Interaction of Pipamperone Augmentation of Citalopram and Genetic Variables in the Prediction of Antidepressant Response

Elisabeth Binder, 1,2,3 Charles Nemeroff, 4 Alan Schatzberg, 1,2 Thomas Schlaepfer, 1 Kees Bo, 5 Ludo Haazen, 6 Didier De Chaffoy, 1,2 Erik Buntinx 1

1Max-Planck Institute of Psychiatry, Munich, Germany; 2Emary University School of Medicine, Atlanta, GA, USA; 3University of Miami Miller School of Medicine, Miami, FL, USA; 4Stanford School of Medicine, Stanford, CA, USA; 5University of Bonn, Germany, and Johns Hopkins University School of Medicine, Baltimore, MD, USA; 6Kinesis Pharma BY, Breda, Netherlands; 7PharmaNeo/Booit N.V., Aaken, Belgium

Abstract
Background: Individual variability in observed therapeutic response to antidepressant treatment is in large part due to genetic differences. It is known that genetic factors influence the pharmacokinetics and pharmacodynamics of antidepressants. Thus, polymorphisms in the genes encoding the serotonin receptor 2A (HTR2A) and dopamine D4 receptor (DRD4) are associated with antidepressant treatment outcome. However, the effect of genetic polymorphisms on the response to combination therapy is less well investigated. The aim of the present study was to evaluate whether patients carrying genetic polymorphisms known to be associated with antidepressant treatment outcomes showed a different response to combination therapy. Methods: A phase II double-blind study (ClinicalTrials.gov identifier: NCT00672659) was performed to investigate the effect of combination therapy with PIP (pipamperone) and CIT (citalopram) on antidepressant treatment outcomes. Patients were treated with CIT plus either PIP or placebo for 12 weeks. Blood samples were collected at baseline and weekly. DNA was isolated from whole blood samples using the QIAamp DNA Blood Mini Kit (QIAGEN). The following polymorphisms were tested: rs6265 (Val66Met, HTR2A); rs7997012 (Gkasloc, HTR2A); rs8034171 (S NP, COMT); rs380067 (C NP, BDNF); rs1800497 (Gkasloc, COMT); and rs6265*rs799012 (Val/Val, HTR2A). Results: A significant main effect on T50 was observed for rs6265 (Val66Met polymorphism had a shorter T50 for Val/Val carriers vs. Met/Met carriers) and rs7997012 (interaction for the rs7997012 risk allele of 6.6 days if they were carriers of the G risk allele of rs7997012 in PIP compared to 4.3 d earlier response in the PIP augmentation). Conclusions: This study suggests that patients carrying genetic polymorphisms known to be associated with antidepressant treatment outcomes showed a different response to combination therapy. PIP augmentation affected the response of patients carrying genetic polymorphisms known to be associated with antidepressant treatment outcomes. PIP augmentation improved the response of patients carrying the rs7997012 risk allele, whereas the response of patients carrying other genetic polymorphisms was less affected. These results are in line with previous findings suggesting that PIP may be a promising treatment option for patients carrying genetic polymorphisms known to be associated with antidepressant treatment outcomes.

References

Disclosures
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Figure 2: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 3: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 4: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 5: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 6: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 7: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 8: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 9: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 10: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.

Figure 11: The PIP group showed a significantly faster improvement than the CIT group on all scales, except for BDI and depression. The CIT group showed a significant improvement from baseline to week 12 for all scales, except for BDI.