if the preterm/term infant survived the neonatal period or 2) unsuccessful if there was a miscarriage/fetal demise/perinatal death. Drug regimen during pregnancy were 1) penicillamine (DPA), 2) zinc (Zn) or 3) DPA/Zn if the patient had switched therapy for any reason. Statistical analysis was carried out using Fisher's test, with significance level at $p<0.05$.

Results and Discussion: Of the 49 pregnancies analyzed, 2 (4.1%) ended in maternal death and 17/49 (34.7%) in miscarriage/fetal or neonatal death. The Table below presents the results. The analysis of medication and pregnancy outcomes combined deteriorating and stable cases. There was a correlation between successful births and asymptomatic patients who had given birth before the onset of WD ($p<0.001$). In stable patients, successful births were slightly above significance ($p=0.062$). There was no significant difference among the outcomes in relation to the medication taken.

Conclusions: Pregnancy in symptomatic WD is potentially harmful to mother and conceptus. Successful births were significantly associated with pregnancies before the onset of WD symptoms, but were also possible with stable disease under treatment. Anti-copper drug regimen was not associated with pregnancy outcome.

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OP-16 FREQUENCY OF ATP7B GENE MUTATIONS IN A BRAZILIAN COHORT OF PATIENTS WITH WILSON'S DISEASE

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Conflict of interest: No

Introduction and Objectives: Wilson's disease (WD) is a rare genetic disease presenting more than 900 mutations in the ATP7B gene. The knowledge of the regional distribution of these mutations can improve the diagnosis of WD. We aimed to evaluate the frequency of ATP7B mutations in a WD Brazilian cohort and the association with disease phenotypes.

Patients / Materials and Methods: We performed molecular analysis by NGS of the 21 exons of ATP7B (Mendelics Genomic Analysis Laboratory) in patients with diagnosis of WD and in first-degree relatives undergoing WD investigation, followed in a single hepatology center. Demographic data and predominant type of WD presentation were assessed.

Results and Discussion: 28 patients were included (60% female; mean age 25 $\pm$ 13 years): 25 had an established diagnosis of WD and 3 were heterozygous relatives without disease. The phenotypes of WD were as follows: 15/25 (60%) with exclusively hepatic manifestation, 8/25 (32%) combination of hepatic and neurological, 1/25 (4.0%) isolated neurological manifestations and 1/25 (4.0%) were pre-symptomatic. We identified 17 ATP7B gene distinct mutations. The pathogenic variants c.3402delC, c.2123T>C and c.3818C>T presented the highest allele frequency, respectively, 25.5%, 15.7% and 15.7%. The majority (80.0%) presented the mutation in compound heterozygosity, 12.0% in homozygosity and 8.0% in simple heterozygosity. The c.2145C>T, c.1552T>C and c.3188C>T variants were considered of undetermined significance; c.2072G>T and c.3071_3072delTG variants were considered probably pathogenic. Regarding the disease phenotype, patients with mutations c.3402delC CG>C and c.2123T>C presented equal distribution of isolated hepatic or hepatic plus neurological phenotype, while c.3818C>T mutation was associated with predominantly hepatic phenotype. Presence of exon 2 deletion was associated with severe neurological manifestations.

Conclusions: The mutations c.3402delC, c.2123T>C and c.3818C>T were the most prevalent. The c.2145C>T and c.3188C>T variants, considered of undetermined significance, were found in confirmed cases of WD. An important heterogeneity of the ATP7B genotype associated with variation in phenotypic presentation was observed.

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P- 1 DEVELOPMENT OF LENTIVIRAL VECTORS FOR INHIBITION OF HEPATITIS B VIRUS, VIA SMALL INTERFERING RNA

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Conflict of interest: No

Introduction and Objectives: INTRODUCTION: Chronic hepatitis B represents a significant global health challenge. Current treatments often fail due to the persistence of HBV DNA as covalently closed circular DNA or integrated into the host genome, leading to viral reactivation. RNA interference (RNAi) emerges as a promising approach for treating chronic hepatitis through post-transcriptional gene silencing. OBJECTIVE: To design and evaluate the efficacy of RNAi lentiviral vectors targeting key HBV proteins (HBsAg, HBcAg, HBeAg) and pregenomic RNA (pgRNA) for silencing.

Patients / Materials and Methods: Silencing vectors were designed to target overlapping open reading frames, allowing simultaneous silencing of multiple viral proteins and pgRNA with a single RNAi construct. Three vector candidates (siHBV-1 to 3) underwent rigorous in silico testing to minimize off-target effects, evaluating stability and secondary structures. Lentiviral vector production was assessed using flow cytometry to detect green fluorescent protein expression in cell culture. Huh7 cells were transfected with 1 μg of purified HBV genotype A circular monomers, followed by infection

with the first lentiviral candidate (siHBV-1), targeting S/Pol genes of HBV (108 TU/mL), three days later. Quantification of HBV proteins using chemiluminescence and HBV DNA using quantitative PCR (qPCR) was performed throughout the post-transfection period.

Results and Discussion: Effective silencing of HBsAg expression was observed in cells infected with siHBV-1, with undetectable levels from the third day post-infection compared to untreated controls ($p<0.002$). Furthermore, HBV DNA was undetectable by qPCR, indicating successful silencing of HBV genotype A in vitro. The production of lentiviral candidates siHBV-2 and siHBV-3 is currently under evaluation. Flow cytometry will be used to determine the transduction rates in Huh7 cells once the tests are completed. Future investigations will explore combinations of these three siHBV vectors to optimize HBV silencing.

Conclusions: Lentiviral vector-mediated RNAi offers a promising approach for sustained suppression of HBV replication and gene expression, potentially promoting HBV clearance in chronic carriers.

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P-2 RECAM VS. RUCAM: ADVANCING THE DIAGNOSIS OF IDIOSYNCRATIC DILI WITH A REVISED ELECTRONIC APPROACH.

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Conflict of interest: No

Introduction and Objectives: Background: RUCAM has been a cornerstone in the causality assessment of DILI for the last three decades. However, the emergence of the Revised Electronic Causality Assessment Method (RECAM) promises enhanced accuracy and efficiency. Aim: to compare both scales and assess RECAM's performance in a prospective DILI registry.

Patients / Materials and Methods: The analysis was conducted on well-vetted DILI cases from a prospective multicenter cohort from a single country, in which RUCAM initially assessed causality. After applying the RECAM, the results and significant causes of discrepancy were analyzed

Results and Discussion: among 180 DILI-suspicions induced by conventional agents, RUCAM excluded 3.8% of cases and classified 38.8% as highly probable, 41.6% as probable, and 15.5% as possible. RECAM upgraded 66 cases (36.7%), downgraded 42 (23.3%), and left 72 (40%) unchanged. RECAM upgraded seven cases excluded by RUCAM to probable (3) or possible (4) and excluded one case considered probable by RUCAM. The figure shows the flow of classifications from RUCAM to RECAM. Variability in results between the RECAM and RUCAM was mainly due to differences in the domains assessing latency, particularly prolonged onsets (>60 days after drug initiation or >30 days after cessation accounted for 42.5% of differences), and the lack of Virus E serology as a determining factor.

Conclusions: RECAM proved to be a straightforward tool for evaluating DILI causality in clinical practice, offering improved objectivity when used prospectively and with all critical information available (particularly hepatitis virus markers). However, it is crucial to remain vigilant and pay particular attention to drugs with a long latency period.

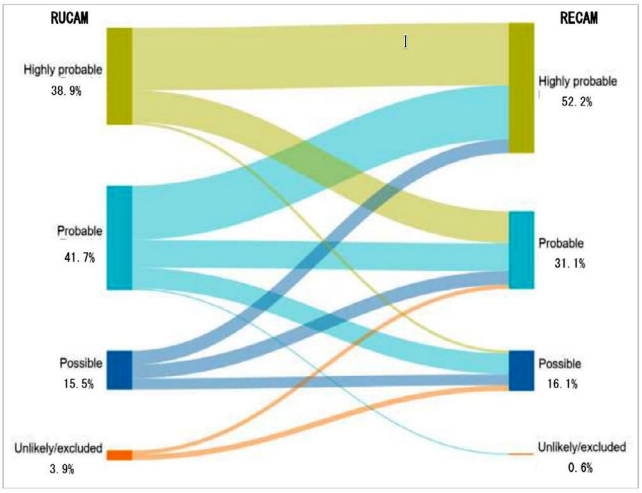

Figure: The flow of classifications from RUCAM to RECAM shows shifts into higher likelihood categories of DILI and how the revised method reclassifies cases initially categorized by the previous method.

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P-3 FACTORS ASSOCIATED WITH AN IMPROVEMENT IN SEQUENTIAL LIVER STIFFNESS MEASURES BY TRANSIENT ELASTOGRAPHY IN MASLD PATIENTS WITH PREDIABETES AND TYPE 2 DIABETES.

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Conflict of interest: No

Introduction and Objectives: There is increasing evidence that a ≥20% decrease in sequential liver stiffness measurements (ΔLSM) by transient elastography (TE) is associated with a lower risk of long-term liver-related outcomes and mortality in patients with MASLD. Objective: We aimed to evaluate factors associated with ≥20% decrease in ΔLSM in MASLD patients with prediabetes (Pre-DM) and type 2 diabetes (T2DM).

Patients / Materials and Methods: MASLD adults with PreDM or T2DM with two consecutive reliable LSMs by transient TE (Fibroscan Touch 502) were included. Clinical, biochemical and elastography data were collected at baseline and follow-up. PNPLA3 (rs738409 C>G) genotypes were determined. A multivariate logistic regression analysis was performed to evaluate the variables independently associated with ≥20% decrease in ΔLSM. All data were analyzed using the statistical package SPSS (vs.24.0,IBM), a p-value < 0.05 was regarded as significant.

Results and Discussion: 294 patients were included (70% female, 60 ± 10 y, 63% with BMI ≥ 30 kg/m2): 14% had PreDM and 86% T2DM. Genotyping of PNPLA3 was identified as CC in 46% and CG+GG in 54%. At the first TE, 10% had LSM > 15kPa [median 7.0 kPa (5.1-10.1)]. Overall, 31% experienced a ≥20% decrease in ΔLSM on a 38 (26-52) months interval.