Mechanisms and Biomarkers of Drug-Induced Liver Injury
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Drug-induced liver injury (DILI) occurs with an annual incidence of about 14 to 19 per 100,000 inhabitants according to surveys in France and Iceland. About 2,000 cases of acute liver failure (ALF) occur annually in the US. About half of ALF cases are due to DILI, the leading drug being paracetamol. Non-paracetamol causes represent about 10 to 15% of DILI cases, especially amoxicillin/clavulanate, isoniazid and NSAIDS. Of note, herbals and dietary supplements are increasingly being recognized as potential causes of liver injury.

Current management of DILI would benefit greatly from novel biomarkers that separate patients with a likelihood of recovering spontaneously from those who are at risk of worsening to a state of advanced liver injury with a requirement for liver transplantation. Examples of idiosyncratic DILI resulting in liver failure include lumiracoxib, troglitazone (withdrawn in May 2000), and bromfenac (withdrawn in June 1998). A biomarker that could predict the clinical course of a patient in whom a drug-induced elevation of alanine transaminase (ALT) has been observed could help to scale the risk of subsequent deterioration, which would also impact on the overall clinical management.

The IMI SAFE-T Consortium (Safer And Faster Evidence-based Translation) was initiated to qualify new biomarkers for drug-induced kidney injury (DIKI), drug-induced liver injury (DILI) and drug-induced vascular injury (DIVI) for human applications. A panel of potential biomarkers for DIKI, DILI, and DIVI was assessed in clinical studies in healthy volunteers and patients with drug- and non-drug induced kidney, liver and vascular injuries and common systemic diseases. Investigations on biologic/mechanistic understanding for DIKI, DILI, and DIVI biomarkers was undertaken to support the clinical scientific qualification strategy of the candidate biomarkers.

Results from the SAFE-T consortium on novel DILI biomarkers will be presented.