Supplementary Content 1. Results of supportive analyses in patients with a P7 cut-off of ≥2 points (at least 'minimal' hostility)

PANSS-EC score change in patients with hostility at baseline (P7 score ≥2)

Short-term analyses: In patients with P7 score ≥2 at baseline, brexpiprazole 4 mg (LSMD: -1.34 [95% CLs: -2.14, -0.55]; p=0.0010), but not brexpiprazole 2 mg (-0.76 [-1.57, 0.05]; p=0.065), was superior to placebo in reducing the PANSS-EC score at Week 6 (Supplementary Figure 1a).

Long-term analyses: Patients with P7 score ≥2 at baseline showed further improvement in PANSS-EC score with long-term brexpiprazole treatment, changing from baseline by a mean (SD) of -6.6 (3.8) points to open-label Week 26 (n=134), and by -7.2 (3.6) points to open-label Week 52 (n=99) (Supplementary Figure 1b).

P7 (hostility) score change in patients with hostility at baseline (P7 score ≥2)

Short-term analyses: In patients with P7 score ≥2 at baseline, brexpiprazole 4 mg was superior to placebo in reducing P7 score at Week 6 (LSMD: -0.34 [95% CLs: -0.55, -0.12]; p=0.0024), independent of improvement in positive symptoms (MMRM Model 1) (Supplementary Figure 2). Similar benefits were observed for brexpiprazole 4 mg when also adjusting for akathisia (MMRM Model 2: -0.32 [-0.54, -0.11]; p=0.0034), or akathisia and somnolence (MMRM Model 3: -0.33 [-0.54, -0.11]; p=0.0033). Brexpiprazole 2 mg showed numerical advantages over placebo in these models (MMRM Model 1: -0.14 [-0.36, 0.08]; p=0.22; MMRM Model 2: -0.12 [-0.34, 0.10]; p=0.28; MMRM Model 3: -0.12 [-0.34, 0.10]; p=0.28).

Long-term analyses: Patients with P7 score ≥2 at baseline showed further improvement in P7 score with long-term brexpiprazole treatment, changing from baseline by a mean (SD) of -1.6 (1.1) points to open-label Week 26 (n=134), and by -1.7 (1.1) points to open-label Week 52 (n=99).

TEAEs in patients with/without hostility at baseline (P7 score ≥2)

Short-term analyses: In patients with P7 score ≥2 at baseline, the incidence of TEAEs over 6 weeks was comparable across treatment groups, in the range of 58.4–60.1% (Supplementary Table 1). A similar incidence of TEAEs was seen in patients with P7 score <2 at baseline, except in the brexpiprazole 2 mg group, which had a lower incidence of TEAEs (53.3%).

The incidence of akathisia over 6 weeks was higher among patients with P7 score ≥2 than those with score <2 (Supplementary Table 1). The highest incidence of akathisia was among patients with hostility at baseline who received the brexpiprazole 4 mg dose (8.1%). The incidences of sedation and somnolence were low (each <5%) in all treatment groups, regardless of hostility status.

Supplement to: Effect of brexpiprazole on agitation and hostility in patients with schizophrenia: post hoc analysis of short- and long-term studies