Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) as a Post-Infectious Autoimmune Disease: Benefits of Intravenous Immunoglobulin (IVIG)

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Introduction

- In the late 1990s, a subgroup of children who presented with obsessive-compulsive disorder (OCD) and/or tic disorders following streptococcal infections were described, and the diagnosis pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) was developed to describe the disorder.[1]
- Due to difficulties in determining a relationship between strep infections and PANDAS symptoms, a new diagnosis, pediatric acute-onset neuropsychiatric syndrome (PANS), was developed to encompass the growing number of infectious agents potentially related to PANS onset.[2]
- Significant findings indicate a relationship between a post-infectious response and behavioral changes[3,4]; this suggests a form of post-infectious autoimmunity through molecular mimicry.[5]
- Given these findings, we hypothesized that an immune defect is the underlying mechanism leading to PANS.[5]
- Based on this hypothesis, we proposed a study to explore the efficacy of IVIG [Octagam 5%] for PANS treatment.

Efficacy Endpoints

- **Changes in Psychological Evaluation Scores from Baseline to Visits 7/8/9**
  - Parent-Rated Symptom Survey
  - Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)
  - Yale Global Tic Severity Scale (YGTSS)
  - Anxiety Disorders Interview Schedule for DSM-IV (ADIS)
  - Clinical Global Impression (CGI)
  - Pediatric Acute Neuropsychiatric Symptom Scale Phone Interview Scores
  - Parent and Patient Artifacts (various)

Results

- Total of 21 participants at 3 clinical sites.
- Mean age: 10.86 yrs; males (13 [62%]); females (8 [38%]).
- Mean follow-up time from Visit 0 to Visit 8 was 186 days (±13 days).
- Late follow-up (Visit 9) occurred 29-46+ weeks after last IVIG infusion to gather data on durability of response.

Study Overview/Schematic

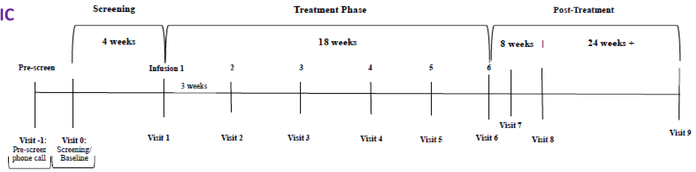
OBJECTIVE
Evaluate the Benefit of Octagam 5% in Subjects with PANS Syndrome

PARTICIPANTS
Male and Female Children Ages 4 – 16 Years with a Diagnosis of PANS

DESIGN
A Multi-site, Open-Label, Pilot Study

STUDY DRUG
Octagam 5% (1g/kg Body Weight Every 21±3 Days/6 Infusions)

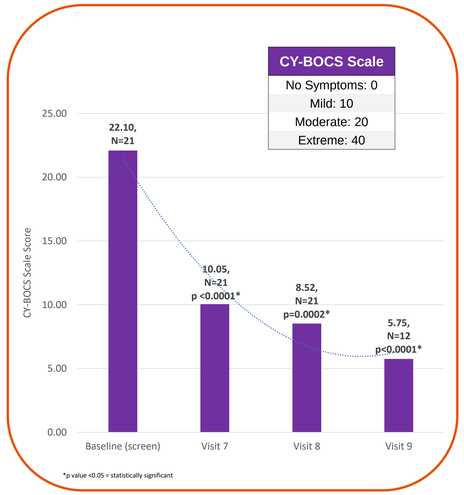
STUDY SCHEMATIC



Results (continued)

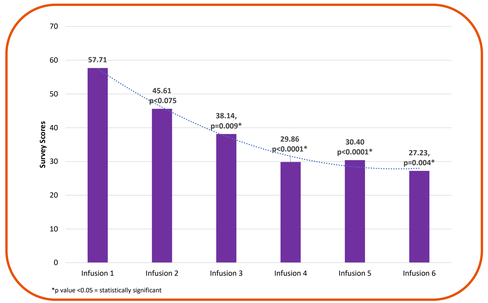
- The primary efficacy endpoints were determined by clinical observation, parent observation, validated psychometric assessments, and interviews by psychologists/psychiatrists.
  - Statistically significant improvements were demonstrated in all psychometric assessments from baseline as compared to Visit 7.
- Results from the **CY-BOCS assessment (Figure 1)** demonstrated significant reductions in obsessive thoughts and behavior at Visits 7/8/9 as compared to treatment initiation (baseline).
- Results from the **Parent-Related Symptom Survey (Figure 2)** demonstrated significant reductions in symptoms beginning at Infusion 3 through Infusion 6 (compared to baseline).
- Results from the **CGI Severity of Illness Scale (Figure 3)** demonstrated significant reductions from baseline as compared to results at Visits 7/8/9, as well as reductions in the follow-up period (Visit 7 to Visit 8; Visit 8 to Visit 9).
- **Cunningham Panel (Moleculera Labs) (Figure 4 [Left])**
  - 100% of subjects demonstrated out of range results.
- **Neural Zoomer (Vibrant Wellness) (Figure 4 [Right])**
  - 71.4% of subjects demonstrated out of range results.

Figure 1. CY-BOCS Assessment Results



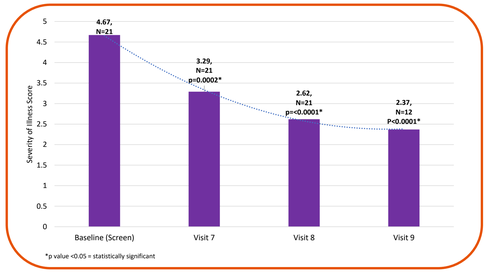
*p value <0.05 = statistically significant

Figure 2. Parent-Rated Symptom Survey Results



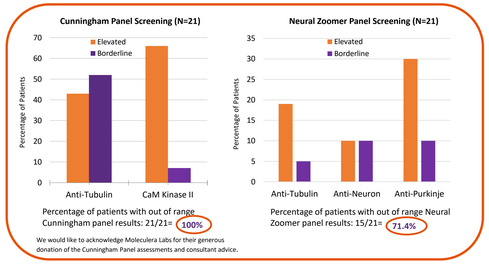
*p value <0.05 = statistically significant

Figure 3. CGI Severity of Illness Scale Results



*p value <0.05 = statistically significant

Figure 4. Brain Autoimmunity Results



We would like to acknowledge Moleculera Labs for their generous donation of the Cunningham Panel assessments and consultant advice.

Conclusions

- In PANS patients, all psychometric endpoints studied exhibited statistically significant decreases following 6 cycles (infusions) of IVIG as well as durability of response for up to 46 weeks in a subset of subjects.
- Patients with PANS can benefit from a 6-cycle course of IVIG.
  - Provisional data demonstrate durability of the positive impact of IVIG treatment.
- PANS is an autoimmune disease; innate immunity and the complement system may play a role in the pathogenesis of PANS.

References

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