

**INTUNIV™ (guanfacine) Extended Release Tablets Q&A
(Presented at AACAP 2009)**

Q1: What was the primary objective of the 307 study?

A1: The primary objective of this randomized, placebo-controlled, flexible-dose study was to assess the reduction of symptoms using the oppositional subscale of the Conners' Parent Rating Scale-Revised: Long Form (CPRS-R:L) in patients aged 6 to 12 years with a primary diagnosis of ADHD with the presence of oppositional symptoms at baseline.¹

Q2: What were the results of the 307 study presented at AACAP?

A2: INTUNIV, identified in the poster as GXR, met the primary objective demonstrating significant efficacy in reducing symptoms as measured by the oppositional subscale.¹ Some of the symptoms measured by this scale include deliberately does things that annoy others, refuses to comply with adults' requests, loses temper, and is touchy or easily annoyed by others.²

In this analysis, GXR demonstrated significant ADHD symptom improvement in the primary and secondary measures as demonstrated on the oppositional subscale of the CPRS-R:L and the ADHD Rating Scale-IV (ADHD-RS-IV), respectively.¹

At the study's end, patients taking INTUNIV showed significant symptom reduction as compared to patients taking placebo (LS mean change from baseline -10.9 versus -6.8; $P < .001$; effect size 0.59) when assessed using the oppositional subscale of the CPRS-R:L.¹ The ADHD-RS-IV scale assesses hyperactive, impulsive, and inattentive ADHD symptoms. At end point, LS mean reduction from baseline in ADHD-RS-IV total score for INTUNIV versus placebo was -23.8 versus -11.5; $P < .001$; effect size 0.92.¹

The effect size is a standardized method of comparing effectiveness of medications as categorized by small (0.2), medium (0.5), and large (0.8) across different studies for the same condition, and was also measured during this study.³

Q3: What were the most common treatment related adverse events reported in the 307 study?

A3: The most commonly reported treatment-emergent adverse events in patients taking INTUNIV (greater than or equal to 10 percent) were somnolence, headache, sedation, upper abdominal pain, and fatigue.¹ The majority of treatment related adverse events were mild to moderate in severity. No syncope, deaths, or serious AEs were reported during the study.¹

Q4: Can you further explain the Conners' Parent Rating Scale-Revised: Long Form (CPRS-R:L)?

A4: CPRS-R:L is a comprehensive scale that uses parent observer and self-report ratings to help assess ADHD symptoms and behaviors in children.²

INTUNIV 2009 Q&A (AACAP Addendum)

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Q5: Were there any other INTUNIV data presented at AACAP?

A5: Yes. Another poster titled “Twenty-Four-Month Effectiveness of Guanfacine Extended Release in Children and Adolescents Aged 6 to 17 Years With Attention-Deficit/Hyperactivity Disorder” was also presented on October 29, 2009.

Q6: What was the objective of the long-term study presented at AACAP?

A6: The objective of this analysis was to assess the efficacy of long-term (24-month) INTUNIV treatment for ADHD in children and adolescents ages 6 to 17 years based on pooled data from two open-label clinical trials. Although the focus of this analysis was effectiveness, the primary objective of both open label trials was to assess the long term safety of INTUNIV. The key effectiveness analysis examined change from baseline to end point in ADHD-RS-IV total score using a 1-sample t-test, both overall and within each actual dose group and weight-adjusted dose group. Baseline ADHD-RS-IV was defined as the measurement obtained at baseline of the preceding short-term trial.⁴

Q7: What were the results of the long-term study presented at AACAP?

A7: Once-daily INTUNIV demonstrated significant ADHD symptom control for up to 24 months. Reductions in ADHD-RS-IV total and subscale scores were maintained for up to 24 months of once-daily INTUNIV treatment (1 or 2 mg/day to 4 mg/day) in patients aged 6 to 17 years with ADHD. At end point, mean decrease from baseline in ADHD-RS-IV total score was -19.5 ± 13.48 versus baseline ($P < 0.001$), and decreases in mean ADHD-RS-IV total scores emerged within 1 week of INTUNIV therapy and were maintained through month 24 ($P < 0.001$ at end point). ADHD symptom improvements were similar among actual and weight-adjusted GXR dose groups.⁴

Q8: What were the safety results from this long term analysis of data from the open-label studies?

A8: Most treatment emergent adverse events were mild to moderate in severity. Most common TEAEs >10% included somnolence, headache, fatigue, sedation, and upper respiratory tract infection. Discontinuations due to adverse events occurred in 16.6% (n=74 of 446) of subjects. AEs that most frequently led to discontinuation ($\geq 2\%$) were somnolence (3.1%) and increased weight (2.0%).⁴

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1. Effects of guanfacine extended release in children aged 6 to 12 with oppositional symptoms and a diagnosis of ADHD. Poster Presented at the American Academy of Child & Adolescent Psychiatry Annual Meeting; October 29, 2009; Honolulu, HI.
 2. Conners CK. Conners' rating scales-revised: technical manual. North Tonawanda, NY: *Multi-Health Systems*.
 3. Faraone S. Understanding the effect size of ADHD medications: implications for clinical care. *Medscape Psychiatry and Mental Health*. 2003;8(2).
 4. Twenty-four-month effectiveness of guanfacine extended release in children and adolescents aged 6 to 17 years with attention-deficit/hyperactivity disorder. Poster Presented at the American Academy of Child & Adolescent Psychiatry Annual Meeting; October 29, 2009; Honolulu, HI.