4th HEPATITIS C TECHNICAL ADVISORY GROUP

TAG Meeting

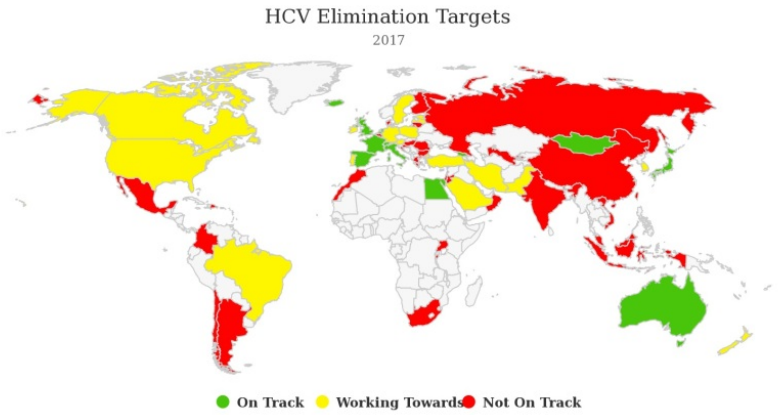
HCV CARE AND TREATMENT
TAG 2017 RECOMMENDATIONS, STATUS OF ACCESS TO HCV CARE AND TREATMENT, KEY ACHIEVEMENTS, KEY CHALLENGES, SIMPLIFIED TESTING AND CURE STRATEGIES IN DECENTRALIZATION OF HCV SERVICES

Tengiz Tsertsvadze MD, PhD
Director General
Infectious Diseases, AIDS and Clinical Immunology Research Center
Professor, Tbilisi State University
Head of Clinical Group, National HCV Elimination Program

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.)



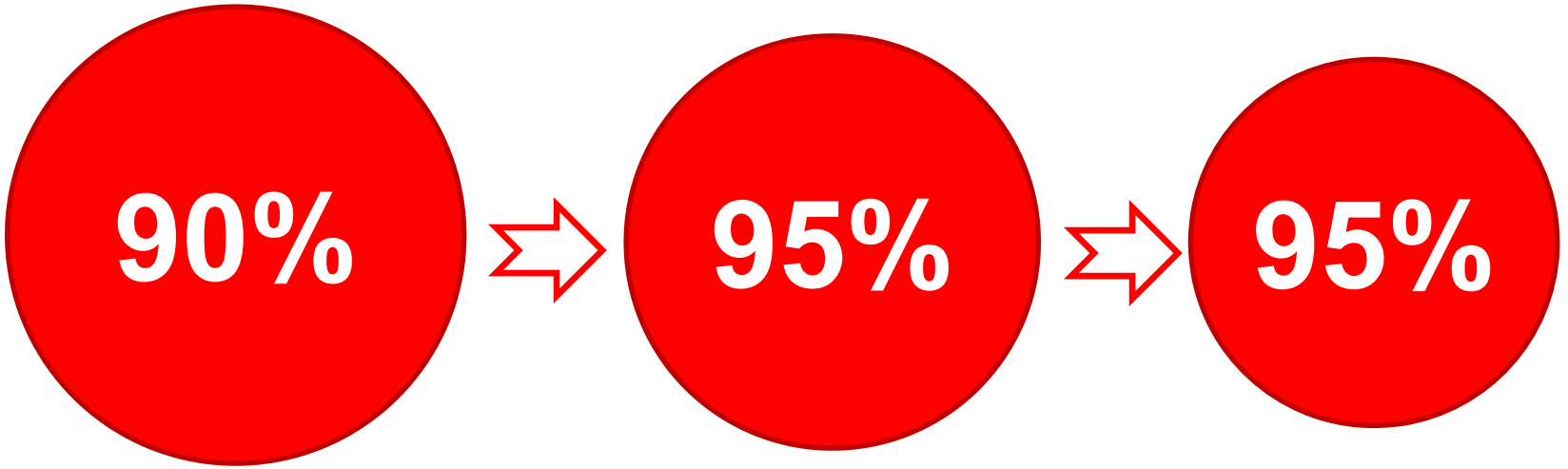
Hepatitis C Elimination Strategy

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

Treatment Protocols

April 2015 – March 2016	**Sofosbuvir (SOF)**
	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

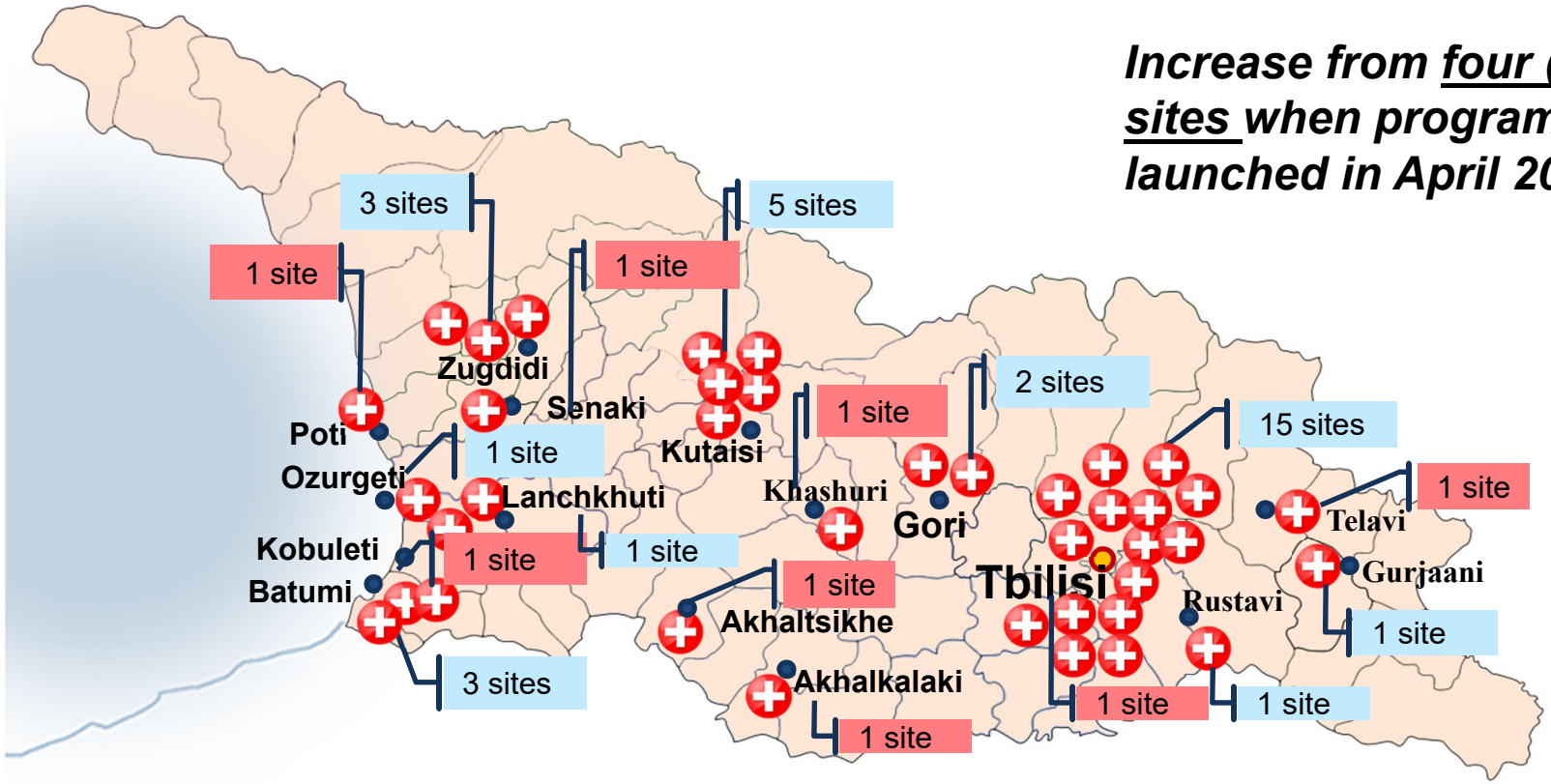
Measurements	Treatment Duration (weeks)								After treatment completion (weeks)
	1	2	4	8	12	16	20	24	12 ѕб 24
Clinical assessment			X	X	X			X	X
HCV RNA Quantitative			X						X
Complete blood count			X	X	X	X	X	X	
ALT			X	X	X	X	X	X	
AST									
Creatinine					X	X	X	X	
Bilirubin					X			X	

Treatment monitoring

Ribavirin free regimens

Measurements	Treatment Duration (weeks)								After treatment completion (weeks)
	1	2	4	8	12	16	20	24	12 sб 24
Clinical assessment			X	X	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)

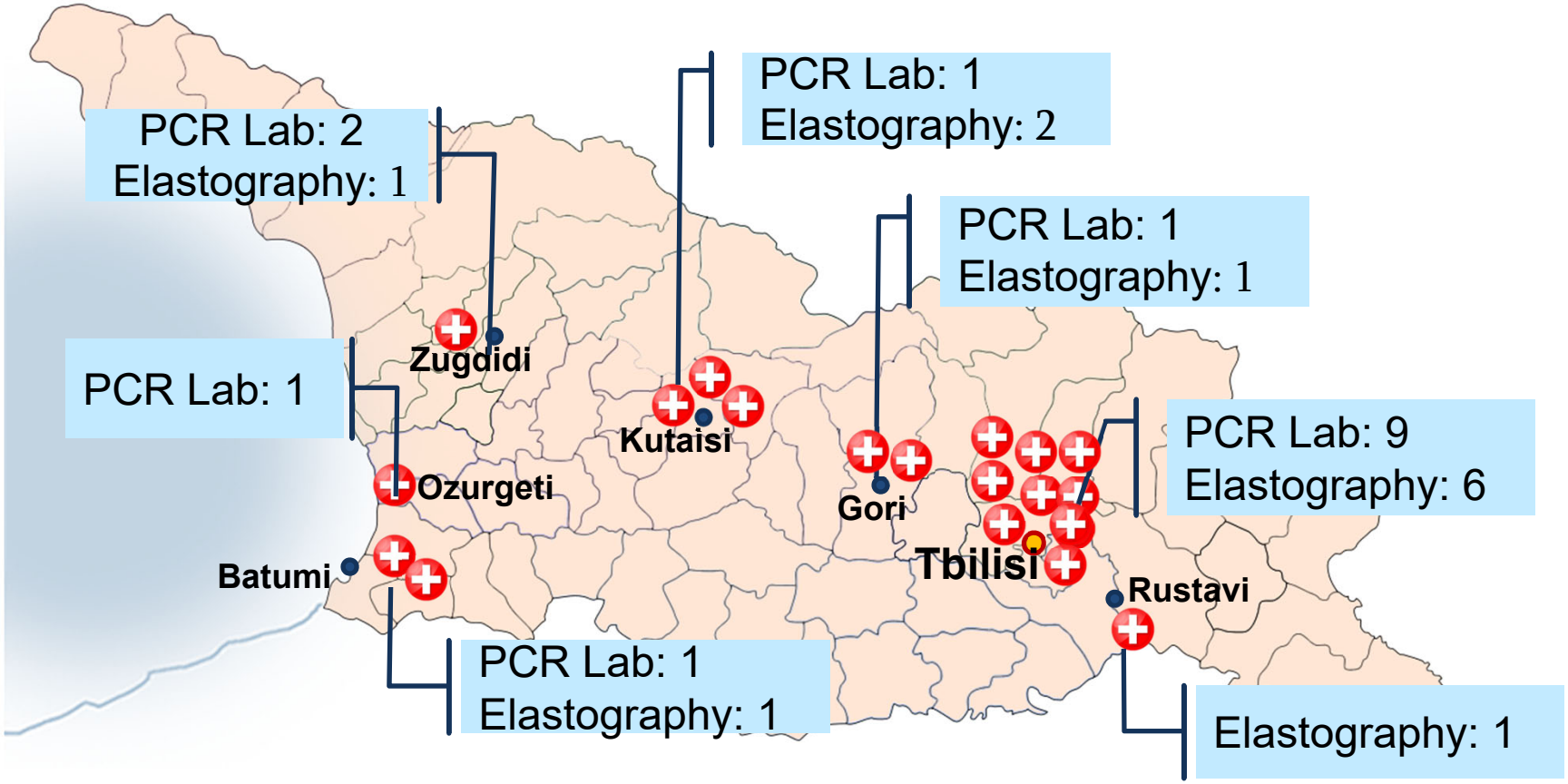


Increase from <u>four (4)</u> <u>sites</u> when program launched in April 2015

<u>Total</u>: **39 sites**
155 physicians (ID specialists, gastroenterologist, primary care specialists)

Source: Georgia's HCV Elimination Program Treatment Database

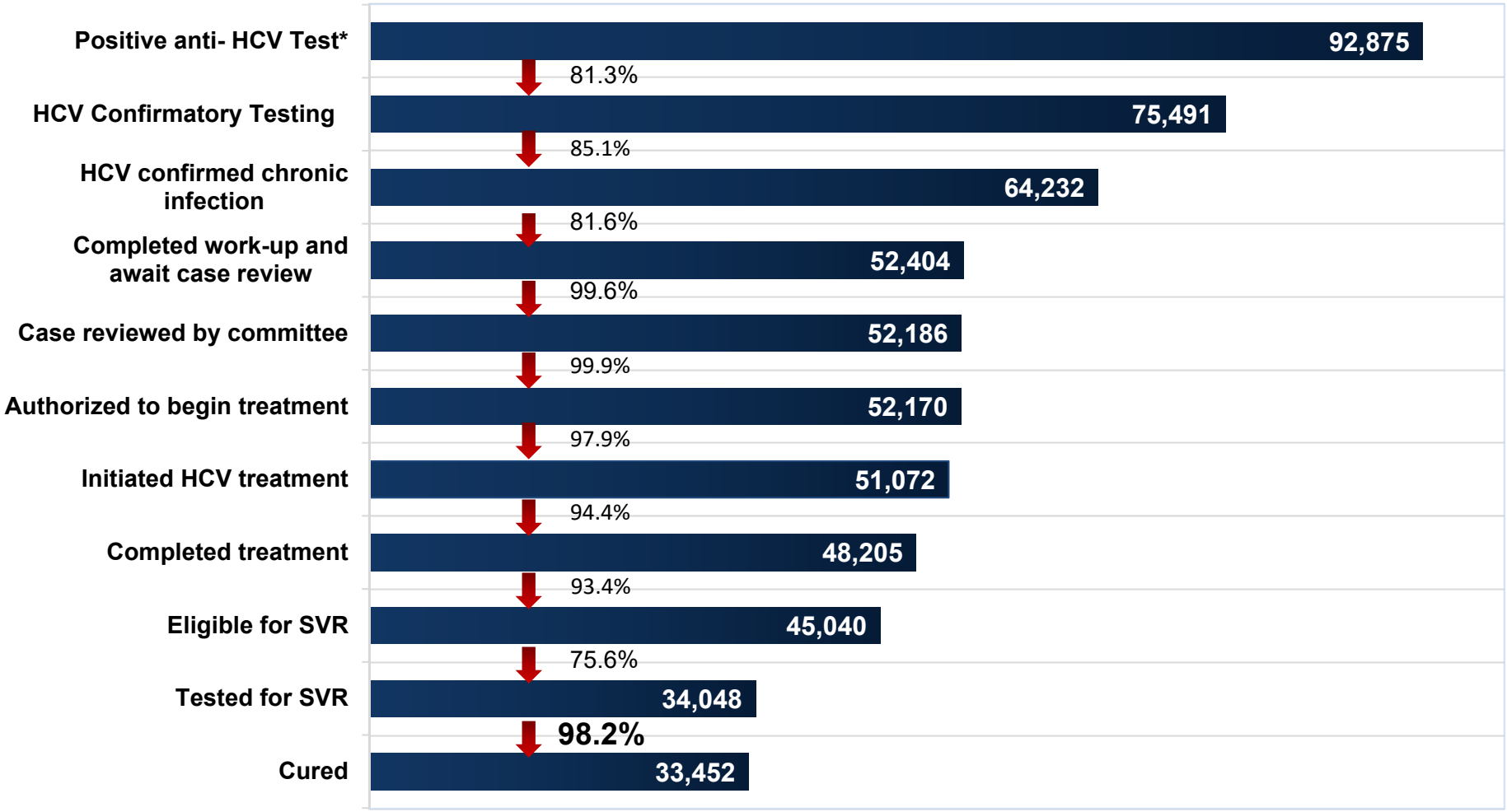
Hepatitis C Diagnostic Capacity at 31 Treatment Sites in Georgia, October, 2018



Total: **15 PCR Labs**
12 Elastography

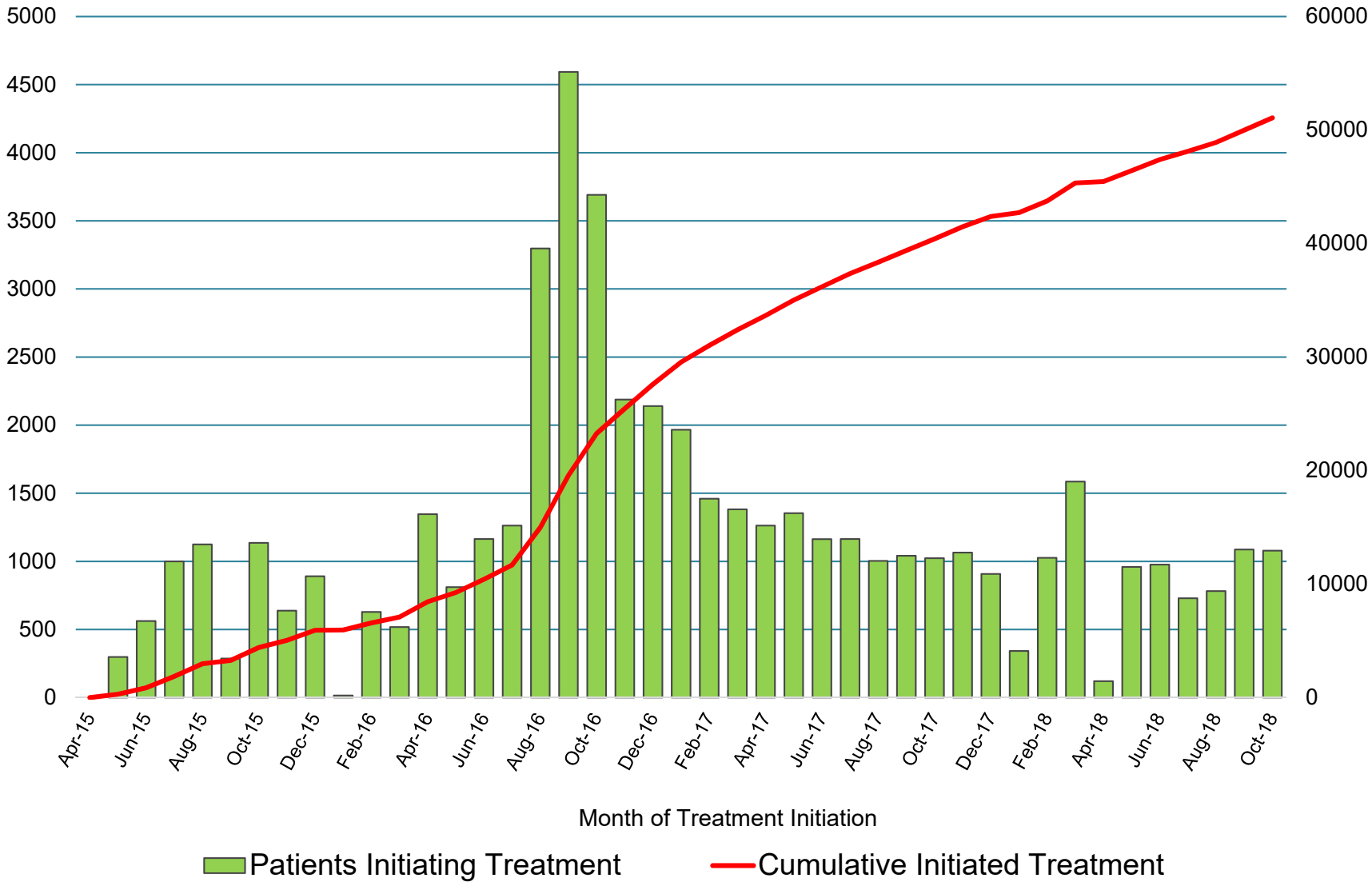
Source: Provisional Data, Georgia Hepatitis C Treatment Program

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

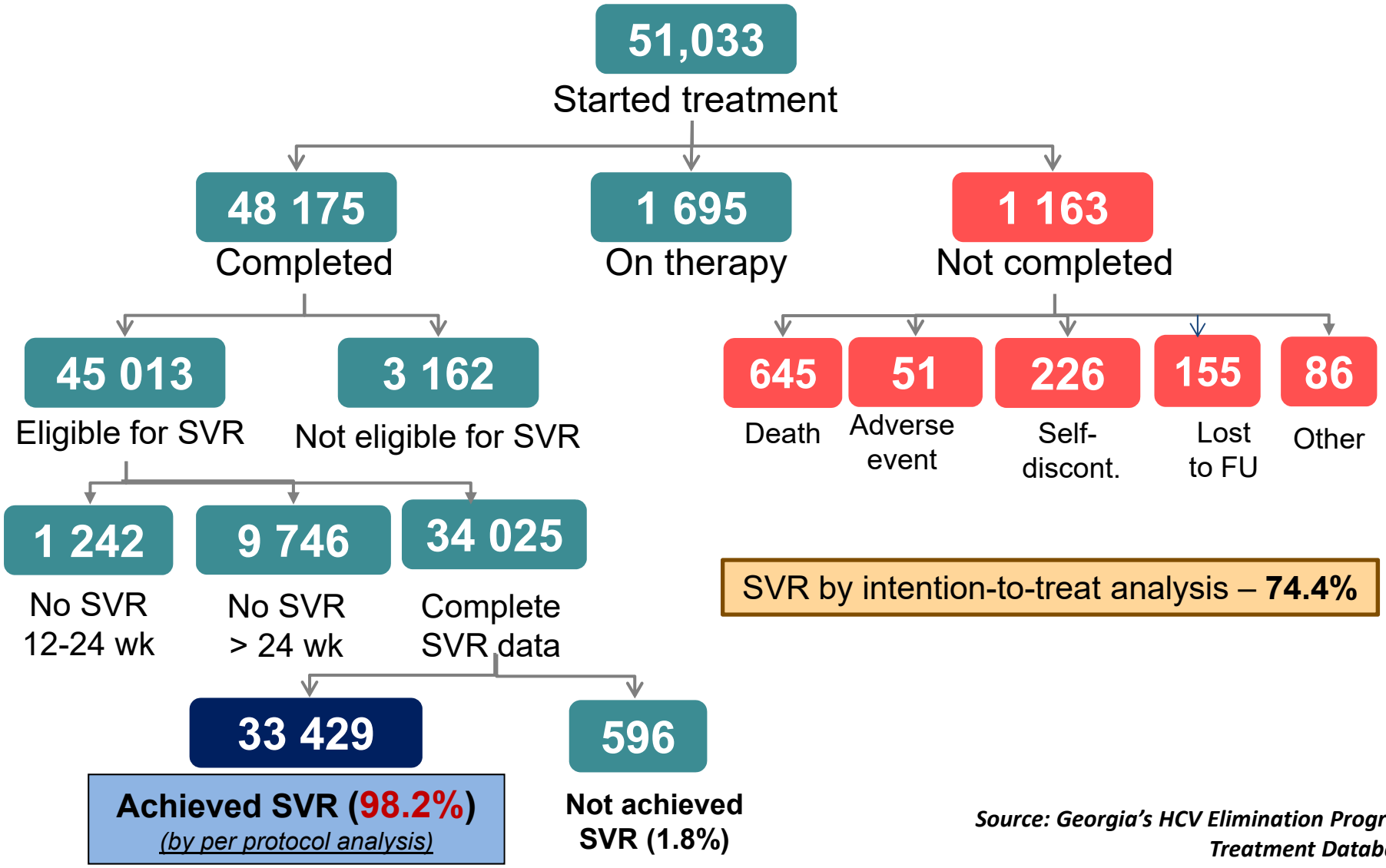


* Among persons age ≥12 with PID screened from January 1, 2015

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



Source: Georgia's HCV Elimination Program Treatment Database

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

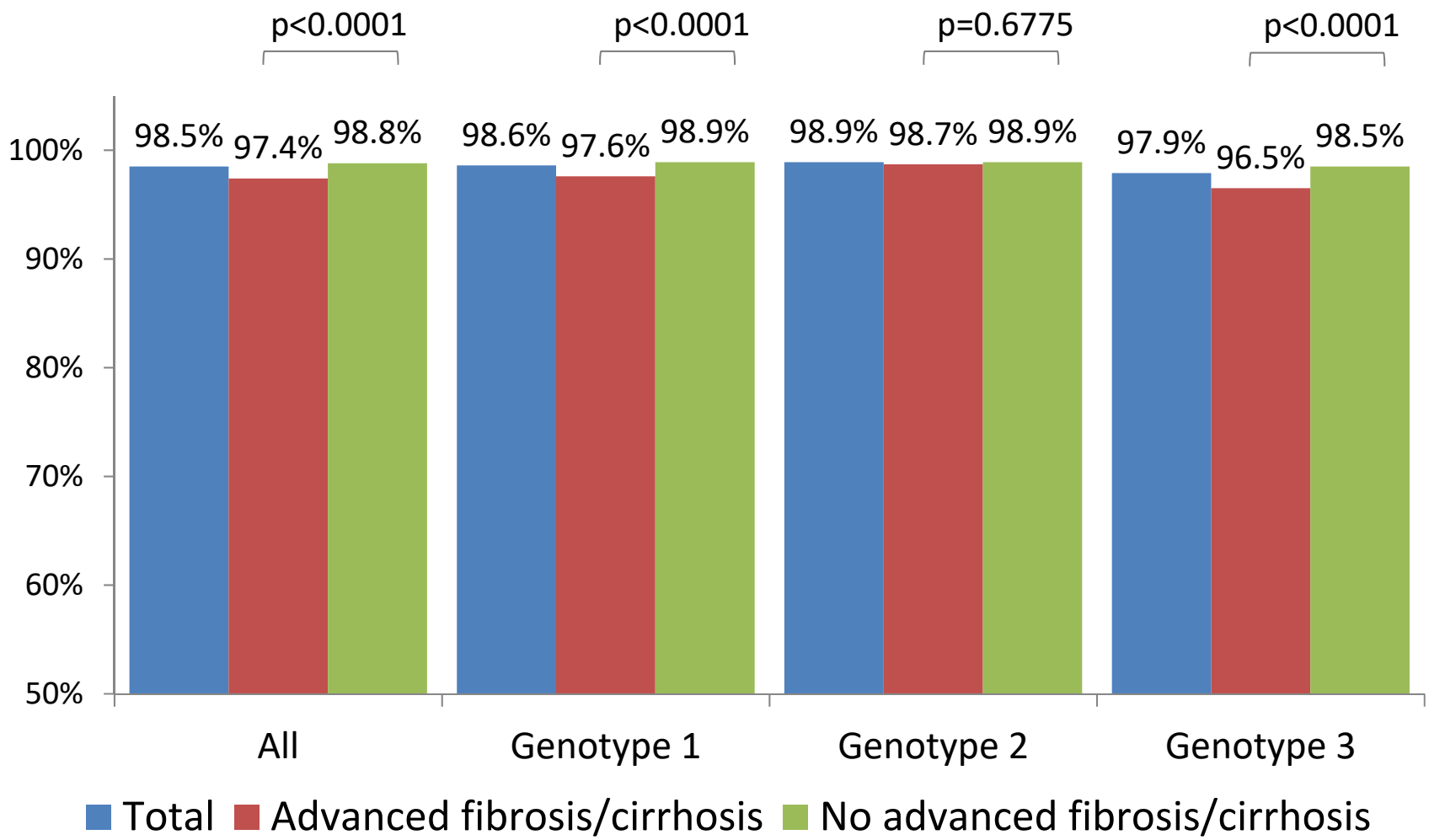
Source: Georgia's HCV Elimination Program Treatment Database

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

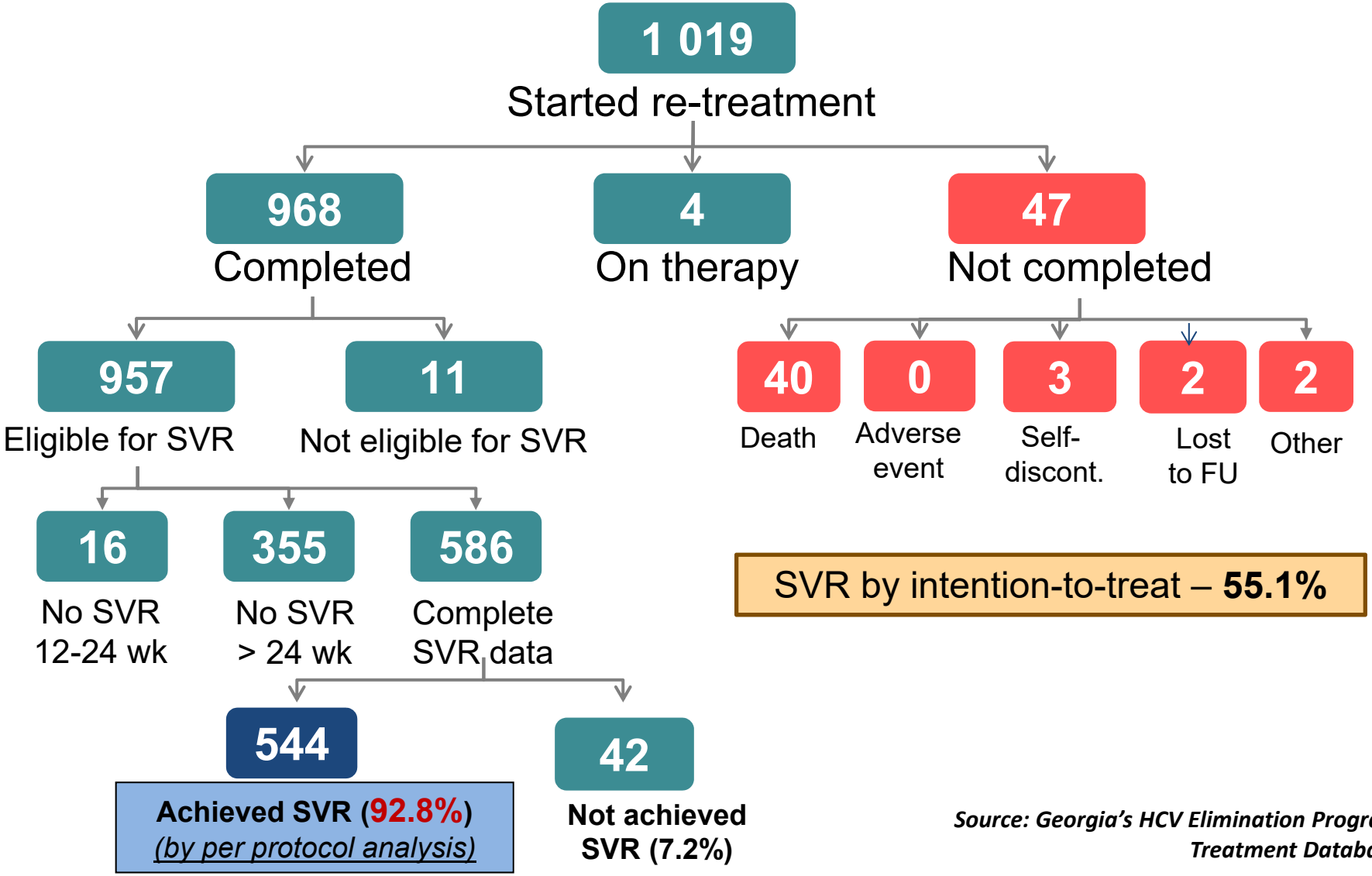
Source: Georgia's HCV Elimination Program Treatment Database

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



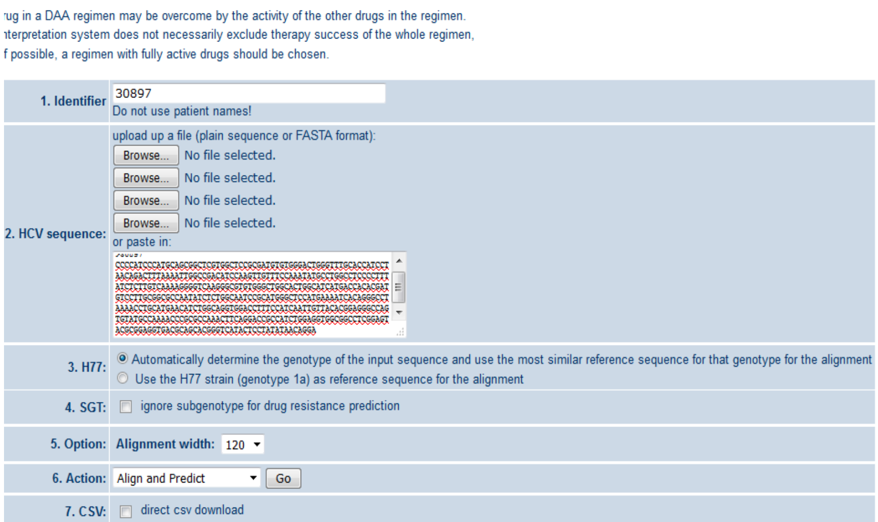
Source: Georgia's HCV Elimination Program Treatment Database

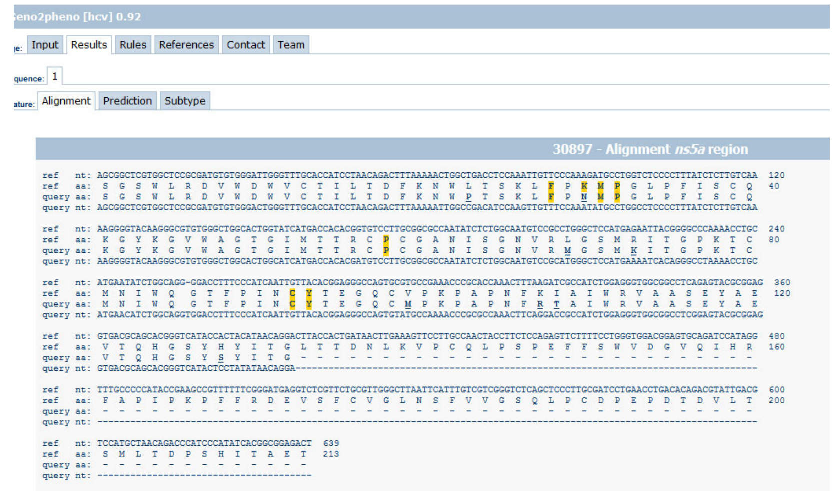
Re-Treatment of patients with LDV/SOF-based regimens who failed prior SOF-based therapy March, 2016 – October 31, 2018

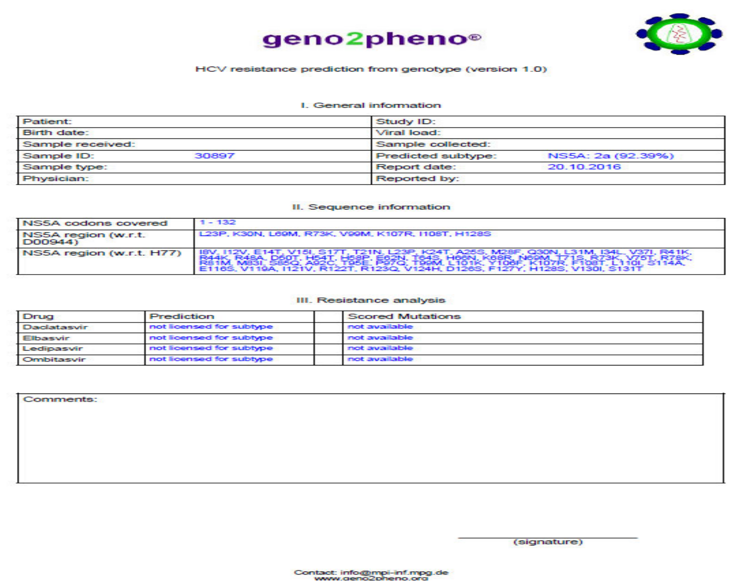


Source: Georgia's HCV Elimination Program Treatment Database

NS5A RAS testing
Geno2pheno [HCV]







Decentralization of HCV treatment and care services

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

L.I.F.E.R.
LIVER INSTITUTE AND FOUNDATION FOR EDUCATION AND RESEARCH

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

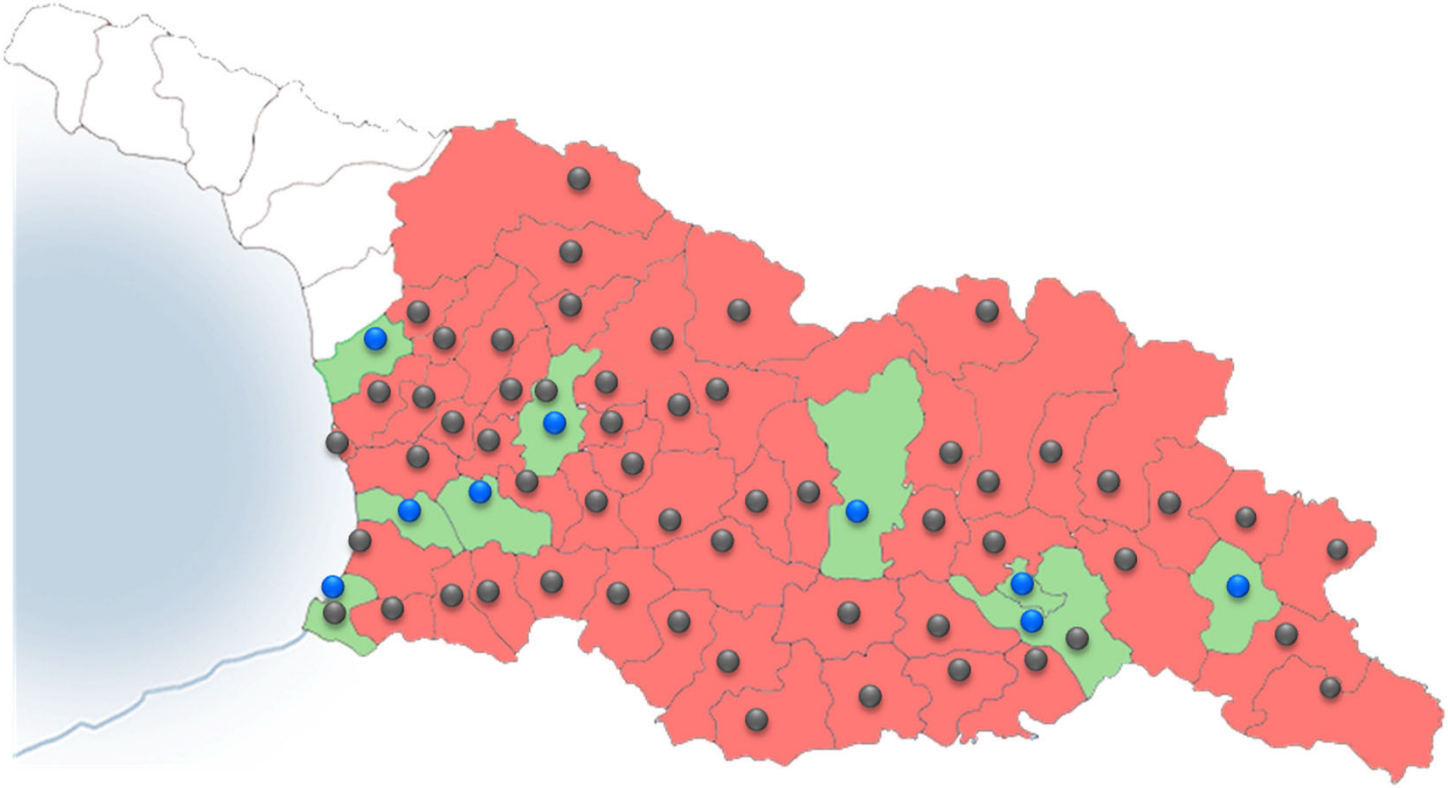
Primary care/hospitals working group established

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

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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 ad-hoc 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.

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MONITORING AND EVALUATION INDICATORS

2015-2018

Objective: Promote universal access to HCV care and treatment

Indicator name	Measurement	Value
1. Proportion of anti-HCV positive persons assessed for viraemic HCV infection	Number of HCV antibody positive persons tested for viraemic HCV infection **75,491** / Number of people with a presence of anti-HCV antibodies **92,875**	= **81.3%**
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 Treatment 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** / Number of persons diagnosed with chronic HCV infection **64,232**	= **79.5%**
	☐ 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** / Number of patients diagnosed with chronic HCV infection who initiated treatment **51,072**	= **94.4%**

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** / Number of patients who completed antiviral therapy and were assessed for SVR 12-24 weeks post treatment **34,048**	= **98.2%**
	☐ 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** / Estimated resident population: **3 010 200**	= **5.1 per 100,000 residents**
7. Number of a/ Primary Healthcare Centers; b) Harm Reduction Sites providing HCV care and treatment	8 primary healthcare sites 3 Harm reduction sites	

Source: Georgia's HCV Elimination Program Treatment Database

Elimination Goal

II

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

Acknowledgements

Technical Advisory Group (TAG)

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Amiran Gamkrelidze

All HCV Clinical Care Provider Clinics