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HEPATITIS

HCV Therapy Overview in 2017

Supported by educational grants from AbbVie; Bristol-Myers Squibb; Gilead Sciences; Janssen Therapeutics; Merck & Co., Inc; and ViiV Healthcare.

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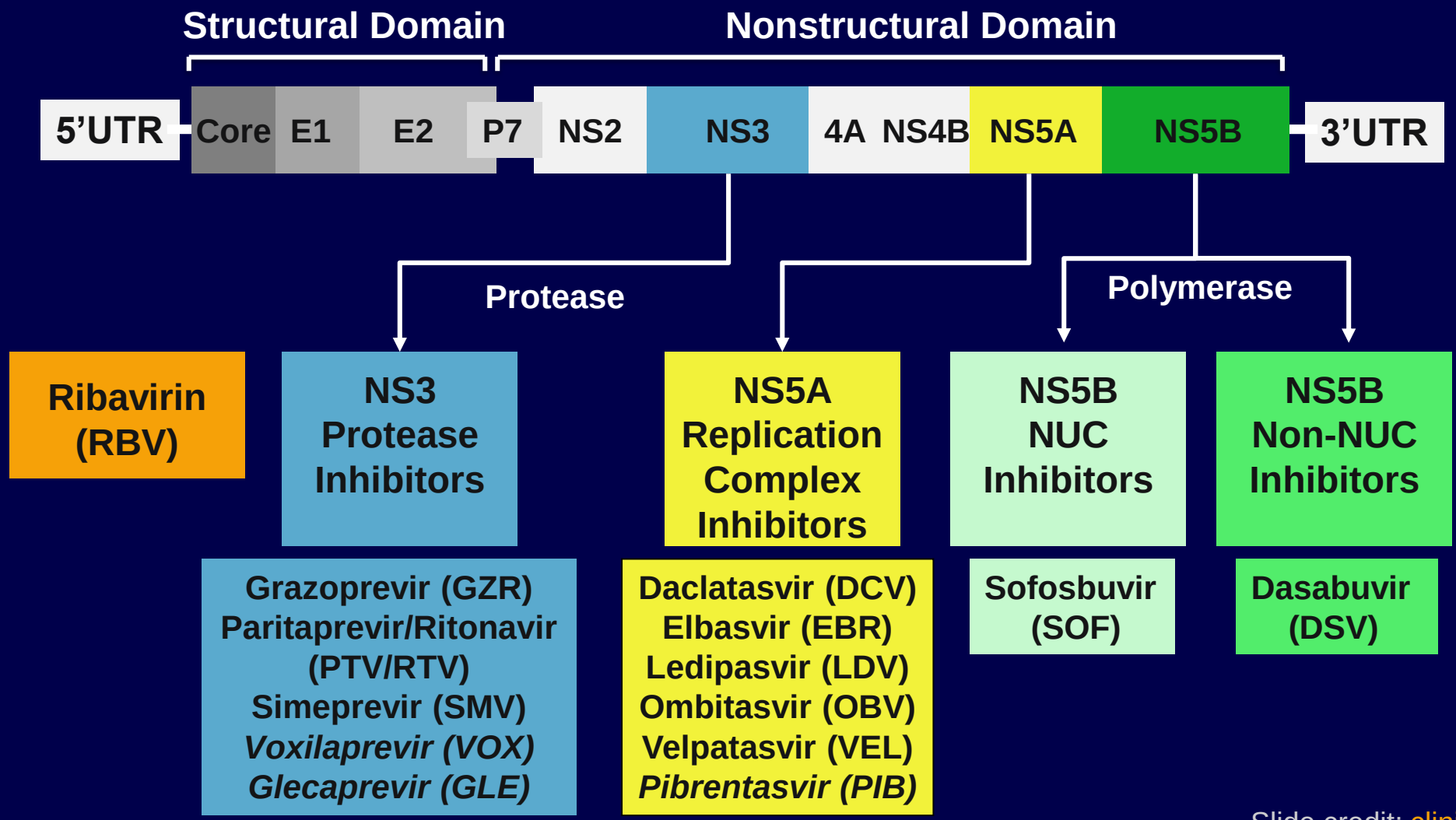
Where HCV Therapy Stands Now

- Interferon is gone in the US; ribavirin . . . not quite
- SVR in > 95% of pts
- “Difficult-to-cure” populations no longer difficult
  - Black race
  - Cirrhosis
  - Renal failure and kidney transplant
  - HIV coinfection
  - Older age
  - Liver transplant
  - Persons who inject drugs (PWID)
  - Genotype 3 remains more challenging (but not by much)
- Emergent issues and controversies:
  - HBV reactivation
  - HCC recurrence after DAA therapy
- Cost and access issues persist but improving

Approved DAAs From Multiple Classes: Basis of 2017 Combination HCV Regimens



Slide credit: clinicaloptions.com

Treatment Options for Genotype 1

Recommended for GT1 Treatment-Naive or IFN-Experienced Pts Without Cirrhosis

HCV GT	Recommended Regimens (All 12 Wks Except as Noted)
1a	▪ LDV/SOF (***8 wks*** *if tx naive, nonblack, no HIV, and HCV RNA < 6 million IU/mL*) ▪ SOF/VEL ▪ DCV + SOF ▪ SMV + SOF ▪ EBR/GZR (Only if no baseline NS5A elbasvir RASs; 16 weeks with RBV if present) ▪ OBV/PTV/RTV/DSV extended release + **RBV** *or* OBV/PTV/RTV + DSV BID + **RBV** ▪ GLE/PIB (**8 wks**)
1b	▪ LDV/SOF (***8 wks*** *if tx naive, nonblack, no HIV, and HCV RNA < 6 million IU/mL*) ▪ SOF/VEL ▪ DCV + SOF ▪ SMV + SOF ▪ EBR/GZR ▪ OBV/PTV/RTV/DSV extended release *or* OBV/PTV/RTV + DSV BID ▪ GLE/PIB (**8 wks)**

*.

AASLD/IDSA. HCV guidance. April 2017.

Slide credit: clinicaloptions.com

Recommended for GT1 Treatment-Naive or IFN-Experienced Pts With Compensated Cirrhosis

HCV GT	Recommended Regimens (All 12 Wks)	
	Treatment Naive	IFN/RBV Experienced
1a	▪ EBR/GZR* ▪ LDV/SOF ▪ SOF/VEL	▪ EBR/GZR* ▪ LDV/SOF + **RBV** ▪ SOF/VEL
1b	▪ EBR/GZR ▪ LDV/SOF ▪ OBV/PTV/RTV/DSV ER ▪ OBV/PTV/RTV+ DSV BID ▪ SOF/VEL	▪ EBR/GZR ▪ LDV/SOF + **RBV** ▪ OBV/PTV/RTV/DSV ER ▪ OBV/PTV/RTV+ DSV BID ▪ SOF/VEL

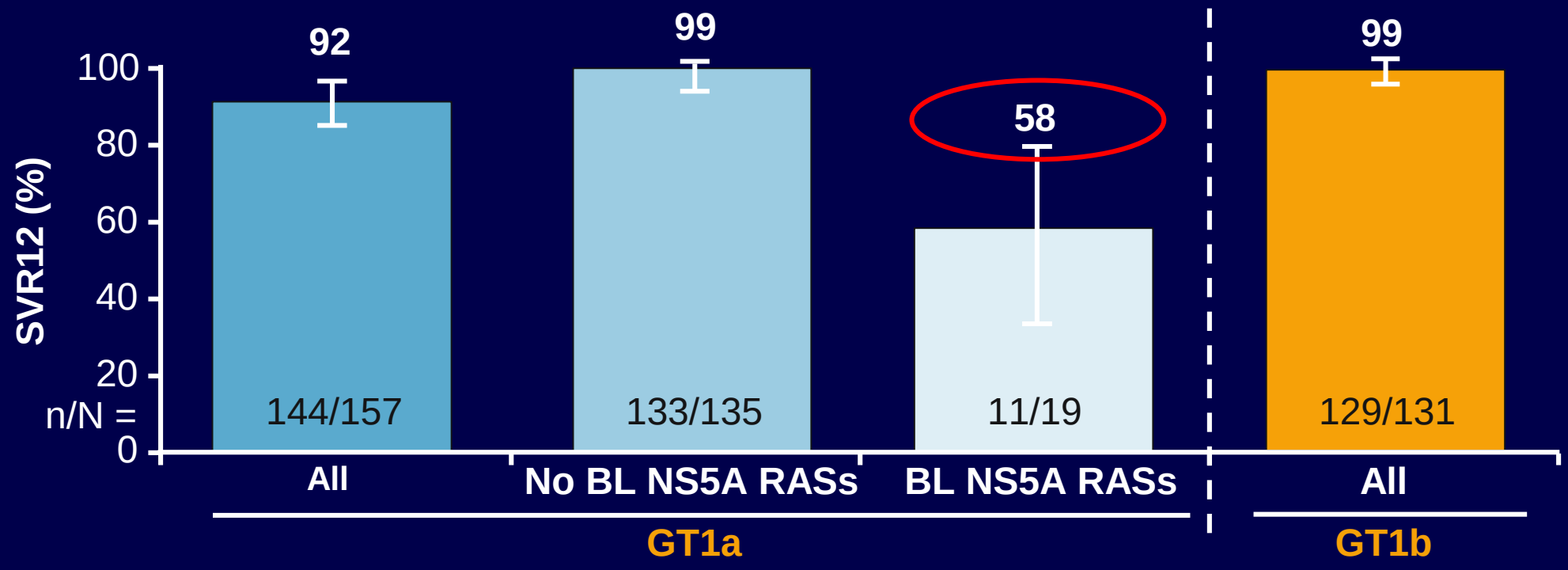
*Only if no baseline NS5A elbasvir RASs detected.

AASLD/IDSA. HCV guidance. April 2017.

Slide credit: clinicaloptions.com

Adjust EBR/GZR Duration Based on Baseline NS5A RASs in GT1a

C-EDGE Treatment Naive: 12 Wks of Elbasvir/Grazoprevir



If NS5A RASs in GT1a, treat with EBR/GZR + RBV for 16 wks (alternative)
No baseline RAS testing needed in GT1b pts

Zeuzem Z, et al. Ann Intern Med. 2015;163:1-13.
Kwo P, et al. J Hepatol. 2015;62(suppl 2):S674-S675.

Slide credit: clinicaloptions.com

Treatment Options for Genotypes 2, 4, 5, 6

Recommended Regimens for Treatment-Naive Pts With GT 2, 4, 5, 6 HCV

- All regimens 12 wks

HCV GT	No Cirrhosis	Compensated Cirrhosis
2	▪ SOF/VEL	▪ SAME
4	▪ OBV/PTV/RTV + **RBV** ▪ SOF/VEL ▪ EBR/GZR ▪ LDV/SOF	▪ SAME
5 or 6	▪ SOF/VEL ▪ LDV/SOF	▪ SAME

AASLD/IDSA. HCV guidance. April 2017.

Slide credit: clinicaloptions.com

Recommended Regimens for PegIFN/RBV-Experienced Pts With GT2, 4, 5, 6 HCV

- All regimens 12 wks unless noted otherwise

HCV GT	No Cirrhosis	Compensated Cirrhosis
2	▪ SOF/VEL	▪ SAME
4	▪ OBV/PTV/RTV + **RBV** ▪ SOF/VEL ▪ EBR/GZR* ▪ LDV/SOF	▪ SAME ▪ SAME ▪ SAME ▪ LDV/SOF + **RBV**
5 or 6	▪ SOF/VEL ▪ LDV/SOF	▪ SAME

*Previous relapse only; pts with previous virologic nonresponse or breakthrough should be treated with 16 wks with addition of RBV.

AASLD/IDSA. HCV guidance. April 2017.

Slide credit: clinicaloptions.com

Sofosbuvir/Velpatasvir: A Single Tablet Regimen (STR)

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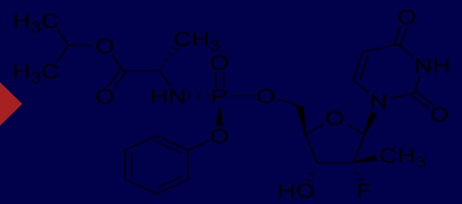
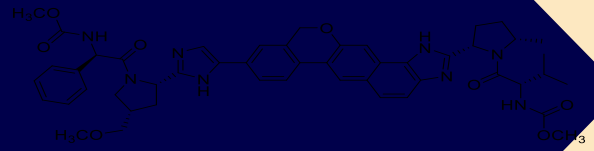
SOF
Nucleotide NS5B polymerase inhibitor



- **Sofosbuvir (SOF)[1,2]**
  - Potent antiviral activity against HCV GT 1–6
  - Once-daily, oral, 400-mg tablet



VEL
NS5A inhibitor

- **Velpatasvir (VEL; GS-5816)[3-5]**
  - Picomolar EC_{50} against GT 1–6
  - 2nd-generation NS5A inhibitor with improved resistance profile
    - Long half-life of ~13-23 h supports once-daily dosing
  - No food effect

SOF + **VEL**

- **SOF/VEL Single Tablet Regimen (STR)**
  - Once daily, oral, STR (400/100 mg)

U.S. Approval June 28, 2016; EU MAA July 2016

MAA marketing authorization application

1. Jacobson IM, et al. N Engl J Med 2013;368:1867-77; 2. Lawitz E, et al. N Engl J Med 2013;368:1878-87; 3. Cheng G, et al. EASL 2013, poster 1191; 4. German P, et al. EASL 2013, poster 1195; 5. Lawitz E, et al. AASLD 2013, poster 1082.

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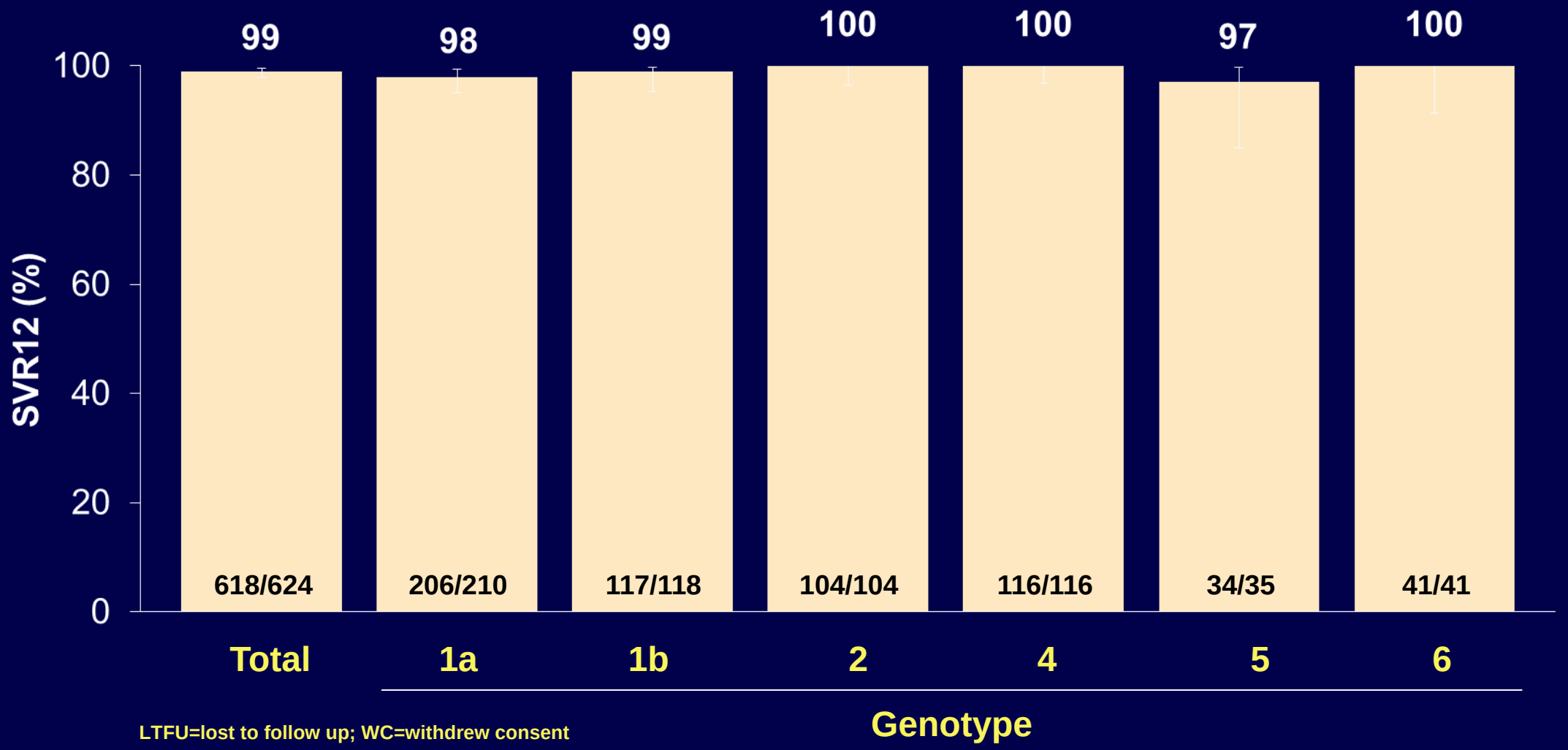
SVR12 by Genotype



LTFU=lost to follow up; WC=withdrew consent

Feld, AASLD, 2015, LB-2. Feld JJ, et al. *N Engl J Med*. 2015. DOI: 10.1056/NEJMoa1512610

SVR12 Depending on Cirrhosis or Treatment

- Total 99%
- Non cirrhotic 99%
- Cirrhosis 99%
- Tx Naïve 99%
- Tx Exp 99%

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Conclusions

- Treatment with SOF/VEL for 12 weeks resulted in a 99% SVR12 rate in patients with HCV GT 1, 2, 4, 5, or 6 infection
  - 99% SVR12 rate in patients with cirrhosis
  - 99% SVR12 rate in patients with prior treatment failure
- Presence of baseline NS5A RAVs did not impact SVR12
- Treatment with SOF/VEL for 12 weeks was well tolerated, with a safety profile similar to that of placebo treatment
- SOF/VEL for 12 weeks provides a simple, safe, and highly effective treatment for patients with HCV GT 1, 2, 4, 5, or 6 infection

Treatment Options for Genotype 3

Recommended for Treatment-Naive Pts With Genotype 3 HCV

Cirrhosis?	RAS Test?	RAS Test Result	Recommended regimens
No	**Don't test**	-	DCV + SOF 12 wks SOF/VEL 12 wks
Yes	**Test**	No Y93	DCV + SOF ± RBV 24 wks SOF/VEL 12 wks
		Y93	DCV + SOF + RBV 24 wks SOF/VEL + RBV 12 wks

AASLD/IDSA. HCV guidance. April 2017.

Slide credit: clinicaloptions.com

ASTRAL-3

‡

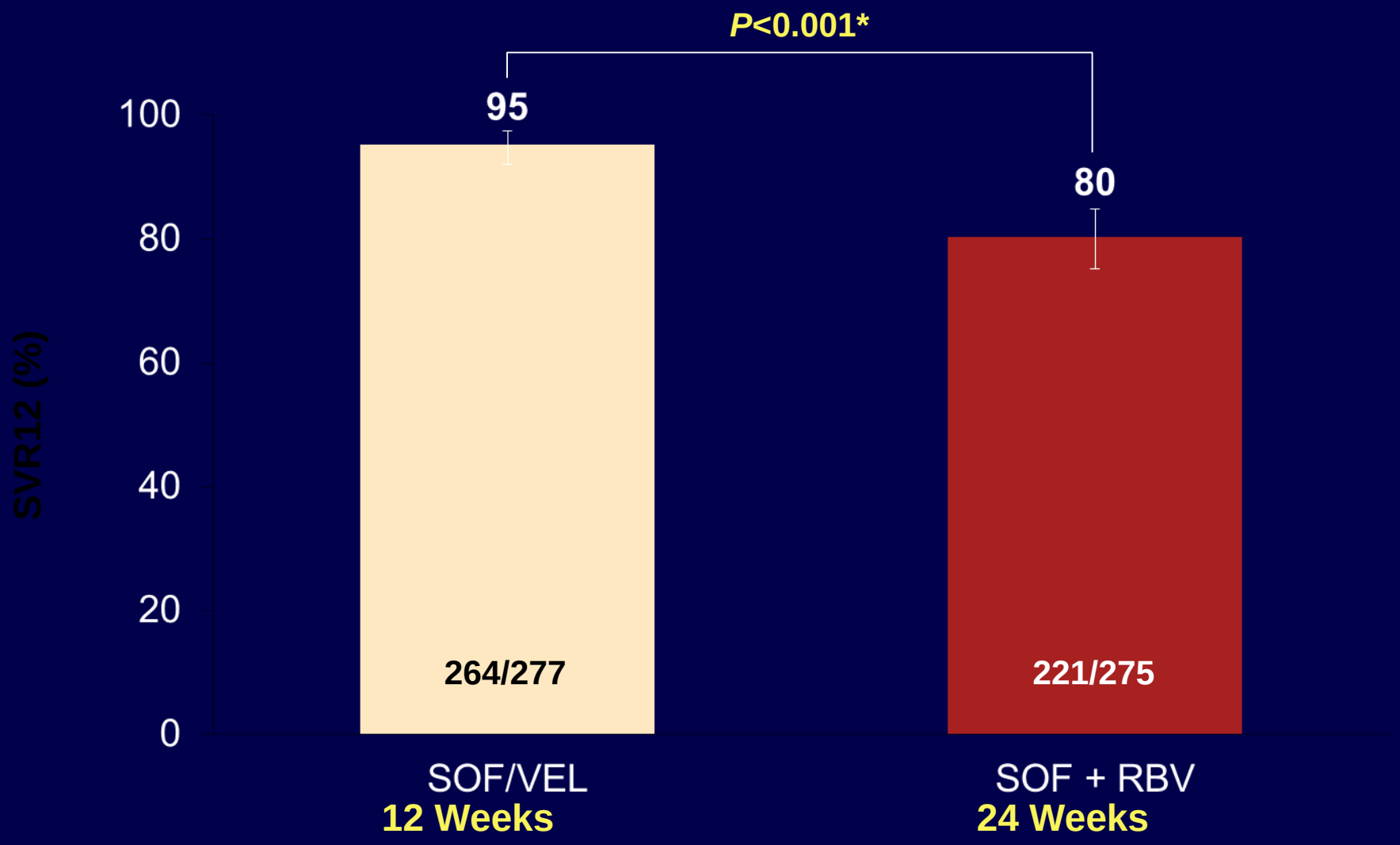
SOF/VEL STR for 12 Weeks Compared to SOF+RBV for 24 Weeks in GT 3 HCV

Phase 3, open-label, randomized study of SOF/VEL for 12 weeks in GT 3

	SOF/VEL 12 Weeks n=277	SOF + RBV 24 Weeks n=275
Mean age, y (range)	49 (21–76)	50 (19–74)
Male, n (%)	170 (61)	174 (63)
White, n (%)	250 (90)	239 (87)
Mean BMI, kg/m^2 (range)	26.4 (16.6–48.2)	26.6 (16.9–56.2)
Cirrhosis, n (%)	80 (29)	83 (30)
Treatment experienced, n (%)	71 (26)	71 (26)
IL28B CC, n (%)	105 (38)	111 (40)
HCV RNA, $\log_{10}$ IU/mL (SD)	6.2 (0.7)	6.3 (0.7)

‡

SVR12



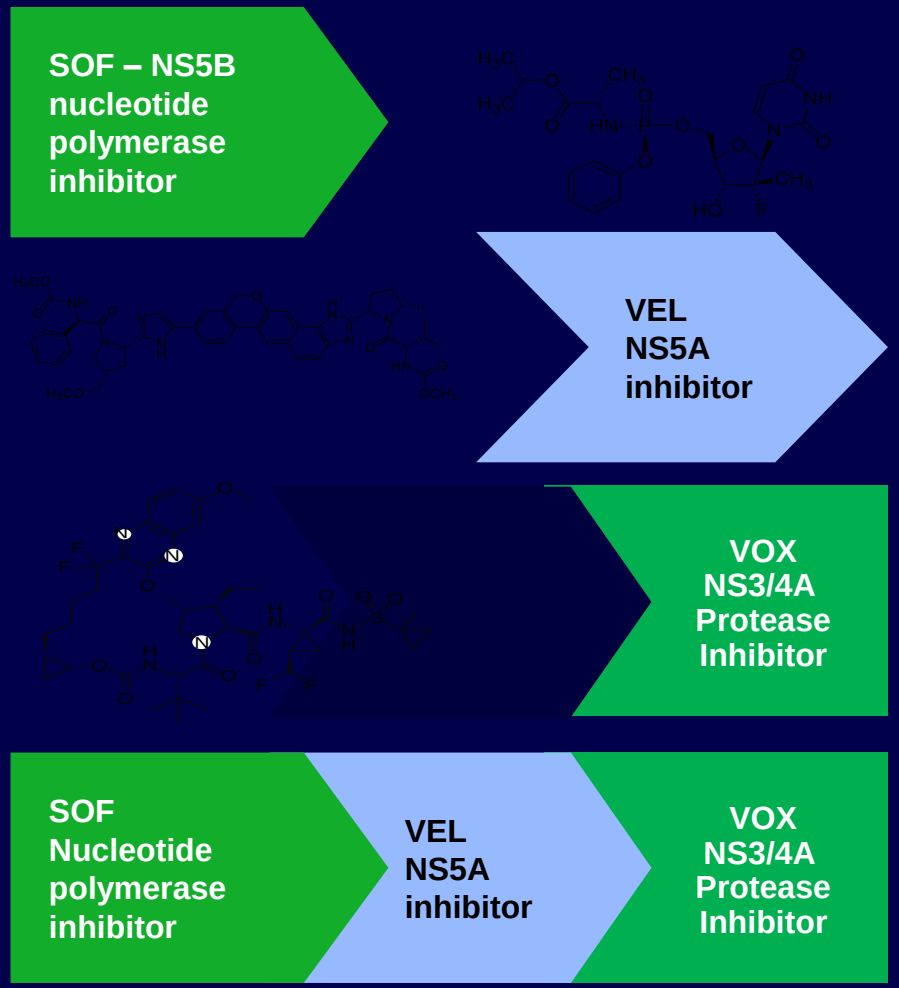
*P-value for superiority of SOF/VEL compared with SOF+RBV.
Error bars represent 95% confidence intervals.
Mangia, AASLD, 2015, 249. Foster GR, et al. *New Engl J Med*. 2015. DOI: 10.1056/NEJMoa1512612

‡

Conclusions

- SOF/VEL for 12 weeks resulted in a 95% SVR12 rate in patients with HCV GT 3 infection
  - Statistically superior to SOF + RBV for 24 weeks ($p < 0.001$)
  - 91% SVR12 rate in patients with cirrhosis
- SOF/VEL was well tolerated and, compared with SOF + RBV, lacked toxicities commonly associated with RBV
- SOF/VEL for 12 weeks provides a simple, safe, highly effective, RBV-free treatment for patients with HCV GT 3 infection

Sofosbuvir/Velpatasvir/Voxilaprevir: A Single Tablet Regimen (STR)



- **Sofosbuvir (SOF)[1,2]**
  - Potent antiviral activity against HCV GT 1–6
- **Velpatasvir (VEL)[3-5]**
  - Picomolar potency against HCV GT 1–6
  - 2nd-generation NS5A inhibitor with improved resistance profile
- **Voxilaprevir (VOX)[6,7]**
  - HCV NS3/4A protease inhibitor with potent antiviral activity against HCV GT 1–6
  - Improved resistance profile compared with other HCV protease inhibitors
- **SOF/VEL/VOX**
  - Once daily, oral, fixed dose combination (400/100/100 mg) for GT 1-6

1. Jacobson IM, et al. N Engl J Med 2013;368:1867-77; 2. Lawitz E, et al. N Engl J Med 2013;368:1878-87; 3. Cheng G, et al. EASL 2013, poster 1191; 4. German P, et al. EASL 2013, poster 1195; 5. Lawitz E, et al. J Viral Hepat 2015;22:1011-9; 6. Taylor JG, et al. EASL 2015, poster 899; 7. Kirby B, et al. EASL 2015, poster 861.

POLARIS Phase 3 Program

‡

DAA-Experienced

POLARIS-1

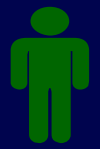
N = 415
NS5A-experienced
± cirrhosis

GT 1 2 3 4 5 6

SOF/VEL/VOX
12 weeks (n=263)

Placebo (n=152)

POLARIS-4



N = 333
Non-NS5A-experienced
± cirrhosis

GT 1 2 3 4 5 6

SOF/VEL/VOX
12 weeks (n=182)

SOF/VEL
12 weeks (n=151)

DAA-Naïve

POLARIS-2

N = 941
± cirrhosis

GT 1 2 3 4 5 6

SOF/VEL/VOX
8 weeks (n=501)

SOF/VEL
12 weeks (n=440)

POLARIS-3

N = 219
Cirrhosis

GT 1 2 3 4 5 6

SOF/VEL/VOX
8 weeks (n=110)

SOF/VEL
12 weeks (n=109)

Bourliere M, et al. N Engl J Med 2017;376:2134-46; Jacobson I, et al. Gastroenterology 2017, doi: 10.1053/j.gastro.2017.03.047.

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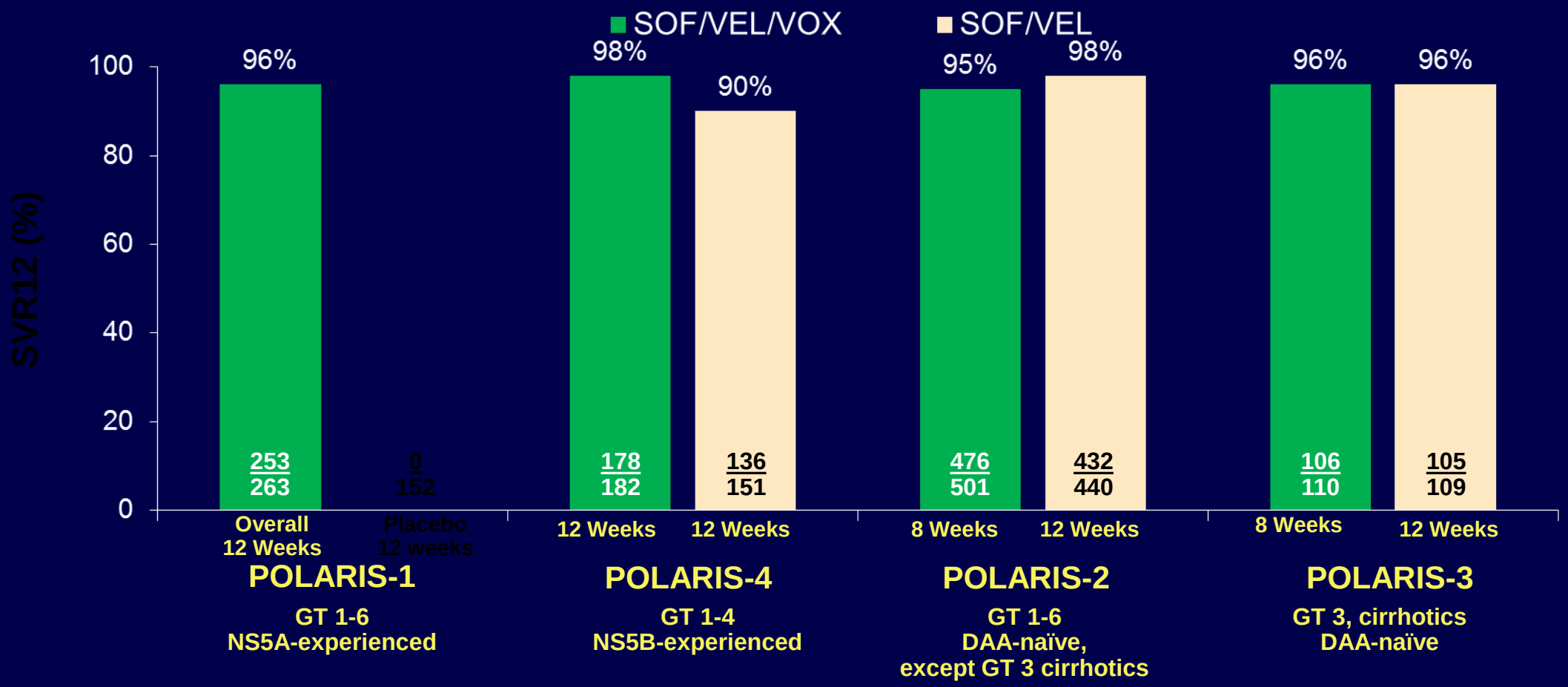
Efficacy Summary (ITT Analysis)*

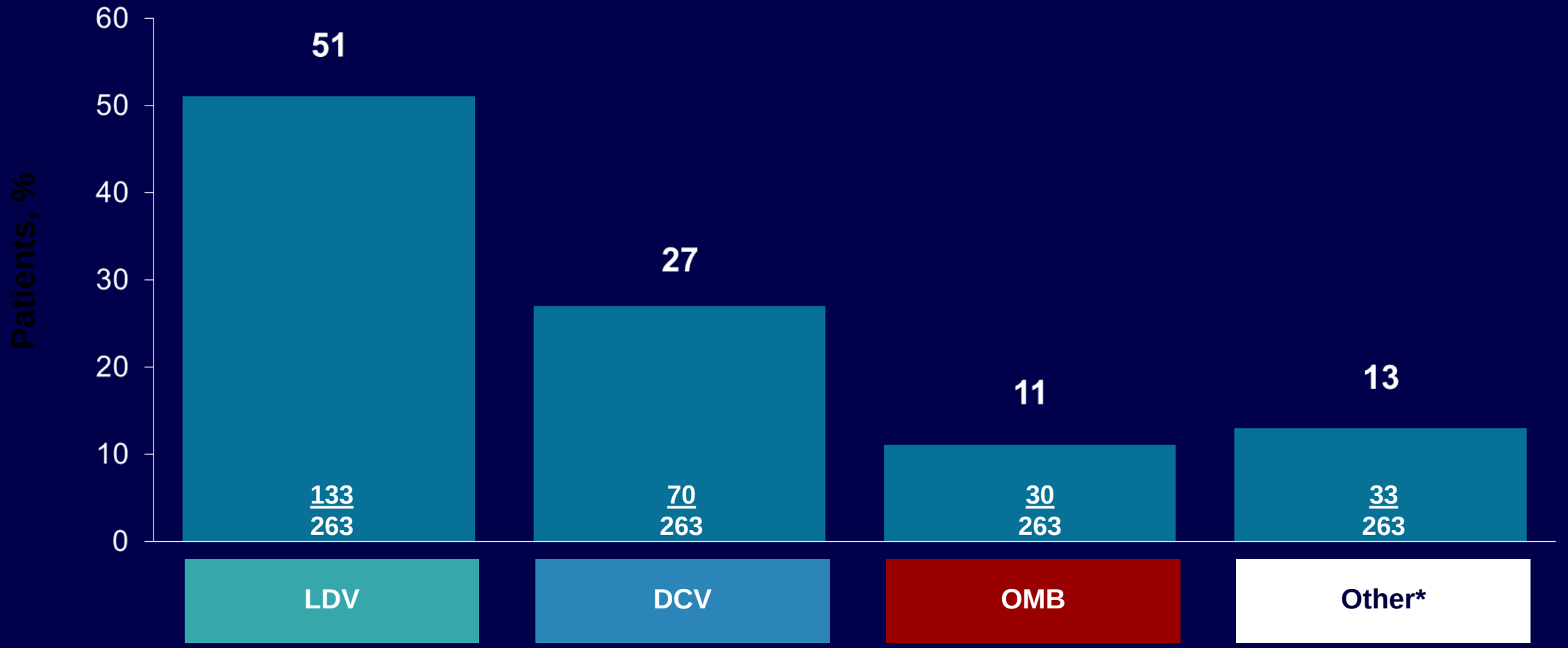


SOF/VEL/VOX for 12 weeks provides a STR for DAA-experienced patients and SOF/VEL for 12 weeks provides a STR for DAA-naive patients regardless of cirrhosis status

*All studies included patients with compensated cirrhosis

‡

Prior NS5A Treatment (%)



*Other included SOF/VEL experienced, EBR/GZR experienced, and other investigational combinations and/or medications from discontinued programs.

3 patients received both LDV and DCV; DCV, daclatasvir; LDV, ledipasivir; OMB, ombitasvir.

Bourliere M, AASLD 2016, Oral 194

‡

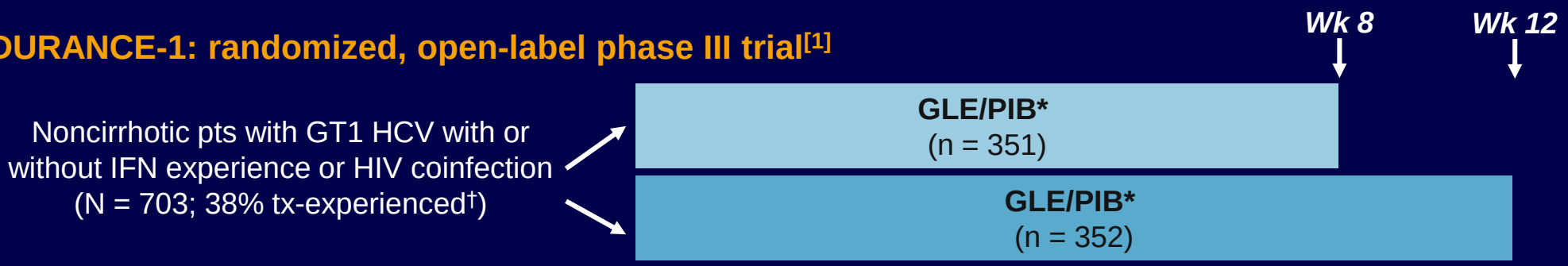
Conclusions

- In a wide variety of DAA-experienced patients across all genotypes SOF/VEL/VOX for 12 weeks resulted in:
  - 96% SVR in NS5A-experienced patients
  - 98% SVR in Non-NS5A inhibitor DAA-experienced patients
  - Including patients with multiple unfavorable characteristics including multiple RASs across NS5A and NS3/4A
  - Baseline RASs did not impact treatment outcome for SOF/VEL/VOX with SVR rates of 97-100%
  - No treatment-emergent RASs were observed among patients who relapsed with SOF/VEL/VOX
- SOF/VEL/VOX was well tolerated with an AE profile similar to that

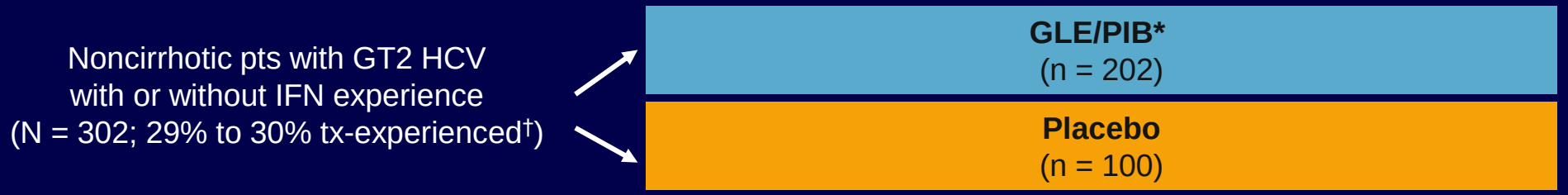
ENDURANCE Studies: Glecaprevir/Pibrentasvir in Noncirrhotic Patients

ENDURANCE-1, -2, -4: GLE/PIB for Treatment of GT1, 2, 4, 5, 6 HCV

ENDURANCE-1: randomized, open-label phase III trial[1]



ENDURANCE-2: randomized, double-blind, placebo-controlled phase III trial[2]



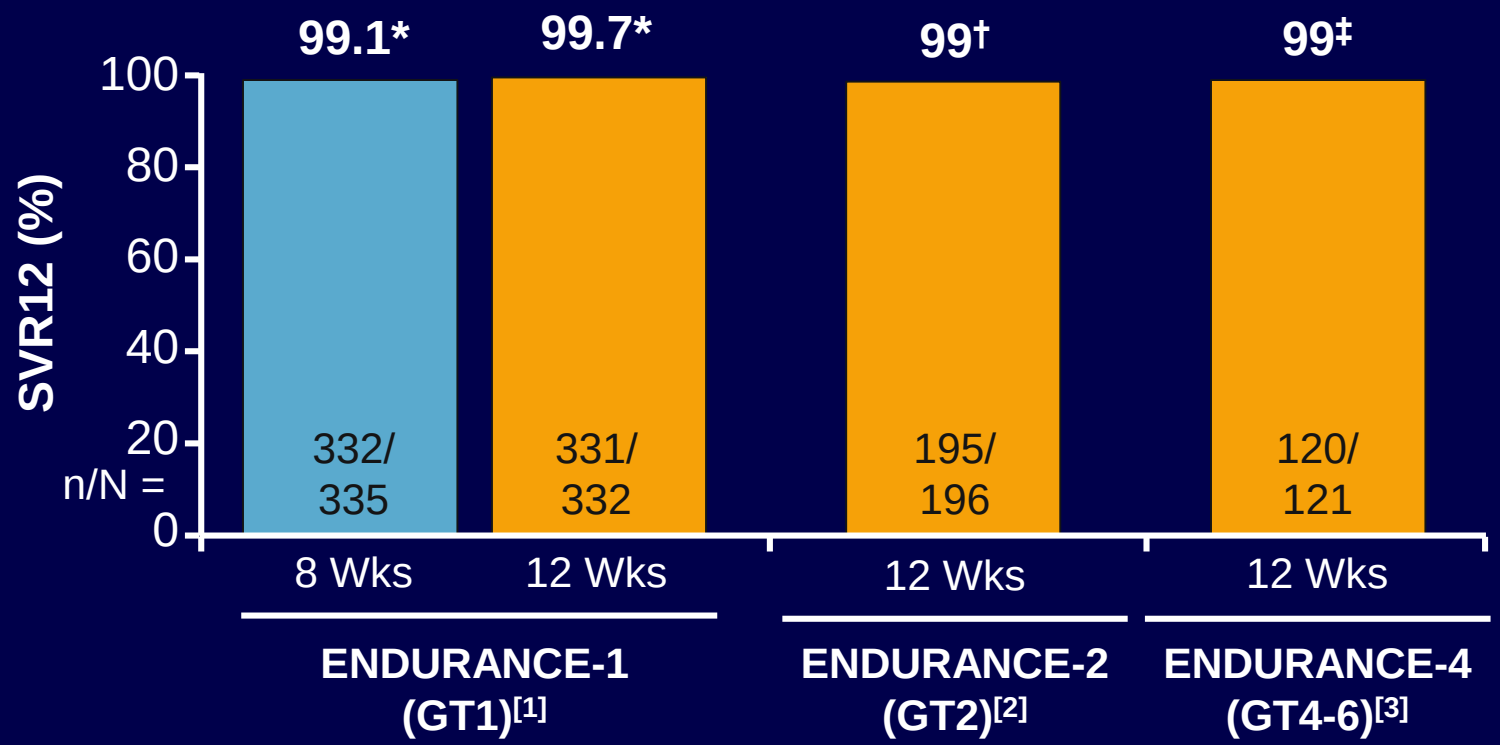
ENDURANCE-4: open-label, single-arm phase III trial[3]

*Dosing: GLE/PIB given as 3 coformulated 100/40-mg tablets QD for a total dose of 300/120 mg.
†Treatment experience permitted: IFN or pegIFN ± RBV or SOF + RBV ± pegIFN.

References in slidenotes.

Slide credit: clinicaloptions.com

ENDURANCE-1, -2, -4 Studies: Efficacy of GLE/PIB for Treating GT1, 2, 4, 5, 6 HCV



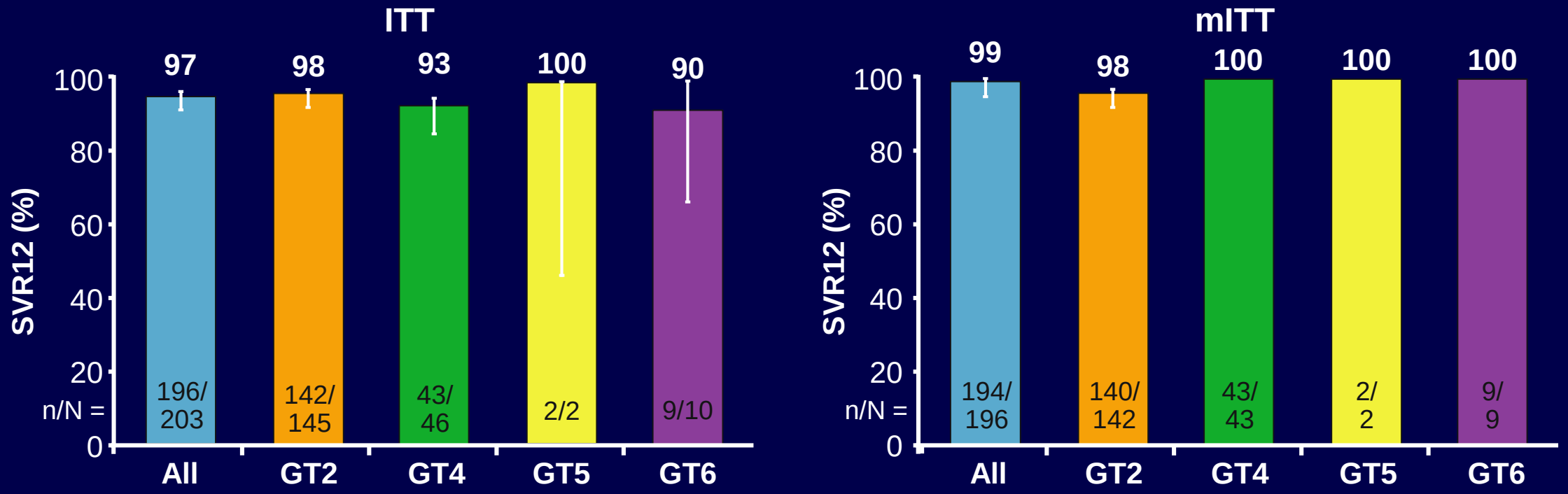
1 case of on-treatment virologic failure at Day 29 in pt with GT1a HCV infection

*ITT-PS analysis: included all pts receiving ≥ 1 dose of study drug; excluded pts with HIV coinfection or SOF experience.
†ITT analysis: excluded pts with SOF experience. ‡ITT analysis.

1. Zeuzem S, et al. AASLD 2016. Abstract 253. 2. Kowdley KV, et al. AASLD 2016. Abstract 73. 3. Asselah T, et al. AASLD 2016. Abstract 114.

SURVEYOR 2, Part 4: 8 Wks GLE/PIB For Pts With GT 2, 4, 5, 6 HCV Without Cirrhosis

- 99% SVR12 rate with 8-wk regimen in DAA-naive pts with GT2 HCV – noninferior to 95% historical control (SOF + RBV for 12 wks)



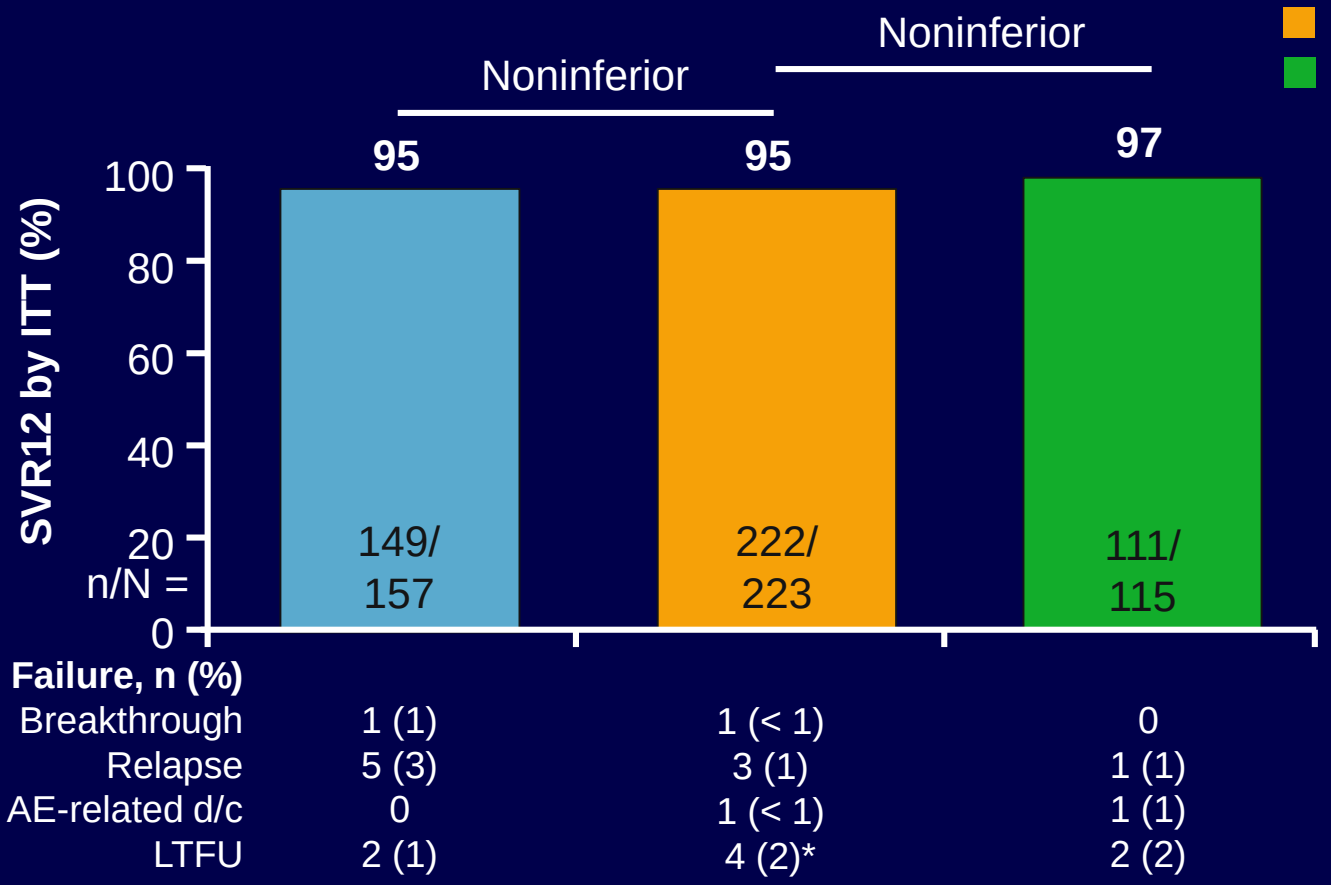
	All	GT2	GT4	GT5	GT6
Relapse	2	2	0	0	0
D/C	2	1	1	0	0
No SVR12 data	3	0	2	0	1

Hassanein TI, et al. AASLD 2016. Abstract LB-15.

Slide credit: clinicaloptions.com

ENDURANCE-3: Glecaprevir/Pibrentasvir in GT3 HCV Without Cirrhosis

- Most pts had history of IDU (63% to 66%)



Failure, n (%)			
Breakthrough	1 (1)	1 (< 1)	0
Relapse	5 (3)	3 (1)	1 (1)
AE-related d/c	0	1 (< 1)	1 (1)
LTFU	2 (1)	4 (2)*	2 (2)

*2 other failures due to consent withdrawal and noncompliance.

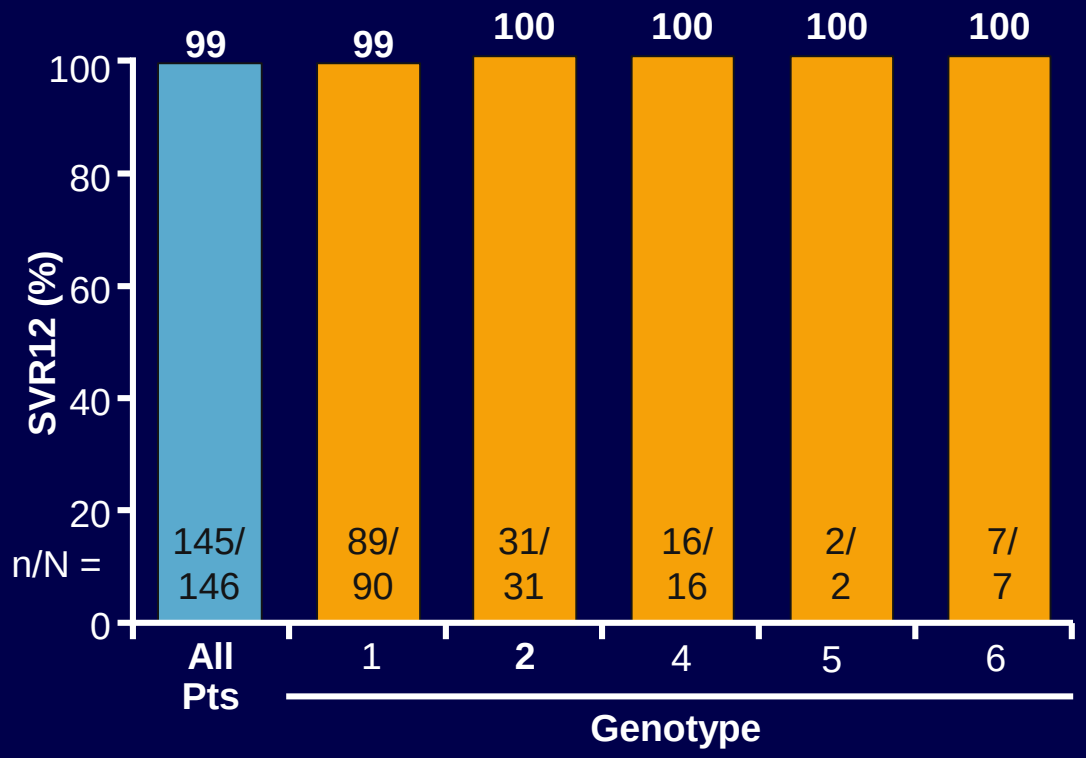
- No serious AEs deemed related to study drug
- No clinically relevant ALT increases, 1 isolated bilirubin increase (G/P 8 wks), 1 isolated neutrophil count decrease (G/P 12 wks)

Foster GR, et al. EASL 2017. Abstract GS-007.

Slide credit: clinicaloptions.com

EXPEDITION-1: Glecaprevir/Pibrentasvir in GT1, 2, 4, 5, or 6 HCV and Compensated Cirrhosis

- Tx-naive and tx-exp'd pts enrolled[1,2]
  - 1 relapse in pt with GT1a HCV with new NS5A mutations (Q30R, H58D)



- No AE-related discontinuations or DAA-related serious AEs[1,2]
  - 1 death deemed unrelated to study drug
- Rare grade 3 laboratory abnormalities

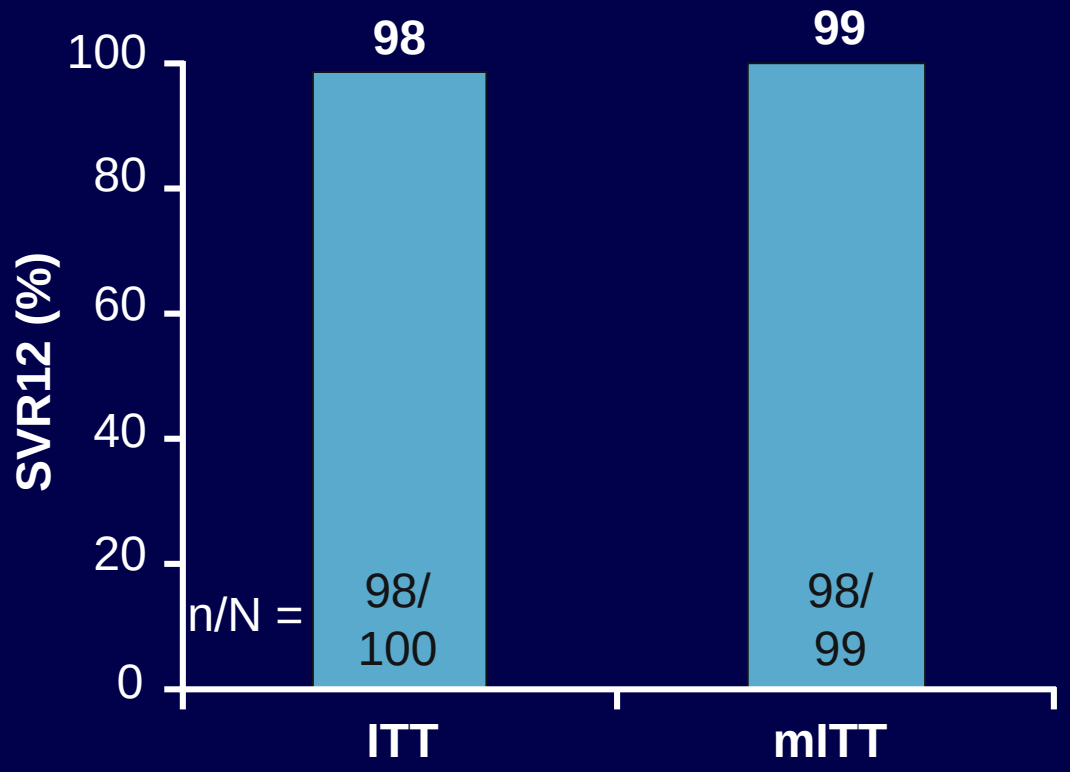
AE,[1,2] n (%)	Pts (N = 146)
Any AE	101 (69)
Any serious AE	11 (8)
AEs occurring in ≥ 10% of pts	
▪ Fatigue	28 (19)
▪ Headache	20 (14)
▪ Pruritus	14 (10)
HCC	2 (1)

- In EXPEDITION-2,[3] 98% SVR12 rate with GLE/PIB for 8 or 12 wks (without vs with cirrhosis) in HCV/HIV-coinfected pts

1. Forns X, et al. EASL 2017. Abstract GS-006. 2. ClinicalTrials.gov. NCT02642432.
3. Rockstroh J, et al. EASL 2017. Abstract LBP-522.

MAGELLAN-2: Glecaprevir/Pibrentasvir for 12 Wks in GT1-6 HCV With Liver or Renal Transplant

- Liver/kidney transplant: 80%/20%
- 1 relapse in pt with GT3a HCV; 1 pt LTFU



- No deaths during study, 1 pt with transplant rejection (unrelated to DAA)

Outcome, %	GLE/PIB (N = 100)
Any AE	85
Serious AE	8
▪ DAA related	2
D/c for AE	1
▪ DAA related	0
AEs in ≥ 10% of pts	
▪ Headache	22
▪ Fatigue	22
▪ Nausea	12
▪ Pruritus	12
Grade ≥ 3 abnormality	
▪ AST	0
▪ ALT	1
▪ Total bilirubin	1
▪ CrCl	2

Reau N, et al. EASL 2017. Abstract LBO-03.

Slide credit: clinicaloptions.com

Glecaprevir-Pibrentasvir

- **Approval Status**: Approval by United States FDA on August 3, 2017
- • **Indications and Usage**

  - Treatment-naïve patients with HCV genotypes 1-6 without cirrhosis and with compensated cirrhosis (Child-Pugh A)

  - HCV genotype 1 previously treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both without cirrhosis and with compensated cirrhosis (Child-Pugh A)

Glecaprevir-Pibrentasvir

- **Class & Mechanism**
- - Glecaprevir (GLE): HCV NS3/4A protease inhibitor
- - Pibrentasvir (PIB): HCV NS5A inhibitor
- • **Dosage Form (Tablet)**: 100 mg Glecaprevir and 40 mg Pibrentasvir
- • **Dosing:** Three tablets orally once daily, with food (total daily dose of Glecaprevir (300 mg)-Pibrentasvir 120 mg)

Glecaprevir-Pibrentasvir
Indications: Treatment-Naïve Patients

HCV Genotype	Treatment Duration	
	No Cirrhosis	**Cirrhosis Child A**
Genotype 1	8 weeks	12 weeks
Genotype 2	8 weeks	12 weeks
Genotype 3	8 weeks	12 weeks
Genotype 4	8 weeks	12 weeks
Genotype 5	8 weeks	12 weeks
Genotype 6	8 weeks	12 weeks

Glecaprevir-Pibrentasvir
Indications: Treatment Experienced-Patients

- **HCV Genotype 1** **Treatment Duration**

Patients Previously Treated With a Regimen Containing: **No cirrhosis** **Child A**

An NS5A inhibitor without prior treatment with an NS3/4A protease inhibitor	16 weeks	16 weeks

Treatment: Ledipasvir/Sofosbuvir/Daclatasvir/PEG/RBV

Glecaprevir-Pibrentasvir
Indications: Treatment Experienced-Patients

- **HCV Genotype 1,2,4,5,6** — **Treatment Duration**

Patients Previously Treated With a Regimen Containing:	**No cirrhosis**	**Child A**
PEG/RBV+/-Sofosbuvir	**8 weeks**	**12 weeks**
HCV Genotype 3	**16 weeks**	**16 weeks**

Glecaprevir-Pibrentasvir
Indications: Treatment Experienced-Patients

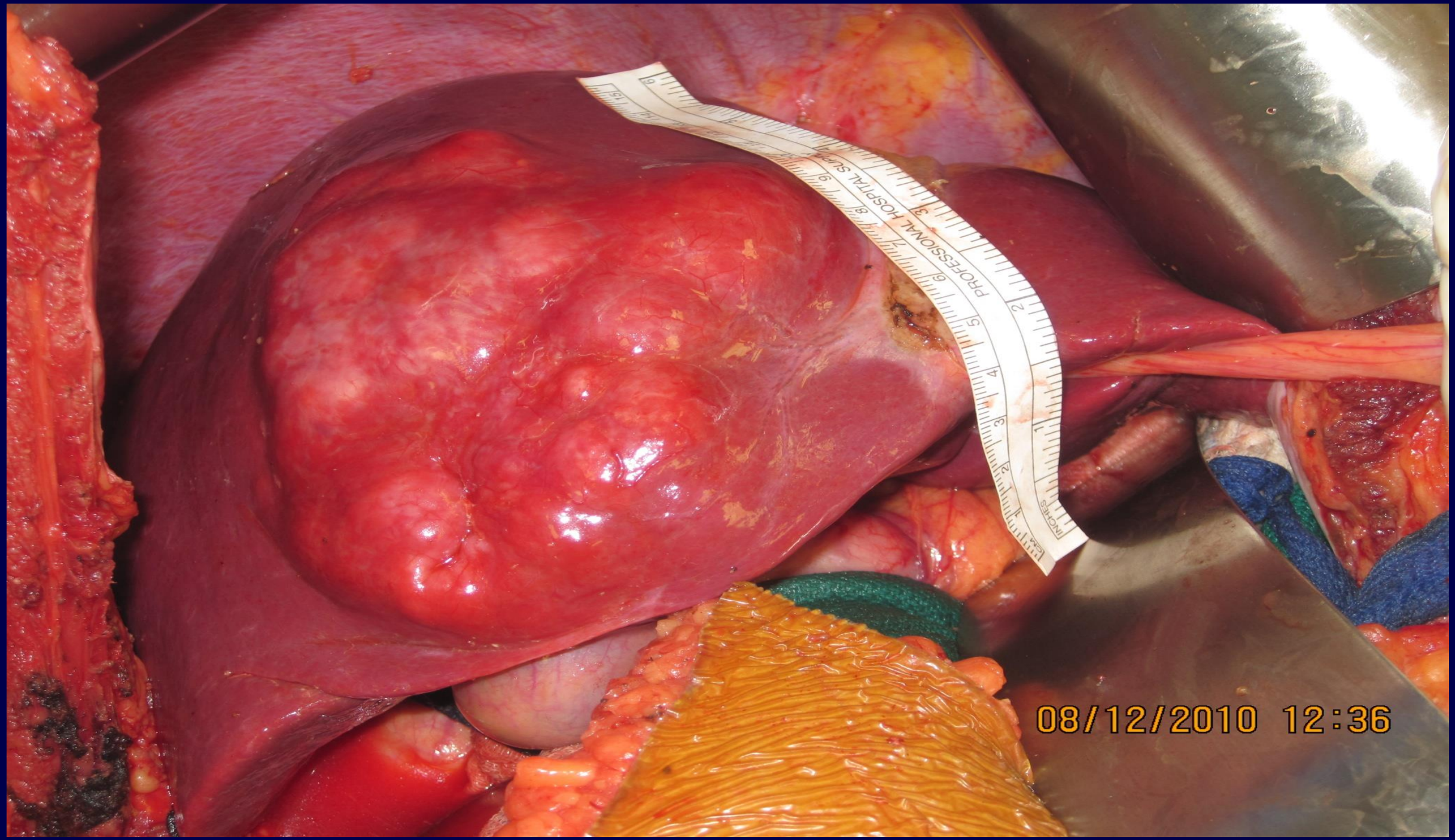
- **HCV Genotype 1** **Treatment Duration**

  Patients Previously Treated With a Regimen Containing: **No cirrhosis** **Child A**

- An NS3/4A PI without prior treatment with an NS5A inhibitor — 12 weeks — 12 weeks

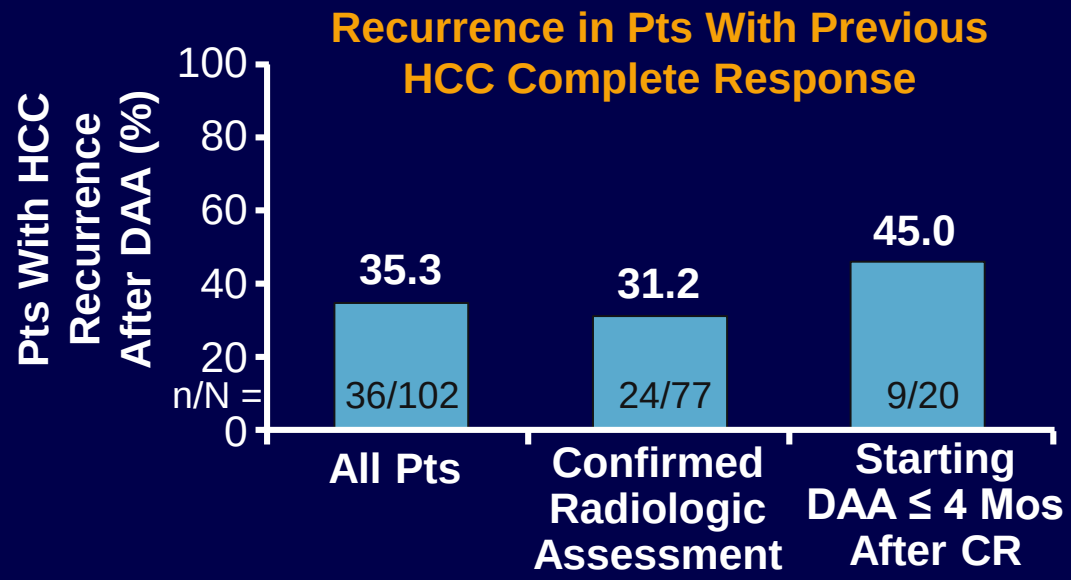
- **Treatment: Simeprevir & Sofosbuvir/Simeprevir, Boceprevir, or Telaprevir with PEG/RBV**

Do DAAs Increase the Risk of de Novo or Recurrent HCC?


PROFESSIONAL HOSPITAL SUPPLY
INCHES
08/12/2010 12:36

High Rate of HCC Recurrence With DAAs

- Retrospective study of pts with history of HCC before starting DAA



- Among pts starting DAAs ≤ 4 mos after CR, 4 pts (20%) died
  - Deaths occurred in Mos 9, 10, 15, 16 after starting DAA

- 10 pts had second HCC recurrence or progression

Endpoint	Pts With Recurrence (n = 24)*
Median time from DAA start to first recurrence, mos (IQR)	3.5 (2-7.6)
Median time from first to second recurrence/progression, mos (IQR)	6.0 (3.2-8.2)
▪ Within 6 mos of first recurrence, n/n (%)	6/20 (30)
▪ Death, n (%)	5 (20.8)

*Pts from cohort with confirmed radiologic assessment, no confounding factors.

Reig M, et al. EASL 2017. Abstract PS-031.

Slide credit: clinicaloptions.com

HCC Occurrence or Recurrence Equivalent in Pts With SVR to DAAs vs IFN

- Meta-analysis and meta-regression analysis of 41 studies (N = 13,875)
  - HCC occurrence in cirrhotic pts who achieved SVR with DAAs or IFN
  - HCC recurrence in pts who had had curative treatment for liver cancer

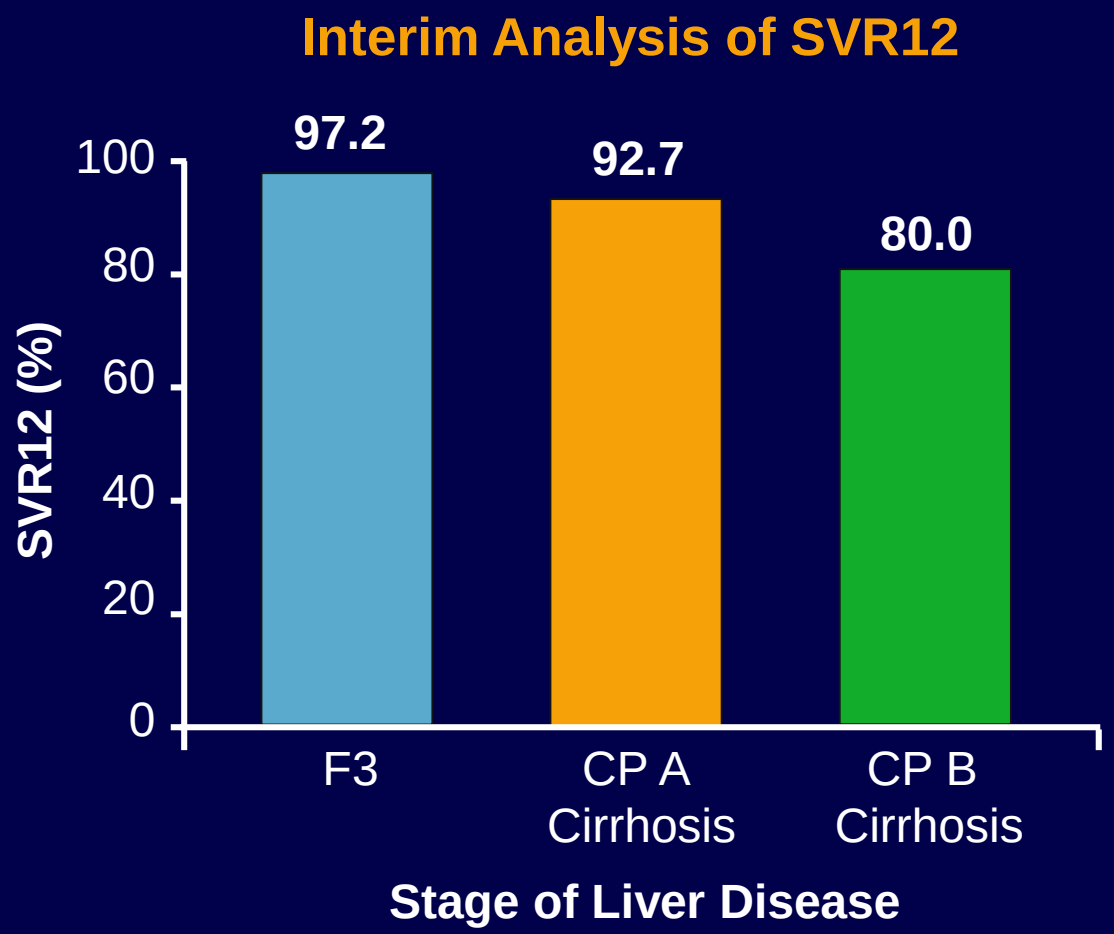
HCC and Risk Factor	Adjusted RR (95% CI)	*P* Value
HCC occurrence		
▪ Average follow-up	0.77 (0.62-0.97)	.03
▪ Average age	1.06 (0.99-1.14)	.08
▪ Treatment (DAA vs IFN)	0.75 (0.22-2.52)	.62
HCC recurrence		
▪ Average follow-up	0.79 (0.55-1.15)	.19
▪ Average age	1.11 (0.96-1.27)	.14
▪ Treatment (DAA vs IFN)	0.62 (0.11-3.45)	.56

Dore G, et al. EASL 2017. Abstract PS-160.

Slide credit: clinicaloptions.com

De Novo HCC in HCV-Infected Pts Treated With Oral DAAs

- Italian pts with HCV and advanced liver disease treated with DAAs and monitored January 2015 - June 2016
  - N = 3075
- Mean follow-up after starting DAA therapy: 300.8 days
  - 41 pts developed HCC
- HCC incidence analyzed by multivariate Cox regression (forward stepwise selection)



Romano A, et al. AASLD 2016. Abstract 19.

Slide credit: clinicaloptions.com

De Novo HCC in HCV-Infected Pts Treated With Oral DAAs

Subgroup	HCC Incidence in Cirrhotic Pts, % per Pt-Yr	*P* Value
Child-Pugh score A/B	1.64/2.92	.58
DAA regimen		.90
▪ SOF + RBV	3.32	
▪ LDV/SOF ± RBV	1.45	
▪ SMV + SOF ± RBV	1.35	
▪ DCV + SOF ± RBV	1.12	
▪ OBV/PTV/RTV + DSV ± RBV	1.88	
APRI score < 2.5/≥ 2.5	1.52/3.27	.02
SVR12 no/yes	8.38/1.55	.001

Romano A, et al. AASLD 2016. Abstract 19.

Slide credit: clinicaloptions.com

De Novo HCC in HCV-Infected Pts Treated With Oral DAAs

Subgroup	HCC Incidence in Cirrhotic Pts, % per Pt-Yr	*P* Value
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APRI score < 2.5/≥ 2.5	1.52/3.27	.02
SVR12 no/yes	8.38/1.55	.001

Cirrhotic pts with HCV treated with DAAs are not at increased risk of developing HCC compared with untreated pts

Romano A, et al. AASLD 2016. Abstract 19.

Slide credit: clinicaloptions.com

HBV Reactivation During HCV DAA Therapy

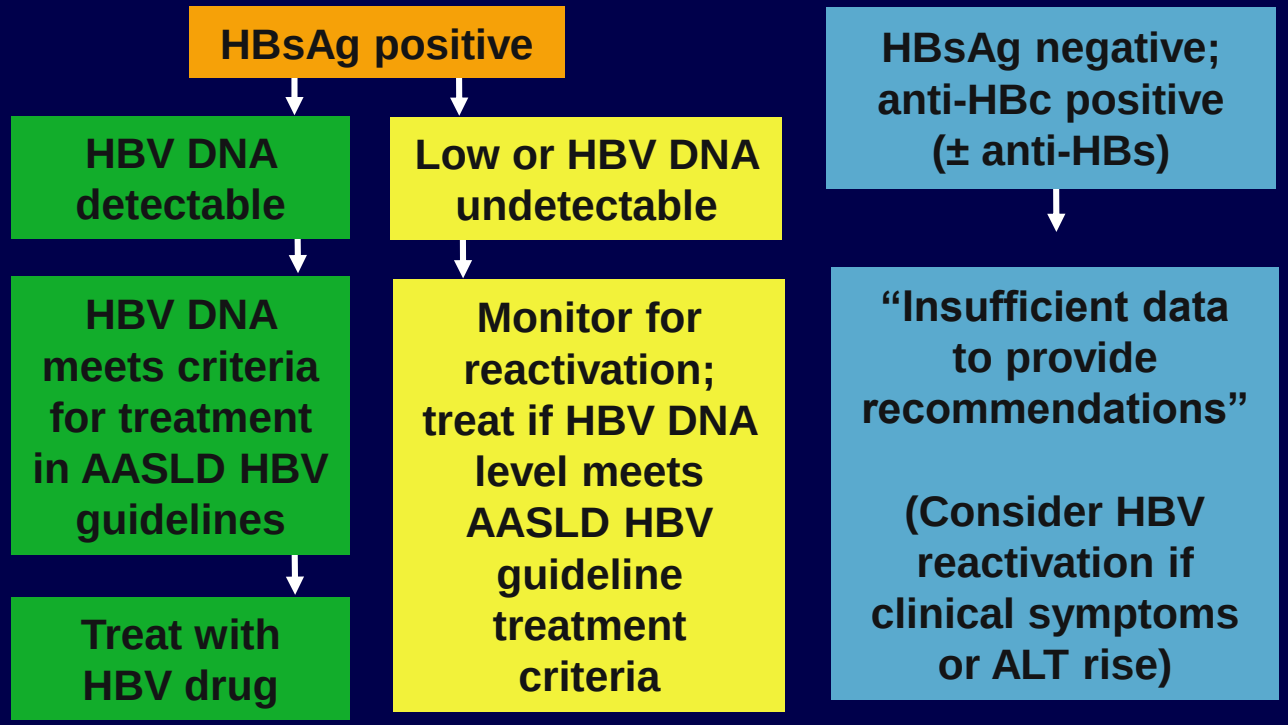
HBV Reactivation in Pts Receiving HCV DAAs

- Case reports of HBV reactivation in pts treated with SMV + SOF ± RBV,[1,2] DCV + ASV,[3,4] and LDV/SOF[5]
  - Possibly due to loss of host immune response to HBV[6]
- 29 confirmed cases of HBV reactivation in HCV DAA recipients in ~ 3 yrs (November 2013 to October 2016)[7]
  - Most cases occurred within 4-8 wks of HCV DAA initiation
- October 2016 FDA issued boxed warning

1. Collins JM, et al. Clin Infect Dis. 2015;61:1304-1306. 2. Ende AR, et al. J Med Case Rep. 2015;9:164. 3. Hayashi K, et al. Clin J Gastroenterol. 2016;9:252-256. 4. Takayama H, et al. Hepatol Res. 2016;46:489-491. 5. De Monte A, et al. J Clin Virol. 2016;78:27-30. 6. Balagopal A, et al. Clin Infect Dis. 2015;61:1307-1309. 7. Bersoff-Matcha SJ, et al. AASLD 2016. Abstract LB-17.

HBV Testing/Monitoring During HCV DAA Therapy

- Test all pts initiating HCV therapy for HBsAg, anti-HBc, and anti-HBs
  - Vaccinate if no HBV markers; follow flow chart below if HBV markers present



AASLD/IDSA. HCV Guidance. April 2017. Graphic adapted from Ira M. Jacobson, MD.

Slide credit: clinicaloptions.com

Conclusions

- Multiple current regimens highly effective and safe across genotypes; confirmed in “real-world” studies
- GLE/PIB is an 8-wk pangenotypic regimen for DAA-naive noncirrhotic pts
- Short duration SOF/VEL/VOX not superior to current regimens for DAA-naive pts; but useful in pts with previous DAA failure
- Controversy persists re: HCC recurrence after DAA-induced SVR
- Little evidence for spike in de novo HCC after SVR
- HBV reactivation very rare in anti-HBc–positive pts; precautions in HBsAg-positive pts especially with HBV viremia
- Only 1 patient out of 1,000 will not be cured today! Need to find every HCV pt!


November 13, 2030