

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

Isaac Melamed, MD, Roger Kobayashi, MD, Maeve O'Connor, MD, Ai Lan Kobayashi, MD, Andrew Schechterman, PhD, Melinda Heffron, Sharon Canterberry, RN, Holly Miranda, RN, Nazia Rashid, PharmD, MS

## 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.<sup>1</sup>
- 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.<sup>2</sup>
- Significant findings indicate a relationship between a post-infectious response and behavioral changes<sup>3,4</sup>; this suggests a form of post-infectious autoimmunity through molecular mimicry.<sup>5</sup>
- Given these findings, we hypothesized that an immune defect is the underlying mechanism leading to PANS.<sup>5</sup>
- 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 ( $\pm 13$  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

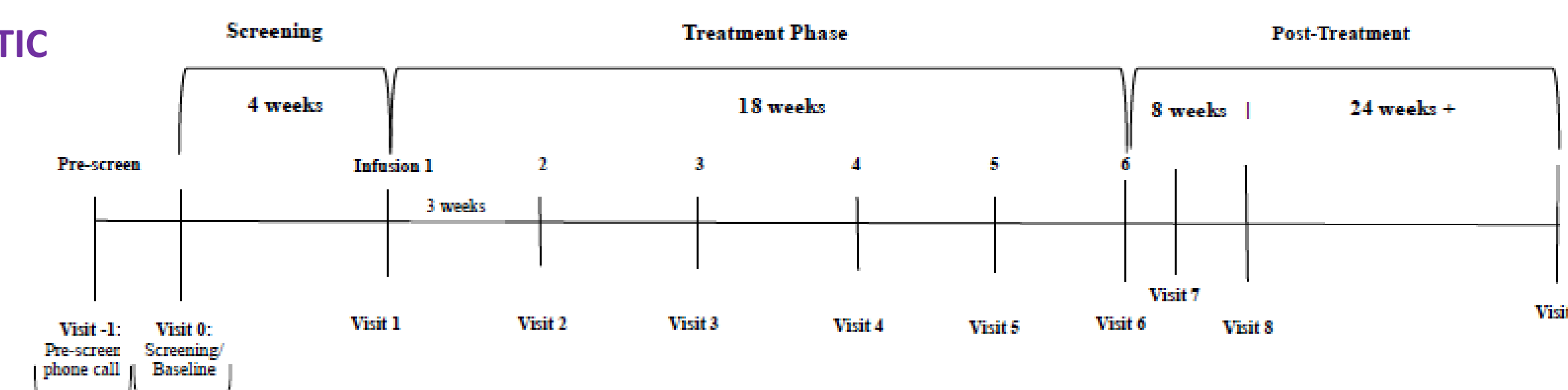


### STUDY DRUG

Octagam 5% (1g/kg Body Weight Every 21 $\pm$ 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 (Moleculara 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

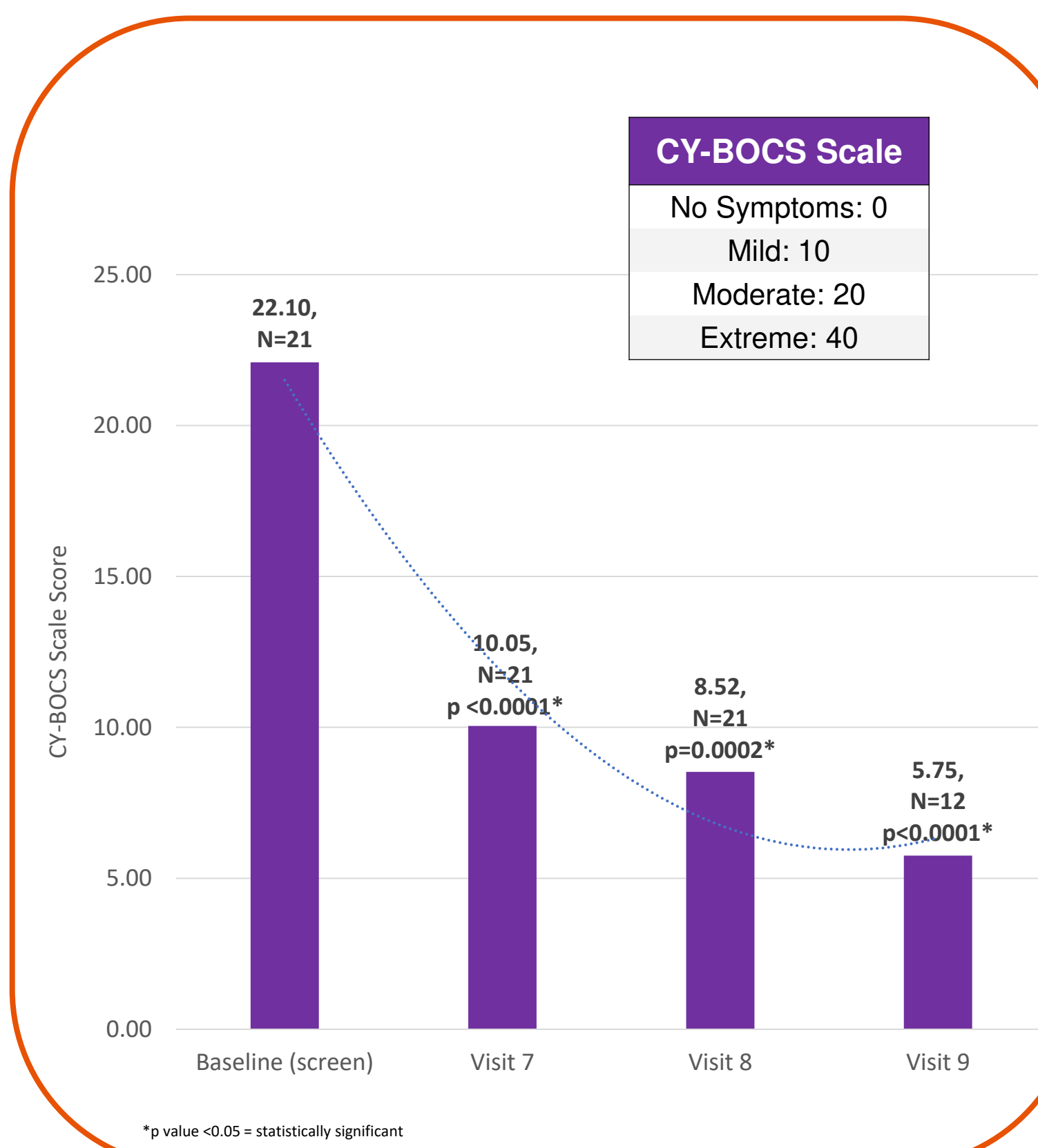


Figure 2. Parent-Rated Symptom Survey Results

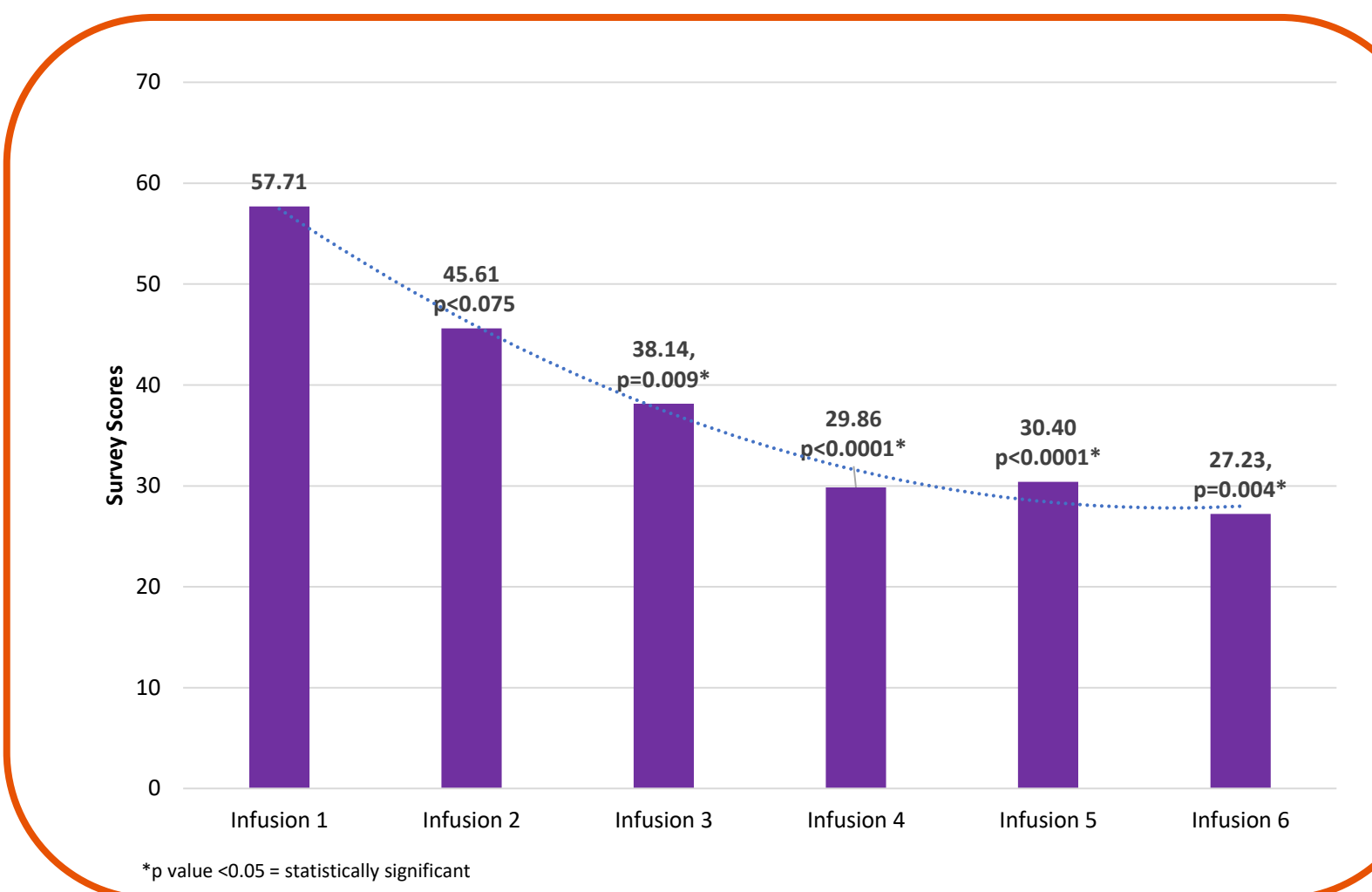


Figure 3. CGI Severity of Illness Scale Results

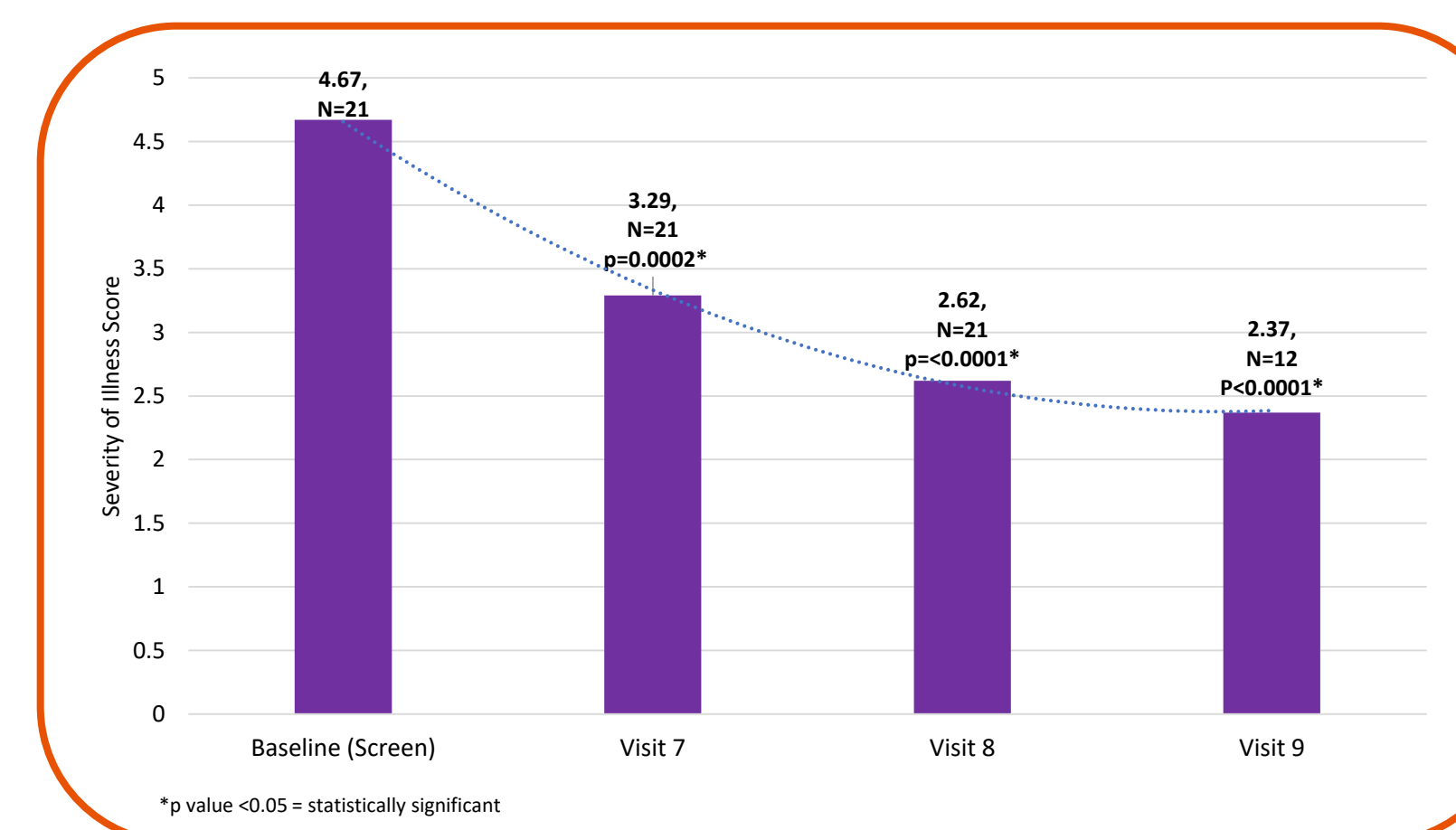
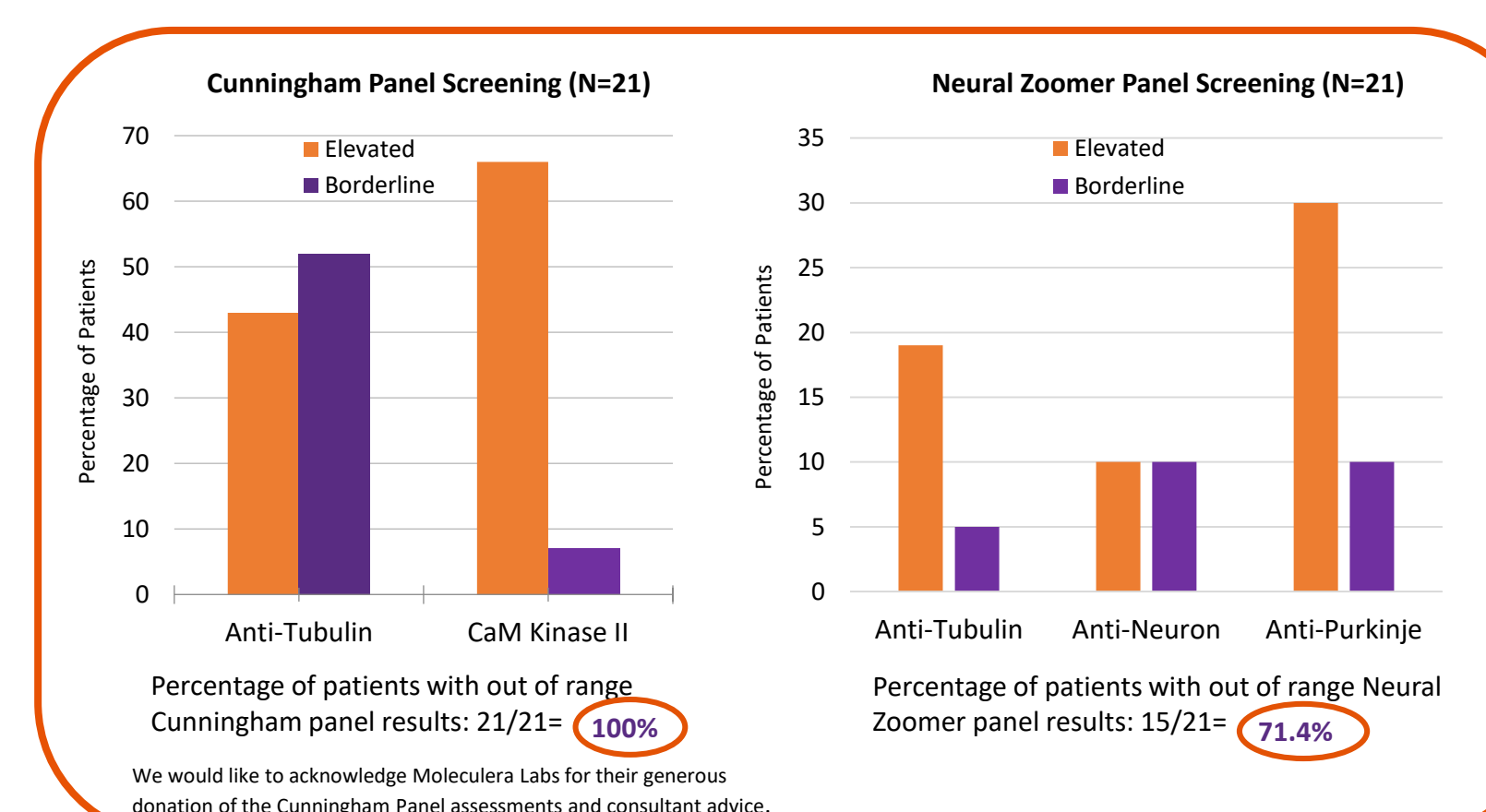


Figure 4. Brain Autoimmunity Results



## 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

- Swedo SE, et al. Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections: clinical description of the first 50 cases. *Am J Psychiatry*. 1998;155:265-271.
- Swedo SE, et al. From research subgroup to clinical syndrome: Modifying the PANDAS criteria to describe PANS (Pediatric Acute-onset Neuropsychiatric Syndrome). *Pediatr Therapeut*. 2012;2:2.
- Bronze MS, et al. Epitopes of streptococcal M proteins that evoke antibodies that cross-react with human brain. *J Immunol*. 1993;15:2820-2828.
- Hornig M. The role of microbes and autoimmunity in the pathogenesis of neuropsychiatric illnesses. *Curr Opin Rheumatol*. 2013;25:488-795.
- Melamed I. Alzheimer's of the immune system: a new variant of immune deficiency. *Immunother Open Acc*. 2016;2:2.

## Acknowledgments

This study was funded by a grant from Octapharma. Cunningham Panel laboratory assessments and consulting expertise were provided by Moleculara Labs. Dunwoody Consulting provided assistance with poster content, statistical analyses, and design.

Presented at: American Academy of Pediatrics National Conference, 2019, New Orleans, Louisiana