Distinguishing the efficacy and sedative effects of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder


Abstract

The present study investigated whether symptom reduction in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) treated with guanfacine extended release (GXR) can be explained by sedative effects of the medication. Data from four double-blind, randomized, placebo-controlled, phase 3 trials of GXR monotherapy (1-7 mg/day; morning administration) in children (aged 6-12 years) and adolescents (aged 13-17 years) with ADHD were analyzed post hoc. Two studies used forced-dose titration and two used flexible-dose titration. Efficacy was determined using ADHD Rating Scale IV (ADHD-RS-IV) scores. Sedative treatment-emergent adverse events (TEAEs) included somnolence, sedation and hypersomnia. The proportion of responders (≥ 30% reduction in ADHD-RS-IV total score) increased from weeks 1 to 4 and remained stable to study endpoint. Sedative TEAEs generally peaked at the first week in which the target dose was achieved and then declined. In subgroup analyses, significant placebo-adjusted improvements in ADHD-RS-IV total scores were observed in participants without any sedative TEAEs in the forced-dose and flexible-dose studies (nominal p < 0.001). In addition, GXR was associated with significant improvements in both inattentive and hyperactive-impulsive symptoms, as assessed by the ADHD-RS-IV subscale scores (nominal p < 0.001) and by the ADHD-RS-IV total score in participants with different ADHD subtypes (nominal p < 0.05). Thus, the efficacy of GXR in children and adolescents with ADHD is not primarily due to sedation, although some contribution to symptom reduction cannot be excluded, especially early in treatment when rates of sedative TEAEs are at their highest.