Clinical Impact of New Viral Hepatitis Data From EASL 2018

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Updated EASL HCV Guidelines

EASL 2018 HCV Treatment Guidelines

- Recommendations for treatment-naive patients and patients previously treated with pegIFN/RBV ± SOF or SOF + RBV, ± compensated cirrhosis

HCV Genotype	SOF/VEL	GLE/PIB	SOF/VEL/ VOX	LDV/SOF	EBR/GZR	OBV/PTV/ RTV + DSV
1a	Yes	Yes	No*	Yes†	Yes‡	No
1b	Yes	Yes	No*	Yes	Yes	Yes
2	Yes	Yes	No*	No	No	No
3	Yes‖	Yes	Yes§	No	No	No
4	Yes	Yes	No*	Yes†	Yes#	No
5 or 6	Yes	Yes	No*	Yes†	No	No

*Triple combination effective but not needed because double combinations comparably effective. †Tx naive ± compensated cirrhosis. ‡Tx naive or tx experienced without cirrhosis or with compensated cirrhosis and HCV RNA ≤ 800,000 IU/mL. ‖Tx naive or tx experienced without cirrhosis. §Tx naive or tx experienced with compensated cirrhosis. #Treatment naive without cirrhosis or with compensated cirrhosis and HCV RNA ≤ 800,000 IU/mL.

EASL HCV Guidelines. 2018. In press.

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EASL 2018 HCV Treatment Guidelines

- Recommendations for patients who experienced DAA regimen (PI and/or NS5AI) failure: management should be in context of multidisciplinary team including experienced treaters and virologists

Failure of DAA (PI and/or NS5AI)-Containing Regimen	Retreatment Recommendation
± Compensated cirrhosis	SOF/VEL/VOX for 12 wks
± Compensated cirrhosis with predictors of lower response*	GLE/PIB + SOF for 12 wks†
Very difficult to cure: NS5A RASs after 2 failures of PI and/or NS5AI-containing regimens	SOF/VEL/VOX or GLE/PIB + SOF: + RBV for 12 wks, no RBV for 16-24 wks, or + RBV for 16-24 wks†
Decompensated cirrhosis	SOF/VEL + RBV for 24 wks†

*Advanced liver disease, multiple courses of DAA-based treatment, complex NS5A RAS profile.
†Based on individual decision.

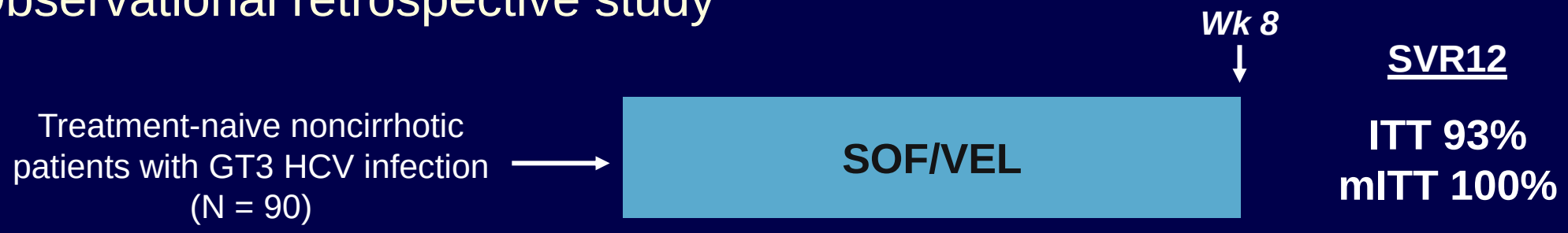
EASL HCV Guidelines. 2018. In press.

Slide credit: clinicaloptions.com

Treatment of HCV Infection

Sofosbuvir/Velpatasvir for 8 Wks in Treatment-Naive Patients With GT3 HCV and F2-F3 Fibrosis

- Observational retrospective study



- 91% receiving OST; 42% receiving daily supervised OST
  - 27 of 49 patients attending addiction center tested positive for current drug use
- Fibrosis: 67% F2; 31% F3
- 84 of 90 (93%) achieved SVR12 (ITT population)
  - 2 lost to follow-up, 2 d/c, 1 death, 1 reinfection
  - 100% SVR12 after excluding loss to follow-up, d/c, death, reinfection (mITT)

Boyle A, et al. EASL 2018. Abstract PS-034.

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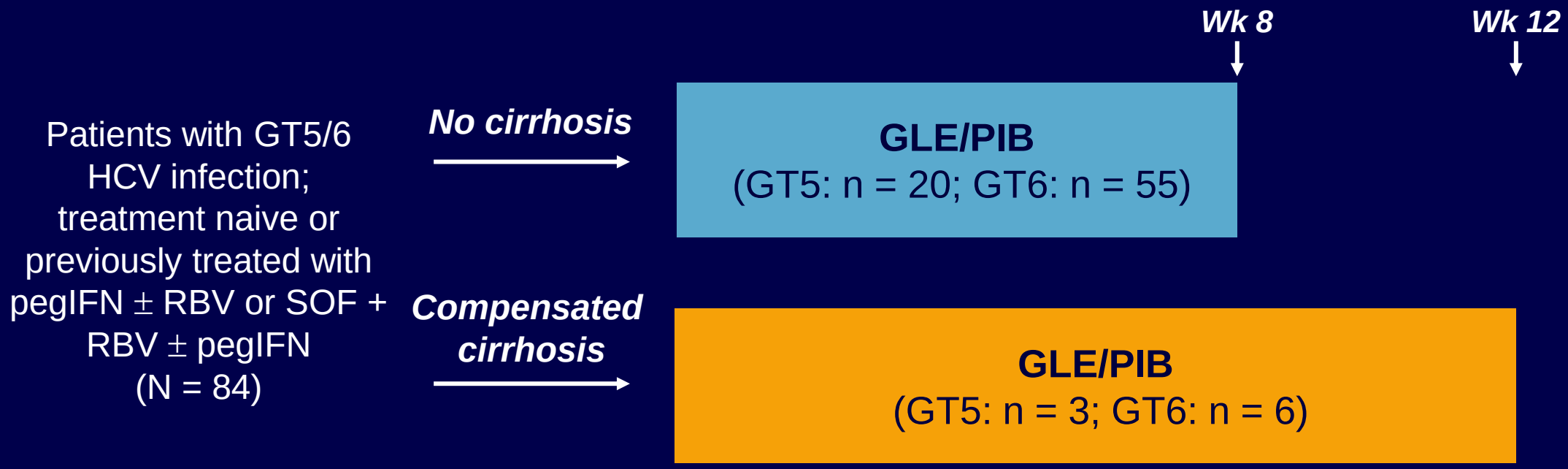
ENDURANCE-5, 6: Glecaprevir/Pibrentasvir in Patients With GT5/6 HCV Infection

- Nonrandomized, ongoing, open-label phase IIIb study
  - Primary endpoint: SVR12



Asselah T, et al. EASL 2018. Abstract GS-012.

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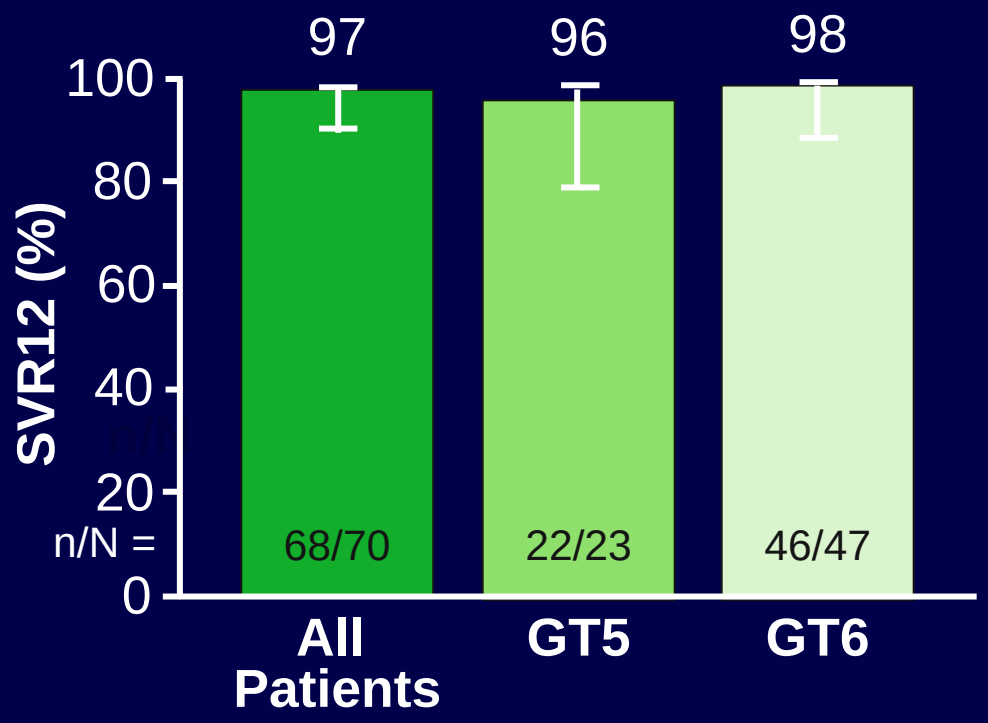
ENDURANCE-5, 6: Efficacy and Safety of Glecaprevir/Pibrentasvir for GT5/6 HCV



- 3 patients with serious AEs
  - None DAA related and none leading to discontinuation of study regimen

- 2 patients with VF, both white males adherent to therapy with high baseline HCV RNA

Characteristic	Patient 1	Patient 2
GT	5a	6f
Cirrhosis	Noncirrhotic	CP A
BL HCV RNA, IU/mL	10,800,000	625,000
Type of VF	Relapse	On-tx
NS3 RASs ▪ BL ▪ At VF	 D168E D168E	 None T93A
NS5A RASs ▪ BL ▪ At VF	 None None	 None A156M

Asselah T, et al. EASL 2018. Abstract GS-012. Reproduced with permission.

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German Hepatitis-C Registry: Real-World Efficacy of Glecaprevir/Pibrentasvir

- Multicenter prospective registry study of GLE/PIB for 8-12 wks in patients ± compensated cirrhosis
  - Included treatment naive or IFN or SOF + RBV experienced (N = 638)
    - 34% GT1a; 17% GT1b; 35% GT3
    - 90% treatment naive; 7% cirrhosis
- n = 96 with SVR12 data
- Per protocol (PP) population: no cirrhosis, treated 8 wks: n = 91; with cirrhosis, treated 12 wks: n = 2

GLE/PIB for 8-12 Wks ± Cirrhosis	SVR12, % (n/N)
Overall	97 (93/96)
Per protocol	100 (93/93)

- 3 nonresponders: 2 discontinued for AEs; 1 lost to follow-up

Berg T, et al. EASL 2018. Abstract GS-007.

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German Hepatitis-C Registry: Real-World Safety and Tolerability of Glecaprevir/Pibrentasvir

Safety Parameter	GLE/PIB Safety Population (n = 321)
Any AE, n (%)	87 (27)
AEs leading to d/c, n (%)	2* (1)
Serious AE, n (%)	6 (2)
▪ Serious AEs related/possibly related to GLE/PIB†	1 (< 1)
AEs occurring in ≥ 5% of patients, n (%)	
▪ Fatigue	30 (9)
▪ Headache	25 (8)

- Laboratory abnormalities infrequent and no deaths occurred in safety analysis
  - Grade ≥ 3 AST increase (> 5 x ULN): 1/284 (< 1%)
  - Grade ≥ 3 ALT increase (> 5 x ULN): 0/306
  - Grade ≥ 3 total bilirubin increase (> 3 x ULN): 2/285 (1%)

*1 patient with IBD, CVD, thyroid dysfunction d/c at Wk 4 for AE of diarrhea; 1 patient with psychiatric disease, drug abuse, HIV, chronic respiratory disease d/c at Wk 1 for AE of nausea. †Meniere's disease, considered possibly related to treatment.

Berg T, et al. EASL 2018. Abstract GS-007.

STREAGER: Elbasvir/Grazoprevir for 8 Wks in Patients With GT1b HCV and Nonsevere Fibrosis

- Interim analysis of an international, open-label, single-arm phase III study

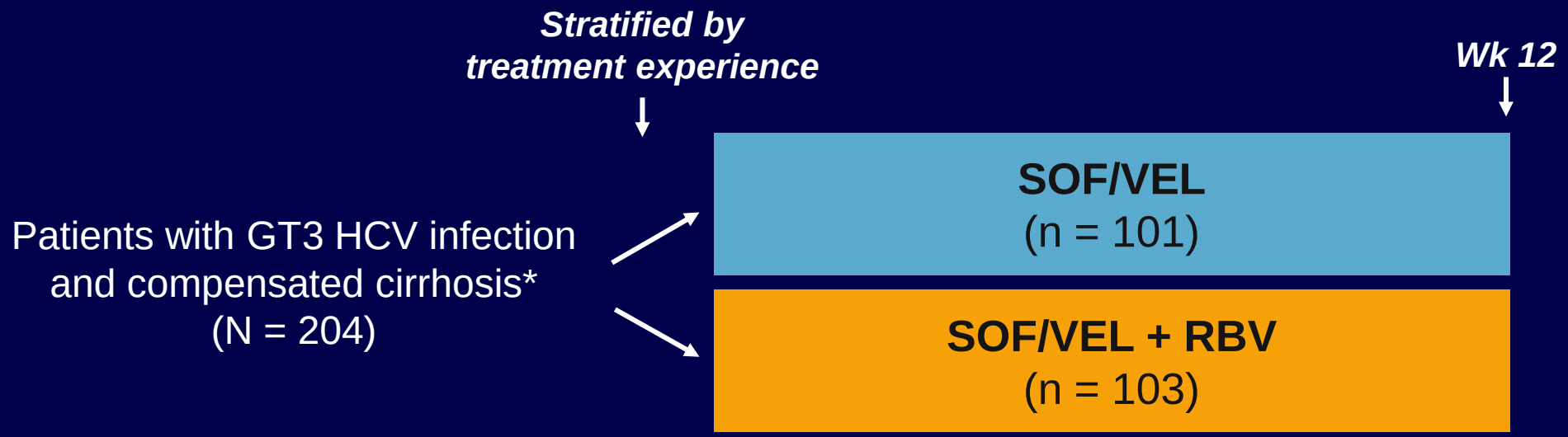
*Nonsevere fibrosis defined as *FibroScan* < 9.5 kPa and *FibroTest* < 0.59. Planned N = 120.

- SVR12 in GT1b: 98% (87/89; excludes 1 patient found to have GT1e HCV)
  - 4 relapses (3 at posttreatment Wk 12, 1 at posttreatment Wk 24 after achieving SVR12), including 1 patient with GT1e HCV
  - RAS detected in 3 of 3 relapsers
- No grade 3/4 AEs

Abergel A, et al. EASL 2018. Abstract LBP-010.

Sofosbuvir/Velpatasvir ± RBV for 12 Wks in Patients With GT3 HCV Infection and Cirrhosis

- Randomized, open-label study
  - Primary endpoint: SVR12



*Patients eligible if treatment naive or experienced, including previous use of NS3/4 PI or NS5B inhibitor. All patients were NS5A inhibitor naive. HIV coinfection permitted. Dosing: SOF/VEL 400/100 mg QD plus weight-based RBV.

Buti M, et al. EASL 2018. Abstract PS-035.

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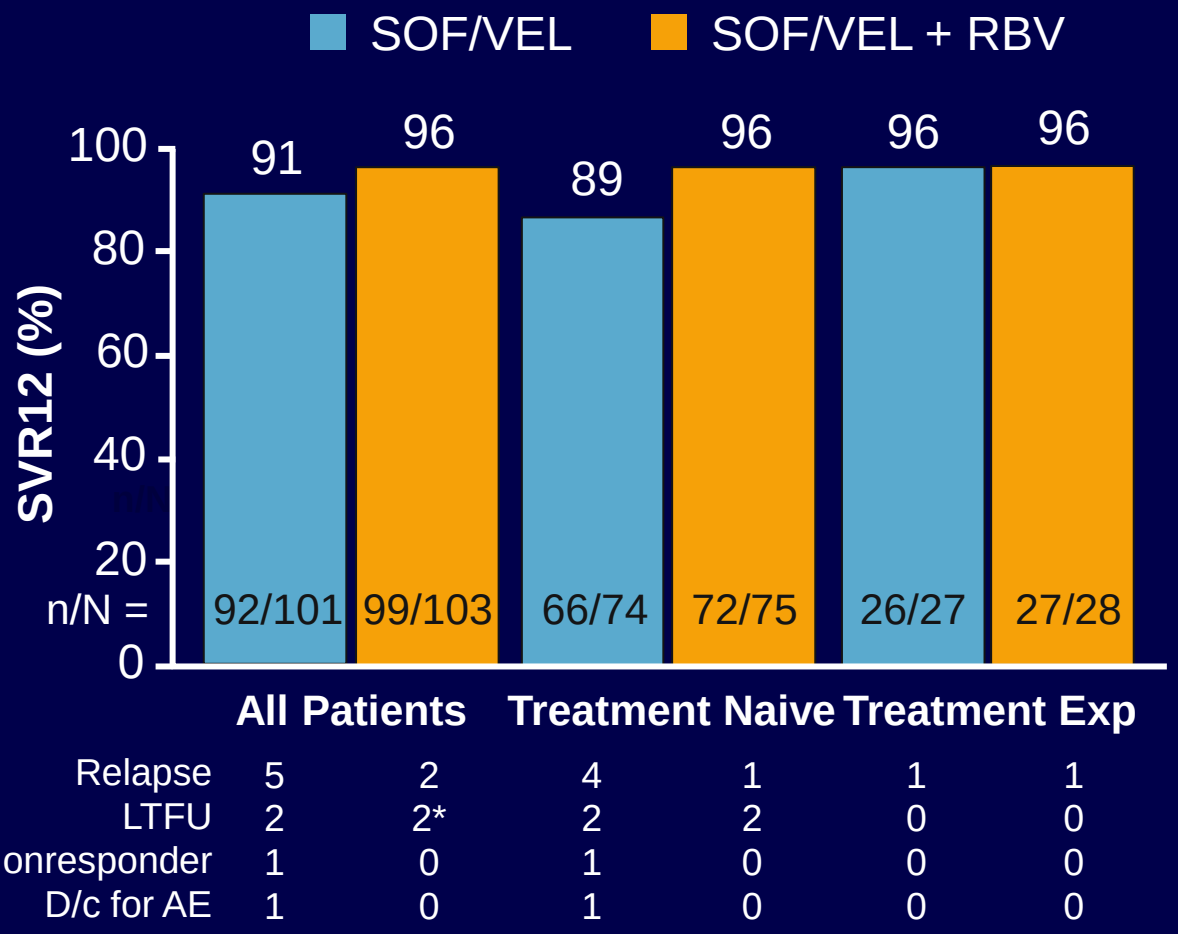
Efficacy of Sofosbuvir/Velpatasvir ± RBV for GT3 HCV With Cirrhosis



*1 LTFU discontinued for AE.

RAS Analysis, n/N (%)	SOF/VEL	SOF/VEL + RBV
Detection of BL RAS		
▪ No	79/98 (81)	79/101 (78)
▪ Yes	19/98 (19)	22/101 (22)
SVR12		
▪ No BL RAS	76/79 (96)	78/79 (99)
▪ BL RAS	16/19 (84)	21/22 (96)
▪ BL Y93H	2/4 (50)	8/9 (89)

Buti M, et al. EASL 2018. Abstract PS-035. Reproduced with permission.

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Safety of Sofosbuvir/Velpatasvir ± RBV for GT3 HCV With Cirrhosis

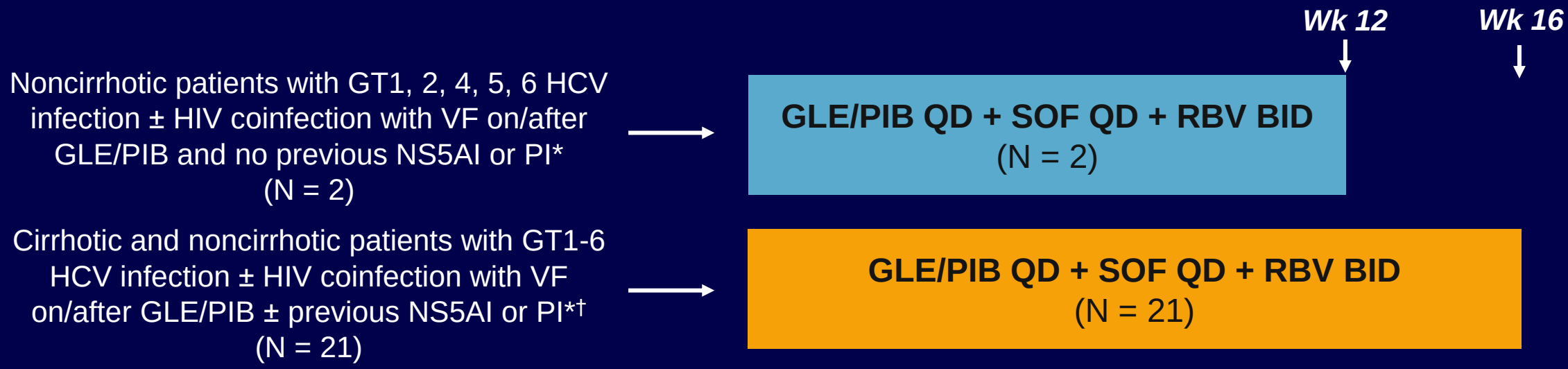
Safety Parameter, n (%)	SOF/VEL (n = 101)	SOF/VEL + RBV (n = 103)
Any AE	48 (48)	77 (75)
Grade 3/4 AE	2 (2)	1 (1)
Serious AE*	4 (4)	2 (2)
D/c of SOF/VEL for AE	1 (1)†	1 (1)‡
D/c of RBV for AE	--	2 (2)
Grade 3/4 lab abnormality	7 (7)	16 (16)
Hemoglobin < 10 g/dL	1 (1)	5 (5)

*Unrelated to study treatment. †D/c on Day 1 for dizziness and anxiety. ‡D/c on Day 20 for abnormal bilirubin.

Buti M, et al. EASL 2018. Abstract PS-035. Reproduced with permission.

MAGELLAN-3: GLE/PIB + SOF + RBV for 12-16 Wks for Retreatment After Failure of GLE/PIB

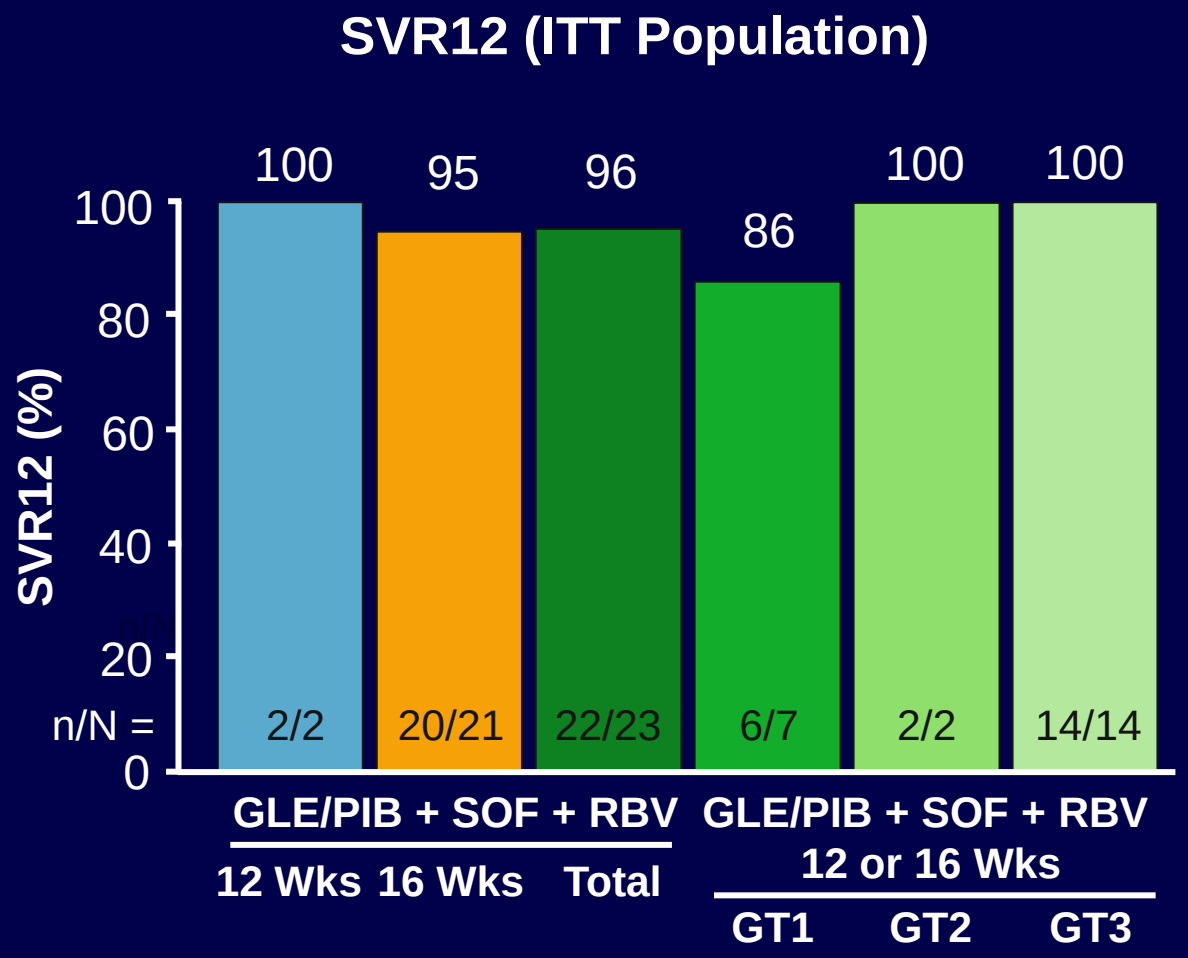
- Ongoing, open-label phase IIIb study
  - Primary endpoint: SVR12



*All patients received GLE/PIB in previous clinical study and either completed treatment or discontinuation ≥ 1 mo before screening. †Includes patients with GT3 ± cirrhosis and ± previous NS5AI or PI, cirrhotic patients with any HCV GT ± previous NS5AI or PI, and patients with any HCV GT ± cirrhosis with previous NS5AI or PI. Dosing: GLE/PIB 300/120 mg QD + SOF 400 mg QD + RBV 1000-1200 mg BID.

Wyles D, et al. EASL 2018. Abstract PS-040.

MAGELLAN-3: Efficacy of GLE/PIB + SOF + RBV in Patients Who Experienced GLE/PIB Failure



- Baseline RAS:
  - NS5A RAS detected in 18 (78%) of 23 patients
    - 12-wk arm: 2/2
    - 16-wk arm: 16/21
  - NS3 + NS5A RAS detected in 5/23 patients, all in 16-wk arm
- VF occurred in 1 patient in 16-wk arm
  - GT1a HCV infection, cirrhosis, previous LDV/SOF, NS5A RAS (Q30K + Y93H), and no NS3 RAS at MAGELLAN-3 BL

Wyles D, et al. EASL 2018. Abstract PS-040. Reproduced with permission.

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MAGELLAN-3: Safety of GLE/PIB + SOF + RBV in Patients Who Experienced GLE/PIB Failure

AEs, n	All Patients (N = 23)
Any AE	19
Serious AE	1*
▪ DAA related	0
AE leading to d/c	0
Grade ≥ 3 serious AE	0
AEs in ≥ 10% of patients	
▪ Headache	6
▪ Pruritus	5
▪ Dizziness	4
▪ Irritability	4
▪ Fatigue	3
▪ Insomnia	3
▪ Upper respiratory tract infection	3

*Cholelithiasis unrelated to study drugs.

Laboratory Abnormalities, n	All Patients (N = 23)
Grade ≥ 3 ALT increase (< 5 x ULN)	1*
Grade ≥ 3 AST increase (> 5 x ULN)	0
Grade ≥ 3 bilirubin increase (> 3 x ULN)	0
Grade ≥ 3 hemoglobin decrease	0
RBV dose reduction for toxicity	0

*Asymptomatic ALT increase in patient with SAE cholelithiasis.

Wyles D, et al. EASL 2018. Abstract PS-040. Reproduced with permission.

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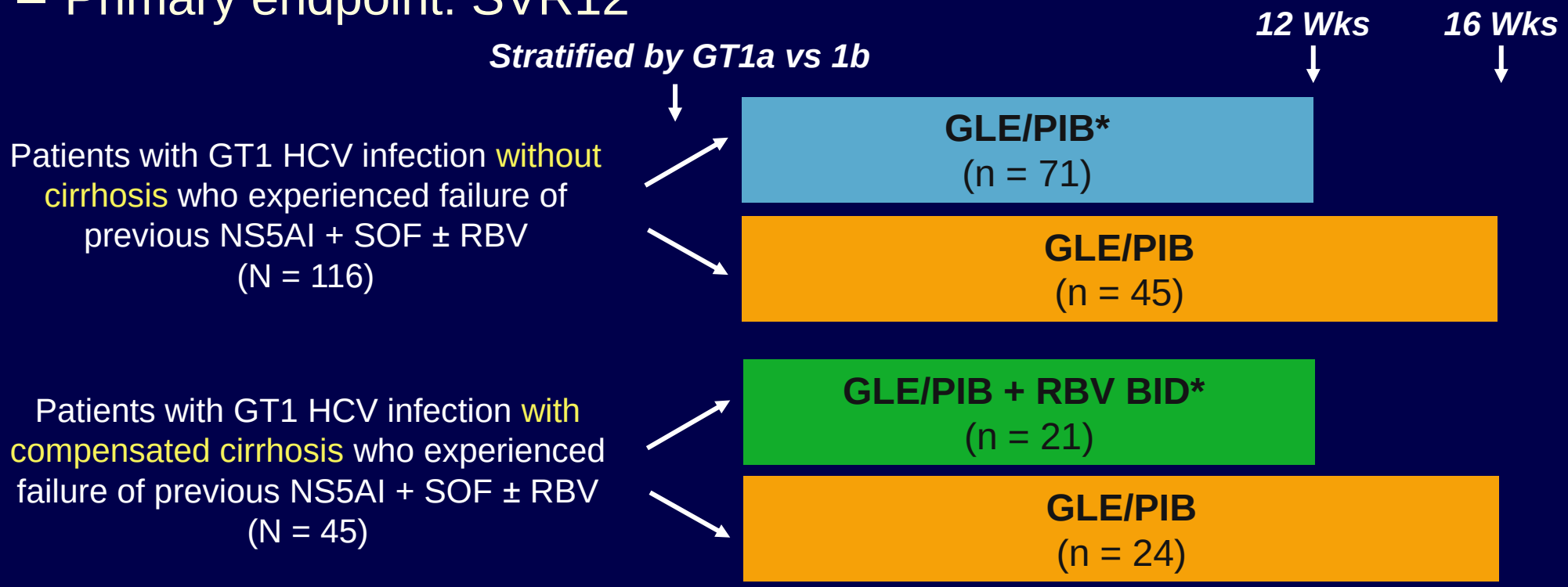
Glecaprevir/Pibrentasvir ± RBV for GT1 HCV After NS5A Inhibitor + Sofosbuvir ± RBV Failure

- Interim analysis of an open-label, randomized phase IIIb trial
  - Primary endpoint: SVR12



*Protocol amendment following FDA approval of GLE/PIB resulted in PI-experienced patients randomized to 12-wk regimens receiving 16 wks of treatment and subsequent analysis in respective 16-wk arms (5 noncirrhotic, 1 cirrhotic).

Lok A, et al. EASL 2018. Abstract LBO-008.

Slide credit: clinicaloptions.com

Efficacy of Glecaprevir/Pibrentasvir ± RBV for GT1 HCV After NS5AI + Sofosbuvir ± RBV Failure

Viral Outcome	No Cirrhosis		Compensated Cirrhosis	
	12-Wk GLE/PIB (n = 68)	16-Wk GLE/PIB (n = 29)	12-Wk GLE/PIB + RBV (n = 21)	16-Wk GLE/PIB (n =21)
SVR4, %	96	96	86	100
Relapse, n	2	1	0	0
Viral BT, n	1	0	3	0

- 12-wk GLE/PIB + RBV arm closed following 3 breakthroughs
- No SVR4 data available for 22 patients

Baseline RAS, n (%)	No Cirrhosis		Compensated Cirrhosis	
	12-Wk GLE/PIB (n = 71)	16-Wk GLE/PIB (n = 45)	12-Wk GLE/PIB + RBV (n = 21)	16-Wk GLE/PIB (n = 24)
Patients sequenced, n	66	29	20	21
NS3*	2 (3)	0	3 (15)	1 (5)
NS3†	21 (47)	10 (34)	9 (45)	11 (52)
NS5A‡	50 (76)	23 (79)	16 (80)	18 (86)

*155, 156, 168. †80. ‡24, 28, 30, 31, 32, 58, 62, 92, 93.

- BL NS5A RAS detected in 6/6 virologic failures, all of whom acquired additional NS5A mutations at failure

Lok A, et al. EASL 2018. Abstract LBO-008.

Safety of Glecaprevir/Pibrentasvir ± RBV for GT1 HCV After NS5AI + Sofosbuvir ± RBV Failure

AEs, n (%)	Noncirrhotic Patients		Cirrhotic Patients	
	12-Wk GLE/PIB (n = 71)	16-Wk GLE/PIB (n = 29)	12-Wk GLE/PIB + RBV (n = 21)	16-Wk GLE/PIB (n = 24)
Any AE	53 (75)	27 (60)	17 (81)	12 (50)
Serious AE ▪ DAA-related AE	3 (4) 0	1 (2) 0	1 (5) 0	0 0
D/c of GLE/PIB for AE	0	0	0	0
Discontinuation/dose reduction of RBV for AE	NA	NA	7 (33)/1 (5)	NA
Most common AEs (in ≥ 10% of patients) ▪ Fatigue ▪ Headache ▪ Nausea	10 (14) 14 (20) 5 (7)	9 (20) 6 (13) 5 (11)	10 (48) 6 (29) 2 (9.5)	7 (29) 6 (25) 1 (4.2)

Lok A, et al. EASL 2018. Abstract LBO-008.

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Posttreatment HCV Outcomes

Scottish National Study: Reduction in Liver Outcomes After Initiation of DAA Therapy

- Retrospective study of Scottish HCV Clinical Database, 2000-2017
  - DAA therapy introduced April 2014
- Endpoint: hospital admission with decompensated cirrhosis
  - Ascites, hepatic encephalopathy, hepatorenal syndrome, bleeding varices
- From April 2014-2017, 4800 persons with HCV initiated on HCV therapy in Scotland

Characteristics, %	Treated Pts (N = 4800)
GT1	54
GT3	38
Other GT	8
F2/F3	24
Compensated cirrhosis	27
Decompensated cirrhosis	5
Treated with DAAs	83

Hutchinson S, et al. EASL 2018. Abstract GS-017.

Slide credit: clinicaloptions.com

Scottish National Study: Results

- From April 2014 to March 2017 compared with previous 3 yrs
  - 1.6 times more patients initiated on HCV therapy
  - 2.8 times more patients with decompensated cirrhosis initiated HCV therapy
- Between 2013 and 2017, 29% reduction in first-time presentations for decompensated cirrhosis
  - 39% reduction for those with chronic HCV infection at time of admission
  - First time admissions for decompensated cirrhosis increased from 10 in 2013 to 20 in 2016 among persons who had previously achieved SVR

Hutchinson S, et al. EASL 2018. Abstract GS-017.

Slide credit: clinicaloptions.com

RESIST-HCV: Long-term Outcomes Following SVR to HCV DAA Therapy

- Prospective cohort analysis of 4668 patients who started DAAs Mar 2015 - Dec 2016 (previous HCC or OLT excluded)
  - 69% with CTP A cirrhosis; 8.8% with CTP B cirrhosis
  - SVR: 90.7%; no SVR: 5%
  - Primary endpoint: survival since initiating HCV DAAs
  - Median follow-up: 72 wks
  - Modified ITT analysis: N = 4468

Calvaruso V, et al. EASL 2018. Abstract PS-149.

Slide credit: clinicaloptions.com

RESIST-HCV: Predictors of Mortality in Patients Treated With HCV DAAs

- SVR associated with reduced risk of liver-related mortality across disease stages, but benefit lower in CTP B cirrhosis
  - Univariate HR for no SVR vs SVR in CTP B: 3.49; *P* = .036

Multivariate Cox Regression	HR (95% CI)	*P* Value
Independent predictors of liver-related mortality in CTP A cirrhosis		
▪ No SVR	18.50 (6.75-50.70)	< .001
▪ Albumin < 3.5 g/dL	6.01 (2.30-15.73)	< .001
Independent predictors of cardiovascular mortality in DAA-treated patients		
▪ No SVR	10.56 (3.43-32.46)	< .001
▪ Diabetes	4.11 (1.30-12.98)	.011

Calvaruso V, et al. EASL 2018. Abstract PS-149.

Slide credit: clinicaloptions.com

Impact of DAAs on Survival in Patients With HCV Infection and Decompensated Cirrhosis

- Incidence of observed deaths in DAA-treated patients with decompensation vs expected deaths in untreated patients in modeling study
  - Observed mortality data derived from SOLAR (LDV/SOF + RBV) and ASTRAL-4 (SOF/VEL ± RBV)
  - Expected mortality model based on pre-DAA era liver transplant list data
- **56% reduction in mortality** 1 yr after DAA treatment initiation for observed deaths vs expected deaths ($P < .05$)
  - Day 100 SMR: 0.54 (95% CI: 0.30-0.98)
  - Day 339-365 SMR: 0.44 (95% CI: 0.30-0.65)

Kim WR, et al. EASL 2018. Abstract PS-151.

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Post HCV SVR Liver Stiffness Measurement (LSM) Not Predictive of HCC

- 828 patients without previous HCC from 2 French treatment centers May 2008 - Nov 2016; SVR: 94% (799/849)
- LSM assessed by *FibroScan* before HCV therapy and ≥ 1 time during 12-48 wks of follow-up
- Post-SVR HCC screening every 6 mos by ultrasound
- Median LSM decrease from baseline to follow-up: -3.6 kPa (-6.2 to -1.1; *P* < .0001)
- At median f/u of 6 mos, 2 patients died and 22 (2.8%) developed HCC

- Factors assoc. with HCC in multivariate analysis: age, sex, diabetes, and baseline LSM, but NOT change in LSM

Factor	HR (95% CI)	*P* Value
Age (per yr)	1.06 (1.02-1.10)	.005
Diabetes	2.70 (1.12-6.51)	.026
Baseline LSM		
▪ Per kPa	1.05 (1.02-1.07)	< .0001
Qualitative baseline LSM		.005
▪ 8-12.5 vs < 8	1.59 (0.14-17.59)	
▪ ≥ 12.5 vs < 8	10.44 (1.38-78.63)	
Change in LSM, per kPa	0.99 (0.94-1.04)	.705

Shili S, et al. EASL 2018. Abstract PS-021.

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HCV Elimination Strategies

TraP HepC: HCV Treatment as Prevention in PWID in Iceland

- Nationwide treatment-as-prevention study focusing on HCV PCR+ patients actively injecting drugs, incarcerated, or with advanced liver fibrosis/cirrhosis
- Enrollment Jan 2016-Jan 2018
  - N = 652 (80% to 85% of estimated total persons with HCV in Iceland)
- Regimens:
  - Jan-Oct 2016: LDV/SOF ± RBV
  - After Nov 2016: SOF/VEL

Characteristics, %	Treated Pts (N = 518)
Living at home	75
Homeless/halfway house	16
Prison	8
Treated at university hospital	65
Treated at addiction hospital	30
Treated in prison	5
Stimulant, preferred drug	85
Opioid user	14
Ever used IV drugs	88
Used IV drug in past 6 mos	37
On OST	12
HCV GT3a/GT1a/GT1b	58/37/14
HIV coinfected	7

Tyrffingsson T, et al. EASL 2018. Abstract PS-095.

Slide credit: clinicaloptions.com

TraP HepC: 2-Yr Results From HCV Treatment as Prevention in PWID in Iceland

- Dramatic reduction in proportion of PWIDs with detectable HCV RNA and new HCV infections between 2015-2017 at National Addiction Hospital
  - **53% reduction in new HCV infections**
  - **72% reduction in proportion PWIDs HCV RNA positive: from 43% to 12%**
- 90% overall cure rate in first 15 mos; 94% for those who completed HCV regimen

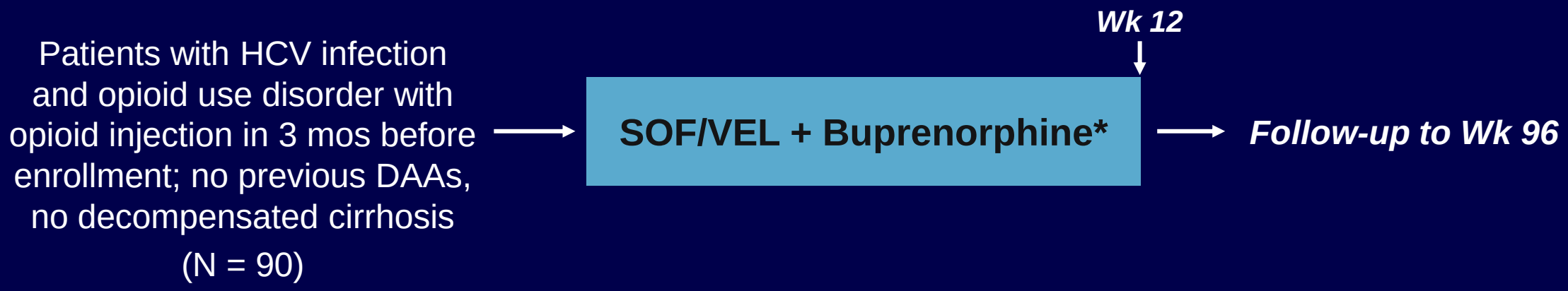
SVR12, %	Treated Pts (N = 518)	*P*
Current IVD use (last 6 mos) Not currently using IVD	87 95	.0033
Homeless Not homeless	74 94	.0005

Tyrffingsson T, et al. EASL 2018. Abstract PS-095.

Slide credit: clinicaloptions.com

ANCHOR Substudy: Colocation of HCV and Buprenorphine Treatment

- Substudy of single-arm HCV treatment trial in Washington, DC
  - Endpoints: adherence to SOF/VEL, SVR12 rate; risk behaviors, HCV reinfection, HIV acquisition



*Buprenorphine started between Wk 0-24 of SOF/VEL treatment initiation with follow-up for 1 yr at same center and with same provider as HCV treatment.

Rosenthal E, et al. EASL 2018. Abstract PS-092.

Slide credit: clinicaloptions.com

ANCHOR Substudy: Efficacy of Colocalized Buprenorphine and HCV Treatment

- HCV treatment visit adherence high, ranging from 77% to 87% over 24 wks
  - 90% to 95% received study drug
- SVR rate 91% among 46 patients who reached Wk 24 with SVR data
- SVR rate among 55 patients in ITT analysis: 76%
  - 7% no SVR, 13% missed visit, 2% awaiting results, 2% deceased
- 39 patients started buprenorphine with 26 (67%) retained
- Patients receiving medication-assisted opioid addiction treatment (MAT) significantly more likely to receive second bottle of SOF/VEL and to receive SOF/VEL at a study visit vs those not receiving MAT
- HIV risk behavior decreased significantly from Day 0 of buprenorphine to Wks 4, 12, and 24 (P = .003 for Wk 4 and 24 difference; P = .001 for Wk 12 difference)

Rosenthal E, et al. EASL 2018. Abstract PS-092.

Slide credit: clinicaloptions.com

Treatment of HBV Infection

Switch From TDF to TAF in Patients With Chronic HBV Infection and TDF Risk Factors

- Study 108 and Study 110: double-blind, randomized, phase III trials comparing TAF vs TDF in 1298 treatment-naive HBeAg-negative (108) and HBeAg-positive (110) patients
  - After 96 wks, 540 patients switched to open-label TAF: TAF→TAF in 360; TDF→TAF in 180 (284 had ≥ 1 and 123 had ≥ 2 TDF risk factors)
  - Study amended and remaining patients continue double-blind therapy to Wk 144 before switch to open-label TAF
  - TDF risk factors: older than 60 yrs of age, hip/spine osteoporosis, stage ≥ 2 CKD, albuminuria, hypophosphatemia, obesity, or comorbidities associated with CKD (HTN, diabetes, CVD, hyperlipidemia)
- Current interim analysis of renal, bone, efficacy parameters 1 yr after switch at 96 wks in subset of patients with baseline TDF risk factors

Gane E, et al. EASL 2018. Abstract PS-156.

Slide credit: clinicaloptions.com

Safety, Efficacy 1 Yr After Switch From TDF to TAF in HBV Patients With TDF Risk Factors

- At Wk 144, antiviral efficacy maintained in both switch groups

Viral Outcome	96 Wks	144 Wks
HBV DNA < 29 IU/mL, % (n/N)		
TAF → TAF	91 (166/183)	89 (162/183)
TDF → TAF	88 (89/101)	84 (85/101)
HBV DNA ≥ 29 IU/mL, %		
TAF → TAF	8	8
TDF → TAF	12	10
Missing data, %		
TAF → TAF	2	3
TDF → TAF	0	6

- Patients switched from TDF to TAF at Wk 96 showed improved renal and BMD parameters at Wk 144

Wk 96-144 Change by Subgroup	*P* Value
Hip BMD increase	
▪ No TDF risk factors	< .001
▪ ≥ 1 TDF risk factor	.002
Spine BMD increase	
▪ No TDF risk factors	< .001
▪ ≥ 1 TDF risk factor	< .001
$eGFR_{CG}$ increase	
▪ No TDF risk factors	.023
▪ ≥ 1 TDF risk factor	.008

Gane E, et al. EASL 2018. Abstract PS-156.

Slide credit: clinicaloptions.com

DARING-B: HBsAg Loss After Long-term ETV or TDF in HBeAg-Negative HBV Without Cirrhosis

- Prospective study of 60 noncirrhotic patients who received ETV or TDF for ≥ 4 yrs, had undetectable HBV DNA for ≥ 3 yrs and consented to discontinue ETV or TDF with close follow-up
- Mean follow-up: 19 mos; no deaths, jaundice or decompensation
- Cumulative viral relapse (HBV DNA > 2000 IU/mL) rates 62%, 68%, and 70% at 6, 12, and 18 mos
- Cumulative HBsAg loss rates 5%, 10%, and 20% at 0, 6, and 12 mos after NA discontinuation
- Independent predictors of HBsAg loss: lower HBsAg levels at d/c, higher ALT or higher IP10 levels 1 mo after d/c

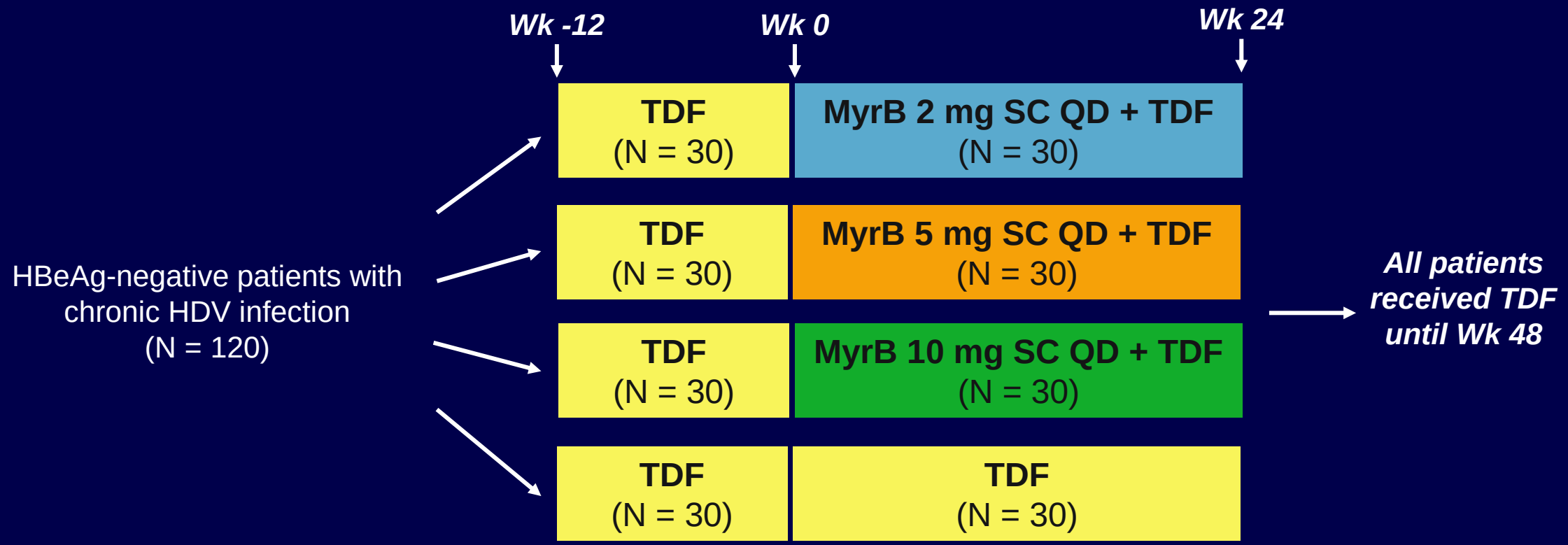
Factor	aHR (95% CI)	*P* Value
Serum HBsAg at d/c (per 100 IU/L)	0.738 (0.590-0.923)	.008
ALT 1 mo after d/c (per 10 IU/L)	1.134 (1.026-1.253)	.0013
IP10 1 mo after d/c (per 10 pgIU/L)	1.103 (1.022-1.191)	.0012

Papatheodoridi M, et al. EASL 2018. Abstract PS-159.

Slide credit: clinicaloptions.com

Phase IIb Study of HBV/HDV Entry Inhibitor, Myrcludex B + TDF in Pts With Chronic HBV/HDV

- Interim results from an open-label, randomized phase IIb study



Allweiss L, et al. EASL 2018. Abstract PS-162.

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Activity of Myrcludex B + TDF in Patients With Chronic HBV/HDV Infection

Median Change at Wk 24 vs BL, log IU/mL	MyrB 2 mg + TDF (n = 30)	MyrB 5 mg + TDF (n = 30)	MyrB 10 mg + TDF (n = 30)	All MyrB + TDF Arms (n = 90)	TDF (n = 30)
HBV pgRNA	0.2	-0.3	-0.9	--	0.0
Total HBV DNA	0.1	-0.0	-0.6	--	0.1
cccDNA/cell	0.3	0.1	-0.1	--	-0.7
Liver HBV DNA	0.1	-0.2	-0.7	--	--
Serum HBsAg	0.1	-0.0	-0.0	--	--
HDV RNA	-0.9	-1.1	-1.4	-1.02	-0.3
HDAg+ hepatocytes	-0.7	-0.9	-1.1	-0.84	--
NTCP	--	--	--	0.1	--
CYP7A1	--	--	--	0.3	--
CXCL10	--	--	--	-0.4	--
IL18	--	--	--	-0.3	--

Allweiss L, et al. EASL 2018. Abstract PS-162.

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