EASL and DDW Hepatology Updates

Bilal Hameed, MD

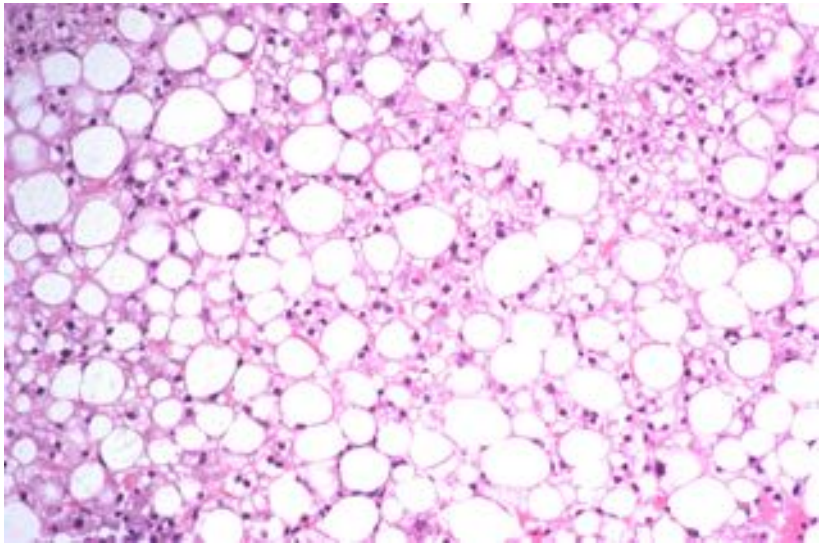
University of California, San Francisco

Email: bilal.hameed@ucsf.edu

Outline

- **Nonalcoholic Steatohepatitis (NASH)**
- **HCC and risk with DAA**
- **Cirrhosis Complications and others**

Nonalcoholic Steatohepatitis



NASH

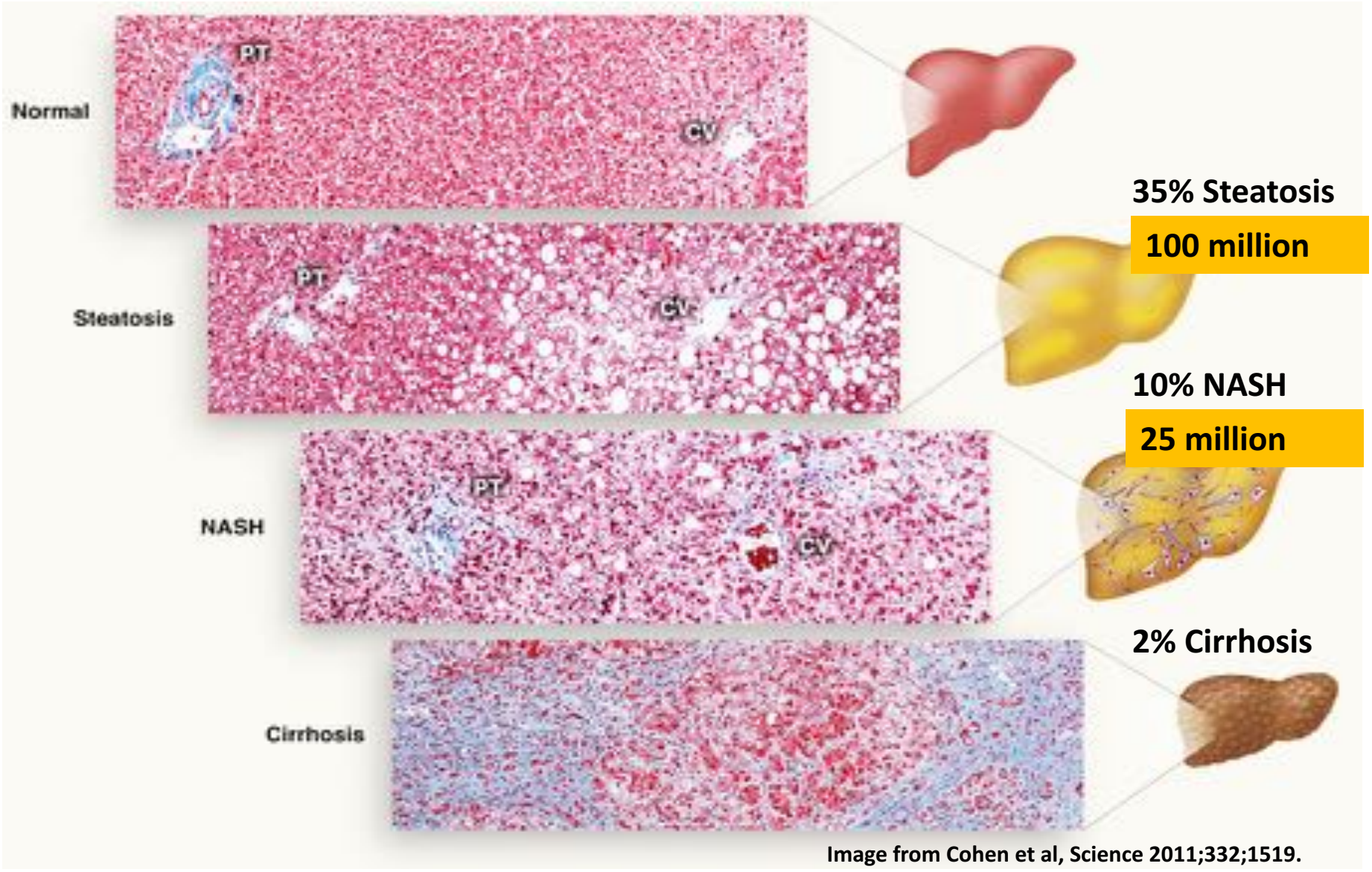


Image from Cohen et al, Science 2011;332;1519.

Subtypes of NAFLD: Who to Treat?

Caveats

- Presence of steatosis in ≥ 5% hepatocytes
- Minimal alcohol use
- Biopsy consistent with NAFLD
- No other etiology for liver disease

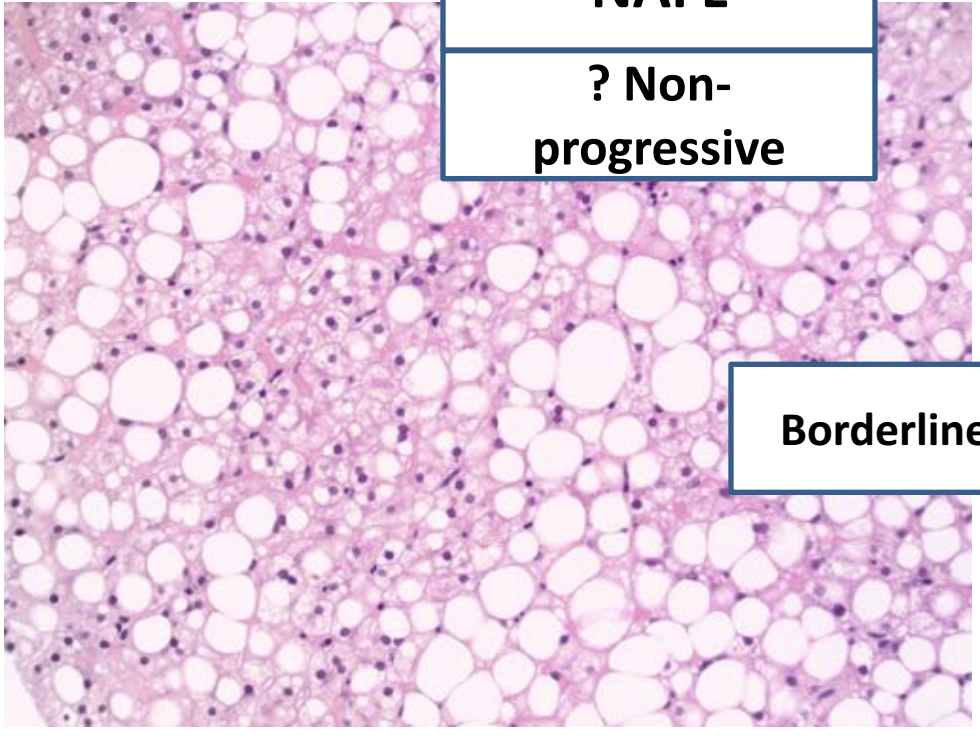
NAFLD

NAFL

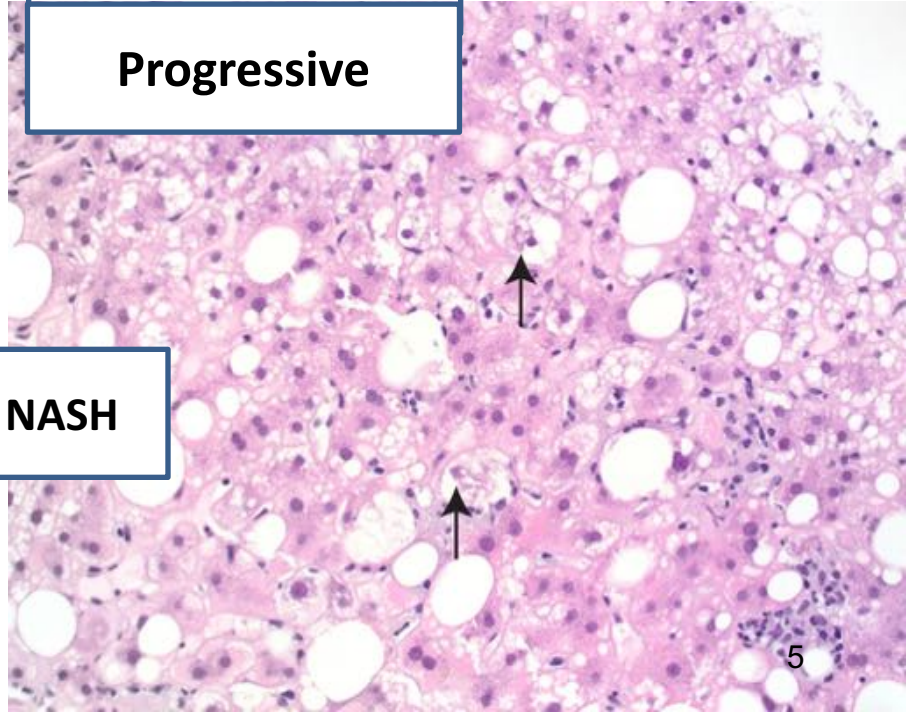
? Non-progressive

NASH

Progressive



Borderline NASH



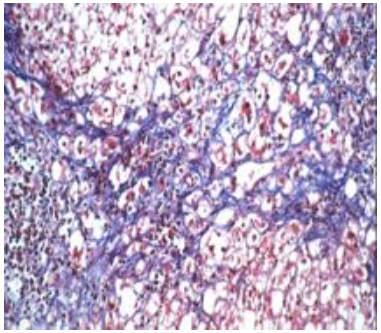
Emerging Therapies in NASH

- **Anti-NASH**
  - Obitecholic acid
  - GFT-505
  - PPAR-ligands
  - Cencriviroc
  - Aramchol
  - ASK-1 inhibitors
  - ACC inhibitors
  - CB1 receptor inhibitors
  - DPP4 inhibitors
  - SGLT-2 inhibitors
  - GLP-1 agonist
  - Emricassan (caspase inhibitors)
  - FGF-19 agonist
  - Resveratrol
  - Ezetimibe
  - JNK-1 inhibitors
  - Intestinal specific FXR
  - ASBT inhibitors
- **Anti-fibrotic**
  - Simtuzamab
  - Obeticholic acid
  - PPAR- α,δ, γ
  - Anti-galectin 3 inhibitors
  - Anti-CTGF
  - Angiotensin-receptor blockers
  - Pentraxin-2
  - Anti-IL-17
  - Anti-TGF-beta
  - JNK-1 inhibitors
  - Intestinal specific FXR

Defining NASH Study End Points

Histological:

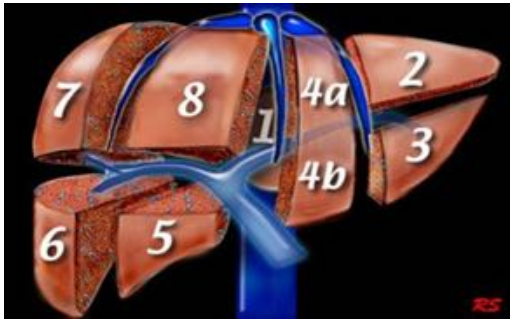
- Resolution of NASH with no worsening of fibrosis
- 2-point improvement in NAS and no worsening of fibrosis



Imaging and Labs

- MRS and MRI-PDFF
- ALT improvement

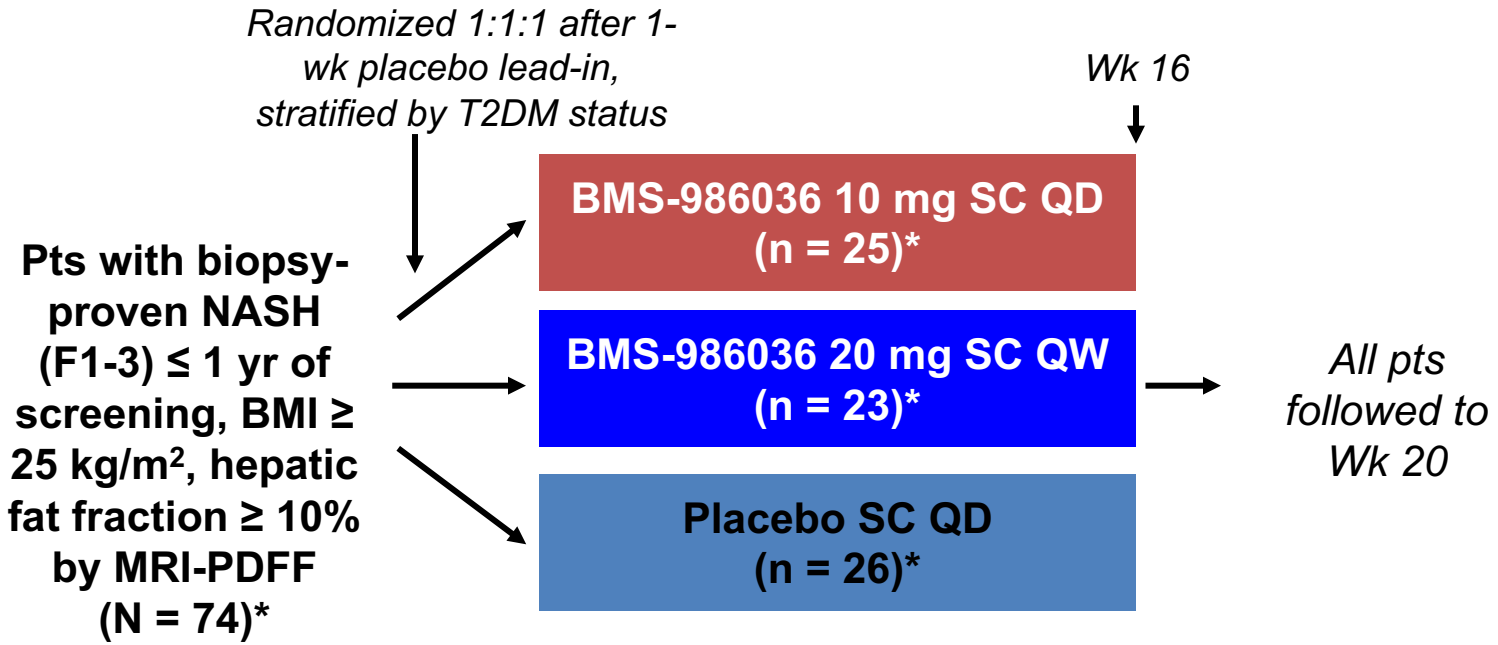
MRI-PDFF



Nonalcoholic Steatohepatitis Investigational Treatments

Pegylated FGF21 Analogue BMS-986036 in Pts With NASH After 16 Wks

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



*Enrollment stopped before planned 30 pts per arm due to significant effect on primary endpoint in preplanned interim analysis at Wk 8.

Primary endpoint: change in hepatic fat fraction from BL to Wk 16

Slide credit: clinicaloptions.com

Sanyal A, et al. EASL 2017. Abstract LBO-02.

BMS-986036 in Pts With NASH After 16 Wks: Efficacy and Safety

- **Significant reduction in hepatic fat fraction with BMS-986036 QD and QW vs placebo**

Change in Liver MRI-PDFF, %	BMS-986036		Placebo (n = 24)
	10 mg QD (n = 23)	20 mg QW (n = 21)	
Mean absolute change	-6.8*	-5.2*	-1.3
≥ 30% relative reduction	57*	52	25
≥ 20% relative reduction	65	71	42
≥ 10% relative reduction	83	76	54

****P* < .05 vs placebo arm (not adjusted for multiple comparisons).**

- **Significantly greater increase from BL in adiponectin with BMS-986036 QD and QW vs placebo (+15.3% vs +15.9% vs -2.3%, respectively; all *P* < .01)**

Sanyal A, et al. EASL 2017. Abstract LBO-02.

Slide credit: clinicaloptions.com

BMS-986036 in Pts With NASH After 16 Wks: Efficacy and Safety

- Triglycerides and HDL levels improved from BL with BMS-986036 QD and QW vs no meaningful changes from BL with placebo
- No deaths, tx-related serious AEs, or AE-related d/c

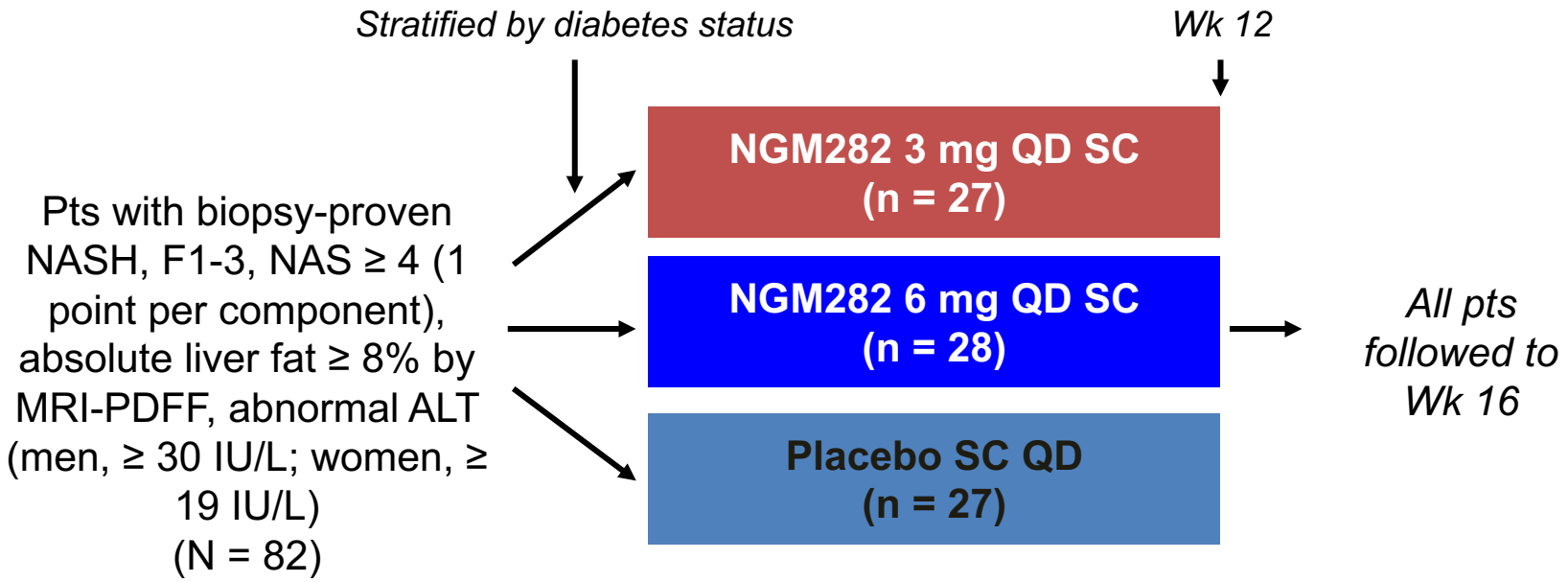
Event, n (%)	BMS-986036		Placebo (n = 26)
	10 mg QD (n = 25)	20 mg QW (n = 23)	
Serious AEs	1 (4)	0	1 (4)
AEs in ≥ 10% of pts			
▪ Diarrhea	3 (13)	5 (22)	2(8)
▪ Nausea	4 (16)	3 (13)	2(8)
▪ Frequent bowel movements	5 (20)	0	0
Tx-emergent grade 3/4 lab abnormalities	1 (4)	2 (9)	2 (8)

Sanyal A, et al. EASL 2017. Abstract LBO-02

Slide credit clinicaloptions.com

FGF19 Variant NGM282 in Pts With NASH After 12 Wks

- International, randomized, double-blind, placebo-controlled phase II trial

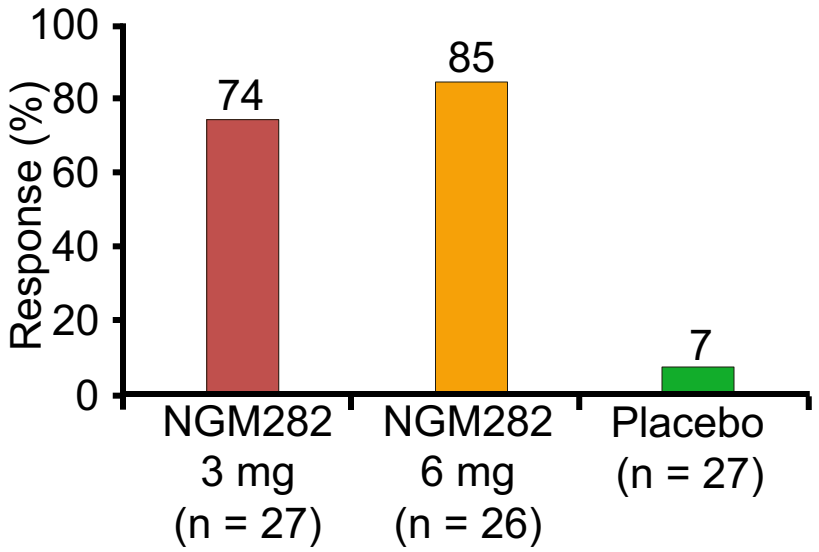


- **Primary endpoint: decrease ≥ 5% in absolute liver fat content**
- Other endpoints: ALT, C4 levels, triglycerides, LDL, antifibrotic markers, safety

Harrison SA, et al. EASL 2017. Abstract LBO-07.

Slide credit: clinicaloptions.com

NGM282 in Pts With NASH After 12 Wks: Efficacy and Safety



- 79% of NGM282-treated pts had absolute decrease in LFC > 5% (decrease greatest in pts with most active disease)
  - ALT normalized in 36% of NGM282-treated pts

Harrison SA, et al. EASL 2017. Abstract LBO-07.

Slide credit: clinicaloptions.com

NGM282 in Pts With NASH After 12 Wks: Efficacy and Safety

- NGM282 antifibrotic activity suggested by significant decreases in PIINP, TIMP-1
- 1 serious AE (acute pancreatitis)

Tx-Emergent AE in > 10% Pts, %*	NGM282		Placebo (n = 27)
	3 mg (n = 27)	6 mg (n = 28)	
Injection-site rxn	40.7	53.6	7.4
Diarrhea	40.7	35.7	22.2
Abdominal pain	29.6	17.9	7.4
Nausea	33.3	14.3	3.7
Headache	11.1	17.9	18.5

*Also included: abdominal distension, vomiting, frequent bowel movements, increased appetite, constipation, injection-site bruising, and decreased weight.

Harrison SA, et al. EASL 2017. Abstract LBO-07.

Efficacy and Safety of Simtuzumab for the Treatment of NASH with Bridging Fibrosis or Cirrhosis: Results of Two Phase 2b, Dose-Ranging, Randomized, Placebo-Controlled Trials

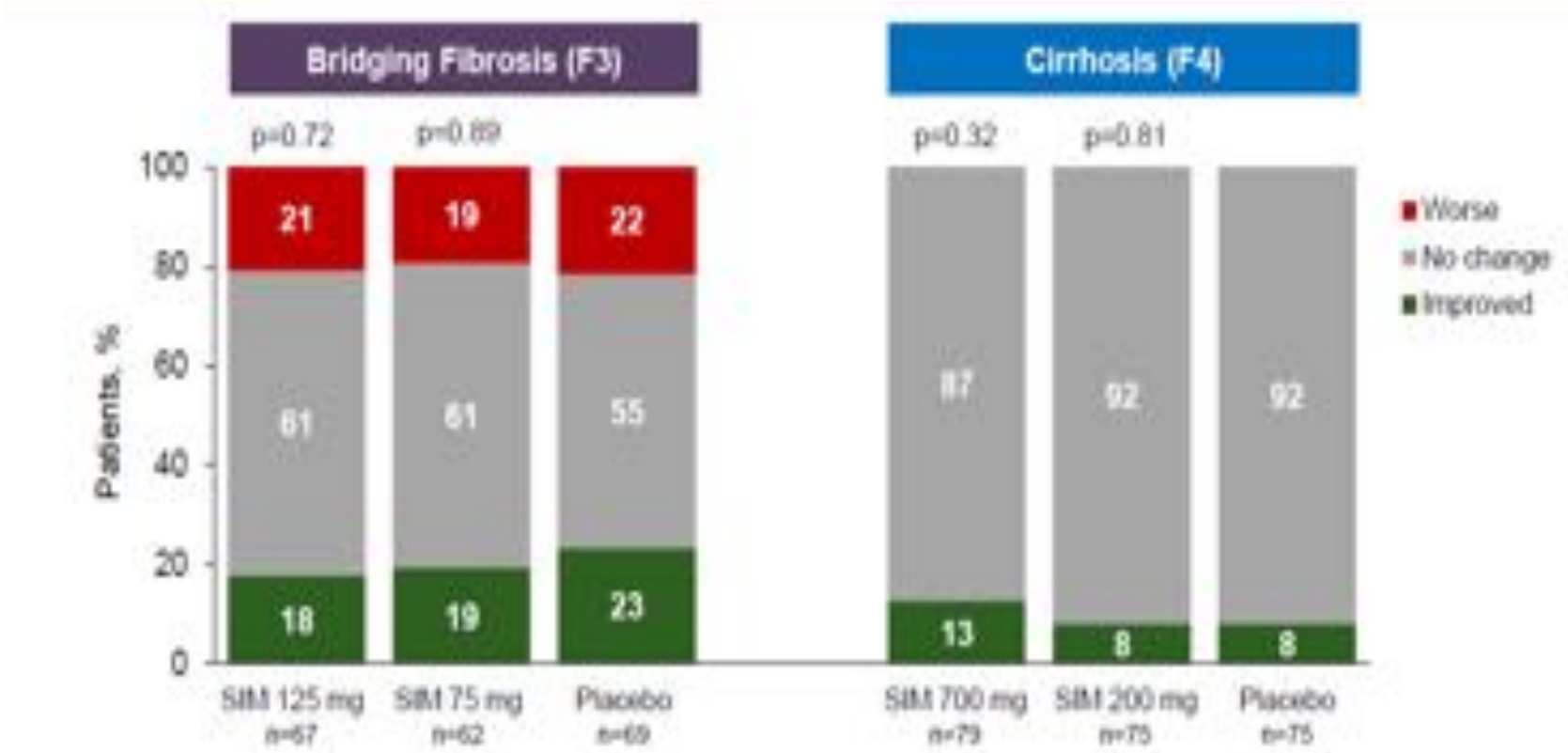
Harrison S et al. EASL 2017. Abstract # PS-094

Study Design

- Key inclusion criteria
  - Histologically confirmed NASH with bridging fibrosis (F3) or compensated cirrhosis (F4)
- 1:1:1 randomization
  - Stratified by diabetes and HVPG ≥10 mmHg (F4 only)
- Studies terminated at Week 96 due to lack of efficacy

Harrison S et al. EASL 2017. Abstract # PS-094

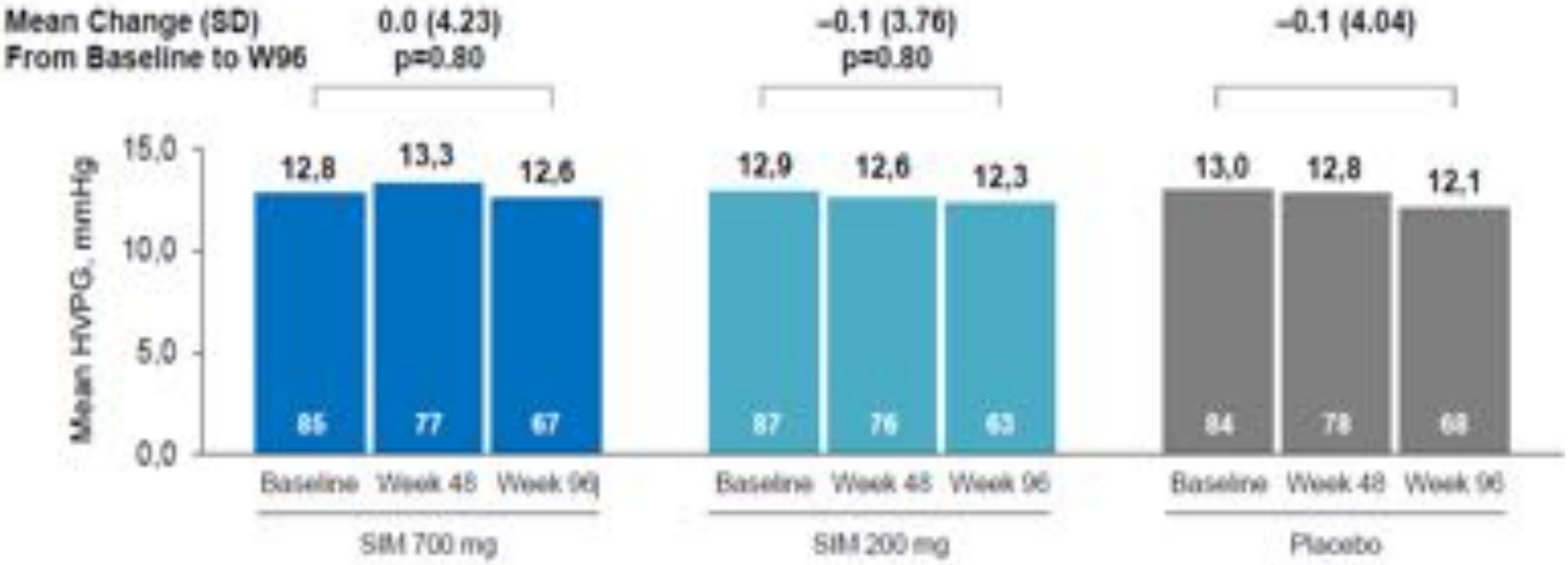
Results: NASH CRN Fibrosis Stage (Week 96)



- SIM had no effect on fibrosis stage through Week 96

Harrison S et al. EASL 2017. Abstract # PS-094

Results: Portal Pressure (F4)



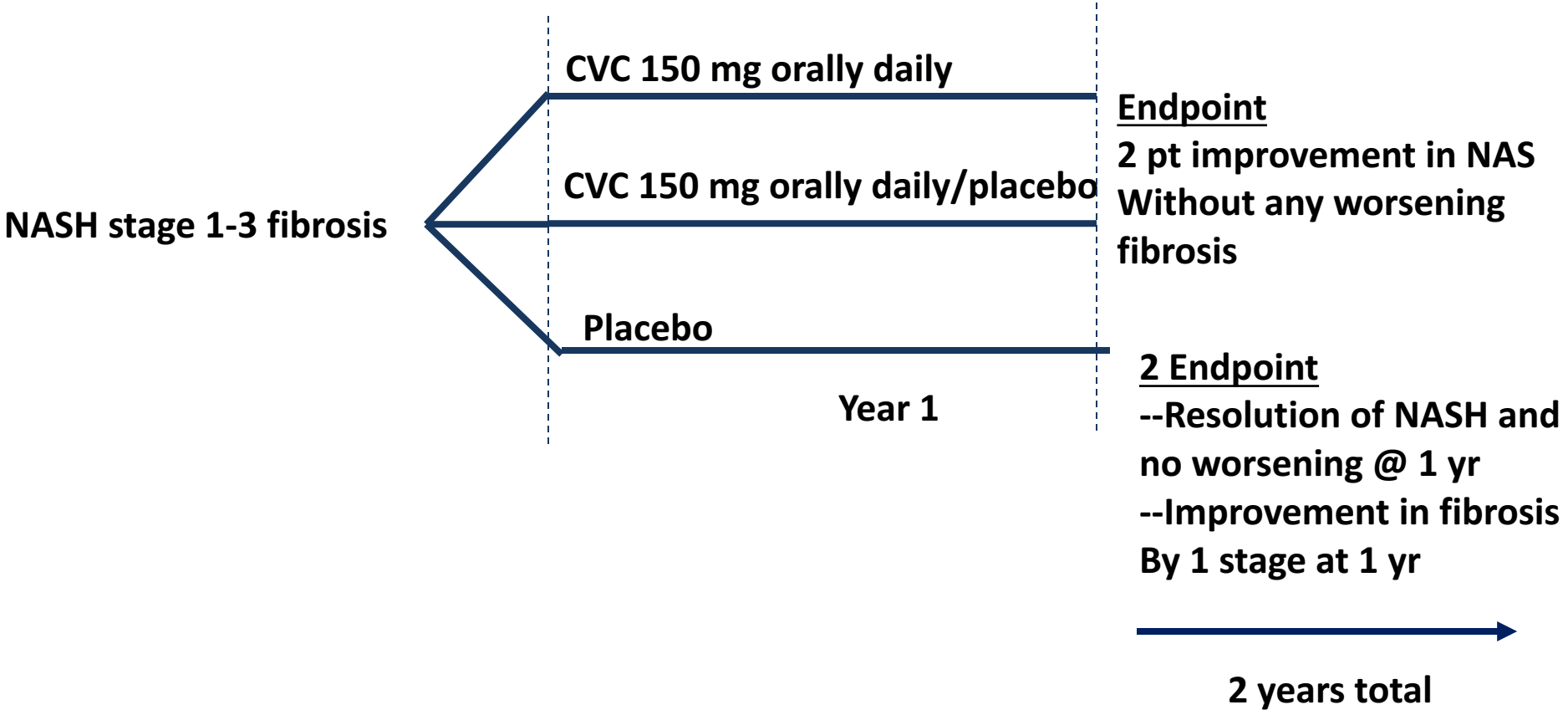
- SIM had no effect on portal pressure

Harrison S et al. EASL 2017. Abstract # PS-094

CENTAUR: Efficacy and Safety Study of Cenicriviroc for the Treatment of Nonalcoholic Steatohepatitis (NASH) in Adult Subjects With Liver Fibrosis

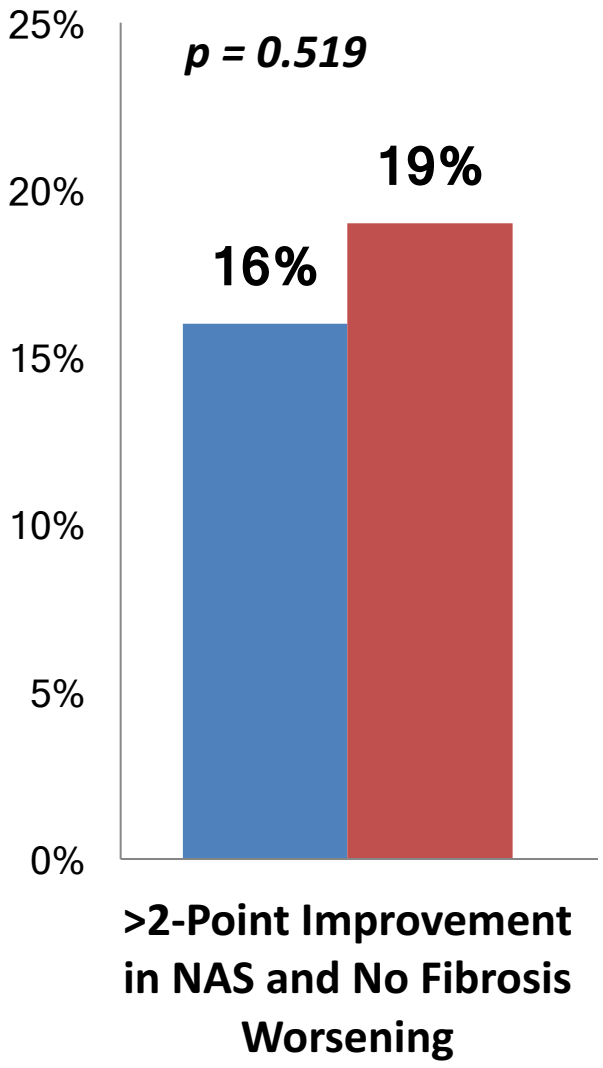
Sanyal et al. AASLD 2016, LB-1

Study Design: Cenicriviroc vs Placebo



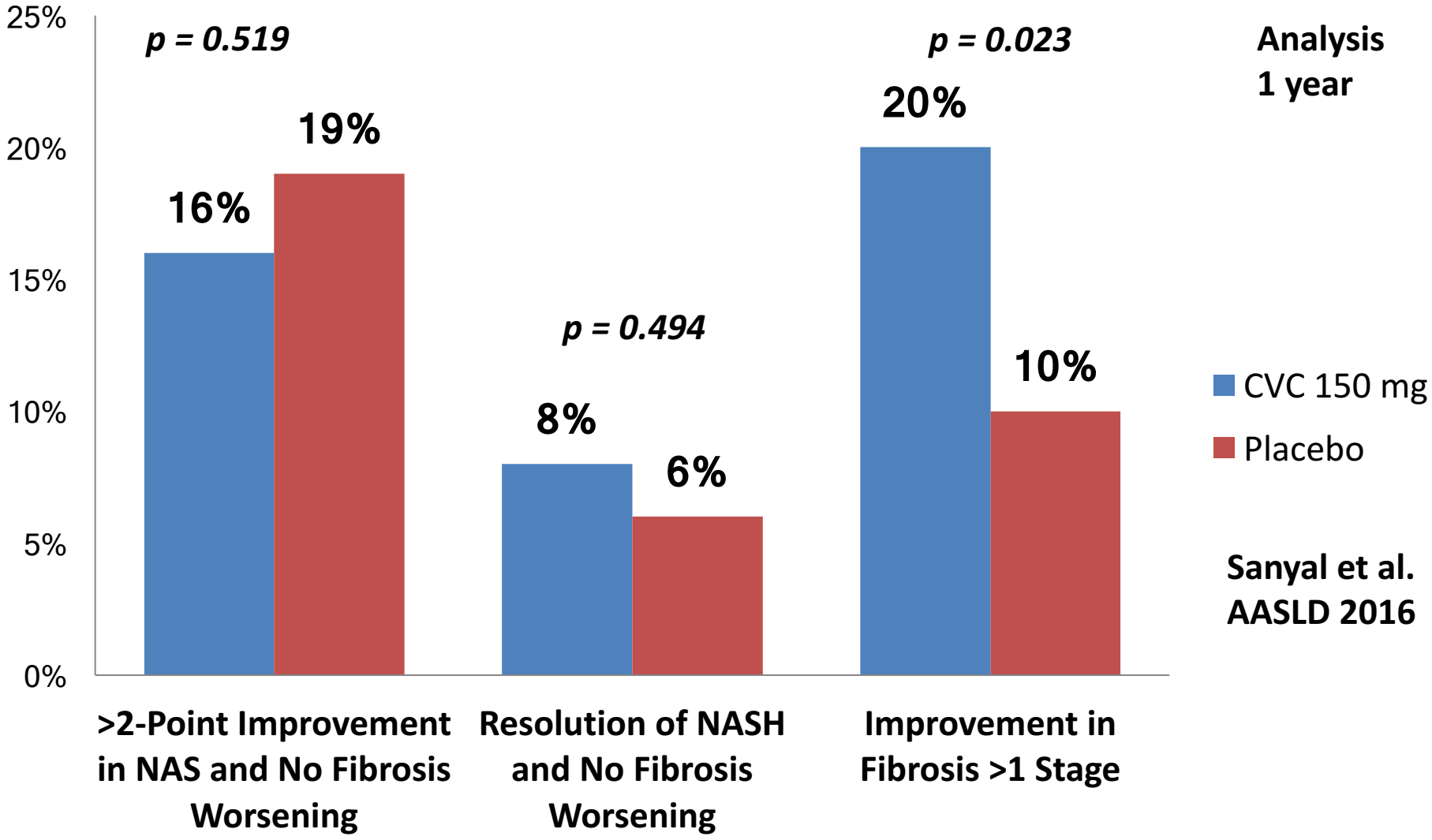
Sanyal et al. AASLD 2016, LB-1

CENTAUR: Cenicriviroc versus Placebo

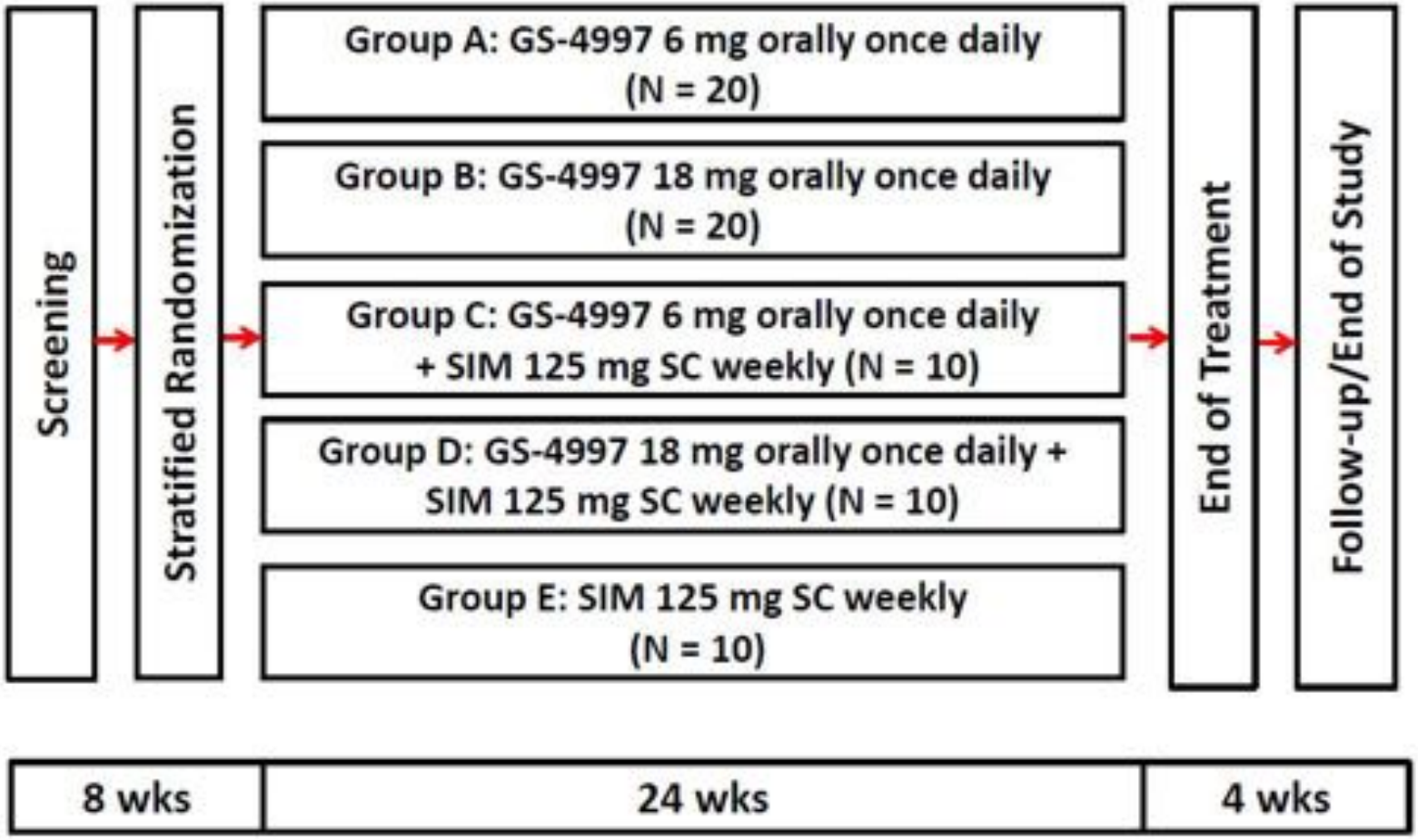


Sanyal et al. AASLD 2016

CENTAUR: Cenicriviroc versus Placebo



Study Design: ASK-I (GS-4997) and Simtuzumab combination trial



Subjects with NASH (n=72)
NAS score 5
F2-F3

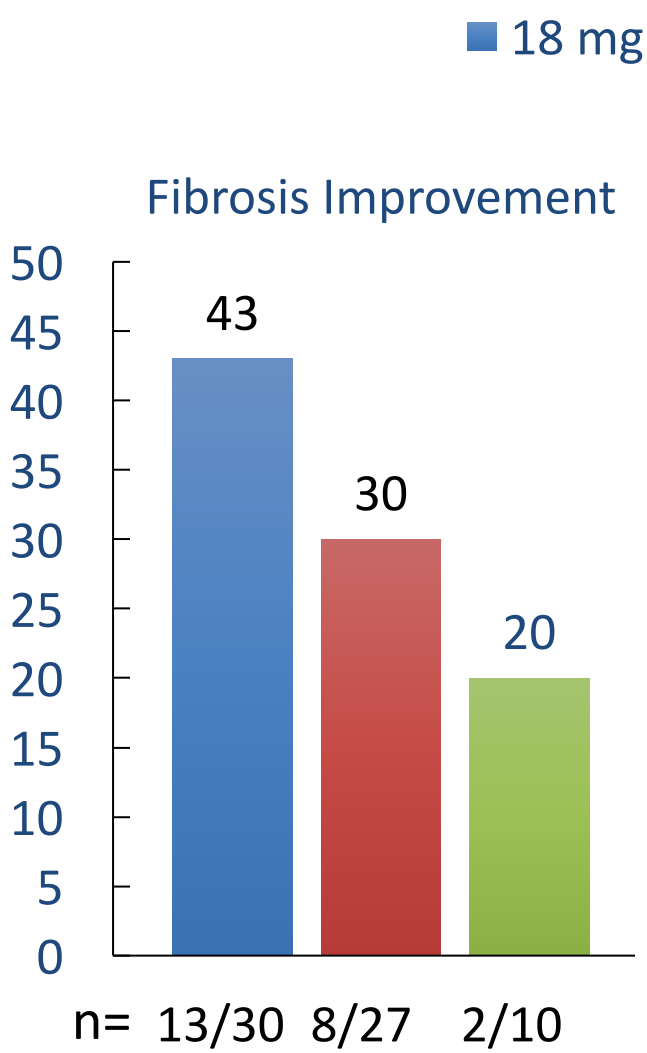
Loomba et al. AASLD 2016. LB-3

Study Design: ASK-I and Simtuzumab combination trial

SAFETY	Adverse Events and Lab abnormalities

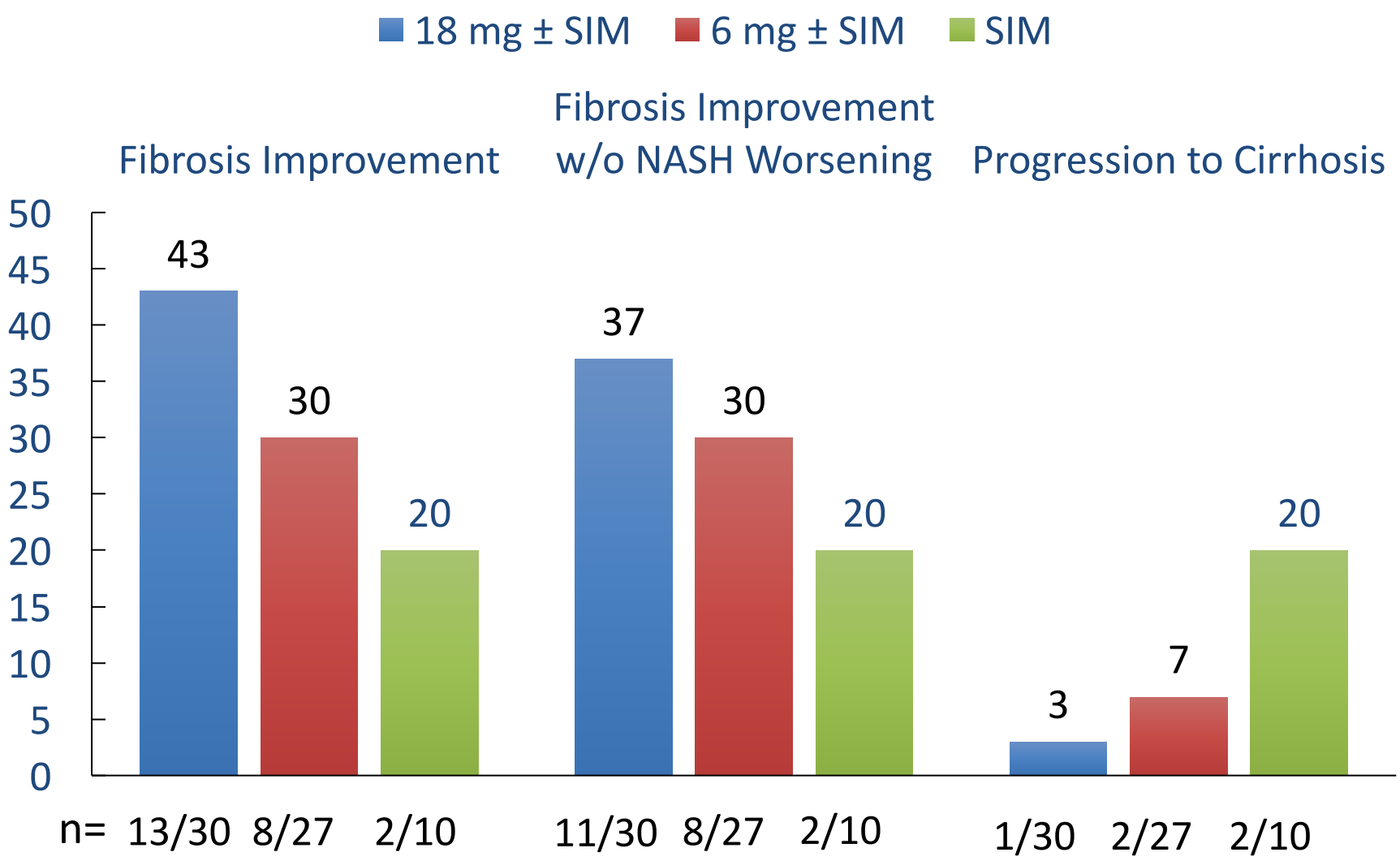
EFFICACY		
	Histology	• Fibrosis improved by 1 stage • Progression to cirrhosis
	Imaging	• >15% reduction in MRE-Stiffness • >30% reduction in MRI-PDFF
	Labs and Biomarkers	• ALT, GGT • CK-18

Study Results: ASK-I and Simtuzumab combination trial



Pts with biopsies at baseline and week 24 n=67

Study Results: ASK-I and Simtuzumab combination trial



Pts with biopsies at baseline and week 24 n=67

Nonalcoholic Steatohepatitis
Other Studies

High Prevalence of Advanced Fibrosis Among U.S. Adults with Nonalcoholic Fatty Liver Disease

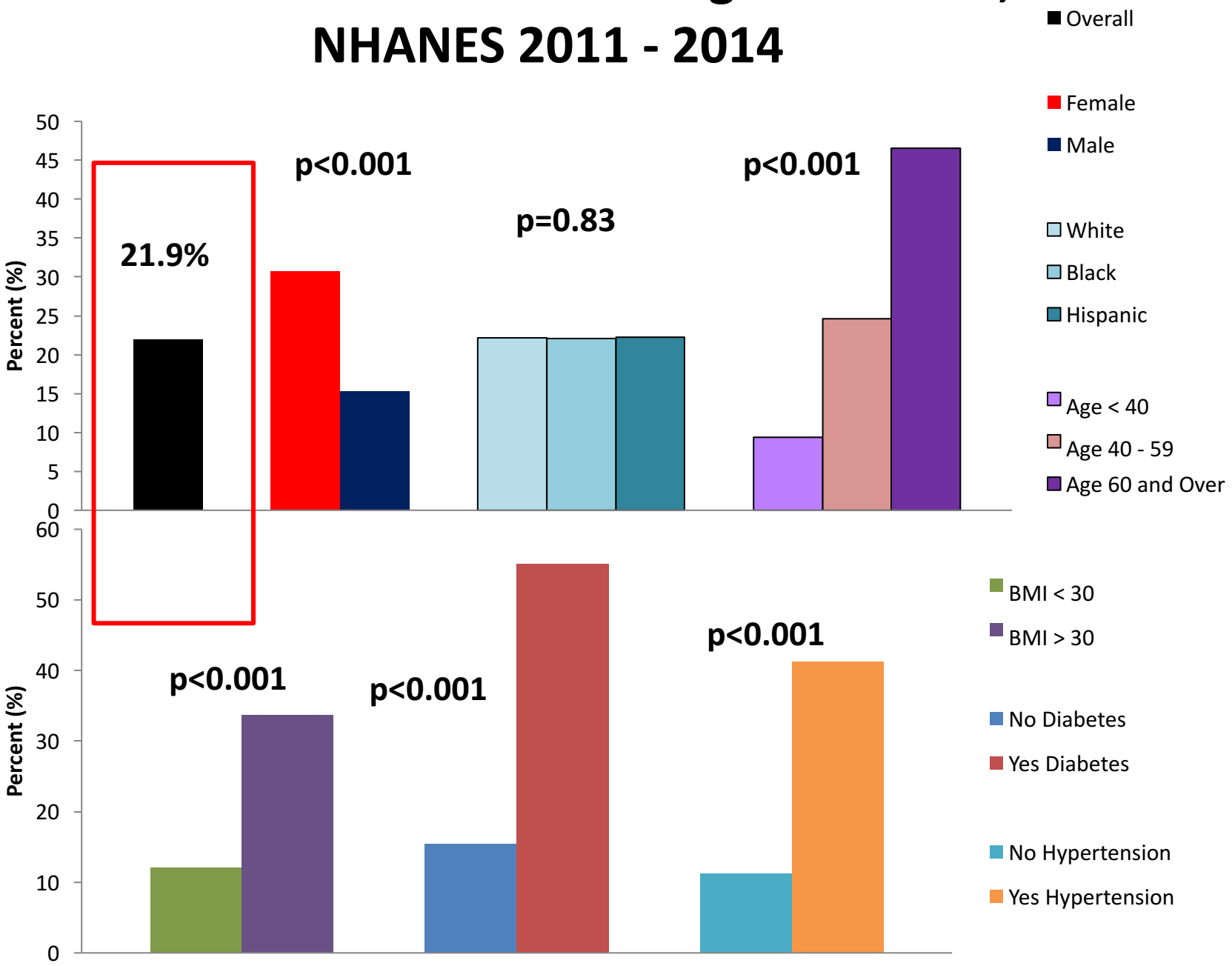
An Analysis of NHANES 2011-2014

Yu-Chi Lapid, Aristeo Lopez, Taft Bhuket, Benny Liu, Robert Wong

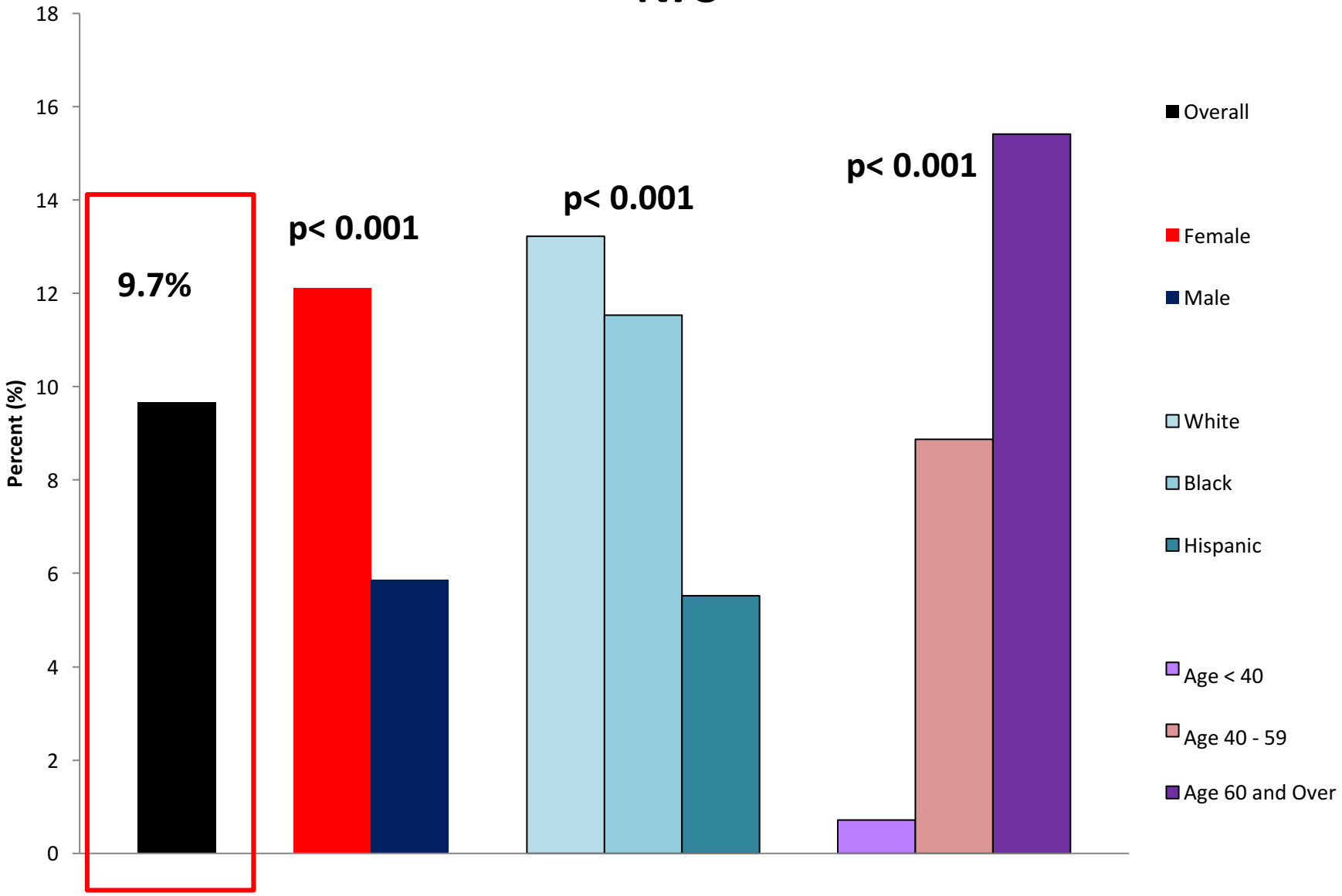
Division of Gastroenterology and Hepatology, Department of Medicine, Alameda Health System – Highland Hospital, Oakland, CA

DDW 2017. Abstract #356

Prevalence of NAFLD Among U.S. Adults, NHANES 2011 - 2014



Prevalence of Advanced Fibrosis (F3-F4) Among NAFLD Using NFS



Lapid Y et al. DDW. Abstract # 356

Predictors of NAFLD and NAFLD-Fibrosis

	NAFLD			NAFLD-AF (NFS)		
	OR	95% CI	p-value	OR	95% CI	p-value
Male (vs. female)	0.32	0.24-0.42	<0.001	0.82	0.31-2.19	0.701
Age	1.04	1.03-1.05	<0.001	**1.08**	1.03-1.13	0.001
White	1.00	Reference	-	1.00	Reference	-
Black	0.60	0.41-0.85	<0.001	0.38	0.13-1.13	0.082
Hispanic	1.04	0.73-1.5	0.796	0.30	0.08-1.07	0.063
BMI ≥ 30	2.70	2.02-3.59	<0.001	**9.10**	2.37-35.0	0.001
Diabetes	3.10	2.33-4.36	<0.001	**18.20**	4.7-70.1	< 0.001
HTN	3.00	2.24-4.1	<0.001	1.20	0.36-4.2	0.752

Lapid Y et al. DDW. Abstract # 356

Conclusion

- Using 2011 – 2014 NHANES data, overall prevalence of NAFLD among U.S. adults is 21.9%
- Using serological markers of fibrosis assessment, 9.7% of NAFLD patients have evidence of advanced fibrosis.
- Increasing age, concurrent diabetes, and obesity were associated with increased risk of advanced fibrosis

Lapid Y et al. DDW. Abstract # 356

Histologic Predictors of Progression in NASH

- In pts with bridging fibrosis (Metavir F3), **21.5%** progressed to cirrhosis after median follow-up of **25 months**
  - No difference in progression between Ishak 3 vs 4 (*P* = .39)
  - BL ballooning score 2 vs 0 associated with progression (aHR: 7.30; 95% CI: 1.72-30.91; *P* = .007)
- Risk of progression increased with greater ELF and hepatic collagen

Parameter	HR (95% CI)	*P* Value
Hepatic collagen, per 5%		
▪ BL	3.28 (2.31-4.85)	< .001
▪ Change from BL	2.99 (2.36-3.78)	< .001
ELF		
BL	3.13 (2.31-4.22)	< .001
Change from BL	1.59 (1.18-2.13)	.002

Sanyal AJ, et al. EASL 2017. Abstract GS-004.

Slide credit: clinicaloptions.com

Histologic Predictors of Progression in NASH

- In pts with cirrhosis (Metavir F4), **19.0%** had a liver-related clinical event after median follow-up of 26.7 mos
  - No difference for Ishak 5 vs 6 (*P* = .50)
- Increased risk of liver-related clinical events with higher BL hepatic collagen and ELF, worsening of fibrosis

Parameter	HR (95% CI)	*P* Value
BL Ishak stage 5 vs 6	1.25 (0.68-2.29)	.48
No improvement vs improvement	9.63 (1.33-69.81)	.025
Hepatic collagen, per 5%		
BL	1.38 (1.15-1.69)	< .001
Change from BL	1.20 (1.03-1.39)	.017
ELF		
▪ BL	2.37 (1.69-3.31)	< .001
▪ Change from BL	1.54 (1.10-2.15)	.002

Sanyal AJ, et al. EASL 2017. Abstract GS-004

Slide credit: clinicaloptions.com

No Benefit from Modest Alcohol Use in Nonalcoholic Fatty Liver Disease

- Aim: Using a well-characterized longitudinal cohort:
- To compare histological progression of NAFLD between modest alcohol users (≤ 2 drinks/day) and those abstaining from alcohol use

Ajmera V et al. AASLD 2016

Change in Histology by Baseline Drinking Status

Characteristic	Non-drinker (n=117)	Modest drinker (n=168)	P
Mean Difference			
Steatosis	-0.49	-0.30	0.04
Lobular Inflammation	-0.25	-0.26	0.86
Hepatocyte Ballooning	-0.24	-0.16	0.43
Fibrosis Stage	0.06	0.08	0.85
NASH Resolution (%)	21	13	0.13

Ajmera V et al. AASLD 2016

Change in Clinical Features by Baseline Drinking Status

Characteristic	Mean Change		P
	Non-drinker (n=117)	Modest drinker (n=168)	
ALT, U/L	-24.7	-17.1	0.09
AST, U/L	-7.3	+2.3	0.04
Alkaline Phosphatase, U/L	-15.9	-13.0	0.42
HOMA-IR	+0.6	+1.0	0.74
Triglycerides, mg/dL	-16.7	-2.9	0.26
HDL, mg/dL	+1.9	+0.5	0.17
BMI, kg/m^2	-0.3	+0.2	0.14

Ajmera V et al. AASLD 2016

Multivariate* Models: OR for NASH Resolution by Drinking History (n=195)

Drinking Status		% (x/N)
Baseline	Follow-up	
Consistent drinking		
Non-drinker	Non-drinker	22% (17/78)
Modest drinker	Modest drinker	11% (7/66)

*Adjusted for Age, Race, Sex, Smoking History

Ajmera V et al. AASLD 2016

Conclusions

- Modest alcohol use had no benefit on NAFLD histology compared to abstention over an average period of four years
- Modest alcohol use was associated with significantly increased AST, less improvement in steatosis and less NASH resolution

Ajmera V et al. AASLD 2016

HCC

HCC Outcomes on HCV DAA Therapy

HCC Recurrence Equivalent With DAAs and IFN

- **Meta-analysis and meta-regression analysis comparing risk of HCC after SVR with DAA- vs IFN-based therapy in 41 studies (n = 13,875)**

Pts With First HCC Occurrence After SVR

Characteristic	DAA	IFN
Age, yrs	60	52
Cirrhosis, %	90	87
Child-Pugh Class B/C, %	34	0
Follow-up, yrs	1.0	5.5

Pts With HCC Recurrence After SVR

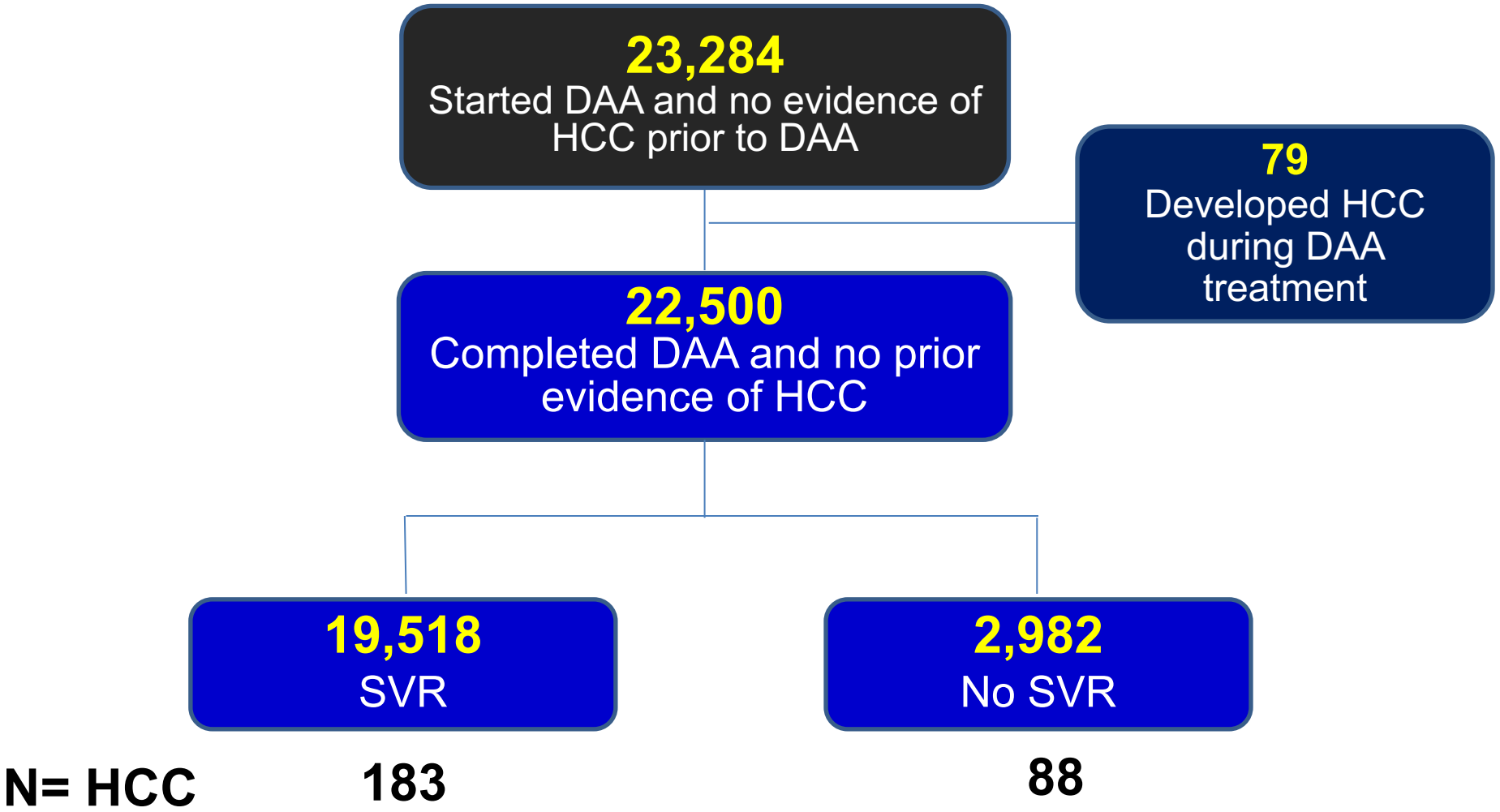
Characteristic	DAA	IFN
Pts with previous curative HCC treatment, %	96	100
Follow-up, yrs	1.3	5.0

- **After adjusting for these factors, no difference in risk of HCC occurrence (aRR: 0.75) or recurrence (aRR: 0.62) between DAAs and IFN**

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

Slide credit: clinicaloptions.com

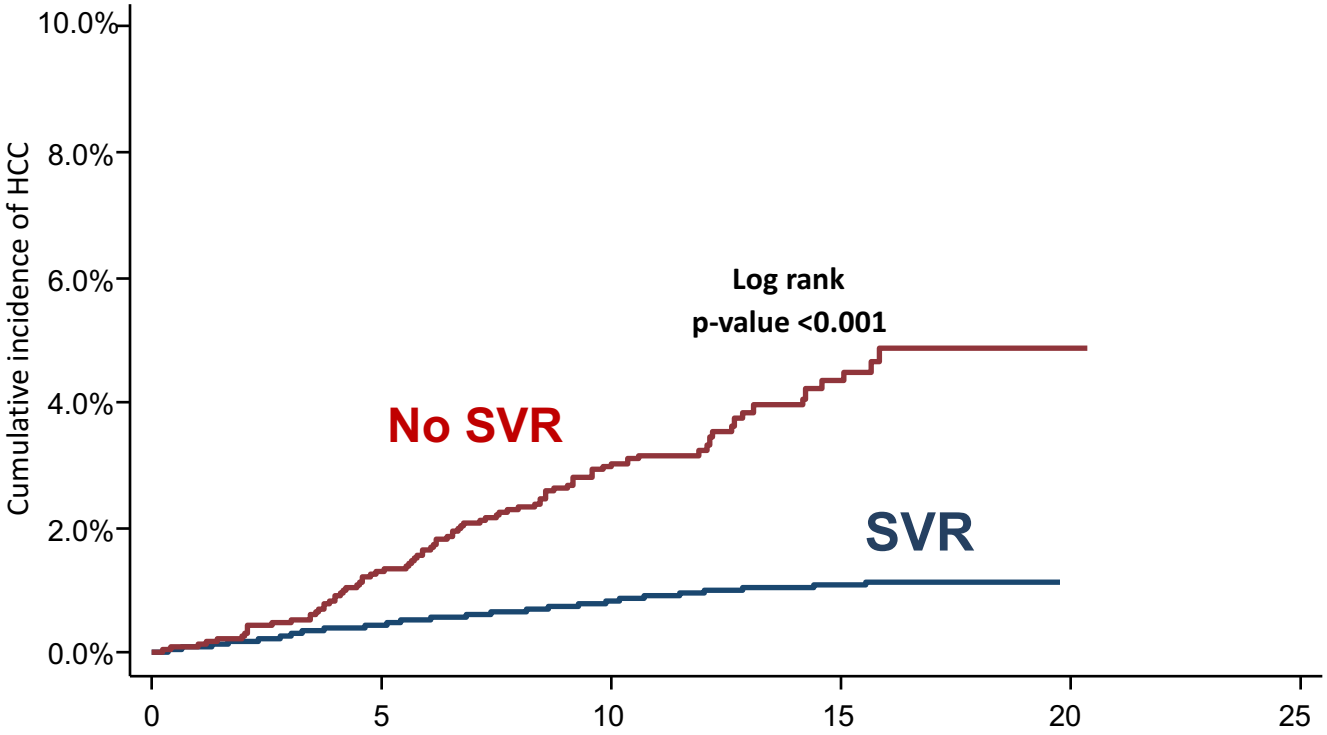
Risk of Hepatocellular Cancer in HCV Patients Treated with Direct Acting Antiviral Agents



Kanwal et al. DDW 2017. Abstract # 419

Results

Cumulative HCC incidence rates by SVR

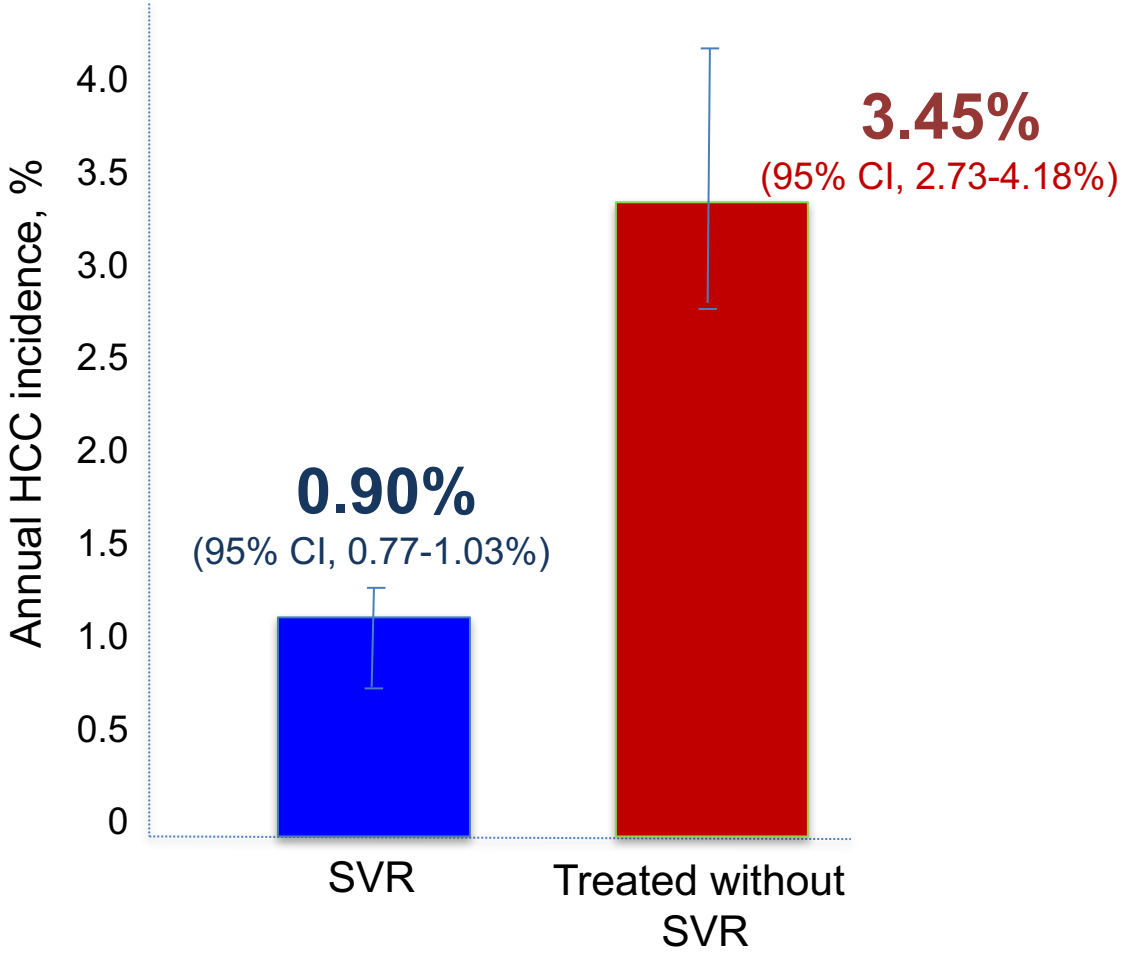


N at risk (N HCC)											
SVR	19518	(85)	19372	(68)	14364	(29)	6128	(1)	0	(0)	0
No SVR	2982	(35)	2453	(36)	1617	(14)	636	(3)	5	(0)	0

Kanwal et al. DDW 2017. Abstract # 419

Results

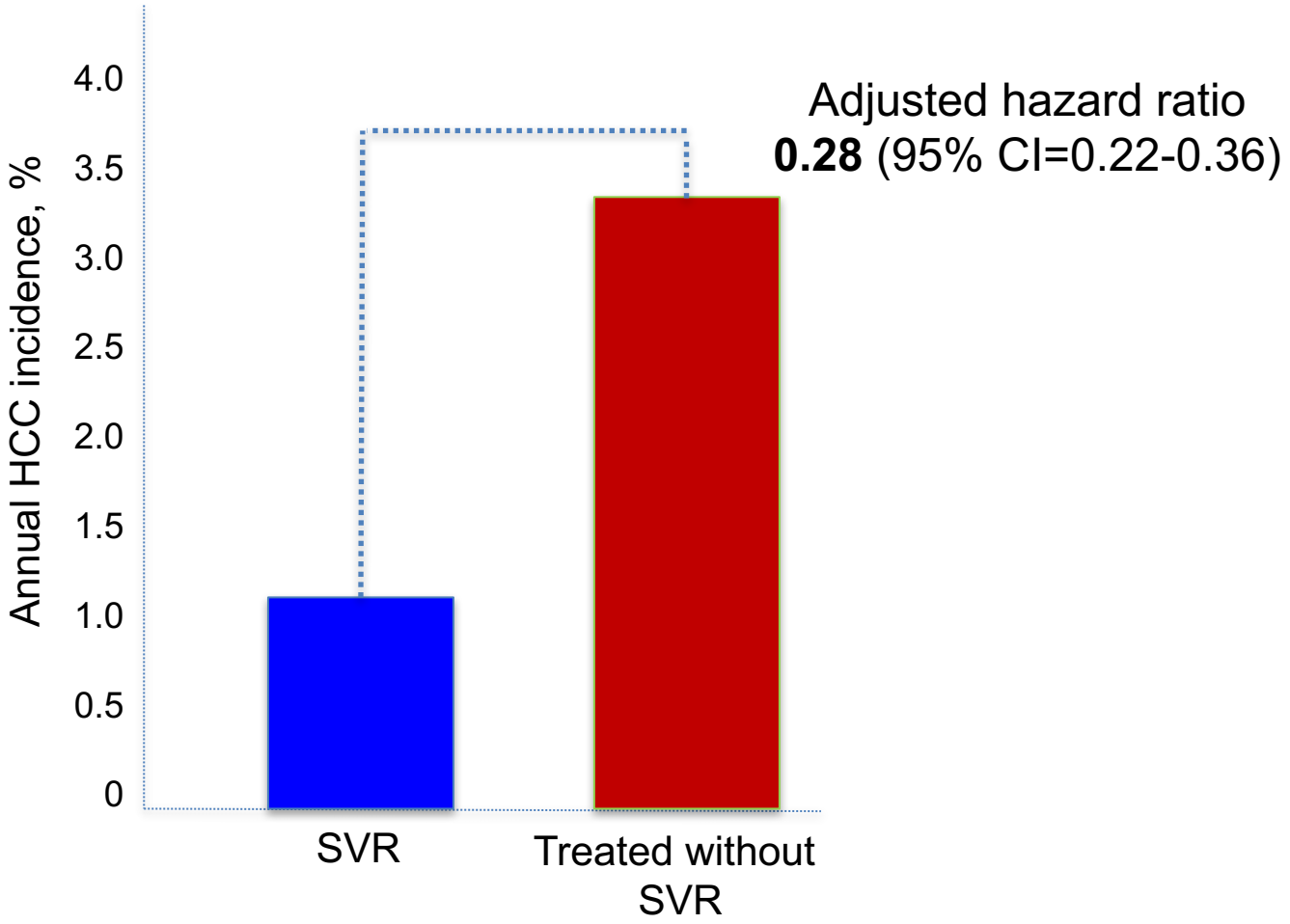
Annual HCC incidence rates by SVR



Kanwal et al. DDW 2017. Abstract # 419

Results

Effect of SVR on risk of HCC



Kanwal et al. DDW 2017

Results

Factors associated with risk of HCC in patients with SVR

Characteristics	Adjusted hazard ratio (95% CI)
Age ≥65 year	1.30 (0.96-1.76)
Female	0.38 (0.10-1.54)
Race (ref: white)	
African Americans	0.56 (0.39-0.81)
Hispanic	1.22 (0.65-2.27)
Cirrhosis	4.73 (3.34-6.68)
HIV coinfection	0.95 (0.42-2.13)
Diabetes	1.28 (0.92-1.78)
Alcohol abuse	1.56 (1.11-2.18)
HCV genotype (ref: GT 1)	
2	0.70 (0.34-1.42)
3	0.72 (0.29-1.75)
4-6	0.56 (0.08-3.99)

Kanwal et al. DDW 2017. Abstract # 419

Results

Characteristics of patients with early *vs*. delayed HCC

Characteristic,%	Early HCC (during treatment) N=79	Late HCC (after treatment) N=271	P value
Cirrhosis	69.6	73.8	0.46
AJCC Stage			0.81
I	44.8	50.6	
II	31.0	24.1	
III/IV	10.4	7.6	
Missing	13.8	17.7	
Tumor size (largest tumor)			0.27
< 2 cm	24.1	26.6	
2-5 cm	51.7	50.6	
More than 5 cm	13.8	3.8	
Missing	10.4	19.0	

Kanwal et al. DDW 2017

Conclusions

- Among patients treated with DAA, SVR resulted in a considerable reduction in the risk of HCC
- Based on this study there is no evidence to suggest that DAAs promote HCC either during or after treatment
- However, the absolute risk of HCC was high in several patient groups who achieved SVR, including ~40% of patients who have already progressed to cirrhosis
  - Annual HCC risk was 1.81% in patients with cirrhosis

Kanwal et al. DDW 2017. Abstract # 419

Direct-acting Antivirals for Hepatitis C Do Not Increase the Risk of Hepatocellular Carcinoma Recurrence After Locoregional Therapy or Liver Transplant Waitlist Dropout

- **AIM** To compare HCC recurrence after locoregional therapy (LRT), waitlist dropout, and liver transplantation (LT) among patients with HCV and HCC on the LT waitlist who had:

1) DAA therapy before HCC diagnosis (n=29)
2) DAA therapy after HCC diagnosis (n=62)
3) No DAA therapy (n=87)

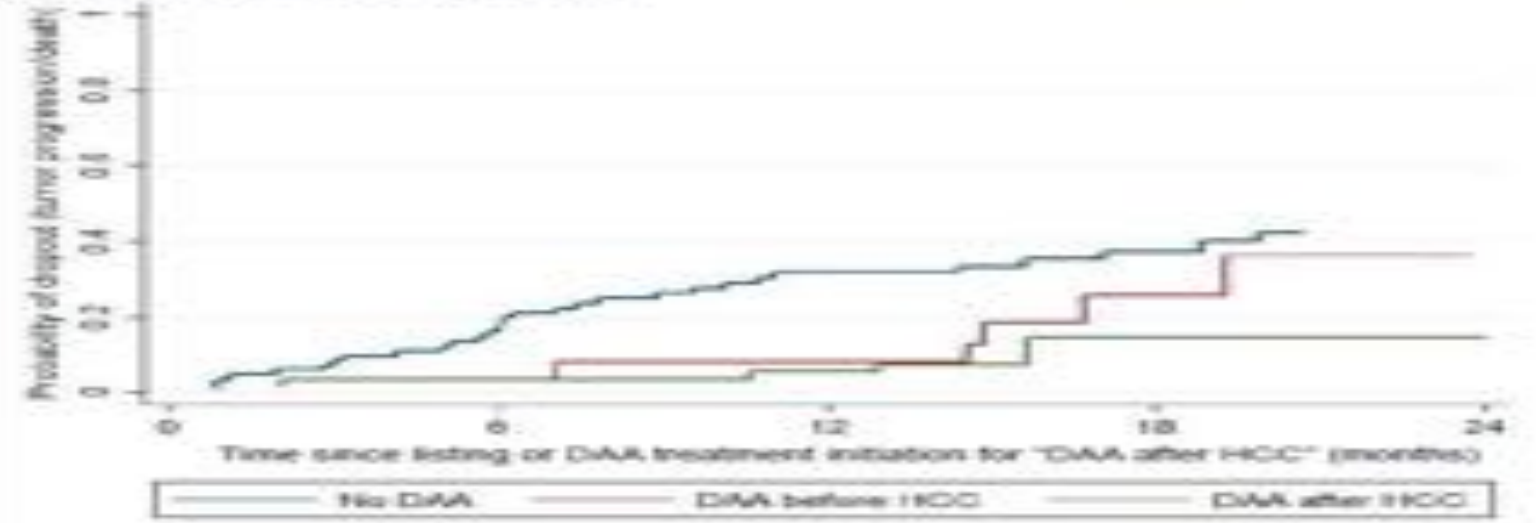
Huang, A et al. EASL 2017, Abstract # LBP-508

DAA for HCV Do Not Increase the Risk of HCC Recurrence After Locoregional Therapy or Liver Transplant Waitlist Dropout

Table: Univariate and multivariate analysis of dropout by competing risk regression

	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)*	p-value
DAA group ("no DAA" as reference)				
DAA before HCC	0.48 (0.21-1.08)	0.08	0.47 (0.19-1.18)	0.11
DAA after HCC	0.20 (0.08-0.48)	<0.001	0.22 (0.09-0.57)	0.002

Figure 1a. Cumulative incidence of waitlist dropout due to tumor progression by DAA group



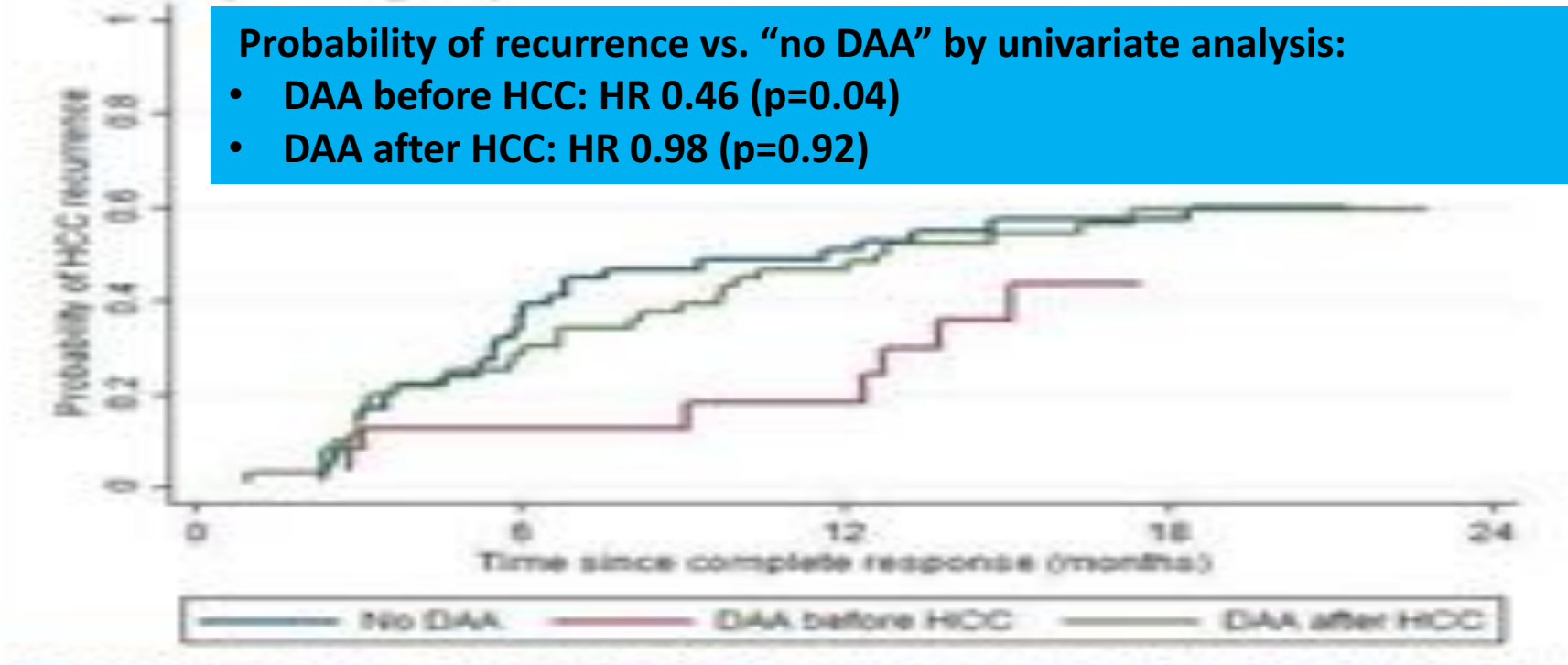
Huang, A et al. EASL 2017, Abstract # LBP-508

DAA for HCV Do Not Increase the Risk of HCC Recurrence After Locoregional Therapy or Liver Transplant Waitlist Dropout

Figure 1b. Cumulative incidence of HCC recurrence while on waitlist by DAA group

Probability of recurrence vs. "no DAA" by univariate analysis:

- **DAA before HCC: HR 0.46 (p=0.04)**
- **DAA after HCC: HR 0.98 (p=0.92)**



Huang, A et al. EASL 2017, Abstract # LBP-508

Conclusion

- In LT candidates with HCV and HCC treated with LRT with initial complete response, DAA use is not associated with increased risk of HCC recurrence or waitlist dropout

- These results support the use of DAA therapy in patients on the transplant waitlist with HCC who have achieved initial response to LRT

Huang, A et al. LB Abstract EASL 2017

HCC Treatment Studies

CheckMate 040: Nivolumab in Sorafenib-Experienced Pts With HCC ± HCV or HBV

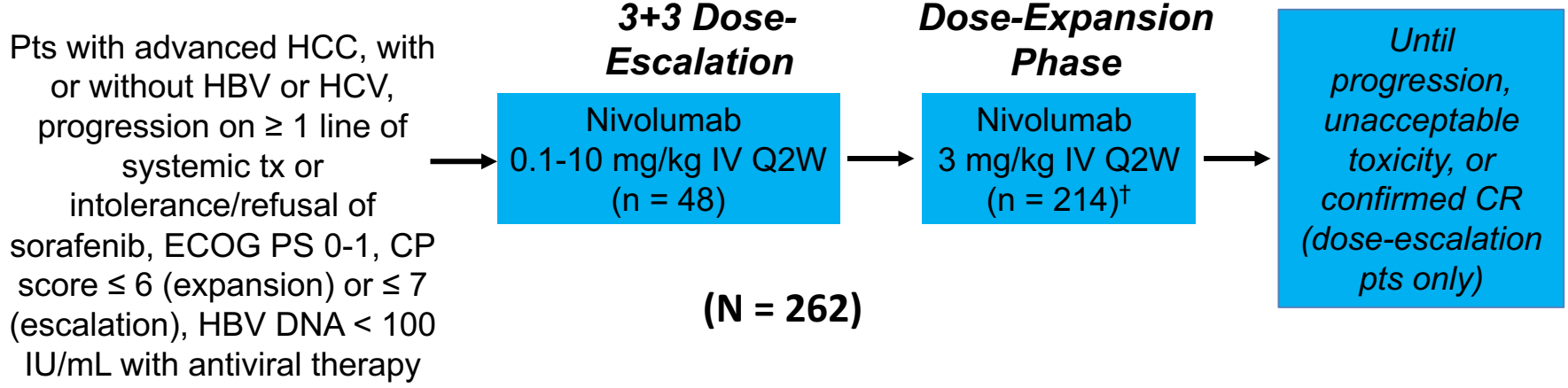
- International, open-label, noncomparative, phase I/II dose-escalation and multicohort dose-expansion study in sorafenib-naive and sorafenib-experienced pts
- **Nivolumab: fully human IgG4 mAb and PD-1 checkpoint inhibitor**

Sangro B, et al. EASL 2017. Abstract GS-010.

Slide credit: clinicaloptions.com

CheckMate 040: Nivolumab in Sorafenib-Experienced Pts With HCC ± HCV or HBV

- International, open-label, noncomparative, phase I/II dose-escalation and multicohort dose-expansion study in sorafenib-naive and sorafenib-experienced pts
- Nivolumab: fully human IgG4 mAb and PD-1 checkpoint inhibitor



- **Primary endpoints: objective response rate, safety (escalation only)**
- **Current analysis: sorafenib-experienced pts in dose-expansion phase (n = 145)**

Sangro B, et al. EASL 2017. Abstract GS-010.

Slide credit: clinicaloptions.com

Nivolumab in Sorafenib-Experienced Pts With HCC ± HCV or HBV: Efficacy

- **Objective response of 14.5% (independent of PD-L1 expression), with 57% of responses in ≤ 3 mos**

Outcome	Infection Status		
	HCV (n = 30)	HBV (n = 43)	Uninfected (n = 72)
Objective response, n (%)*	6 (20.0)	6 (14.0)	9 (12.5)
▪ Complete	1 (3.3)	1 (2.3)	0
▪ Partial	5 (16.7)	5 (11.6)	9 (12.5)
▪ Stable	9 (30.0)	14 (32.6)	37 (51.4)
▪ Progressive	11 (36.7)	22 (51.2)	23 (31.9)
▪ Not evaluable	4 (13.3)	1 (2.3)	3 (4.2)
Median time to response, mos (range)	2.1 (1.2-7.0)	2.0 (1.2-6.8)	4.0 (2.6-6.8)
1-yr OS, % (95% CI)	67.1 (46.2-81.4)	55.6 (39.6-69.0)	59.7 (47.4-70.0)

Sangro B, et al. EASL 2017. Abstract GS-010.

*By BICR using RECIST v1.1.

Slide credit: clinicaloptions.

Nivolumab in Sorafenib-Experienced Pts With HCC ± HCV or HBV: Safety

- Safety profile consistent with other tumor types, with most ALT/AST elevations reversible

Endpoint, n (%)	Infection Status		
	HCV (n = 30)	HBV (n = 43)	Uninfected (n = 72)
Study tx d/c	22 (73)	35 (81)	59 (82)
▪ Progression	17 (57)	34 (79)	51 (71)
▪ Toxicity	2 (7)	0	2 (3)
Tx-related AE*	25 (83)	30 (70)	53 (74)
▪ Grade 3/4	9 (30)	4 (9)	11 (15)
Grade 3/4 ALT increase	1 (3)	0	2 (3)
Grade 3/4 AST increase	2 (7)	0	2 (3)

*In ≥ 5% pts: fatigue, pruritus, rash, diarrhea, nausea, dry mouth,

- **No SVR in HCV-infected pts**
- **No anti–HBs seroconversion in HBV-infected pts**

Sangro B, et al. EASL 2017. Abstract GS-010.

Slide credit clinicaloptions.com

SARAH: Selective Internal Radiation vs Sorafenib in HCC

Open-label, randomized phase III trial of SIRT with yttrium-90 microspheres vs sorafenib 400 mg BID in pts with HCC (N = 459)

Parameter	SIRT (n = 237)	Sorafenib (n = 222)	*P* Value
Median overall survival, mos	8.0	9.9	.179
Median progression-free survival, mos	4.1	3.7	.765
Response rate, %	19.0	11.6	.042
Treatment-related AEs			
Overall, n	1297	2837	--
Grade ≥ 3, n	230	411	--
Pts with ≥ 1, n (%)	173 (76.5)	203 (94.0)	< .001
Pts with ≥ 1 grade ≥ 3, n (%)	92 (40.7)	136 (63.0)	< .001

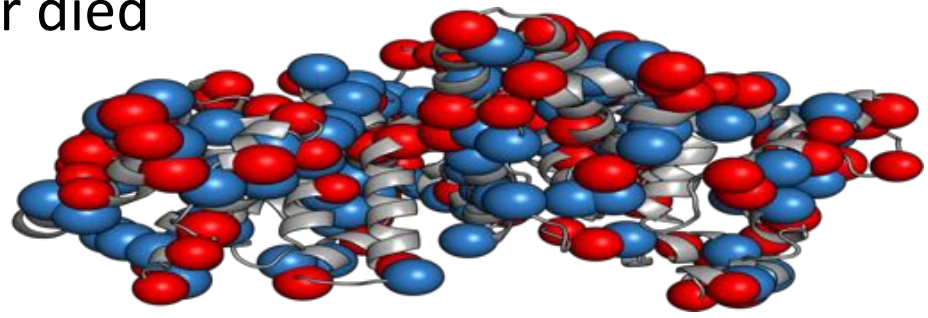
Vilgrain V, et al. EASL 2017. Abstract GS-012

Slide credit: clinicaloptions.com

Cirrhosis Complications and Other

Long Term Albumin Improves Survival in Decompensated Cirrhosis: “ANSWER” study

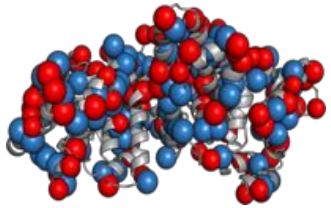
- 431 pts, cirrhosis and uncomplicated ascites
- All on diuretics (aldactone around 200 mg/day and furosemide at least 25 mg/day)
- 218 patients were randomized to receive human albumin 40 g twice a week for the first 2 weeks, and thereafter received 40 g per week. 213 in SMT
- Patients were followed for 18 months or until frequent refractory ascites, TIPS, OLT or died



Carceni, P et al. EASL. LB-4191

Long Term Albumin Improves Survival in Decompensated Cirrhosis: "ANSWER" study

- Overall survival at 18 months — was significantly better in the albumin group than in the SMT group



(78% vs 66%; P = .028. 38% RR reduction)

Outcome	Incidence Rate Ratio	P Value
Hospitalization	**0.65**	**<.0001**
Paracentesis	**0.46**	**<.0001**
Refractory ascites	**0.54**	**<.0001**
SBP	**0.32**	**<.0001**
Renal dysfunction	**0.50**	**<.0001**
HE grades III and IV	**0.48**	**<0.0001**

Carceni, P et al. EASL. LB-4191

FMT is Safe, Associated with lower hospitalization and improved cognitive function in recurrent HE

- **Aim**: To define the safely profile, impact on liver and cognition of FMT for recurrent HE using rationally-derived stool donor

- FMT arm received 5 days of antibiotics then a single FMT enema (90ml) from the same donor (OpenBiome)
- 20 cirrhotic men (all on lactulose/rifaximin), last HE 4 months ago, randomized 1:1 to FMT or SOC
- Both arms were similar in age, MELD, albumin and etiology
- F/u: Day 5,6,12,35 & 150

Bajaj J et al. EASL 2017. Abstract# PS-085

FMT is Safe, Associated with lower hospitalization and improved cognitive function in recurrent HE

Event (150 day period)	Transplant Group, n=10	Standard-Care Group, n =10
Hospitalization	2	11
Hospitalization to HE	0	6
Infections	0	2
Variceal bleeding	0	2

Bajaj J et al. EASL 2017. Abstract# PS-085

The BEZURSO study (Bezafibrate in Combination with Ursodeoxycholic Acid in PBC)

- 2-year double-blind, multicenter, placebo-controlled
- Incomplete response to ursodiol
- All patients on ursodiol 13 to 15 mg/kg
- 50 patients were randomized to daily bezafibrate 400 mg and 50 to placebo

The primary outcome — a complete biochemical response at 2 years — was defined as normal bilirubin, alkaline phosphatase, ALT was seen more in bezafibrate group than in the placebo group (30% vs 0%; $P < .001$).

Corpechot et al. EASL 2017 LBO-01

The BEZURSO study (Bezafibrate in Combination with Ursodeoxycholic Acid in PBC)

Changes (%) BS to 24 m	Bezafibrate Group (n=50)	Placebo Group (n=50)	*P* Value
Alkaline phosphatase, %	–60	0	<0.0001
Total bilirubin, %	–14	18	<0.0001
ALT	–36	0	<0.0001
IgM	–21	–2	0.25
Cholesterol	–16	0	<0.0001
Itch Score	–75	0	<0.01

BZF in combination with UDCA normalizes biochemical prognostic markers, improves pruritus in PBC patients with inadequate response to UDCA

Corpechot et al. EASL 2017 LBO-01

Thank you

Email: bilal.hameed@ucsf.edu