Failure with All-Oral DAA Regimens: Academic and Community Treatment of a Real-World Population from the TRIO Network

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Trio Health

1. BACKGROUND

DAA therapies ledipasvir-sofosbuvir (LDV-SOF) and ombitasvir-paritaprevir-ritonavir+dasabuvir (VKP) have yielded SVR12 rates over 95% in clinical trials. Given the remarkable efficacy in clinical trials, understanding factors associated with treatment failure in clinical practice remains challenging due to the relatively few patients who do not achieve an SVR.

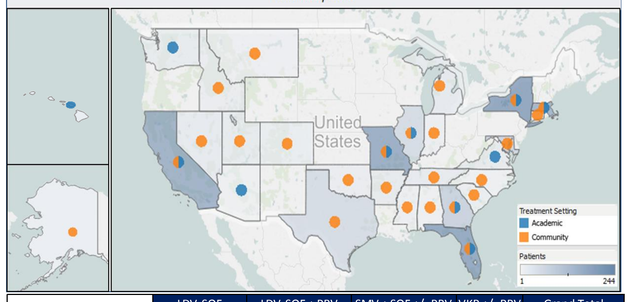
2. AIM

The purpose of this study is to examine a large real-world population to assess the characteristics of patients with genotype 1 HCV who failed 12 week LDV-SOF, VKP or other all-oral DAA therapies.

3. METHODS

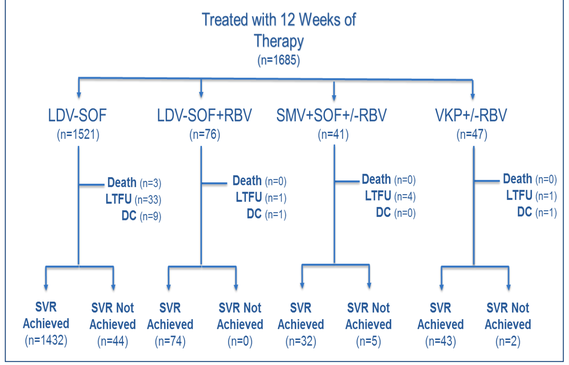
Data were collected from providers and specialty pharmacies including AcariaHealth, Allcare Plus, Aureus Health, BioCure, Encompass Rx, Islandcare, Pharmacare Hawaii, Premier, SkyeMed, and other pharmacies through Trio Health's Innervation Platform, a cloud-based disease management program. All genotype 1 HCV patients who initiated treatment with 12 week LDV-SOF, VKP or simeprevir + sofosbuvir (SMV+SOF)-based regimens between Oct 2014 and Mar 2015 were included in the analysis (n = 1685).

Patients by State



	LDV-SOF	LDV-SOF + RBV	SMV + SOF +/- RBV	VKP +/- RBV	Grand Total
	12	12	12	12	Total
Academic: n (%)	611 (40%)	65 (86%)	23 (56%)	19 (40%)	718 (43%)
Community: n (%)	910 (60%)	11 (14%)	18 (44%)	28 (60%)	967 (57%)
Total:	1521	76	41	47	1685

4. PATIENT DISPOSITION



5. BASELINE CHARACTERISTICS

Patients on a 12 week regimen, n = 1685

Patient Demographics and Clinical Characteristics at Baseline

Group - no. (%)	LDV-SOF 12 Week	LDV-SOF + RBV 12 Week	SMV + SOF +/- RBV 12 Week	VKP +/- RBV 12 Week
	n= 1521	n= 76	n= 41	n=47
Academic Practice – no. (%)	611 (40%)	65 (86%)	23 (56%)	19 (40%)
Age - mean (range)	60 (19-89)	59 (40-73)	60 (38-80)	58 (32-80)
Male - no. (%)	868 (57%)	56 (74%)	23 (56%)	28 (60%)
Patient Ethnicity - no. (%)				
Asian	53 (3%)	1 (1%)	0 (0%)	1 (2%)
Black	234 (15%)	11 (14%)	5 (12%)	9 (19%)
Hispanic/Latin	100 (7%)	5 (8%)	2 (5%)	4 (9%)
Pacific Islander	8 (1%)	0 (0%)	0 (0%)	0 (0%)
White	742 (49%)	52 (68%)	16 (39%)	23 (49%)
Other	12 (1%)	0 (0%)	0 (0%)	0 (0%)
Unknown	372 (24%)	7 (9%)	18 (44%)	10 (21%)
Baseline Labs				
ALT - mean (s.d.)	68 (59), n=1391	82 (53), n=74	66 (79), n=33	83 (108), n=45
AST - mean (s.d.)	62 (45), n=1382	78 (48), n=74	60 (50), n=32	64 (44), n=45
Hb - mean (s.d.)	14 (7), n=1464	14 (2), n=73	14 (1), n=34	15 (2), n=45
Platelets <100 K/ml - no. (%)	142 (11%)	15 (21%)	7 (21%)	6 (14%)
Platelets >=100 K/ml - no. (%)	1197 (89%)	58 (79%)	27 (79%)	38 (86%)
Genotype - no. (%)				
1a	1017 (67%)	57 (75%)	28 (68%)	26 (55%)
1b	433 (28%)	16 (21%)	13 (32%)	21 (45%)
1Mixed	7 (0%)	0 (0%)	0 (0%)	0 (0%)
1Unknown	64 (5%)	3 (4%)	0 (0%)	0 (0%)
Initial Viral Load - no. (%)				
<800K IU/ml	389 (26%)	25 (33%)	17 (41%)	13 (28%)
800K<2MM IU/ml	352 (23%)	12 (16%)	9 (22%)	11 (23%)
2MM<6MM IU/ml	443 (29%)	23 (30%)	7 (17%)	16 (34%)
6MM+ IU/ml	326 (21%)	15 (20%)	8 (20%)	7 (15%)
Unknown	11 (1%)	1 (1%)	0 (0%)	0 (0%)
Fibrosis - no. (%)				
0 - No Fibrosis	90 (6%)	4 (5%)	2 (5%)	3 (6%)
1 - Mild	229 (16%)	15 (20%)	3 (7%)	12 (26%)
2 - Moderate	332 (22%)	19 (25%)	4 (10%)	12 (26%)
3 - Severe	253 (17%)	6 (8%)	6 (15%)	6 (13%)
4 - Cirrhosis	448 (29%)	31 (41%)	18 (44%)	7 (15%)
No Cirrohosis - Score Unknown	121 (8%)	1 (1%)	6 (15%)	4 (9%)
Unknown	38 (2%)	0 (0%)	2 (4%)	3 (5%)
Prior Treatment - no. (%)				
PEG + RBV	305 (66%)	26 (57%)	12 (75%)	13 (86%)
BOC + PEG + RBV	32 (8%)	0 (0%)	1 (6%)	0 (0%)
TVR + +PEG + RBV	51 (11%)	10(22%)	0 (0%)	0 (0%)
SMV + SOF	7 (2%)	5 (11%)	0 (0%)	1 (7%)
SOF + PEG + RBV	4 (1%)	1 (1%)	0 (0%)	0 (0%)
SOF + RBV	9 (2%)	3 (8%)	1 (6%)	0 (0%)
VKP +/- RBV	1 (0%)	0 (0%)	0 (0%)	0 (0%)
LDV-SOF	2 (0%)	0 (0%)	0 (0%)	0 (0%)
Prior Regimen Unknown	48 (10%)	1 (1%)	2 (13%)	1 (7%)

6. SVR12 RATES

SVR12 Rates Inside Approved FDA Labeling vs. Outside Approved FDA Labeling

	LDV-SOF +/-RBV	VKP +/-RBV	SMV+SOF +/-RBV	Total
Outside Approved FDA Labeling	85% (115/135)	83% (5/6)	63% (5/8)	84% (125/149)
Inside Approved FDA Labeling	95% (1391/1462)	93% (38/41)	82% (27/33)	95% (1456/1536)
Total	94% (1506/1597)	91% (43/47)	78% (32/41)	94% (1581/1685)

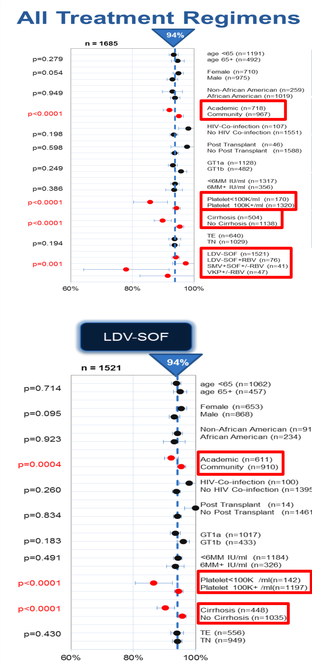
*Patients prescribed outside approved FDA labeling: GT1a on VKP without RBV, tx failure cirrhotic patients on 12 weeks of VKP+/RBV, LDV-SOF without RBV, or SMV+SOF+/-RBV

Numerator = SVR Achieved; Denominator = Intent to Treat (ITT) Whiskers = 95% confidence intervals.

8. SUMMARY

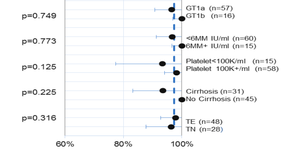
Overall SVR in real world Genotype 1 HCV patients is 94% across all DAA therapies. SVR rates for LDV-SOF, LDV-SOF+RBV, SMV+SOF+/-RBV, and VKP+/-RBV are 94%, 97%, 78% and 91% respectively. 149 patients were treated outside of approved FDA labeling and saw a significantly lower SVR rate (84% SVR outside vs. 95% SVR inside). Platelets <100k/ml, cirrhosis, prescribing outside approved FDA labeling, and males all had a negative association with achieving SVR. Practice type, ethnicity, genotype subtype, baseline viral load, post transplant, age, treatment status, and HIV had no clear association with achieving SVR. Overall discontinuation rate was <1% (12/1685).

7. PREDICTORS OF RESPONSE

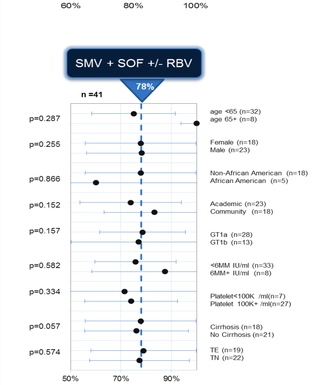


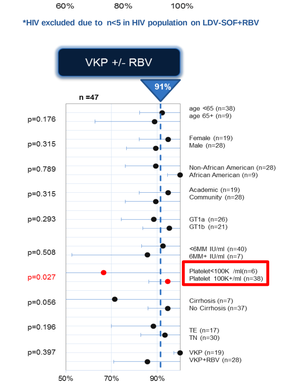
Variable	Full Population Distribution % (n)	Treatment Failure Distribution % (n)	p-value
Platelets<100k/ml Platelets 100l+/ml	11% (170) 89% (1320)	40% (19) 60% (29)	<0.001
Cirrhosis No Cirrhosis	31% (504) 69% (1138)	70% (35) 30% (15)	<0.001
Outside Approved FDA Labeling Inside Approved FDA Labeling	10% (149) 90% (1536)	33% (17) 67% (34)	<0.001
Male Female	58% (975) 42% (710)	76% (39) 24% (12)	0.008

*Patients prescribed outside approved FDA labeling: GT1a on VKP without RBV, tx failure cirrhotic patients on 12 weeks of VKP+/RBV, LDV-SOF without RBV, or SMV+SOF+/-RBV



*HIV excluded due to n<5 in HIV population on LDV-SOF+RBV





*Closed circles= proportions; whiskers = 95% confidence interval; dotted lines = overall SVR12; 2-side asympt. p-value via Pearson χ^2.

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