REAL-WORLD EFFECTIVENESS OF HEPATITIS C VIRUS (HCV) TREATMENT WITH DIRECT-ACTING ANTIVIRALS (DAA) IN POPULATIONS WITH FATTY LIVER/NON-ALCOHOLIC STEATOHEPATITIS (FL/NASH), DECOMPENSATED CIRRHOSIS (DCC), HEPATOCELLULAR CARCINOMA (HCC), AND/OR POST LIVER TRANSPLANT (PTX)

ISPOR Improving healthcare decisions

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1. OBJECTIVES

DAA therapies are highly effective for treatment of HCV, however their efficacy in patients with existing advanced liver disease (ALD) has not been well described, especially in real-world populations. This study assessed utilization patterns and outcomes with DAAs in patients with HCV and ALD (FL/NASH, DCC, HCC, and/or PTX).

2. METHODS

Data were collected using Trio Health's disease management program and are specific to patients with physician-reported ALD at therapy initiation occurring between October 2015 to February 2019 and with ≥9 months follow-up.

Patient characteristics were summarized using N (%), and comparisons between patient characteristics and SVR were computed using Fisher's Exact Test.

SVR confidence intervals were computed using binomial exact method.

3. RESULTS

Of 667 patients with ALD, 9% had NASH, 22% FL, 31% DCC, 31% HCC, and 21% were PTX. Overall, 70% were male, 35% age >65, 50% (299/602) FIB4 >3.25, 20% (122/617) eGFR < 60 ml/min, 25% diabetes, 55% hypertension, 17% (110/653) >6M HCV viral load, and 74% (491/666) treatment-naïve. Majority (91%, 538/667) were treated with ledipasvir-sofosbuvir (51%), sofosbuvir-velpatasvir (18%), glecaprevir-pibrentasvir (12%), elbasvir-grazoprevir (6%), or sofosbuvir-velpatasvir-voxilaprevir (5%) [Table 2].

In intent to treat (ITT) ALD patients, sustained virologic response [SVR] was 84% (CI 81%-86%); per protocol (PP) SVR was 95% (CI 93%-96%) with 5% virologic failure. Differences in ITT vs PP SVRs were due to loss of follow-up (37 patients, 6%), death (22, 3%), and treatment discontinuation (20, 3%). Within this ALD study population, ITT SVR [95% CI] was lowest in patients with DCC (74% [68%-80%]) due to a higher rate of patient death relative to the overall study population (9% v. 3%, respectively) [Table 3; Figure 2].

PP SVRs were similar between overlapping ALD subgroups and ranged from 92% to 97% [Table 4; Figure 2].

TABLE 1: PATIENT DISPOSITION

	N	%
Advanced liver disease not indicated	19315	97%
With advanced liver disease	667	3%
Total	**19982**	**100%**

FIGURE 1: REGIMEN DISPENSE BY ADVANCED LIVER DISEASE

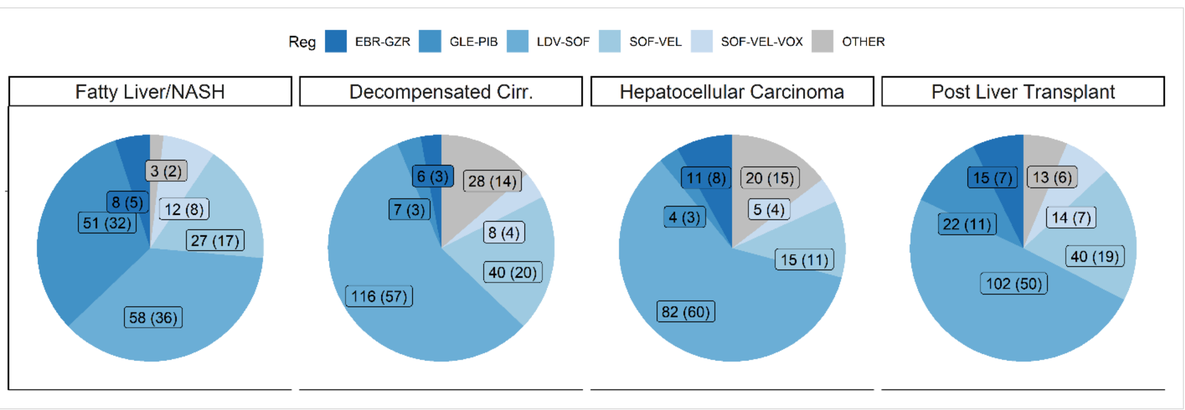

FIGURE 2: ITT AND PP SVR RATES BY ALD

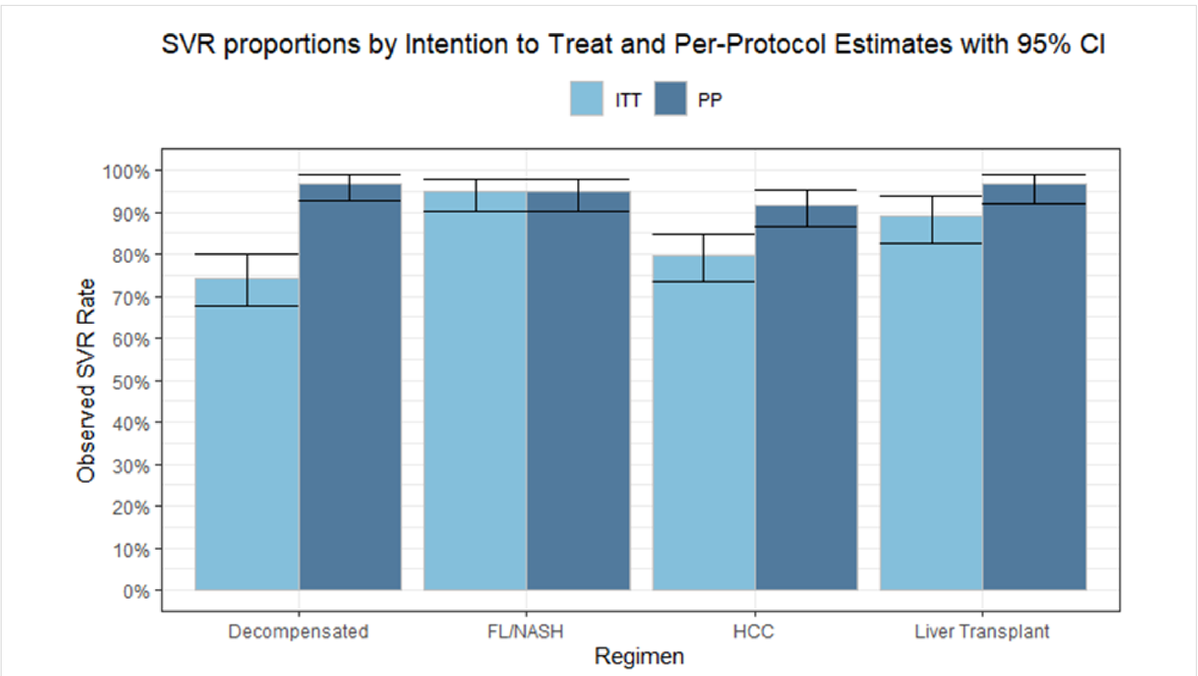

TABLE 2: PATIENT CHARACTERISTICS

	Advanced Liver Disease n/N (%)
Gender	
Female	202/667 (30.3)
Male	465/667 (69.7)
Race/Ethnicity	
Asian	15/530 (2.8)
Black or African-American	89/530 (16.8)
Declined to Answer	111/530 (20.9)
Hispanic or Latino	50/530 (9.4)
Other Race	13/530 (2.5)
White	252/530 (47.5)
Age at Treatment Initiation	
18-49	69/667 (10.3)
50-64	366/667 (54.9)
65+	232/667 (34.8)
Practice Type	
Academic	175/667 (26.2)
Community	492/667 (73.8)
Payer Type	
Commercial	172/667 (25.8)
Medicaid	126/667 (18.9)
Medicare	357/667 (53.5)
Other Payer	12/667 (1.8)
eGFR <60ml/min	122/617 (19.8)
FIB4 >3.25	299/602 (49.7)
HCV Viral Load >6MM	110/653 (16.8)
Genotype	
GT1	502/659 (76.2)
GT2	58/659 (8.8)
GT3	86/659 (13.1)
GT4-6	13/659 (2.0)
Prior Treatment	
Treatment Naive	497/667 (74.5)
SOF Regimen	57/170 (33.5)
PEG or PEG +RBV	90/170 (52.9)
Other DAAs	12/170 (7.1)
Unspecified	11/170 (6.5)
Advanced Liver Diseases (Overlapping Categories)	
Fatty Liver/NASH	159/667 (23.8)
Decompensated cirrhosis	205/667 (30.7)
Hepatocellular Carcinoma	206/667 (30.9)
Post Liver Transplant	137/667 (20.5)
Comorbidities	
HIV	12/667 (1.8)
HBV	20/667 (3.0)
Anxiety	102/667 (15.3)
Depression	127/667 (19.0)
Diabetes	169/667 (25.3)
Hyperlipidemia	91/667 (13.6)
Hypertension	370/667 (55.4)

4. LIMITATION

SVR outcomes were not adjusted for patient characteristics at therapy initiation.

TABLE 3: UNADJUSTED ITT OUTCOMES (OVERLAPPING POPULATIONS)

N (%)	Fatty Liver/NASH	DCC	HCC	Post Liver Tx	Any ALD
Discontinued	0 (0)	11 (5)	6 (3)	5 (4)	20 (3)
Lost to Follow Up	0 (0)	18 (9)	14 (7)	6 (4)	37 (6)
Patient Expired	0 (0)	19 (9)	7 (3)	0 (0)	22 (3)
SVR Achieved	151 (95)	152 (74)	164 (80)	122 (89)	557 (84)
SVR Not Achieved	8 (5)	5 (2)	15 (7)	4 (3)	31 (5)
Grand Total	159	205	206	137	667

TABLE 4: UNADJUSTED OUTCOMES WITHIN ALD GROUPS (OVERLAPPING POPULATIONS)

		ITT			PP		
ALD	Cure	N	SVR	SVR 95% CI	N	SVR	SVR 95% CI
FL/NASH	151	159	0.95	(0.90-0.98)	159	0.95	(0.90-0.98)
DCC	152	205	0.74	(0.68-0.80)	157	0.97	(0.93-0.99)
Post Liver Transplant	122	137	0.89	(0.83-0.94)	126	0.97	(0.92-0.99)
HCC	164	206	0.80	(0.74-0.85)	179	0.92	(0.87-0.95)
Any ALD	557	667	0.84	(0.81-0.86)	588	0.95	(0.93-0.96)

5. CONCLUSIONS

Virologic failures with DAAs in patients with ALD were limited and consistent with reported outcomes in real-world studies of patients with less severe disease. The reduced cure rate in this intent to treat ALD population was predominantly due to patients lost to follow up.

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