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THE INTERNATIONAL SERIOUS ADVERSE EVENTS CONSORTIUM ANNOUNCES PRED4 STUDY RESULT -- HLA DQA1-DRB1 VARIANTS PREDISPOSE TO PANCREATITIS INDUCED BY THE THIOPURINE IMMUNOSUPPRESSANTS

A PRED Study finds patients with a particular genetic variation are four times more likely to develop pancreatitis if they are prescribed a widely used group of drugs.

Chicago, IL (September 14, 2014) – The International Serious Adverse Events Consortium (iSAEC) announced today results from the Predicting Serious Drug Side Effects in Gastroenterology (PRED) study, being executed in conjunction with Royal Devon & Exeter Hospital (UK) (http://www.rdehospital.nhs.uk/), which also serves as the coordinating center for this international research effort. 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.

The PRED Study has been led by Tariq Ahmad, MD, PhD, and Professor of Gastroenterologist and Graham Heap, MD at the Royal Devon & Exeter Hospital in England. Through a study focused on the genetics of thiopurine induced pancreatitis, PRED researchers have discovered patients with a particular genetic variation are four times more likely to develop pancreatitis if they are prescribed thiopurines. Pancreatitis is a serious adverse effect of several drug therapies and occurs in approximately 4 to 7% of patients treated with the thiopurines azathioprine or mercaptopurine. The drugs, which include azathioprine and mercaptopurine, are some of the most effective and most commonly used drugs to suppress the immune system in the treatment of Inflammatory Bowel Disease (IBD), rheumatoid arthritis and after some organ transplants. The development of pancreatitis is unpredictable and almost always leads to drug withdrawal.

The PRED researchers identified 441 inflammatory bowel disease (IBD) patients who had developed pancreatitis within three months of starting these drugs from 168 sites around the world. Strong evidence of association was identified within the class II HLA region with the most significant association at rs2647087 (Odds ratio 2.59, 95% CI 2.07 – 3.26 P=2x10-16). These findings were replicated in an independent set of 78 cases and 472 IBD controls matched for drug exposure. Imputation fine mapping of the HLA region identified association with the HLA-DQA1*02:01-HLA-DRB1*07:01 haplotype. Patients homozygous for the at-risk allele have a 17% risk of developing pancreatitis after administration of azathioprine or mercaptopurine.

“It is extremely exciting to identify genetic markers which can predict patients who are at risk for develop pancreatitis when prescribed thiopurines associated with the treatment of Crohn's disease and ulcerative colitis.” said Arthur L. Holden, Chairman and CEO of the iSAEC. “As we expected, these results indicate similar patterns of genetic contribution, as we have seen in our ground breaking research into the genetics of drug-induced liver and skin injury."

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.

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