# Serum autoantibody profiling of primary Sjögren's syndrome patients reveals novel biomarkers associated with the disease, disease activity, and clinical response to VAY736

SAT0301

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## Introduction

- Overexpression of B cell activating factor (BAFF) in salivary glands contributes to the pathogenesis of primary Sjögren's syndrome (pSS) by promoting autoantibody (AAB) production.
- Treatment of pSS patients with VAY736, an anti-BAFF receptor mAb, appears promising and was associated with a depletion of circulating B cells and a positive therapeutic effect [1].
- In addition to the classical anti-SS-A/Ro and anti-SS-B/La, a broader set of AABs may reflect B cell disturbances in pSS and could serve as markers during clinical development of novel pSS therapeutics.

## Objectives

- The study was undertaken to explore novel AABs in pSS and their associations with the disease, disease activity, and clinical response to VAY736.

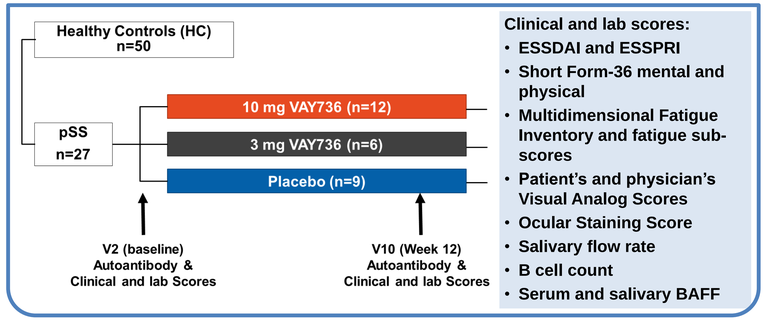


***Fig. 1: Study design***

- Serum samples were collected from pSS patients pre- and post-VAY736 administration, and from age and gender-matched HCs (Fig. 3). Statistical analysis was conducted as detailed in Table 1.

| Goal | Statistical approach |
|---|---|
| Identification of AABs associated with pSS | **Parameters:** AAB levels in HCs and in pSS patients at baseline<br>**Tests:** Wilcoxon rank sum test, significance analysis of microarrays, and comparison of the 90$^{th}$ quantiles between groups. |
| Identification of AABs associated with pSS activity | **Parameters:** AAB levels in pSS patients at baseline and week 12, as well as relative changes<br>**Tests** Pearson correlation with clinical and lab scores |
| Assessment of VAY736 treatment-specific changes in AAB levels | **Parameters:** AAB levels in pSS patients at baseline and Week 12<br>**Test:** linear mixed-effects models adjusting for dosage, age, and gender effects |

***Table 1: Statistical approach***

## Methods

- A discovery screen was designed comprising 1,596 antigens, which are directly relevant to pSS associated processes (Fig.2 ).

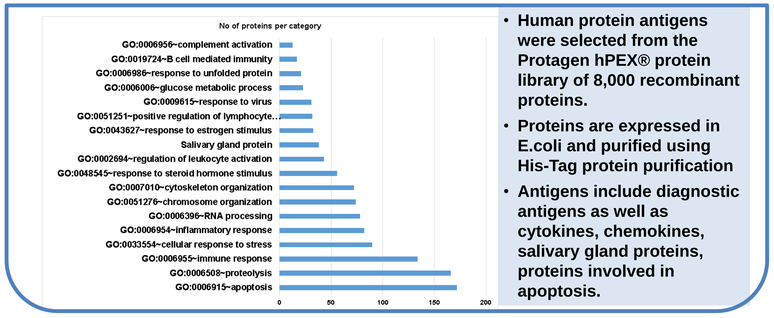


***Fig. 2: Overview of antigens included in this study***

- IgG antibodies were measured using the bead-based Luminex® xMAP® platform SeroTag® (Fig.3).

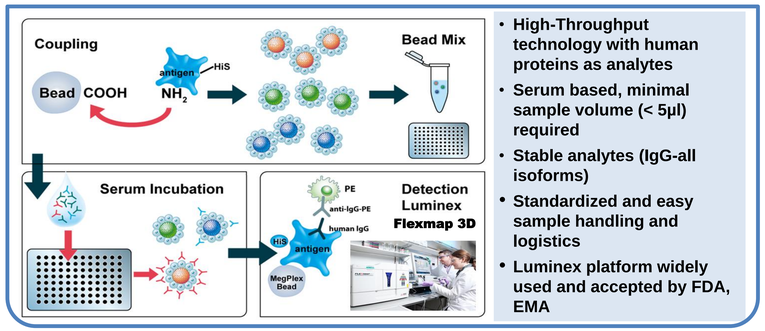


***Fig. 3: Schematic SeroTag workflow of bead-based assays***

## Results

- Compared to HC, pSS patients had increased IgG AAB levels to 36 antigens, including the known SSA and SSB ($p<0.05$). Examples are shown in Fig.4.

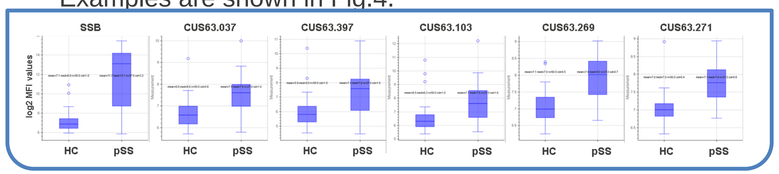


***Fig. 4: Box and Whisker plots showing novel autoantibodies in HC and pSS***

## Results (continued)

- SS-A/Ro and SS-B/La AABs were not associated with disease activity or response to treatment.
- When combining all treatment arms, 48 AABs were significantly correlated with different clinical outcome measures ($p<0.05$, $|r|>0.46$). Fig. 5A shows AABs associated with ESSDAI.
- 12 baseline AABs correlated with change in clinical outcome measures over 12 weeks in VAY736-treated patients (Fig 5B).

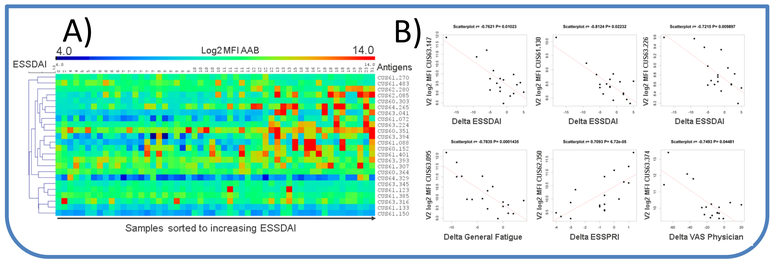


***Fig. 5: Autoantibodies correlating with clinical outcome scores***

- 51 serum AAB levels correlated with salivary BAFF levels, but not BAFF serum levels ($p<0.05$, $|r|>0.55$).

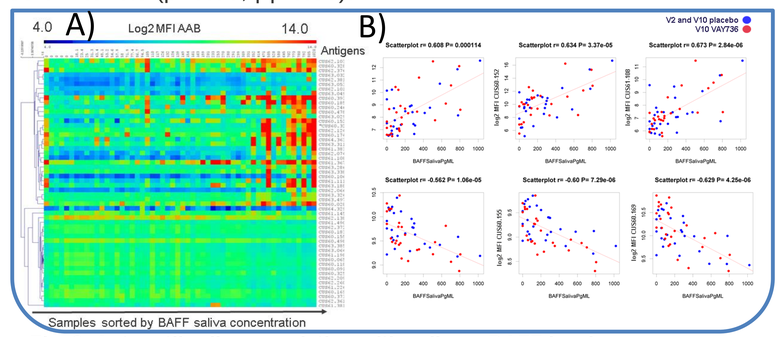


***Fig. 6: Autoantibodies correlating with salivary BAFF levels***

- No reduction in AABs levels was observed in response to VAY736 at week 12.

## Conclusions

The genes encoding novel antigens are involved in apoptotic, anti-viral, metabolic, inflammatory, blood coagulation and B-cell processes, suggesting a possible link to the disease pathology. Further large-scale studies are needed to confirm the value of these markers.

### References

1. Dörner T et al. Arthritis Rheum 2016; 68(suppl S10):4051