VANDERBILT UNIVERSITY MEDICAL CENTER

Real World Assessment of Interferon Free Oral Sofosbuvir Based Therapy in Hepatitis C Patients

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BACKGROUND

- Multiple, all orally administered, direct acting antivirals (DAA) have been introduced to the Hepatitis C (HCV) therapeutic arena with remarkable clinical cure rates over previously available therapies.
- These new medications have drastically improved efficacy, side effect profiles and therapy completion rates compared with the interferon-based previous standard of care in most chronic hepatitis c infected patients.
- However, many more obstacles appear in clinical care outside of clinical trials such as medication access, medication adherence, and increased medical diversity of exposed patients population.

PURPOSE

- To evaluate the efficacy, safety and discontinuation rates of sofosbuvir based, all oral DAA HCV Therapy in a real-world (RW) population compared to results reported in clinical trials (CT).

METHODS

Study Design
- IRB Approved Retrospective Chart Review
- Clinical Trial Comparison: ION-1, 2, 3; COSMOS: SOLAR 1, 2; OPTIMIST-1, 2; FISSION; VALENCE; POSITRON; FUSION; BOSON

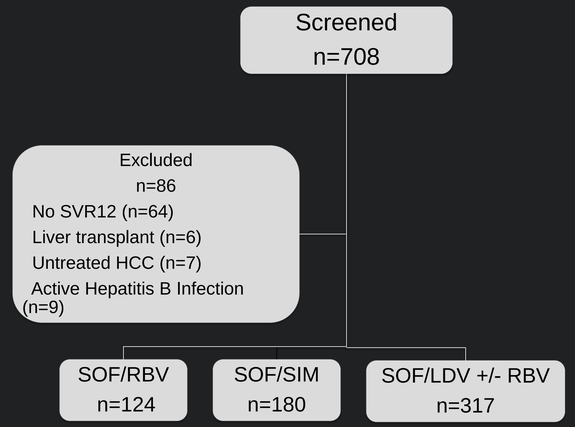
Inclusion Criteria	Exclusion Criteria
≥ 18 years age, HCV treatment naïve or experienced	Completed therapy but final SVR not collected/available
HCV initiated by Vanderbilt Provider between 12/1/13 and 5/31/15	Liver transplant prior to or during HCV therapy
On HCV regimen consisting of: • Sofosbuvir/Ribavirin (SOF/RBV) • Sofosbuvir/Simeprevir (SOF/SIM) • Sofosbuvir/Ledipasvir +/- Ribavirin (SOF/LDV+/-RBV)	Untreated hepatocellular carcinoma Active Hepatitis B infection

ENDPOINTS

Primary
- SVR12 rates stratified by drug regimen

Secondary
- Discontinuation rates
- SVR12 rates by genotype and cirrhosis status
- Factors associated with lower SVR 12 rates
- Adverse drug reactions

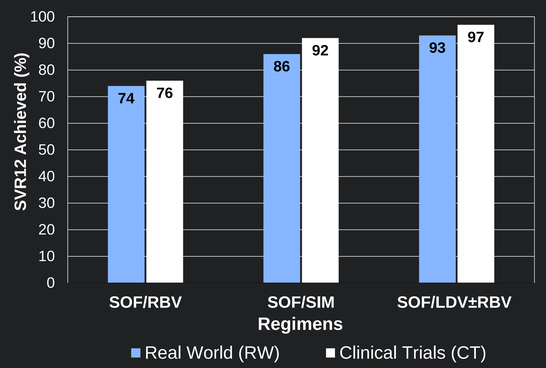
RESULTS



Characteristics	SOF/RBV n=124	SOF/SIM n=180	SOF/LDV ± RBV n=317
Median age, years	55 (51-60)	58 (53-62)	57 (52-62)
Body-mass index	29 (25-34)	28 (25-34)	28 (25-32)
Gender, male	78 (63)	105 (58)	191 (60)
Race White African American	 109 (88) 10 (8)	 148 (82) 29 (16)	 241 (76) 59 (20)
HCV genotype (%) 1a 1b 2 3	 21 (17) 1 (1) 59 (48) 37 (30)	 134 (74) 41 (22) - -	 223 (70) 62 (19) 2 (1) -
HCV RNA – $\log_{10}$ IU/mL	6.24 (5.57-6.71)	6.24 (5.84-6.66)	6.22 (5.65-6.65)
Cirrhosis (%) Decompensated	66 (53) 34 (27)	142 (79) 65 (46)	141 (45) 46 (33)
Treatment Experienced	34 (27)	105 (58)	124 (40)

RESULTS

Overall SVR12 Rates



SVR 12 Rates Sub-Group Analysis

Genotype	SOF/RBV		SOF/SIM		SOF/LDV ± RBV	
	RW %	CT %	RW %	CT %	RW %	CT %
1a			**84**	**92**	91	93
1b			90	92	97	97
2	**85**	**92**				
3	70	66				
Naïve	74	77	85	95	**94**	**96**
Experienced	59	77	86	89	**91**	**97**
No Cirrhosis	90	81	92	95	**98**	**97**
Cirrhosis	61	58	84	86	**86**	**96**
CTP A	75	62	88	85	93	96
CTP B/C	47	-	78	-	**74***	**87****

* <1% of RW patients received RBV **100% of CT patients received RBV

RESULTS

Discontinuation Rates	SOF/RBV		SOF/SIM		SOF/LDV ± RBV	
	RW n=124	CT n=1393	RW n=180	CT n=473	RW n=317	CT n=1952
Discontinued Early (%)	18 (15)	16 (1.2)	6 (3)	5 (1.1)	8 (3)	38 (2)
Reason						
Adverse Events	8 (6)	16 (1.2)	2 (1)	4 (0.8)	0	13 (0.7)
Death	1 (1)	-	1 (1)	1 (0.2)	6 (2)	-
Noncompliance	3 (2)	-	0	-	0	-
Poor Response	2 (2)	-	0	-	0	-
Medication Access	4 (3)		3 (2)	-	2 (1)	-

Adverse Events (AE)	SOF/RBV (n=124)		SOF/SIM (n=180)		SOF/LDV ± RBV (n=317)	
	RW (%)	CT (%)	RW (%)	CT (%)	RW (%)	CT (%)
Any AE	81	64	68	68	58	79
Common AEs						
Fatigue	42	38	28	13	28	29
Headache	25	28	27	15	34	23
Insomnia	15	20	6	0	12	12
N/V/D	25	28	19	10	14	21
Anemia	15	7	0	0	20	5

CONCLUSIONS

- SVR12 rates achieved in the real world population are quite comparable to those demonstrated by clinical trials for oral sofosbuvir based regimens.
- Compensated cirrhotic patients also achieved SVR12 rates similar to clinical trials.
- The addition of ribavirin was associated with a higher rate of any adverse event but clearly enhances the efficacy in decompensated cirrhosis. RBV was not recommended in the guidelines during the study period for decompensated cirrhotic patients. However, ongoing data collection since the guidelines where changed and clinical practice followed is showing an SVR12 improvement from 74% to 91% for SOF/LDV+RBV in decompensated cirrhotic patients in the real world patients.
- Discontinuation rates are higher than those reported in the literature for sofosbuvir/ribavirin but similar for ribavirin sparing regimens of SOF/SIM and SOF/LDV demonstrating the excellent tolerability profile even when applied to a medically diverse population not hindered by strict study exclusion criteria.