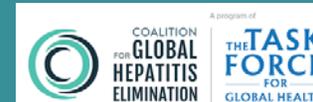


Retreatment for HCV: Preliminary results from a retrospective analysis of pooled national program data across low- and middle-income countries

Christian B. Ramers¹, Lindsey Hiebert², Caroline E. Boeke¹, Imam Waked³, Tengiz Tsertsvadze⁴, Lali Sharvadze⁵, Maia Butsashvili⁶, Mamuka Zakalashvili⁷, Win Naing⁸, Neil Gupta⁹, Fred Kateera⁹, John W. Ward²

1. Clinton Health Access Initiative, Boston, MA, United States 2. Coalition for Global Hepatitis Elimination, Task Force for Global Health, Decatur, GA, United States 3. Hepatology Department, National Liver Institute, Menoufia University Shebeen El Kom, Egypt 4. Infectious Diseases, AIDS, and Clinical Immunology Research Center, Tbilisi, Georgia 5. Hepatology Clinic Hepa, Tbilisi, Georgia 6. Clinic Neolab, Tbilisi, Georgia 7. Clinic Mrchevili, Tbilisi, Georgia 8. Yangon Speciality Hospital, Liver Unit, Yangon, Myanmar 9. Partners in Health/ Inshuti Mu Buzima, Kigali, Rwanda



INTRODUCTION

Global HCV elimination relies heavily on a public health approach using affordable generic DAA regimens. Generic first-line therapy (FLT) combinations, such as sofosbuvir/daclatasvir (SOF/DCV), cure roughly 95% of those treated, with the remainder requiring retreatment with second line therapy (SLT). The patented originator product recommended by WHO as SLT, sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX), is typically unavailable in low- and middle-income countries (LMICs). The near-100% cure rates using licensed, WHO pre-qualified generic FLT suggest that volumes of SLT required are too small to warrant generic licensing and manufacturing of SOF/VEL/VOX. Clinicians in LMICs are therefore left to consider other SLT options using available generic DAA regimens +/- Ribavirin.

AIM

To inform clinical decision-making and future WHO treatment guidelines, a multi-country retrospective study was launched to document current real-world HCV retreatment practices with SLT and outcomes in LMICs.

METHODS

A centralized, secure data portal was established for LMIC programs to share previously collected, de-identified data on HCV patients with FLT failure, SLT regimens used and re-treatment outcomes. Data on patients receiving Interferon-containing regimens were excluded. To date, national programs from Egypt, Georgia, and Myanmar and clinical sites from Rwanda have shared datasets on FLT failures, retreatments with SLT, or both. Descriptive statistics were used to assess patient demographics and SLT regimens as well as sustained virologic response at 12-weeks post-treatment (SVR12).

RESULTS

De-identified data on 1,462 patients who failed HCV FLT and were re-treated with SLT was shared from Egypt (N=639), Georgia (N=807), and Myanmar (N=16); Data from Rwanda included only FLT failures (N=37) and was not included in the analysis. The median age of re-treated patients was 53 (IQR: 47-59) years, 73.8% were male (N=1,079) and 72.6% were cirrhotic (N=1,061). The most common SLT regimens and treatment durations were SOF/LDV+RBV for 24 weeks (31.8%), SOF/DCV+RBV for 24 weeks (30.7%), SOF/VEL+RBV for 24 weeks (14.0%), SOF/DCV+RBV for 12 weeks (5.4%), SOF/LDV+RBV for 12 weeks (5.3%), and SOF+SIM+DCV+RBV for 12 weeks (5.3%). Of 1,070 patients who completed retreatment and received SVR12 testing, all regimens were at least 91.4% effective in achieving SVR12, and overall 93.8% were cured.

	Percent of retreated patients receiving SLT regimen and duration [‡] , across countries (%)				Percent of retreated patients achieving SVR12 [±] , by SLT regimen and duration (%)
	Egypt (N=639)	Georgia (N=807)	Myanmar (N=16)	Overall (N=1,462)	Overall (N=1,070)
12 weeks					
SOF/LDV+RBV (N=77)	-	9.5%	-	5.3%	98.4%
SOF/DCV+RBV (N=79)	12.4%	-	-	5.4%	92.2%
SOF+SIM+DCV+RBV (N=77)	12.1%	-	-	5.3%	97.4%
Other (N=87)	5.3%	5.0%	81.3%	6.0%	98.3%
24 weeks					
SOF/LDV+RBV (N=465)	-	57.6%	-	31.8%	91.4%
SOF/DCV+RBV (N=449)	70.3%	-	-	30.7%	93.6%
SOF/VEL+RBV (N=204)	-	24.9%	18.8%	14.0%	94.1%
Other (N=24)	-	3.0%	-	1.6%	100.0%

[‡]For SLT regimen and duration combinations >5%, all other combinations grouped into the "Other" category

[±]Among patients completing retreatment and receiving SVR12 testing

Abbreviations. SLT: second-line therapy; DCV: daclatasvir LDV: ledipasvir; RBV: ribavirin; SIM: simeprevir; SOF: sofosbuvir; SVR12: Sustained viral response at 12 weeks; VEL: velpatasvir

Figure 1. Summary of SLT regimens and durations across countries and associated SVR12

CONCLUSION

This preliminary analysis reveals effective SLT options are available in LMICs for successful retreatment of patients who fail FLT for HCV, even where the WHO-recommended regimen of SOF/VEL/VOX is unavailable. Additional retrospective data may be collected to study strengths and limitations of these SLT options. These preliminary data can reassure the public, clinicians, and policymakers that effective and affordable SLT options are feasible for national programs in diverse LMICs settings.

DISCLOSURES

None

CONTACT INFORMATION:
cramers.IC@clintonhealthaccess.org