4th HEPATITIS C TECHNICAL ADVISORY GROUP TAG Meeting

HCV CARE AND TREATMENT TAG 2017 RECOMMENDATIONS, STATUS OF ACCESS TO HCV CARE AND TREATMENT, KEY ACHIEVEMENTS, KEY CHALLENGES, SIMPLIFIED TESTING AND CURE STRATEGIES IN DECENTRALIZATION OF HCV SERVICES

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12 COUNTRIES WORLDWIDE ON TRACK TO ELIMINATE HEPATITIS C INFECTION BY 2030

Georgia is almost the only country implementing the national HCV elimination program with comprehensive approach

- Baseline and follow-up seroprevalence surveys
- Nationwide HCV screening
- Active case finding
- Treating (including retreatment) all HCV-infected persons
- Unified secure web-based information system
- Extensive prevention and control of HCV infection (increasing public awareness and education, improving infection control, promoting harm reduction, improving surveillance etc.)



Hepatitis C Elimination Strategy

Care and Treatment

Goal:

Provide universal access to HCV care and treatment

Targets: 90-95-95 by 2020



Reducing the HCV prevalence by 90% by 2020



ACCOMPLISHMENTS

How Georgia Differs from Other Countries

Georgia's approach builds on delivering comprehensive response to HCV

Other countries Georgia Nationwide HCV screening No active case finding Active case finding Only those aware of their disease and referring to Treatment of all patients physicians are treated (including F0 fibrosis) Treatment prioritization Re-treatment Wide-scale prevention programs

Treatment Protocols

April 2015 – March 2016	Sofosbuvir (SOF)
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IFN-containing and IFN-free SOF regimens recommended based on various clinical scenarios (genotype, cirrhosis, previous treatment experience)

Since March 2016	Ledipasvir/Sofosbuvir (LDV/SOF)
	LDV/SOF is recommended in all genotypes
	 Evidence supporting this recommendation included: High prevalence of 2k/1b recombinant in Georgia Results of some trials and observational studies indicating that LDV/SOF could be more effective that SOF alone

Hepatitis C Pre-Treatment Evaluation

- Clinical assessment
 HCV RNA quantification
 HCV genotyping
 Complete blood count
 ALT, AST, creatinine, bilirubin, albumin, INR alkaline phosphatase, G-GT, glucose
 HBsAg, anti-HBc total
 - FIB-4 for liver fibrosis assessment**
 - Abdominal ultrasound

^{*} Patients with FIB-4 score between the lower and upper cut-off values undergo liver elastography to assess fibrosis stage.

Treatment monitoring

Ribavirin containing regimens

Measurements			Trea	tment (wee	Durat eks)	ion			After treatment completion (weeks)		
	1	1 2 4 8 12 16 20 24									
Clinical assessment			X	X	X			X	X		
HCV RNA Quantitative			X						X		
Complete blood count			X	x	X	X	x	X			
ALT			X	X	X	X	X	X			
AST											
Creatinine					X	X	x	X			
Bilirubin					X			X			

Treatment monitoring

Ribavirin free regimens

Measurements			Trea	tment (wee	Durati eks)	ion			After treatment completion (weeks)			
	1	1 2 4 8 12 16 20 24										
Clinical assessment			X	Х	X			X	X			
HCV RNA Quantitative			X						x			
Complete blood count			X		X			X				
ALT			X	X	X	X	X	X				
AST												
Creatinine					X			X				
Bilirubin					X			X				

HCV Treatment Sites within Elimination Program, March 31, 2018 (Total=39)



155 physicians (ID specialists, gastroenterologist, primary care specialists)

Source: Georgia's HCV Elimination Program Treatment Database

Hepatitis C Diagnostic Capacity at 31 Treatment Sites in Georgia, October, 2018



Source: Provisional Data, Georgia Hepatitis C Treatment Program

Georgia Hepatitis C Elimination Program Care Cascade, April 28, 2015 – October 31, 2018



* Among persons age ≥12 with PID screened from January 1, 2015

Patients initiating treatment, Georgia HCV elimination program, April 2015 – October 2018



Cascade of HCV care and treatment outcomes among patients receiving Sofosbuvir-based and Ledipasvir/Sofosbuvir-based regimens within the national hepatitis C elimination program, April 28, 2015 – October 31, 2018





Treatment Outcomes of SOF-Based Treatment

Treatment Outcomes in Patients with Complete SVR Data Receiving SOF-based Regimens Apr 28, 2015 – October 31, 2018 (n=5,079)

			SVR Rate		
	G1	G2	G3	G4	TOTAL
12 weeks	<mark>80.8%</mark>	<mark>96.3%</mark>	<mark>96.9%</mark>	<mark>100.0%</mark>	<mark>91.3%</mark>
IFN/SOF/RBV	(731/905)	(231/240)	(1453/1500)	(1/1)	(2416/2646)
12 weeks	<mark>66.7%</mark>	<mark>75.8%</mark>	<mark>100%</mark>	<mark>0%</mark>	<mark>75.8%</mark>
SOF/RBV	(2/3)	(273/360)	(1/1)	(0/0)	(276/364)
20 weeks	<mark>33.3%</mark>	<mark>76.8%</mark>	<mark>0%</mark>	<mark>0%</mark>	<mark>76.5%</mark>
SOF/RBV	(1/3)	(301/392)	(0/0)	(0/0)	(302/395)
24 weeks	<mark>54.8%</mark>	<mark>71.4%</mark>	<mark>82.8%</mark>	<mark>100%</mark>	<mark>69.0%</mark>
SOF/RBV	(381/695)	(5/7)	(591/714)	(2/2)	(979/1418)
48 weeks	<mark>70.3%</mark>	<mark>87.5%</mark>	<mark>80.0%</mark>	<mark>0%</mark>	<mark>76.9%</mark>
SOF/RBV	(83/118)	(42/48)	(72/90)	(0/0)	(197/256)
TOTAL	<mark>69.4%</mark>	<mark>81.4%</mark>	<mark>91.8%</mark>	<mark>100%</mark>	<mark>81.9%</mark>
	(1198/1724)	(852/1047)	(2117/2305)	(3/3)	(4170/5079)

Source: Georgia's HCV Elimination Program Treatment Database

Treatment Outcomes in Patients with Complete SVR Data Receiving LDV/SOF Based Regimens (n=29 100) April 28, 2015 – October 31, 2018

		SVR rates												
	G1	G2	G3	G4	Indeterminate	Total								
SOF/LDV– 12 wk.	<mark>98.7%</mark>	<mark>100%</mark>	<mark>72.7%</mark>	<mark>100%</mark>	<mark>100%</mark>	<mark>98.7%</mark>								
	(12967/13140)	(16/16)	(8/11)	(16/16)	(7/7)	(13014/13190)								
SOF/LDV– 24 wk.	<mark>98.8%</mark>	<mark>100%</mark>	<mark>100%</mark>	<mark>0%</mark>	<mark>100%</mark>	<mark>98.8%</mark>								
	(158/160)	(1/1)	(2/2)	(0/0)	(1/1)	(162/164)								
SOF/LDV/RBV– 12 wk.	<mark>95.5%</mark>	<mark>98.9%</mark>	<mark>98.2%</mark>	<mark>100%</mark>	<mark>98.9%</mark>	<mark>98.4%</mark>								
	(358/375)	(5817/5884)	(7868/8012)	(1/1)	(605/612)	(14649/14884)								
SOF/LDV/RBV– 24 wk.	<mark>94.7%</mark>	<mark>100%</mark>	<mark>95.9%</mark>	<mark>0%</mark>	<mark>100%</mark>	<mark>95.9%</mark>								
	(18/19)	(5/5)	(777/810)	(0/0)	(11/11)	(811/845)								
IFN/SOF/LDV/RBV– 12	<mark>0%</mark>	<mark>0%</mark>	<mark>100%</mark>	<mark>0%</mark>	<mark>0%</mark>	<mark>100%</mark>								
wk.	(0/0)	(0/0)	(7/7)	(0/0)	(0/0)	(7/7)								
IFN/SOF/LDV/RBV– 24	<mark>0%</mark>	<mark>0%</mark>	<mark>90.0%</mark>	<mark>0%</mark>	<mark>0%</mark>	<mark>90.0%</mark>								
wk.	(0/0)	(0/0)	(9/10)	(0/0)	(0/0)	(9/10)								
TOTAL	<mark>98.6%</mark>	<mark>98.9%</mark>	<mark>97.9%</mark>	<mark>100%</mark>	<mark>99.7%</mark>	<mark>98.5%</mark>								
	(13501/13694)	(5839/5906)	(8671/8852)	(17/17)	(624/631)	(28652/29100)								

Source: Georgia's HCV Elimination Program Treatment Database¹⁸

Treatment Outcomes of LDV/SOF-based Regimens by Advanced fibrosis/cirrhosis status. March 1, 2016 – October 31, 2018



Re-Treatment of patients with LDV/SOF-based regimens who failed prior SOF-based therapy March, 2016 – October 31, 2018



NS5A RAS testing Geno2pheno [HCV]

ug in a DAA regimen may be overcome by the activity of the other drugs in the regimen. terpretation system does not necessarily exclude therapy success of the whole regimen, f possible, a regimen with fully active drugs should be chosen.

30897

IIS5A

1 - 132

D0094 Scored mutations

not available

2a (Similarity of DNA to closest reference = 92.39%)

L23P, K30N, L69M, R73K, V99M, K107R, 1108T, H128S

e: Input Results Rules References Contact Team

ture: Alignment Prediction Subtype

Identifier:

Genetic region:

Predicted subtype

Codons covered in #S5A re

Mutations in *IIS5A* region

Warnings //S5A region:

Reference used:

Drugs Dadatasvir

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1 Identifier	30897
i. identifier	Do not use patient names!
2. HCV sequence:	upload up a file (plain sequence or FASTA format): Browse No file selected. Browse No file selected. Browse No file selected. or paste in:
3. H77:	 Automatically determine the genotype of the input sequence and use the most similar reference sequence for that genotype for the alignment Use the H77 strain (genotype 1a) as reference sequence for the alignment
4. SGT:	ignore subgenotype for drug resistance prediction
5. Option:	Alignment width: 120 -
6. Action:	Align and Predict Go
7. CSV:	irect csv download

no2pheno [hcv] 0.92

e: Input Results Rules References Contact Team

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ature: Alignment Prediction Subtype

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geno2pheno®

HCV resistance prediction from genotype (version 1.0)

	I. General information	
Patient:	Study ID:	
Birth date:	Viral load:	
Sample received:	Sample collected:	
Sample ID: 30897	Predicted subtype:	NS5A: 2a (92.39%)
Sample type:	Report date:	20.10.2016
Physician:	Reported by:	

		11. 5	Sequ	ence information
NS5A codons cov	ered	1 - 132		
NS5A region (w.r.t D00944)	L:	L23P, K30N, L69M, R	73K. 1	V99M, K107R, H08T, H128S
NS5A region (w.r.t	. H77)	18V, 112V, E14T, V151 844K, R48A, D60T, H R81M, M831, S850, A E110S, V119A, 1121V	817 826 812	T, T21N, L23P, K24T, A25S, M28F, G30N, L31M, I34L, V37I, R41K H58P, E02N, T04S, H00N, K08P, M09M, T71S, R73K, V76T, R78K T06E, P07G, T06M, L101K, V100F, K107R, F108T, L110I, S114A, 2T, R123G, V124H, D120S, F127Y, H128S, V130I, S131T
			Res	istance analysis
Drug	Predict	tion		Scored Mutations
Daclatasvir	not licen	sed for subtype		not available

Drug	Prediction	Scored Mutations	
Daclatasvir	not licensed for subtype	not available	
Elbasvir	not licensed for subtype	not available	
Ledipasvir	not licensed for subtype	not available	
Ombitasvir	not licensed for subtype	not available	

Elbasvir	not available	not acensed for subtype
Ledipasvir	not available	not licensed for subtype
Ombitasvir	not available	not licensed for subtype
Mutation	Resistar	ice analysis
Resistance class	Descriptio	n
Resistant	Well-characterized resistance-associated mutation	•
Possibly resistant	Association to resistance, insufficient evidence for clinical outcome (characterized resistance variated	nt in other HCV genotypes)
Substitution on scored position	Uncharacterized substitution on a scored position	
Susceptible		
Not licensed for genotype	Drug not licensed for the predicted genotype.	

Resistance analysis

not licensed for subtype

Contact: info@mpi-inf.mpg.de

(signature)



Decentralization of HCV treatment and care services



Pilot project

Integrating HCV screening and simplified treatment services in primary healthcare

This model will provide the basis for the decentralization of treatment and care in PHCs and hospitals nationwide

Primary care/hospitals working group established

Objective

Develop a practical model for HCV screening and treatment in primary health care centers and district hospitals that maximizes HCV screening, enrollment, and retention in the HCV program of the general population.

Clinical group of HCV elimination program responsible for HCV treatment decentralization activities

Decentralization of HCV diagnostics, treatment and care services in Primary healthcare centers (PHCs) in Georgia



Integration of HCV diagnostics, treatment and care services in at least one PHC of each district of Georgia

HCV diagnostics, treatment and care services should be integrated in 69 PHCs across the country during the first phase of the program

Preliminary Results from Senaki PHC

- Number of screened on anti-HCV: 1415
- Anti-HCV+: 154 (10.9%)
- 135 specimens sent for confirmation using HCV Core Ag
- Chronic infection was confirmed in 131 cases. 124 persons returned for pretreatment evaluation.
- 40 Persons had FIB4 score <1.45. Of them 23 persons already started HCV treatment at Senaki PHC.
- 48 patients with FIB4 score ≥1.45 were referred to specialty hepatology clinics
- 36 persons are under pretreatment evaluation

4th HEPATITIS C TECHNICAL ADVISORY GROUP TAG Meeting

CHALLENGES/GAPS & PROPOSED ACTIONS

Clinical Challenges/Gaps Proposed Actions

Limited options of DAA medications

Anticipate introduction of SOF/VEL and/or SOF/VEL/VOX in Georgia

Limited treatment options for kidney disease patients including hemodyalisis

Resistance to NS5A Inhibitors

Resistance testing already implemented at IDACIRC

• Establishing drug resistance surveillance required on national level

Programmatic Challenges/Gaps Proposed Actions

Scarcity of treatment centers in some geographic and especially in rural areas

- Increase from original 4 sites to 39 sites by October, 2018
- Pilot project: integrated HCV screening and treatment model in 4 rural primary healthcare clinics (PHCs)
- Full scale of HCV care decentralization in PHCs (69 PHCs across the country)

Information Systems (STOP-C and Elimination-C) limited capacity

New high-quality IT system created in August 2018 capable for routine or adhoc queries for analytic and reporting activities

Programmatic Challenges/Gaps Proposed Actions

Declined enrollment in the treatment program

- lack of access to the treatment program (financial barriers)
- HCV screening and linkage modality currently used is not adequately effective



- Free confirmatory testing
- Decentralization of HCV confirmatory testing and increase number of providers in rural areas (including PHCs)

Missing SVR Data (21%)

Identify reasons for missing data and design response activities

TAG 2017 Recommendations

 Rapidly Increase the number of providers in primary care or medical specialties other than ID, gastroenterology and hepatology trained to test and treat HCV

> Integrated HCV screening and treatment model in primary care already started. Primary care physicians at 8 PHCs currently involved in the elimination program were trained.

 Strengthen referral relationships between the current major HCV treatment sites and primary care, corrections and other non-tertiary providers

The major HCV treatment sites provide mentorship and education to primary care sites to guide HCV testing and treatment.

TeleECHO clinics between treatment hubs and PHCs will be started in nearest future.

4th HEPATITIS C TECHNICAL ADVISORY GROUP TAG Meeting

MONITORING AND EVALUATION INDICATORS

2015-2018

Objective: Promote universal access to HCV care and treatment

Indicator name	Measurement	Value
 Proportion of anti-HCV positive persons assessed for viraemic HCV infection 	Number of HCV antibody positive persons tested for viraemic HCV infection 75,491	= 81.3%
	Number of people with a presence of anti-HCV antibodies 92,875	
2. Proportion of persons, diagnosed with chronic HCV infection	Number of persons diagnosed with chronic HCV infection based on virological biomarker testing 64,232	
	Number of persons tested for viraemia after a positive serological result 75,491	= 85.1%
	□ Target of identifying 90% of persons infected with hepatitis C infection N=135,000	47.6%
	Source: Georgia's HCV Elimination Program Tree	atment Database

Objective: Promote universal access to HCV care and treatment

Indicator name	Measurement	Value
3. Proportion of persons with chronic HCV infection initiated antiviral therapy	Number of persons diagnosed with chronic HCV infection who initiated antiviral therapy 51,072	= 79.5%
	Number of persons diagnosed with chronic HCV infection 64,232	
	□ Target of treating 95% of persons with chronic HCV infection: N=128,250	39.8%
4. Proportion of patients engaged in antiviral therapy who have completed treatment	Number of patients with chronic HCV infection who have completed treatment 48,205	= 94.4%
	Number of patients diagnosed with chronic HCV infection who initiated treatment 51,072	

Source: Georgia's HCV Elimination Program Treatment Database

Objective: Promote universal access to HCV care and treatment

Indicator Name	Measurement	Value	
5. Proportion of patients achieving SVR to HCV infection	Number of patients who completed treatment and achieved SVR (undetectable viral load 12-24 weeks after the end of treatment 33,452	= 98.2%	
	Number of patients who completed antiviral therapy and were assessed for SVR 12-24 weeks post treatment 34,048		
	□ Target of curing 95% of persons treated for their HCV infection: N=121,838	27.4%	
6. Number of physicians providing HCV services OR provider/resident ratio	Number of physicians providing HCV services 155	= 5.1 per 100,000 residents	
	Estimated resident population: 3 010 200		
7. Number of a/ Primary Healthcare Centers; b) Harm Reduction Sites providing HCV care and treatment	8 primary healthcare sites 3 Harm reduction sites		

Elimination Goal

Reduce prevalence of HCV infection by 90% (to 0.5%)

Acknowledgements

Technical Advisory Group (TAG)











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Sanjeev Arora, Karla Thornton

David Sergeenko, Valeri Kvaratskhelia, Multisectoral Commission on Hepatitis C

Amiran Gamkrelidze

All HCV Clinical Care Provider Clinics