgAV patients from HC, and might play a key role in the pathogenesis of IgAV. Our study sets the basis for the identification of novel, serum-based disease biomarkers in vasculitis.

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SAT0235

BIOLOGICAL THERAPY IN NEUROBEHÇET. MULTICENTER STUDY OF 29 PATIENTS

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Background: Behçet's disease (BD) is a variable vessel vasculitis and typically presents with mucocutaneous involvement. However, any organ can be affected, being the neurological affection (neurobehçet, NB) one of the most serious manifestations.

Objectives: Our aim was to assess the efficacy and safety of biological therapy as treatment of NB.

Methods: We set up a multicenter observational study of 29 patients with NB on treatment with biological therapy (BT). NB diagnosis was made by neuroimaging, CSF analysis and/or suggestive clinical signs of central and/or peripheral nervous system involvement, excluding infectious causes or more prevalent pathology. Results are expressed as mean $\pm$ SD or as median and interquartile range (IQR) as appropriate.

Results: 29 patients (15 σ /14 ϕ) with an average age of 39.6 ± 10.5 years. HLA-B51 was positive in 48.3% of the patients. Table shows the non-neurological manifestations. Regarding the neurological manifestations, 23 patients (79.3%) had parenchymal involvement (hemiparesis (n=6),

brainstem involvement (n=1), encephalopathy (n = 4), optic neuropathy (n=3), dysphasia (n=1), polyneuropathy (n=6), cognitive impairment (n=4), and non-steroidal psychosis (n=1), while the remaining 6 patients (20.7%) presented aseptic meningitis as a non-parenchymal affection (Table).

Prior to BT, patients had received the following treatment: oral prednisone (n=27), methylprednisolone bolus (n=9), CsA (n=8), AZA (n=16), MTX (n=14) and mycophenolate (n=2).

After a median of 31 [10-60] months since the beginning of the neurological symptoms, the following BT was initiated: infliximab (IFX)(n=17), adalimumab (ADA)(n=7), tocilizumab (TCZ) (n=2), golimumab (GOL) (n=2) and Etanercept (ETN) (n=1). A first switch to ADA was necessary in 8 patients with IFX due to primary failure. In addition, 2 of them needed a second switch to TCZ, getting a partial response. The BT was discontinued in 5 patients, 2 of them for obtaining clinical remission and the remaining 3 for inefficacy.

After a median follow-up of 5.4±4.6 years, complete response was obtained in 15 patients, partial response in 11 and no response in the remaining 3. We observed an anaphylactic reaction and psoriasis induced by IFX, without other serious adverse events (Table).

Conclusion: BT, especially anti-TNF, seems effective and safe for treatment in NB.

Table.	
Demographical parameter	
- Patients, n	29
- Sex, n (%)	15, /14, (51.7/48.3)
- Age, year (mean±SD)	39.6±10.5
- HLA-B51 +	14 (48.3)
Non Neurological manifestation	
- Oral ulcers	28 (96.6)
- Genital ulcers	23 (79.3)
- Uveitis	16 (55.2)
- Skin lesions	20 (69)
- Arthritis	6 (20.7)
- Arthralgia	19 (65.6)
- Venous/arterial thrombosis	7 (24.1)/3 (10.3)
Neurological manifestation	
Parenchymal Disease, n (%)	
- Hemiparesis	23 (79.3)
- brainstem syndrome	6 (20.7)
- encephalopathy	1 (3.4)
- optic neuropathy	4 (13.8)
- dysphasia	2 (6.8)
- polyneuropathy	1 (3.4)
- cognitive dysfunction	6 (20.7)
- psychosis	4 (13.8)
- Non-parenchymal Disease (aseptic meningitis), n (%)	1 (3.4)
- Time from diagnosis to BT onset, months (median[IQR])	6 (20.7)
Previous immunosuppressants	
- Oral corticoids	31 [10-60]
- Bolus MTP	27 (93.1)
- Azathioprine	9 (31)
- Methotrexate	16 (55.2)
- Cyclosporine	14 (48.3)
- Mycophenolate	8 (27.6)
- First Biological therapy	2 (6.9)
- Infliximab	17 (58.6)
- Adalimumab	7 (24.1)
- Tocilizumab	2 (6.9)
- Golimumab	2 (6.9)
- Etanercept	1 (3.4)
Follow-up, months (median[IQR])	
- 1 st /2 nd Switch, n (%)	22 [18.5-74]
- Discontinued (inefficacy)	8 (27.6) / 2 (6.9)
- Severe adverse events	3 (10.3)
-	0 (0)

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SAT0236 RELATIONSHIP BETWEEN RITUXIMAB CONCENTRATION AND AUTOANTIBODY LEVELS IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS

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Background: Rituximab is approved in patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV). Antibodies to proteinase 3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA) decrease with therapy (1) and may therefore be used as biomarkers.

Objectives: To investigate the relationship between rituximab concentration and ANCA levels in AAV patients.

Methods: 92 AAV patients from the RAVE trial (rituximab for ANCA-associated vasculitis) were assessed. Both MPO-ANCA, and PR3-ANCA antibody levels were used as biomarkers. ANCA levels were measured at baseline, at months 1, 2, 4, 6, 9, 18, and every 6 months until the second rituximab cycle if any, using ELISA supplied by Euroimmun. A semi-mechanistic model including a deep compartment which was sensitive to rituximab and a feedback mechanism, and a blood compartment were tested to describe the concentration-ANCA autoantibodies relationship. A population modeling approach using sequential methods was used for model building. Influence of sex, body surface area (BSA), BVAS/WG score, newly diagnosed status, major renal involvement at baseline, and relapse were investigated as covariates on pharmacodynamics parameters.

Results: A two compartment model including feedback mechanism from the circulating ANCA well described the concentration autoantibody relationship. The mean (interindividual standard deviation) estimated rituximab IC50, assessing potency, in patients with MPO-ANCA and PR3-ANCA were 21.9 mg/l (28%) and 11.2 mg/l (48.6%), respectively. Moreover, among patients with PR3-ANCA, rituximab IC50 was higher in patients with major renal involvement at baseline (p=2.47 x 10⁻²) and newly diagnosed status (p=6.42 x 10⁻⁵) than in others.

Figure 1. Simulations of ANCA-time profile in patients with MPO-ANCA (red line) and PR3-ANCA (purple line), using typical pharmacodynamic parameters. The central curve are the median dynamics of ANCA and the shadow are 90% prediction intervals.