SUMMARY AND CONCLUSION

DILI is becoming a significant public health issue because of its potential impact, not only on patients but also on the development of new drugs. DILI events are the main cause of regulatory action pertaining to drugs, including denial of marketing approval, restrictions with respect to clinical indications, and withdrawal from the marketplace. What makes DILI so difficult to manage is that it often occurs in only a small fraction of the treated population. Because it is not possible to identify thesesusceptible patients before they actually develop DILI, the physician must view all treated patients as being at risk for DILI during treatment with potentially hepatotoxic drugs***(Watkins, et al 2008).***

Jaundice and other symptoms of liver injury may indicate severe or even life-threatening liver injury. In order to detect DILI at the early, presymptomatic stage, it is often recommended that the patients undergo frequent monitoring of serum alanine aminotransferase (ALT) levels, although there is no clear evidence that this practice has been effective in reducing the incidence of DILI***(Senior 2009).***

For many drugs, it is not necessary to stop treatment in the face of asymptomatic elevations in liver biochemical parameters because these elevated levels will frequently resolve even if the drug treatment is continued. This phenomenon of “adaptation” has been observed in relation to most of the drugs that have potential to cause acute liver failure, including isoniazid, troglitazone, and ximelagatran. It is believed that severe liver injury occurs in the subset of patients with elevations in ALT level that cannot adapt to the initial mild toxicity. It is not currently

possible to distinguish patients with benign and reversible elevations in ALT level from those in whom the liver injury will progress. Genetics has had some success in helping to avert hypersensitivity drug reactions***;*** however, to date, genetic markers of DILI susceptibility have not been sufficiently predictive to make their way into the clinic. It is likely that susceptibility to DILI is often not a function of genetic predisposition alone and that environmental factors play an important role. For example, patients who develop clear-cut DILI with the use of a particular drug may not experience DILI again when re-treated with the same drug months or years later. ***(Watkins, et al 2008)***.

Serum adducts, lymphocyte transformation test, anti-liver antibodies, metabolomics, transcriptomics, and Proteomics are promises and challenges in developing and validating biomarkers that could improve the diagnosis and management of DILI. ***(Connell, Watkins 2010)***.