iSAE Consortium Ltd.

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THE INTERNATIONAL SERIOUS ADVERSE EVENTS CONSORTIUM ANNOUNCES RESEARCH RESULT

Clozapine-induced agranulocytosis is associated with rare HLA-B and HLA-DQB1 alleles

Chicago, IL (September 16, 2014) – The International Serious Adverse Events Consortium (iSAEC) announced today results of a genetics research study, completed in conjunction with the Clozapine-Induced Agranulocytosis Consortium (CIAC). The CIAC was led by Patrick F Sullivan, MD, who is in the Departments of Genetics & Psychiatry at the University of North Carolina in Chapel Hill, NC. The iSAEC is a novel, non-profit international research consortium, funded by the global pharmaceutical industry and the Wellcome Trust, to better understand the role genetics plays in drug safety and response.

Although clozapine is a particularly effective antipsychotic, its use is curtailed by the risk of agranulocytosis, a severe adverse drug reaction which occurs in up to 1% of treated individuals. Identifying genetic risk factors for clozapine-induced agranulocytosis (CIA) will likely enable safer and more widespread usage of clozapine for the treatment of schizophrenia. The CIAC performed the largest genetic study of CIA to date by interrogating a cohort of 163 cases using genome-wide SNP genotyping and whole exome sequencing to test common and rare variants for association. It found two loci in the major histocompatibility complex to be independently associated with CIA: a single amino acid in HLA-DQB1 (126Q) (P=4.7x10-14, OR=0.19, 95% CI 0.12-0.29) and an amino acid change in the extracellular binding pocket of HLA-B (158T) (P=6.4x10-10, OR= 3.3, 95% CI 2.3-4.9).

"Clozapine-induced agranulocytosis is associated with rare HLA-B and HLA-DQB1 alleles". Patrick F Sullivan, Jackie I. Goldstein, et al., Nature Communications, DOI: 10.1038/ncomms 5757, 4 September, 2014.

About the iSAEC (http://www.saeconsortium.org)

The International Serious Adverse Event Consortium (iSAEC) is a 501(c) organization dedicated to identifying and validating DNA-variants useful in predicting the risk of drug-related serious adverse events. The Consortium brings together the pharmaceutical industry, regulatory authorities and academic centers to address clinical and scientific issues associated with drug-related serious adverse events. iSAEC partners are providing financial support, in-kind donations, and participation in data collection to the Stage II research. The iSAEC is the only privately-funded international partnership dedicated to studying the genomics of drug induced serious adverse events.

iSAEC Membership and Collaborators

The iSAEC's participants include representatives from the pharmaceutical industry, the scientific community, and government.

- Pharmaceutical industry members are closely involved in all aspects of the Consortium's research, providing ongoing consultation on the development and structure of the Consortium's scientific models, and contributing cohort data and underwriting costs of the iSAEC's research/operations. The iSAEC's Phase 2 funding members include: Abbott, Amgen, AstraZeneca, Daiichi Sankyo, GlaxoSmithKline, Merck, Novartis, Pfizer, Takeda and the Wellcome Trust.
- iSAEC provides researchers with open access to its data through a controlled-access database (www.saeconsortium.org). Twelve months after genotyping studies are complete, data is released without any patent or intellectual property constraints, allowing for further use and study by interested researchers.