Drug-induced liver injury registries are important

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Abbreviations

DILI - Drug-induced liver injury, **Pro-Euro-DILI-** prospective European DILI study**, MARS-** Molecular Adsorbent Recirculating System

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We would like to thank Steven Trinh et al. for interest in our paper recently published in the journal (1). We are particularly happy to hear about the increasing interest for DILI in Australia. Apart from characterizing the most important drugs leading to DILI major objective of the Pro-Euro-DILI registry is to try to detect novel biomarkers in patients with DILI that may better distinguish DILI from other liver diseases (2). Patients who are suspected to have DILI but in the diagnostic work-up found have another liver disorder such as viral or autoimmune hepatitis are used as controls. Using this nested case-control design, we have identified, evaluated and validated novel biomarkers which can distinguish DILI from acute liver injury resulting from alternative aetiology (3) Furthermore, this prospective study has also the aim to analyze biomarkers that might be useful for prognostic assessment in patients with DILI, an important case of need in this field (4). However, the study is not population based and most of the participating centers from Spain, England, Germany, Switzerland and Iceland are from tertiary referral centers. As in other DILI studies from referral centers, 60-70% of patients present with jaundice (~~3-5~~5-7). However, in population based studies, approximately 25-30% of DILI patients present with jaundice in prospective population based studies (~~6-7~~8-9), which is in line with the Australian experience (1).

Steven Trinh et al. suggest that there is a need to determine the role of medical therapy for DILI. Currently, the management of patients with DILI is mainly symptomatic and there is no evidence based pharmacological treatment that has been shown to be able to change the natural course of the liver injury in DILI patients in general, other than withdrawing the suspected offending agent and providing supportive care (~~8-11~~10-13). Therefore, there is a medical need to identify an effective therapy for DILI in patients who otherwise might develop acute liver failure and/or have prolonged jaundice and itching. In the Spanish hepatotoxicity registry (20%) received treatment according to the physician's criteria (~~4~~6). Usually cases were more severe, patients were jaundiced and hospitalized, 52% received corticosteroids, 39% ursodeoxycholic acid, 9.4% MARS (~~4~~6).
Corticosteroid group had much higher mortality but they were also sicker to start with (~~4~~7). Indeed, the association between corticosteroid treatments and clinical outcomes could be confounded by various factors influencing physicians' decisions. Therefore, the question would be, are corticosteroids helping patients or hurting them? Clearly, the data included in the registry cannot address the role of medical therapy for DILI and other approaches are necessary. Interestingly, in a propensity score-matched analysis with 724 well-characterised

DILI cases (with and without hypersensitivity features) prospectively included in the Spanish DILI Registry and Indiana University School of Medicine, corticosteroid administration was not associated with an increased risk of developing acute liver failure and seemed to be safe. (~~12~~14). Furthermore, patients receiving corticosteroids had a significantly higher normalisation rate of liver enzymes than untreated patients (~~12~~14).

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