

Article: 0094

Topic: S36 - Symposium 38: Crestar: Personalized medicine in schizophrenia - Development of pharmacogenomics biomarkers

How Can Pharmacogenomics Biomarkers Be Translated into Patient Benefit

D. Collier¹, E. Achilla², G. Breen³, S. Curran³, D. Dima³, R. Flanagan⁴, J. Frank⁵, S. Frangou⁶, C. Gasse⁷, I. Giegling⁸, M. Rietschel⁵, D. Rujescu⁸, M. Helthuis⁹, J. Maccabe¹⁰, P. McCrone², J. Mill¹¹, E. Sigurdsson¹², H. Stefansson¹³, J. Walters¹⁴, M. Verbelen³

¹Neuroscience Genetics, Eli Lilly and Company Ltd, Windlesham Surrey, United Kingdom ; ²Health Services and Population Research, King's College London, London, United Kingdom ; ³Social Genetic and Developmental Psychiatry, King's College London, London, United Kingdom ; ⁴Clinical Biochemistry, King's College Hospital, London, United Kingdom ; ⁵Genetic Epidemiology in Psychiatry, Central Institute of Mental Health, Mannheim, Germany ; ⁶Psychiatry, Mount Sinai School of Medicine, New York, USA ; ⁷National Centre for Register-Based Research, Aarhus University, Aarhus, Denmark ; ⁸Psychiatry, University of Halle-Wittenberg, Halle, Germany ; ¹⁰Psychosis Studies, King's College London, London, United Kingdom ; ¹¹Medical School, University of Exeter Medical School, Exeter, United Kingdom ; ¹²Psychiatry, Landspítali National University Hospital, Reykjavik, Iceland ; ¹³Genetics, deCODE Genetics, Reykjavik, Iceland ; ¹⁴MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, United Kingdom

Treatment resistant schizophrenia (TRS) is one of the most disabling of psychiatric disorders, affecting about 1/3 of patients. First-line treatments include both atypical and typical antipsychotics. The original atypical, clozapine, is a final option, and although it has been shown to be the only effective treatment for TRS, many patients do not respond well to clozapine. Clozapine use is related to adverse events, most notably agranulocytosis, a potentially fatal blood disorder which affects about 1% of those prescribed clozapine and requires regular blood monitoring. This as a barrier to prescription and there is a long delay in access for TRS patients, of five or more years, from first antipsychotic prescription. Better tools to predict treatment resistance and to identify risk of adverse events would allow faster and safer access to clozapine for patients who are likely to benefit from it. The CRESTAR project (www.crestar-project.eu) is a European Framework 7 collaborative project that aims to develop tools to predict i) treatment response, particularly patients who are less likely to respond to usual antipsychotics, indicating treatment with clozapine as early as possible, ii) patients who are at high or low risk of adverse events and side effects, iii) extreme TRS patients so that they can be stratified in clinical trials for novel treatments. CRESTAR has addressed these questions by examining genome-wide association data, genome sequence, epigenetic biomarkers and epidemiological data in European patient cohorts characterized for treatment response, and adverse drug reaction using data from clozapine therapeutic drug monitoring and linked National population medical and pharmacy databases, to identify predictive factors. In parallel CRESTAR will perform health economic research on potential benefits, and ethics and patient-centred research with stakeholders.