DAA TREATMENT FAILURE AND RETREATMENT STRATEGIES FOLLOWING NAT+ HCV SOLID ORGAN TRANSPLANTATION IN HCV-NEGATIVE RECIPIENTS: A CASE SERIES

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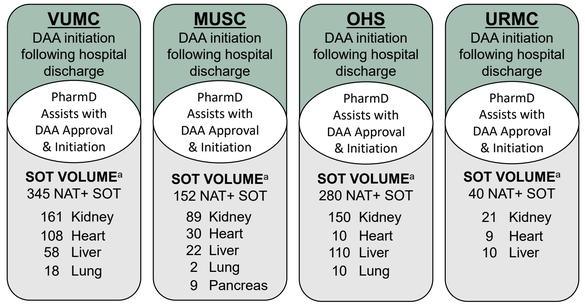
BACKGROUND

- Data demonstrating safety and efficacy of direct-acting antivirals (DAAs) in hepatitis C virus (HCV) negative solid organ transplant (SOT) recipients receiving nucleic acid testing (NAT) positive HCV organs continues to emerge.
- Given high sustained virologic response rates (SVR) in this population, limited data exist to guide DAA re-treatment selection in NAT+ HCV organ recipients when initial DAA failure occurs.
- **OBJECTIVE:** To pool data from multiple treatment facilities to better describe the population of HCV-SOT recipients who fail initial DAA, retreatment strategies, and subsequent SVR rates.

METHODS

Design	Multi-site, retrospective case series
Sample	Adult HCV negative patients who received HCV NAT+ SOT and failed to achieve SVR following initial DAA treatment at four tertiary medical centers: Vanderbilt University Medical Center (VUMC), Medical University of South Carolina (MUSC), Ochsner Health System (OHS) and University of Rochester Medical Center (URMC)
Study Period	September 2016 - June 2022
Primary Outcome	Achievement (rate) of SVR following DAA retreatment
Secondary Outcomes	Describe population failing initial DAA treatment, DAA retreatment strategies and concomitant medications of concern

FIGURE 1: PRACTICE SITES



[a]Data provided are estimates during time of the study period

RESULTS

TABLE 1: PATIENT CHARACTERISTICS, DAA TREATMENT REGIMENS AND OUTCOMES

ID	Gender	Race	Age	SOT Type	GT	Initial DAA Treatment	Reported Missed Doses	Initial DAA Treatment Outcome	RAS Post Initial DAA	DAA Retreatment	Reported Missed Doses	DAA Retreatment Outcome
1	Male	White	73	Kidney	1	SOF/VEL x12 weeks	0	+viral load 4 weeks post EOT	Y93N	GLE/PIB + RBV x16 weeks	0	Achieved SVR34
2	Male	White	70	Kidney	1a	LDV/SOF x12 weeks	0	+viral load 4 weeks post EOT	N/A	SOF/VEL/VOX x12 weeks	1	Achieved SVR41
3	Female	Black	69	Kidney	1a	SOF/VEL x12 weeks	0	+viral load 9 weeks post EOT	N/A	SOF/VEL/VOX x12 weeks	0	Achieved SVR98
4	Female	White	63	Kidney	1a	SOF/VEL x12 weeks	0	+viral load 5 weeks post EOT	N/A	SOF/VEL/VOX x12 weeks	0	Achieved SVR13
5	Male	Black	44	Kidney	1a	GLE/PIB x12 weeks	0	+viral load increased while on GLE/PIB **(GLE/PIB stopped week 11)[a]**	K24R M28G Q30R	SOF/VEL/VOX + RBV x12 weeks	0	Achieved SVR25
6	Male	Black	47	Kidney	1a	SOF/VEL x12 weeks	0	+viral load at EOT	N/A	SOF/VEL/VOX x12 weeks	0	Achieved SVR38
7	Male	Black	42	Kidney	2	GLE/PIB x12 weeks	0	+viral load week 9 **(GLE/PIB stopped week 10)[b]**	N/A	SOF/VEL/VOX x12 weeks	0	Achieved SVR24
8	Male	White	57	Kidney	3	GLE/PIB x12 weeks	0	+viral load 3 weeks post EOT	M28I/K L31L/P	SOF/VEL/VOX + RBV x24 weeks[c]	7	Achieved SVR25
9	Male	Black	37	Kidney	3	SOF/VEL x12 weeks	0	+viral load 1 week post EOT	N/A	SOF/VEL/VOX x12 weeks	2	**+viral load 3 weeks post EOT[d]**
10	Male	White	70	Kidney	3	GLE/PIB x12 weeks	0	+viral load 11 weeks post EOT	N/A	SOF/VEL/VOX x12 weeks	0	Achieved SVR16
11	Male	White	57	Lung	1a	LDV/SOF x12 weeks	0	+viral load 8 weeks post EOT	N/A	SOF/VEL/VOX x24 weeks[e]	0	Achieved SVR27
12	Male	White	66	Heart	3	GLE/PIB x12 weeks	0	+viral load at EOT	N/A	SOF/VEL/VOX x12 weeks	0	Achieved SVR13
13	Female	White	31	Liver	1a	SOF/VEL x12 weeks	0	+viral load 5 weeks post EOT	N/A	SOF/VEL/VOX + RBV x12 weeks	0	Achieved SVR75

Abbreviations: DAA, direct-acting antiviral; EOT, end of treatment; GLE/PIB, glecaprevir/pibrentasvir; GT, genotype; HCV, hepatitis C virus; LDV/SOF, ledipasvir/sofosbuvir; NAT, nucleic acid test; N/A, not available; RAS, resistance-associated substitutions; RBV, ribavirin; SOF/VEL, sofosbuvir/velpatasvir; SOF/VEL/VOX, sofosbuvir/velpatasvir/voxilaprevir; SOT, solid organ transplant; SVR, sustained virologic response

[a]GLE/PIB stopped early at discretion of the hepatology service due to rising viral load and emergence of RAS polymorphisms.

[b]GLE/PIB stopped early at discretion of the hepatology service due to rising viral load.

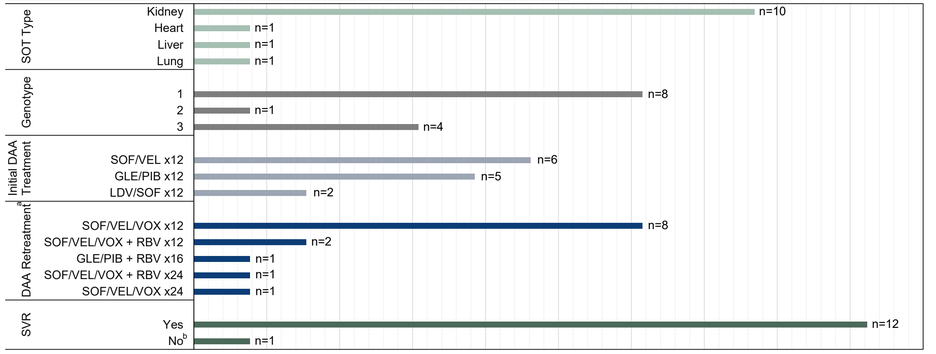
[c]Initially prescribed for 12 weeks; extended to 24 weeks at the discretion of the hepatology service due to persistent viremia and persistently elevated alanine transaminase (ALT).

[d]Underwent third round of DAA treatment with sofosbuvir + GLE/PIB + RBV x 24 weeks. No RAS testing available. No reported missed doses. Achieved SVR14.

[e]Initially prescribed for 12 weeks; extended to 24 weeks at the discretion of the hepatology service due to persistent viremia.

RESULTS

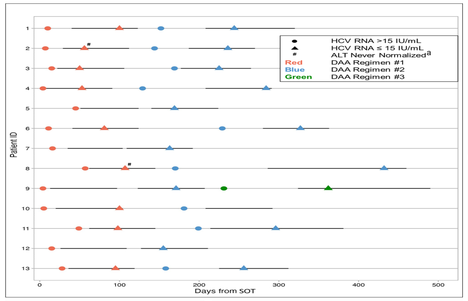
FIGURE 2: SOT TYPE, DAA TREATMENT REGIMENS AND SVR RATES



[a]3rd DAA regimen for Patient ID 9 SOF + GLE/PIB + RBV x24 weeks not included in graph

[b]Patient ID 9 failed SOF/VEL/VOX x12 weeks initially, then achieved SVR after 3rd DAA regimen

FIGURE 3: DAA MONITORING TIMELINES



Time from SOT to DAA #1
Median Days 35, IQR [22-41]

Time to DAA failure to Retreatment
Median Days 35, IQR [17-76]

[a]ALT normalization defined as ≤33 IU/l for males and ≤ 25 IU/l for females

FIGURE 4: CONCOMITANT MEDICATIONS OF CONCERN[a]

DAA FAILURE

	LDV/SOF (n=2)	SOF/VEL (n=6)	GLE/PIB (n=5)	SOF/VEL/VOX (n=1)	SOF + GLE/PIB (n=0)	TOTAL (n=14)
PPI	2	0	2	0	N/A	4
H2RA	0	4	2	1	N/A	7
Antacid	3	4	0	1	N/A	8

SVR ACHIEVED

	LDV/SOF (n=0)	SOF/VEL (n=0)	GLE/PIB + RBV (n=1)	SOF/VEL/VOX +/- RBV (n=11)	SOF + GLE/PIB + RBV (n=1)	TOTAL (n=13)
PPI	N/A	N/A	0	1	0	1
H2RA	N/A	N/A	1	9	0	10
Antacid	N/A	N/A	0	9	0	9

Abbreviations: H2RA, histamine 2 receptor antagonist; PPI, proton-pump inhibitor

[a]Medications that have potential to affect the absorption of DAA

CONCLUSIONS

- SVR rates were high in SOT NAT+ HCV organ recipients requiring DAA retreatment following initial DAA failure and all patients achieved SVR following one or two DAA retreatment courses.
- DAA retreatment regimens varied, however, SOF/VEL/VOX-containing regimens were prescribed most frequently and most commonly for a period of 12 weeks.
- Times to start DAA from SOT and from DAA failure were similar.
- Fewer PPIs were prescribed to patients who achieved SVR, however, this can be explained by the differences in DAA regimen interaction profiles of those who failed DAA and those who achieved SVR.

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