
2021 SCSG
LIVER
SYMPOSIUM

# Update: Viral Hepatitis Abstracts from AASLD

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# Disclosures

- I receive institutional grant support from Gilead Sciences Inc.

# Updates on…

1. Epidemiology and Elimination
2. Viral Hepatitis and HCC
3. Considerations with Current Treatments

# Epidemiology and Elimination

# Global HBV Cascade of Care: The Pre-COVID-19 Baseline

## BACKGROUND & AIMS

- 2019 is an important baseline year for global hepatitis elimination targets to evaluate pre- and post-COVID-19 efforts
- **AIM**:
  - To estimate the global cascade of care for HBV in 2019 prior to impact of COVID-19
  - To quantify the progress of prevention programs using 5-year-old prevalence as proxy

## METHODS

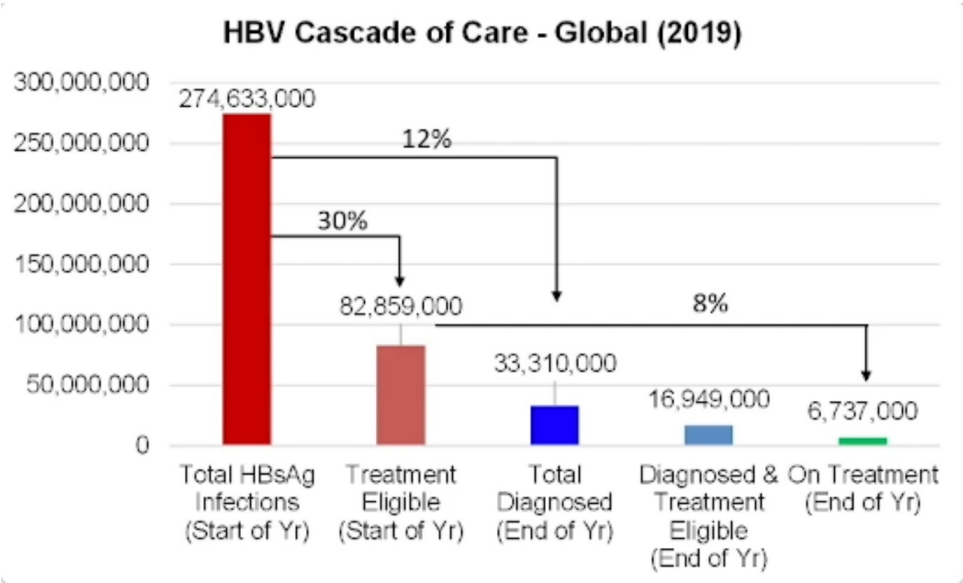
- Used the PRoGReSs model for all output= fully dynamic HBV disease burden and transmission Markov model
  - Diagnosis data collected from national registries
  - Treatment data from country reports and sales data
- 166 country specific fully dynamic disease burden and transmission models
  - 94 received feedback from country experts (Delphi method)
  - 40 based on country data
  - 32 extrapolated by GBD region

# Global HBV Cascade of Care: The Pre-Covid-19 Baseline

**RESULTS**

- 2020 targets for HBV diagnosis were not reached by any continent, though Europe came close (25%)
  - The road to 2030 targets is long for all
- 90% of all HBV treated cases are in 8 countries
- MTCT disparity exists
  - Asia accounts for 69% of all infections but only 33% of 5-year-olds
  - Africa (65%) has highest proportion of 5-year-olds infected
  - More prominent in low-middle income countries

## Global HBsAg prevalence = 3.6% (3.1-4.2%)




**CONCLUSION** **Global increases in screening and treatment are necessary. Lower-middle and low-income countries require additional measures beyond standard of care to prevent MTCT.**

*Razavi-Shearer D, et al. AASLD TLMdX 2021*

# Global Status Update on HCV Prevalence and Cascade of Care Entering 2020

## BACKGROUND & AIMS

- 5 years since global hepatitis elimination targets were set
- Countries had been making progress towards HCV elimination before COVID-19
- **AIM**: to evaluate national, regional, and global progress towards HCV elimination at the start of 2020

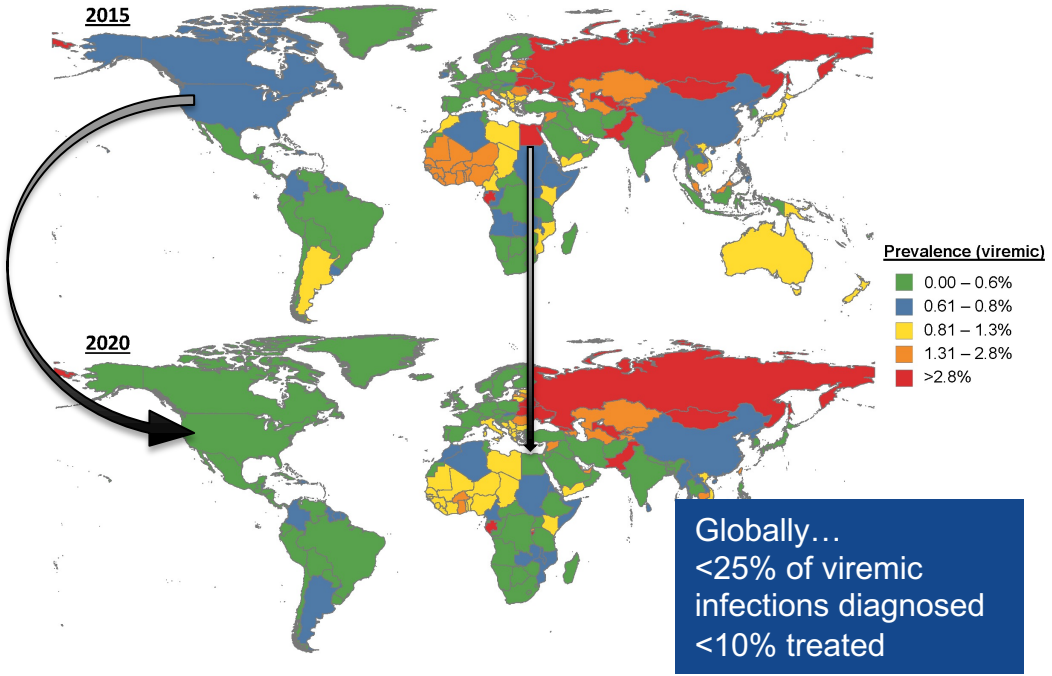
## METHODS

- Integrated literature review, Delphi process and modeling
- Epidemiological data were collected from published and unpublished sources
  - Validated in collaboration with country experts
- Collected data entered into country-level Markov models (HCV Bright model)
  - Used natural history of disease to forecast HCV prevalence and disease burden
  - Regional and global averages were calculated and used to extrapolate for countries with insufficient data

# Global Status Update on HCV Prevalence and Cascade of Care Entering 2020

**RESULTS**

- 110 countries with models (80 approved by country experts)
- **Global prevalence of *viremic* HCV estimated to be 0.75% (0.6-0.8%) at start of 2020**
  - Equal to 59 million viremic infections
  - ↓ 7 million from 2015 estimate
- In 2019:
  - 1.3 million newly diagnosed
  - 2.9 million started on treatment
  - 9.4 million treated between 2015-2019
    - more than one-third in Egypt




Globally…
<25% of viremic infections diagnosed
<10% treated

**CONCLUSION** **Global prevalence of HCV has declined. 59 million viremic infections remain, providing a jumping off point for continued efforts toward HCV elimination.**

*Blach S, et al. AASLD TLMdX 2021*

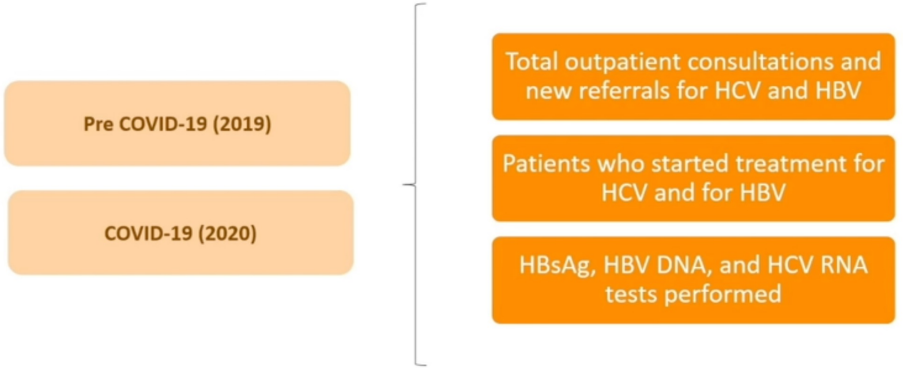
# COVID-19 Impact on Viral Hepatitis B and C Elimination: Preliminary Results in 31 Centres Worldwide

## BACKGROUND & AIMS

- Real-world impact of COVID-19 on viral hepatitis elimination is unknown
- Cannot rely on mathematical models alone for accurate estimates
- **AIM**: to compare practices on viral hepatitis elimination goals pre- and post-COVID-19 pandemic through an international survey

## METHODS

- *Prospective web-based survey (10 items)*
- Delivered to active EASL members, global viral hepatitis experts and large clinical centers in Europe
- Available starting May 2021




*Buti M, et al. AASLD TLMdX 2021*

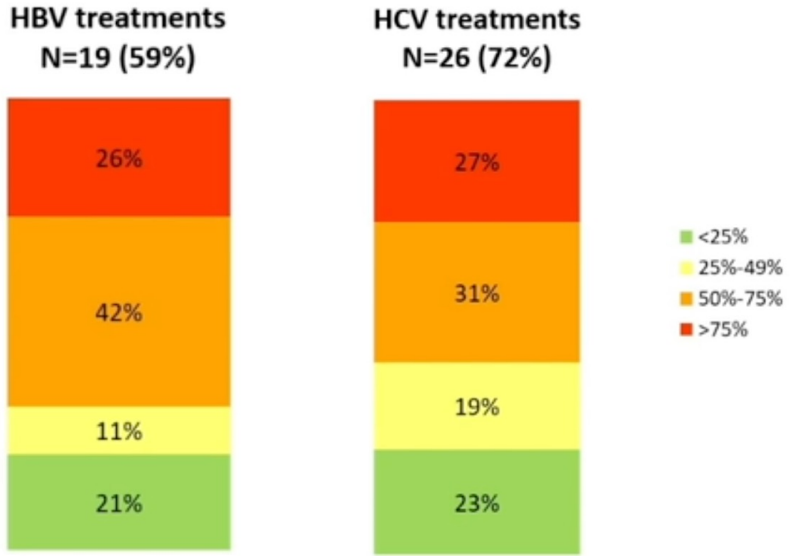
# COVID-19 Impact on Viral Hepatitis B and C Elimination: Preliminary Results in 31 Centres Worldwide

**RESULTS**

- 37 centers from 5 continents responded to the survey as of July 2021 (primarily referral centers)
  - Europe n=20
  - Outside Europe n=17
- All centers except for 1 treated COVID-19

| Metric | Result |
|---|---|
| Total # of HBV consultations | ↓ 30% |
| Total # of HCV consultations | ↓ 45% |
| HBsAg testing | ↓ 39% |
| HCV RNA testing | ↓ 4% |

**Proportion of centers reporting tx reductions**




**CONCLUSION** **The COVID-19 pandemic has substantially impacted the care of patients with chronic viral hepatitis with declines in testing, referral/consultations, and treatment at most centers.**

*Buti M, et al. AASLD TLMdX 2021*

# Cost-Effectiveness Analysis of Treating All HBsAg+ Individuals in the United States

## BACKGROUND & AIMS

- The US is behind in elimination targets for HBV (90% diagnosis, 80% treated, 65% reduction in deaths)
- Modelling studies have shown mortality target will still not be reached if diagnosis/treatment targets are achieved
- **AIM**: to examine economic impact of extending treatment to **all** individuals who are HBsAg-positive
  - Rationale: simplifying screening and linkage to care to help achieve all elimination targets

## METHODS

- US Markov model employed (PRoGReSs)
  - Previously developed to consider impact of immigration
  - Estimates HBV-related morbidity and mortality
  - Base annual treatment cost of $5400 was estimated utilizing weighted average of drug sales
  - Cost of diagnostics estimated with Medicaid data

Considered three scenarios compared to standard of care:

1. Treat all (screen and treat HBsAg+ by 2030)
2. Treat all $2000 (reduced annual cost of tx by 2025)
3. Cost-saving (which price point was necessary by 2025 to make this scenario cost-saving by 2050)

*Razavi-Shearer D, et al. AASLD TLMdX 2021*

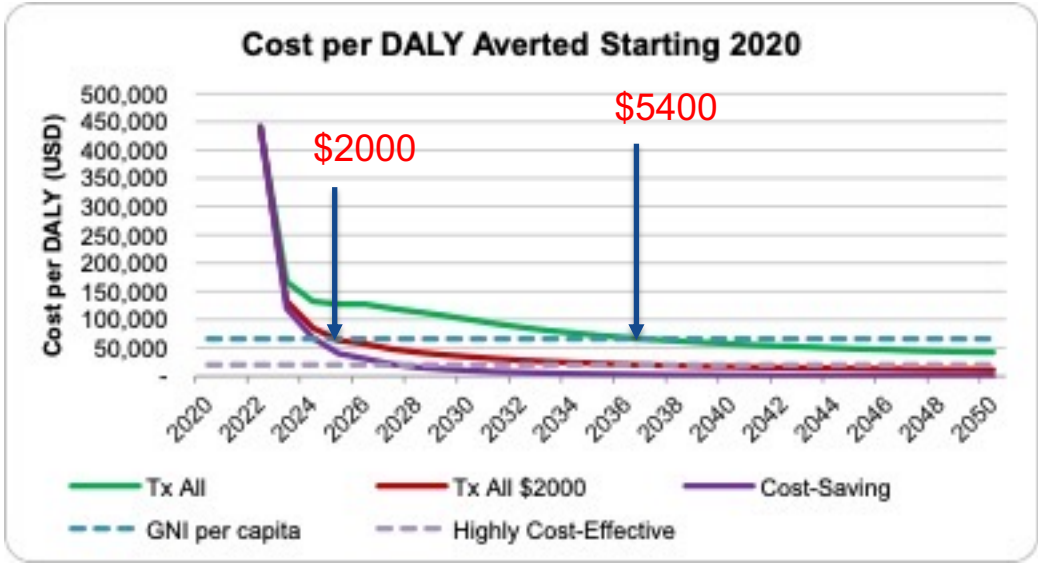
# Cost-Effectiveness Analysis of Treating All HBsAg+ Individuals in the United States

## RESULTS

1) Tx ALL strategy with current pricing was cost-effective with cost/DALY averted of $41,900
2) If price $2000, cost/DALY averted = $10,900 = highly cost-effective
3) Annual price would need to be $750/year to be cost-saving

In this model, compared with base scenario, Tx ALL would avert:

- 10,000 incident cases of HBV
- 49,000 decompensated cirrhosis
- 132,000 cases of HCC
- **Save 157,000 lives through 2050**




*Treating all HBsAg positive cases in the US is cost effective by 2037 at current prices*

**CONCLUSION** **Treating all HBsAg+ individuals may result in significant reductions in HCC, incident infections and mortality. Decreasing treatment costs may lead to cost-savings.**

*Razavi-Shearer D, et al. AASLD TLMdX 2021*

# Hepatitis D-Associated Hospitalizations in the United States: 2010-2018

## BACKGROUND & AIMS

- Burden of HDV infection in the United States is unclear
- Recent treatment advances necessitate more accurate estimates of disease burden
- **AIM**: to estimate the incidence of hepatitis D-associated hospitalizations in the US
  - Describe clinical, demographic, and geographic characteristics

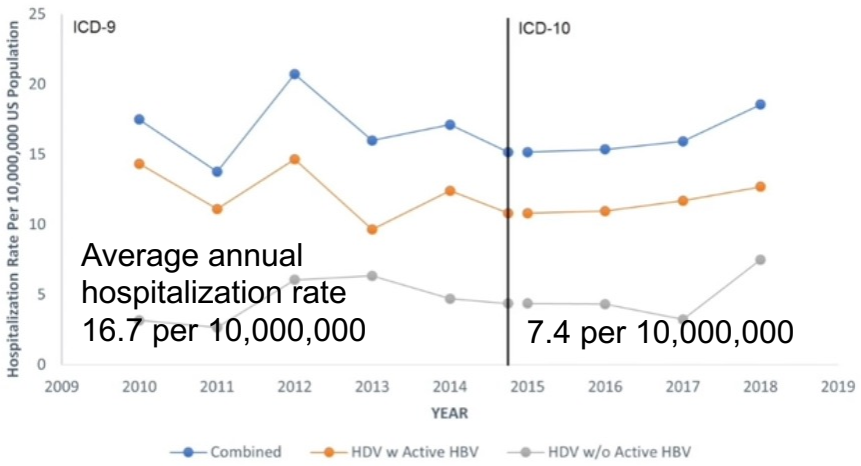
## METHODS

- National Inpatient Sample 2010-2018
- All hospitalizations with hepatitis D (cases) and hepatitis B without hepatitis D (controls) were identified by ICD-9/10 coding
- Frequencies were compared using Chi-squared testing
- Primary endpoint was in-hospital mortality
  - Risk factors were evaluated with logistic regression

# Hepatitis D-Associated Hospitalizations in the United States: 2010-2018

## RESULTS

- **Prevalence of hepatitis D among those hospitalized with hepatitis B was 0.6%**




| Variables | Hepatitis D | Hepatitis B | p value |
|---|---|---|---|
| No. hospitalizations | 3035 | 413355 | |
| Male sex, % | 66.3% | 61.3% | 0.05 |
| White, % | 43.1% | 41.6% | <0.001 |
| Asian, % | 10.4% | 13.5% | <0.001 |
| Hispanic, % | 14.5% | 6.4% | <0.001 |
| Urban, teaching % | 73.2% | 70.0% | 0.09 |
| Northeast, % | 41.4% | 24.9% | <0.001 |
| Ascites, % | 16.5% | 10.8% | <0.001 |
| Portal HTN, % | 12.9% | 6.8% | <0.001 |
| **Mortality, %** | **3.7%** | **3.7%** | **0.99** |

- Age >65 (OR 3.79, p=0.02) and ETOH cirrhosis (OR=3.37, p=0.04) increased mortality among HDV-infected

**CONCLUSION** **HDV-associated hospitalizations are uncommon but associated with severe complications. HDV burden is disproportionately greater in males, Hispanics, and Northeast US.**

*Wasuwanich P, et al. AASLD TLMdX 2021*

# Key Takeaways

- Prior to COVID-19, elimination targets for HBV/HCV elimination remained elusive, particularly for HBV
- Survey of treating providers shows the pandemic will have substantial negative impact on global progress
- Innovative screening and treatment strategies are needed – and potentially cost-effective
- HDV burden in US remains unclear – better data (more testing?) is needed

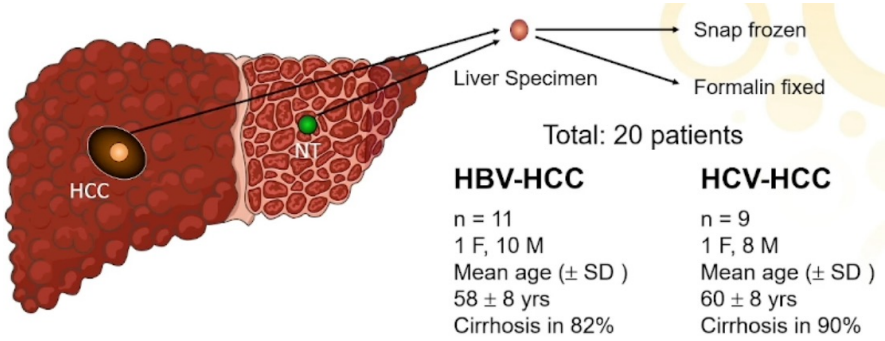
# Viral Hepatitis and HCC

# HBV- and HCV-Associated Hepatocellular Carcinoma Showed Distinct Molecular Signature and Immune Landscape

## BACKGROUND & AIMS

- Viral hepatitis accounts for >70% of worldwide HCC cases – 3rd leading cause of cancer-related deaths
- Immune-based therapies are increasingly used for solid tumors, including HCC
- Immunologic microenvironment of HCC is of interest, but currently limited information on immune-cell infiltration by different viral etiologies
- **AIM**: to characterize/compare immune landscape of HBV- and HCV-associated HCC

## METHODS



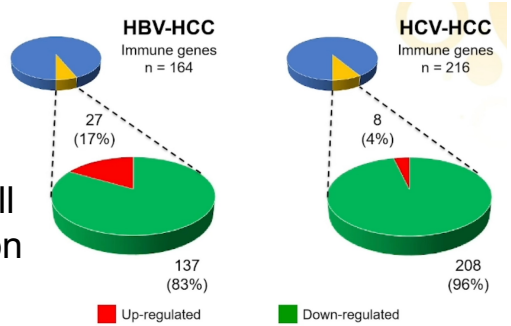

- RNA-seq was performed on the tumor and non-tumor tissue
- A curated list of immune-related genes were examined with IHC:
  - Alpha-SMA, CD3, CD4, CD8, CD20

*De Battista D, et al. AASLD TLMdX 2021*

# HBV- and HCV-Associated Hepatocellular Carcinoma Showed Distinct Molecular Signature and Immune Landscape

## RESULTS

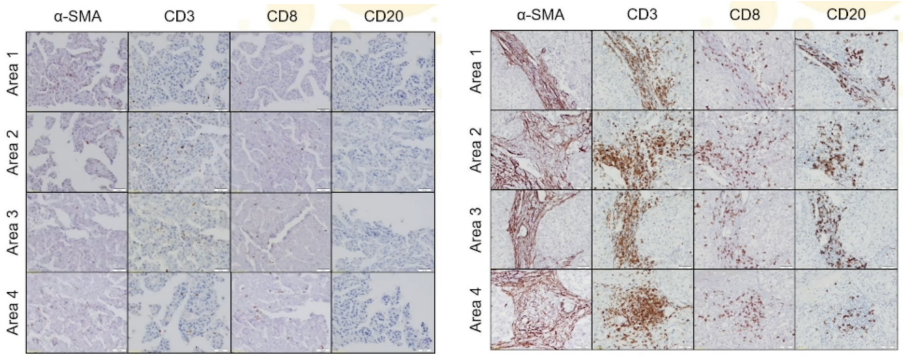
- Majority of genes were down-regulated for both viruses (67% HBV, 74% HCV)
- HCV-HCC: prominent dysregulation of genes involved in T-cell activation and oxidative stress
- HBV-HCC: 4 distinct pathways involved in cyclins and cell cycle regulation and control




**Two distinct immune-cell infiltration patterns were observed**

HCV
9/9 “Cold Tumors”

HBV
4/11 “Hot Tumors”




- Hot tumors were characterized by abundant immune-cell infiltration with higher expression of genes involved in the innate and adaptive immune response regulation

**CONCLUSION** **HBV- and HCV-related HCC has a distinctive molecular signature and immune landscape, which has implications for molecular pathogenesis and treatment selection.**

*De Battista D, et al. AASLD TLMdX 2021*

# Entecavir vs. Tenofovir on the Risk of HCC in a U.S. Cohort with Chronic Hepatitis B Virus

## BACKGROUND & AIMS

- Controversy around the difference in HCC risk reduction in HBV patients treated with tenofovir (TDF) vs entecavir (ETV) is ongoing
- Previous study in the VA database reported no significant differences (Su Gut 2021)
  - Concerns around HCC misclassification and incomplete measurement of medication exposure
- **AIM**: to examine TDF vs ETV and HCC risk in an updated cohort in the VA with extended f/u to Dec 2018

## METHODS

- Retrospective cohort study of VA database patients with positive HBsAg test between 1999-2018
  - With at least 1 filled TDF or ETV prescription between 2008-2018
  - Excluded prevalent HCC and HIV
- Outcome of HCC identified by VA Central Cancer Registry, HCC ICD code, and verified by chart review through 7/31/2019 → **eliminated 22% of HCC cases (misclassified by ICD)**
- Medication exposure: 1) time updating of current drug (yes/no) and 2) time-updating of cumulative duration
- Derived propensity score for receiving drug, tested in Cox regression

# Entecavir vs. Tenofovir on the Risk of HCC in a U.S. Cohort with Chronic Hepatitis B Virus

**RESULTS**

- N=3,735 patients
  - 47.4% TDF, 52.6% ETV
  - Mean age was 55.9 years
  - 95.3% were male; 43.2% white, 36.4% black
- Cirrhosis by ICD/FIB-4>2.67 present in ETV 14.9% vs TDF 15.3% (p=0.07)
- Slightly higher HBeAg+ and HBV DNA for ETV (p<0.01)
- Mean follow-up of 4.1 years
  - Incident HCC: 12.5/1000 PY on ETV and 11.6/1000 PY on TDF

| Antiviral Therapy | # HCC | Person Years | IR (%) | Unadjusted HR | Adjusted HR* |
|---|---|---|---|---|---|
| **Overall** | 186 | 15366.9 | 1.21 (1.04-1.40) | -- | -- |
| **Duration** | | | | | |
| Tenofovir | 59 | 4396.4 | 1.34 (1.02-1.73) | 0.91 (0.81-1.01) | **0.89 (0.79-0.99)** |
| Entecavir | 72 | 4647.2 | 1.55 (1.21-1.95) | 1.0 | |
| **Current Use** | | | | | |
| Tenofovir | 84 | 7230.0 | 1.16 (0.93-1.44) | 0.87 (0.62-1.23) | 0.86 (0.60-1.21) |
| Entecavir | 102 | 8136.9 | 1.25 (1.02-1.52) | 1.0 | |

*age, gender, race, DM, obesity, ETOH, HCV, CKD, baseline HBV DNA, HBeAg status, cirrhosis, prior IFN/lamuvidine tx

**CONCLUSION** **There was a significant trend toward slightly lower risk of HCC in patients treated with TDF in this national VA cohort. Whether this small difference justifies practice change is still unclear.**

*El-Serag H, et al. AASLD TLMdX 2021*

# De Novo Hepatocellular Carcinoma Occurrence Following the HCV Viral Eradication by Direct Acting Antivirals: Medium to Long Term Observations from the Ongoing PITER Cohort

## BACKGROUND & AIMS

- Risk of *de novo* HCC development still persists after HCV eradication by DAA therapy in patients with liver cirrhosis
- Longer term impact of DAA treatment on HCC risk is less well-characterized
- **AIM**: to evaluate the medium/long-term DAA treatment impact on HCC development in patients with HCV-induced liver cirrhosis in a prospective multicenter cohort

## METHODS

- Study population:
  - Consecutive DAA treated patients with cirrhosis in the PITER cohort from 30 centers in Italy
- Inclusion criteria:
  - Liver cirrhosis with >1 year follow-up after end of DAA tx
- Exclusion criteria:
  - Patients who underwent liver transplantation or with prior dx of HCC
- Statistical analysis:
  - Cox regression, KM survival to evaluate factors associated with and time to occurrence of de novo HCC

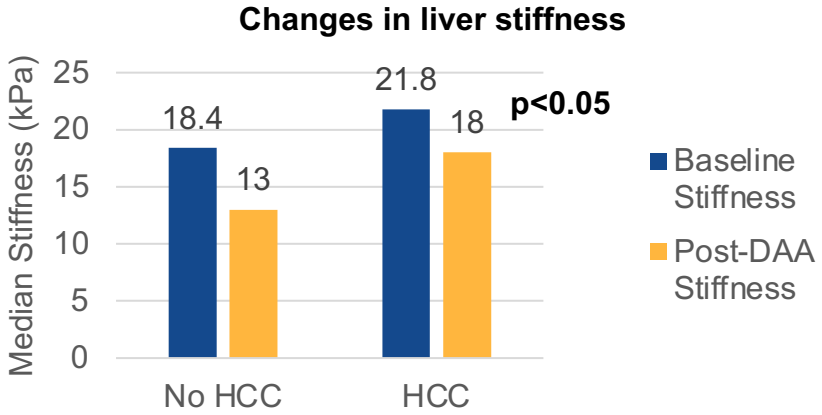
# De Novo Hepatocellular Carcinoma Occurrence Following the HCV Viral Eradication by Direct Acting Antivirals: Medium to Long Term Observations from the Ongoing PITER Cohort

## RESULTS

| Baseline Data | No HCC N=2065 | | De Novo HCC N=149 | | p value |
|---|---|---|---|---|---|
| Age (years)* | 64 (54-71) | | 67 (60-71) | | <0.01 |
| Liver stiffness (kPa) | 18.8 | | 21.8 | | 0.01 |
| | N | % | N | % | |
| Plt count <150* | 1409 | 70.6 | 127 | 87.6 | <0.01 |
| Albumin <3.5* | 438 | 23.7 | 63 | 44.4 | <0.01 |
| FIB-4>3.25 | 1328 | 67.0 | 119 | 82.6 | <0.01 |
| CPT B | 310 | 15.0 | 32 | 21.5 | 0.04 |
| Ascites | 147 | 7.1 | 20 | 13.4 | 0.01 |
| Esophageal varices | 436 | 21.1 | 53 | 35.6 | <0.01 |

*Associated with *de novo* HCC in MV models (also GT3 - not shown)

- Of 2214 DAA tx patients, 149 (6.7%) developed HCC over median 30 months (20-43) of follow-up
- Incidence rate = 2.8 x 100 person-years
- SVR: 5.8% with HCC, **NO SVR (n=150): 20%**
- 80% diagnosed at BCLC B/C stage




**CONCLUSION** **HCC incidence and risk factors after DAA therapy in this prospective cohort is similar to previous data. Higher baseline and post-tx liver stiffness were observed in those with HCC.**

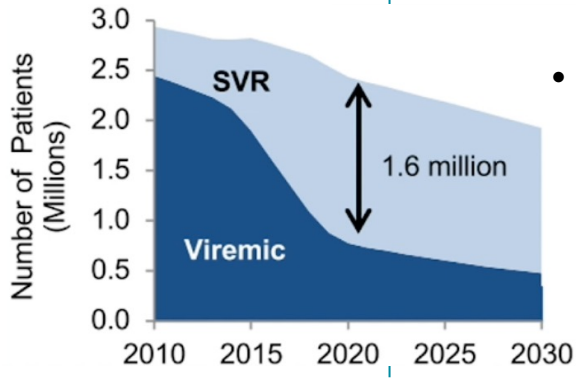
*Kondili L, et al. AASLD TLMdX 2021*

# HCC Incidence Threshold for Routine Surveillance is Much Lower in HCV Cirrhosis Individuals Who Achieve Virological Cure

## BACKGROUND & AIMS

- AASLD recommends biannual surveillance for HCC in HCV-infected with cirrhosis IF HCC incidence >1.5/100 person-years
- Incidence threshold for surveillance among those with SVR is unknown →lower competing risk

**AIM**: to estimate the HCC incidence above which routine HCC surveillance is cost-effective in HCV patients with SVR



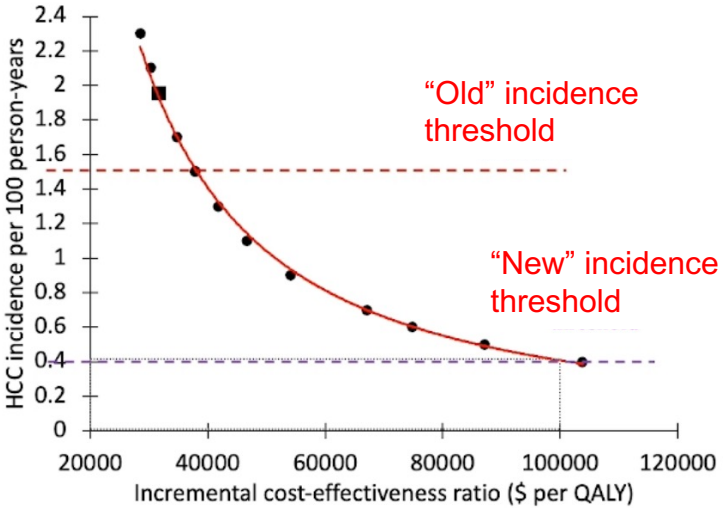

## METHODS

- *Developed microsimulation model of natural history of HCC in patients with SVR*
- Accounted for:
  - Competing risk post-SVR
  - HCC tumor progression rates
  - Real-world HCC surveillance adherence
  - Contemporary treatment options, cost, and utilities
    - Updated willingness-to-pay (WTP) threshold of $100,000/QALY

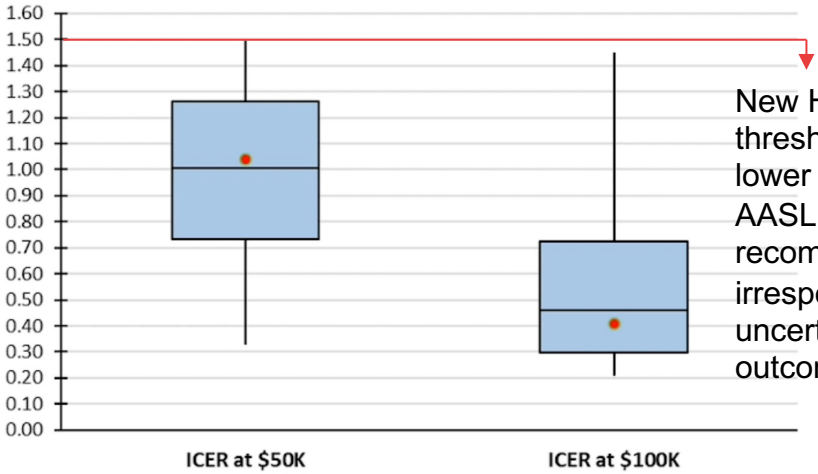
*Chhatwal J, et al. AASLD TLMdX 2021*

# HCC Incidence Threshold for Routine Surveillance is Much Lower in HCV Cirrhosis Individuals Who Achieve Virological Cure

**RESULTS**




Probabilistic sensitivity analysis




New HCC incidence threshold remains lower than current AASLD recommendations irrespective of uncertainty in model outcomes

**CONCLUSION** **In HCV patients with SVR, HCC surveillance could be cost-effective if the annual incidence rate of HCC exceeds 0.4 per 100 PY, much lower than previous thresholds used to guide surveillance decisions.**

*Chhatwal J, et al. AASLD TLMdX 2021*

# Key Takeaways

- The differing “immune landscape” in HBV- versus HCV-associated HCC tumors may have implications for diagnosis and treatment
- Tenofovir may confer lower HCC risk compared to entecavir when treatment duration is considered – jury is still out on clinical impact
- Risk of HCC persists 2.5 years post-SVR and HCC surveillance may be cost-effective at very low incidence thresholds

# Current Treatment Considerations

# Nucleos(t)ide Analogue Withdrawal in Chronic Hepatitis B Patients Leads to Limited Sustained Remission in the Absence of HBsAg Loss: Results from the RETRACT-B Study

## BACKGROUND & AIMS

- NA withdrawal may lead to higher rates of HBsAg loss, but safe discontinuation remains controversial
- Hypothesize that patients who do not achieve HBsAg loss by certain time point may be better off restarted on tx
- **AIM**: to examine the long-term virological and biochemical response after NA cessation
  - Focus on patients who did not achieve HBsAg loss

RETRACT-B
THE GLOBAL STUDY GROUP

## METHODS

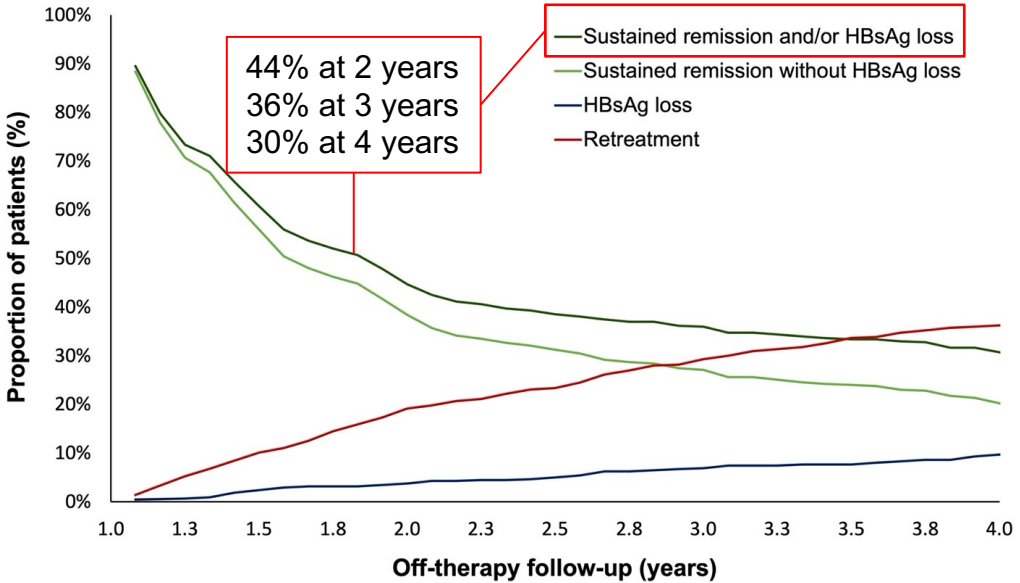
- *Retrospective multicenter cohort study of CHB patients who discontinued NAs from 2001-2020*
- Inclusion / Exclusion
  - Inclusion: HBeAg negative and HBV DNA undetectable at time of NA cessation
  - Excluded: co-infection with HCV, HDV or HIV, received Peg-IFN 1 year prior to NA cessation
  - **Patients allowed to have variable HBV DNA and ALT in 1st year**
  - Those with HBsAg loss, retreatment, hepatic decompensation, HCC, HBeAg seroreversion, death or ltfu ≤1 year excluded (n=612)
- Survival analysis to estimate:
  - Proportion who remained off-therapy and in disease remission **>1 yr** after withdrawal
  - Remission defined as HBeAg- with HBV DNA ≤2000 IU/mL and ALT ≤1.5x ULN

*Hirode G, et al. AASLD TLMdX 2021*

# Nucleos(t)ide Analogue Withdrawal in Chronic Hepatitis B Patients Leads to Limited Sustained Remission in the Absence of HBsAg Loss: Results from the RETRACT-B Study

## RESULTS

- N=945 CHB patients met inclusion criteria
- 72% male, 91% Asian, 9% Caucasian
- 62% ETV, 29% TDF, 9% other
- Post-1 year follow-up: 4 visits (IQR 2-6) with 5.5 months (2.7-8.8) between visits
- **At 4-years off-therapy:**
  - 9.7% achieved HBsAg loss
  - 36% retreated
- **≥1 elevation of HBV DNA >2000 and ALT >1.5x during 1st year (n=604):**
  - 2% achieved HBsAg loss
  - 43% retreated
  - 55% remained off therapy




Caucasian, HBeAg+ at SOT, qHBsAg<100 and no relapse in 1st yr associated with favorable outcomes

**CONCLUSION** **NA withdrawal patients with relapse in 1st year and no HBsAg loss have low likelihood of sustained remission and may benefit from earlier re-treatment.**

*Hirode G, et al. AASLD TLMdX 2021*

# Tenofovir Alafenamide Used Throughout Pregnancy in Chinese Active Chronic HBV Mothers: A Multicenter Prospective Study

## BACKGROUND & AIMS

- Prevention of mother-to-child transmission (MTCT) is critical to viral elimination
- TAF has a better safety profile compared to TDF
- Data on TAF for pregnant women with active CHB are lacking
- **AIM**: to investigate the efficacy and safety of TAF (compared to TDF) in active CHB mothers and their infants

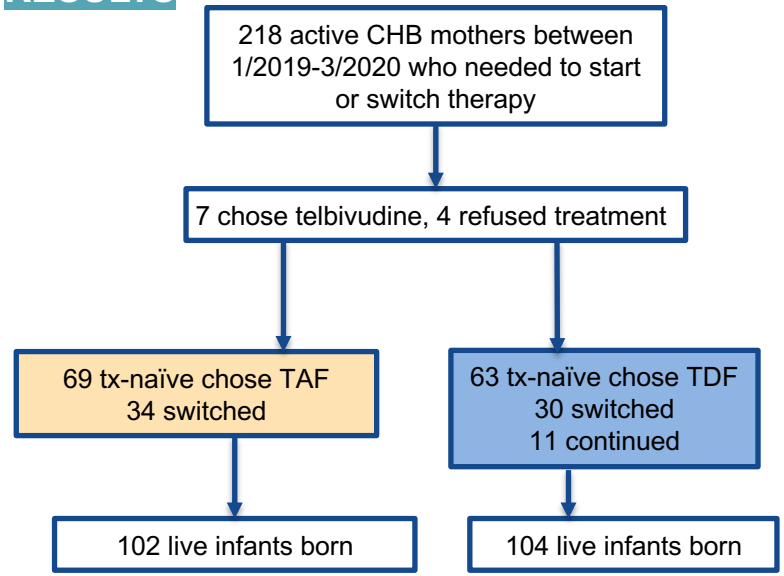
## METHODS

- Multicenter prospective study in China
- Inclusion criteria: >20 years old pregnant women with new diagnosis of treatment-naïve or previously treated active CHB who switched
- Monitoring performed at treatment initiation, 3 month intervals during pregnancy, delivery, postpartum month 3 and 6
- All infants received HBIG and HBV vaccine (birth, one and 6 months)
- Primary endpoint: Rates of adverse events in mothers and infants
- Secondary endpoint: Effectiveness for mothers (i.e. viral suppression) and infants (HBV+)

*Zeng QL, et al. AASLD TLMdX 2021*

# Tenofovir Alafenamide Used Throughout Pregnancy in Chinese Active Chronic HBV Mothers: A Multicenter Prospective Study

**RESULTS**




## Effectiveness Outcomes with TAF vs TDF

| Outcome Variables | TAF | TDF | p value |
|---|---|---|---|
| Tx naïve HBV DNA- at delivery | 51.5% | 47.6% | >0.05 |
| Tx naïve normal ALT at delivery | 63.2% | 65.1% | >0.05 |
| Tx naïve HBeAg seroconversion at PPM18 | 22.0% | 21.1% | >0.05 |
| Switch HBeAg seroconversion at PPM18 | 30.4% | 29.0% | >0.05 |
| MTCT transmission | 0% | 0% | >0.05 |

- Induced abortion was performed on one infant with fetal cleft lip and palate at week 23 (TAF started at week 12 of pregnancy)
- No mothers discontinued tx due to AEs
- At 12 and 18 months, infant height, weight, head circumference were comparable between two groups and national standards
- No serious adverse events in mothers or infants

**CONCLUSION** **TAF and TDF had comparable safety and effectiveness profiles for active CHB mothers and reduced MTCT to 0% with combination standard immunoprophylaxis.**

*Zeng QL, et al. AASLD TLMdX 2021*

# HBV Reactivation in Rheumatic Patients with Resolved Hepatitis B Ongoing Biologics Treatment

## BACKGROUND & AIMS

- Risk of reactivation among core-antibody positive patients on biologics remains unclear
- Accurate characterization of risk is essential to determining need for prophylaxis
- **AIM**: to examine incidence of and factors associated with reactivation by different classes of biologic disease-modifying anti-rheumatic drugs (bDMARDs)

## METHODS

- Retrospective study of 1937 patients with RA who had HBsAg and anti-HBc data in Taipei Veterans General Hospital between 6/2003-5/2019
  - N=1022 classified as resolved HBV
  - N=487 of above received bDMARDs
- No prophylaxis as not reimbursed
- Liver function monitored q2-3 months, HBsAg monitored q6 months
- bDMARDs = anti-TNF, abatacept, rituximab, and anti-IL-6 (tocilizumab)
- **Primary outcome = reappearance of HBsAg**

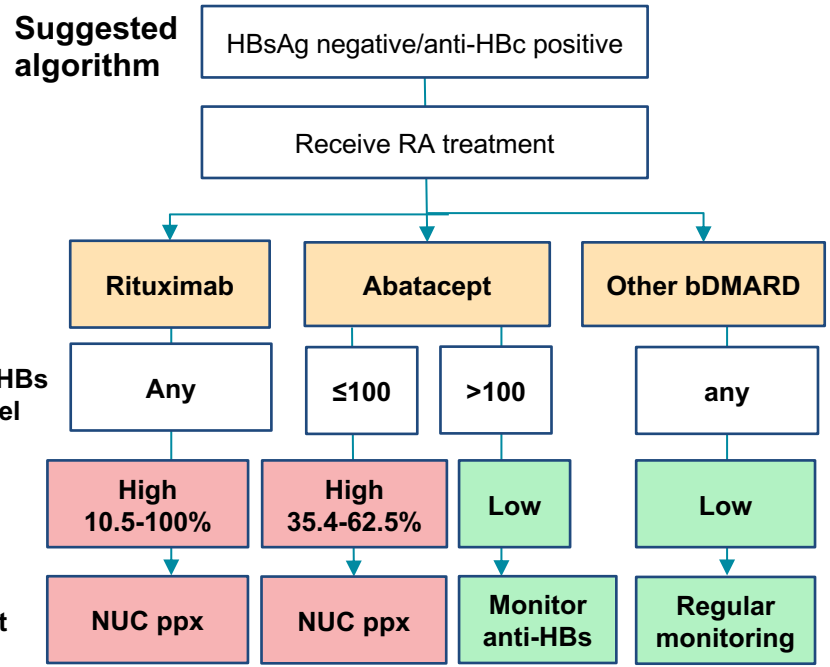
*Huang YH, et al. AASLD TLMdX 2021*

# HBV Reactivation in Rheumatic Patients with Resolved Hepatitis B Ongoing Biologics Treatment

**RESULTS**

| | # | PY | IR (per 1000) | Adjusted HR |
|---|---|---|---|---|
| **Anti-TNF** | 3 | 3023 | 0.99 | ref |
| **Tocilizumab** | 0 | 947 | 0.00 | -- |
| **Abatacept** | 6 | 640 | 9.38 | 15.4 (3.1-77.0) |
| **Rituximab** | 18 | 1016 | 17.72 | 35.7 (8.2-155.8) |

- Steroids: 55.6% in RS+ vs 37.4% in RS- (p=0.07)
- 70.4% vs 29.0% received ≥1 bDMARD (p<0.01)
- **Cumulative incidence of RS+ was highest among those who were anti-HBS negative (24.3% at 16 years vs 2.4% if anti-HBs >100)**
- Baseline negative anti-HBs, abatacept and rituximab associated with reactivation




**CONCLUSION** **Anti-viral prophylaxis should be considered in core-antibody positive RA patients on abatacept therapy with low anti-HBs titers.**

*Huang YH, et al. AASLD TLMdX 2021*

# Excellent Efficacy and Safety of Sofosbuvir, Glecaprevir, Pibrentasvir and Ribavirin for Retreatment of Chronic Hepatitis C After Sofosbuvir, Velpatasvir and Voxilaprevir Failure

## BACKGROUND & AIMS

- Some HCV patients have undergone multiple DAA treatments without SVR
- Guidelines recommend use of sofosbuvir (SOF), glecaprevir (GLE), pibrentasvir (PIB) and ribavirin (RBV) for 16-24 weeks for patients who have failed SOF/VEL/VOX based on limited case reports
- **AIM**: to report larger experience with SOF+GLE/PIB+RBV HCV re-treatment among treatment failures

## METHODS

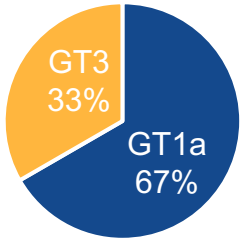
- Retrospective cohort study of all patients at KPNC and UCSF who:
  - failed SOF/VEL/VOX
  - treated with SOF+GLE/PIB+RBV
- Outcomes
  - Efficacy defined as SVR at 12 weeks
  - Adverse events on treatment including hospitalization

# Excellent Efficacy and Safety of Sofosbuvir, Glecaprevir, Pibrentasvir and Ribavirin for Retreatment of Chronic Hepatitis C After Sofosbuvir, Velpatasvir and Voxilaprevir Failure

## RESULTS

- **12 patients met inclusion criteria**
- Median age 66 (54-67); 83% male
- 88% White, 8% Black, 8% AIAN

- 50% with cirrhosis
- 2 with solid organ txp
- 3 with HCC




- 50% on weight-based RBV dosing vs 50% on 600mg/day; no EPO use
- No treatment discontinuations or AEs requiring hospitalization

Table: Pre-Treatment Details, Treatment Duration and SVR12

| ID | Transplant? | HCV Genotype | Cirrhosis? | Previous Tx History | Resistance Associated Substitutions* | SOF/GLE/PIB /RBV Duration | SVR12? |
|---|---|---|---|---|---|---|---|
| 1 | No | 3 | Yes | SOF/VEL/VOX/RBV | M28, L31M | 16 wks | Yes |
| 2 | No | 1a | Yes | Peg/RBV; EBR/GZR; SOF/VEL/VOX | None | 24 wks | Yes |
| 3 | No | 3a | Yes | Peg/RBV; SOF/RBV; SOF/DAC/RBV; SOF/EBR/GZR/RBV; SOF/VEL/VOX/RBV | Y93H | 24 wks | Yes |
| 4 | No | 1a | No | SOF/LDV; GLE/PIB; SOF/VEL/VOX | Q30, L31M | 24 wks | Yes |
| 5 | No | 1a | Yes | SOF/LDV/RBV; SOF/VEL/VOX | Y93C | 24 wks | Yes |
| 6 | No | 1a | Yes | SOF/LDV; SOF/VEL/RBV; SOF/VEL/VOX | None | 16 wks | Yes |
| 7 | Yes, liver | 3 | No | SOF/VEL; SOF/VEL/VOX | L31, Y93 | 24 wks | Yes |
| 8 | No | 1a | Yes | Peg/RBV; SMV/SOF; SOF/VEL/VOX | None | 16 wks | Yes |
| 9 | No | 1a | No | SOF/LDV; SOF/VEL/VOX | Y93N | 16 wks | Yes |
| 10 | No | 3a | No | SOF/VEL; SOF/VEL/VOX | A30K | 16 wks | Yes |
| 11 | No | 1a | No | SOF/LDV; SOF/VEL/VOX | L31M | 16 wks | Yes |
| 12 | Yes, kidney | 1a | No | SOF/LDV; SOF/VEL/VOX | None | 16 wks | Yes |

*tested prior to SOF/GLE/PIB/RBV retreatment

DAC – daclatasvir; EBR – elbasvir; GLE – glecaprevir; GZR – grazoprevir; HCV – Hepatitis C Virus; LDV – ledipasvir; PIB – pibrentasavir; RBV – ribavirin; SMV – simeprevir; SOF – sofosbuvir; VEL – velpatasvir; VOX – voxilaprevir

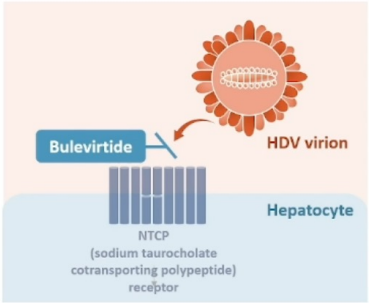
**CONCLUSION** **In the largest reported cohort to date of SOF/VEL/VOX failures, SOF+GLE/PIB+RBV for 16-24 weeks results in 100% SVR12 rates without any safety concerns.**

*Saxena V, et al. AASLD TLMdX 2021*

# Safety and Efficacy of 2mg Bulevirtide in Patients with Chronic HBV/HDV Co-Infection: First Real-World Results

## BACKGROUND & AIMS

- Bulevirtide is a first-in-class entry inhibitor for treatment of chronic HDV infection




- BLV 2mg once daily by subcutaneous injection received conditional EMA approval in 2020
- **AIM**: to present real-world 6 and 12-month results of HDV/HBV patients receiving BLV 2mg

## METHODS

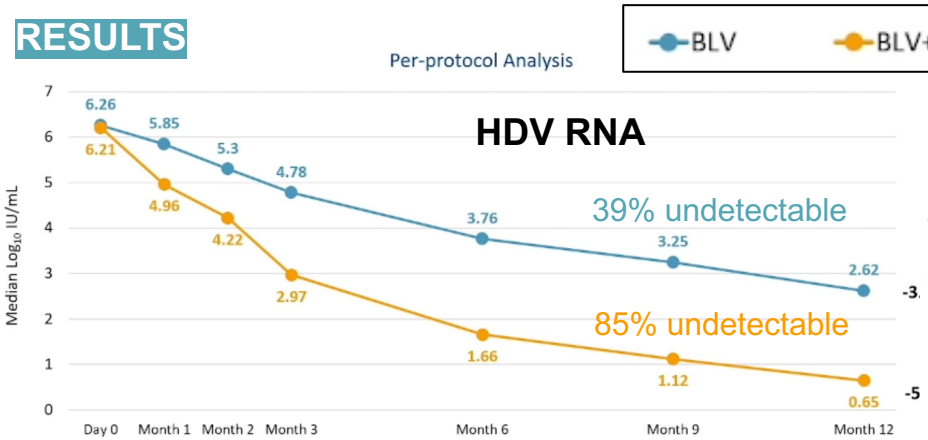
- French Early Access Program (cATU)
  - Sept 2019– Sept 2020
  - Eligible patients: compensated cirrhosis OR F3 fibrosis OR F2 with persistent ALT>2x ULN for >6 months

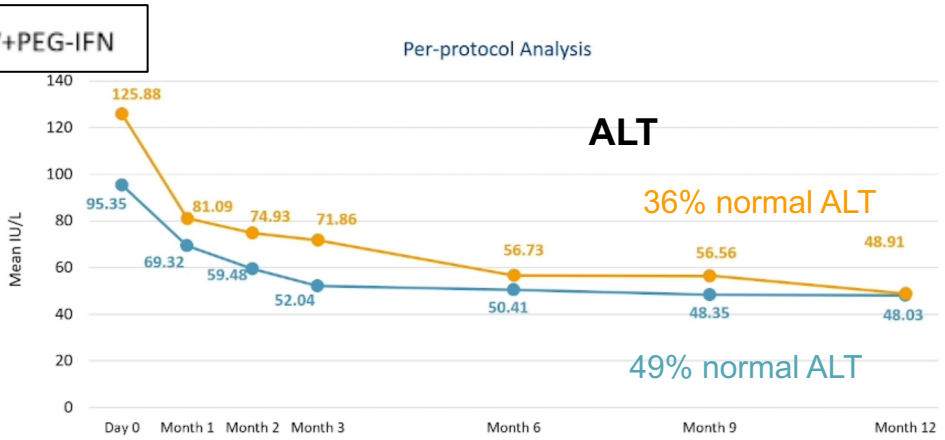

- Treatment regimen and modifications per treatment physician
- **Primary endpt** = undetectable HDV RNA or ≥2 $\log_{10}$ decrease from baseline
- Per-protocol analysis

*De Ledingham V, et al. AASLD TLMdX 2021*

# Safety and Efficacy of 2mg Bulevirtide in Patients with Chronic HBV/HDV Co-Infection: First Real-World Results

**RESULTS**




- Mean age 41; ~62% with cirrhosis, 8% HBeAg+
- At 12 months, 68.3% BLV vs 93.9% +PEG had met primary endpt
- Respective 39.0% vs 30.3% had both virological endpt + ALT<40 U/L

| AEs | BLV 2mg N=77 | +PEG-IFN N=68 |
|---|---|---|
| Grade 3-4 AE | 7 | 6 |
| D/C due to AE | 2 | 3 |
| Liver-related AE | 4 | 2 |
| ↑ Bile acids | 76 | 68 |

**CONCLUSION** **In this real-world study, BLV 2mg shows favorable HDV RNA declines and ALT normalization over 12 months and was well-tolerated with asymptomatic elevations in bile acids.**

*De Ledingham V, et al. AASLD TLMdX 2021*

# Key Takeaways

- Patients who do not achieve desired HBsAg loss in 1st year after NA withdrawal have low chance of sustained remission
- TAF is safe & effective for both prevention of MTCT and tx of active CHB in pregnant women
- HBV ppx should be considered in HBcAb+/anti-HBs- with abatacept immunosuppression
- In real-world settings:
  - SVR12 is highly achievable with SOF+GLE/PIB+RBV x16-24 months for patients with difficult-to-treat HCV
  - Bulevirtide for HDV has comparable efficacy to clinical trials and low frequency of severe adverse events

# Thank You!

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