need to come up with a study design, with adequate endpoints to assess effect of an intervention on DILI clinical outcomes and to set up a Network of centers for clinical research including Transplant centers to achieve this goal.

The multidisciplinary collaborative approach of ProEuroDILINet (https://proeurodilinet.eu) provides an ideal environment for innovation.

COST's support for networking led to important effects at the level of individual researchers and their institutions, which included the building of trust of the participating partners and the promotion of interdisciplinary partnerships and STSMs, fostering international publications that would smooth the further joint international research projects and a road map on DILI. Actions to compromise ECI, increase their leadership, provide mentorship and ease their way forward are underway.

The exceptional situation of COVID 19 pandemic represents a major scientific challenge that have clearly hampered the full intended achievements and objectives of EU COST Actions. The COVID-19 pandemic has highly reduced the mobility and networking possibilities that our COST Action wanted to develop. Indeed, traveling and the movement of people has been severely affected. To mitigate impact on the COST Action goals we have organized virtual meetings – across the COST-DILI Action. Hopefully we may resume on-site meetings in the second semester of 2021.

COST DILI Lecture 1

MAFLD & DILI: Clinical and Pathophysiological Interactions

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Introduction: MAFLD, metabolic associated fatty liver disease describes all liver diseases associated with metabolic dysfunctions, being the hepatic manifestation of a systemic and heterogeneous disorder. It is characterized by great variability among affected patients, based on age, gender, ethnicity, genetic predisposition, metabolic disease and gut microbiota, which in turn generate different phenotype of high level of clinical complexity. MAFLD patients have an increased cardiovascular risk and thus, are exposed to polypharmacy. DILI, which acts synergistically with MAFLD, refers to adverse drug reactions involving the liver due to xenobiotics, at the usual dose.

Main text: Several studies have shown that patients with chronic liver disease have increased risk of death or liver transplant after DILI. A prospective study carried on by DILIN, showed that 10 % of patients developing DILI with pre-existing liver diseases had grater mortality, maybe due to such comorbidities, as diabetes. This study confirmed previously obtained results in which patients with visceral adiposity had a fourfold increase of DILI risk when exposed to common drugs. Recently, it has been clarified that MAFLD patients are at major risk of DILI development with more severe outcomes, because of impaired drug processing, modified toxicological responses and immune or inflammatory response modified by metabolic factors. On this regard, some drugs, as glucocorticoids, valproate, didanosine, methotrexate, tamoxifen and others are responsible of a clinical picture of drug-induced steatohepatitis, in which such drugs may acts as inducing de novo steatosis or worsen a pre-existing condition.

Conclusion: Given the increased risk of MAFLD patients for developing severe DILI, several studies are needed in order to establish criteria for early diagnosis, comorbidities and risk stratification.

COST DILI Lecture 2

Clinical Trials and Drug-Induced Liver Injury: Where do We Stand and Future Perspectives

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Introduction: There is no specific therapy approved for idiosyncratic drug-induced liver injury (DILI). Therapeutical options tested in randomized clinical trials (RCTs) have yielded inconclusive findings. Within the Working Group 4 of the COST ACTION 17112 (PRO-EURO DILI NETWORK), we performed a systematic review and meta-analysis to summarize the design and findings of RCTs in the prevention and management of idiosyncratic DILI.

Main text: A systematic literature search up to January 31st, 2020, was performed. We used a recognized scale to assess methodological bias. After screening and review candidate manuscripts, we included 22 RCTs, 12 on prevention and 10 on management of DILI. Silymarin, bicyclol, magnesium isoglycyrrhizinate and N-acetylcysteine were the most common compounds tested. Only a minor proportion of RCTs showed a strong methodological design with low risk of bias. There was a great heterogeneity on DILI diagnostic criteria, and only few trials reported about the causality assessment method. Based on the scarce number of trials available, tested agents showed limited efficacy in DILI prevention and management. Altogether, the tested agents showed a safe profile.

Conclusions: Due to the methodological flaws in RCTs in DILI, international research networks are needed to establish a standardized framework on RCTs design and therapeutic endpoints.

KLINICKÁ FARMAKOLÓGIA A COVID-19

Controversies and New Trends in the Treatment of COVID-19

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Introduction: COVID-19 has become a global pandemic with severe health issues around the world. Although COVID-19 primarily affects respiratory system, it is generally accepted that it is a complex multisystemic disease. Its pathogenesis involves a biphasic immune response. The initial stage is characterized by viral replication induced tissue damage and, in