CLINICAL CARE OPTIONS®
HEPATITIS

CCO Independent Conference Coverage: Clinical Impact of New Data From EASL 2021

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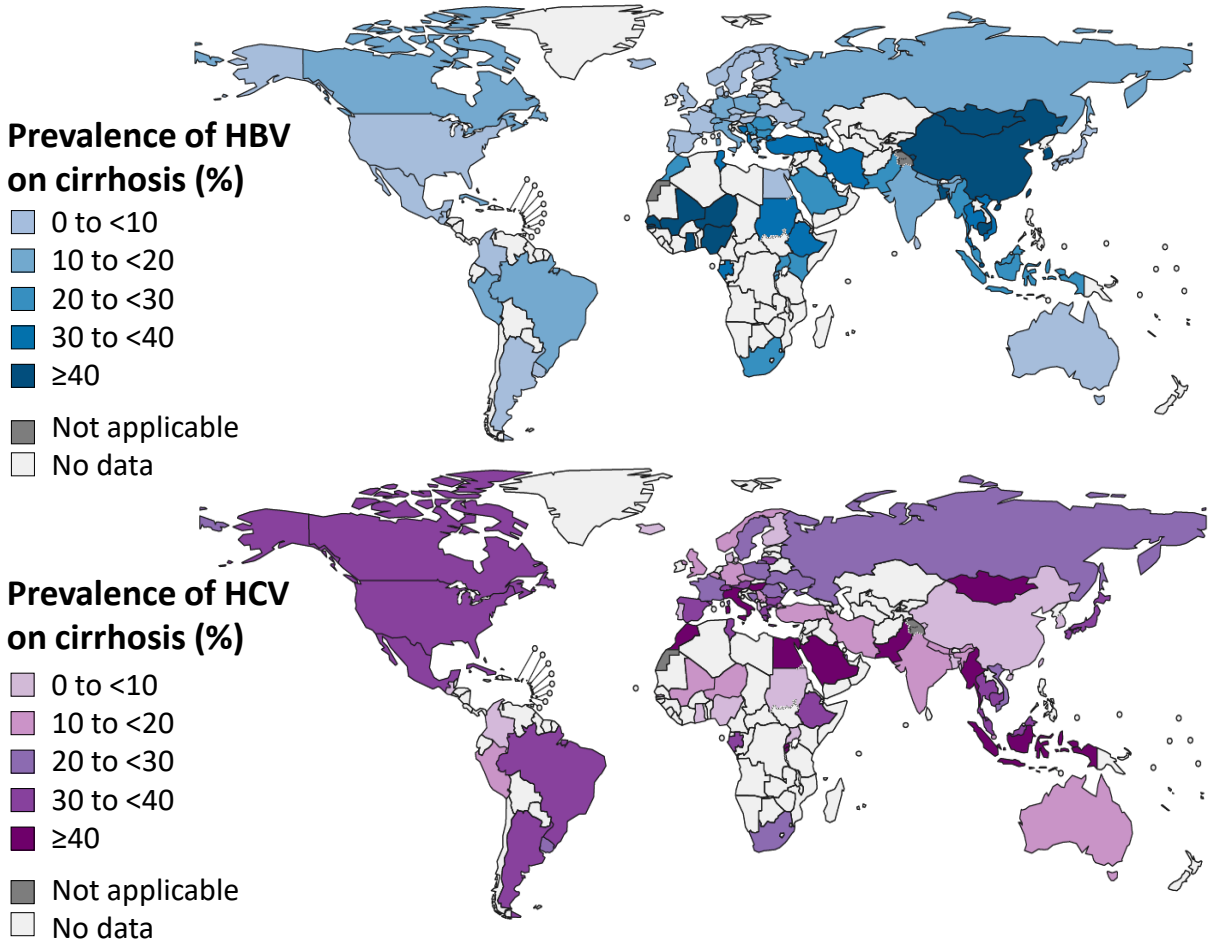
WHO: Estimating HBV and HCV Prevalence Among Patients With Cirrhosis Worldwide

- Systematic literature review from 1993-2021



Alberts. EASL 2021. Abstr 2750.

- Among patients with cirrhosis:
  - Prevalence of HBV highest in Asian and African countries
  - Prevalence of HCV varies regionally, highest in Egypt and Pakistan (>60%)
  - Prevalence of heavy alcohol consumption >40% in America, Australia, and Western Europe; <10% in Northern Africa and Western Asia
  - Prevalence of NAFLD varies between 2%-15% in North America and Europe
- Prevalence of both HBV and HCV higher in patients with HCC vs patients with cirrhosis

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Impact of Chronic Liver Disease and Alcohol Use Disorders on COVID-19 Mortality in France

- Retrospective, observational study in French National Hospital Discharge database
  - N = 259,110 adults discharged from hospital in 2020 with COVID-19 diagnosis
  - Mean age 70 yr (IQR: 54-83); 52% male; 6% chronic liver disease; 4% alcohol use disorders
- Increased risk of COVID-19 death with decompensated cirrhosis, chronic liver disease, and alcohol use disorders

Population	Adjusted OR (95% CI)	*P* Value
30-Day Mortality		
Alcohol use disorders	1.11 (1.05-1.17)	<.001
Chronic liver disease	1.79 (1.71-1.87)	<.001
Compensated cirrhosis	0.71 (0.63-0.80)	<.001
Decompensated cirrhosis	2.21 (1.94-2.51)	<.001
Mechanical Ventilation		
Alcohol use disorders	0.82 (0.76-0.89)	<.001
Chronic liver disease	1.54 (1.44-1.64)	<.001
Compensated cirrhosis	0.64 (0.53-0.76)	<.001
Decompensated cirrhosis	0.65 (0.52-0.81)	<.001

Mallet. EASL 2021. Abstr GS-1587.

Slide credit: clinicaloptions.com

Hepatitis B Studies

Extrahepatic Malignancies in Treated vs Untreated Patients With CHB in NHIS Database in Republic of Korea

- 90,944 patients newly diagnosed from 2012-2014 with CHB compared with 685,346 controls matched for age, sex, socioeconomic status, and area of habitation
  - CHB patients further classified as NA treated (n = 6539) and NA untreated (n = 84,405)
- Mean follow-up: 47.4 mo
- 30,413 (3.9%) developed extrahepatic malignancy

- NA-untreated CHB patients significantly more likely to develop extrahepatic malignancy vs NA-treated CHB patients or controls

Development of Overall Malignancy: Primary Outcome*	aSHR (95% CI)	*P* Value
NA-untreated CHB vs controls	1.22 (1.18-1.26)	<.001
NA-untreated CHB vs NA-treated CHB	1.27 (1.11-1.45)	.003
NA-treated CHB vs controls	0.96 (0.85-1.09)	.55

*IPTW applied for balancing.

Chung. EASL 2021. Abstr 691.

Slide credit: clinicaloptions.com

Extrahepatic Malignancies in Treated vs Untreated Patients With CHB: Landmark 12-Mo, 18-Mo, 24-Mo Periods

- At 12, 18, and 24 mo, NA-untreated CHB patients significantly more likely to develop extrahepatic malignancy vs NA-treated CHB patients or control

Patient Groups	Development of Malignancy: Sensitivity Analysis					
	12 Mo		18 Mo		24 Mo	
	aSHR (95% CI)	*P* Value	aSHR* (95% CI)	*P* Value	aSHR (95% CI)	*P* Value
NA-untreated CHB vs controls	1.24 (1.20-1.28)	<.001	1.17 (1.13-1.21)	<.001	1.20 (1.16-1.24)	<.001
NA-untreated CHB vs NA-treated CHB	1.22 (1.08-1.39)	.002	1.22 (1.06-1.39)	.005	1.22 (1.08-1.39)	.002
NA-treated CHB vs controls	1.01 (0.89-1.15)	.85	0.96 (0.84-1.10)	.53	0.98 (0.87-1.11)	.76

*Before IPTW.

Chung. EASL 2021. Abstr 691.

Slide credit: clinicaloptions.com

Extrahepatic Malignancies in Treated vs Untreated Patients With CHB: Cancer Types

- NA-untreated patients at **greater risk vs controls** for development of both solid tumors and hematologic cancer

Cancer Type	aSHR (95% CI) NA Untreated vs Control	*P* Value
Thyroid cancer	1.25 (1.13-1.38)	<.001
Stomach cancer	1.28 (1.16-1.41)	<.001
Lung cancer	1.13 (1.01-1.26)	.03
Prostate cancer	1.23 (1.13-1.34)	<.001
Pancreatic cancer	1.64 (1.46-1.84)	<.001
Gallbladder/biliary tract cancer	1.65 (1.41-1.95)	<.001
Kidney cancer	1.30 (1.08-1.55)	.01
NHL	1.92 (1.51-2.44)	<.001

- NA-treated patients at **greater risk vs controls** for development of breast and kidney cancer

Cancer Type	aSHR (95% CI) NA Treated vs Control	*P* Value
Breast cancer	1.62 (1.14-2.29)	.007
Kidney cancer	2.12 (1.26-3.55)	<.001

- NA-treated patients at **lesser risk vs NA-untreated patients** for development of prostate, pancreatic cancer but greater risk for breast cancer

Cancer Type	aSHR (95% CI) NA Treated vs Untreated	*P* Value
Prostate cancer	0.59 (0.40-0.86)	.007
Pancreatic cancer	0.41 (0.23-0.74)	.003
Breast cancer	1.69 (1.18-2.44)	.005

Chung. EASL 2021. Abstr 691.

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Mortality and Cause of Death in Individuals With CHB in Denmark

- Nationwide cohort study conducted in Denmark to determine the adjusted all-cause mortality and cause of death in persons with CHB compared with the general population in a low prevalence setting
  - Included 6988 adults diagnosed with CHB between 2002-2016 and 69,847 age- and sex-matched controls
  - Individuals followed from 6 mo after first CHB registration until death, emigration, or December 31, 2017
  - Mortality rate ratios adjusted for age, sex, employment, region of origin, and comorbidity

- Median follow-up: 7.7 (range: 0-15.5) yr
- 315 (5%) individuals with CHB and 1525 (2%) individuals in general population died
- Liver disease largest contributor to mortality

Outcome	CHB (N = 6988)	Controls (N = 69,847)
Death, n (%)	315 (5)	1525 (2)
Adjusted all-cause mortality rate ratio (95% CI)	1.5 (1.2-2.0)	1 (ref)
Mortality rate ratio by cause of death (95% CI)		
▪ Liver disease	12.3 (8.6-17.7)	---
▪ Neoplasm (excluding HCC)	1.6 (1.2-2.0)	
▪ Endocrine disease	3.2 (1.8-5.4)	
▪ Genitourinary disease	3.2 (1.2-7.6)	
▪ External causes	3.3 (2.5-4.7)	

Bollerup. EASL 2021. Abstr 2202.

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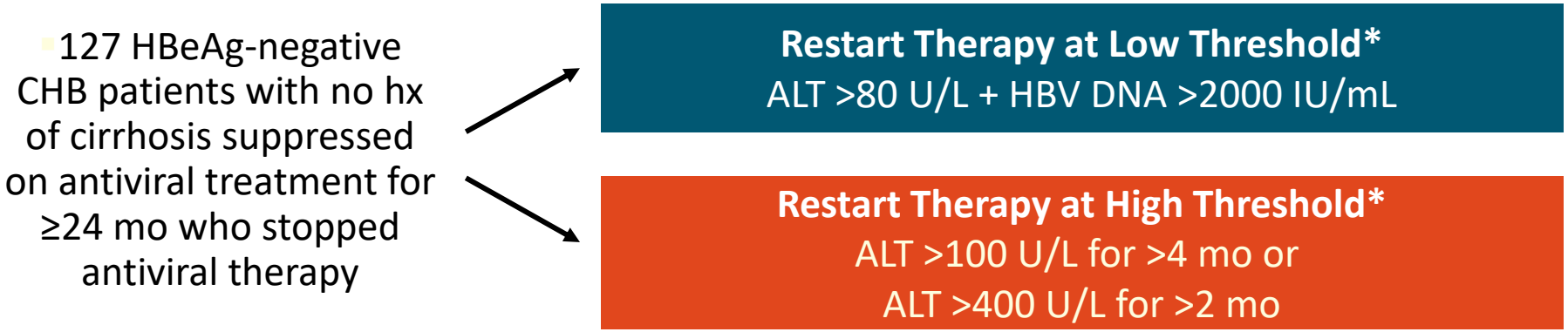
Nuc-Stop Study in HBV: Design

- Randomized, multicenter open-label trial from 11 centers in Norway, Sweden, Denmark, and Ethiopia



*All patients restarted therapy upon severe flare (ALT >800 U/L; ALT flare with INR ≥1.4 or bilirubin >38 mmol/L)

- Median duration of antiviral treatment before inclusion: 45 mo (IQR: 32-76)
- 90 (70.9%) patients on TDF; 30 (23.6%) patients on ETV
- Primary endpoint: HBsAg loss not reported here; safety results *only* in this report

Johannessen. EASL 2021. Abstr 111.

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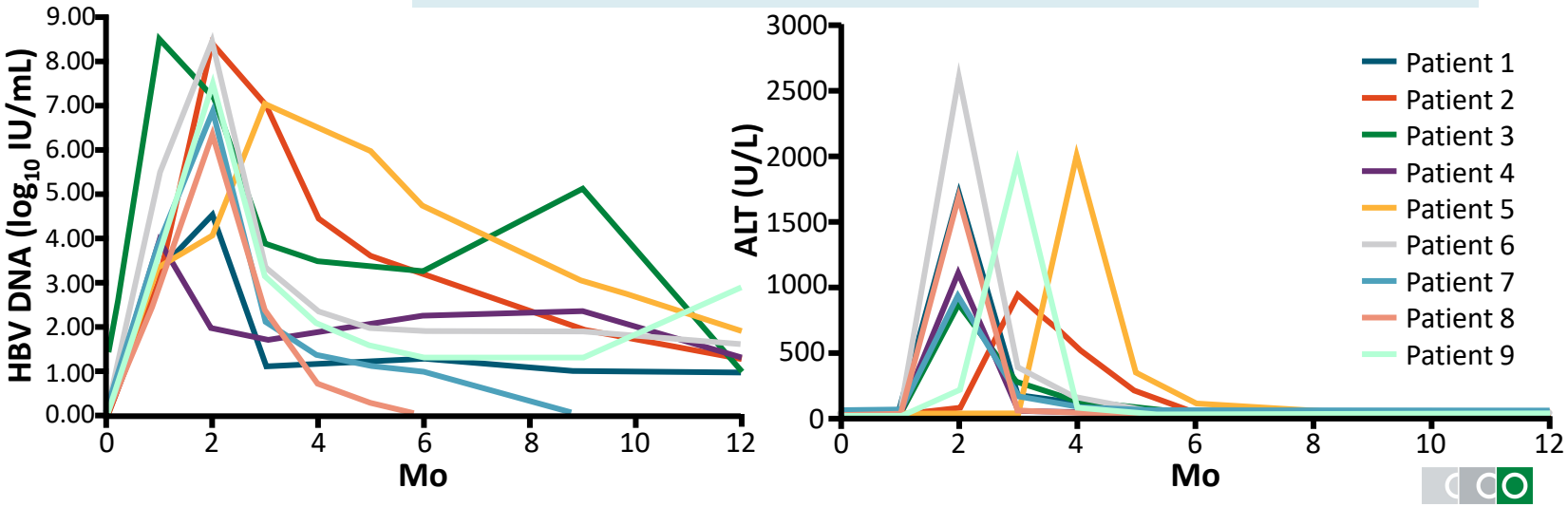
Nuc-Stop Study in HBV: Safety Results at 1 Yr

- 9 (7.1%) patients with severe flare in first yr
  - 1 patient with bilirubin >38 mmol/L
- All 9 cases of severe flare occurred among patients who stopped TDF therapy
  - Severe flare not associated with age, sex, or duration of previous antiviral treatment

Result After Therapy Cessation, n (%)	Patients (N = 127)
Virologic relapse*	108 (85)
Clinical relapse†	44 (34.6)
Severe flare	9 (7.1)

*HBV DNA >2000 IU/mL
†ALT >80 U/L and HBV DNA >2000 IU/mL

- Additional serious AEs related to treatment interruption not observed
- Undetectable HBV DNA and normalized ALT levels observed for 8 patients with severe flare after restart of therapy
  - 1 patient with spontaneous decline of HBV DNA without restarting therapy



Johannsen. EASL 2021. Abstr 111.

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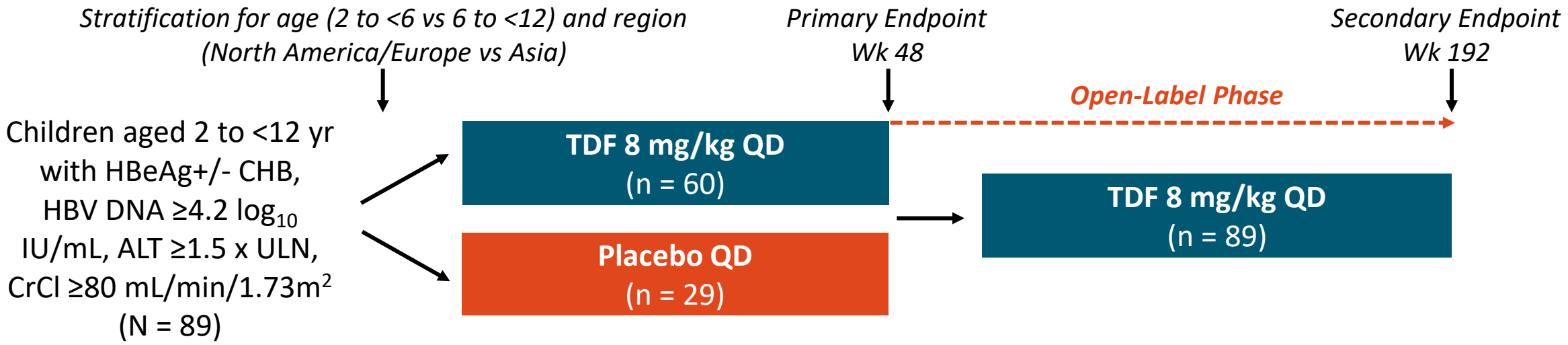
TDF Study 0144: Long-term Efficacy of TDF in Children With Chronic Hepatitis B

- Multicenter, randomized, double-blind, placebo-controlled phase III trial



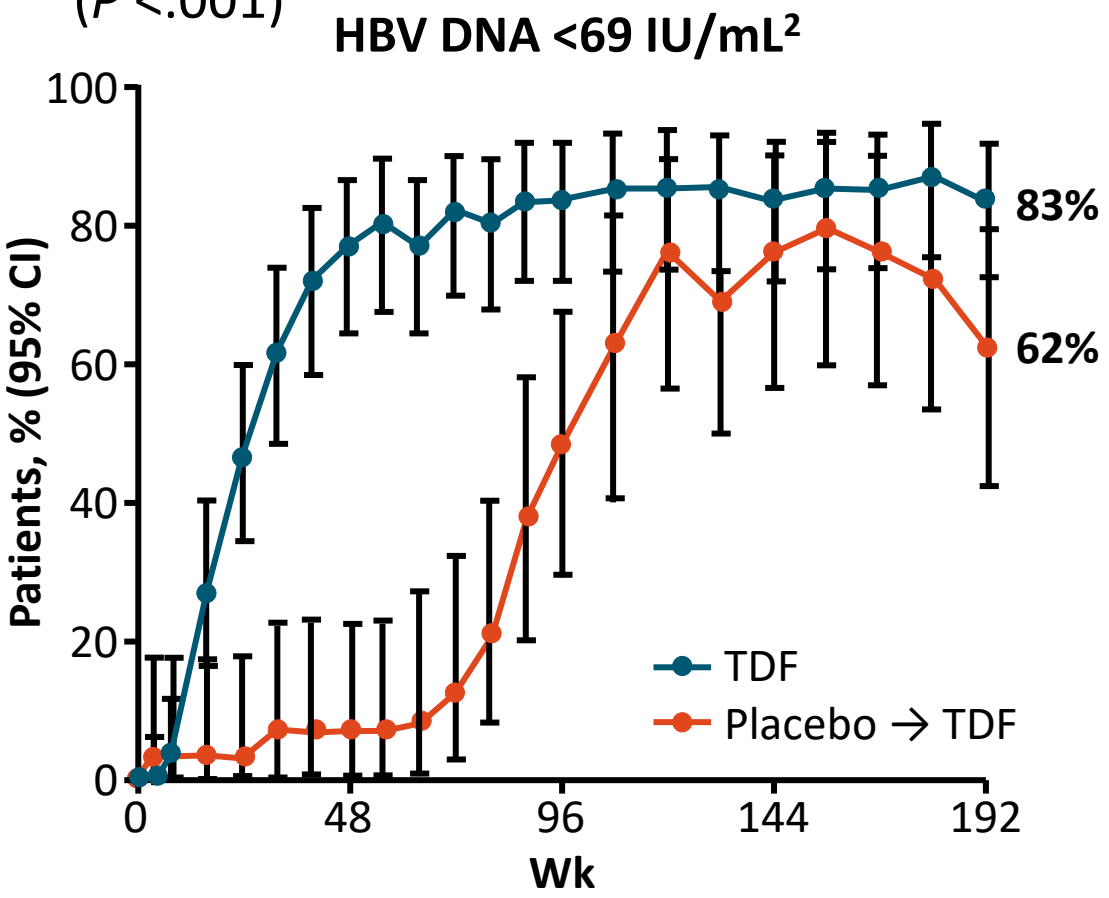
- Primary endpoint: HBV DNA <69 IU/mL at Wk 48
- Secondary endpoints: Wk 192 HBV DNA <69 IU/mL or <29 IU/mL, ALT normalization, serology, composite endpoint (virologic, biochemical, serologic endpoints), safety

Chang. EASL 2021. Abstr OS-2283.

Slide credit: clinicaloptions.com

TDF Study 0144: Virologic Response Through Wk 192

- At Wk 48, 77% of patients on TDF vs 7% of patients on placebo with HBV DNA <69 IU/mL (*P* <.001)[1]



Virologic Outcomes at Wk 192 (M=F), n (%)[2]	TDF (n = 60)	Placebo to TDF (n = 29)
HBV DNA <69 IU/mL	50 (83)	18 (62)
▪ 95% CI	72-92	42-79
HBV DNA <29 IU/mL	49 (82)	18 (62)
HBV DNA ≥69 IU/mL	10 (17)	11 (38)
▪ ≥69 IU/mL	2 (3)	2 (7)
▪ Missing data	8 (13)	9 (31)

1. Chang. AASLD 2018. Abstr 76. 2. Chang. EASL 2021. Abstr OS-2283.

Slide credit: clinicaloptions.com

TDF Study 0144: Other Efficacy Endpoints at Wk 192

Outcome (M=F)	TDF (n = 60)	Placebo to TDF (n = 29)
ALT normalization, %		
▪ Central laboratory	79	59
▪ AASLD criteria	72	50
HBeAg, n/N (%)		
▪ Loss	30/56 (54)	10/29 (34)
▪ Seroconversion	19/56 (34)	10/29 (34)
HBsAg, n/N (%)		
▪ Loss	6/60 (10)	0/29 (0)
▪ Seroconversion	0/60 (0)	0/29 (0)

Composite Endpoints (M=F), n/N (%)	TDF (n = 60)	Placebo to TDF (n = 29)
2-endpoint composite ▪ HBV DNA <69 IU/mL with ALT normalization by central laboratory	44/58 (76)	15/27 (56)
3-endpoint composite ▪ HBV DNA <69 IU/mL with ALT normalization by central laboratory and HBeAg loss	24/54 (44)	9/27 (33)

- No virologic breakthrough or resistance on TDF during open-label phase
- No grade 3/4 or serious TRAEs on TDF

Chang. EASL 2021. Abstr OS-2283.

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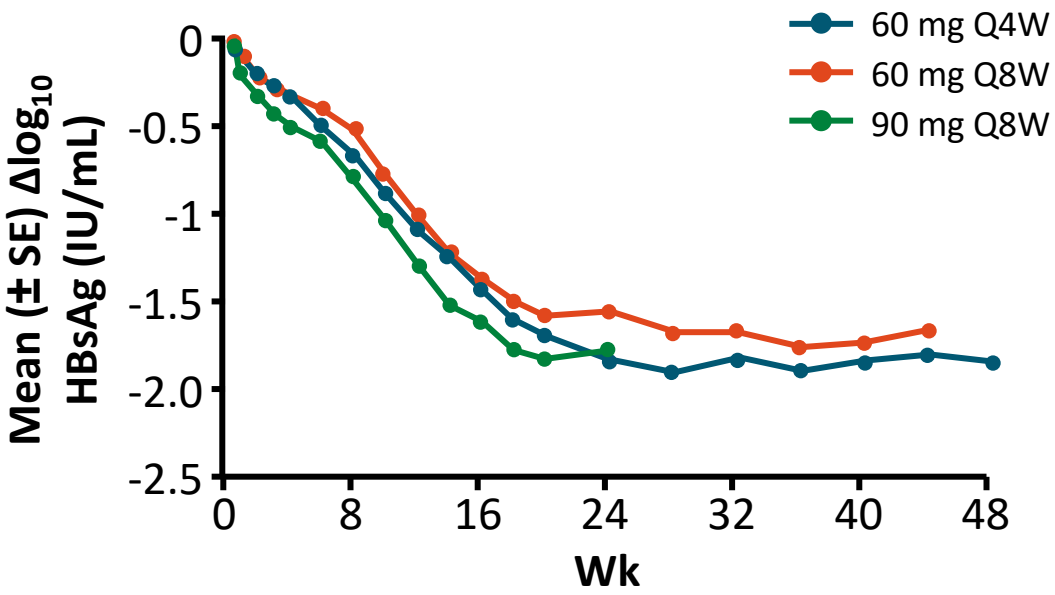
Selected Studies of Investigational Compounds for HBV Cure Strategies

Investigational HBV Cure Strategies: AB-729

- GalNAc-conjugated single-trigger RNA interference agent that blocks all HBV RNA transcripts
- Single dose of AB-729 (90 mg SC) in the absence of NA therapy blocked resulted in reductions in HBsAg, HBV DNA, HBV RNA, and HBcrAg in small cohort of 5 HBe-neg patients[1]
- Repeat doses at different dosing levels and intervals in HBV DNA-neg patients result in similar declines in HBsAg, all plateauing at Wk 20[2]
  - 15/20 achieve HBsAg <100 IU/mL

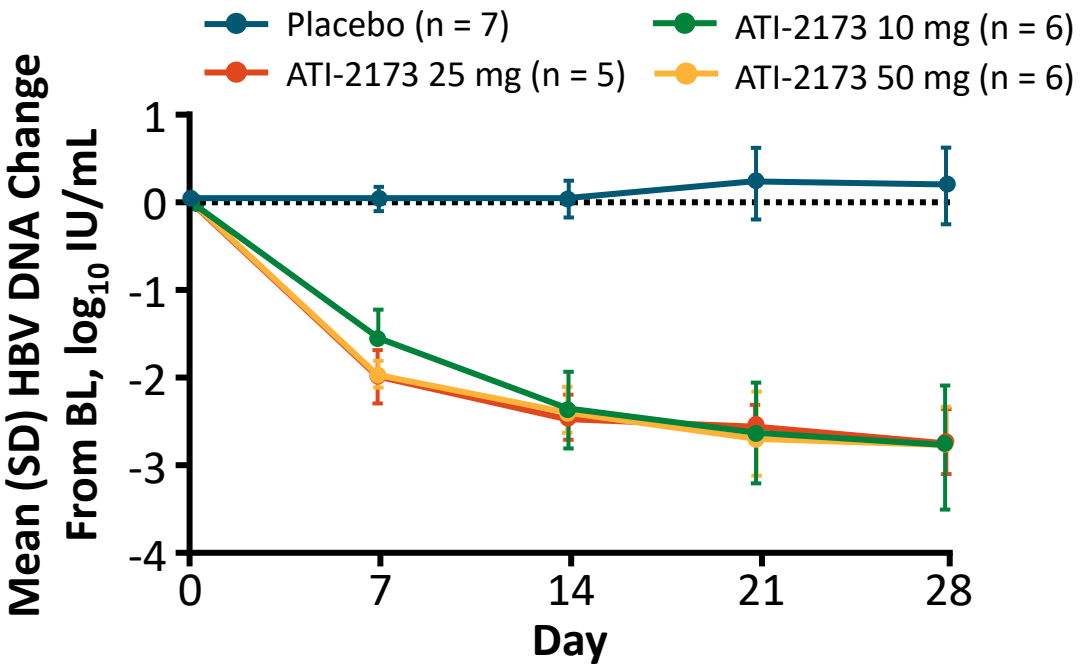


1. Gane E. EASL 2021; Abstr 2879. 2. Yuen. EASL 2021. Abstr LBO2764.

Slide credit: clinicaloptions.com

Investigational HBV Cure Strategies: ATI-2173

- Phosphoramidate prodrug of clevudine-5'-triphosphate[1,2]; functions as an active site polymerase inhibitor nucleotide
- In phase Ib ascending-dose trial, potent anti-HBV responses seen at 28 days. Sustained off-treatment responses seen[2]
- Antiviral effect seen at ~1/4 oral dose of clevudine, increasing safety

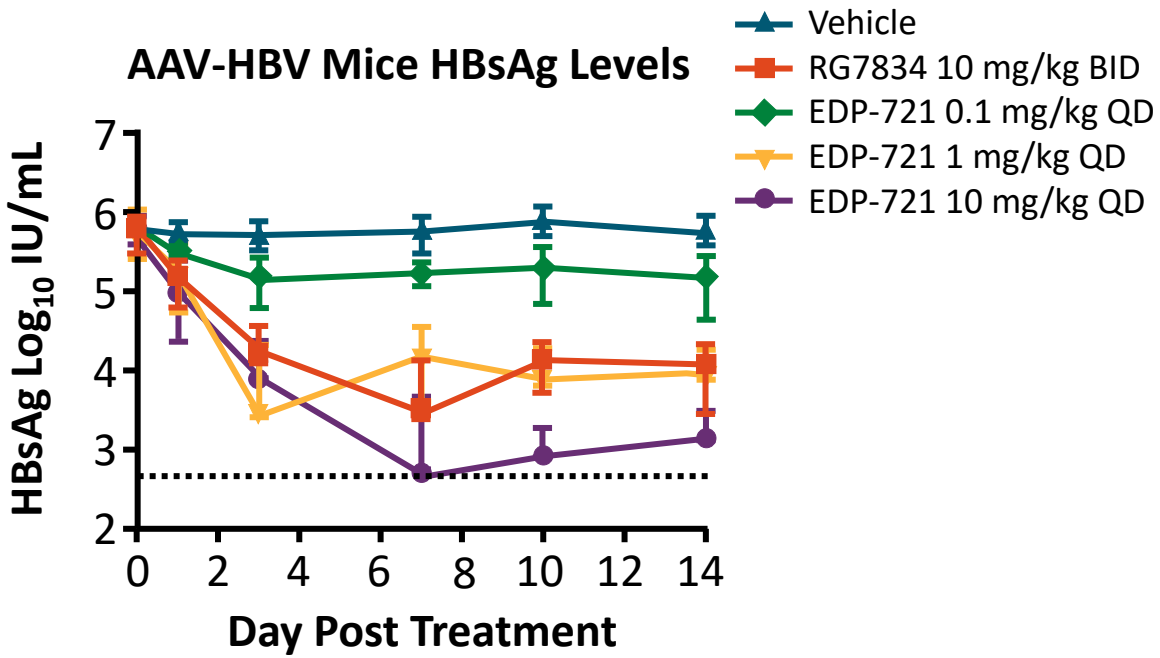


1. Mayers. EASL 2021. Abstr 1251. 2. Squires. EASL 2021. Abstr 1240.

Slide credit: clinicaloptions.com

Investigational HBV Cure Strategies: EDP-721

- Selective inhibitor of noncanonical poly(A) polymerase domain-containing proteins PAPD5 and PAPD7
- Destabilizes HBV RNA and blocks production of viral proteins, including HBsAg
- Active against all HBV genotypes tested (A-H)
- Displays synergy with other antivirals in vitro
- Declines in HBsAg, HBeAg seen within 24 hr in mouse model

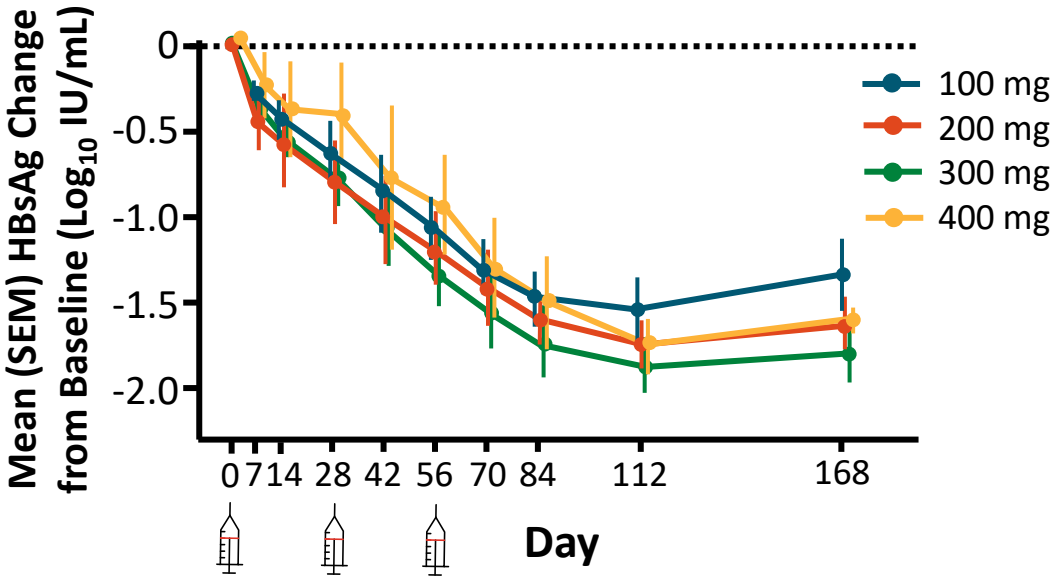


Vaine. EASL 2021. Abstr 942.

Slide credit: clinicaloptions.com

Investigational HBV Cure Strategies: JNJ-3989

- siRNA that prevents transcription of mRNAs involved in the production of viral proteins, including HBV polymerase and HBsAg
- Treatment with JNJ-3989 100 mg-400 mg SC Q4W, in combination with TDF or ETV, resulted in sustained reductions of HBsAg, HBeAg, HBcrAg, and HBV RNA in both HBeAg-positive and HBeAg-negative patients



Gane. EASL 2021. Abstr 1430.

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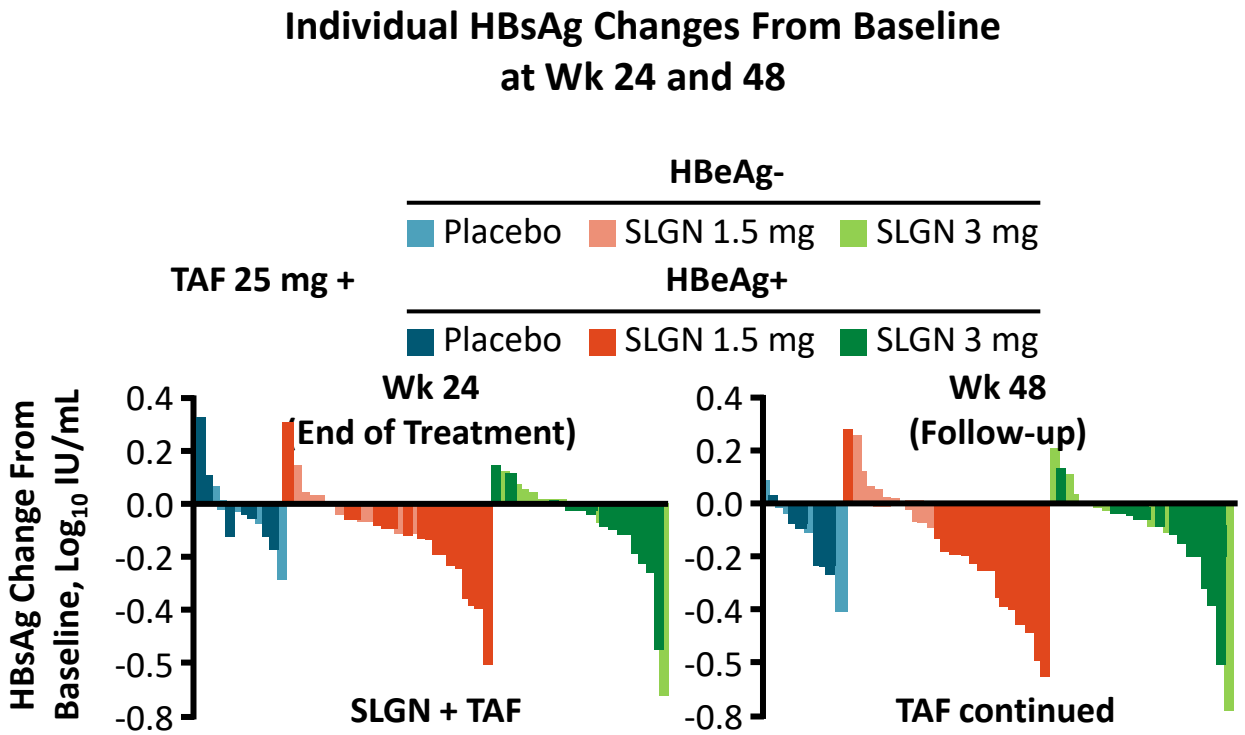
Investigational HBV Cure Strategies: Selgantolimod

- Selective, oral, small molecule agonist of toll-like receptor 8
- Induces intrahepatic HBV immunity through migration, activation, and proliferation of intrahepatic CD8+ T-cells, B-cells, NK cells, and MAIT cells
- Phase II study of SLGN vs placebo for 24 wk with daily TAF, followed by TAF for 24 wk, showed sustained declines of HBsAg ≥0.5 log_{10}/mL from BL in patients treated with SLGN
  - No patient achieved primary endpoint of HBsAg decline ≥1.0 log_{10}/mL at Wk 24



Janssen. EASL 2021. Abstr 2429.

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Investigational HBV Cure Strategies: VIR-2218

- Investigational GalNAc-conjugated siRNA that is effective across all genotypes
- Wk 48 results of phase II trial in 24 noncirrhotic, virologically suppressed participants with CHB showed that 2 doses of VIR-2218 20-200 mg SC 4 wk apart resulted in substantial reductions in HBsAg in both HBeAg- and HBeAg+ participants

Mean Maximum Decline in HBsAg, log_{10}/mL	HBeAg- (n = 18)	HBeAg+ (n = 6)
VIR-2218 20 mg	-1.03	ND
VIR-2218 50 mg	-1.23	-1.16
VIR-2218 100 mg	-1.50	ND
VIR-2218 200 mg	-1.65	-1.57

Gane. EASL 2021. Abstr 44.

Slide credit: clinicaloptions.com

Summary: HBV

- National Database of Korea: Patients with CHB left untreated more likely to develop extrahepatic malignancies than treated patients or uninfected controls
- Nuc-Stop: Stopping NA treatment in virologically suppressed noncirrhotic HBeAg-negative CHB patients may be safe, with low levels of flare seen among the 127 patients included
- TDF shown to be effective in children <12 yr of age for endpoints of HBV DNA <69 IU/mL at Wk 48 and normalization of ALT at Wk 192
- In nationwide cohort study in Denmark, liver disease largest contributor to mortality in patients with CHB
- Multiple novel therapeutic agents in development with ideal endpoint of HBsAg seroconversion
  - Several different modes of action are being investigated, including combination of DAAs and immune modulators

Hepatitis C Studies

Automated Liver Function Testing: Background

- Estimated 21,000 people in Scotland with HCV infection
  - 50% estimated to be undiagnosed
  - Older patients without overt risk factors likely represent undiagnosed cases (ie, “hard to reach” patients)
- iLFT: “intelligent” liver function testing automatically added if standard LFTs above reference rates (ALT >30 IU/mL)
  - Ordered by general practitioners
  - Algorithm uses blood results, fibrosis score, and clinical data to generate a likely diagnosis and management plan from 32 possible outcomes
- Current retrospective cohort analysis assessed if iLFT can help identify “hard-to-reach” patients with HCV infection

Livingstone. EASL 2021. Abstr 1390.

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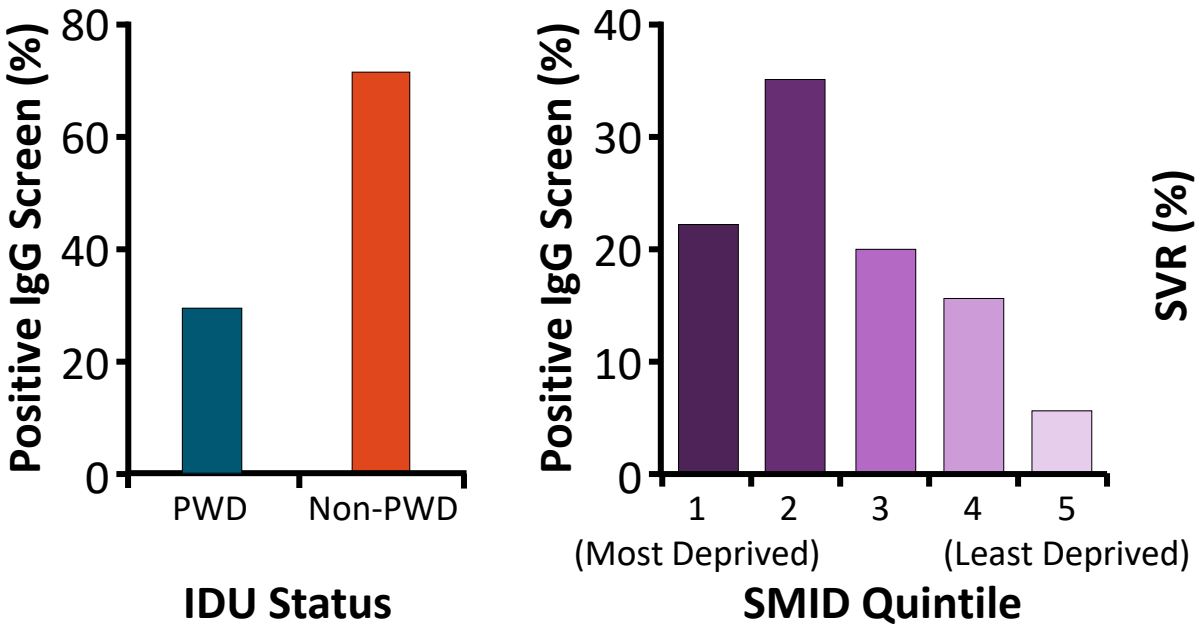
Automated Liver Function Testing: Results

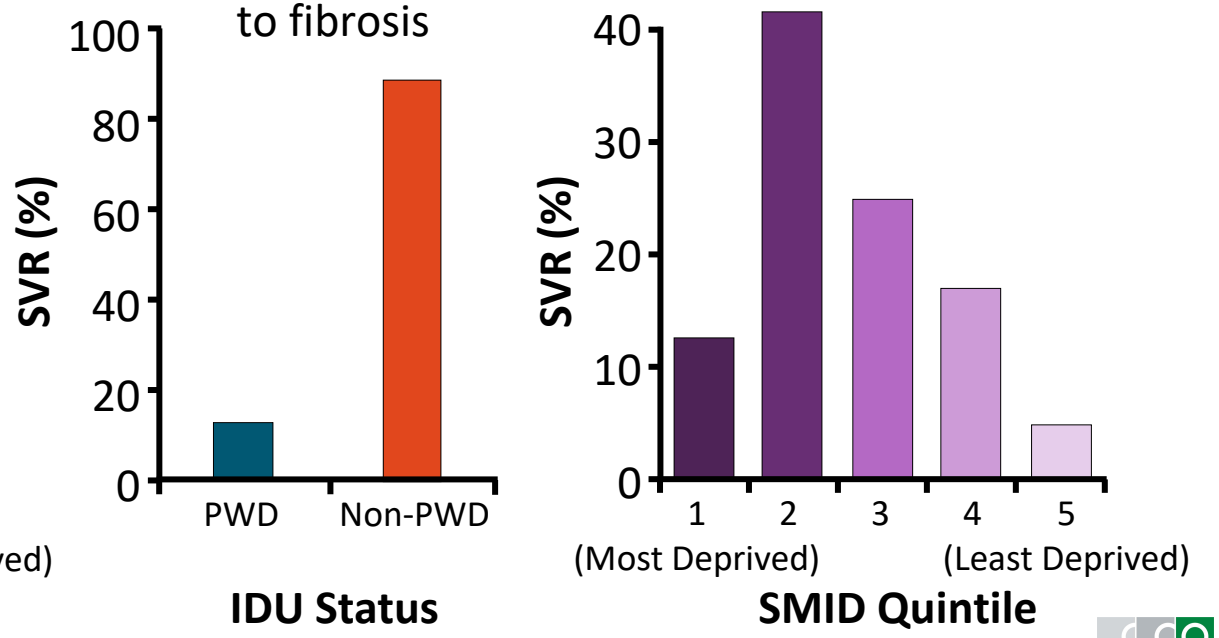
HCV Antibodies

- 49/6791 patients who underwent iLFT were positive for HCV antibodies
  - Average age: 51 yr



SVR

- 24/26 patients who began and completed HCV therapy achieved SVR
  - Average age: 53 yr
  - 21 discharged; 3 remained under review due to fibrosis



Livingstone. EASL 2021. Abstr 1390.

Slide credit: clinicaloptions.com

Feasibility of Point-of-Care HCV Testing in Pharmacies in France

- Pharmacists enrolled on a voluntary basis and received training and education on PoC HCV testing
  - Planned 10 tests per wk per pharmacy for 12 mo for a total of 5000 tests
- Screening conducted only for patients with ≥1 risk factor
- Persons with positive HCV test referred for follow-up HCV viral load testing and assessment for liver fibrosis with *FibroScan*
- Patients then eligible for treatment with HCV antiviral agents

- 29 pharmacies completed ≥1 PoC test
  - Testing decreased during a flu vaccination campaign and during the COVID-19 pandemic
- 656 tests performed
  - 46 persons with positive tests (serological prevalence: 7.0%) referred for additional assessment

HCV RNA Result	n	Risk Factors	Mean *FibroScan* Score
Negative	33	1-2	4.5 (F1)
Positive	13	3-9	8.6 (F2)

- All patients effectively treated and cured with HCV antiviral agents

Remy. EASL 2021. Abstr 690.

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Data From the German Hepatitis C-Registry (DHC-R): Lost to Follow-up After DAA Therapy

- Outcomes of patients with HCV from the DHC-R (German Hepatitis C-Registry) with LTFU before and after EOT compared with outcomes from patients with data on SVR 12/24
  - LTFU before EOT: reported lost before treatment was ended as scheduled
  - LTFU after EOT: lost after a full course of therapy but without SVR12/24 data
- ITT population: N = 7898 patients treated with GLE/PIB, SOF/LDV, SOF/VEL, SOF/VEL/VOX and GZR/EBR (± RBV)

Outcome	Patients (N = 7898)
Loss to follow-up, n (%)	908 (11.5)
▪ Before EOT, n	432
▪ After EOT, n	476
SVR in ITT population (N = 7989), %	86
SVR in mITT* population (N = 6990), %	98

*mITT = patients with SVR12/24 data.

Christensen. EASL 2021. Abstr 51. *Data derived from DHC-R, a project of the German Liver Foundation, managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German Gastroenterologists in Private Practice (bng). DHC-R is financially supported by AbbVie Deutschland GmbH & Co. KG, Gilead Sciences GmbH, MSD Sharp & Dohme GmbH as well as Bristol-Myers Squibb Gmbh & Co. and Janssen-Cilag GmbH (each until 2020-07-14) and Roche Pharma AG (until 2017-07-14).*

Data From the German Hepatitis C-Registry (DHC-R): Predictors of Loss to Follow-up After DAA Therapy

Baseline Characteristic	mITT Population (N = 6990)	Lost Before EOT (n = 432)	*P* Value*	Lost After EOT (n = 476)	*P* Value†
Male, n (%)	4164 (59.6)	313 (72.5)	<.001	338 (71.0)	<.001
Mean age, yr (SD)	52.5 (12.9)	46.5 (13.2)	<.001	46.4 (12.4)	<.001
Psychiatric disorders, n (%)	1040 (14.9)	48 (11.1)	.030	63 (13.2)	.350
HCV/HIV coinfection, n (%)	605 (8.7)	20 (4.6)	.002	18 (3.8)	<.001
Non-OST/NDU, n (%)	4680 (67.0)	191 (44.2)	<.001	176 (37.0)	<.001
Non-OST/IDU, n (%)	1403 (20.1)	121 (28.0)	<.001	153 (32.1)	<.001
OST, n (%)	907 (13.0)	120 (27.8)	<.001	147 (30.9)	<.001

**P* value not lost vs lost before EOT. †*P* value not lost vs lost after EOT.

- In multivariate regression analysis, higher risk of LTFU before and after EOT associated with being male or of younger age and having a history of drug abuse and/or an OST; lower risk of LTFU associated with HCV/HIV coinfection and psychiatric disorders

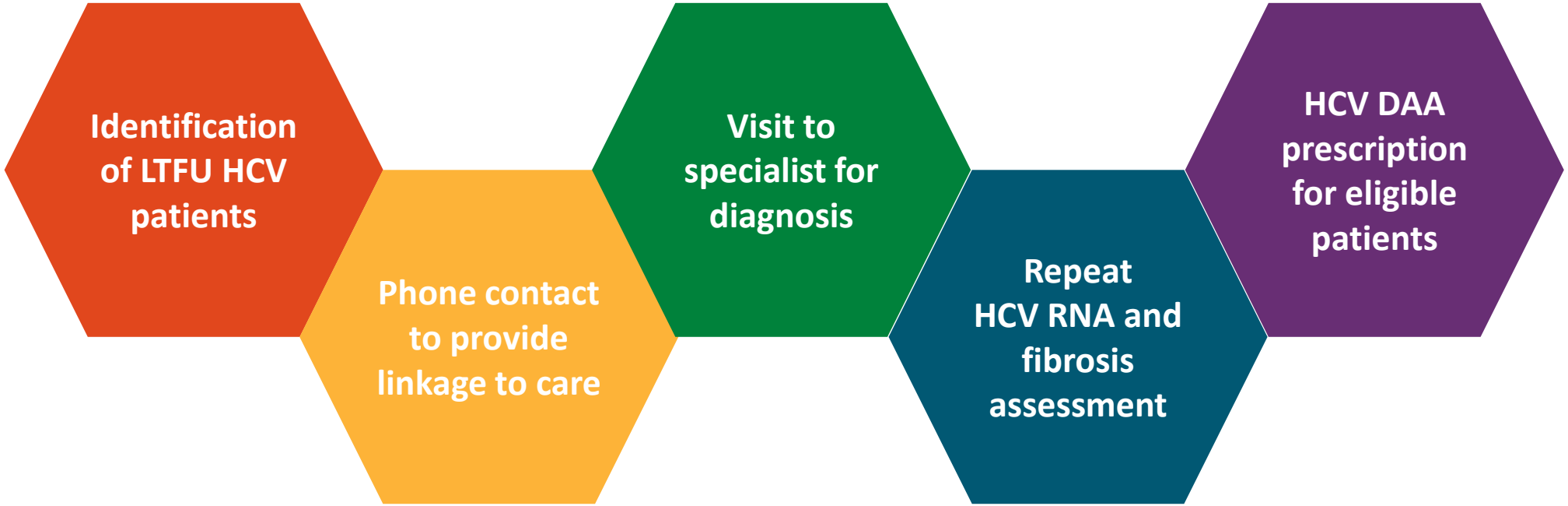
- Investigators conclude that alternative treatment approaches (ie, intense monitoring or directly observed treatment) tailored to specific groups at varying risks of LTFU should be considered

Christensen. EASL 2021. Abstr 51.

Slide credit: clinicaloptions.com

Relink-C Strategy to Retrieve Lost to Follow-up HCV Patients in Spain

- Retrospective search for LTFU HCV RNA-positive patients in Barcelona database carried out between January-December 2019



Martinez-Campreciós. EASL 2021. Abstr 1341.

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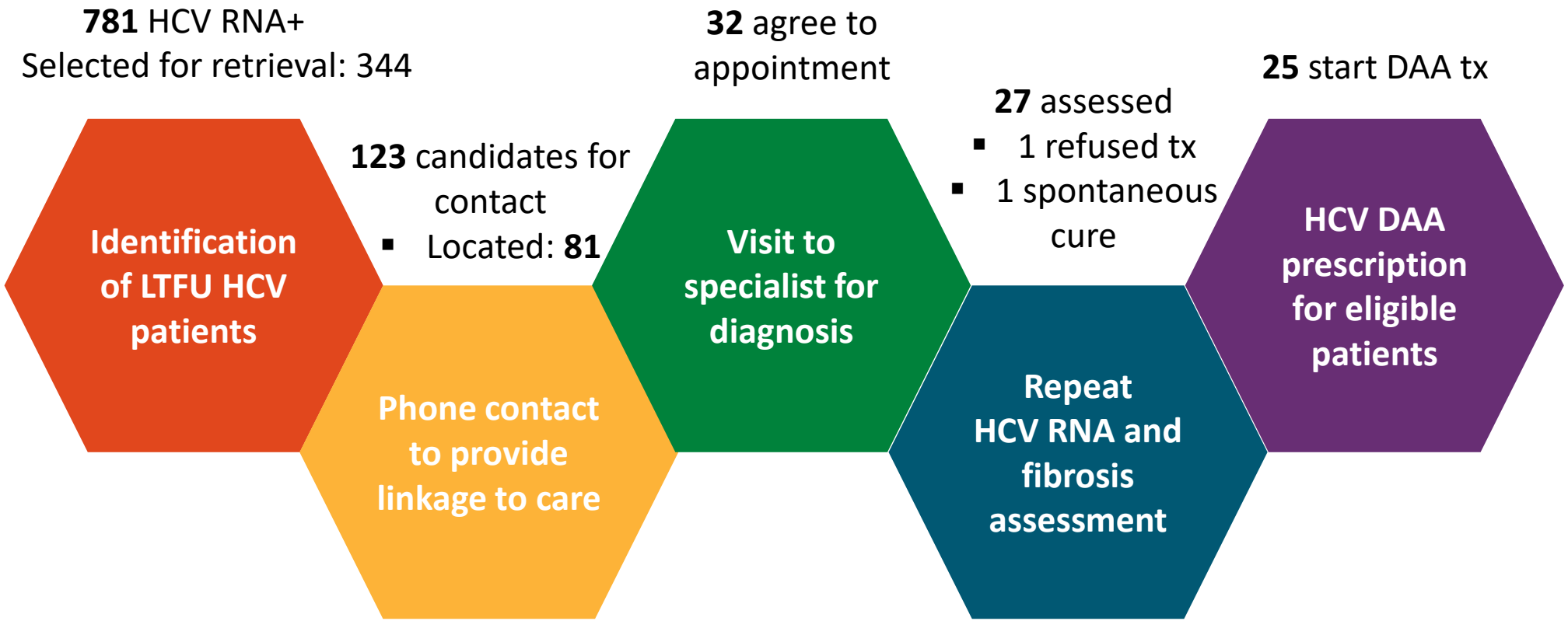
Relink-C Strategy: Treatment Cascade

- Out of 781 identified patients, 32 agreed to specialist appointment and 25 started treatment



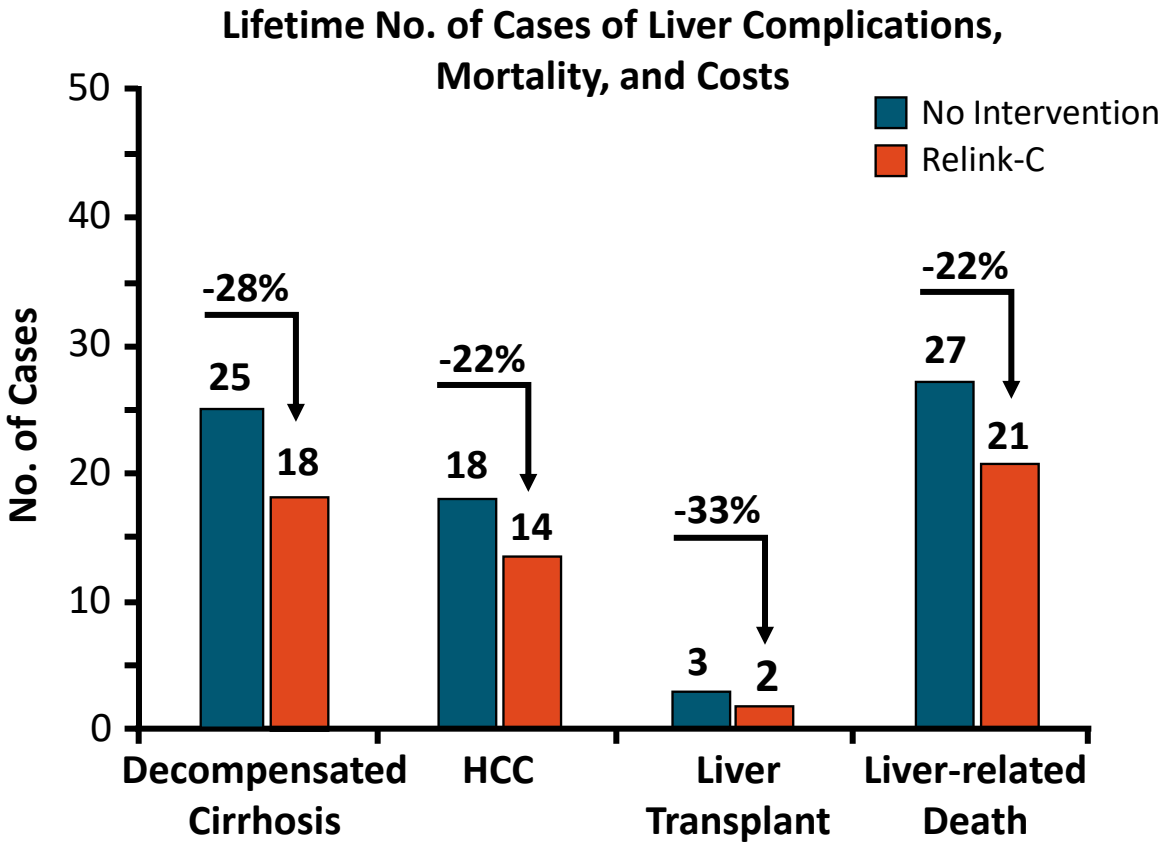
Martinez-Campreciós. EASL 2021. Abstr 1341.

Slide credit: clinicaloptions.com

Relink-C Strategy: Morbidity, Mortality Reductions, and Cost Savings

- Markov model demonstrates that treating 25 patients reduced mortality and liver complications
- €278,534 of healthcare savings projected

Costs, €	No Intervention	After Linkage to Care
Decompensated Cirrhosis	200,086	154,085
HCC	299, 816	239,065
Liver Transplant	788,953	617,171

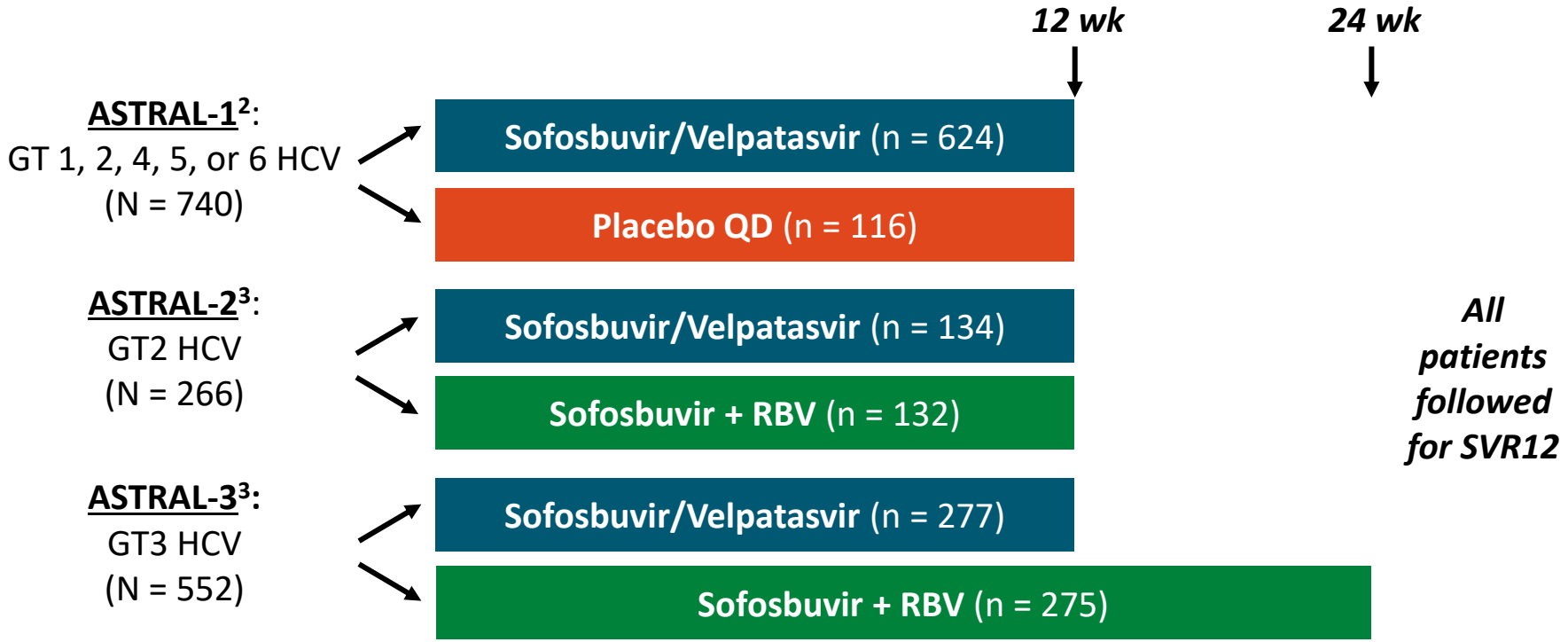


Martinez-Campreciós. EASL 2021. Abstr 1341.

Slide credit: clinicaloptions.com

Concordance of SVR4, SVR12, and SVR24 Following Sofosbuvir/Velpatasvir FDC Treatment in ASTRAL Trials

- Post hoc analysis of 3 multicenter, randomized phase III trials in tx-naive and tx-experienced patients (n = 1035 receiving sofosbuvir/velpatasvir; n = 1558 receiving sofosbuvir + RBV or placebo)[1]
  - Concordance analysis conducted in patients with SVR4 and SVR12 data, or SVR12 and SVR24 data



Sofosbuvir/velpatasvir dosed 400/100 mg QD.

1. Sulkowski. EASL 2021. Abstr 983. 2. Feld. NEJM. 2015;373:2599. 3. Foster. NEJM. 2015;373:2608.

Slide credit: clinicaloptions.com

Concordance of SVR4, SVR12, and SVR24

SVR4 and SVR12 Concordance		SVR12, n	
		Yes	No
SVR4	Yes	1002	3
	No	0	10

SVR12 and SVR24 Concordance		SVR24, n	
		Yes	No
SVR12	Yes	991	0
	No	0	2

- High concordance observed between:
  - SVR4 and SVR12 (99.7% PPR, 100% NPR)
  - SVR12 and SVR24 (100% PPR, 100% NPR)
- Suggests that SVR4 can be utilized to predict long-term SVR in patients at risk of not attending later assessments (eg, incarcerated patients or those without a secure living situation)

Sulkowski. EASL 2021. Abstr 983.

Slide credit: clinicaloptions.com

C-Free Child Project: Program Design

- Global prevalence of HCV in children ≤18 yr of age in 2018 was 3.26 million (95% CI: 2.07-3.90)[1]
- Children and adolescents often marginalized populations neglected in policies and guidelines
- Egyptian Liver Care Society–sponsored C-Free Child Project (Phase IV) developed to treat children and adolescents (≥35 kg) with generic oral DAA therapy at specialized pediatric hepatitis treatment centers within university and teaching hospitals[2]
  - Includes baseline and follow-up laboratory tests, ultrasound, and *FibroScan;* dispensing of medication; distribution of prevention and personal care items during therapy and at SVR
  - Trains physicians, nurses, and IT staff
  - Holds health awareness workshops for children and their families
  - Regularly audits treatment centers

1. Schmelzer. Lancet Gastroenterol Hepatol. 2020;5:374. 2. El Sayed. EASL 2021. Abstr 2306.

C-Free Child Project: Outcomes

- 535 pediatric patients treated with generic ledipasvir/sofosbuvir 90 mg/400 mg for 12 wk
  - Median age : 16 yr (range 11.5-17.5)
  - Male-to-female ratio: 1.4:1
- 249/264 (94%) patients assessed for SVR achieved SVR
  - SVR rate was 100% on per-protocol analysis
  - 2 patients discontinued treatment; 13 lost to follow-up

Health History/Comorbidity, n		Patients (N = 535)
HCV risk factors	▪ Vaginal delivery	396
	▪ Multiple injections	222
	▪ Mother with HCV infection	198
	▪ Dental procedures	133
	▪ Informal health care	132
	▪ Surgery	123
	▪ Hospital admission	92
	▪ Blood transfusion	85
	▪ Circumcision by informal health care	44
Comorbidities	▪ Cardiac	2
	▪ Hemophilia	4
	▪ Thalassemia	3
	▪ Lymphoma	3
Cancer survivor		51
Clinical exam finding	▪ Splenectomy	3
	▪ Splenomegaly	3
	▪ Hepatomegaly	26

El Sayed. EASL 2021. Abstr 2306.

Slide credit: clinicaloptions.com

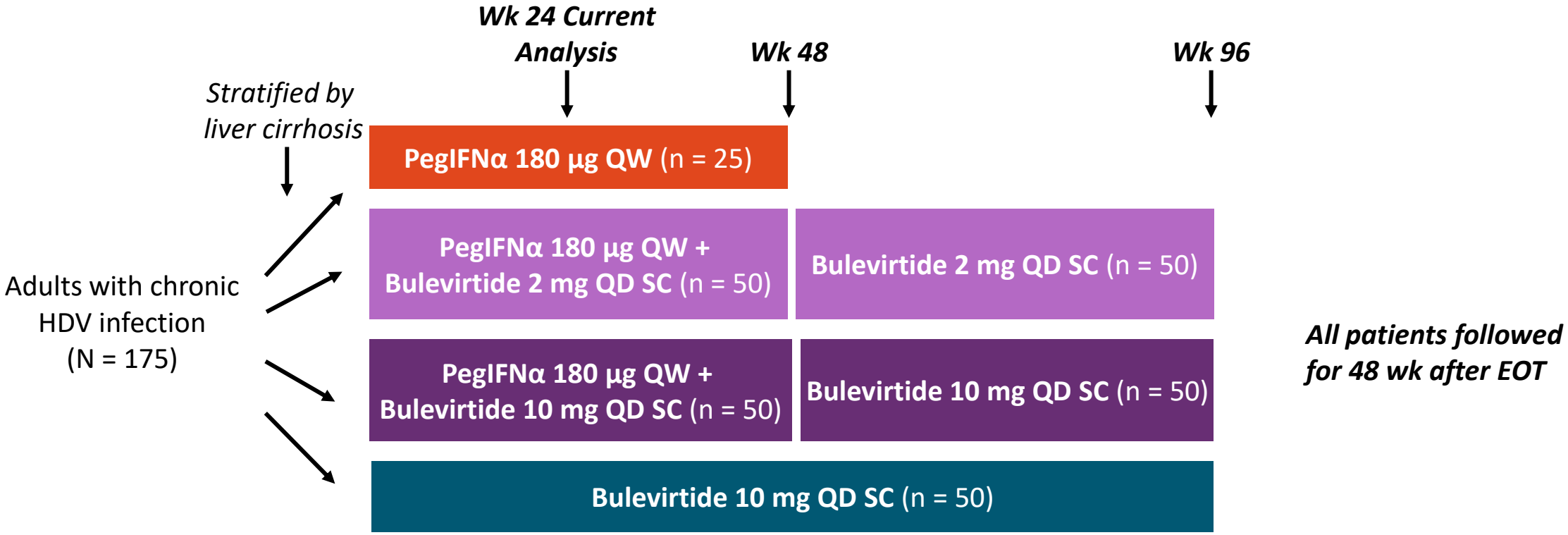
Summary: HCV

- Many strategies are being developed to link HCV+ patients to care with the goal of HCV elimination
- ASTRAL studies of SOF/VEL indicate that SVR4 may be a predictor of long-term treatment succuss
- High rates of SVR seen with ledipasvir/sofosbuvir 90 mg/400 mg for 12 wk in children and adolescents in NGO project in Egypt

Hepatitis D Studies

MYR204: Bulevirtide Alone and Combined With PegIFNα-2a for Chronic HDV Infection: Wk 24 Analysis

- Multicenter, international, open-label, randomized phase IIB trial of bulevirtide, entry inhibitor approved by EMA for use in adults with chronic HDV infection and compensated cirrhosis

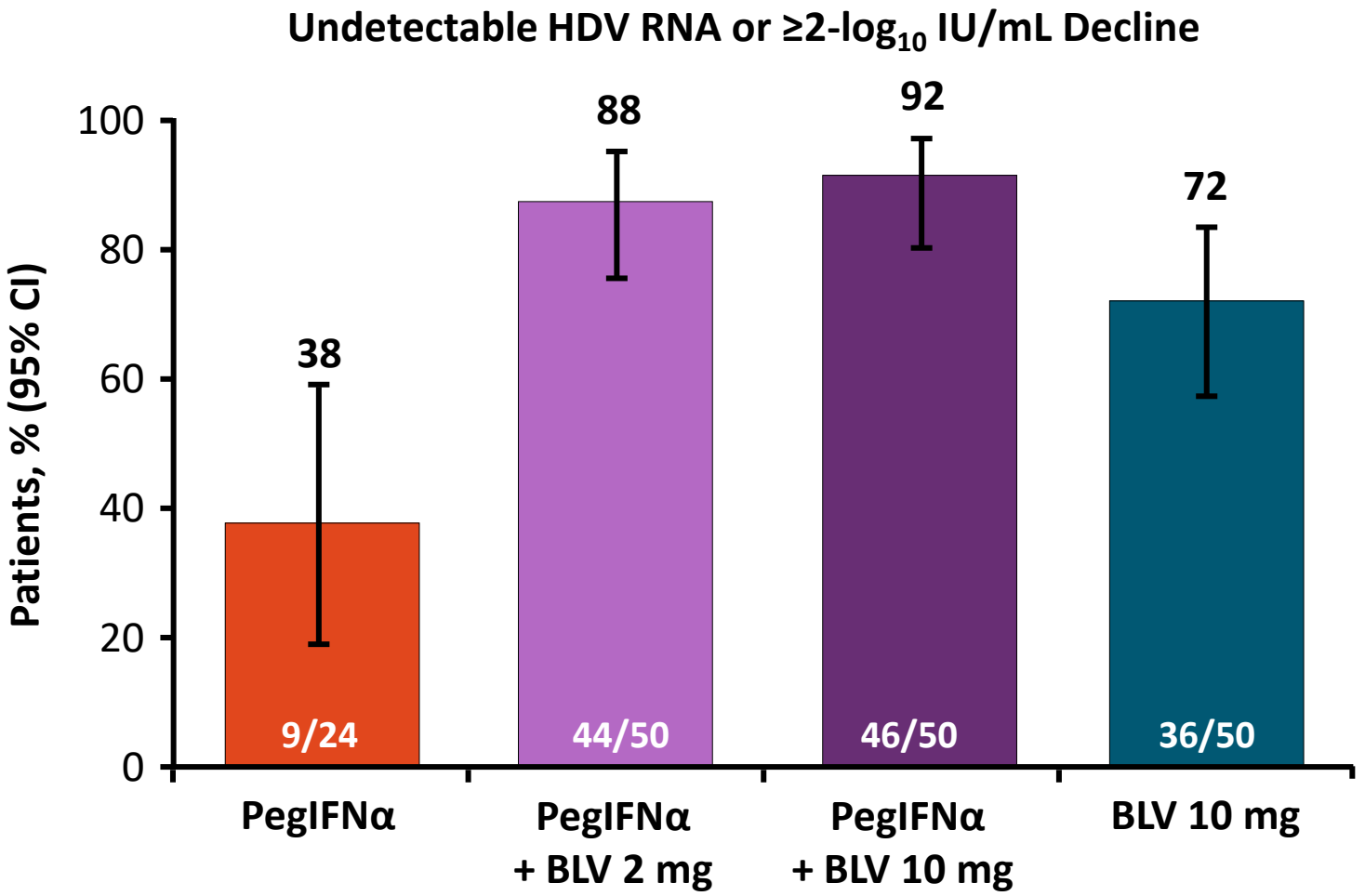


- Primary endpoint: undetectable HDV RNA (LLD: 6 IU/mL) at Wk 24 after EOT

Asselah. EASL 2020. Abstr 2717.

Slide credit: clinicaloptions.com

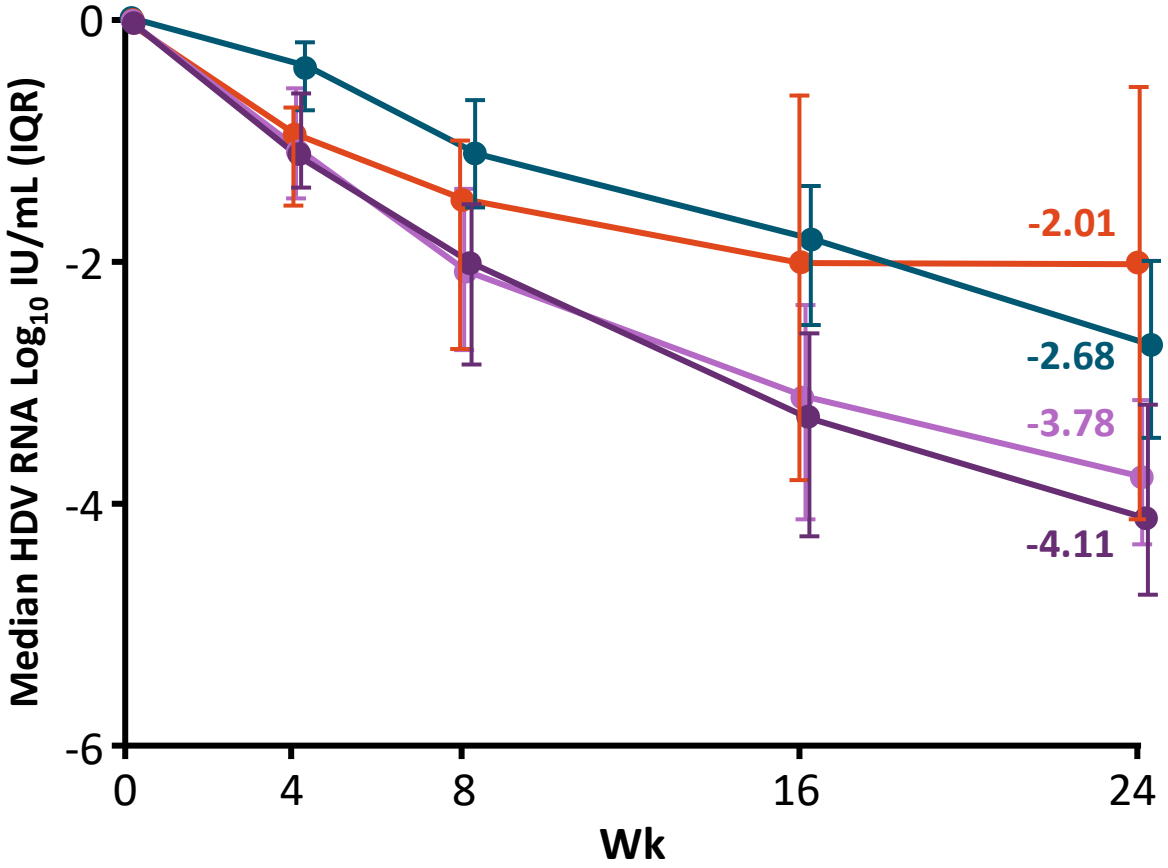
MYR204 Interim Wk 24 Analysis: Virologic Response

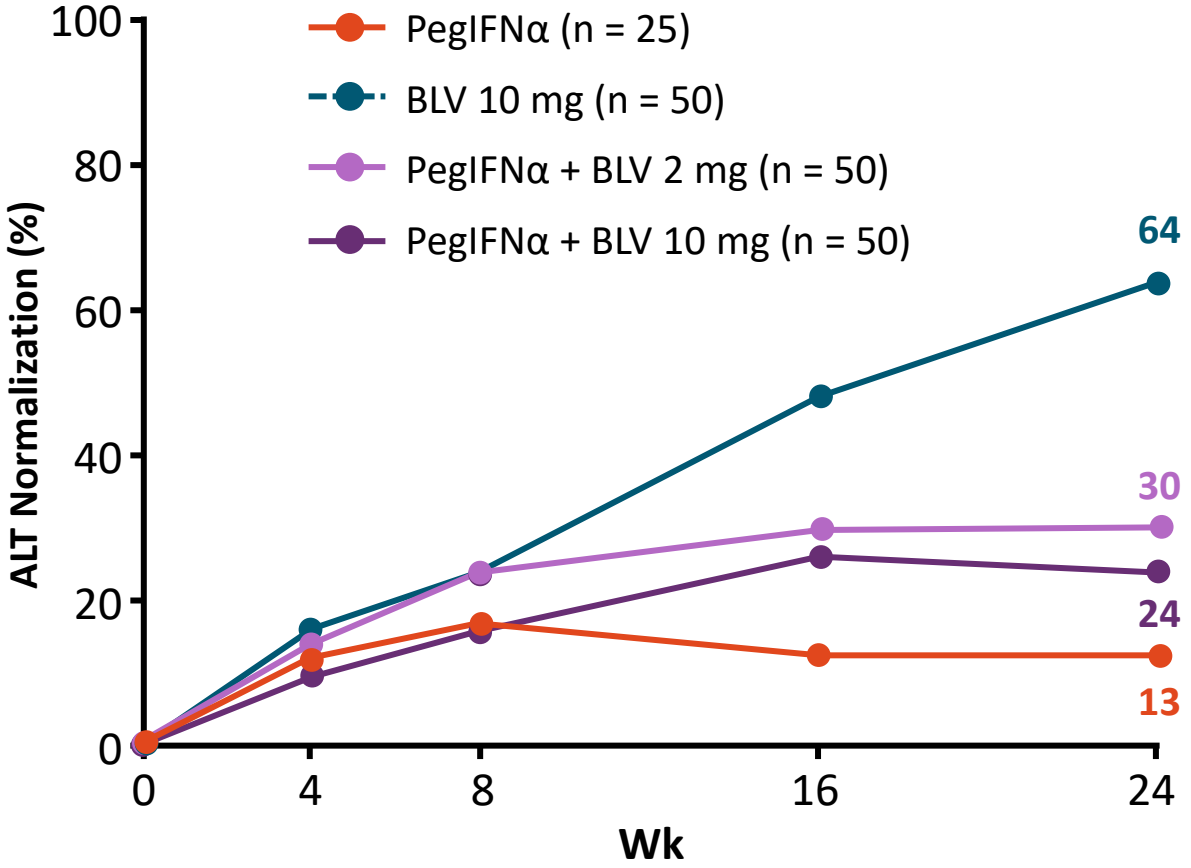


Asselah. EASL 2020. Abstr 2717.

Slide credit: clinicaloptions.com

MYR204 Interim 24-Wk Analysis: HDV RNA





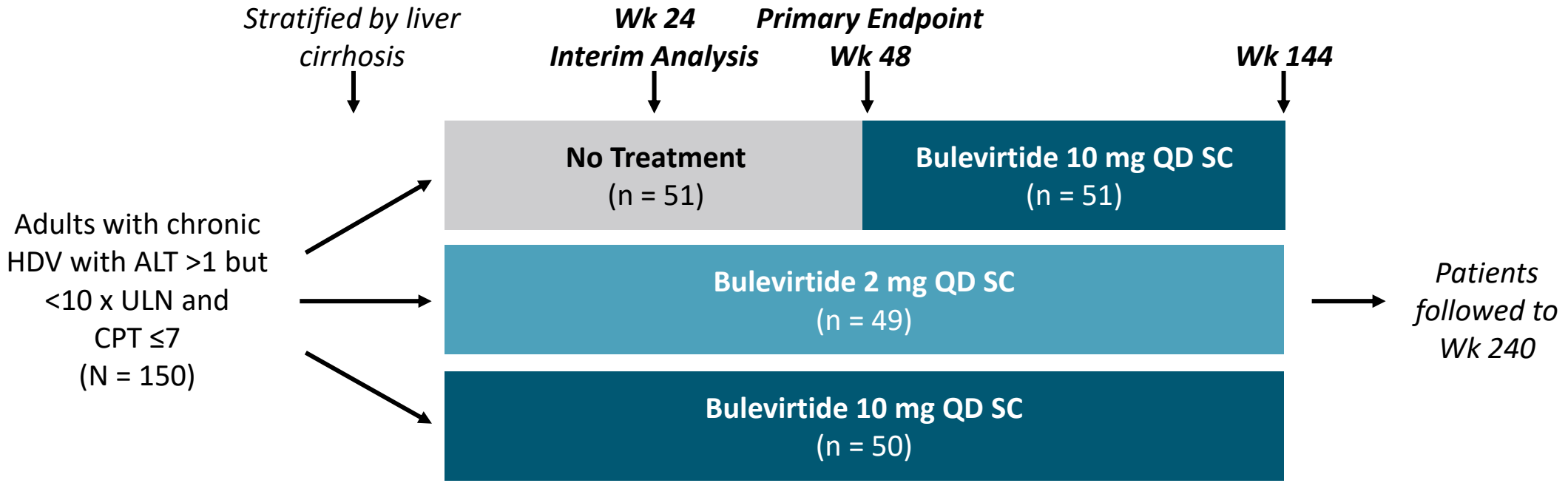
- No serious AEs related to bulevirtide use or AEs leading to d/c in BLV-treated patients
- ISRs observed in patients receiving BLV mostly mild; frequency 8% to 16% across arms

Asselah. EASL 2020. Abstr 2717.

Slide credit: clinicaloptions.com

MYR301: High- vs Low-Dose Bulevirtide Monotherapy in Patients With Chronic HDV Infection

- Multicenter, open-label, randomized, phase III trial

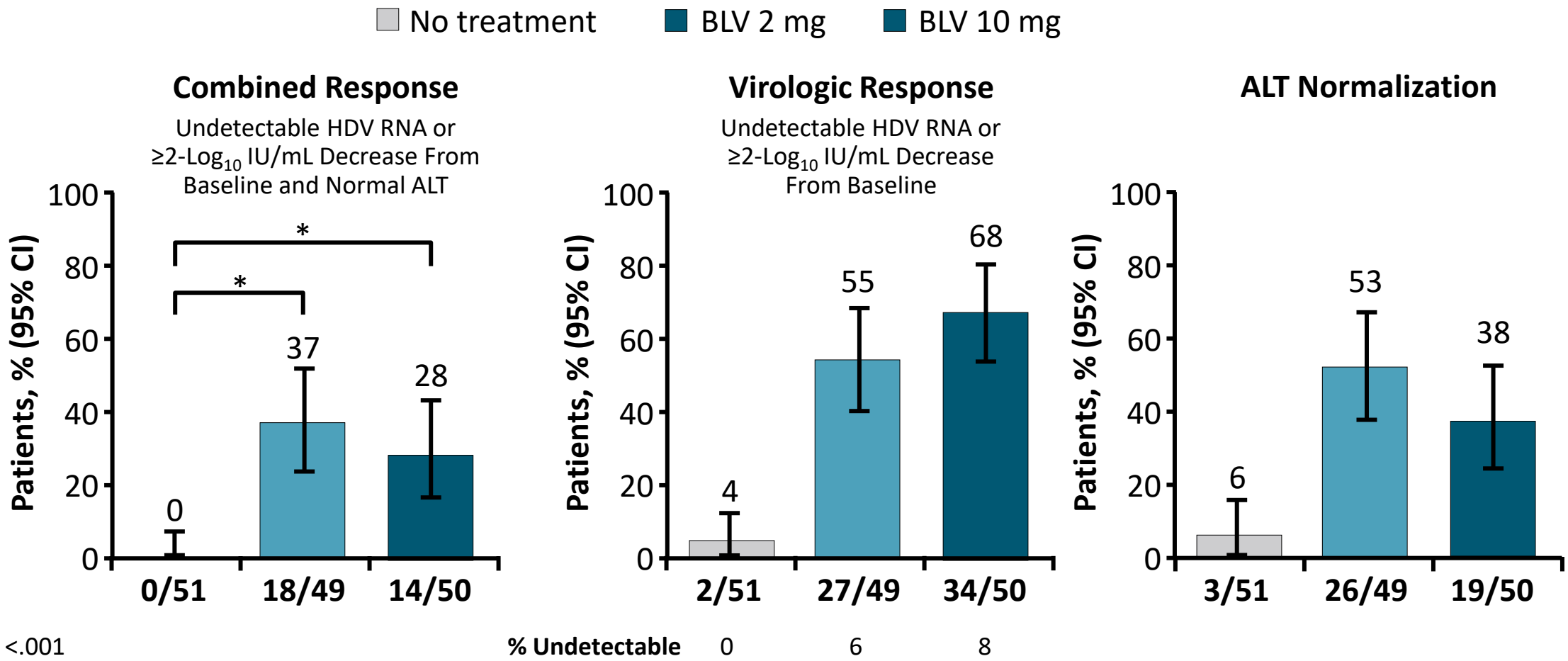


- Primary endpoint: combined response defined by undetectable HDV RNA or decrease by ≥2 $\log_{10}$ IU/mL from baseline **+** normalized ALT at Wk 48

Wedermeyer. EASL 2020. Abstr 2730.

Slide credit: clinicaloptions.com

MYR301 Interim Analysis: Virologic Efficacy at Wk 24



Wedermeyer. EASL 2020. Abstr 2730.

Slide credit: clinicaloptions.com

MYR301 Interim Analysis: Safety

- No serious AEs causing discontinuation of study drug; more ISRs with bulevirtide 10 mg vs 2 mg
- Elevations in total bile salts across all bulevirtide arms were asymptomatic

Safety Outcome, n (%)	No Treatment (n = 51)	Bulevirtide 2 mg (n = 49)	Bulevirtide 10 mg (n = 50)
AEs			
▪ Any AE	25 (51)	32 (65)	36 (72)
▪ Grade 3/4 AE	2 (4)	2 (4)	1 (2)
▪ Any serious AE	1 (2)	0	0
▪ D/c due to AE	0	0	0
▪ Death	0	0	0
AEs of interest			
▪ ISRs	0	3 (6)	13 (26)
▪ Liver-related AEs	0	0	0
Grade 3/4 laboratory abnormalities			
▪ Thrombocytopenia	2 (4)	0	0
▪ Leukopenia	1 (2)	0	1 (2)
▪ Neutropenia	1 (2)	0	0

Wedermeyer. EASL 2020. Abstr 2730.

Slide credit: clinicaloptions.com

Long-term Bulevirtide in Patients With Compensated HDV Cirrhosis

- Case reports (N = 3) of patients with HDV cirrhosis treated with self-administered bulevirtide 10 mg/day SQ added to ongoing TDF therapy for 3 yr
  - All patients previously treated with pegIFN
- Monitoring Q4W by LFTs, total bile acids, and HBV, HDV virologic markers for 2 yr; then, Q8W for third yr

Patients Included in Case Studies

Female, 69 yr of age
- Thrombocytopenia
- No HCC/no esophageal varices
- Diabetes treated with diet therapy
- Liver stiffness at BL: 17.3 kPa
- Platelet count: 95 x 10^9/L

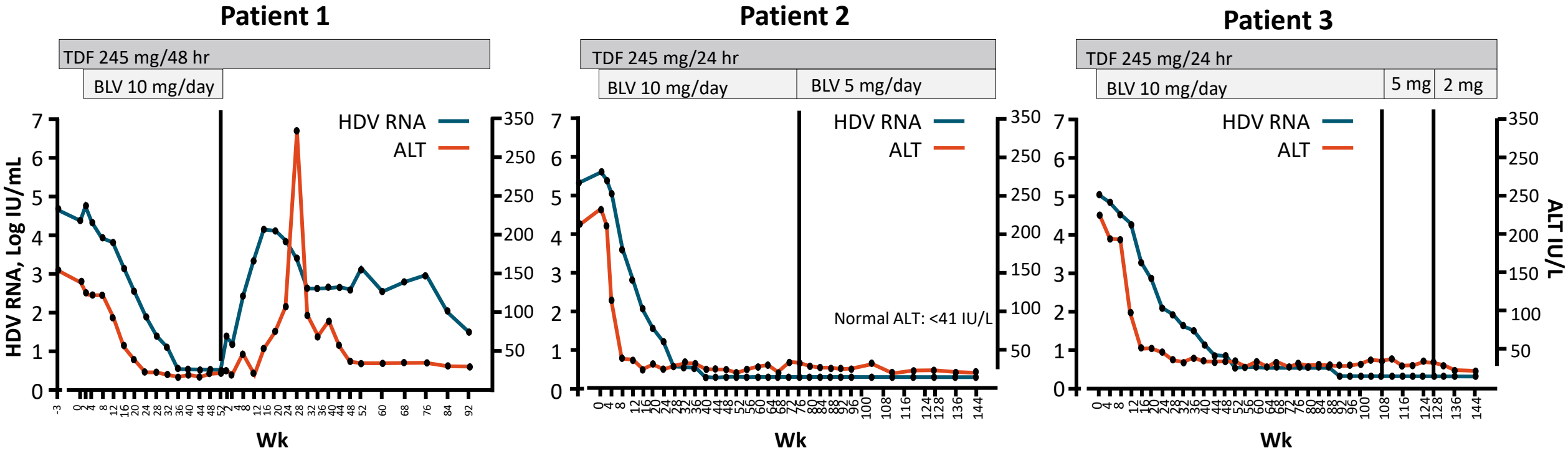
Male, 51 yr of age
- Large plasma cellular component on liver biopsy
- No HCC/small esophageal varices
- Diabetes treated with diet therapy
- Liver stiffness at BL: 17.6 kPa
- Platelet count: 74 x 10^9/L

Female, 58 yr of age
- Autoimmune thrombocytopenia seen during previous treatment
- No HCC/no esophageal varices
- Platelet count: 210 x 10^9/L

Loglio. EASL 2021. Abstr 1448.

Slide credit: clinicaloptions.com

Long-term Bulevirtide in Patients With Compensated HDV Cirrhosis: Results



- HDV DNA reduction and ALT normalization over course of 3 yr
- Regression of esophageal varices in Patient 2 over course of treatment
- Treatment associated with asymptomatic increase in bilirubin
  - Bulevirtide dose decreased in all patients; antiviral effect maintained

Loglio. EASL 2021. Abstr 1448.

Slide credit: clinicaloptions.com

Summary: HDV

- Interim data from studies MYR204 and MYR301 demonstrate that treatment with BLV associated with significant HDV RNA decline and normalization of ALT
  - Combination with pegIFN-α2a demonstrates synergistic antiviral activity
  - These findings further support conditional approval of BLV 2 mg in the EU
- Long-term real-world study of 3 patients with chronic HDV infection shows HDV DNA reduction and ALT normalization over course of 3 yr of treatment with BLV and reduction of portal hypertension in 1 patient

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