2018

NCSCG 15TH ANNUAL POST-DDW SYMPOSIUM

Rehoboth McKinley Christian Health Care Services

Northern California Society for Clinical Gastroenterology

Jointly provided by the New Mexico Medical Society (NMMS) through the joint providership of Rehoboth McKinley Christian Health Care Services (RMCHCS) and the Northern California Society for Clinical Gastroenterology.

2018 NCSCG 15TH ANNUAL POST-DDW SYMPOSIUM

High-Impact Presentations and Posters of Liver Disease at DDW and EASL

Paul Y Kwo

Cochrane

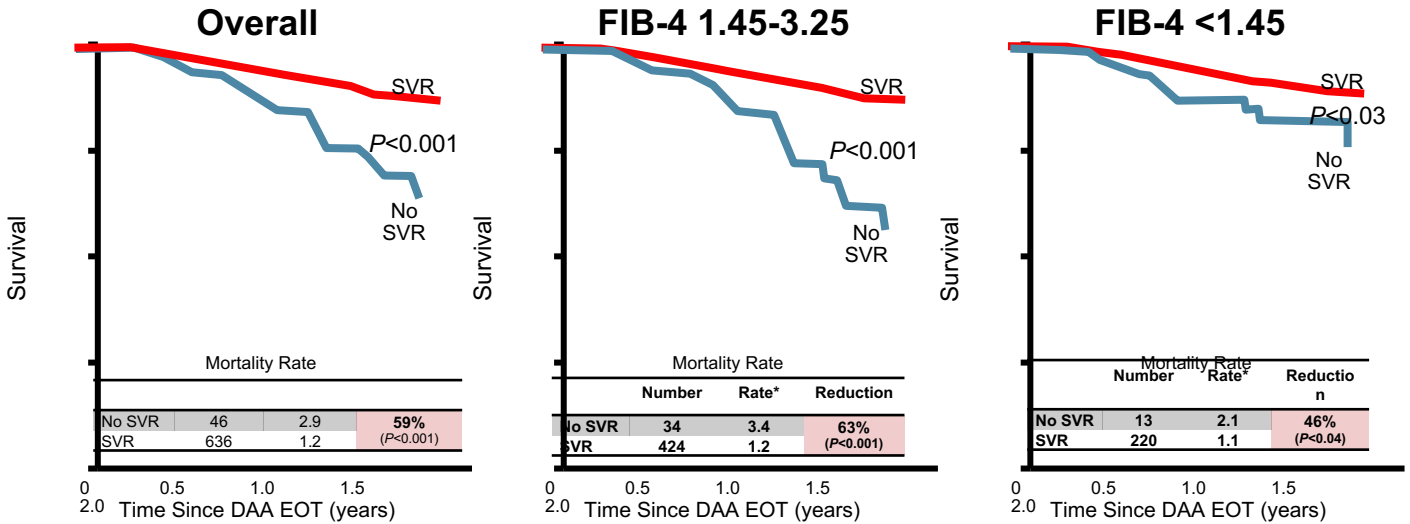
Authors' conclusions

Overall, DAAs on the market or under development do not seem to have any effects on risk of serious adverse events. Simeprevir may have beneficial effects on risk of serious adverse event. In all remaining analyses we could neither confirm nor reject that DAAs had any clinical effects. DAAs seemed to reduce the risk of no sustained virological response. The clinical relevance of the effects of DAAs on no sustained virological response is questionable, as it is a non-validated surrogate outcome. All trials and outcome results were at high risk of bias so our results presumably overestimate benefit and underestimate harm. The quality of the evidence was very low.

Direct-acting antivirals for chronic hepatitis C (Review)

Jakobsen JC, Nielsen EE, Feinberg J, Katakam KK, Fobian K, Hauser G, Poropat G, Djurisic S, Weiss KH, Bjelakovic M, Bjelakovic G, Klingenberg SL, Liu JP, Nikolova D, Koretz RL, Gluud C

Survivial Benefit: VA HCV Clinical Case Registry (Non-ACLD Group):Impact of SVR With DAA Treatment on Mortality



*per 100 patient-years.
Overall: SVR (n=39,373), no SVR (n=1290); FIB-4 1.45-3.35: SVR (n=25,121), no SVR (n=810); FIB-4 <1.45: SVR (n=14,233), no SVR (n=480).

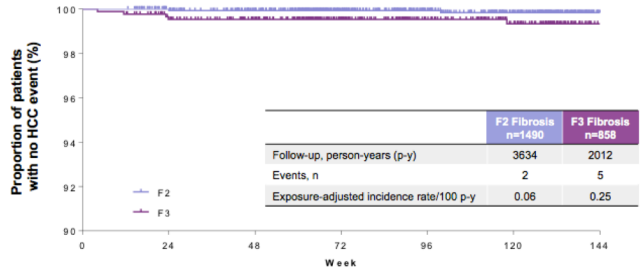
Backus LI, et al. *Hepatology*. 2018;Jan 29. [Epub ahead of print].

Long-Term Follow-up of Patients with Chronic HCV and F2–F3 Fibrosis After Achieving SVR with DAA-Based Therapy: Results from the Gilead SVR Registry

Demographics and Characteristics

		F2 Fibrosis n=1490	F3 Fibrosis n=858
Demographics and Baseline Characteristics	Mean age, y (range)*	55 (19–80)	57 (19–82)
	Male, n (%)*	856 (57)	615 (72)
	White, n (%)	1231 (83)	710 (83)
	Mean BMI, kg/m² (range)	28 (17–53)	27 (17–49)
	HCV GT, n (%)		
	1	916 (62)	549 (64)
	2	189 (13)	81 (9)
	3	265 (18)	176 (21)
	4	70 (5)	34 (4)
	5	27 (2)	8 (1)
	6	22 (2)	9 (1)
	Missing or Mixed	3 (<1)	1 (<1)
	Mean Fibrotest scores (SD)	0.46 (0.08)	0.66 (0.04)
	Cirrhosis determined by another test, n (%)	93 (6)	129 (15)
Mean Pretreatment Laboratory Values (SD)	ALT, U/L	67 (54)	87 (65)
	AST, U/L	52 (33)	65 (42)
	Total bilirubin, mg/dL	0.5 (0.3)	0.6 (0.3)
	Albumin, gm/dL	4.2 (0.3)	4.1 (0.4)
	Platelets, x10³/µL	224 (64)	209 (66)
	INR	1 (0.17)	1 (0.11)

Kaplan-Meier Plot of Patients Without HCC Since Achieving SVR12



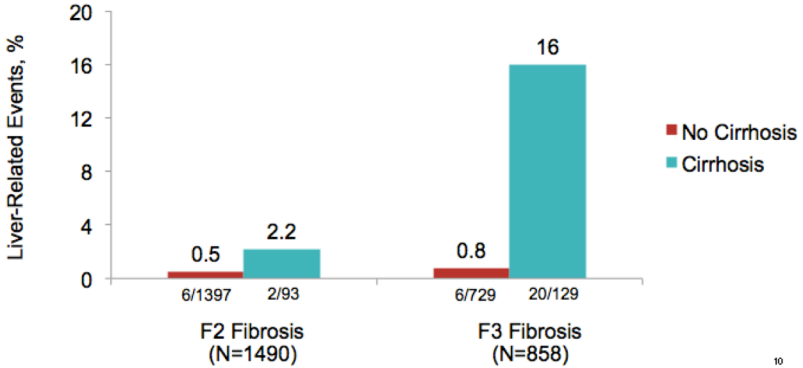
	F2 Fibrosis n=1490	F3 Fibrosis n=858
Follow-up, person-years (p-y)	3634	2012
Events, n	2	5
Exposure-adjusted incidence rate/100 p-y	0.06	0.25

At risk (cumulative events)

F2	1490 (0)	1453 (1)	1380 (1)	1176 (1)	1070 (1)	965 (2)	776 (2)
F3	858 (0)	832 (4)	782 (4)	648 (4)	572 (4)	508 (5)	417 (5)

Liver events were uncommon among patients with F2–F3 fibrosis by FibroTest

- Patients determined to have cirrhosis by another assessment method were more likely to experience a liver event, including HCC, than those without cirrhosis



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Proportions of Patients With F2–F3 Fibrosis Maintaining SVR

F2 Patients	SVR24	SVR 48	SVR 96	SVR 144
Cumulative virologic failure, n	0	0	4	4
HCV relapse	0	0	0	0
HCV re-infection	0	0	4	4
Censored patients, n*	0	60	363	605
Patients remaining at risk, n	1489	1429	1122	880
Patients maintaining SVR, %†	100	100	100	100

F3 Patients	SVR24	SVR 48	SVR 96	SVR 144
Cumulative virologic failure, n	0	1	3	3
HCV relapse	0	1	1	1
HCV re-infection	0	0	2	2
Censored patients, n*	0	41	238	393
Patients remaining at risk, n	858	816	617	462
Patients maintaining SVR, %†	100	99.9	99.9	99.9

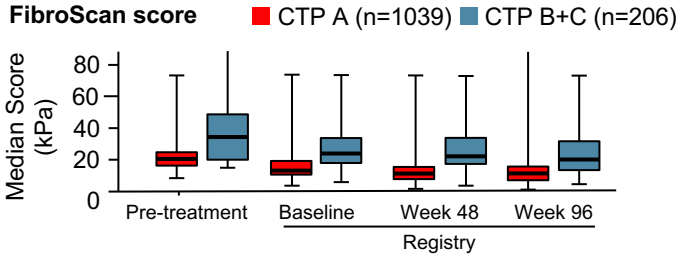
*Includes early discontinuations, lost to follow-up, reinfection, and still on study; †Kaplan-Meier estimate. SVR 24/48/96/144, SVR 24/48/96/144 wk after treatment end.

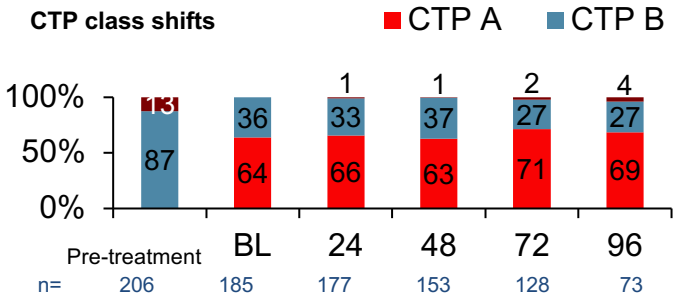
When assessing fibrosis
In HCV patients
Use multiple methods

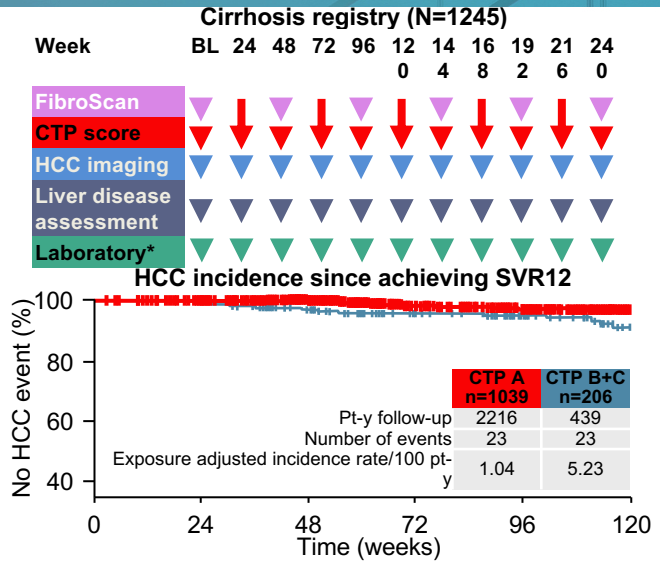
Jacobson et tl Digestive Disease Week
02nd - 05th June, 2018 Washington, D.C

Long-term follow-up of patients with CHC and compensated or decompensated cirrhosis following SOF-based regimens

- Long-term virological and clinical outcomes in patients with cirrhosis who achieve SVR after DAA treatment are being evaluated in the DALTON cirrhosis registry study
- **Objective:** to evaluate clinical progression or liver disease reversal after SVR and SVR durability







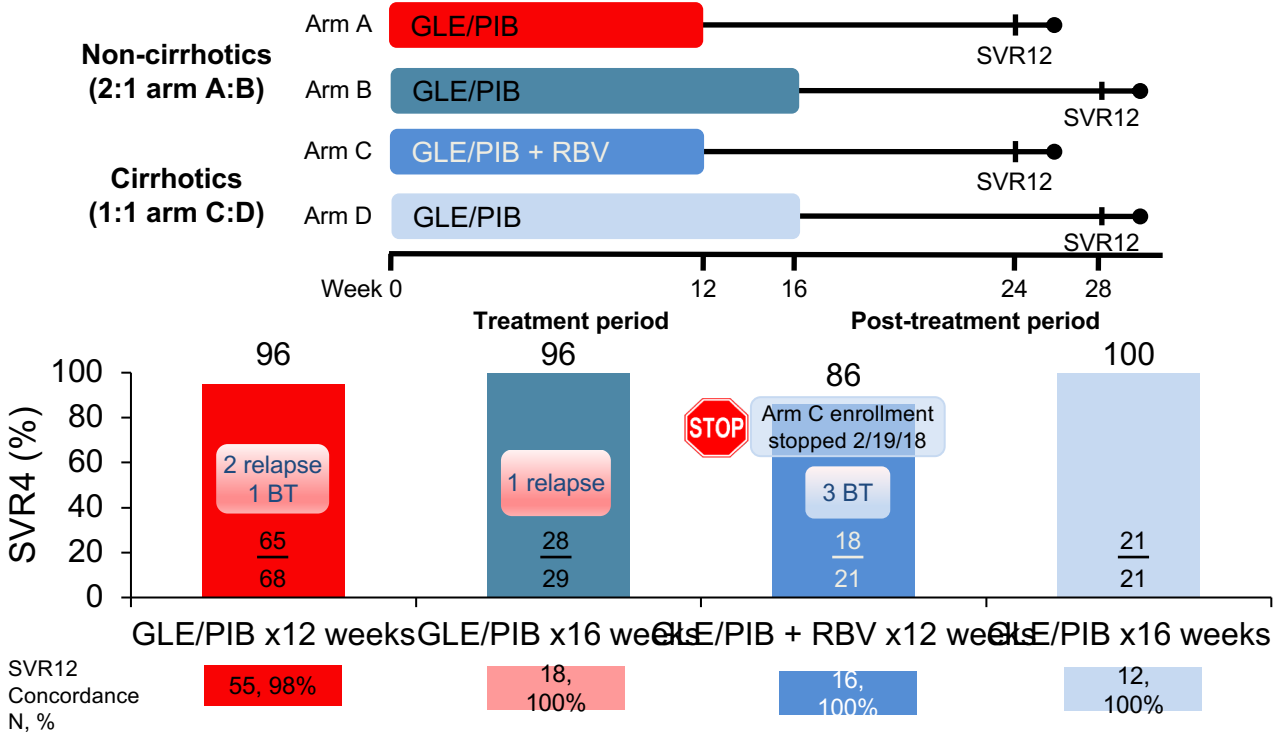
- **Conclusions**
  - SVR maintained in >99.9% of patients
  - Improvements in fibrosis scores maintained
  - Most patients show CTP improvement
  - HCC decreased, in keeping with prior literature

*Includes haematology, chemistry, lipids, HbA1C, coagulation, HCV RNA, markers of fibrosis and biomarkers. Other assessments: quality of life survey, DNA, endoscopy and optional biopsy

Mangia A, et al. ILC 2018, #1773 (GS-018)

Phase 3b study of GLE/PIB ± RBV in GT 1 HCV subjects previously treated with an NS5A inhibitor + SOF therapy

Phase 3b, multi-center, randomized, open-label, pragmatic study



GLE, glecaprevir; PIB, pibrentasvir; RBV, ribavirin; SOF, sofosbuvir; BT, breakthrough

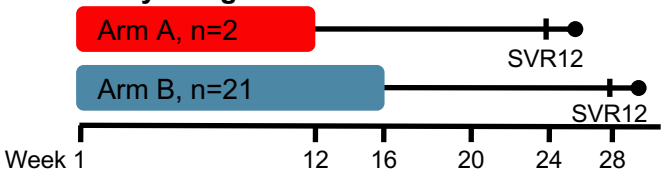
Lok A, et al. JLC 2018. #5667 (LBO-008)

HCV-TARGET Network Study

Retreatment of HCV infection in patients who failed GLE/PIB: MAGELLAN-3 study

Objective: ongoing study to evaluate efficacy and safety of 12 or 16 weeks of GLE/PIB + SOF + RBV in patients who previously failed GLE/PIB treatment

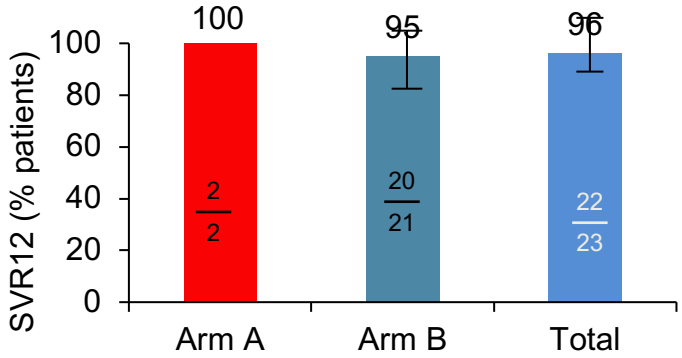
Study design:



Treatment arm	GT	Cirrhosis status	Prior NS5Ai and/or PI*
A	1, 2, 4, 5, 6	NC	No
B	3	Any	Any
B	Any	C	Any
B	Any	Any	Yes

- **Results:**
  - 30% cirrhosis, 26% failed PI and/or NS5Ai before GLE/PIB treatment failure, and 65% had ≥2 NS5A RASs at baseline
  - One GT 1a cirrhotic patient with prior experience of SOF/LDV relapsed
  - 100% (14/14) SVR12 in GT 3 patients
  - No D/Cs and no DAA-related SAEs
- **Conclusion:**
  - Preliminary analysis shows retreatment with GLE/PIB + SOF + RBV yields a high SVR12 rate in HCV-infected patients who have experienced virological failure following GLE/PIB treatment

Efficacy of GLE/PIB + SOF + RBV



*Either treatment or combination received before treatment with GLE/PIB

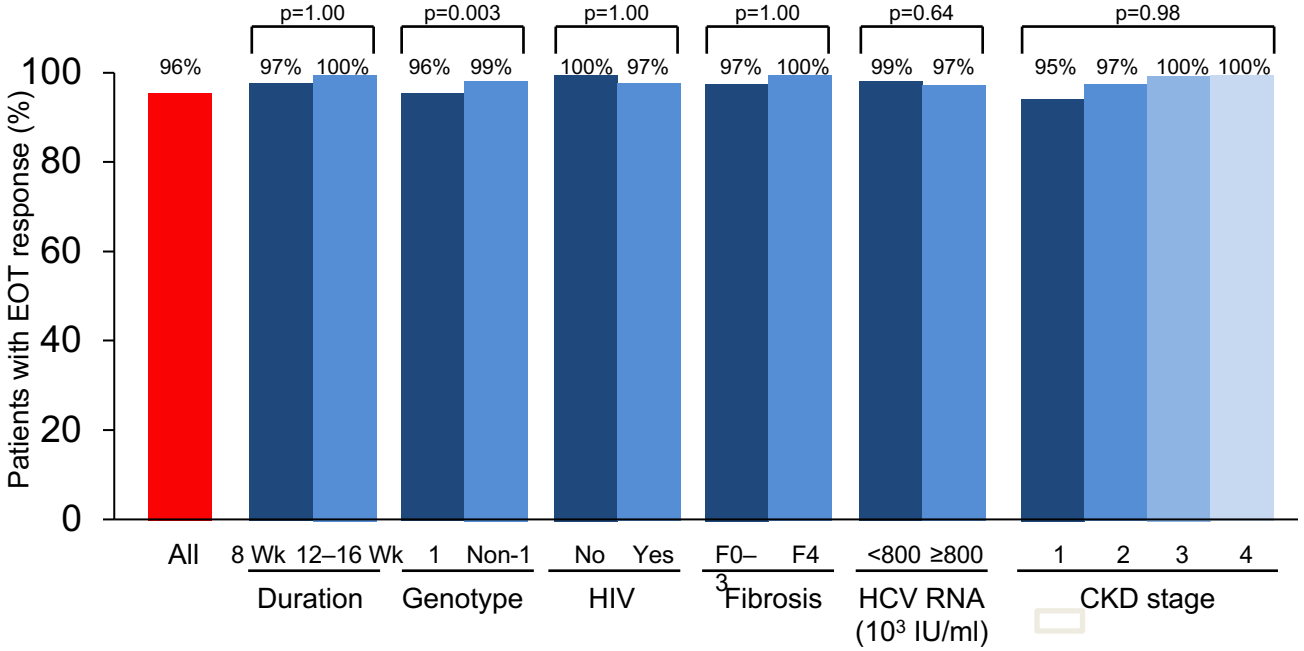
Wyles D, et al, et al. ILC 2018, #2563 (PS-040)

Real World Data for DAAs

- Ledipasvir/sofosbuvir
- Grazoprevir/Elbasvir
- Robust real world SVR data that mirrors clinical trial efficacy
  - Target, Trio, VA

Real-life effectiveness and safety of GLE/PIB in patients with CHC: NAVIGATOR-II study

- 723 Italian patients, 58 (21–89) years, 49% males
- LSM 6.1 (2.5–43) kPa, 7% cirrhotics, 50% HCV GT 1, 6% HCV/HIV+



- **Conclusions:** excellent virologic response and safety profile in a real-world population

D'Ambrosio R, et al. ILC 2018. #5616 (GS-013)

First real-world data on safety and effectiveness of GLE/PIB for CHC infection: German Hepatitis C Registry (DHC-R)

- **Objective:** to confirm whether the high SVR12 rates seen in GLE/PIB clinical trials are consistent with real-world effectiveness and safety of GLE/PIB
- **Methods:**
  - Patients treated within the DHC-R: ongoing, non-interventional, multicentre, prospective registry
  - Adult patients with chronic HCV genotype 1–6 infection were treated with GLE/PIB for 8, 12, or 16 weeks according to the local label

Baseline Population (N=638)	
HCV GT 1	34%
HCV GT 3	35%
History of drug abuse	37%
Treatment-naïve	90%
Without cirrhosis	93%

- 100% (92/92) SVR12 (per protocol)
- 97% (93/96) SVR12 (total effectiveness population)
- GLE/PIB was safe; discontinuations due to AEs were rare (1%)

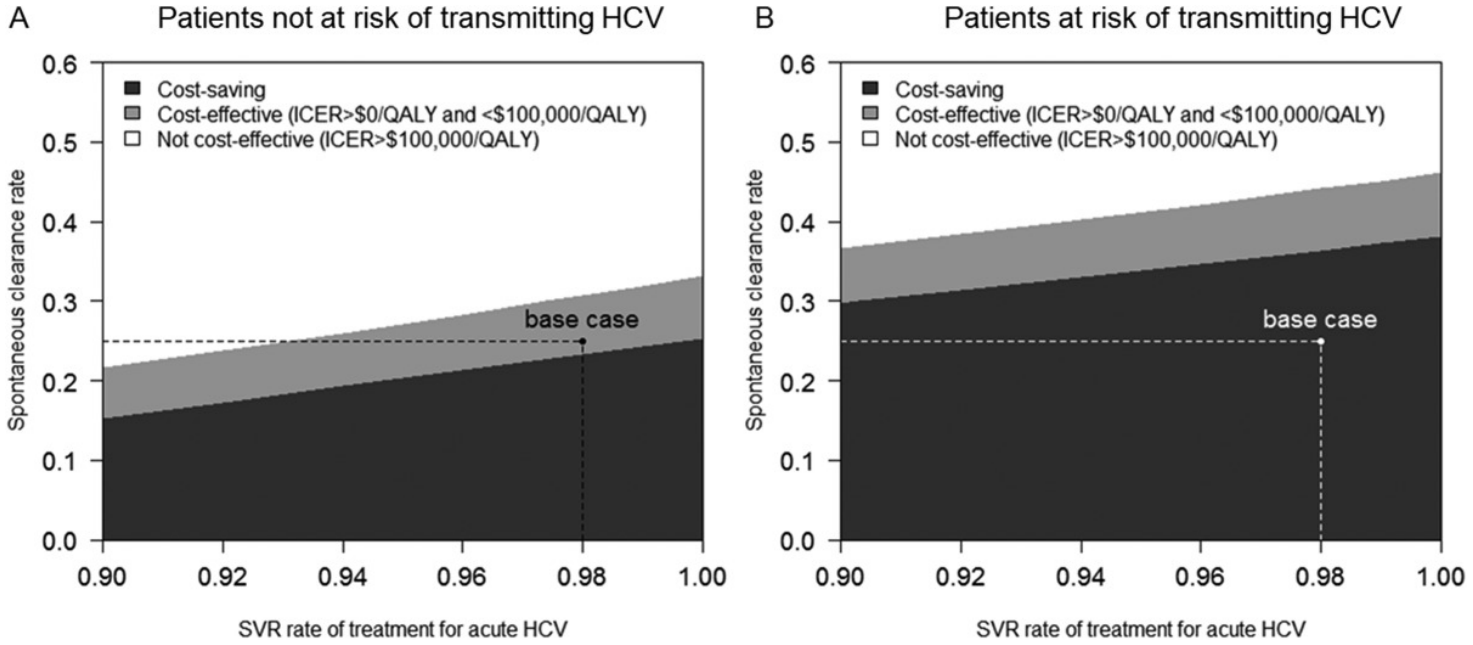
- **Conclusions:**
  - First real-world results of GLE/PIB confirm the high SVR12 rates and favorable safety profile observed in clinical trials

*66 patients excluded from the analysis (e.g. for off-label treatment). 162 enrolled patients have yet to begin treatment

Berg T, et al. ILC 2018, #5395 (GS-007)

Cost-effectiveness: Treatment of acute HCV

- In patients at risk of transmitting HCV, treating acute HCV became cost-saving, increasing QALYs by 0.03 and decreasing costs by $3,655.

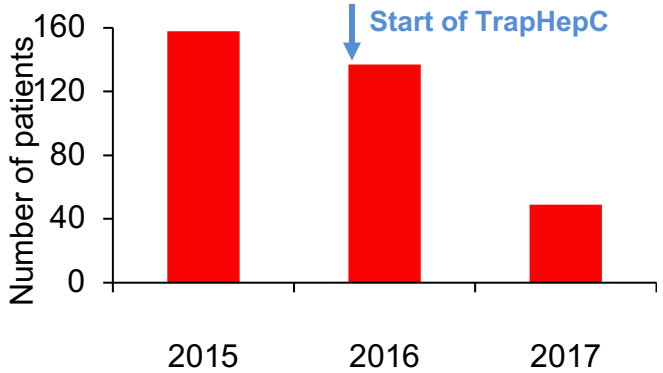


Bethea ED et al. Hepatology 2018;67:837–846

Marked reduction in the prevalence of HCV among PWID during 2nd year of the Treatment as Prevention (TraP HepC) programme in Iceland

- Nationwide treatment programme initiated Jan 2016, aiming for elimination of CHC infection as a public health threat. Estimated 800–1000 HCV-infected individuals in Iceland
- Vogur Addiction Hospital, a key sentinel site where most PWID in Iceland seek treatment; provides an opportunity to monitor trends in HCV prevalence among PWID

HCV PCR positive PWID at Vogur Hospital 2015–17



- After 2 years of TrapHep C, 80–85% of all patients evaluated or initiated on DAA treatment
- HCV prevalence among PWID:
  - 2015: 42.6% – among those admitted for addiction treatment prior to TraP HepC
  - 2017: 11.6% – representing a 73% reduction ($p<0.001$)

- Conclusion:
  - A major scale-up in HCV treatment all patient groups has been successfully initiated in Iceland
  - This has already translated into a significant reduction in prevalence among PWID
  - Key population, should be the focus of treatment scale-up to curtail spread of HCV

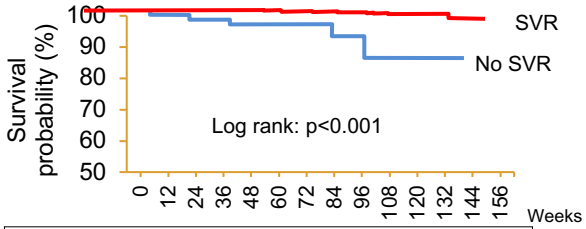
Runarsdottir V, et al. ILC 2018, #1705 (PS-095)

Disease outcomes after DAA-induced SVR: Data from the RESIST-HCV Cohort

- Cohort: 4468 patients treated with DAAs (March 2015–Dec 2016), followed for a median of 73 weeks

63 patients died during the follow-up	Chronic hepatitis 991 (22.2%)	Child–Pugh A cirrhosis 3095 (69.2%)	Child–Pugh B cirrhosis 383 (8.8%)
Overall death, n (%)	7 (0.7)	32 (1.0)	24 (6.3)
Liver-related death, n (%)	0	17 (0.5)	14 (3.7)
Cardiovascular death, n (%)	5 (0.5)	6 (0.2)	8 (2.1)
Other causes, n (%)	2 (0.2)	9 (0.3)	2 (0.5)

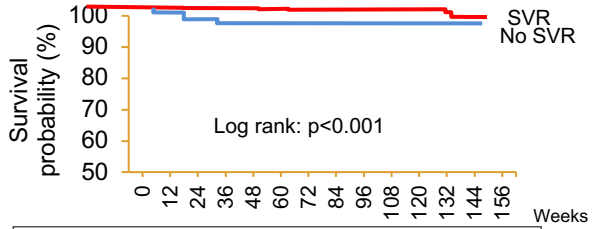
Liver mortality in 3095 patients with Child–Pugh A (mITT)



No. at risk														
No SVR	156	156	156	96	73	61	45	33	21	13	8	4	0	0
SVR	2939	2939	2939	2587	2324	2039	1623	1147	849	538	308	104	19	0

	HR (95% CI)*	p-value
Albumin <3.5 g/dl	6.01 (2.30, 15.73)	<0.001
No SVR	18.50 (6.75, 50.70)	<0.001

CV mortality in 4468 patients (mITT)



No. at risk														
No SVR	234	234	234	143	109	92	68	55	40	25	18	7	1	0
SVR	4234	4234	4234	3659	3282	2860	2179	1524	1113	698	385	137	24	0

	HR (95% CI)*	p-value
Diabetes	4.38 (1.42, 13.36)	0.01
No SVR	10.56 (3.43, 32.46)	<0.001

- **Conclusions:**
  - Patients with Child–Pugh A cirrhosis and SVR to DAAs have a better outcome than non-SVR patients
  - Patients with Child–Pugh B cirrhosis retain significant risk of liver events and death even after HCV eradication
  - Deaths linked to CV diseases seem to be reduced after viral eradication regardless of fibrosis stage

*Multivariate Cox regression

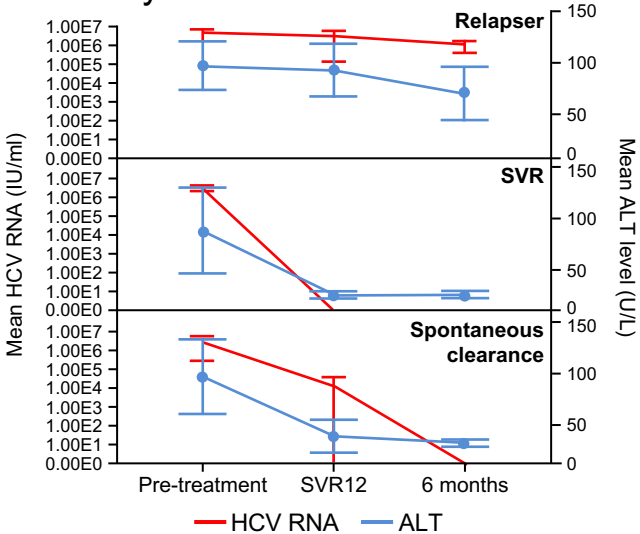
Calvaruso V, et al. ILC 2018, #4253 (PS-149)

Spontaneous clearance of HCV RNA after documented relapse following DAA therapy: A case-control study

Case control study to compare clinical and virologic characteristics of patients with spontaneous clearance after relapse (n=12) with those with SVR (n=24) or relapse without clearance (n=24)

93 cases of documented relapse after DAA; 12 (13%) spontaneously cleared HCV within 6 months

		Relapse (n=24)	SVR (n=24)	Spontaneous clearance (n=12)	p
Male, n (%)		17 (70.8%)	17 (70.8%)	6 (50.0%)	0.39
Treatment experienced, n (%)		12 (50.0%)	7 (30%)	5 (41.7%)	0.34
Cirrhosis, n (%)		17 (70.8%)	15 (62.5%)	6 (50.0%)	0.47
GT, n (%)	1	13 (54.2%)	18 (75.0%)	10 (83.3%)	0.20
	Non-1	11 (45.8%)	6 (25%)	2 (16.7%)	
Age, median (range)		59 (38-77)	59 (27-90)	59 (53-65)	0.97
FibroScan (mean ± SD)		15±4.5	14.1±2.5	13.3±3.5	0.96
ALT (mean ± SD)	Week 0	98±61	85±108	91±62	0.85
	SVR12	93±64*	17±8	28±28*	0.00
HCV RNA log IU/ml (mean ± SD)	Week 0	6.7+6.9	6.5+6.4	6.4+6.5	0.26
	SVR12	6.5+6.8**	Undetected*	4.1+4.6***	0.03



- Spontaneous clearance may occu mented relapse after DAA therapy
- Low HCV RNA levels and normal or near-normal ALT may be predictors of spontaneous clearance
- HCV RNA must be rechecked prior to retreatment after a documented relapse

GT, genotype; SVR, sustained virologic response

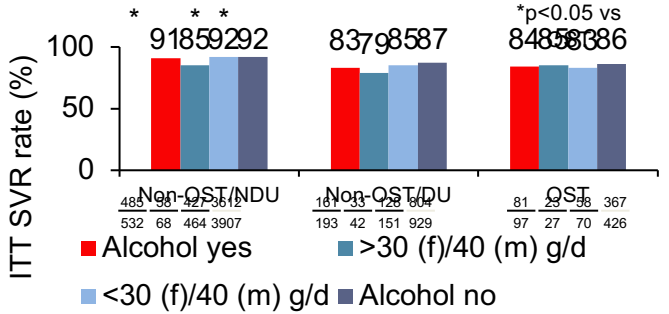
Kuriry H, et al. ILC 2018, #1936 (PS-038)

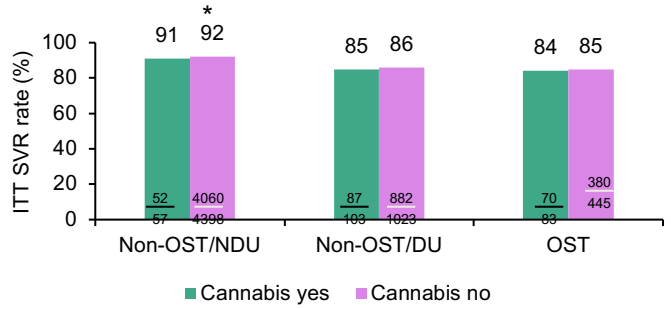
Scaling up HCV DAA treatment in patients on OST: Does alcohol or cannabis consumption diminish cure rates?

- **Aim: to investigate the effect of alcohol and cannabis on SVR and LTFU**
  - German Hepatitis C-Registry (DHC-R)
    - 7747 CHC patients starting DAA treatment
    - ITT: completed therapy and had ≥1 follow-up documentation (528 OST; 5,582 non-OST)

	n	Alcohol consumers	Cannabis consumers
OST	739	17.9%	19.2%
Non-OST/DU	1500	17.5%	9.6%
non-OST/NDU	5508	11.6%	1.2%

  - High SVR in OST and non-OST patients
  - LTFU and SVR 12/24† rates were significantly higher in OST vs. non-OST/NDU
  - Cannabis use did not significantly influence SVR12/24 or LTFU
  - LTFU was more likely in patients with current/former drug use or high alcohol use
  - LTFU occurred mainly after EOT, leaving a high chance for HCV elimination





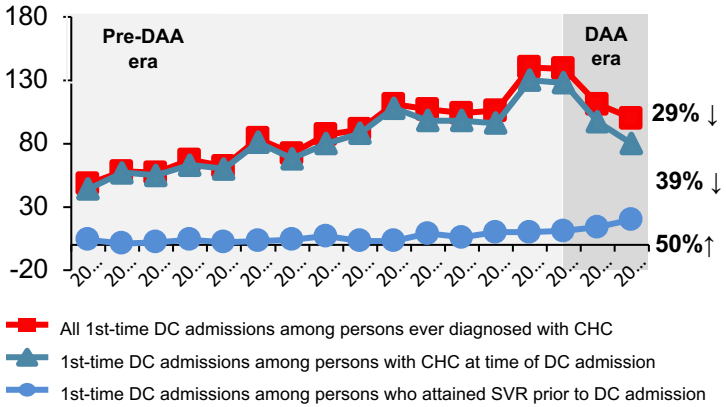
†Except for high alcohol intake group

Christensen S, et al. ILC 2018, #337 (PS-036)

Reduction in hepatitis C-related decompensated cirrhosis associated with national scale-up of DAA therapies targeting advanced liver fibrosis

- **Background:** Scotland has national surveillance of HCV treatment/disease. DAAs (first licensed May 2014) were prioritized to patients with advanced liver fibrosis (F2+); target was set to reduce HCV-related decompensated cirrhosis (DC) by 75% by 2020
- **Aim:** to examine the early impact of DAAs on HCV-related DC at the population level
- **Methods:**
  - Data on persons starting HCV therapy up to March 2017 obtained from the Scottish HCV Clinical database
  - Record linkage of Scotland's HCV Diagnosis database to national hospital inpatient database: linked patients with CHC diagnosis admitted to hospital for the first time with DC (2000–2016)
- **Results:**
  - Since the introduction of DAAs: 4800 patients have started HCV therapy (54% GT 1, 38% GT 3; 24% F2/3; 27% compensated, 5% decompensated; 83% on DAAs; 94% SVR)*
  - Number starting therapy (April-14–March-17 vs. prior 3 years) was 1.6-fold higher for all patients and 2.8-fold higher for compensated cirrhosis
- **Conclusions:**
  - First country-level evidence of immediate impact that DAAs can have in averting HCV-related DC
  - Need to address comorbidities that pose a risk of liver disease progression among patients attaining SVR

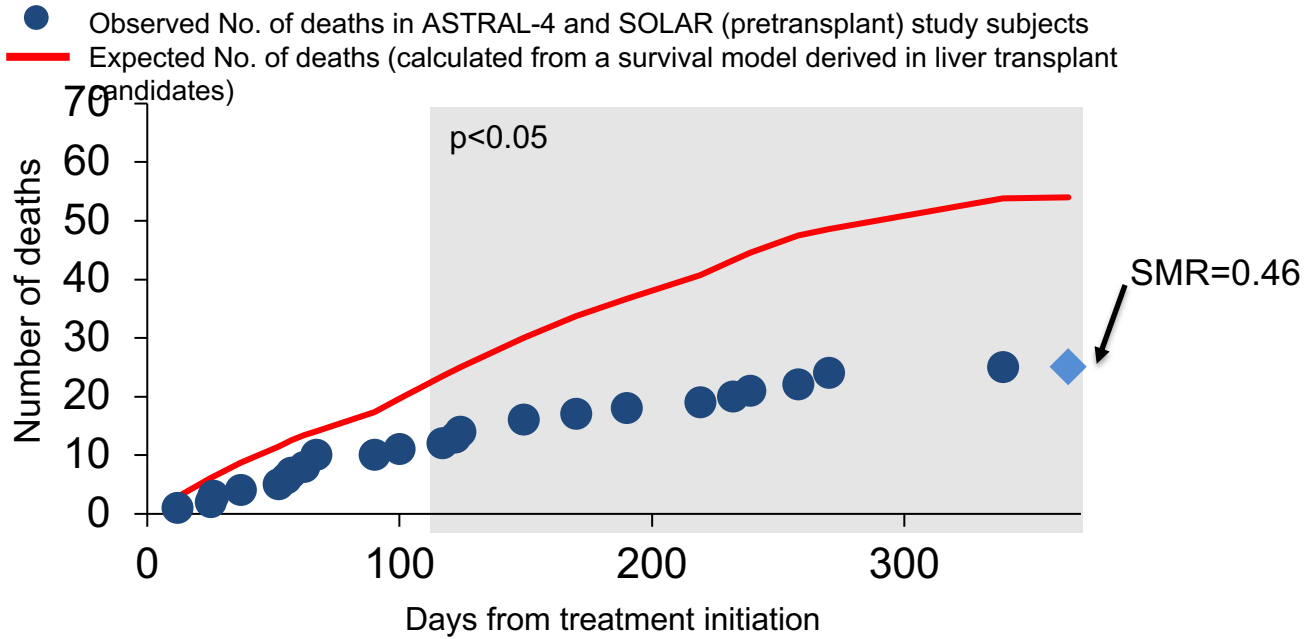
Annual number of new presentations for HCV-related DC



*Based on 3,240 with available data to date

Hutchinson S, et al. ILC 2018, #4515 (GS-017)

Decreased mortality after DAA therapy in decompensated HCV cirrhosis



- Observed and expected survival diverged significantly beginning on Day 117 (p=0.02)
- LDV/SOF or SOF/VEL therapy led to a 54% reduction in mortality by Day 365 (p<0.01)

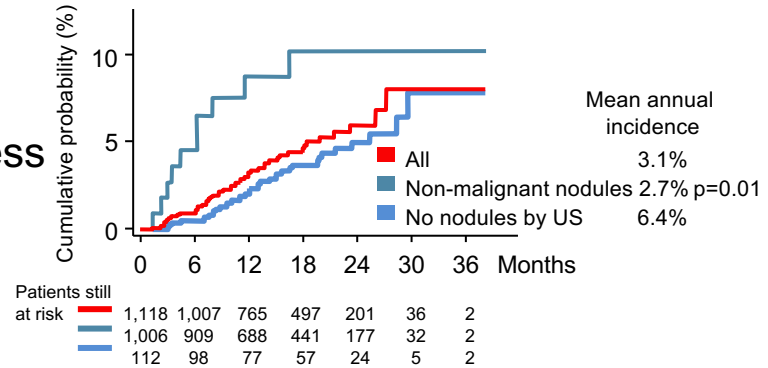
Kim, et al. ILC 2018, #1835 (PS-151)

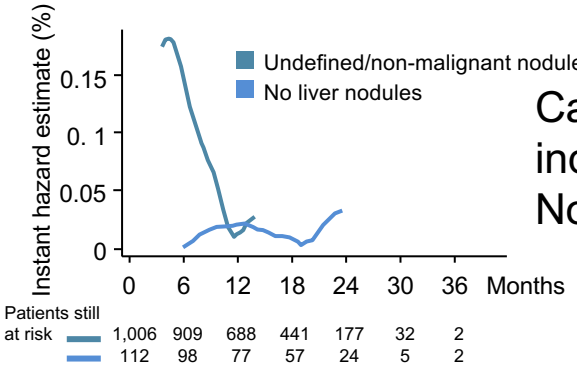
IFN-free DAA treatment of cirrhotic HCV patients with or without history of HCC: multicentre prospective trial in Italy

- **Aim:** to evaluate whether the incidence of *de novo* or recurrent HCC increases after starting DAA treatment and which variables are associated with HCC development in SVR cirrhotic patients
- **Methods:** consecutive cirrhotic patients undergoing IFN-free DAA treatment*
  - Group 1 (n=1160), no history of HCC: Child–Pugh A 1066 (92%), non-malignant nodules 113 (10%), SVR 1,118 (96%)
  - Group 2 (n= 125), history of HCC and complete response to HCC treatment: Child–Pugh A 112 (90%), SVR 119 (95.2%)

De novo HCC incidence and instant hazard ratio according to presence of non-malignant nodules

Carefully assess indeterminate Nodules!





Carefully assess indeterminate Nodules!

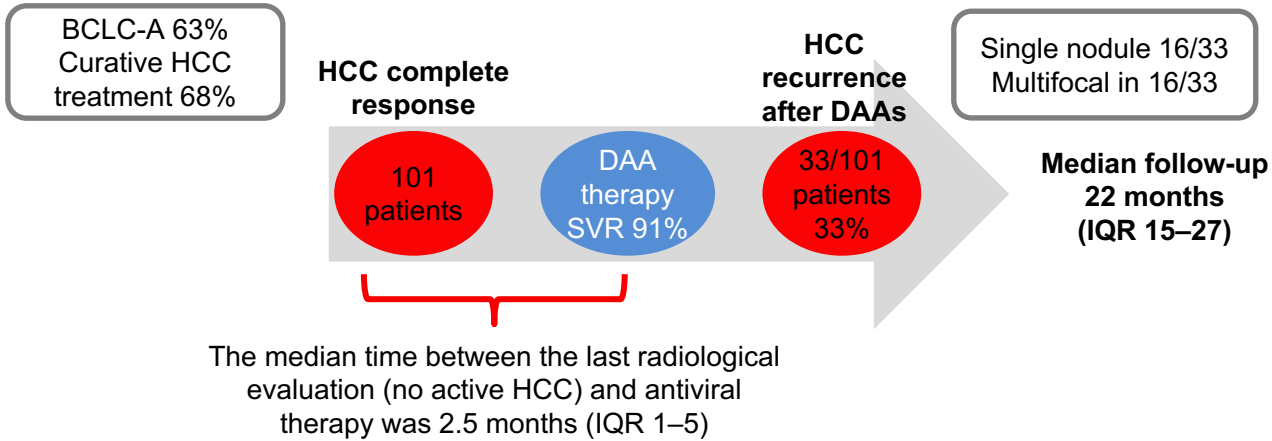
- **Conclusions**
  - Increased instant HR of HCC observed at 47 weeks in Group 1 and 35 weeks in Group 2
  - *De novo* HCC was independently associated with undefined/non-malignant liver nodules (HR 2.4 95% CI 1.2, 4.9; p=0.02), ascites (HR 1.9, 95% CI 1.1, 3.5, p=0.03) and Log_{10} AFP (HR 3.7, 95%CI 1.6, 9.0, p=0.003)

*13 Italian referral centres for liver disease, January 2015 to June 2017

Sangiovanni A, et al. ILC 2018, #3126 (PS-152)

HCC recurrence under all-oral DAA-based antiviral therapy in HCV-infected patients: Navigatore web platform

- **Methods:**
  - Navigatore web platform is a regional data network (Veneto region, Italy), registering all consecutive patients with chronic HCV infection receiving DAA treatment (>5000 participants)
  - HCV-infected patients (n=132) with prior HCC who underwent IFN-free DAA-based therapy (January 2015 to April 2017) and included in the Navigatore Web platform were included



Gambato M, et al. ILC 2018, #4010 (PS-153)

Risk of total non-hepatic cancer following treatment for HCV infection with DAAs

- IFN-based treatment may have anti-tumour effects but has low tolerability and SVR
- DAAs are well tolerated and with SVR >90%
- **Objective:** examine risk of non-hepatic cancer associated with DAAs vs. pre-DAA era IFN
- **Methods:**
  - US administrative claims data for HCV patients enrolled Jan 2006–March 2017
    - DAA cohort: Dec 2013 through March 2017
    - Pre-DAA IFN cohort: receiving IFN prior to May 2011 (follow-up through Nov 2013)
  - Patients with prior cancer at baseline were excluded (by total and specific cancers)

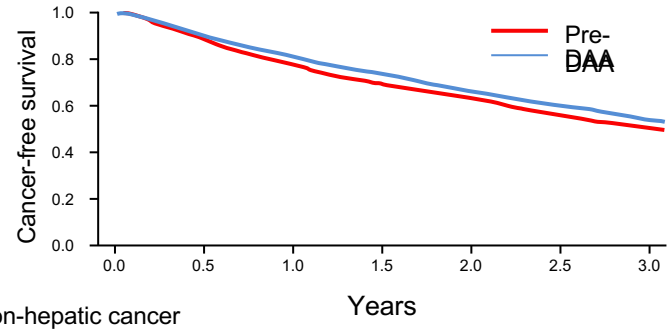
Risk of total non-hepatic cancer

Exposure	N	Years of follow-up	N events	Adjusted HR (95% CI)*
DAA	22,894	25,944	1576	0.86 (0.80, 0.93)
Pre-DAA IFN	10,989	30,522	1684	1.00 (ref)

Risk of specific non-hepatic cancers

Cancer	Exposure	N	Pt-y follow-up	N events	Adjusted HR (95% CI)*
NHL	DAA	31,112	38,197	73	0.88 (0.60, 1.29)
	Pre-DAA IFN	13,108	40,402	64	1.00 (ref)
Pancreas	DAA	31,454	38,703	17	0.62 (0.31, 1.23)
	Pre-DAA IFN	13,222	40,853	22	1.00 (ref)
Bile duct	DAA	31,417	38,601	43	0.81 (0.50, 1.31)
	Pre-DAA IFN	13,218	40,819	34	1.00 (ref)

Adjusted total non-hepatic cancer-free survival



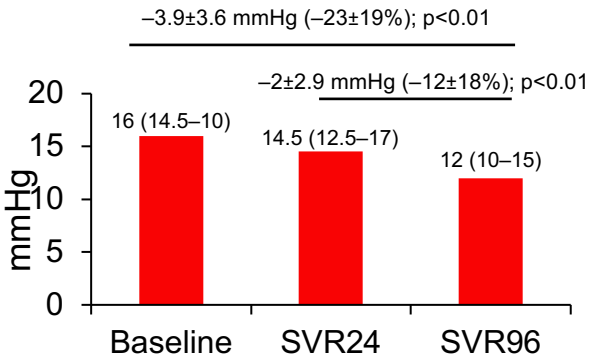
- **Conclusions:**
  - Relative to pre-DAA IFN, DAAs are associated with reduced risk of total non-hepatic cancer (similar results for specific cancers: NHL, pancreas, bile duct (but based on smaller numbers)
  - Indicates long-term impact of successful HCV treatment on non-hepatic cancer at population level

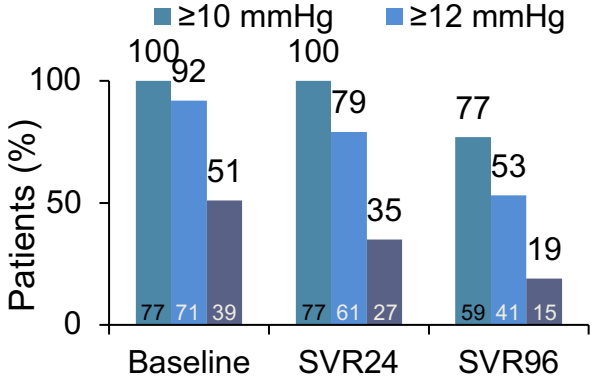
*Cox regression, after adjustment for covariates and treatment propensity

Chokkalingam A, et al. ILC 2018, #3702 (PS-155)

Long-term impact of HCV eradication after all-oral therapy in patients with clinically significant portal hypertension (CSPH)

- Multicentre prospective study of patients with HCV-related cirrhosis and CSPH (HVPG ≥10 mmHg) achieving SVR after all-oral antiviral therapy[1]
- Patients with CSPH 24 weeks after therapy underwent a new haemodynamic assessment 96 weeks after EOT (SVR24 and SVR96, respectively)



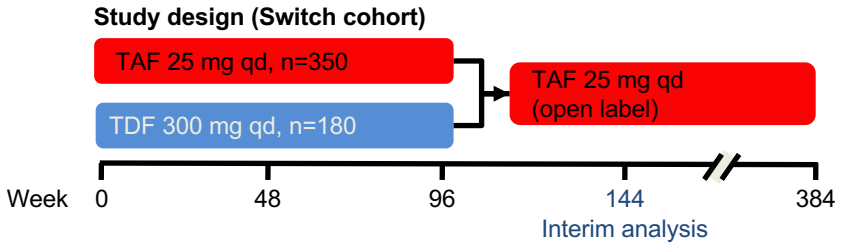


- SVR after IFN-free regimens is associated with time-dependent reduction in portal pressure in patients with baseline CSPH. However, a significant proportion of patients still present with CSPH in the long term and remain at risk of clinical decompensation and OV development or progression
- Baseline HVPG (OR 1.55 [95% CI 1.18, 2.1]; p<0.01) or previous liver decompensation in absence of HVPG assessment (OR 10 [95% CI 1.4, 80]; p=0.02) were independently associated with lower rate of HVPG decrease <10 mmHg 2 years after therapy

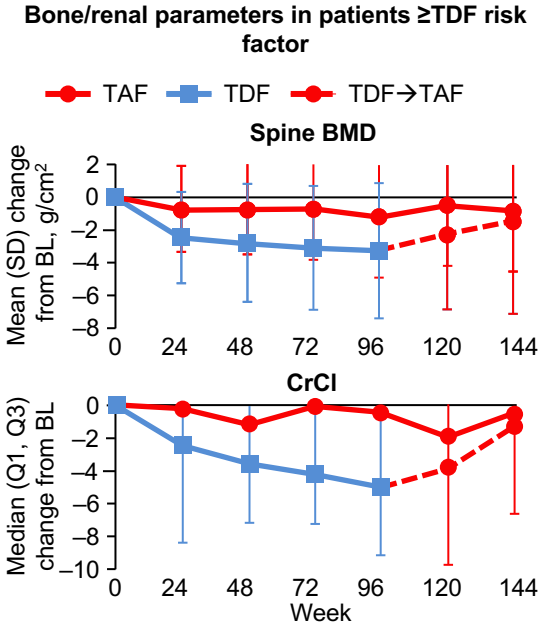
1. Lens S, et al. Gastroenterology 2017;153:1273–83;
Lens S, et al. ILC 2018, #2505 (PS-150)

Safety and efficacy at 1 year after switching from TDF To TAF in CHB patients with risk factors for TDF use

- **Background:** TAF monotherapy is a preferred regimen in the 2017 EASL HBV guidelines, especially in patients with risk factors for TDF-associated renal and bone effects
- **Objective/methods:** to assess 1 year renal and bone safety, antiviral efficacy (HBV DNA <29 IU/ml) and ALT normalization in a subset of patients with CHB and baseline risk factors for TDF* switching to open-label TAF at Week 96



- **Results:**
  - 1298 patients randomized and treated, 540 switched to OL TAF at Week 96; 284 (53%) had ≥1 TDF risk factor
  - Baseline demographics and HBV DNA suppression 1 year following switch were similar for both groups
  - Switch patients had increased rate of ALT normalization and improved bone and renal safety parameters
- **Conclusion:** CHB patients with TDF risk factors who switched to TAF had improved bone and renal safety and increased rates of ALT normalization whilst maintaining efficacy at 1 year

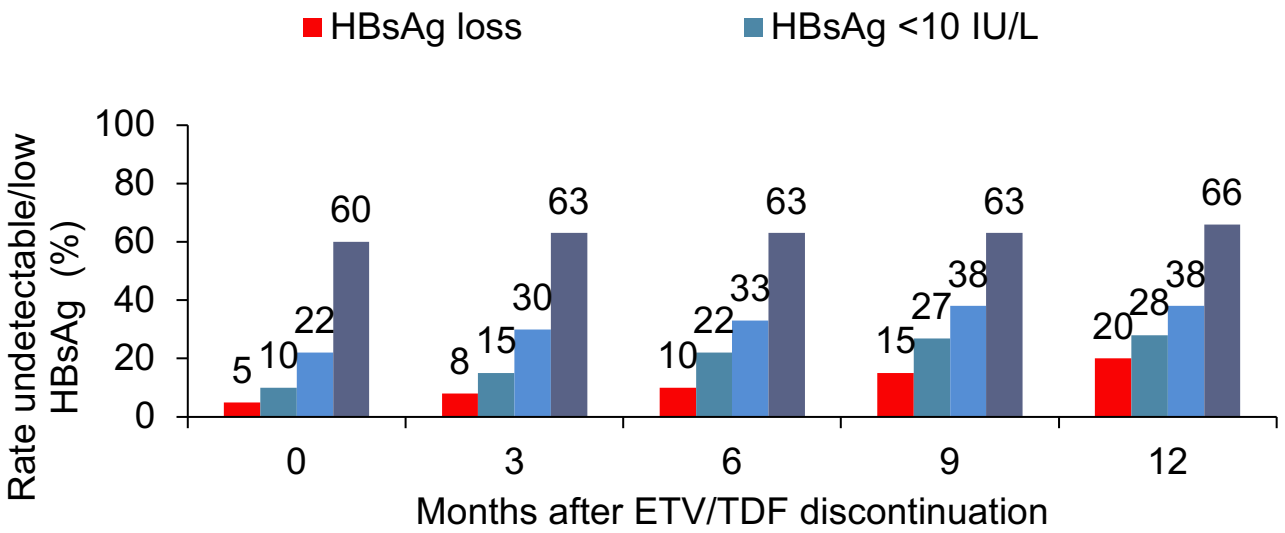


*TDF risk factors: age >60 years, osteoporosis of hip/spine, ≥stage 2 CKD, albuminuria (UACR >30 mg/g), hypophosphataemia (PO_4 <2.5 mg/dl), or comorbidities associated with CKD (e.g. HTN, DM, obesity)

Gane E, et al. ILC 2018, #1722 (PS-156)

Discontinuation of effective ETV/TDF therapy in patients with HBeAg-negative chronic hepatitis B

Cumulative rates of undetectable or low levels of HBsAg



- Independent predictors of HBsAg loss
  - HBsAg at Month 1 (per 100 IU/ L): adjusted HR 0.772 (95% CI 0.637, 0.936), p=0.008
  - IP-10 at Month 1 (per 10 pg/ml): adjusted HR 1.182 (95% CI 1.082, 1.291), p<0.001

Papatheodoridi M, et al. ILC 2018, #3405 (PS-159)

Safety, PK and antiviral activity of CAM JNJ-56136379 (JNJ-6379) in treatment-naïve CHB patients without cirrhosis

- Capsid assembly modulator (CAM) JNJ-6379 25 mg, 75 mg or 150 mg administered orally qd for 28 days is well tolerated and displayed dose-proportional PK
- Potent reduction of HBV DNA and RNA; no relevant changes in HBsAg

	HBV DNA				HBV RNA*			
	Baseline		Day 29		Baseline		Day 29	
Treatment arm	N	Mean (SD) log_{10} IU/mL	Mean (SD) change from BL log_{10} IU/ml	<LLOQ n (%)	N	Mean (SD) log_{10} cp/ml	Mean (SD) change from BL log_{10} cp/ml	Not detected n (%)
25 mg qd	8	6.90 (1.91)	–2.16 (0.49)	0	8	5.59 (2.37)	–2.30 (0.59)	3 (38%)
75 mg qd	8	5.26 (1.50)	–2.89 (0.48)	3 (38%)	8	3.39 (2.21)	–1.85 (1.42)	6 (75%)
150 mg qd	9	5.10 (1.56)	-2.70 (0.53)†	3 (38%)†	9	3.37 (1.66)	-1.67 (0.99)‡	4 (80%)‡
Pooled placebo	11	5.10 (1.64)	-0.04 (0.28)	0	11	3.33 (2.58)	0.02 (0.86)	3 (27%)

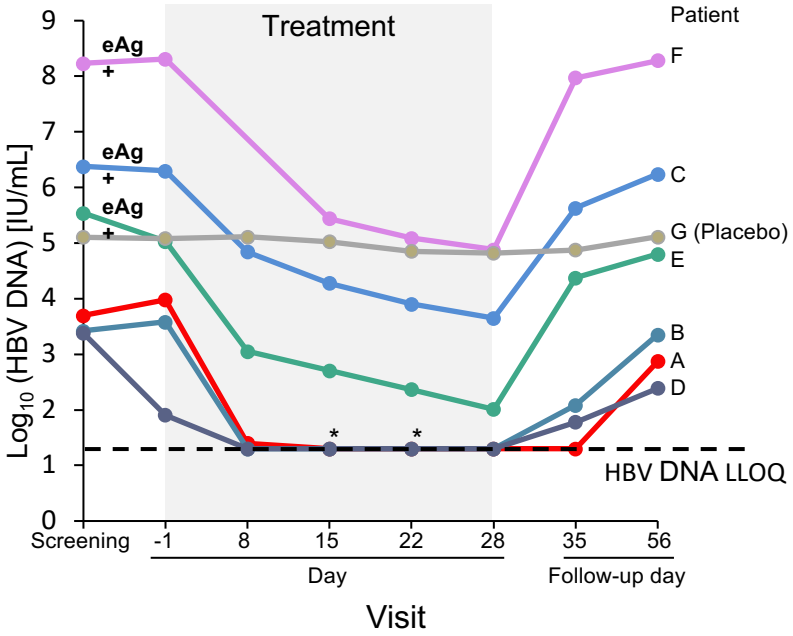
- An oral dose regimen of 250 mg daily for 28 days is being evaluated
- Phase 2a study is ongoing in treatment-naïve and virologically suppressed CHB patients (NCT03361956)

*RNA analysis was carried out in an exploratory setting; †n=8; ‡n=5;
Zoulim F, et al. ILC 2018, #5729 (LBO-004)

RO7049389, a core protein allosteric modulator (CpAM), is effective against HBV and well tolerated in CHB patients

- RO7049389 is and oral small molecule, Class I HBV CpAM
- **Methods:**
  - YP39364 is a Phase I study investigating safety, PK and anti-viral activity of RO7049389
  - SAD and MAD cohorts in healthy volunteers have been completed
  - Dosing in the first patient cohort at 200mg bid for 28 days is complete
- **Results:**
  - To date, RO7049389 is well tolerated with no clinically significant changes or trends evident in safety data
  - Robust HBV DNA declines: median (maximal) –2.7 (–3.4) $\log_{10}$ IU/ml, observed to Day 28 of dosing
    200 mg bid (n=6)
  - Future cohorts will explore higher doses and once daily dosing

Absolute HBV DNA change over time

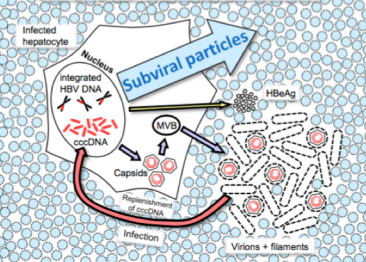


*HBV DNA Values <LLOQ and below the lower limit of detection

Gane E, et al. ILC 2018, #5513 (LBO-003)

Nucleic Acid Polymers REP 2139 For Hepatitis Be Ag negative patients in combination with TDF and IFN

almost all HBsAg is derived from subviral particles which are mostly derived from integrated HBV DNA **not affected by targeting viral replication**



HBsAg clearance is crucial to restoring functional control of HBV infection

Subviral particles are the primary immunosuppressive agent:

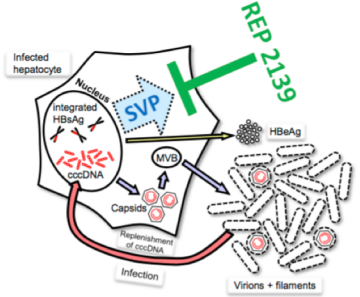
- Mask the anti-HBs response
- Block signalling mechanisms required for innate and adaptive immune function
- Exhaust B- and T-cell responses
- Inhibit the activity of immunotherapy
  - cytokine or TLR-based
  - therapeutic vaccines

Dembeck et al., Curr. Op. Virol. 2018; 30: 58-67.
Aillot et al., Antimicro. Agents Chemother. 2018; 62: e01741-17
Rydell et al., Virol. 2017; 509: 67-70
Bazinet et al., 2017 Lancet Gastro. Hep 2: 877-889
Al-Mahtab et al., 2016 PLOS One 11: e0156667
Yang et al., Int. Immunopharmacol. 2016; 38: 291-297
Jiang et al., J. Viral Hep. 2014; 21: 860-872
Wang et al., J. Immunol. 2013; 190: 5142-5151
Kondo et al., ISRN Gastro. 2013; 2013:935295

REP 2139 blocks subviral particle assembly and release **from cccDNA or integrated HBV DNA**

→ Efficient HBsAg clearance from the blood

Inhibition of SVP release is associated with reduction in intracellular HBsAg



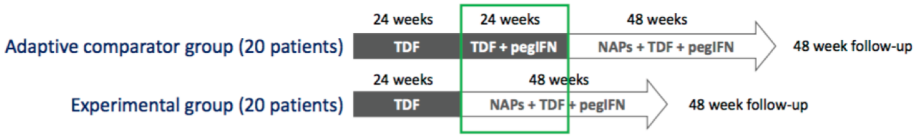
REP 2139 only prevents replenishment of circulating HBsAg

HBsAg clearance is dependent on the clearance of SVP by host immune function.

NCT02565719

Treatment naive chronic HBeAg negative infection, HBsAg > 1000 IU/mL, HBV DNA > 10,000 IU /mL

Advanced fibrosis allowed but cirrhosis excluded



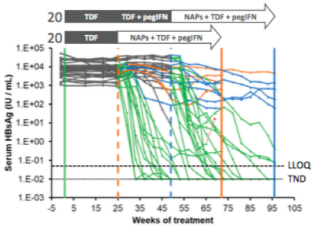
Poor HBsAg response of the patient population to TDF + pegIFN can be demonstrated

NAP drug products used (1:1 ratio):

250mg REP 2139-Mg qW IV
lead candidate

250mg REP 2165-Mg qW IV
suitable for high frequency dosing to rescue the small proportion patients with weak HBsAg response (< 1 log reduction)

HBsAg



REP 2139-Mg = REP 2165-Mg

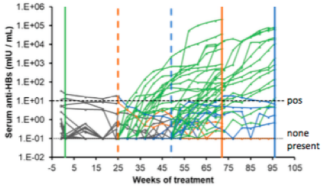
4/40 non-responders (HBsAg reduction < 1 log_{10})

8/40 HBsAg > 1 log_{10} reduction but < 1 IU/mL

28/40 HBsAg < 1 IU/mL

24/40 HBsAg loss (0.00 – 0.05 IU/mL)

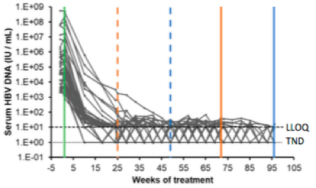
Anti-Hbs



Anti-Hbs dramatically increased with the introduction of pegIFN

(but only in patients with HBsAg declines to < 1 IU/mL)

HBVDNA



TDF-induced HBV DNA declines unaffected during therapy

Frequency and outcomes of liver transplantation for NASH in Europe

Aims:

- Describe the changing frequency of LTx for NASH in Europe
- Determine clinical outcomes and prognostic factors

Methods:

- Retrospective analysis of data from the ELTR database on 68,950 adult patients who underwent primary LTx for chronic liver disease between 01/01/2002 and 31/12/2016 at 174 centres in 33 countries

Results:

- Changing indications for LTx
  - Primary indication was NASH (2,741 [4%] pts)
  - ↑ proportion of LTx performed for patients with NASH: 1.2% (2002) ➔ 8.4% (2016)
  - ARLD was the most common indication (n=22,226; 32.3%)

Recipient differences

	NASH	Non-NASH
Age years; (IQR)	60 (54–64)	55 (48–61)
BMI kg/m^{-2} (SD)	32.6 (4.57)	25.8 (4.45)
HCC (%)	39.1	28.9

- NASH was not an independent predictor of post-LTx patient survival*
  - Patient survival HR 1.06 (95% 0.97–1.17)
  - Graft survival HR 0.90 (95% 0.79–1.04)

*Multivariable Cox regression; adjusted for donor and recipient factors

Haldar D, et al. ILC 2018, PS-041

Determinants of post-LT survival in NASH recipients

For recipients without HCC	HR
Recipient age (years)	
61–65	1.96 (1.29–2.98)
>65	1.77 (1.11–2.82)
MELD >23	1.54 (1.04–2.30)
Recipient BMI (kg/m^2)	
<18.5	5.04 (1.18–21.56)
18.5–25	2.34 (1.28–4.26)
>40	2.24 (1.30–3.87)
Donor blood group B	0.41 (0.23–0.72)

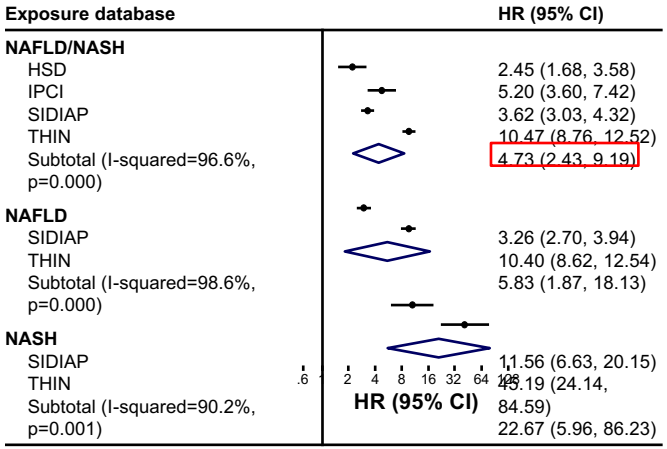
Conclusions:

- The proportion of LTxs performed for patients with NASH has risen more than for any other indication
- Significantly higher proportion of NASH recipients with concomitant HCC than for other indications.
- NASH is not an independent predictor of post-LTx patient or graft survival
- Amongst NASH recipients, older age, higher MELD and extremes of BMI carry a post-LTx mortality risk, ➔ can aid risk stratification and careful selection of patients with NASH for LTx

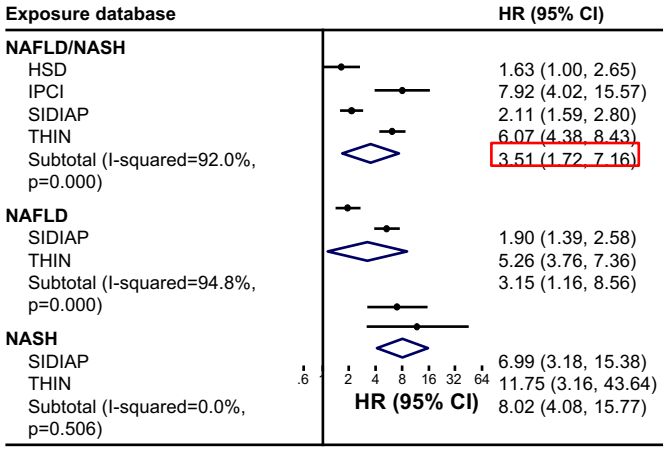
NAFLD and increased risk of incident NASH, cirrhosis and HCC in 18 million European electronic healthcare records

- 134,854 NAFLD or NASH patients
  - From Italy, Spain, the Netherlands, and UK
- Matching 100:1 by practice site, gender, age ±5 years, and visit
- Mean follow-up 3.5 years (>500,000 person years)

Association with cirrhosis



Association with HCC



HR values adjusted for age, smoking status and BMI
Alexander M, et al. ILC 2018, PS-106

Cenicriviroc (CVC), a CCR2 and CCR5 inhibitor, in patients with NASH: Phase 2b CENTAUR study Year 2 analysis

Study design

- Randomized, double-blind, placebo-controlled; 3 serial biopsies: Screening, Year 1 and 2
- N=289 adults with NASH (NAS ≥4; F1–3)

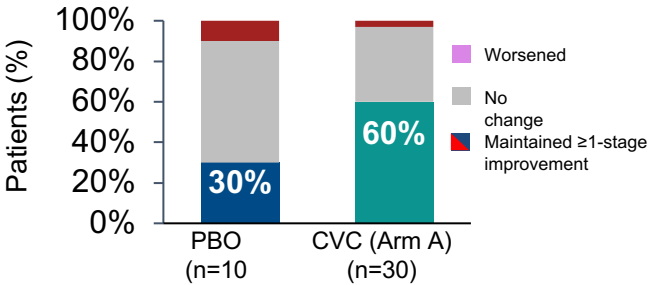
- **Arm A:** CVC (150 mg qd) for 2 years (n=121)
- **Arm B:** Placebo Year 1; cenicriviroc Year 2 (n=61)
- **Arm C:** Placebo for 2 years (n=60)

n for patients who entered Year 2

Results

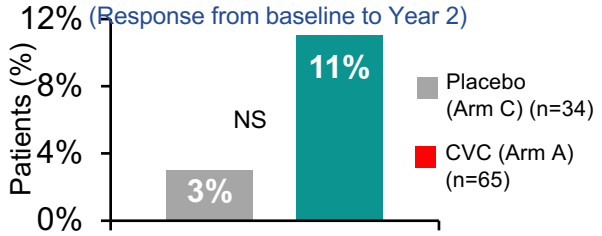
Durability of antifibrotic response

(Response[a] from Year 1 to Year 2) (mITT)



More CVC-treated patients achieved improvement in fibrosis by ≥2 stages AND no worsening of NASH

(Response from baseline to Year 2)



- 2x CVC-treated patients achieving ≥1-stage fibrosis improvement at Year 1 maintained benefit at Year 2 vs. placebo, particularly in Stage 3 fibrosis
- Further supports Cenicriviroc's antifibrotic MoA

Conclusions

- Cenicriviroc was well tolerated and provided antifibrotic activity in adults with NASH and liver fibrosis; Year 2 exploratory analyses supported Year 1 primary endpoint findings
- Phase 3 evaluation of cenicriviroc for treatment of liver fibrosis associated with NASH is underway (NCT03028740)

[a] ≥1-stage fibrosis improvement

Ratziu V, et al. ILC 2018, GS-002

MGL-3196, a selective thyroid hormone receptor beta (THR-β) agonist: Phase 2 NASH study

Background

- MGL-3196 lowers LDL-C and TGs; and could reduce NASH by increased β-oxidation of liver lipids and improved mitochondrial function
- Safe and well tolerated in >300 dosed subjects (Phase 1)

Methods

- 125 patients with biopsy-proven NASH* and ≥10% liver fat on baseline MRI-PDFF randomized 2:1 to oral
  MGL-3196 qd or placebo for 36 weeks; blinded increase or decrease in dose possible based on exposure
- Serial liver biopsies performed

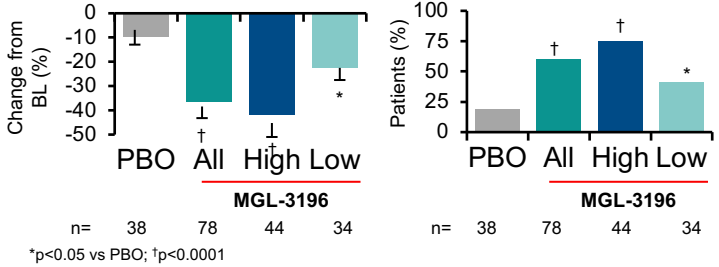
Results (Week 12)

- **Liver enzymes:** Decreases in ALT and AST in high-exposure MGL-3196 vs. PBO (p=0.04, 0.02, respectively)
- **Fibrosis biomarkers**: MGL-3196 significantly decreased ELF™ and Pro-C3 (up to 40% vs. PBO; p=0.009, 0.002, respectively) in patients with >ULN levels at baseline
  (reflective of more advanced fibrosis stage)
- **Safety**
  - Study still blinded; MGL-3196 shows very good tolerability: mostly mild–moderate AEs, balanced between all groups
  - Three SAEs, all unrelated to drug
  - No change in thyroid axis, heart rate or vital signs
  - Significant decreases in S/DBP for MGL-3196 vs. PBO

Conclusions

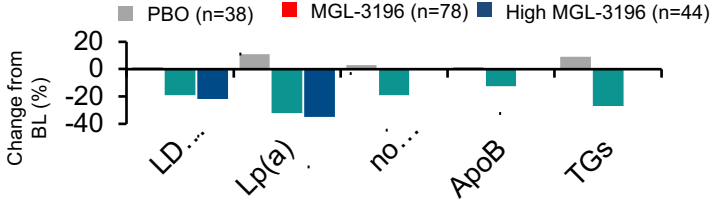
- MGL-3196 reduced NASH and liver fibrosis
- Histopathological assessment (36-week liver biopsy) will allow for correlations with baseline biopsy and multiple
  12- and 36-week non-invasive imaging and biomarkers

- **Primary endpoint:** Relative change in liver fat on MRI-PDFF at 12 weeks
- Patients achieving ≥30% fat ↓

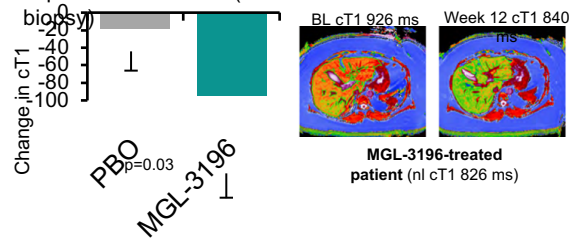


*p<0.05 vs PBO; †p<0.0001

- **Lipids:** meaningful reductions in atherogenic lipids (p<0.0001)



- **Multiparametric MRI-PDFF substudy:** Statistically sig. improvements in cT1 (shown to correlate with inflammation on liver biopsy)

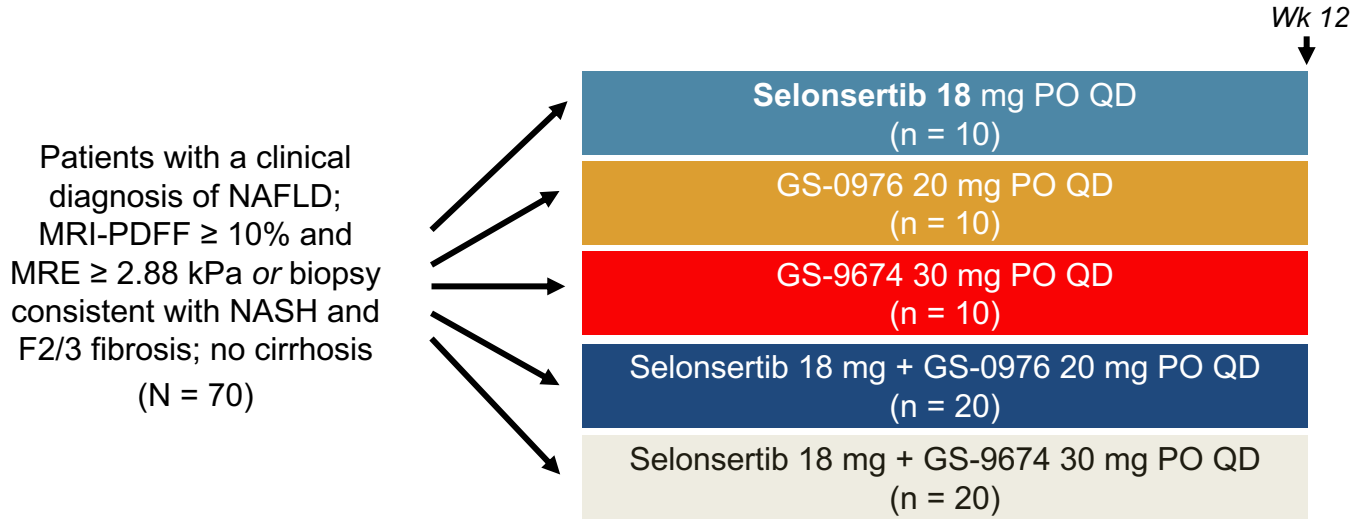


*NAS ≥4, F1–3

Harrison A, et al. ILC 2018, GS-009

Selonsertib, GS-0976, and GS-9674—Alone or in Combination—for Patients With NASH

- Open-label, proof-of-concept phase II study
  - Selonsertib: ASK1 inhibitor, GS-0976: ACC inhibitor, GS-9674: FXR agonist

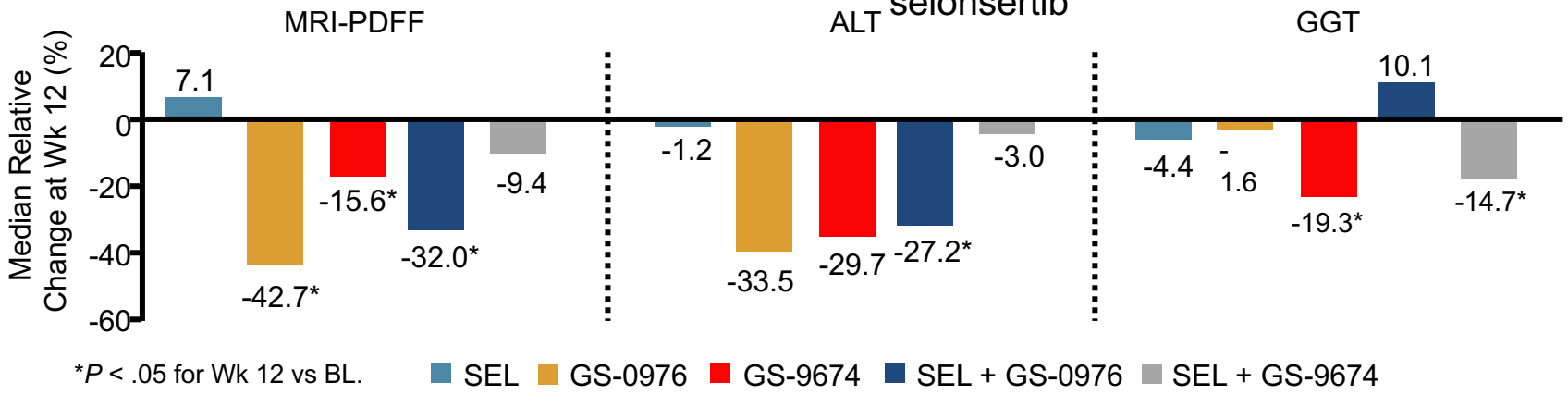


- Endpoints: change in liver fat by MRI-PDFF, liver stiffness by MRE; safety

Lawitz E, et al. EASL 2018. Abstract PS-105.

Combination Regimens Improved Liver Fat, Biochemistry at Wk 12

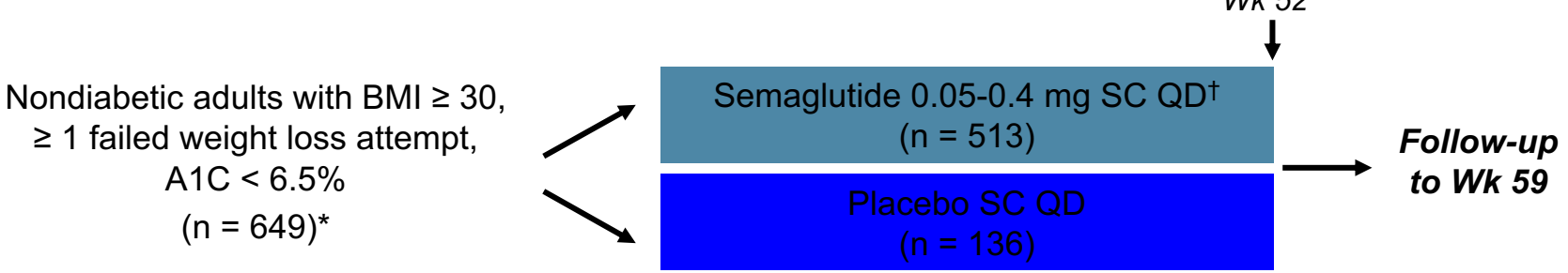
- Robust reductions in liver fat and ALT with GS-0976 ± selonsertib
- Reduction in ALT with GS-9674 monotherapy, in GGT with GS-9674 ± selonsertib



Median Relative Change at Wk 12, %	SEL (n = 10)	GS-0976 (n = 10)	GS-9674 (n = 10)	SEL + GS-0976 (n = 20)	SEL + GS-9674 (n = 20)
MRE-stiffness	-8.6 (-15.6 to 13.6)	-8.9 (-15.1 to -6.3)	-8.3 (-14.7 to 6.7)	-4.5 (-17.7 to 9.3)	-5.2 (-15.3 to 13.8)

Semaglutide vs Placebo in Obese, Nondiabetic Patients

- Post hoc analysis of randomized, double-blind phase II trial that explored use of Semaglutide for weight loss[1,2]
  - Semaglutide: GLP-1 receptor agonist
  - Superior, dose-related mean reductions in body weight at Wk 52 with semaglutide vs placebo in primary analysis (6.0% to 13.8% vs 2.3%, respectively; *P* < .0001)[3]



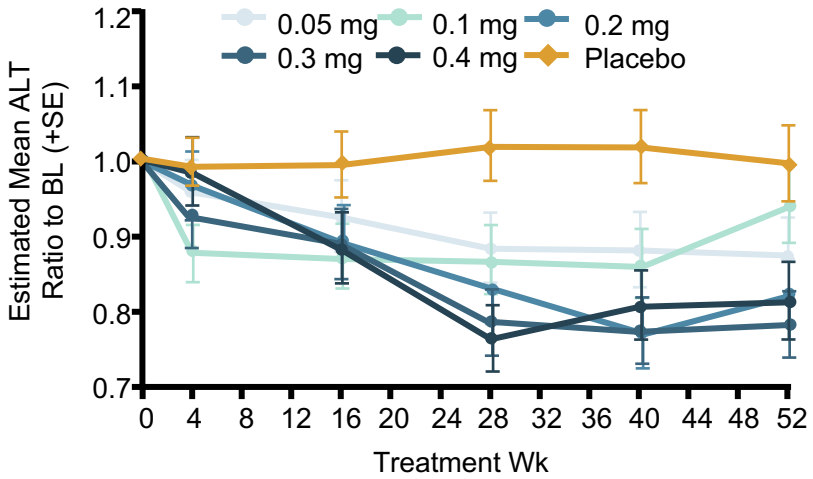
- ALT changes evaluated in subgroups with vs without elevated ALT at BL; 18% (174/954) predicted to be at risk for or have NAFLD/NASH with advanced fibrosis

All patients received lifestyle intervention of -500 kcal/day diet and physical activity. *Examined population within larger trial of 957 participants from 8 countries. †Dose groups: 0.05 mg, n = 103; 0.1 mg, n = 102; 0.2 mg, n = 103; 0.3 mg, n = 103; 0.4 mg, n = 102.

References in slideshow

Elevated ALT Declined, Often Normalized With Semaglutide Treatment by Wk 52

- ALT decline most marked around Wk 28 but generally continued through EOT with semaglutide in patients with BL ALT elevation
- By Wk 52, ALT normalized in 25% to 46% of patients receiving semaglutide vs 18% receiving placebo



Outcome at Wk 52, % (n/n)	Semaglutide					Placebo
	0.05 mg	0.1 mg	0.2 mg	0.3 mg	0.4 mg	
Normalized ALT	29 (17/58)	25 (15/59)	38 (19/50)	43 (23/54)	46 (21/46)	18 (14/76)

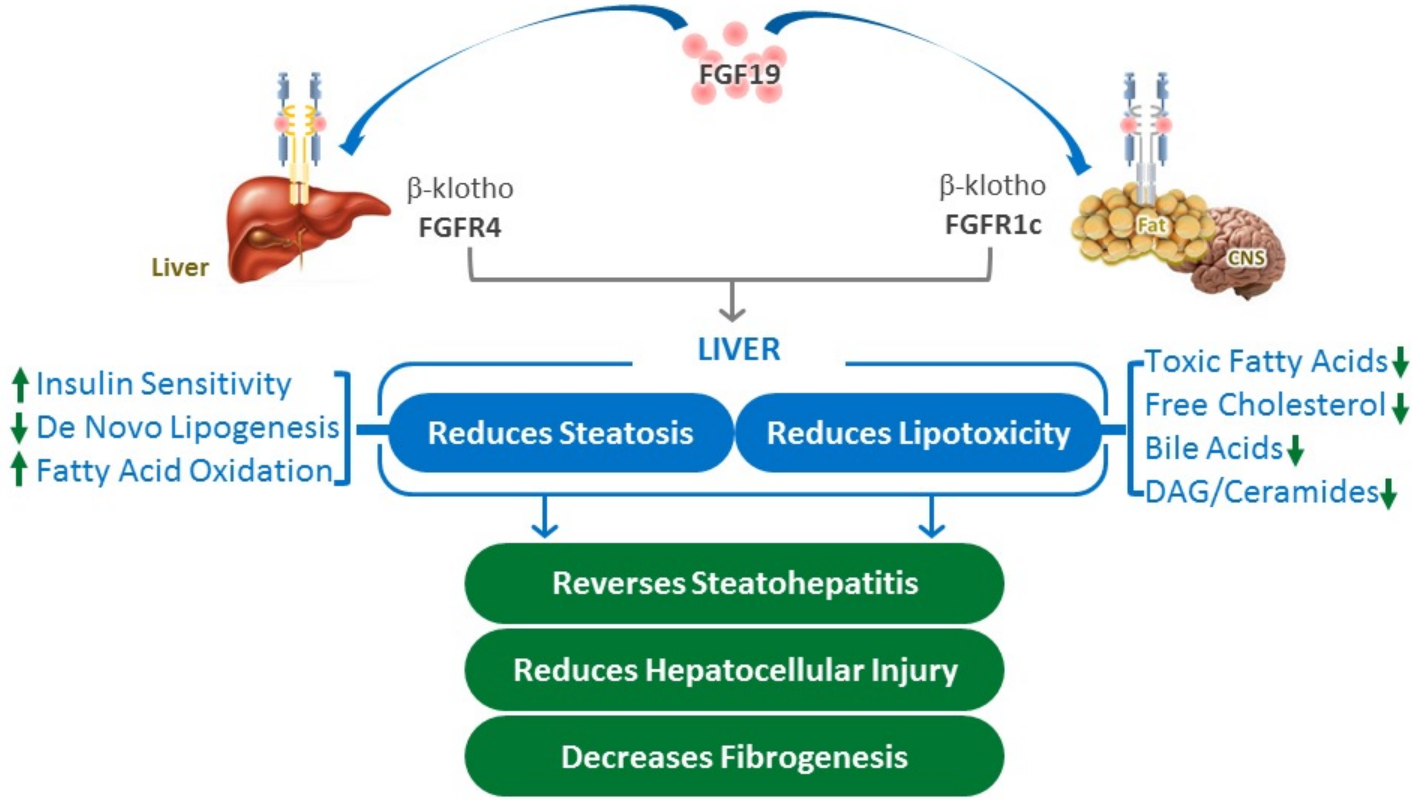
Newsome P, et al. EASL 2018. Abstract FRI-483.

NGM282

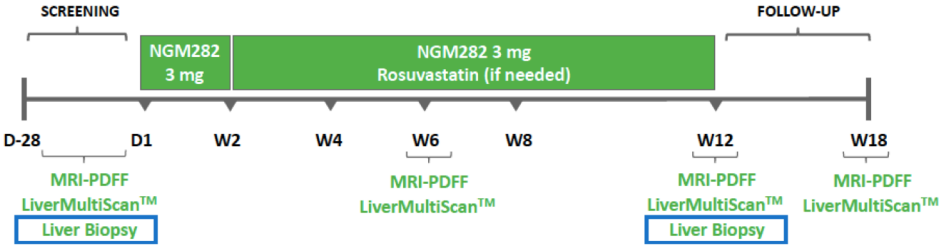
NGM282 Improves Fibrosis and NASH-Related Histology in 12 Weeks in Patients With Biopsy-Confirmed NASH, Which is Preceded By Significant Decreases in Hepatic Steatosis, Liver Transaminases and Fibrosis Markers at 6 Weeks

Stephen A. Harrison, Stephen J. Rossi, Mustafa R. Bashir, Cynthia D. Guy, Rajarshi Banerjee, Mark J. Jaros, Sandra Owers, Bryan A. Baxter, Lei Ling, Alex M. DePaoli

FGF19 Has Multiple Biological Activities Relevant to the Pathogenesis of NASH



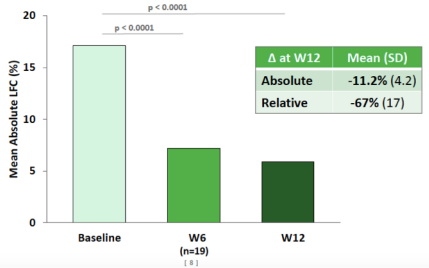
Study Design and Key Enrollment Criteria



- Twenty-two subjects enrolled with biopsy-confirmed NASH at a single center
  - NAS ≥4 (at least 1 point in each component)
  - Stage 1-3 fibrosis
  - LFC ≥ 8% (MRI-PDFF)

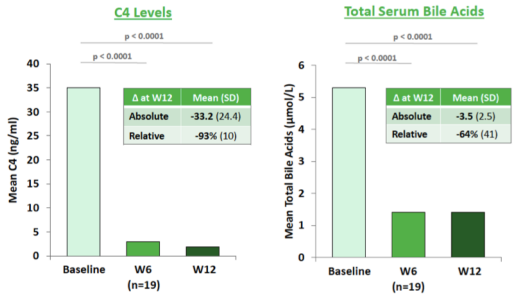
Significant Decrease in Absolute and Relative LFC by MRI-PDFF After 6 and 12 Weeks of NGM282

- *100% of subjects achieved primary endpoint of ≥ 5% absolute LFC reduction and a decreased relative LFC ≥ 30% at W12*
- *12 (63%) of subjects normalized LFC (≤ 5%) by W12*



[8]

Suppression of C4 and Serum Bile Acids by NGM282 Reflects Potent Target Engagement

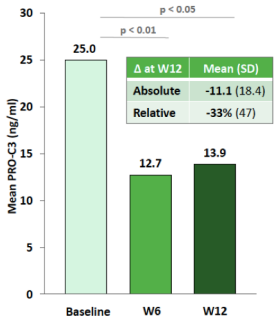


C4 = 7α-hydroxyl-4-cholesten-3-one
Lower Limit of C4 Quantitation = 0.9 ng/ml

[7]

Fibrosis Markers are Significantly Reduced by NGM282 as Early as Week 6

PRO-C3 Levels



Δ at W12	Mean (SD)
Absolute	-11.1 (18.4)
Relative	-33% (47)

ELF Score and Components

Mean (SD)	Baseline	W6	W12
ELF Score	10.1 (1.0)	9.6* (0.8)	9.5* (1.0)
Hyaluronic Acid	*91.4 (79.7)*	*67.3 (60.2)*	*72.1 (90.3)*
PIIINP	*13.4 (4.6)*	*9.7* (3.5)*	*10.3* (3.4)*
TIMP-1	*270.8 (67.7)*	*233.6* (51.4)*	*232.0* (62.5)*

*p < 0.01

Subjects with severe disease (ELF ≥ 10.1) decreased ELF Score by 0.8 at W12

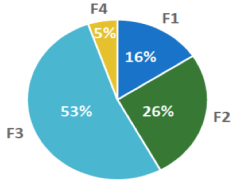
[10]

Rapid Regression of Fibrosis at Week 12 in Patients Treated with NGM282

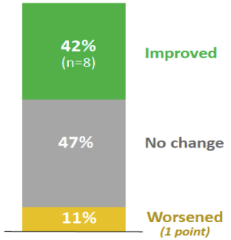
Fibrosis Stage at Baseline

(% patients; n=19)

Mean fibrosis stage = 2.5



Fibrosis Histologic Response at W12



- **Mean change from Baseline in fibrosis stage = -0.5**
- **Three subjects had a 2-stage improvement in fibrosis: all F3 → F1**
- **Mean decrease in NAS in subjects with improved fibrosis = -3.5**

[14]

Reduction in LIF and cT1 on Multi-Parametric MRI are Consistent with Other Non-Invasive Markers

Correlation of LMS Parameters and Disease Severity

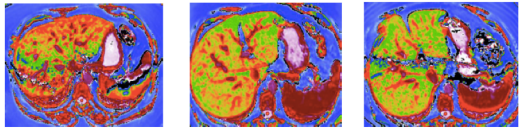
	LIF Score	Mean Corrected T1 (cT1; ms)
Severe Fibrosis	≥ 3.0	≥ 950
Decreased Liver-Related Events	≤ 2.0	≤ 875
No Fibrosis	≤ 1.0	≤ 800

Mean (SD) Change in LIF Score and cT1

	Baseline	W6	W12
LIF (SD)	2.80 (0.43)	2.25 (0.52)*	2.05 (0.56)*
cT1 (SD)	891 (56)	831 (56)*	812 (58)*

*p < 0.0001

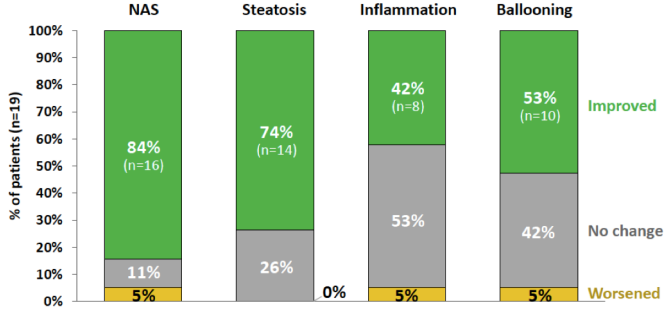
Baseline *W6* *W12*



LMS = LiverMultiScanTM
LIF = Liver Inflammation-Fibrosis

[1] Banerjee et al, J Hepatol. 2014; 60(1): 69-77
[2] Data on file, Perspectum Diagnostics

NAS HISTOLOGICAL RESPONSE AT W12

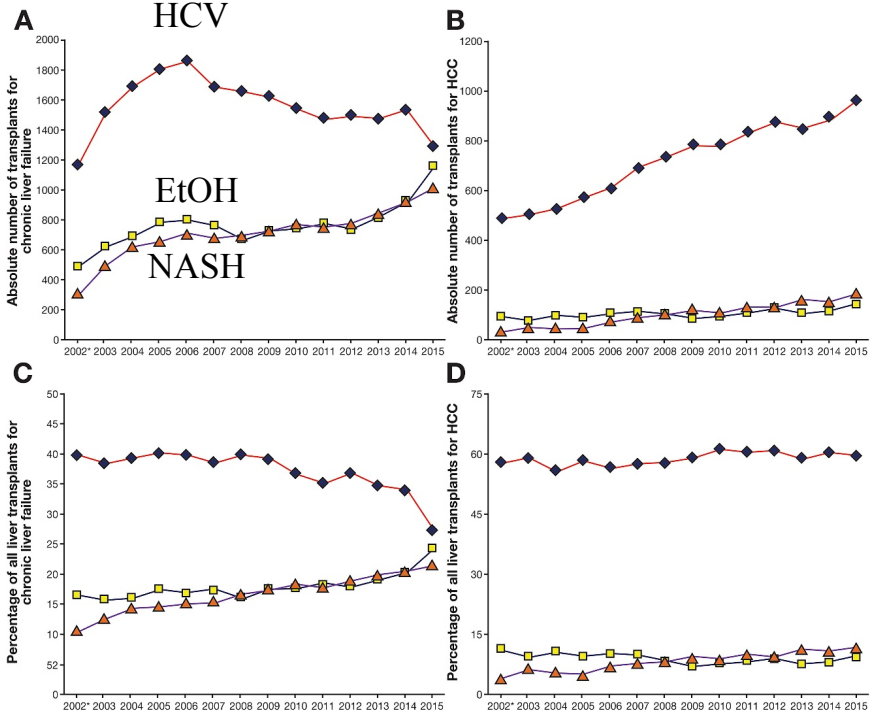


Mean change at W12 (SD)	NAS	Steatosis	Inflammation	Ballooning
	-2.3 (1.8)	-1.1 (0.9)	-0.5 (0.8)	-0.7 (0.9)

Alcoholic Liver Disease

- Acute alcoholic hepatitis rising
- Changing demographics
- Younger women
- High acuity levels
- Increasing demand for LT
- Controversies remain

Absolute number of patients listed for decompensated liver disease



Gastroenterology. 2017 Apr;152(5):1090-1099

The ‘six-month’ rule

Allow time for recovery and obviate need for LT

Examine commitment to sobriety while implementing strategies against future recidivism

Strategy has enabled similar if not better 5 year survival rates than LT for other indications

ALD is a self-inflicted condition and we risk “wasting a liver” in a high-demand region

Mackie, J et al. Liver Transpl. 2001 May;7(5):418-27
Leong , J et al. Clinics in Liver Disease 2012;16:4, 851-863
Lucey , M et al. Transplantation. 1998 Oct 15;66(7):956-62
Dureja J, et al. J Hepatol. 2010 May;52(5):759-64
O’Shea, R et al. Hepatology. 2010 Jan;51(1):307-28

Relapse after LT for alcoholic liver disease more common in younger patients

- Retrospective review of patients who underwent LT for alcoholic liver disease between 1999 and 2015 to
  - establish the rate of alcohol relapse posttransplant and define predictive factor
- 928 patients included, 203 underwent LT for the first time due to alcoholic liver disease,
  - 28 patients relapsed within a median follow-up of 6.5 years
- Patients who relapsed were significantly more likely to be younger than those who did not relapse (49.8 vs. 54.1 years; P = .011).
  - Multivariate analysis confirmed the significance of age related to relapse (HR = 1.083; 95% CI, 1.027-1.142).
- Patients transplanted under a standardized exception pathway (without 6 months prior sobriety were also more likely to relapse compared with those who followed normal pathway (40% vs. 12.4%))
- Patients who relapsed within 1 year had lower survival compared with those who relapsed after 1 year and those who did not relapse at all
  - difference was not significant.

Al-Qaisi MTA, et al. Abstract 503. Presented at: Digestive Disease Week; June 2-5, 2018; Washington, D.C.

Impact of baclofen in alcohol-dependant patients: the French “OBADE-ANGH” series

Aims: Evaluate the use of baclofen, a $GABA_B$ receptor agonist, for the reduction of alcohol cravings/consumption and safety, especially in ALD patients

Methods: Patients in hepato-gastroenterology units in France initiated on baclofen for alcohol misuse between March 2012–Dec 2016

Results:

- Patients were 79.2% male, mean age 50.8 years, 25.1% had non-cirrhotic ALD, 38% had cirrhosis
- Median dose at Month 12: 66 (20–210) mg/d; 59 (20–200) mg/d in patients with cirrhosis

Management of alcoholic liver disease

Management of alcohol use disorder

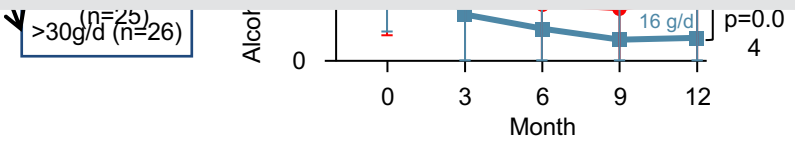
4. In patients with ALD, baclofen is effective in preventing alcohol relapse (Conditional recommendation, low level of evidence)

5. In patients with ALD, brief motivational interventions are effective in reducing alcohol relapse compared with no intervention (Conditional recommendation, very low level of evidence)

Alcoholic hepatitis

Improvement of hepatic function at Month 12

	Day 1	Month 12	p-value
PT, %	70.4	76.5	0.0034
Bilirubin, µmol/l	29.6	20.6	0.0279
Albumin, g/l	34.5	36.6	0.012

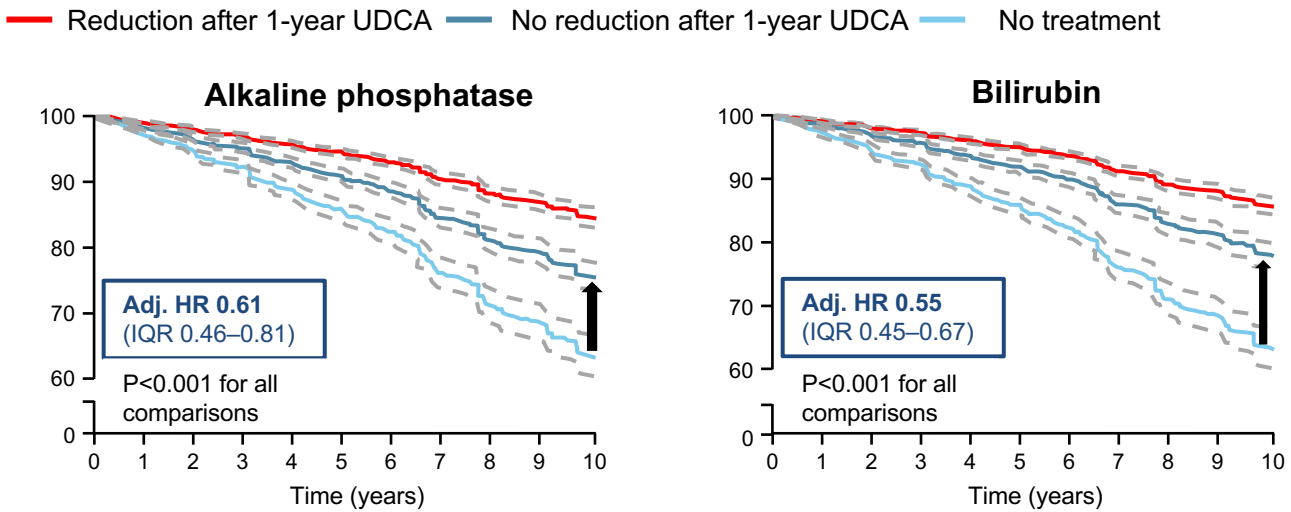


Conclusions: Baclofen is well tolerated and combined with medical and psychosocial monitoring, can help patients reduce or stop alcohol consumption

Barrault C, et al. ILC 2018, PS-072

UDCA is associated with prolonged transplant-free survival of PBC patients: even in the absence of biochemical improvements

- **Global PBC study**, n=3902 patients, 90% **UDCA-treated**
- IPTW-adjusted Cox regression analyses
- Overall IPTW-adjusted **HR of UDCA: 0.46** (IQR 0.40–0.52, p<0.001)



- **Conclusion: UDCA** independently associated with prolonged transplant-free survival

Harms MH, et al. ILC 2018, #PS-008

Statins are associated with reduced mortality and morbidity in PSC

Swedish, register-based cohort study of PSC patients with IBD (n=2914) diagnosed between 2005 and 2016

Cox regression used to analyze associations between different drugs and: death, LTx, CCA, and bleeding oesophageal varices

Statin exposure: 13.9% (n=404)

Hazard ratios (95% CIs)

Drug	All-cause mortality (n=2914)	Mortality and liver transplantation (n=2794)	Adverse liver events* (n=2740)
UDCA	1.04 (0.87, 1.25)	1.34 (1.12, 1.62)	3.10 (2.36, 4.07)
Statins	**0.68 (0.54, 0.88)**	**0.50 (0.28, 0.66)**	**0.53 (0.36, 0.80)**
NSAIDs	0.86 (0.72, 1.02)	0.82 (0.68, 0.99)	0.87 (0.68, 1.62)
ASA	0.99 (0.80, 1.21)	2.16 (1.72, 2.70)	3.35 (2.46, 4.55)
Antibiotics	1.70 (1.27, 2.29)	2.27 (1.70, 3.05)	3.03 (2.09, 4.41)
Antimycotics	2.78 (2.24, 3.44)	3.13 (2.48, 3.94)	1.74 (1.20, 2.51)
Metronidazole	1.27 (1.06, 1.53)	1.20 (0.99, 1.47)	1.58 (1.23, 2.03)
AZA/mercaptopurines	0.66 (0.52, 0.84)	0.65 (0.50, 0.83)	0.80 (0.60, 1.08)
Steroids	1.94 (1.60, 2.34)	2.14 (1.75, 2.60)	1.28 (1.00, 1.65)

Conclusions: statin use associated with decreased risk of death and LTx in PSC

*Liver-related death, LTx, CCA or variceal bleeding

Stokkeland K, et al. ILC 2018, #PS-128

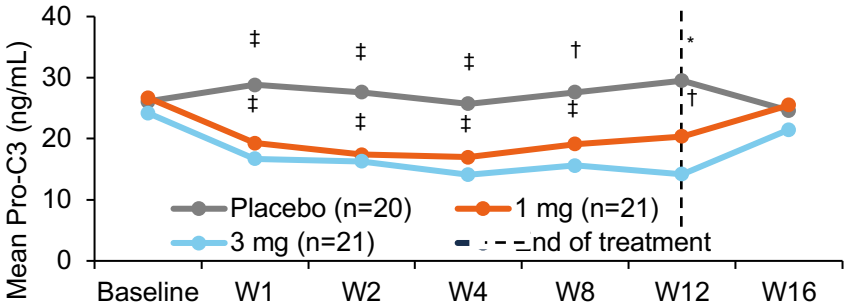
NGM282 significantly improves markers of bile acid synthesis, hepatic injury and fibrosis in PSC

Randomized, double-blind, placebo-controlled Phase 2 trial evaluating the safety and efficacy of NGM282, an engineered analogue of FGF19, in patients with PSC† (n=62)

SC NGM282 1 mg, 3 mg or placebo qd for 12 weeks

Significant reductions from baseline in C4 (0.4, –7.9 and –14.7 ng/ml) and serum BA‡ (–4.03, –12.6 and –16.8) for placebo, 1 mg and 3 mg doses, respectively

	Placebo (n=20)			NGM282 1 mg (n=21)			NGM282 3 mg (n=21)		
	Day 1	Week 12	p	Day 1	Week 12	p	Day 1	Week 12	p
Mean AP (U/L)	365	355	0.78	383	409	0.22	354	351	0.73
Mean ALT (U/L)	90	86	0.26	117	114	0.41	96	56	<0.001
Mean change in ELF score from baseline	Placebo			NGM282 1 mg			NGM282 3 mg		
From baseline of ≤9.8	0.08			0.12 (p=0.90 vs. placebo)			–0.24 (p=0.23 vs. placebo)		
From baseline of >9.8	–0.01			–0.52 (p=0.016 vs. placebo)			–0.58 (p=0.029 vs. placebo)		



- **Conclusions:**
  - Primary endpoint of decreased ALP not met
  - Decreases in markers of hepatic inflammation fibrogenesis
  - Favourable safety profile
  - Significant improvements in Pro-C3, ELF and ALT/AST

*p<0.05; †p<0.01; ‡p<0.001 (all vs. placebo); †patient population included those with features of AIH, small duct disease, stable dominant strictures and compensated cirrhosis; ‡total serum BA minus UDCA

Hirschfield G, et al. ILC 2018, #LBO-002

Primary SBP prophylaxis is associated with greater ICU admission and 30-day mortality compared to secondary SBP prophylaxis

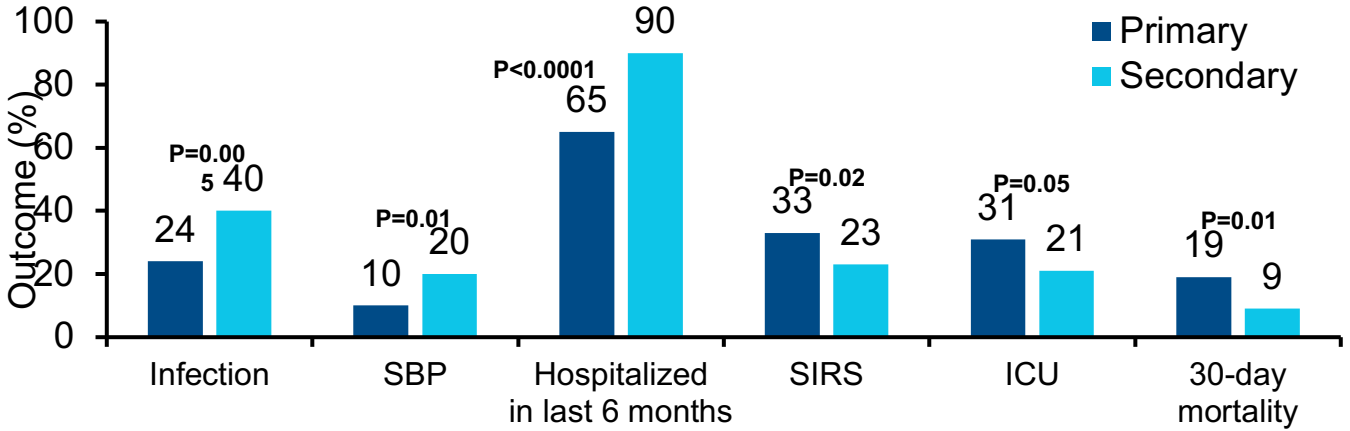
Aim: Comparison of primary vs. secondary prophylaxis for spontaneous bacterial peritonitis (SBP) in patients with cirrhosis from a large inpatient cohort (the NACSELD database)

Methods:

- Inpatients with cirrhosis and on primary or secondary prophylaxis (n=154 each) were propensity matched for admission MELD score and serum albumin

Results:

Rifaximin use may be confounding



Conclusions:

- Despite prophylaxis, a significant number of patients developed SBP
- Unexpectedly, patients on primary prophylaxis had poorer outcomes
- The value of both primary and secondary prophylaxis requires re-evaluation

Bajaj JS, et al. ILC 2018, GS-015

Summary

- Real World data from GLE/PIB similar to other DAAs
- The benefits of SVR are becoming more apparent
- SVR is durable, carefully assess fibrosis levels in your HCV patients
- DC of nucleotides/nucleosides in HBeAg – patients may lead to clearance of HBsAg
- Novel agents for HBV are coming
- NASH: Lots of trials, keep working on lifestyle modifications, GLP-1 class, while not approved for NAFLD should be considered in management of T2DM if appropriate

Summary

- PBC: There are long term benefits to UDCA even without complete response
  - Can add obeticholic acid as indicated for non-responders
- PSC: Multiple trials in place, statins may be beneficial
- Alcoholic Liver Disease: More data required to optimize those who are transplanted via exception pathway
- Baclofen may be combined with other strategies to reduce relapse