IDDF2020-ABS-0053 PREDICTION OF PATIENT MORTALITY RELATED TO THE LIVER DYSFUNCTION IN ICU BASED ON MACHINE LEARNING

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Background The traditional mortality prediction method for patients related to the liver dysfunction is to use the APACHE scoring system for mortality prediction. To evaluate the prediction of patient mortality related to the liver dysfunction in ICU based on machine learning.

Methods It directly extracts patient data from the MIMIC-III and Philips eICU collaboration databases. For the missing value part of the sample set, we analyzed the significance of sample characteristics Gini, chose to use the median to fill missing values on the MIMIC-III sample set, and use the majority to fill missing values on the eICU sample set. After normalizing the data, principal component analysis (PCA) was used to reduce the dimensionality of the sample set's sample features, and the effect of the predictive model trained on the sample sets before and after dimension reduction was compared. Next, we used machine learning methods such as random forest, support vector classification, and multi-layer perceptron neural network to achieve liver dysfunction prediction, mortality prediction, and liver dysfunction on the MIMIC-III and eICU sample sets, respectively.

Results In the process of analyzing the predictive model, we found that some of the sample features showed higher importance in the prediction of patient mortality by comparing the Gini importance of sample features. At the same time, compared with the original sample set, the anion gap shows a higher Gini importance when predicting the mortality of the liver dysfunction sample set, and the liver dysfunction sample set after removing the anion gap. The rate of death predictions has slipped, suggesting a potential link between anion gaps and the liver dysfunction.

Conclusions Compared with the original sample set, the lactic acid shows a higher Gini importance when predicting the mortality of liver dysfunction sample set, and the liver dysfunction sample set after removing the lactic acid. The rate of death predictions has slipped, suggesting a potential link between lactic acid and liver dysfunction.

IDDF2020-ABS-0057 RISK OF INCIDENT HEPATOCELLULAR CARCINOMA (HCC) IN CHRONIC HEPATITIS B (CHB) VIRUS-INFECTED PATIENTS TREATED WITH TENOFOVIR DISOPROXIL FUMARATE (TDF) VERSUS ENTECAVIR (ETV): A US ADMINISTRATIVE CLAIMS ANALYSIS

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Background TDF and ETV are first-line treatments for CHB virus infection. A recent analysis of nationwide insurance data from Korea suggested that the risk of HCC may vary by type of CHB treatment; however, this finding was based on a limited follow-up period following TDF approval in Korea in 2012 and has not been replicated in large datasets outside of Asia. The objective of this analysis was to explore the long-term risk of HCC with TDF vs. ETV in treatment naïve (TN) CHB patients in a US administrative claims dataset.

Methods Among 158,272 patients with evidence of CHB and administrative medical claims between January 2006 and September 2018, we identified TN patients exposed to TDF (N=6,145) or ETV (N=4,046) with at least 1 year of continuous enrollment prior to cohort entry. Exclusion criteria included coinfection with HCV, HDV, or HIV; prior exposure to peginterferon or nucleos(t)ide analogues; HCC or liver transplant prior or up to 6 months after initiating treatment. Absolute rates and corresponding 95% CIs were determined for each treatment group, Cox proportional hazards methods were used to estimate the risk of incident HCC associated with TDF vs ETV. To account for the effects of potential differences in demographics and baseline health status, we incorporated multivariable adjustment and weighting based on treatment propensity scores.

Results Median follow-up duration was comparable in TDF- vs ETV-treated patients among TDF-treated CHB patients, the absolute rate of HCC was approximately half that of patients treated with ETV (0.32 per 100 PY (CI: 0.23 – 0.43) vs 0.61 per 100 PY (CI: 0.45 – 0.80)). After adjustment for age group, sex, baseline health conditions and propensity score weighting, TDF remained associated with a significantly decreased risk of HCC compared to treatment with ETV (HR: 0.56, CI: 0.37 – 0.86).

Conclusions In this analysis of commercially insured, TN CHB patients in the US, the absolute rate of HCC was lower in those treated with TDF than with ETV. After adjustment, treatment with TDF remained associated with a significantly decreased long term risk of HCC, consistent with recent findings from Asia.

IDDF2020-ABS-0058 48-WEEK SAFETY AND EFFICACY OF SWITCHING TO TENOFOVIR ALAFENAMIDE (TAF) FROM TENOFOVIR DISOPROXIL FUMARATE (TDF) IN CHRONIC HBV ASIAN PATIENTS WITH TDF RISK FACTORS (RF)

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Background In a recent Phase 3 study (Study 4018) in HBV patients suppressed on TDF treatment, switching to TAF demonstrated non-inferior efficacy to continued TDF with superior bone and renal safety at Week 48. This study is to assess the safety and efficacy of switching to TAF from TDF in patients of Asian descent with risk factors for TDF toxicity as per current EASL and AASLD guidelines.

Methods Virally suppressed patients (HBV DNA <20 IU/mL at screening) on TDF were randomized (1:1) to switch to TAF or continue TDF for 48 weeks in a double-blind fashion. Viral suppression and changes in bone (BMD by DXA) and renal (creatinine clearance [$eGFR_{CG}$]) parameters were assessed over 48 weeks.

Results Among the 400 Asian patients enrolled, 288 (72%) had at least 1 TDF RF. At Week 48, similar proportions with ≥1 RF had HBV-DNA <20IU/mL (TAF 97%; TDF 97%) and normal ALT by 2018 AASLD criteria (TAF 76%; TDF 73%). TAF subjects with ≥1 RF had increases in $eGFR_{CG}$compared to decreases on TDF [median (Q1, Q3) change; TAF: +2.6 (-2.01, 7.34); TDF: -2.7 (-7.56, +15.79); p<0.0001)]. Among patients with ≥1 RF, improvements were seen in BMD for TAF vs. continued declines in TDF patients at both spine (p<0.0001) and hip (p<0.0001).

Conclusions Virally suppressed Asian patients with CHB and risk factors for TDF who switched to TAF showed improved bone and renal safety while efficacy was well-maintained.

IDDF2020-ABS-0059 SAFETY AND EFFICACY OF SOFOSBUVIR/VELPATASVIR (SOF/VEL) IN PEDIATRIC PATIENTS 6 TO < 18 YEARS OLD WITH CHRONIC HEPATITIS C (CHC) INFECTION

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Background DAA regimens have been approved for CHC treatment in 12 to <18 years, but for younger children, the standard of care is still pegylated-interferon plus ribavirin for ≤48 weeks. We evaluated the safety and efficacy of the pangenotypic regimen of SOF/VEL in children 6 to <18 years.

Methods Patients 6 to <18 years with CHC of any genotype (GT) were enrolled in this open-label, ongoing study. Patients 6 to <12 years received SOF/VEL 200 mg/50 mg and 12 to <18 years SOF/VEL 400 mg/100 mg QD for 12 weeks. Key efficacy endpoint was SVR12. Safety was assessed by adverse events (AEs) and clinical/laboratory data. Intensive pharmacokinetic sampling on Day 7 in a subgroup of patients of each age group was done to confirm the appropriateness of the chosen dose.

Results 102 patients 12 to <18 years and 73 patients 6 to <12 years were enrolled. GT distribution was 75% GT1, 5% GT2, 13% GT3, 3% GT4, 3% GT6; 51% female, 80% white, 85% treatment naïve, and 91% vertically infected. Intensive pharmacokinetics confirmed that the doses selected were appropriate. SVR12 rate was 95% (97/102) and 92% (67/73) among patients 12 to <18 years and 6 to 12 years respectively; 1 patient in each age group had virologic failure, the remaining patients did not achieve SVR for non-virologic reasons. Most AEs were mild or moderate. 5 subjects had serious AE none of which was attributed to treatment, 2 patients discontinued treatment due to AEs and considered treatment unrelated. The most common AEs (>15%) were headache, fatigue, and nausea in adolescents and vomiting, cough and headache in 6 to <12 years.

Conclusions In patients 6 to <18 years with GT1, 2, 3, 4 or 6 CHC infection, treatment with SOF/VEL for 12 weeks resulted in ≥ 92% SVR12 rate. SOF/VEL was well tolerated, supporting its potential as a treatment option for children 6 to 17 years of age. The study is ongoing in children aged 3 to <6 years old.

IDDF2020-ABS-0060 IMPACT OF PRIOR TENOFOVIR DISOPROXIL FUMARATE (TDF) TREATMENT DURATION ON TENOFOVIR ALAFENAMIDE (TAF) SAFETY PROFILE IN VIRALLY SUPPRESSED CHRONIC HBV PATIENTS SWITCHED FROM TDF TO TAF

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Background TAF demonstrated noninferior efficacy to TDF with a superior bone and renal safety profile, in viremic chronic HBV (CHB) patients through week 96, and in virally suppressed patients switched from TDF to TAF at 48 weeks. The duration of prior TDF therapy may influence the degree and rate of recovery of bone and renal function following switch to TAF. Here, we evaluate the impact of prior TDF treatment duration on the safety profile of TAF in virally suppressed patients.

Methods In a double-blind, randomized, multicenter, active-controlled, Phase 3 study, 488 CHB patients who were virologically suppressed on TDF for 1 year, and on TDF monotherapy for 6 months were randomized 1:1 to switch to TAF or continue TDF for 48 weeks. In patients originally randomized to receive TAF, renal, bone, and lipid parameters were categorically evaluated by the duration of prior TDF treatment:

Results Of the 243 patients switched to TAF from TDF, 105 (43%) and 138 (57%) had received TDF for 50 years, 74% male, 80% Asian, median $eGFR_{CG}$91 mL/min, 4% and 12% had osteoporosis at hip and spine, respectively. Similar changes in renal, bone, and lipid parameters following 48 weeks of TAF treatment were observed by TDF treatment duration. A