EASL-ILC 2017: Viral Hepatitis

Heiner Wedemeyer

Hannover Medical School, Germany

EASL The Home of Hepatology | THE INTERNATIONAL LIVER CONGRESS™ 2017
19-23 APRIL, AMSTERDAM, THE NETHERLANDS

Conflicts of Interest

Honoraria for consulting or speaking (last 5 years):

Abbott, Abvie, Biolex, BMS, Boehringer Ingelheim, Eiger, Falk Foundation, Gilead, ITS, JJ/Janssen-Cilag, Medgenics, Merck/Schering-Plough, Novartis, Roche, Roche Diagnostics, Siemens, Transgene, ViiV

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Abbott, Abbvie, BMS, Falk Foundation, Gilead, Merck, Novartis, Roche, Roche Diagnostics, Siemens

Selection of abstracts is biased by personal interest!

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and all presenters providing slides!

Hepatitis A

Hepatitis A

- Acute hepatitis, no chronicity
- Vaccine provides long-term protection, almost no vaccine non-responder
- Change in HAV epidemiology *e.g. Jeong et al., THU-139, Korea*
  e.g. Zhang et al., SAT-133, China

Importance of HAV infections for acute-on-chronic liver failure?

Importance of HAV infection for acute-on-chronic liver failure?

Poovorawan et al., Abstract Thu-138

- 1,481 patients with acute hepatitis A in Thailand (347 hospitals)

➢ Analysis of al-cause mortality

Factors (n)	30-day mortality (%)	Adjusted Hazard Ratio
Overall(1,481)	2.2	-
Age ≥ 60 years(136)	10.3	6.36
Cirrhosis (29)	24.1	8.12
Alcoholic liver diseases (17)	17.6	1.46
Chronic hepatitis B(17)	11.7	5.83
Chronic hepatitis C(5)	20	21.11

➢ Still high mortality rate for HAV infections in Thailand, in particular in patients with chronic liver disease

Hepatitis A

- Acute hepatitis, no chronicity
- Vaccine provides long-term protection, almost no vaccine non-responder
- Change in HAV epidemiology *e.g. Jeong et al., THU-139, Korea*
  e.g. Zhang et al., SAT-133, China

Importance of HAV infections for acute-on-chronic liver failure!

Possible role of HAV and HEV infections for the development of AIH (Taubert et al., LBP-532)

Hepatitis E

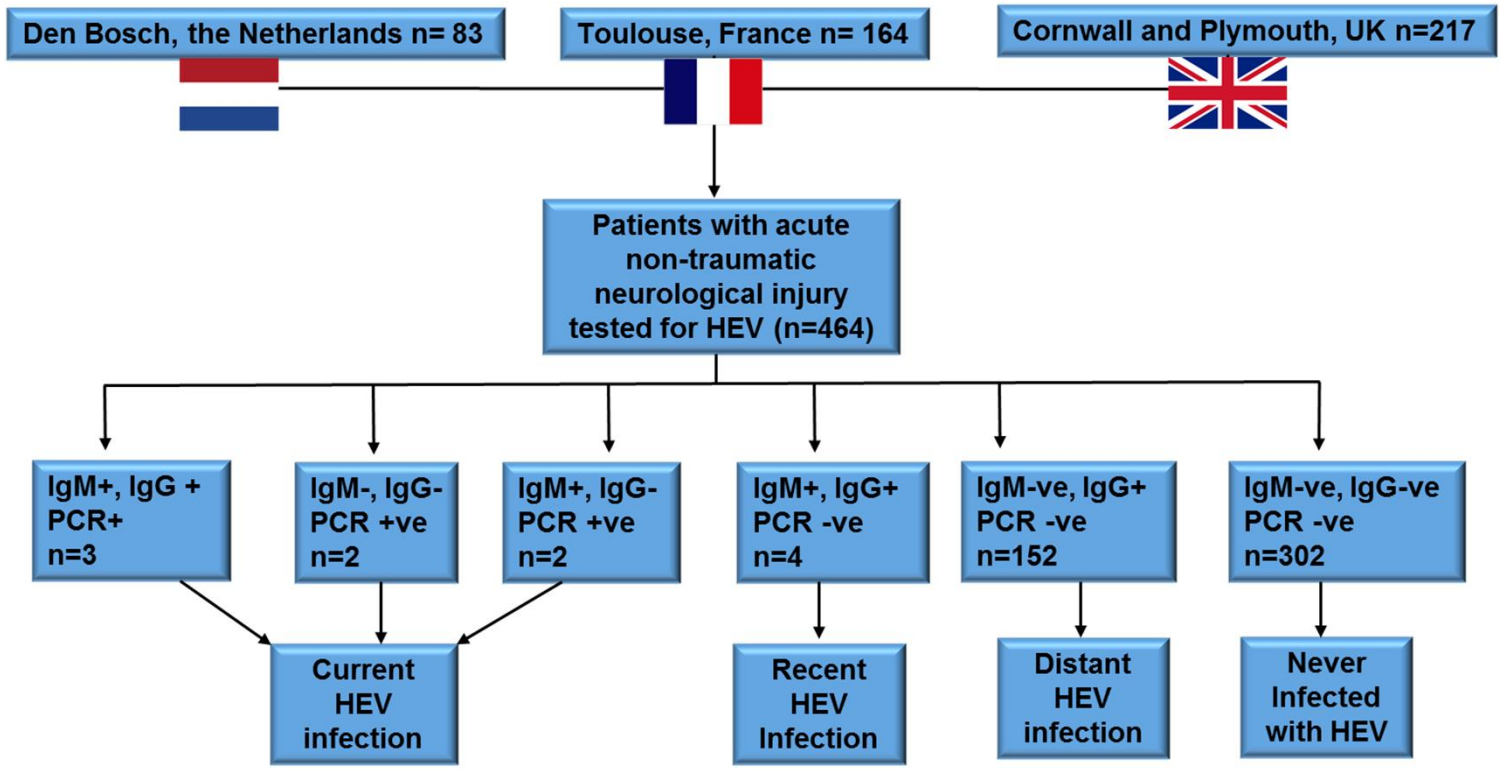
Hepatitis E

- Acute hepatitis, chronicity in immunocompromised patients *Komolmit et al., SAT-137*
  (also during treatment with tyrosine kinase inhibitors) *Protin et al, THU-140*
- Severe courses in patients with chronic liver disease *Fraga-Christinet et al., SAT-298*
- Clinical courses differ between HEV genotypes *Sayed et al., THU-130*
- HEV is mainly a zoonosis in Europe but infections by blood transfusions are possible *(e.g. Germany 1:896 donations HEV-RNA(+))* *Westhölter et al., PS-110*
- Ribavirin is a treatment option, treatment failure may occur *Tjwa et al., THU-323*
  (in particular during ibrutinib therapy?) *Protin et al, THU-140*
- HEV is discussed as a cause for extrahepatic symptoms *Pischke et al., J Hepatol 2017*

Role of HEV in acute non-traumatic neurological injury

Webb, Dalton et al., PS-103:

- Prospective HEV screening of patients with neurological injury (non-traumatic)



Role of HEV in acute non-traumatic neurological injury

Webb, Dalton et al., PS-103:

- Prospective HEV screening of patients with neurological injury (non-traumatic)

- 2.4% of acute neurology patients have evidence for HEV infection

Jones et al., PS-104:

- HEV-associated neuralgic amyotrophy has a different phenotype than HEV-neg. NA:
  - bilaterial;
  - more neurol. Damage
  - involvement outside brachial plexus

Acute neurological event	Number tested (n=)	HEV infection n= (%)
Neuralgic amyotrophy	**5**	**3 (60%)**
Guillain-Barré **syndrome**	11	0 (0%)
Encephalitis	**7**	**1 (14%)**
Meningitis	7	0 (0%)
Cranial Nerve palsies	**31**	**1 (3%)**
Seizure(s)	**44**	**3* (7%)**
Cerebrovascular accident	**170**	**4 (2%)**
Transient ischaemic attack	68	0 (0%)
Migraine/headaches	51	0 (0%)
Multiple sclerosis	12	0 (0%)
Myelitis	14	0 (0%)
Miscellaneous	25	0 (0%)
Other	28	0 (0%)

Extrahepatic manifestations of HEV infection

- Extrahepatic HEV replication

Drave et al., J Viral Hepatitis 2016
EASL ILC-2017: Qu et al., FRI-138

- T cell cross-reactivity

Soon et al., THU-313
(Al-Ayoubi et al., THU-285)

Wedemeyer & Cornberg, Liver International 2016
Pischke et al., Journal of Hepatology 2017

Hepatitis E: ILC-2017

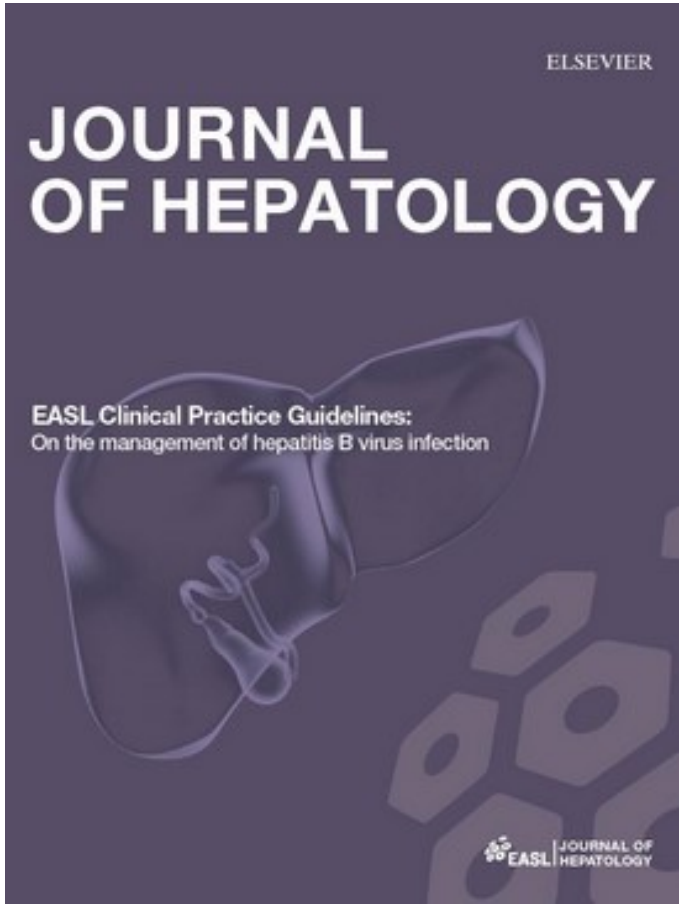
- Robust tools and models to study HEV virology and immunity

  e.g. Sayed et al, THU-130van der Garde et a., FRI-290,

- New data on epidemiology and natural history
- HEV may cause neurological symptoms, specifically neuralgic amyotrophy
- New treatment options are needed for ribavirin treatment failures

  e.g. NUC 2CMC Qu et al., FRI-138

Hepatitis B



Clinical Practice Guidelines

EASL | JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver *

Chair: Pietro Lampertico

Panel members:
Kosh Agarwal, Thomas Berg, Maria Buti, Harry L.A. Janssen, George Papatheodoridis, Fabien Zoulim; EASL Governing Board representative: Frank Tacke

Reviewers:
EASL Governing Board, Maurizia Brunetto, Henry Chan, Markus Cornberg

Natural history of HBV - New nomenclature

	HBeAg positive Chronic *infection*	HBeAg positive Chronic hepatitis	HBeAg negative Chronic *infection*	HBeAg negative Chronic hepatitis
HBsAg	High	High/Intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10E7 IU/mL	10E4-10E7 IU/mL	<2,000 IU/mL°°	>2,000 IU/mL
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative Chronic hepatitis

*Persisitently or intermittently
°° HBV-DNA levels can be between 2,000 and 20,000 IU/mL in some patients without sings of chronic hepatitis

Hepatitis B

TDF → TAF

(*tenofovir disoproxil fumarate → tenofovir alafenamide*)

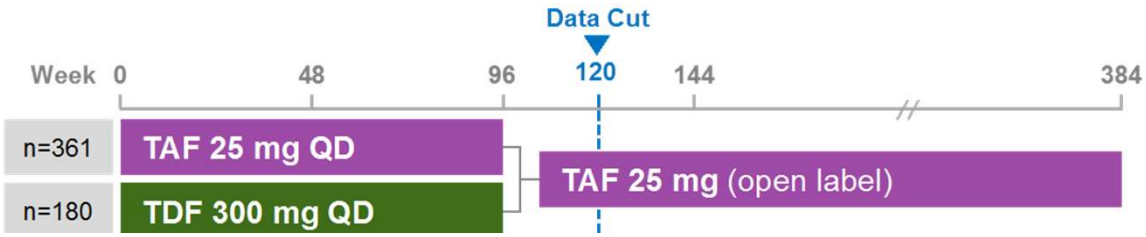
Week 48 Data:
Buti et al.., Lancet Gastroenterol & Hepatol 2016; 1: 196-206 (HBeAg-negative)
Chan et al. Lancet Gastroenterol & Hepatol 2016; 1: 185-195 (HBeAg-positive)

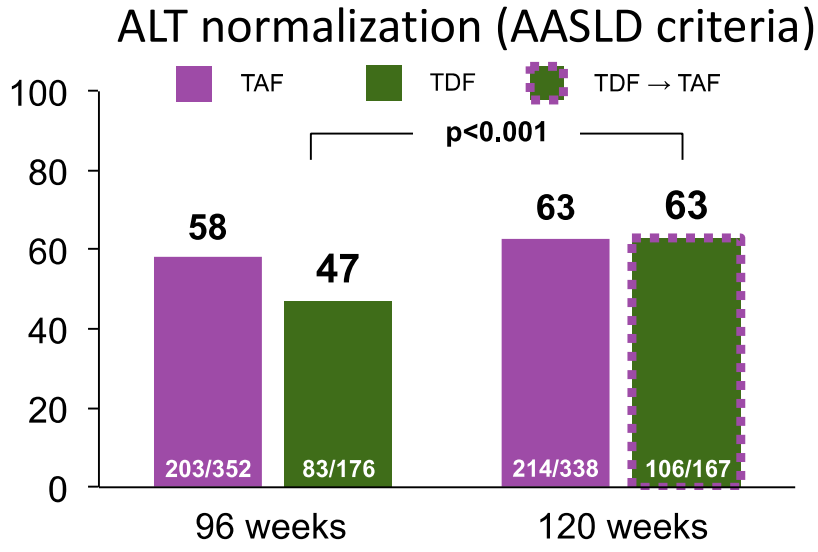
TAF: Week 96 data and switching from TDF

Brunetto et al., PS-042 & Argawal et al., FRI-153: Week 96 data

- HBV-DNA <29 IU/ml 90% (HBeAg-negative) and 73% (HBeAg-positive)
- Non-inferior to TDF

Chan et al., PS-041: Switch from TDF to TAF after week 96





Switching:

- Improvement in ALT normalization
- Improvement in bone density
- Improvement in GFR

Indications for selecting ETV or TAF over TDF*

1. Age >60 year
2. Bone disease
Chronic steroid use or use of other medications that worsen bone density
History of fragility fracture
Osteoporosis
3. Renal alteration**
eGFR <60 min/ml/1.73 m^2
Albuminuria >30 mg or moderate dipstick proteinuria
Low phosphate (<2.5 mg/dl)
Hemodialysis

* TAF should be preferred to ETV in patients with previous exposure to nucleoside analogues.

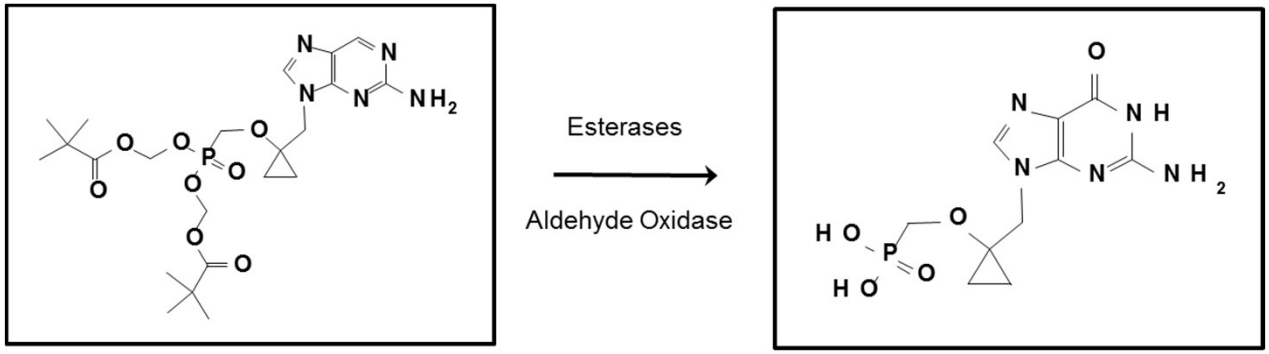
** ETV dose needs to be adjusted if eGFR <50 ml/min; no dose adjustment of TAF is required in adults or adolescents (aged at least 12 years and of at least 35 kg body weight) with estimated creatinine clearance (CrCl) 15 ml/min or in patients with CrCl <15 ml/min who are receiving haemodialysis.

EASL 2017 CPG HBV, J Hepatol 2017 in press

Hepatitis B

Besifovir Phase 3 Study

Novel nucleotide (guanosine monophosphate)



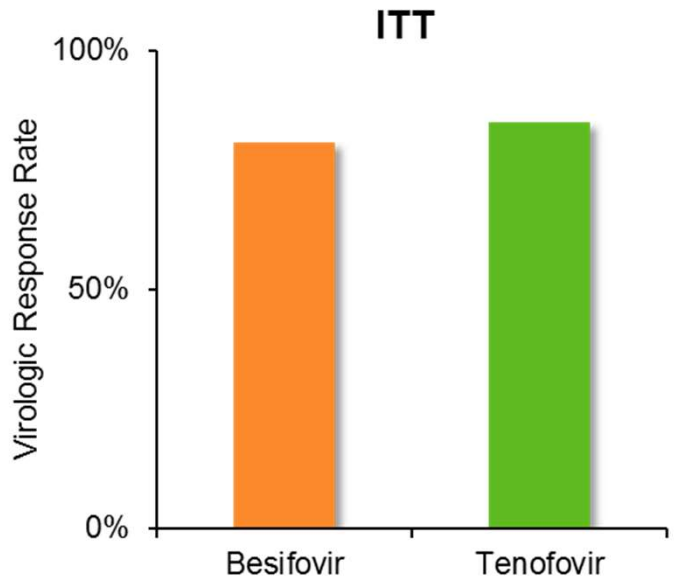
Prodrug (LB80380)

Active (LB80317)

Besifovir phase 3 study

Ahn et al., GS-017: Week 48 data

- 193 patients in Korea
- Randominzed trial vs. TDF
- Addition of L-carnitine required



	Besifovir	Tenofovir	One sided 97.5% CI
VR (n,%)	76 (80.85)	79 (84.95)	-0.149, ∞
Total	94	93	

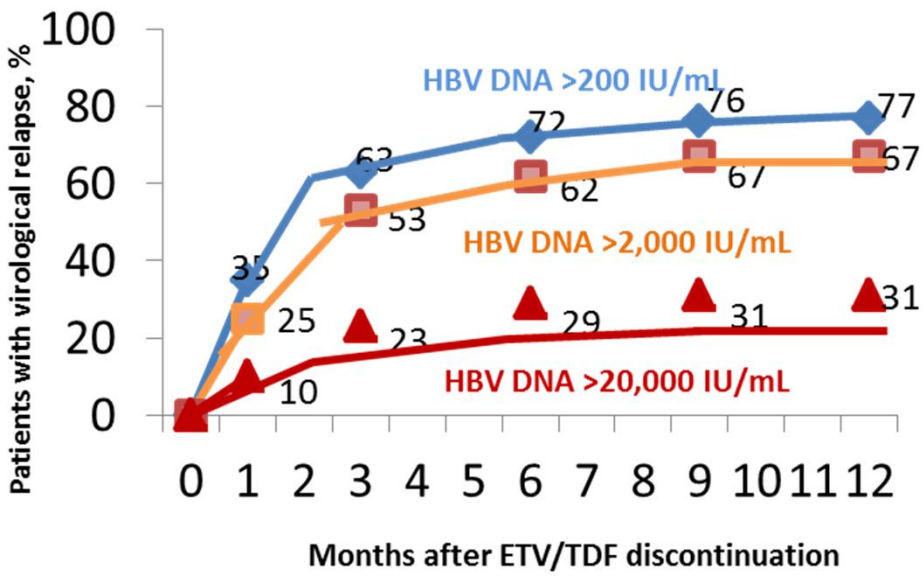
Hepatitis B

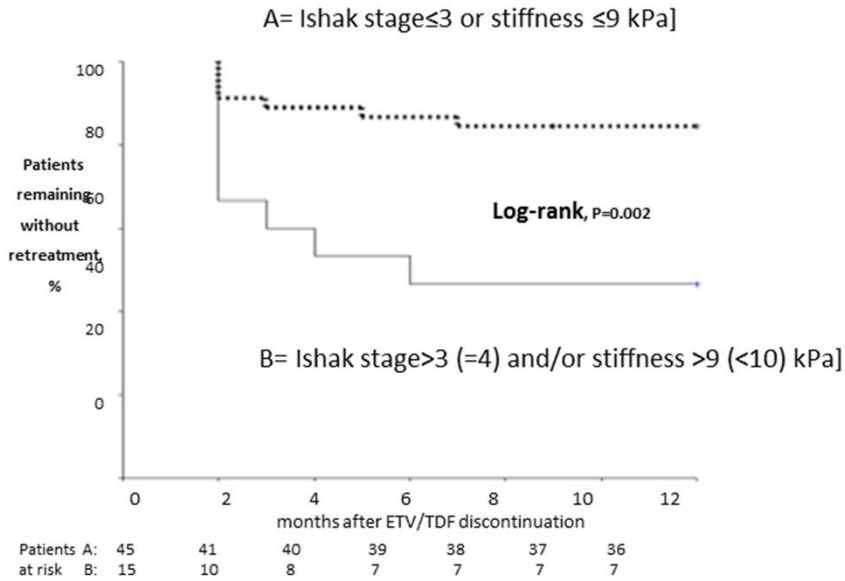
NUC-discontinuation

DARING-B: Discontinuation of ETV or TDF

Papatheodoridis et al., PS_043: Prospective trial in Greece

- 60 patients; ETV/TDF for ≥ 4 years and HBV DNA undetectable ≥ 3 years





Hepatitis B

New drugs to achieve HBV cure

"functional cure", HBsAg loss, HBs seroconversion, …

TARGETS FOR HBV "Cure"

Entry inhibitors
- Myrcludex

Therapeutic vaccination
TLR Agonists
Checkpoint Inhibitors
Bispecific Antibodies
T-cell transfer

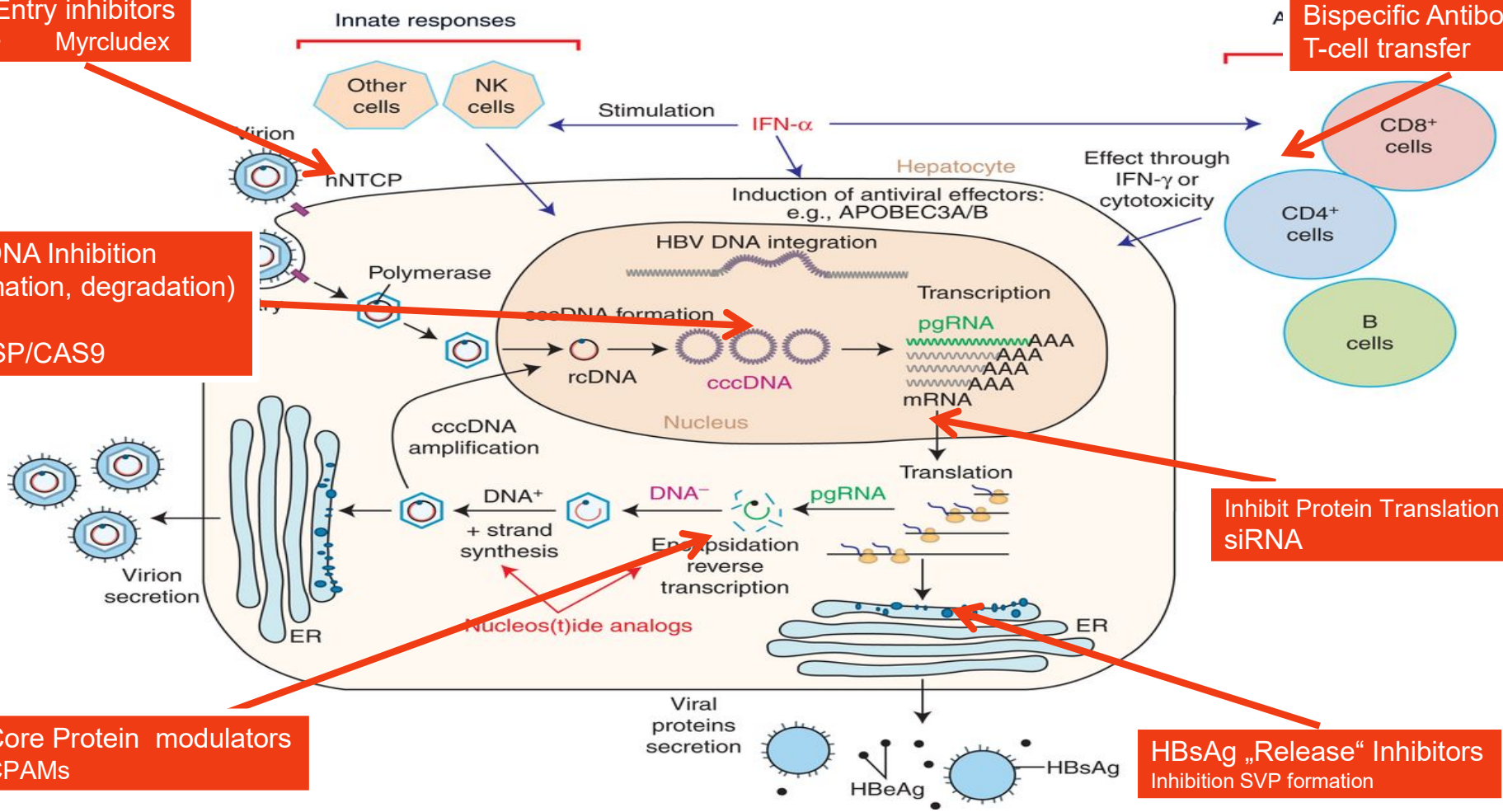
cccDNA Inhibition
(formation, degradation)

CRISP/CAS9

Inhibit Protein Translation
siRNA

Core Protein modulators
CPAMs

HBsAg „Release" Inhibitors
Inhibition SVP formation



Fabien Zoulim, and David Durantel Cold Spring Harb Perspect Med 2015;5:a021501

TARGETS FOR HBV "Cure"

Entry inhibitors
- Myrcludex

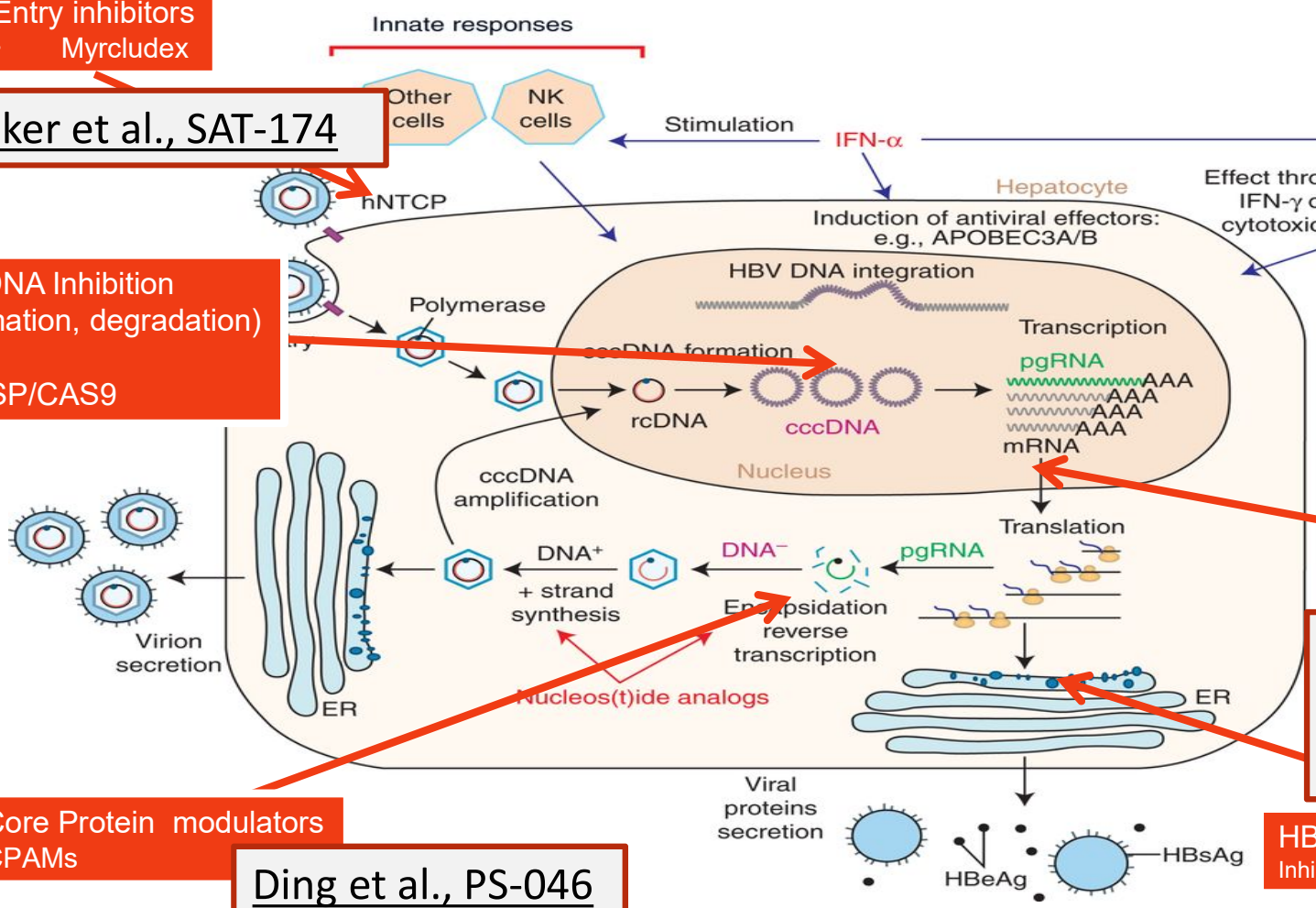
Donker et al., SAT-174

Therapeutic vaccination
TLR Agonists
Checkpoint Inhibitors
Bispecific Antibodies
T-cell transfer

Boni et al., PS-050
Wisskirchen et al, PS-051
Schuch et al., PS-052
Fisciaro et al, PS-053
Gane et al., PS-044

cccDNA Inhibition
(formation, degradation)

CRISP/CAS9



Inhibit Protein Translation
siRNA

Yuen et al., PS-045
Gane et al., THU-176
Streinu-Cercel et al., SAT-155

Core Protein modulators
CPAMs

Ding et al., PS-046

HBsAg „Release" Inhibitors
Inhibition

Bazinet et al., THU-154-6

Fabien Zoulim, and David Durantel Cold Spring Harb Perspect Med 2015;5:a021501

Hepatitis D

Hepatitis D (delta)

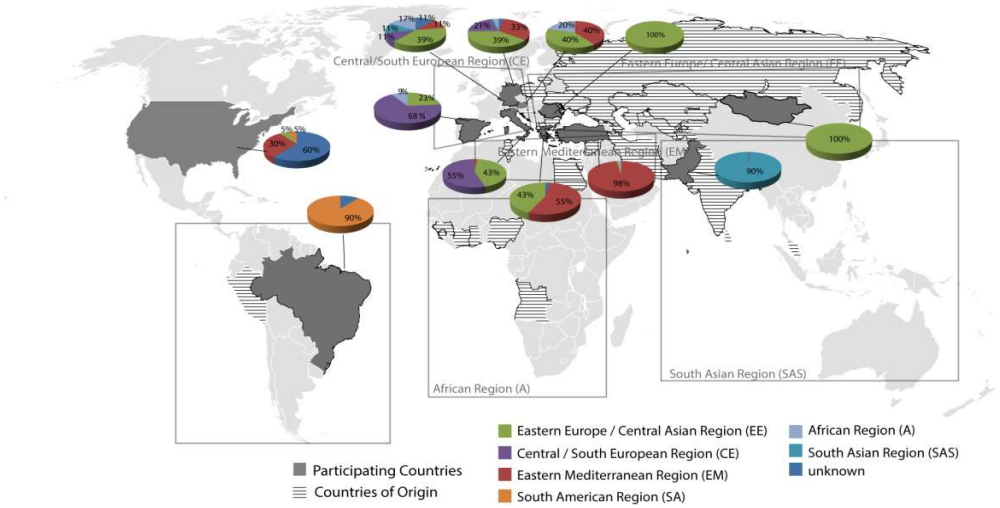
- Most severe form of chronic viral hepatitis
  - possibly less aggressive in African patients *Spaan et al., THU-152*
  - also higher risk for HCC development *Keskin et al., SAT-153*
- HDAg shows high variability *Colagrossi et al., THU-142*
  Reduced HBV quasispecies complexity *Godoy et al., FRI-166*
- PEG-IFNa is effective in only 20-25% of patients
  Viral dominance patterns associated with response *Lutterkort et al., FRI-17*

Clinical and virological characteristics of hepatitis D worldwide?
Alternative antiviral treatment options?

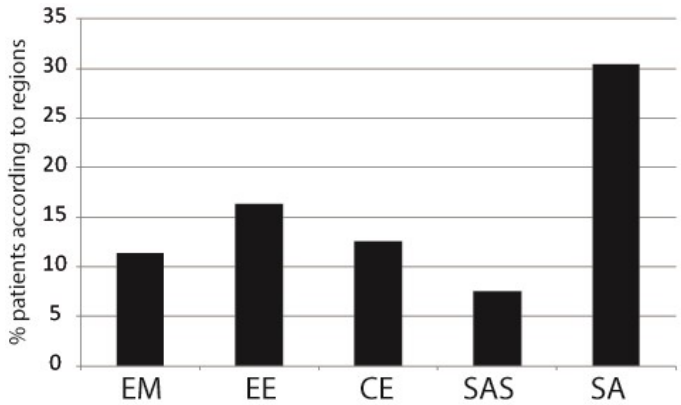
Heterogeneity of hepatitis delta world-wide: the HDIN network

<u>Wranke et al., THU-157:</u>

- The Hepatitis Delta International Network (HDIN)
- 1579 anti-HDV+ or HDV-RNA+ patients from 15 countries



Hepatic clinical complications



- Giersch et al., SAT-175: HDV-G3 leads to higher infection rates in mouse models
- Shirazi et al., SAT-154: HDV in Israel (6.5% prevalence)

Novel treatment options for HDV infection

Novel antiviral strategies against HDV in clinical development

	Target	Drug	Structure/function	Clinical Phase
Entry inhibitors	• Sodium taurocholate co-transporting polypeptide (NTCP)	Myrcludex B	• Myristoylated lipopeptide obtaining 47 amino acids of the pre S1 domain of L-HBsAg	Phase II
Prenylation inhibitors	• Farnesyl or geranylgeranyl prenyl lipids	Lonafarnib	• Inhibitor of an essential step in viral propagation and assembly	Phase II
Nucleic acid polymers	• Amphipathic alpha-helices in class I surface glycoproteins	REP 2139-Ca	• Blocks release of HBsAg particles: entry and post-entry antiviral activity	Phase II

Wranke & Wedemeyer, Current Opinion Virology 2016

- Buchmann et al., Thu-158: kinase inhibitors with activity against HDV
- Donkers et al., SAT-174: NTCP inhibitors (e.g. rosiglitazone)
- Bazinet et al., REP-2139 long-term follow-up; LBP-507

Lonafarnib for HDV infection

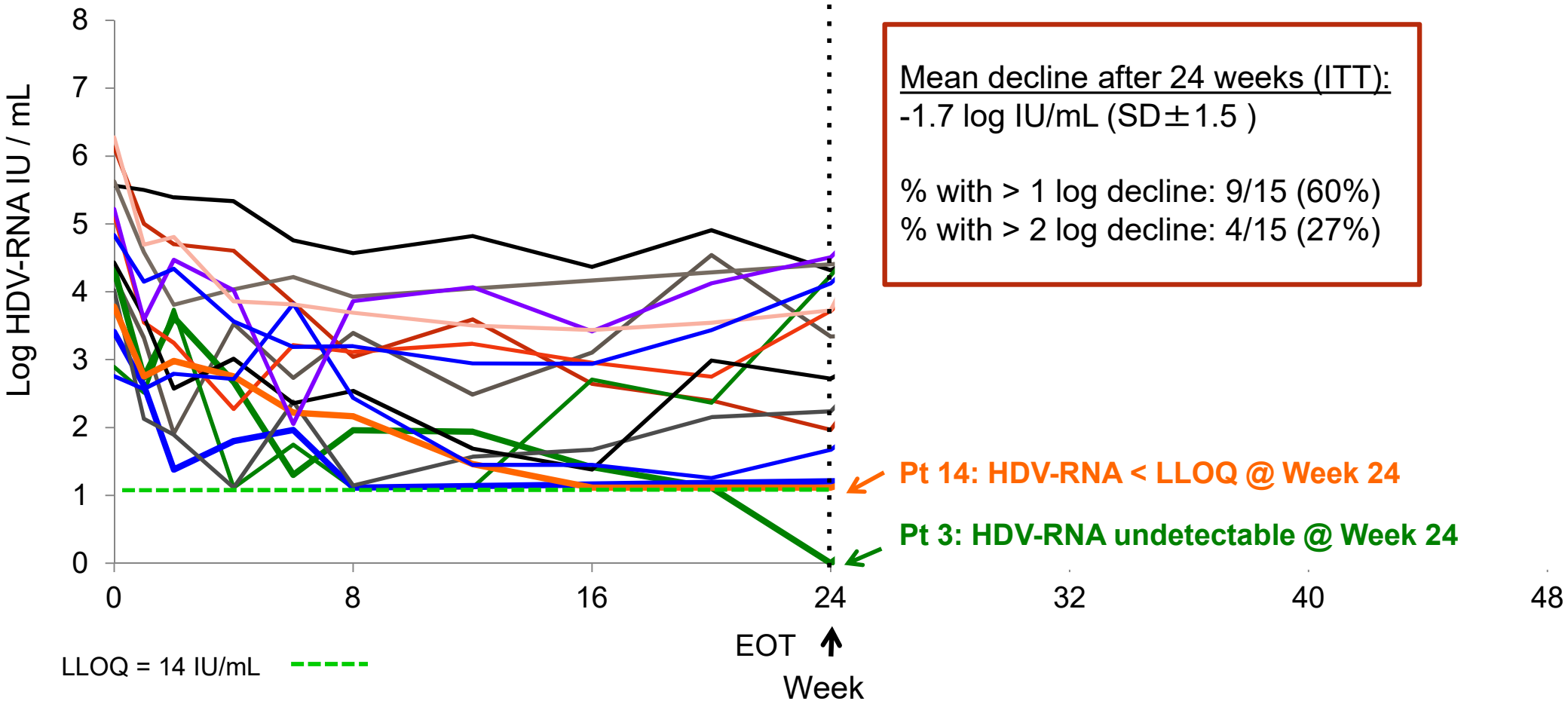
- Final step in HDV replication involves prenylation (i.e. farnesylation): Farnesyl transferase is a host enzyme which can be targeted by drugs
- Lonafarnib for 28 days induced a dose-dependent HDV-RNA decline

Koh et al., Lancet Infect. Dis. 2015; 15: 1167-74

<u>EASL-ILC 2017:</u>
Wedemeyer et al., PS-039: → Lonafarnib dose escalation, treatment 24 weeks
Yurdaydin et al., GS-008: → Lonafarnib dose finding, 12-24 weeks
Koh et al., LPB-519: → Lonafarnib once daily dosing, 24 weeks
Yurdaydin et al., THU-161: → post-treatment HDV RNA clearance

Lonafarnib for HDV infection

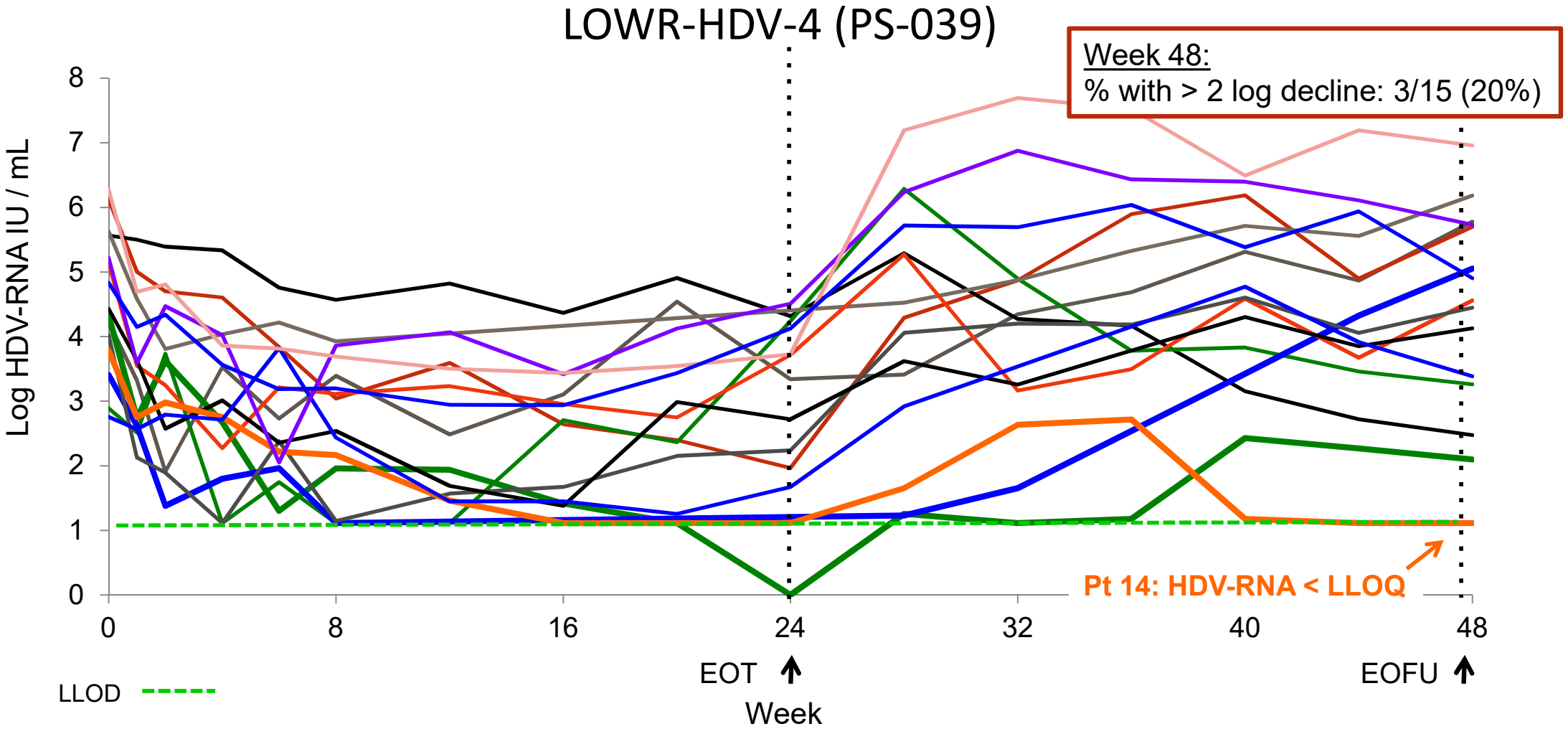
LOWR-HDV-4 (PS-039)



Mean decline after 24 weeks (ITT):
-1.7 log IU/mL (SD±1.5)

% with > 1 log decline: 9/15 (60%)
% with > 2 log decline: 4/15 (27%)

Lonafarnib for HDV infection



Lonafarnib for HDV infection

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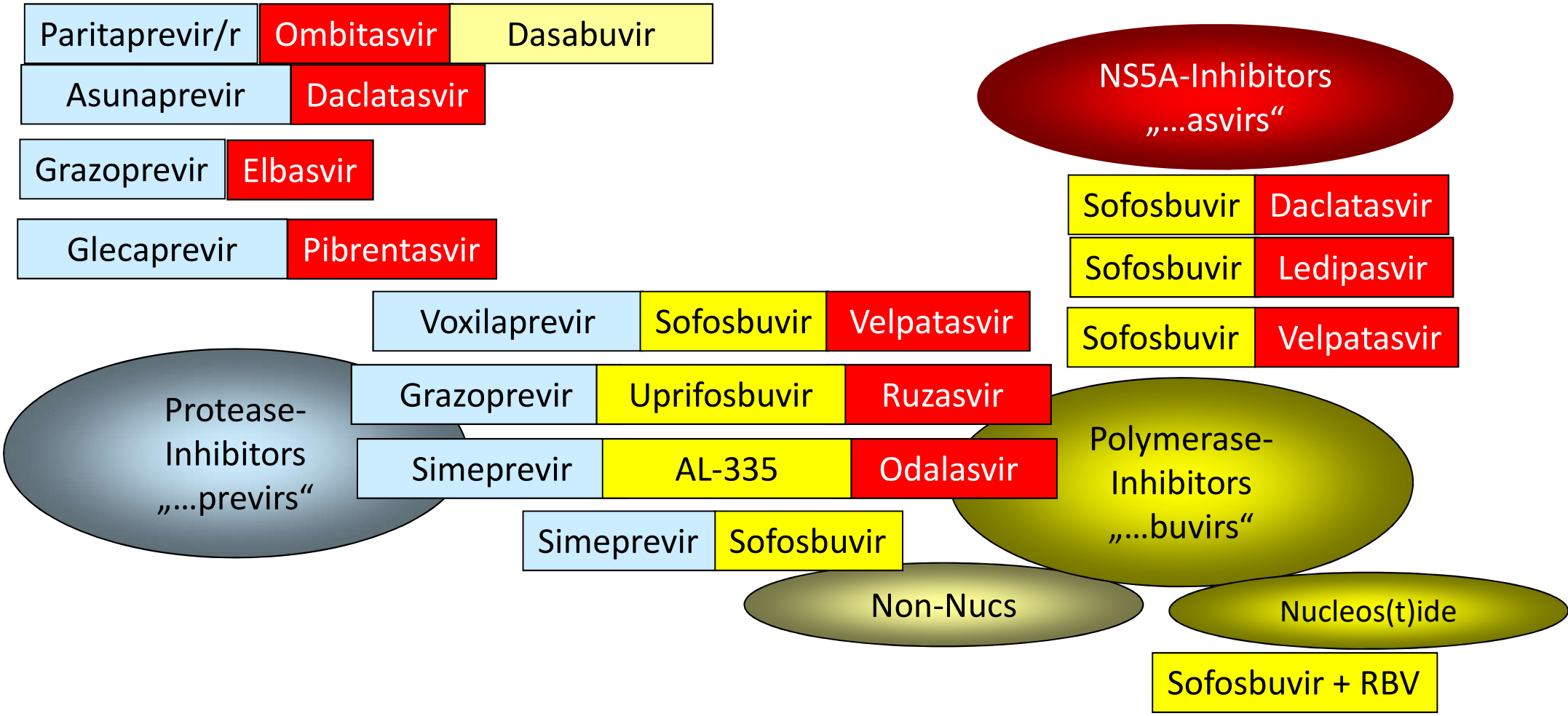
Yurdaydin et al., THU-161: → post-treatment HDV RNA clearance

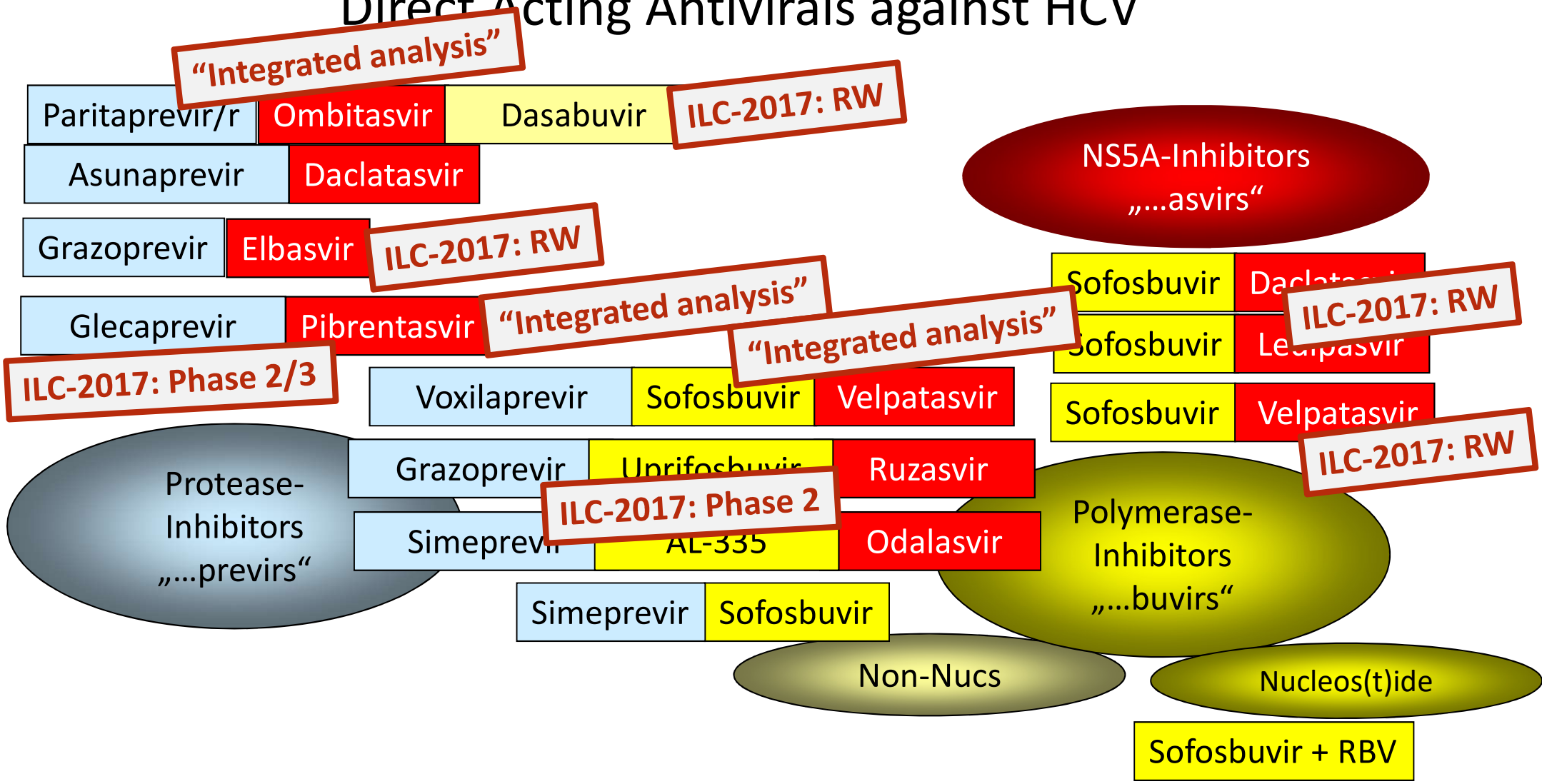
- Antiviral efficacy confirmed for up to 24 weeks
- GI side effects are dose-limiting
- Off-treatment viral control is possible in some patients (can be associated with hepatitis flares)
- Longer therapies/combination therapies may be needed

Hepatitis C

Direct Acting Antivirals against HCV



Direct Acting Antivirals against HCV



HCV treatment ILC-2017: Phase 3 studies

Forns et al., GS-005:

- glecaprevir/pibrentasvir in GT 1,2,4,5,6 cirrhosis (n=146) (Expedition-1); **SVR: 145/146**

Forster et al., GS-006:

- GT 3 (Endurance-3)

glecaprevir/pibrentasvir 12 weeks	**SVR 95% (222/233)**
sofosbuvir/daclatasvir 12 weeks	**SVR 97% (111/115)**
glecaprevir/pibrentasvir 8 weeks	**SVR 95% (149/157)**

Chayama et al., FRI-262 and FRI-262:

- glecaprevir/pibrentasvir in Japanese patients with GT 1 & 2 (Certain 1&2 studies): **SVR 100%**

Wei et al., FRI-266

- elbasvir/grazoprevir in GT1,4,6 (C-CORAL) (Asia, Russia, Australia; n=250), 12 weeks
- **SVR 92.8% (GT1b 98.9%; GT6 62.9%)**

Reau et al., LBO-03

- glecaprevir/pibrentasvir in liver or renal transplant patients (Magellan-2): **SVR 98%**

Hepatitis C

Efficacy and safety of approved regimens in “real-world” cohorts

HCV treatment ILC-2017: cohort studies/registries

- TRIO Network: 7,550 patients; e.g. Flamm et al., SAT-279:
- HCV TARGET: >10,000 patients; e.g. Sulkowski et al., SAT-229:
- French HEPATHER and ANRS cohorts: >5,000 patients; e.g. Salmon et al. PS-131
- German Hepatitis C Registry: >10,000 patients; e.g. Deterding et al. PS-096
- Spanish registry Hepa-C: >6000 patients; e.g. Badia Aranda et al., THU-275
- Italian PITER platform: 3,936 patients; e.g. Kondili et al., FRI-280
- RESIST-HCV (Sicily): >5,000 patients; e.g. Cacciola et al., FRI-228
- Scottish HCV Clinical Database: nation-wide; e.g. Innes et al., PS-035
- … and many more registries/cohorts (e.g. Egypt, VA, etc.)

HCV treatment ILC-2017: Real-world Velpatasvir/Sofosbuvir

Curry et al., PS-102:

- sofosbuvir/velpatasvir in GT2-6 (TRIO Network) (n>600); SVR: GT2 97%, GT3 97%, GT4-6 91%

Vermehren et al., PS-155:

- GT3 treatment according to baseline RASs with SOF/DAC or SOF/VEL

Khalili et al., SAT-222:

- sofosbuvir/velpatasvir in GT1-6 (HCV-TARGET Study)

Buggisch et al., SAT-254:

- sofosbuvir/velpatasvir, single center Germany

Christensen et al., SAT-275:

- sofosbuvir/velpatasvir, German GECCO (n=165 started therapy)

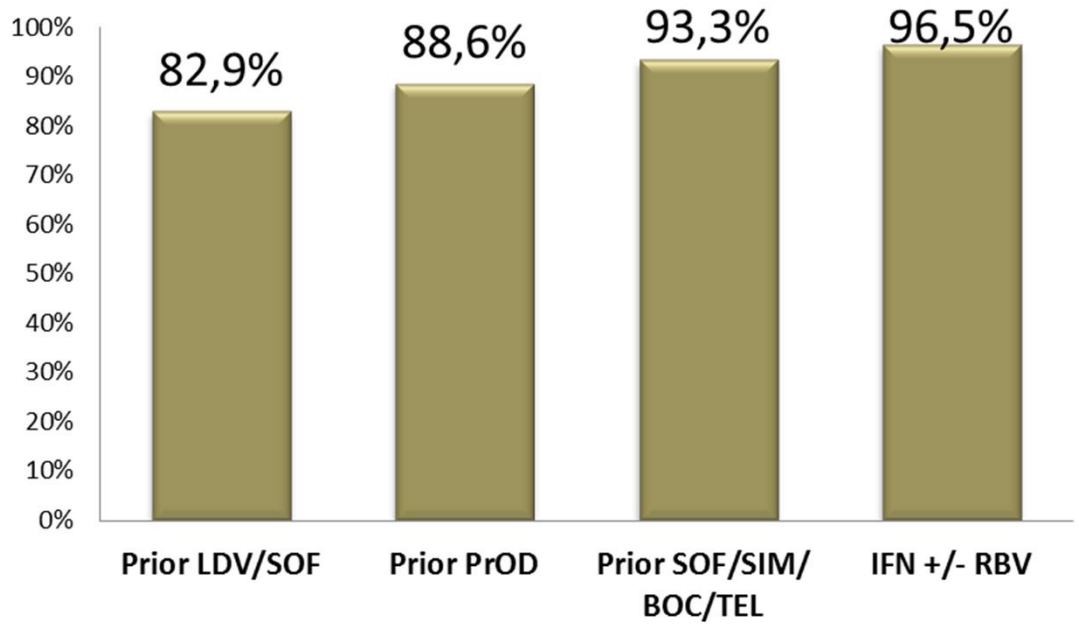
Elbasvir/Grazoprevir experience in the VA healthcare system

Kramer, Puenpatom et al., PS-095:

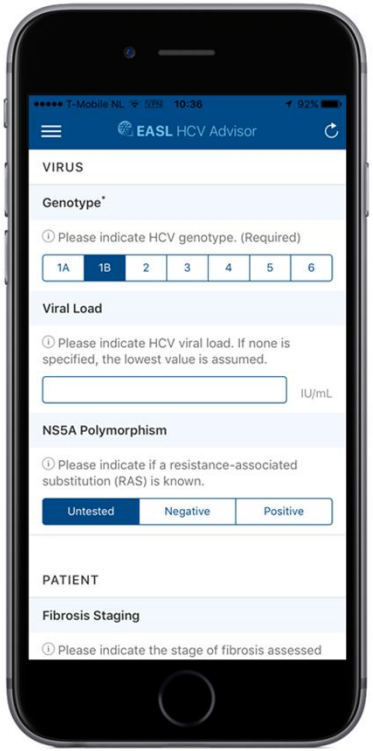
- 2,436 patients (evaluable population) starting EBR/GZR between 2/2016 and 8/2016

- SVR 95.6% (EP) and 97% (PP)
- Similar high SVR rates in
  - pts. with history of acohol abuse
  - pts. with history of drug abuse
  - cirrhosis (n=808)
  - CKD stage 4-5 (n=407)
  - HIV infection (n=74)
  - GT4 (n=64)
  - Afr. Americ (n=1400)
  - Hispanics (n=81)

SVR according to prior treatments



EASL HCV Advisor



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Hepatitis C

Antiviral treatment of patients with HCV-related lymphoproliferative disorders and cyroglobulinemia

HCV-clearance improves extrahepatic manifestations

Venezia et al., PS-100:

- HCV treated in Torino, 67 patients, all achieved SVR
- 44 pts. with lymphoprolifertive diseases; 32 cyrogobulinemia (5 pts both)

- Mixed cryoglobulinemia: 77% improvement of symptoms, in particular vasculitis
- B-NHL group: 52% maintained complete regression; 39% maitained stable disease

Saadoun et al., PS-099:

- HCV cyrogobulinemia-vasculitis (41 pts both); treated with SOF/DAC

- SVR 12: 100%
- 37/41 (90.2%) complete clinical response
- Improvement in kidney function and skin ulcer

Hepatitis C

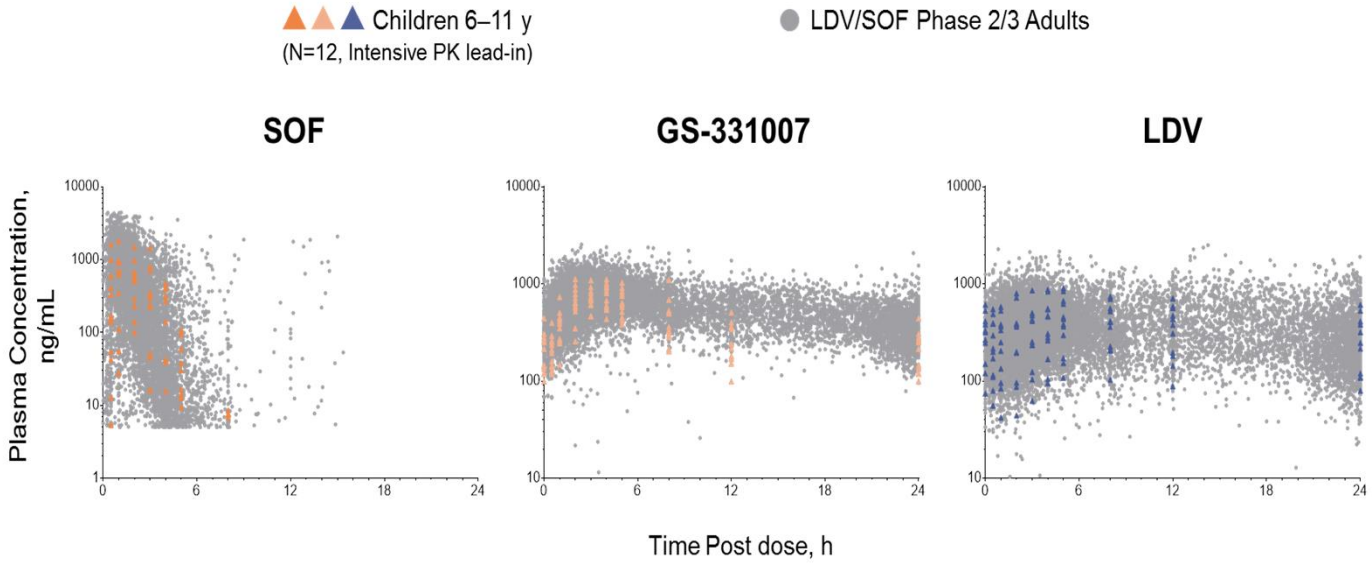
Antiviral treatment of children

Ledipasvir/Sofosbuvir (half dose) is effective and safe in children (6-11 years)

Murray et al., PS-101:

- Children agred 6-11 years
- Ledipasvir/sofosbuvir (45/200mg) for 12 weeks (n=87) or 24 weeks (n=3)

- SVR 99%
  (1 relapse in 1 GT1a patient with cirrhosis)
- 1 SAE (not related)



Hepatitis C

Antiviral treatment in HBV co-infection

Low risk for clinical HBV reactivation during and after HCV clearance

Liu et al., PS-098:

- Ledipasvir/sofosbuvir in HBsAg+/HCV-RNA+ patients (n=111)
- no current HBV treatment, 99% HBeAg-negative
- HBV-DNA undetectable 33%; Mean baseline HBV-DNA 2.1 log10 IU/ml

- HCV-SVR: 100%
- HBV DNA increase in 63%
- Two patients started HBV therapy
- Factors associated with HBV↑ + ALT >2xULN (n=5):
  - baseline ALT
  - HBV-DNA

n, %	Overall N=111	BL HBV DNA <LLOQ n=37	BL HBV DNA ≥LLOQ n=74
Increase to >LLOQ	31 (28)	31 (84)	—
+ ALT >2x ULN	0	0	—
Increase >1 – <2 $\log_{10}$ IU/mL	38 (34)	11 (30)	27 (36)
+ ALT >2x ULN	2 (2)	0	2 (1)
Increase ≥2 $\log_{10}$ IU/mL (any visit)	23 (21)	11 (30)	12 (16)
+ ALT >2x ULN	3 (3)	0	3 (4)

- No patient had AEs of jaundice, liver decompensation, liver failure or liver transplant

Hepatitis C

HCC risk and IFN-free antiviral therapy

HCCs still occur after HCV clearance

Journal of Hepatology October 2016

- Reig et al., earlier and more frequent recurrence

- Pol et al., 0.73 HCC/100 person months, no increased incidence

- Conti et al., de-novo HCC 3,16%

- Cheung et al., de-novo HCC 5.4% in SVR

- Kozbial et al., de-novo HCC 5.2% in SVR

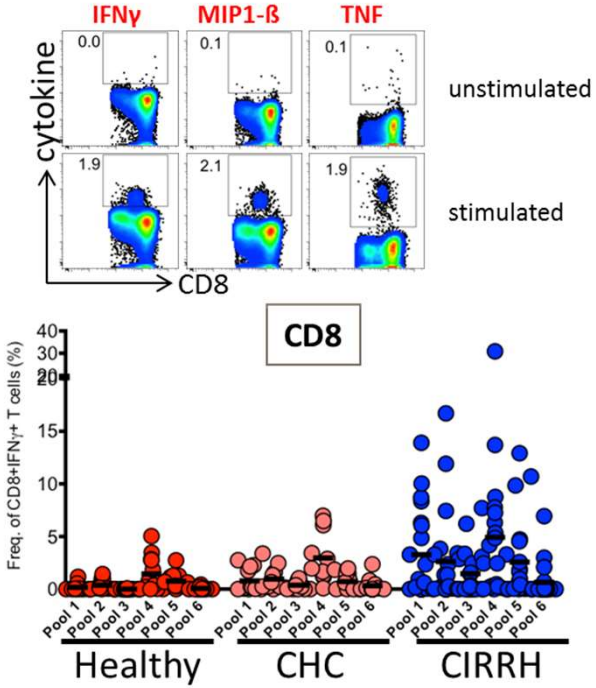
de novo incidence vs. recurrence!

IFN-free clearance of HCC could affect HCC immune surveillance

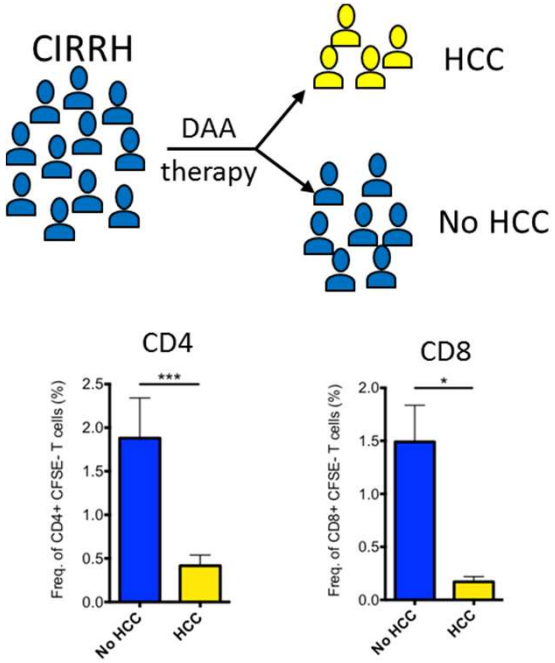
Owusu-Sekyere et al., GS-03:

- Role of HCC-specific T cells in patients with cirrhosis receiving IFN-free HCV therapy

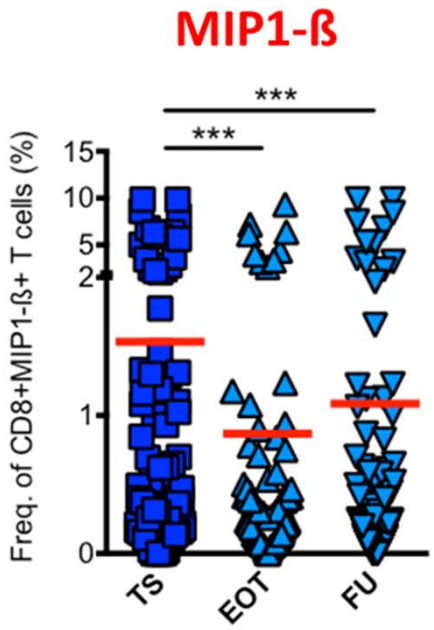
HCC-specific T cells are detectable in patients with HCV cirrhosis w/o HCC



HCC-specific T cells are weak in pts. who develop HCC after DAA therapy



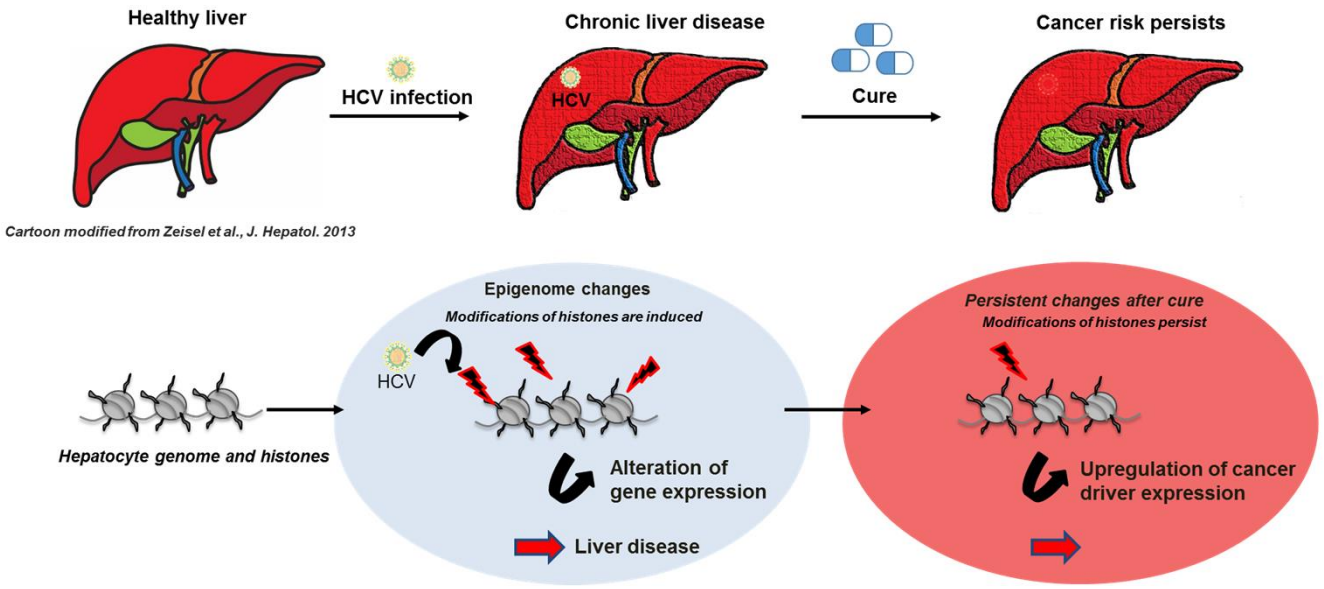
HCC-specific T cells decline during IFN-free therapy



HCC risk and HCV clearance:
HCV-induced epigenetic changes persist despite HCV clearance

<u>Jühling, Hamdane et al., PS-033:</u>

- Genome-wide ChIP-Seq mapping of HCV-induced epigenetic changes
- Cell culture and patient samples



Hepatitis C

HCC risk and IFN-free antiviral therapy

de novo HCC incidence

IFN-free SVR does not alter the short-term HCC risk in HCV cirrhosis

- Calvaruso et al., PS-038:
- Waziry et al., PS-160
- Innes et al., PS-035

- Mettke et al., THU-081
- Ji et al., PS-037
- Korenega et al., PS-036

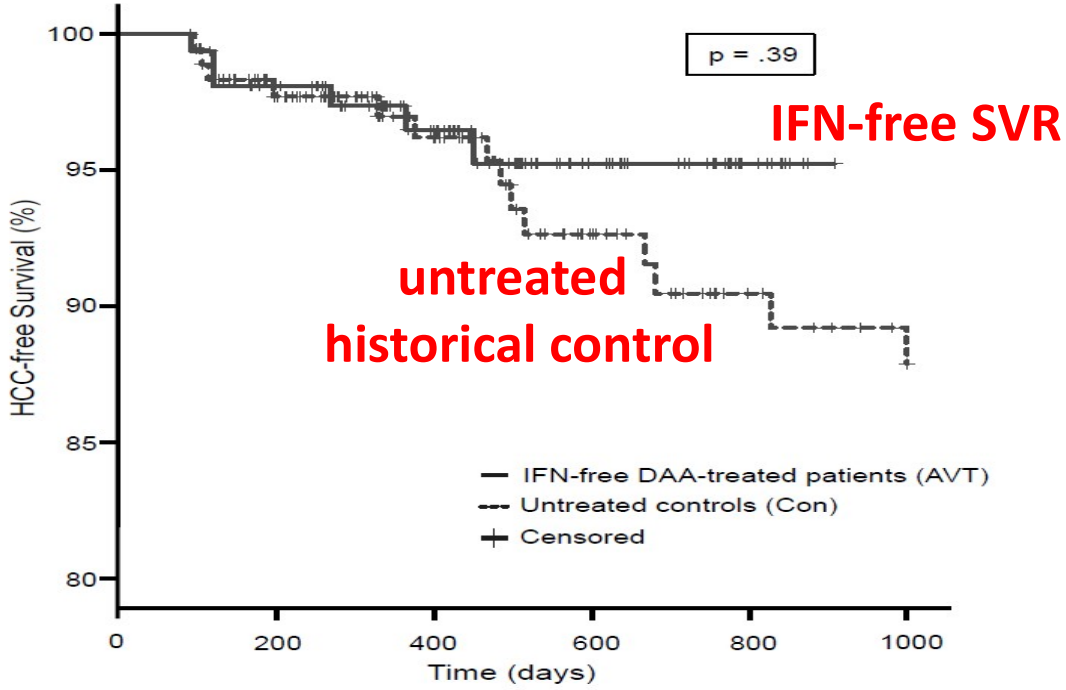
IFN-free SVR does not alter the short-term HCC risk in HCV cirrhosis

Mettke, Schlevogt et al., THU-081:

- 158 cirrhotic HCV patients Hannover Medical School who started DAA therapy after 1/2014

IFN-free SVR vs. untreated historical control

- Factors associated with HCC:
  - higher MELD scores
  - higher AFP levels
- HCC incidence:
  2.9 / 100 person years vs.
  4.5 / 100 person years (control)



Patients at risk							
	(AVT)	158	150	106	37	12	-
	(Con)	184	155	124	91	73	67

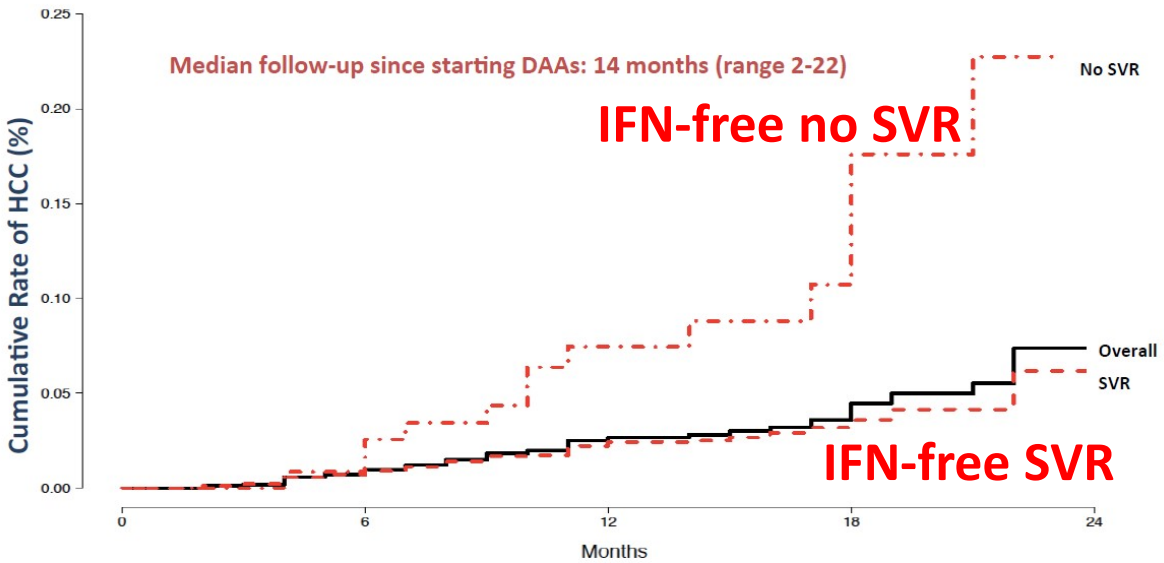
SVR reduces the HCC risk in pts. with HCV cirrhosis receiving DAA therapy

Calvaruso et al., PS-038:

- 2466 patients in the RESIST HCV-cohort who started DAA between 3/2015 and 7/2016

SVR vs. no-SVR

- Factors associated with HCC:
  - Low albumin
  - Low platelet counts
  - No SVR
- Risk of HCC in SVR patients remains proportional to the stage of liver disease



Overall HCC occurrence		
Time	Events, N. (%)	Cumulative Rate (Kaplan – Meier estimates x 100)
6 months	24 (1.0)	1.0%
12 months	59 (2.4)	2.7%
18 months	73 (2.9)	4.4%
24 months	78 (3.1)	7.4%

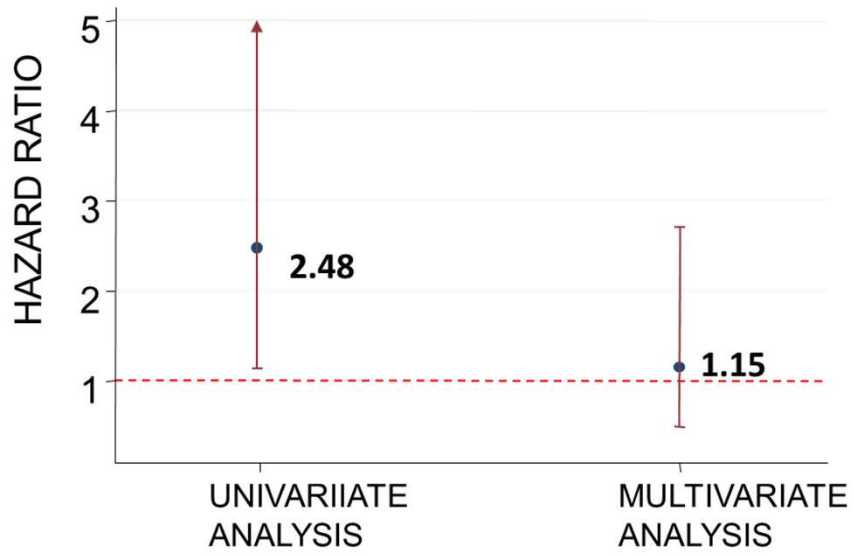
No evidence for higher risk of HCC recurrence

Innes et al., PS-035:

- Scottish HCV clinical database: 857 patients with cirrhosis treated with DAA vs. SVR after IFN-containing therapies

- Patients treated with DAA were
  - older
  - lower platelet counts
  - more often Child B/C
- HCC Association (univariate):
  - DAA therapy
  - Age
  - Child-Pugh & platelets
  - treatment experienced

Association between IFN-free versus IFN-containing therapy and HCC occurrence



Hepatitis C

HCC risk and IFN-free antiviral therapy

HCC recurrence

More aggressive pattern of HCC recurrence after IFN-free therapy

Reig et al., PS-031:

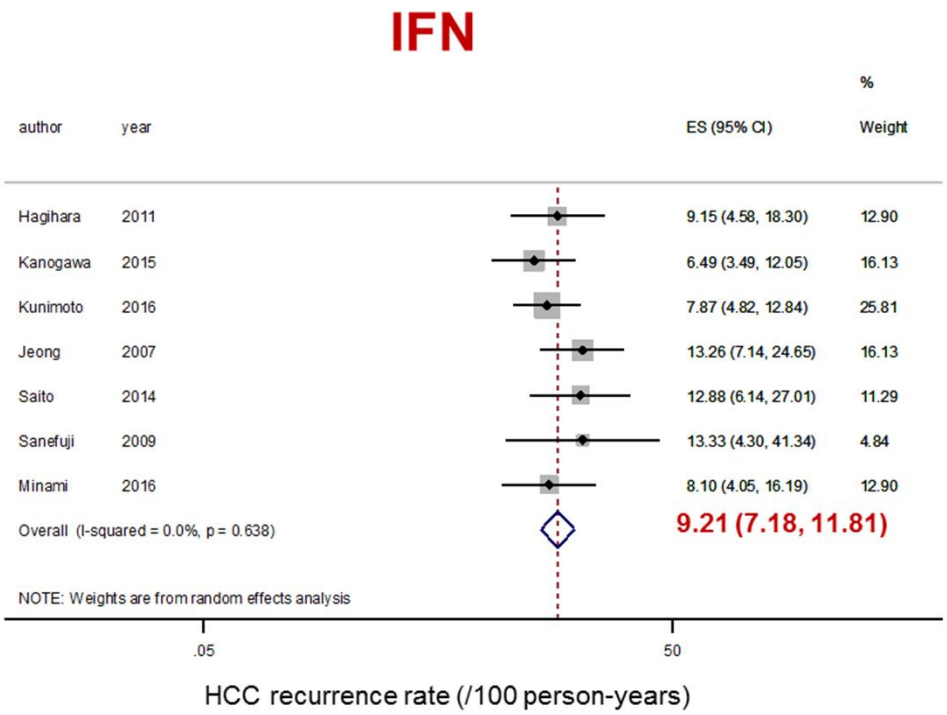
- Follow-up of the J Hepatol 2016 paper
- 77 HCC/HCV patients with complete response to HCC therapy
- HCV therapy initiated in all patients

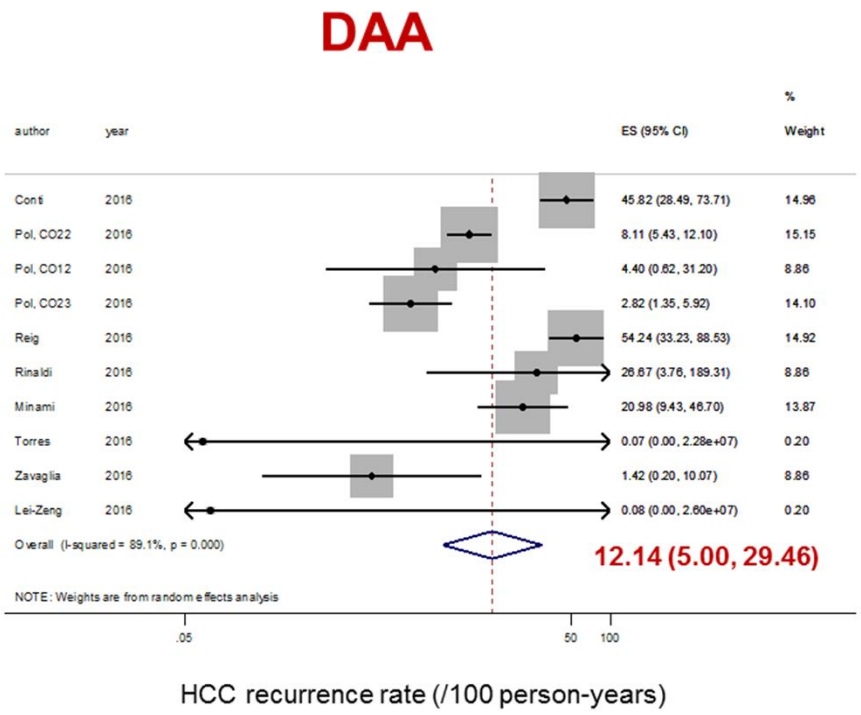
- 31.2% HCC recurrence
- More agrressive pattern and faster tumor growth

No evidence for higher risk of HCC recurrence

<u>Waziry et al., PS-160:</u>

- Systematic review, metanalysis & meta-regression





No evidence for higher risk of HCC recurrence

Waziry et al., PS-160:

- Systematic review, metanalysis & meta-regression

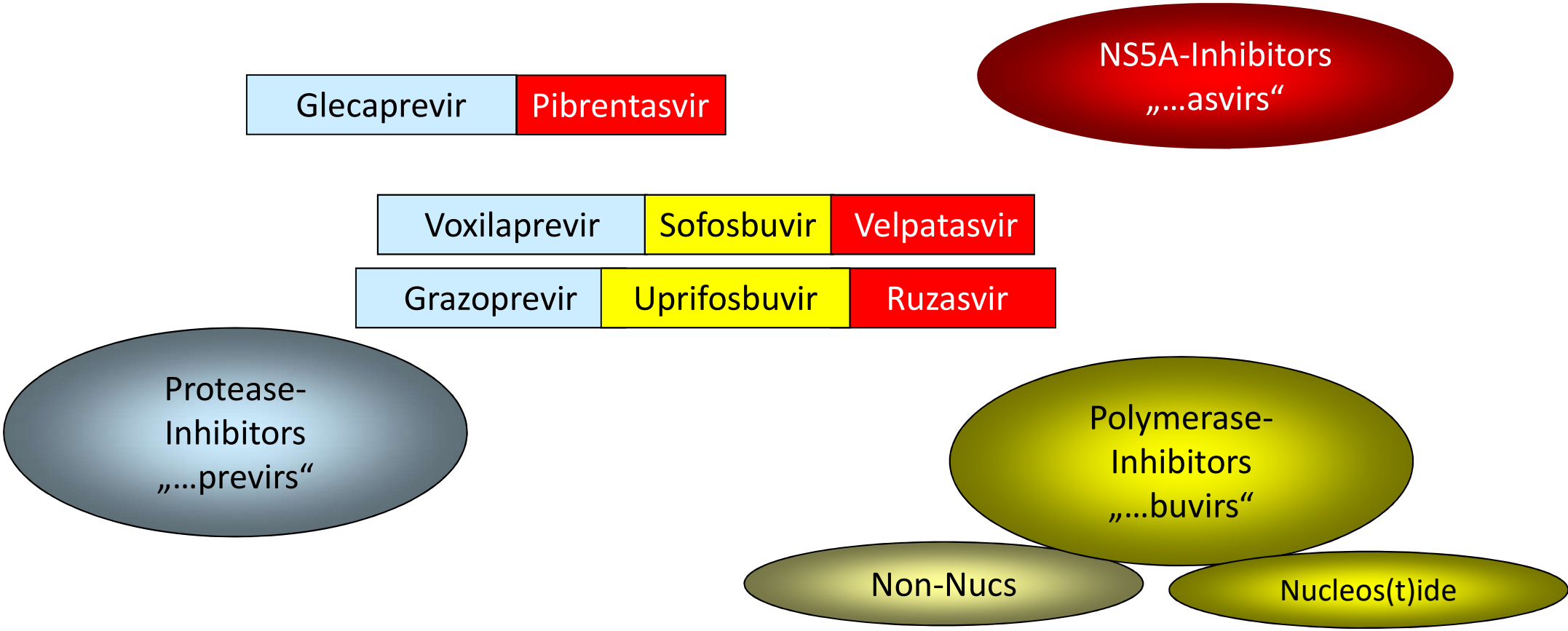
HCC recurrence

	Unadjusted RR	Adjusted RR	95% CI	P value
Average follow-up	0.86	0.79	0.55, 1.15	0.19
Average age	1.11	1.11	0.96, 1.27	0.14
Treatment	1.36	0.62	0.11, 3.45	0.56

Hepatitis C

Treatment of DAA failures

Treatment of DAA failure patients



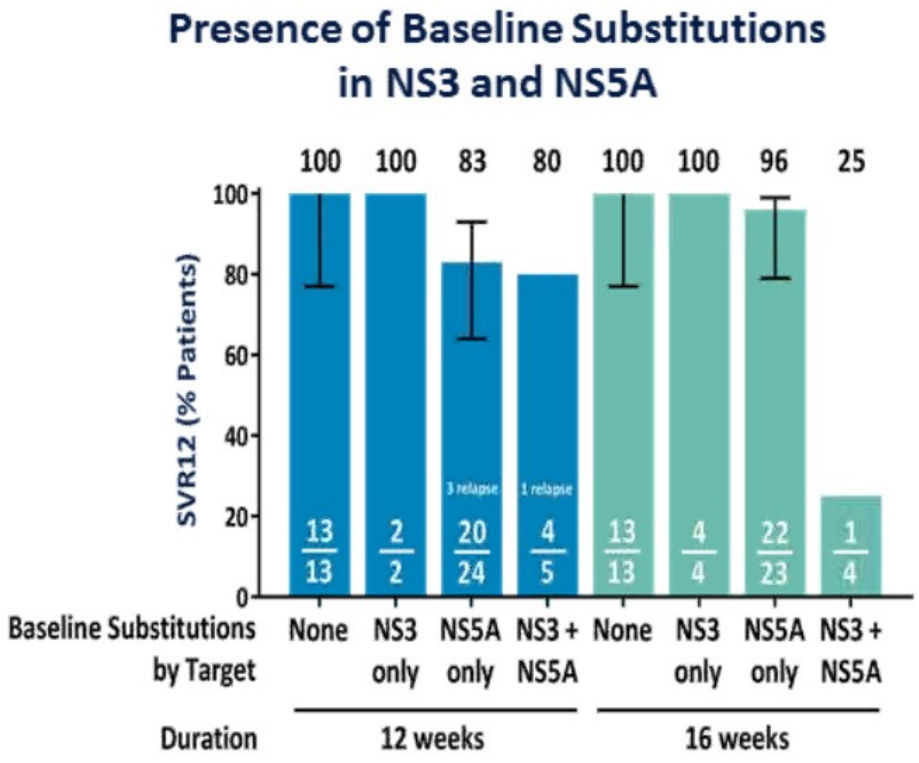
Treatment of DAA failure patients

Glecaprevir	Pibrentasvir

Poordad et al., PS-156:

- Magellan-1, Part 2: 91 patients; 30% PI failure; 37% NS5A failure; 33% PI+NS5A failure
- 30% cirrhotic

- 12 weeks: **SVR 89% (39/44)**
  16 weeks: **SVR 91% (43/47)**



Treatment of DAA failure patients

Voxilaprevir	Sofosbuvir	Velpatasvir

Sarrazin et al., THU-248:

- Integrated analysis of Polaris-1 and Polaris-4 study
- No impact of baseline RASs on virological responses in DAA-experienced patients

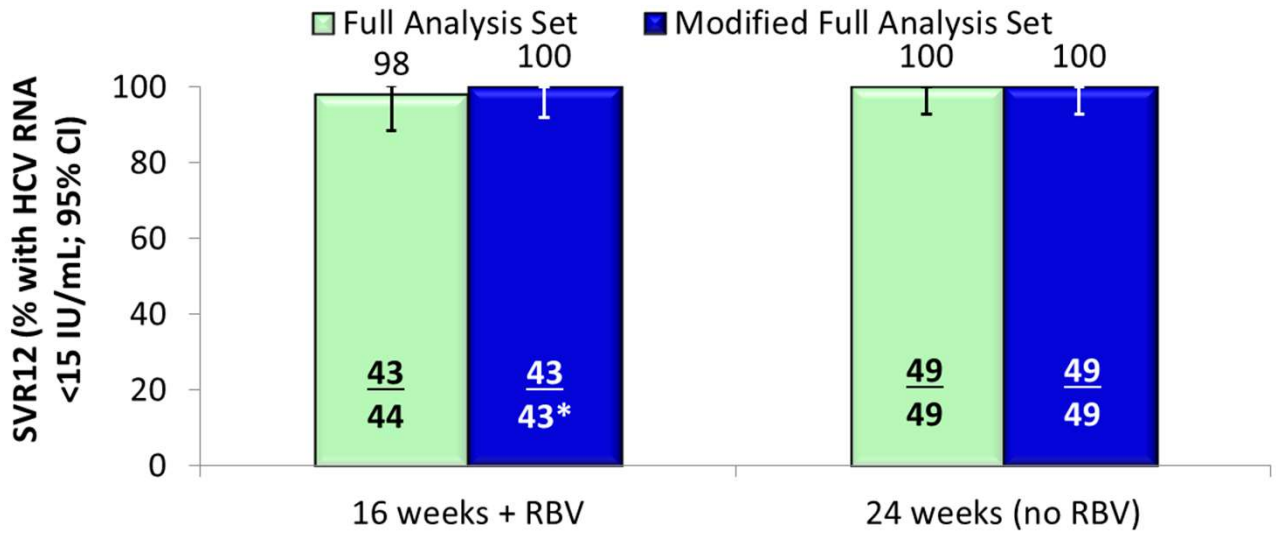
	SOF/VEL/VOX 12 Weeks	
	POLARIS-1 (N = 260)	POLARIS-4 (N = 178)
No VOX and/or VEL RASs	90/93 (97%)	134/135 (99%)
Any VOX and/or VEL RASs	151/155 (97%)	33/33 (100%)
NS3 VOX RASs	3/3 (100%)	3/3 (100%)
R155any	3/3 (100%)	1/1 (100%)
A156G	1/1 (100%)	-
D/Q168any	13/13 (100%)	6/6 (100%)
NS5A VEL RASs	143/147 (97%)	30/30 (100%)
Y93any	63/66 (95%)	4/4 (100%)
A/L/Q/R30any	86/89 (97%)	15/15 (100%)

Treatment of DAA failure patients

Grazoprevir	Uprifosbuvir	Ruzasvir

Wedemeyer et al., PS-159:

- C-SURGE: 94 patients; 76% LDV/SOF failure; 24% EBR/GZR failure
- 43% cirrhotic
- 84% NS5A RASs; 65% NS3 RASs; 55% Dual RASs



Hepatitis C

Is HCV elimination possible?
Effects of elimination programs?

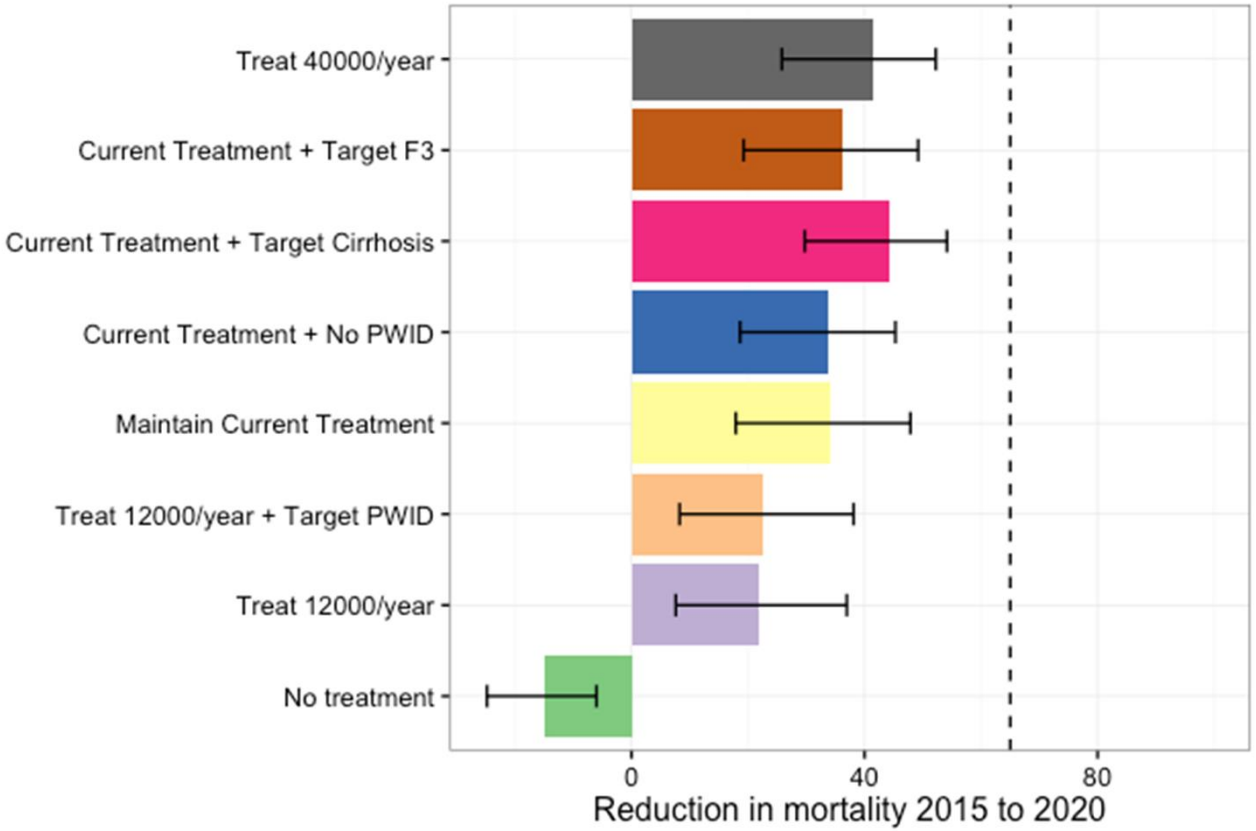
Projected impact of HCV elimination program in Georgia

Walker et al., PS-125:
- Projected impact (model)

Georgia: HCV elimination program launched 2015

- Target: 90% reduction in prevalence by 2020
- >27.000 pts. treated by the end of 2016

Impact on mortality

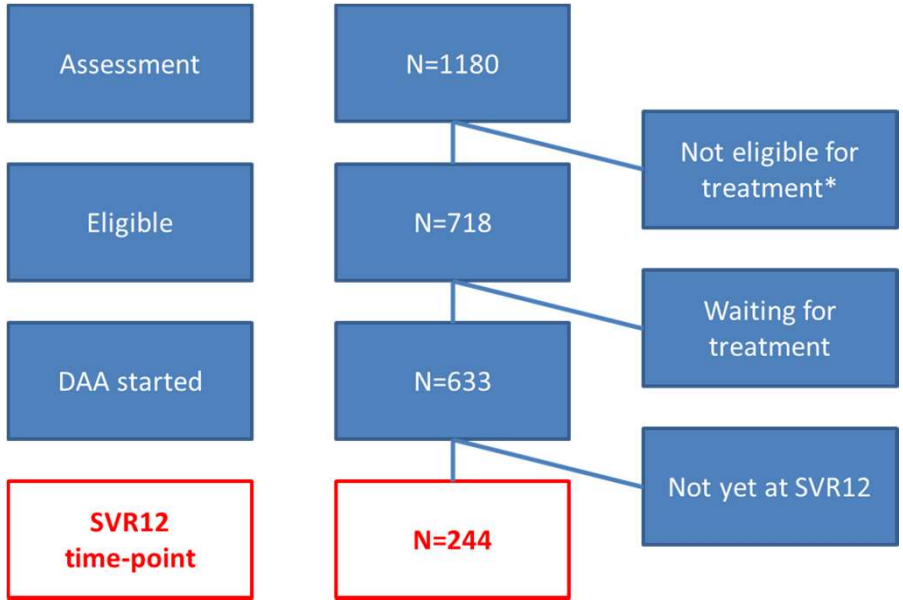


Prison hepatitis programs should be part of elimination programs

McDonald et al., PS-126:

➢ Treatment of HCV infection in the Prison Setting in Victoria, Australia

- Nurse-led
  - 2 full-time nurse specialists
  - protocol-driven assessment & management
  - portable FibroScan
  - delivers care locally to each prison
    - minimizes prisoner movement
  - state-wide service – central medical record (J-Care)
- Supervising hepatologists
  - 2 part-time hepatologists
  - F2F and via tele-medicine



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Prof. Tom Hemming Karlsen

Prof. Frank Tacke