4th HEPATITIS C TECHNICAL ADVISORY GROUP

TAG Meeting

ASSESSMENT OF THE NATIONAL HEPATITIS C ELIMINATION PROGRAM: TREATMENT OUTCOMES AND ASSOCIATED FACTORS

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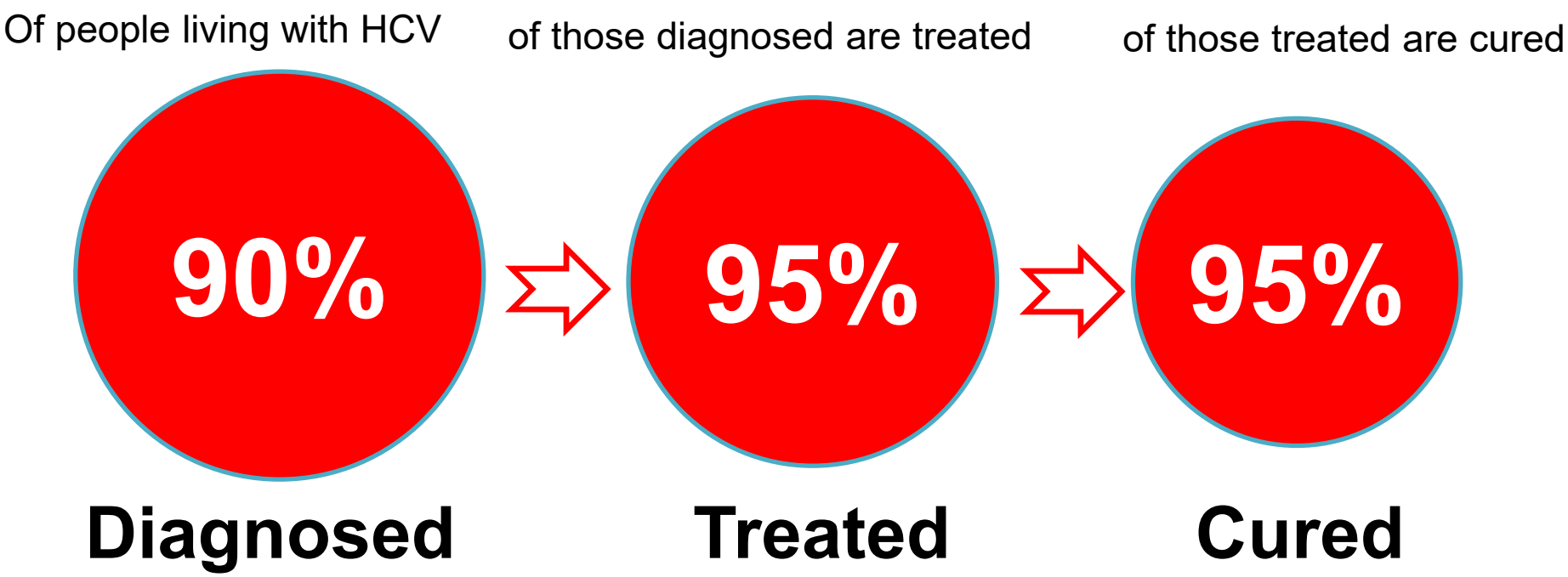
Hepatitis C Elimination Strategy

Care and Treatment

Goal:

Provide universal access to HCV care and treatment and to achieve high cure rates

Targets: 90-95-95



Reducing the HCV prevalence by 90% by 2020

National Hepatitis C Elimination Program

program has been implemented in two phases.

April 2015- June 2016

Treated more than 9,000 patients:

- **F3/F4 fibrosis**
- **Severe extrahepatic manifestations**
- **HIV/HCV co-infection**

From June 2016

Treatment of all patients:
Treatment naive
Treatment experience
(including F0 fibrosis)

National treatment protocols

developed by the clinical group in collaboration with leading international experts:
Drs. Afdhal, Zeuzem, Dusheiko, Arora and Thornton.

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 for 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

This approach had serious opponents, but results exceeded all expectations

New Protocol was approved

Sofosbuvir/Velpatasvir(Epclusa)

Will be available very soon

Ledipasvir/Sofosbuvir (Harvoni)	For all Treatment naïve genotype 1 patient
Sofosbuvir/Velpatasvir (Epclusa)	For all Treatment naïve genotype 2 and genotype 3 patients For all Treatment experienced patients (regardless of genotype)

Hepatitis C Pre-Treatment Evaluation (simplified)

Since April 2017

- ✓ Clinical assessment
- ✓ HCV genotyping
- ✓ Complete blood count
- ✓ ALT, AST, creatinine, bilirubin, albumin, INR alkaline phosphatase, G-GT, glucose
- ✓ HBsAg, Anti-HBc total, HIV
- ✓ 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.***

Simplified treatment Monitoring

Since April 2017

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

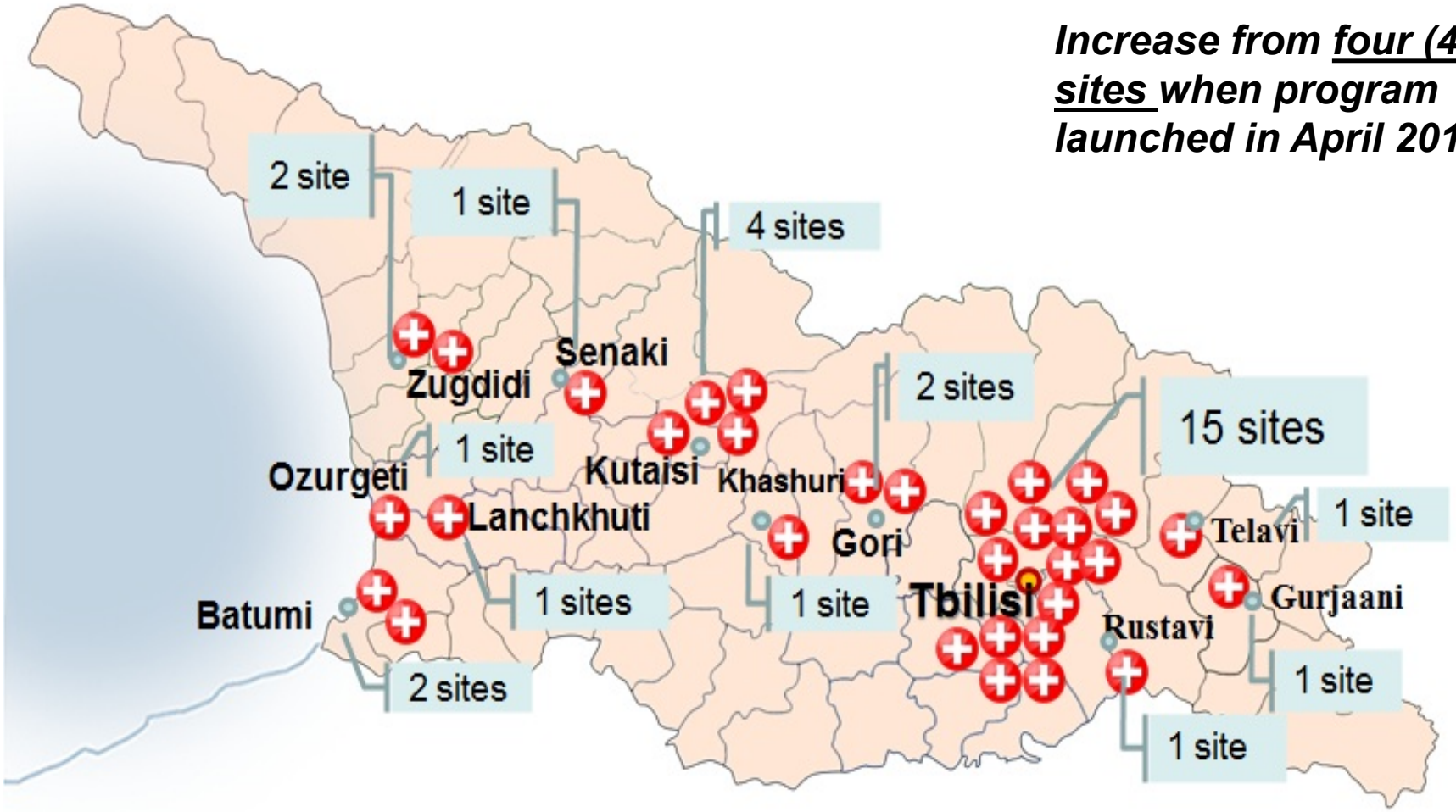
* *for ribavirin -containing regimens.*

** *for ribavirin free regimens.*

*** *HCV RNA level is measured at week 4 and 12 or 24 after treatment termination*

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

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

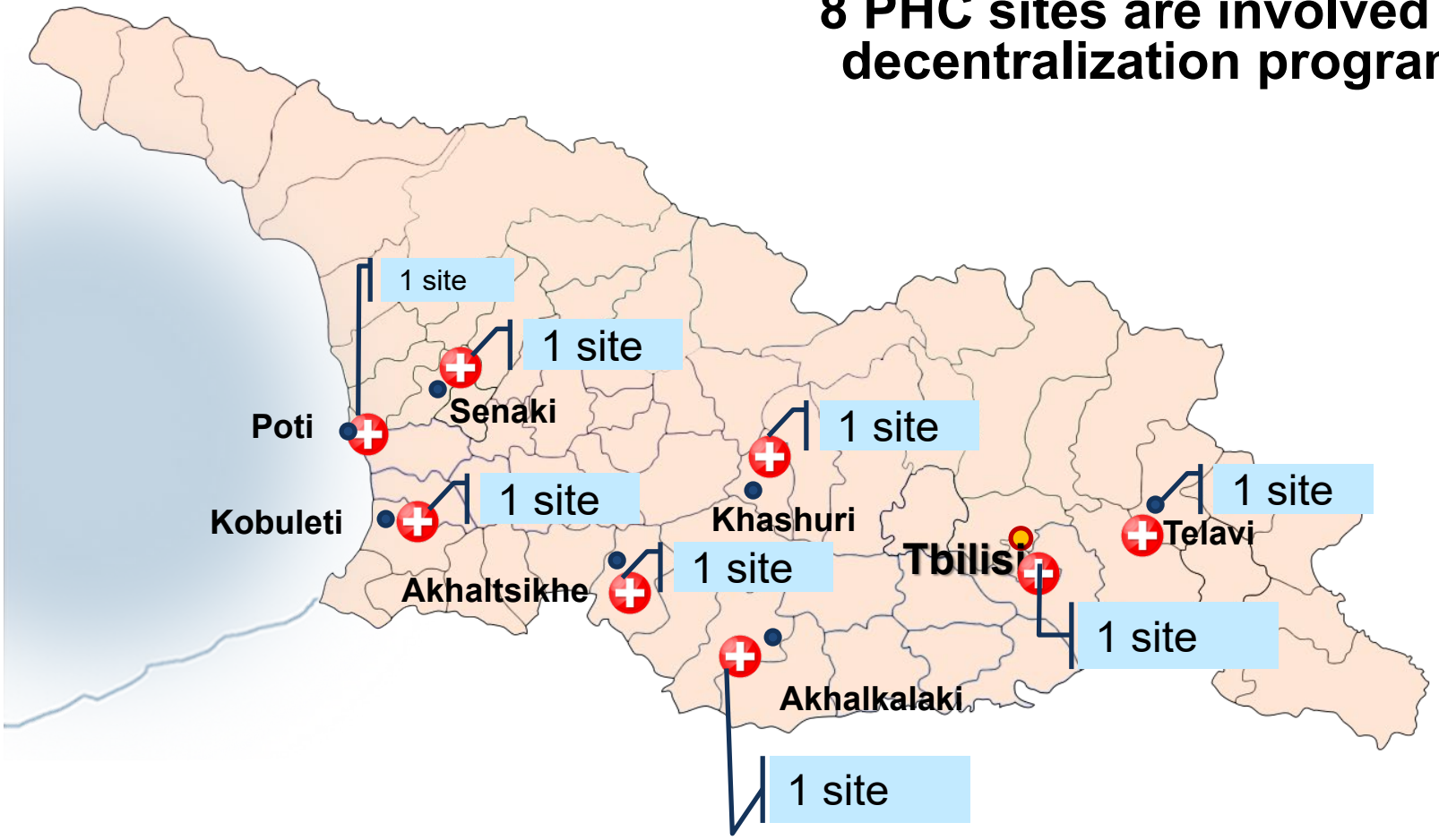


<u>Total:</u> **39 sites**
155 physicians (ID specialists, gastroenterologist, primary care specialists)

Source: Georgia's HCV Elimination Program Treatment Database

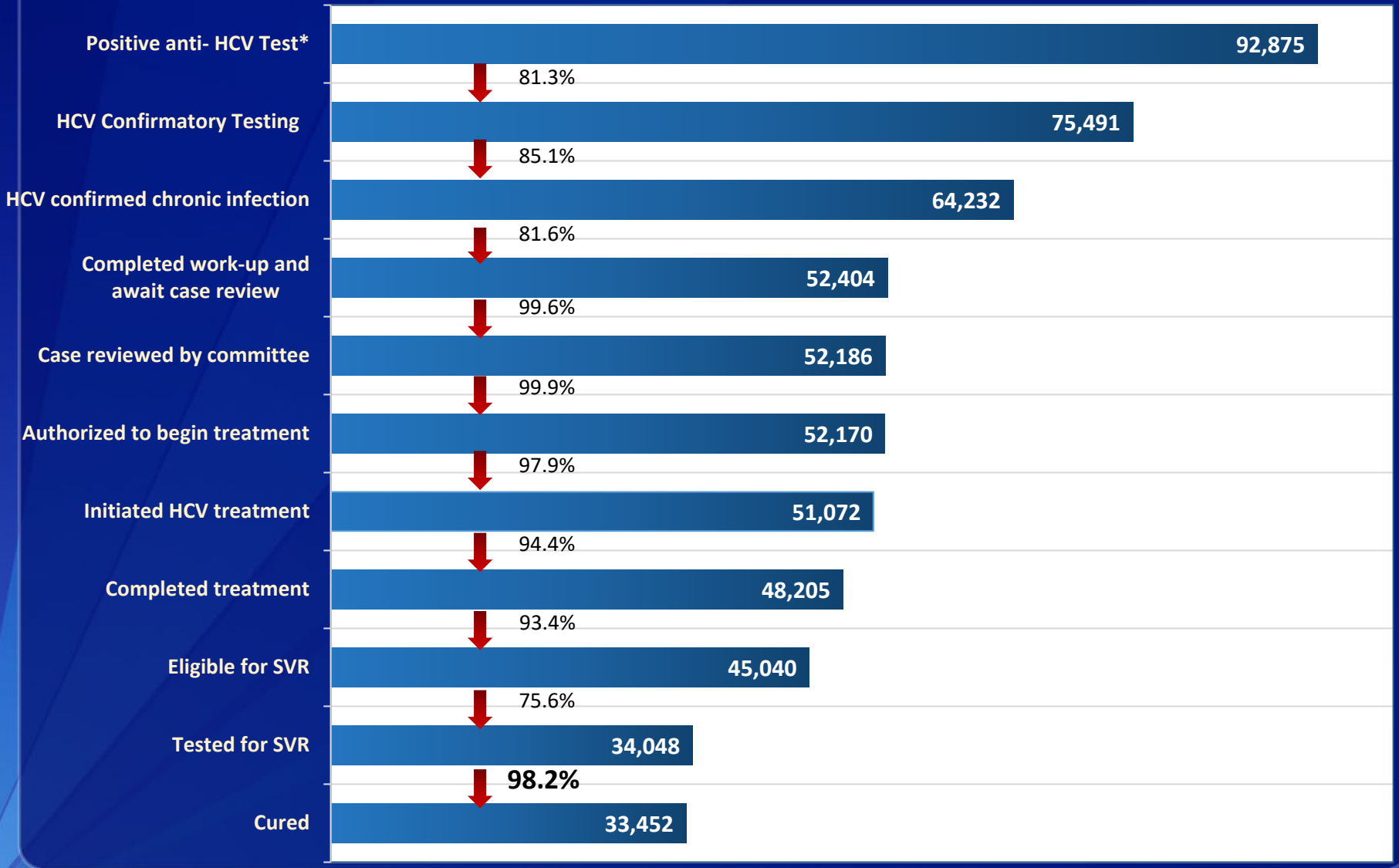
PHCs providing treatment and care within the HCV elimination program

8 PHC sites are involved in decentralization program



Georgia Hepatitis C Elimination Program Care Cascade,

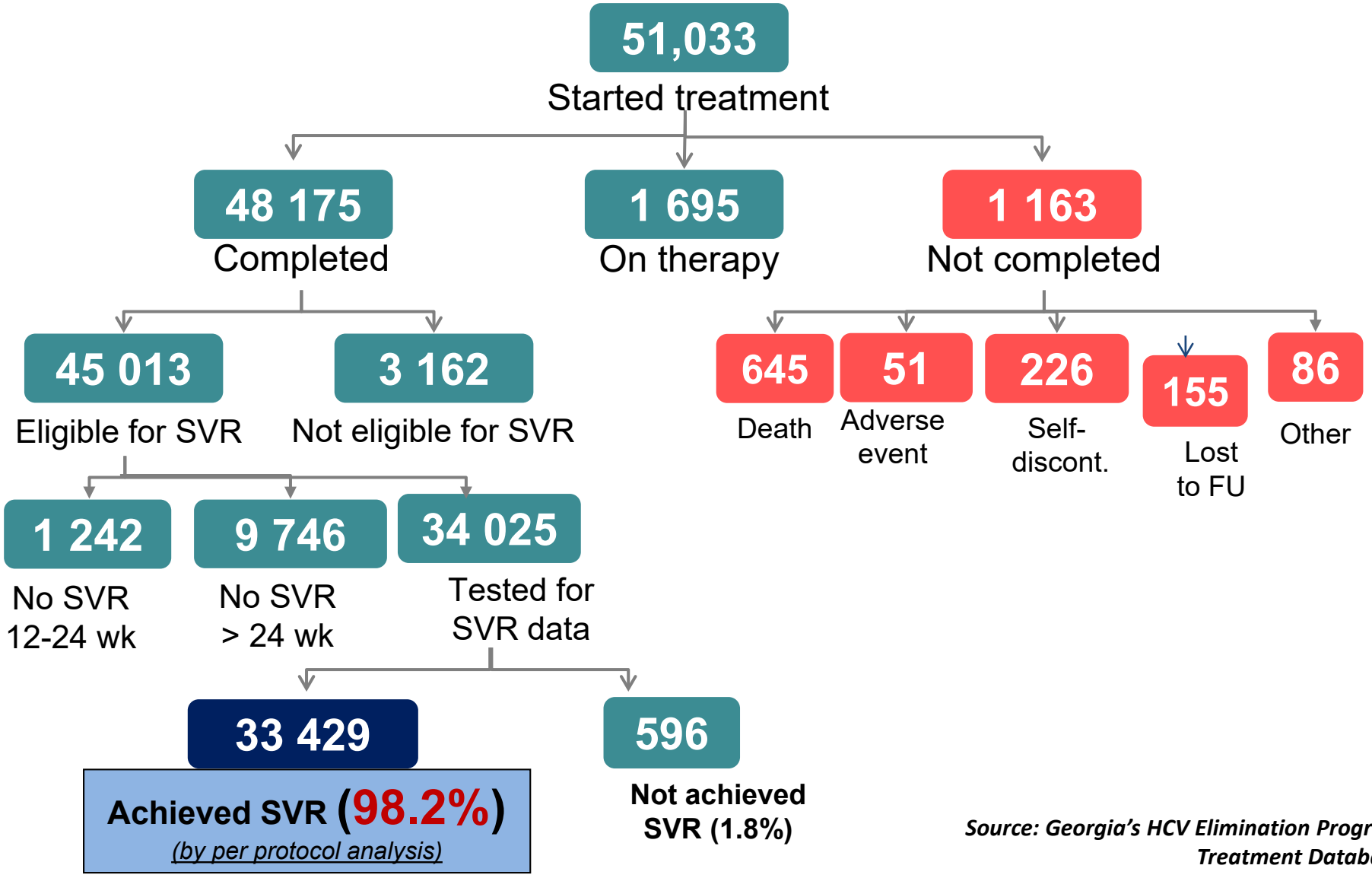
April 28, 2015 – October 31, 2018



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

Cascade of HCV care and treatment outcomes

among patients receiving SOF-based and LED/SOF-based regimens within the national hepatitis C elimination program, April 28, 2015 – October 31, 2018



Source: Georgia's HCV Elimination Program Treatment Database

Results

Treatment Outcomes
According treatment regimens.

METHODS

- All data on persons tested for chronic HCV infection through SVR achievement **were extracted from the national HCV treatment database.**
- HCV RNA or HCV core antigen tests are used for confirming chronic HCV infection. **SVR is defined as undetectable HCV RNA 12-24 weeks after treatment termination**.
- SVR rates were calculated using **per-protocol analysis**, which included only those with complete SVR data,
- All analyses were performed with SAS version 9.3 software (SAS Institute, Inc., Cary, NC, USA).

Treatment Outcomes of SOF-Based regimens

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)

** Last patient received SOF-based therapy was in Dec 2017*

Source: Georgia's HCV Elimination Program Treatment Database

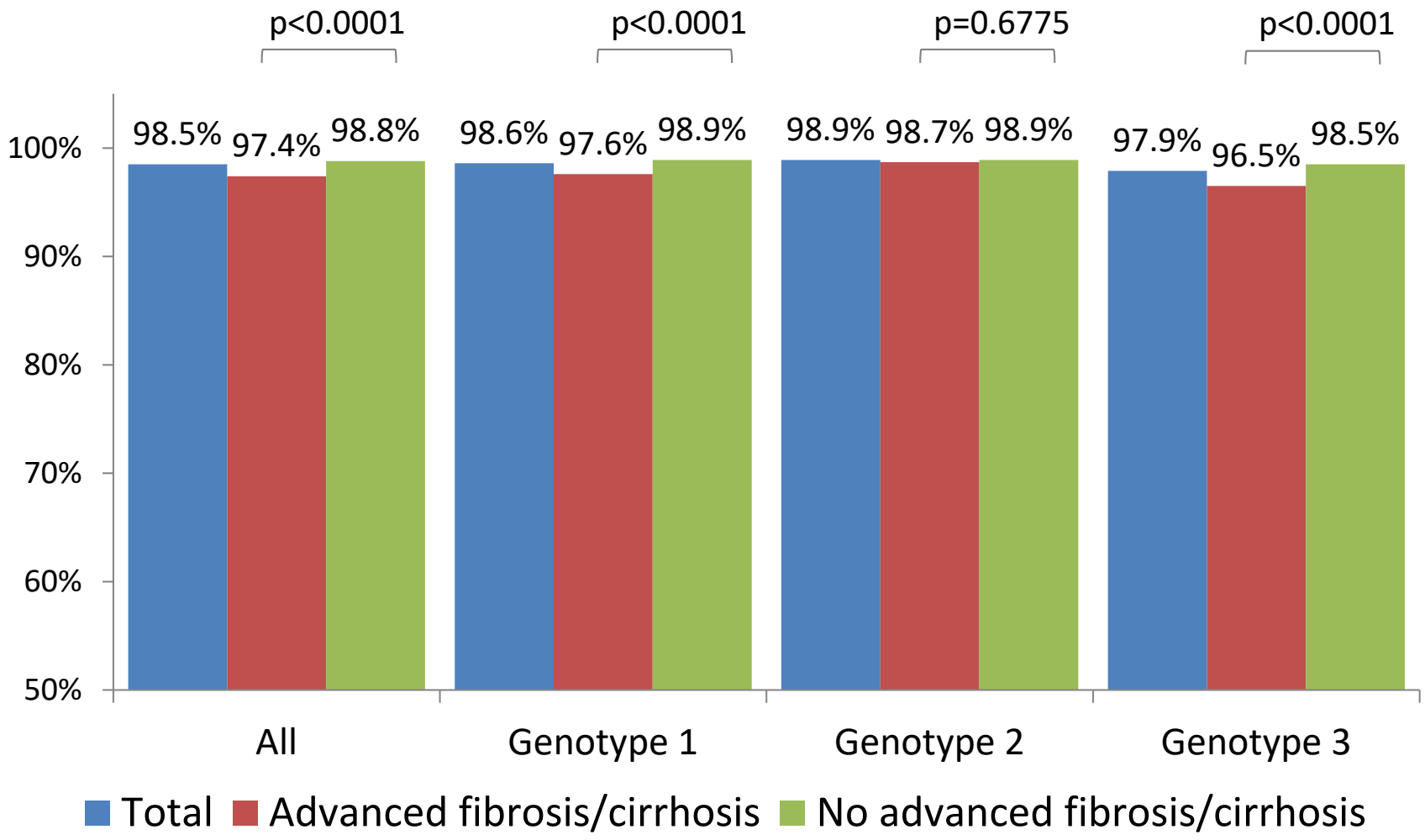
Treatment Outcomes of SOF/LED-Based regimens

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)

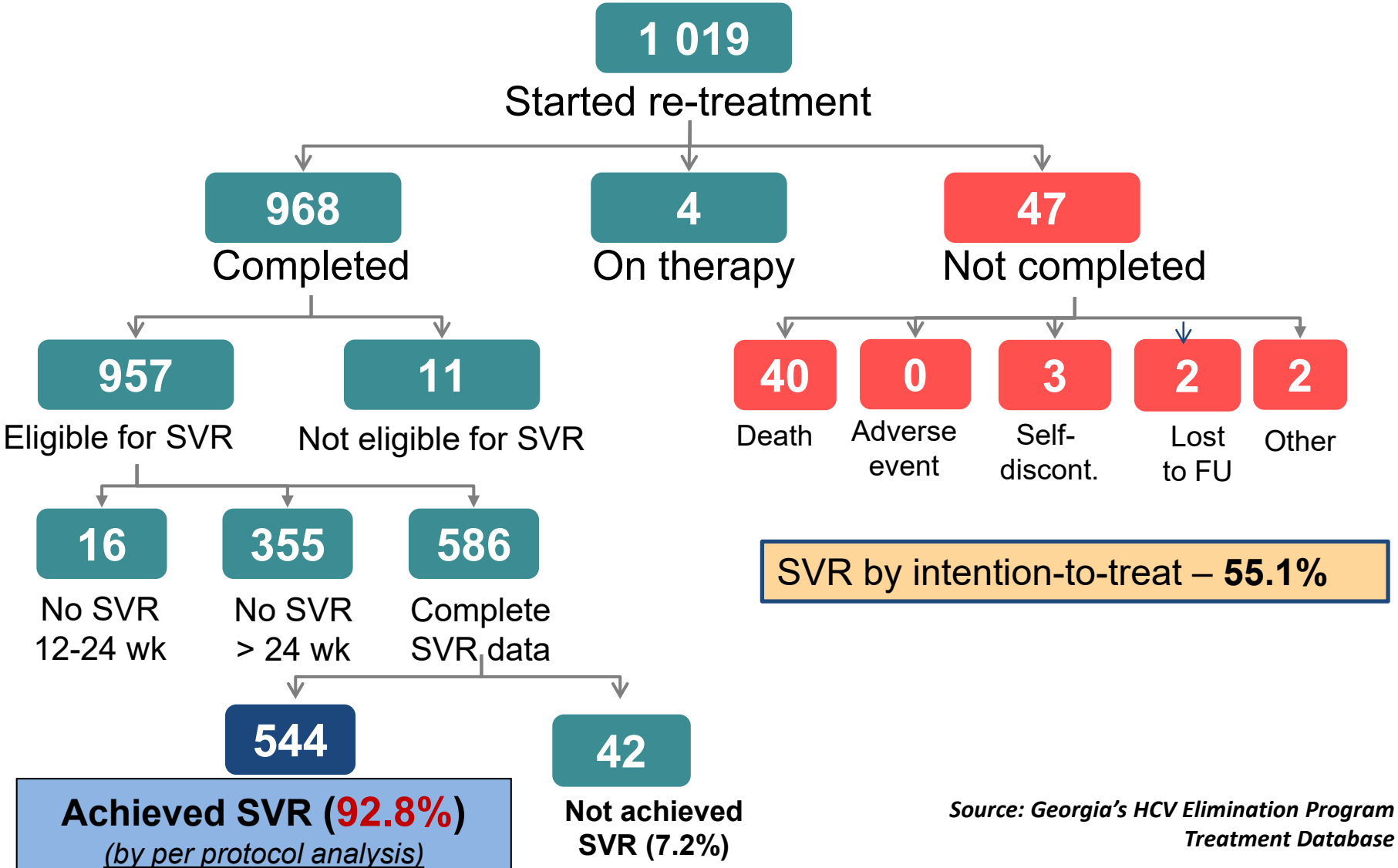
Source: Georgia's HCV Elimination Program Treatment Database

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

CHALLENGES:

- Treatment for **patients with hemodyalisis** is still an issue. Unfortunately Sofosbuvir-based regimens are contraindicated for this category of patients.
- Availability of **Glecaprevir/Pibrentasvir (Mavyret**) would be ideal, since Mavyret does not contain Sofosbuvir, has a pangenotypic effect and is used without Ribavirin.
- There are still some problematic patients in whom ribavirin is contraindicated (**heart diseases, COPD, chronic anemia etc**)
- Introduction of (Epclusa)-SOF/VEL **will optimize treatment** of these patients
- After introduction of Epclusa treatment will be provided **with simplified regimens** (mainly ribavirin free) and it will further improve linkage to treatment and care

Conclusions:

- There is significant progress towards elimination of hepatitis C achieving high cure rates. **Overall SVR is 98.2%**

- LDV/SOF achieved high cure rate in genotype 1 patients in our Georgian cohort similar to data from clinical trials and **real-world studies** (98.6%)

- LDV/SOF in combination with RBV is highly effective for genotypes 2 and 3 and can be considered as a **pangenotypic combination at least in Georgian settings.**

- High cure rates were observed in both patients **with or without advance liver fibrosis/cirrhosis** (97.4% vs. 98.8%) as well as in treatment experienced patients (overall SVR=92.8%)

- **High cure rate (**97.9 %) were observed **with LDV/SOF +RBV in** difficult to treat **HCV genotype 3 patients**

- LDV/SOF achieved high cure rate (98.9%) in genotype 2 patients. This can be explained by **high prevalence of RF1_ 2k/1b recombinant forms** in Georgia

Acknowledgements

Technical Advisory Group (TAG)

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