HCV TEDAVİSİNDE NEREDEYİZ?
- TÜRKİYE'DE MAVİRET GERÇEK YAŞAM VERİLERİ -

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Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Anabilim Dalı
KAYSERİ

HCV infeksiyonunda tedavinin amaçları

Viral eradikasyonu sağlamak

- **Siroz, dekompanse siroz**
- **Hepatoselüler kanser (HSK)**
- **Ekstrahepatik hastalıkların gelişmesini önlenmek**
- **Mortaliteyi azaltmak**
- **HCV bulaşmasını önlemek**

EASL. J Hepatol. 2020;.73:1170-218.

Tedavi endikasyonları

HCV nedenli kompanse ve dekompanse kronik karaciğer hastalığı olan, tedavi olmak isteyen, tedavi kontrendikasyonu olmayan, tüm tedavi naiv ve deneyimli hastalar tedavi edilmelidir!

Zaman kaybetmeden tedavi başlanması gereken hastalar

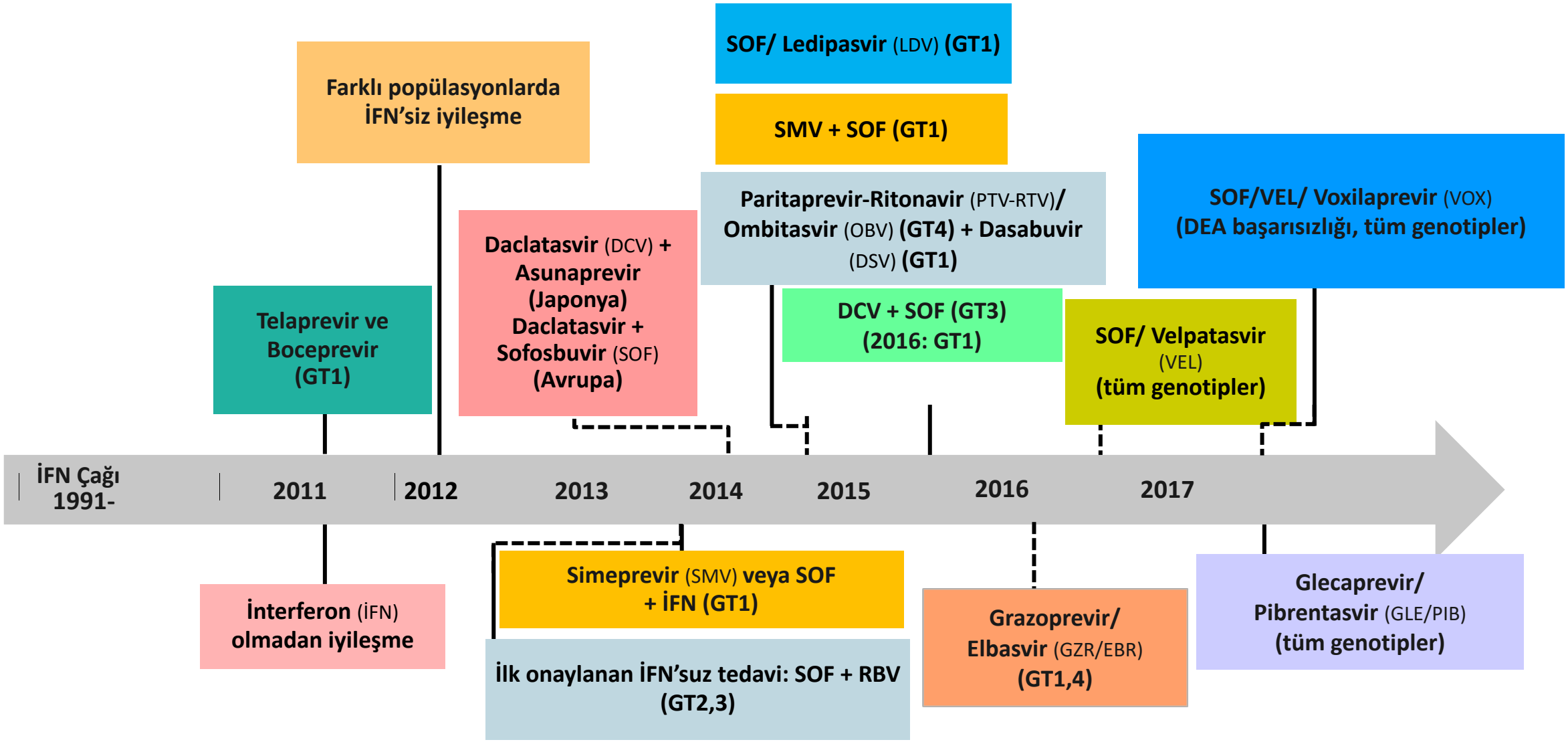
- İleri fibrozu olan hastalar (Metavir F2 ya da F3) / sirotik hastalar (Metavir F4)

  - Dekompanse sirotik hastalar ve anlamlı ekstrahepatik tutulumları olan hastalar dahil -
- Nakil sonrası nüks yaşayan hastalar
- Ko-morbid hastalığı bulunanlar
- Bulaştırma riski yüksek olan hastalar
  - Damar içi madde kullanıcıları
  - Eşcinsel erkekler
  - Gebe kalmak isteyen kadınlar
  - Hemodiyaliz hastaları
  - Mahkum hastalar

Karaciğer dışı nedenlerle yaşam beklentisi kısa olan hastalara tedavi önerilmez!

EASL. J Hepatol. 2020;.73:1170-218.

HCV tedavisinin evrimi



AASLD-IDSA. https://www.hcvguidelines.org/treatment-naive. Last update: September 29, 2021.

Pangenotipik antiviraller (1)

- **GLE/PIB**
  - GLE: Potent pangenotipik, NS3/4A proteaz inhibitörü
  - PIB: Potent pangenotipik, NS5A inhibitörü
  - GLE/PIB: HCV GT 1-6 infeksiyonlarında günde bir kez, gıdalarla 3 tablet, fiks doz kombinasyon (100/40 mg)
  - Orta (Child Pugh B) ve ağır (Child Pugh C) karaciğer yetmezliğinde kullanılmaz

AASLD-IDSA. https://www.hcvguidelines.org/treatment-naive. Last update: September 29, 2021.

Pangenotipik antiviraller (2)

- **SOF/VEL/VOX**
  - SOF: Potent pangenotipik, nükleozid polimeraz inhibitörü
  - VEL: Potent pangenotipik, NS5A inhibitörü
  - VOX: Potent pangenotipik, NS3/4A proteaz inhibitörü
  - SOF/VEL/VOX: HCV GT 1-6 infeksiyonlarında günde bir kez, tek tablet, fiks doz kombinasyon (400/100/100 mg)
  - Orta (Child Pugh B) ve ağır (Child Pugh C) karaciğer yetmezliğinde kullanılmaz

AASLD-IDSA. https://www.hcvguidelines.org/treatment-naive. Last update: September 29, 2021.

Tedavi seçenekleri

Tedavi seçenekleri	Genotipler
GZR/EBR*	1, 4
SOF/LDV	1, 4, 5, 6
SOF/VEL	1, 2, 3, 4, 5, 6
SOF/VEL/VOX	1, 2, 3, 4, 5, 6
GLE/PIB*	1, 2, 3, 4, 5, 6

*Böbrek yetmezliği ve hemodiyaliz hastalarında onaylanmıştır

- Günlük tek veya üç tabletlik rejimler
- Her genotip için etkili tedavi seçeneği
- RBV içermeyen tedavi seçenekleri ile %95 veya daha yüksek kür oranları

AASLD-IDSA. https://www.hcvguidelines.org/treatment-naive. Last update: September 29, 2021.

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

IDSA Infectious Diseases Society of America

Last update: September 29, 2021

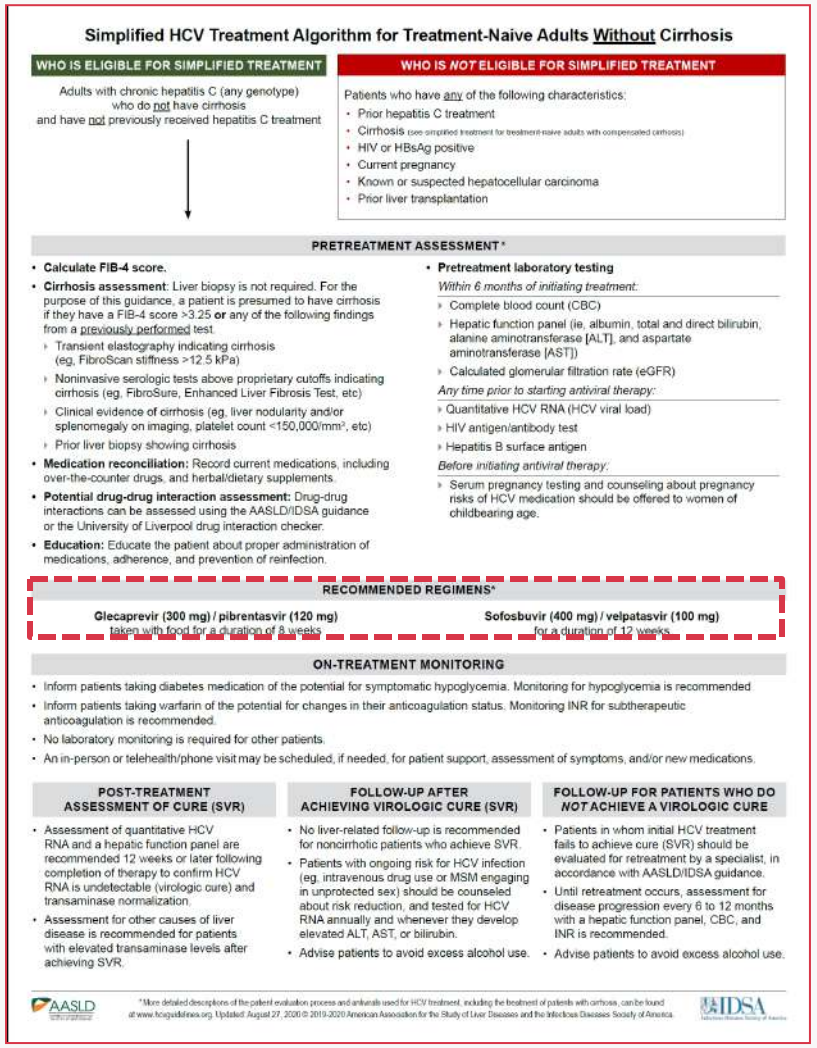
Tedavi tipi	Genotip	Siroz durumu	SOF/VEL	GLE/PIB	SOF/VEL/VOX	GZR/EBR	SOF/LDV
Tedavi-naiv genotip /subtip temelli tedavi	Genotip 1a	NS	12 hafta	8 hafta	Hayır	12 hafta	12 hafta
		KS				Hayır	
	Genotip 1b	NS				12 hafta	
		KS					
	Genotip 2	NS				Hayır	Hayır
		KS					
	Genotip 3	NS					
		KS					
	Genotip 4	NS				12 hafta	12 hafta
		KS					
	Genotip 5-6	NS				Hayır	
		KS					

NS: “Non”- sirotik, KS: kompanse sirotik

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

Last update:
September 29, 2021

- Basitleştirilmiş tedavi -



Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Adults with chronic hepatitis C (any genotype) who do not have cirrhosis and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:
- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Cirrhosis assessment**: Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm³, etc)
  - Prior liver biopsy showing cirrhosis
- **Medication reconciliation:** Record current medications, including over-the-counter drugs, and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing**

Within 6 months of initiating treatment:
- Complete blood count (CBC)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy:
- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen

Before initiating antiviral therapy:
- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg) taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg) for a duration of 12 weeks

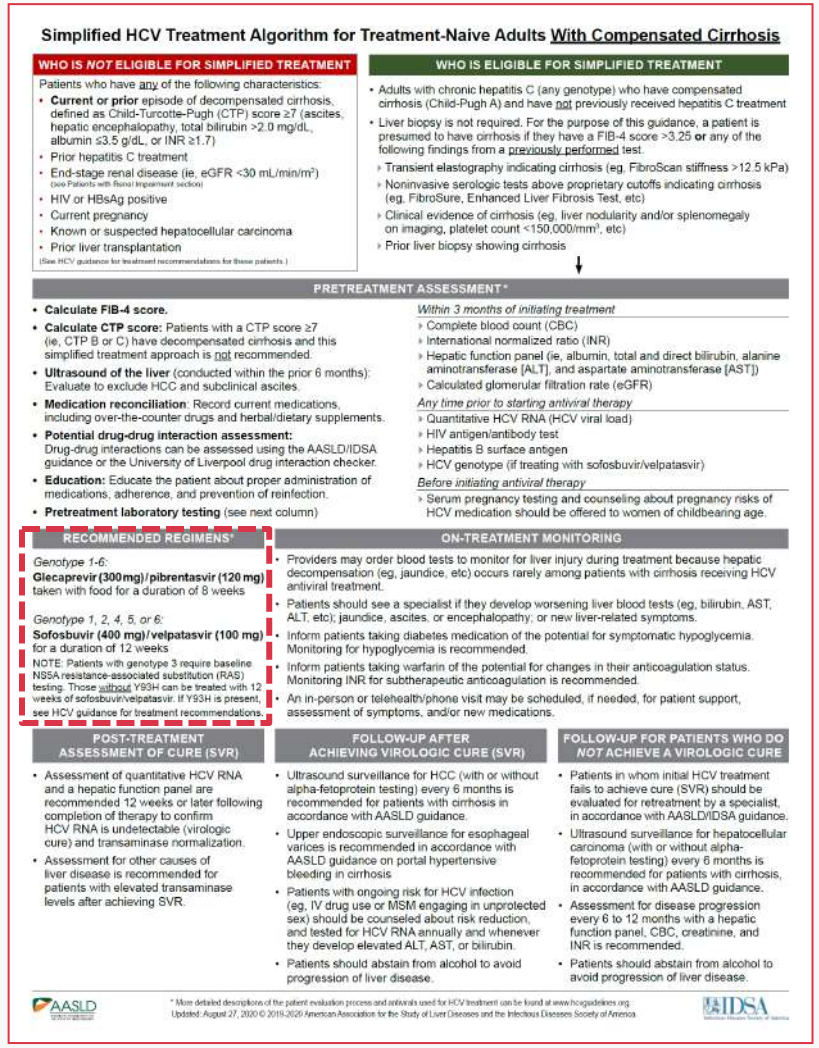
ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)
- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)
- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Advise patients to avoid excess alcohol use.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE
- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Until retreatment occurs, assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Advise patients to avoid excess alcohol use.



Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:
- **Current or prior** episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m²) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these patients.)

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

- Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment
- Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm³, etc)
  - Prior liver biopsy showing cirrhosis

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Calculate CTP score:** Patients with a CTP score ≥7 (ie, CTP B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **Medication reconciliation**: Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing** (see next column)

Within 3 months of initiating treatment
- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy
- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen
- HCV genotype (if treating with sofosbuvir/velpatasvir)

Before initiating antiviral therapy
- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Genotype 1-6:
Glecaprevir (300 mg) / pibrentasvir (120 mg) taken with food for a duration of 8 weeks

Genotype 1, 2, 4, 5, or 6:
Sofosbuvir (400 mg) / velpatasvir (100 mg) for a duration of 12 weeks

NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, see HCV guidance for treatment recommendations.

ON-TREATMENT MONITORING

- Providers may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment.
- Patients should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms.
- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)
- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)
- Ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis in accordance with AASLD guidance.
- Upper endoscopic surveillance for esophageal varices is recommended in accordance with AASLD guidance on portal hypertensive bleeding in cirrhosis
- Patients with ongoing risk for HCV infection (eg, IV drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Patients should abstain from alcohol to avoid progression of liver disease.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE
- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis, in accordance with AASLD guidance.
- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, creatinine, and INR is recommended.
- Patients should abstain from alcohol to avoid progression of liver disease.

Practice Guidelines

JOURNAL OF HEPATOLOGY

Journal of Hepatology 2020 vol. 73 | 1170–1218

EASL recommendations on treatment of hepatitis C: Final update of the series☆

European Association for the Study of the Liver*

Tedavi tipi*	Genotip	Siroz durumu	Önceki tedavi deneyimi	SOF/VEL	GLE/PIB	SOF/VEL/VOX	GZR/EBR
Genotip /subtip temelli tedavi	Genotip 1a, 1b, 2, 4, 5 and 6	NS	TN	12 hafta	8 hafta	Hayır	12 hafta (GT1b sadece)
			TD				
		KS (CP A)	TN				
			TD		12 hafta		
	Genotip 3	NS	TN	12 hafta	8 hafta	Hayır	Hayır
			TD		12 hafta		
		KS (CP A)	TN	12 hafta + RBV	8-12 hafta	12 hafta	
			TD		16 hafta		
	Subtip 1l, 4r, 3b, 3g, 6u, 6v veya doğal olarak herhangi NS5A RAS bulunduran subtipler	NS	TN	Bilinmiyor	Bilinmiyor	12 hafta	
		KS (CP A)	TD				
			TN				
			TD				

*** HCV ile mono-infekte veya HCV-HIV ko-infekte 18 yaş üzeri erişkinler ile 12-17 yaş arası adölesanlar**

TN :Tedavi naiv, TD :Tedavi deneyimli (Peg-İFN+RBV, Peg-İFN+RBV+SOF, SOF+RBV kullanan hastalar), RBV: Ribavirin, KS:kompanse sirotik, CP-A: Child Pugh A

Practice Guidelines

JOURNAL OF HEPATOLOGY

Journal of Hepatology 2020 vol. 73 | 1170–1218

EASL recommendations on treatment of hepatitis C: Final update of the series☆

European Association for the Study of the Liver*

- Basitleştirilmiş tedavi -

Tedavi tipi*	Genotip	Siroz durumu	Önceki tedavi deneyimi	SOF/VEL	GLE/PIB	SOF/VEL/VOX	GZR/EBR
Basitleştirilmiş tedavi: Genotip ve subtip tayini yapılmaz	Tüm genotipler	Siroz yok	TN	12 hafta	8 hafta	Hayır	Hayır
			TD				
		Kompanse siroz	TN				
			TD		12 hafta		

*** HCV ile mono-infekte veya HCV-HIV ko-infekte 18 yaş üzeri erişkinler ile 12-17 yaş arası adölesanlar**

TN: Tedavi naiv, TD: Tedavi deneyimli (Peg-İFN+RBV, Peg-İFN+RBV+SOF, SOF+RBV kullanan hastalar)

1 Haziran 2022 ÇARŞAMBA **Resmî Gazete** Sayı : 31853

TEBLİĞ

Sosyal Güvenlik Kurumu Başkanlığından:

SOSYAL GÜVENLİK KURUMU SAĞLIK UYGULAMA TEBLİĞİNDE DEĞİŞİKLİK YAPILMASINA DAİR TEBLİĞ

Naiv hastalarda tedavi

Tedavi seçenekleri	"Non"-Sirotik	Kompanse sirotik (Child Pugh A)	Dekompanse sirotik (Child Pugh B,C)*
GLE/PIB	8 hafta	8 hafta	-
SOF/VEL/VOX	8 hafta	12 hafta	-
SOF/LDV+RBV			12 hafta

* HCV genotip 1a, 1b, 4, 5, 6 ile infekte hastalarda

Tedavi deneyimli hastalarda yeniden tedavi

NS5A harici tedavi deneyimli hastalar	"Non"-Sirotik	Kompanse sirotik (Child Pugh A)	Dekompanse sirotik (Child Pugh B,C)
GLE/PIB	8 hafta	12 hafta	-
SOF/VEL/VOX	12 hafta	12 hafta	-

NS5A veya proteaz inhibitörü tedavi deneyimi olan hastalar	"Non"-Sirotik	Kompanse sirotik (Child Pugh A)	Dekompanse sirotik (Child Pugh B,C)**
GLE/PIB veya GLE/PIB+…	16 hafta*	16 hafta*	-
SOF/VEL/VOX	12 hafta	12 hafta	-
SOF/LDV+RBV			24 hafta

* Rapor onayı ile, ** HCV genotip 1a, 1b, 4, 5, 6 ile infekte hastalarda

Maviret kısa ürün bilgisi

	GT1		GT2		GT3		GT4		GT5		GT6	
	Sirotik Olmayan	Kompanse Sirotik	Sirotik Olmayan	Kompanse Sirotik	Sirotik olmayan	Kompanse Sirotik	Sirotik Olmayan	Kompanse Sirotik	Sirotik olmayan	Kompanse Sirotik	Sirotik Olmayan	Kompanse Sirotik
Tedavi Naif Hastalar	8 HAFTA											
NS5A* inhibitörü dışında herhangi bir tedavi deneyimi olan hastalar	8 hafta	12 hafta	8 hafta	12 hafta	16 HAFTA		8 hafta	12 hafta	8 hafta	12 hafta	8 hafta	12 hafta
NS5A* inhibitörü içeren herhangi bir tedavi deneyimi olan hastalar	16 HAFTA											

Türkiye'de tedavide ne kadar yol aldık?

Austin Pharmacology & Pharmaceutics

Open Access

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Volume 3 Issue 1 - 2018

Research Article

Sofosbuvir Plus Ledipasvir Treatment in Patients with Hepatitis C Genotype 4d Infection who Previously Failed to Achieve Sustained Virological Response with Telaprevir or Boceprevir Combination Therapies

Aygen B[1], Yıldız O[1*], Gökahmetoğlu S[2], Taheri S[3] and Baltac S[1]

Table 1: The demographic characteristics and treatment outcomes of the patients

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10*
Age (years)	57	46	39	52	27	64	56	61	55	62
Gender	F	M	M	F	F	F	M	F	F	F
Prior type of response										
PegIFN/RBV	Null response	Null response	Null response	Null response	Null response	Relapse	Partial response	Null response	Null response	Null response
TVR or BOC/ PegIFN/RBV	Null response	Null response	Null response	Null response	Null response	Null response	Relapse	Null response	Null response	Null response
Baseline ALT level (IU/L)	40	29	32	27	25	15	35	43	57	63
Baseline AST level (IU/L)	37	25	30	22	24	14	29	48	68	80
Viral load at baseline (IU/mL)	3,653,928	2,784,848	17,900,000	10,900,000	1,630,000	3,860,000	1,730,000	15,600,000	12,190,215	1,160,000
Liver biopsy**										
Necroinflammatin score	10	3	5	5	6	3	3	7	10	9
Fibrosis score	3	1	1	2	1	0	0	6	6	6
IL28B rs12979860 C/T gene polymorphism	CT	CT	TT	CT	CT	CT	CT	TT	TT	CT
On-treatment and post-treatment virologic responses (HCV RNA <15 IU/mL)										
At week 4	Negative	Negative	Negative	Negative	Positive	Positive	Negative	Positive	Positive	Positive
At week 8	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
At week 12	Negative (ETR)	Negative (ETR)	Negative (ETR)	Negative (ETR)	Negative (ETR)	Negative (ETR)	Negative (ETR)	Negative	Negative	Negative
At week 24	Negative (SVR)	Negative (SVR)	Negative (SVR)	Negative (SVR)	Negative (SVR)	Negative (SVR)	Negative (SVR)	Negative (ETR)	Negative (ETR)	Negative (ETR)
At week 36								Negative (SVR)	Negative (SVR)	Negative (SVR)

Received: 9 August 2018 | Accepted: 11 January 2019
DOI: 10.1111/jvh.13075

ORIGINAL ARTICLE

WILEY JVH
J Viral Hepat. 2019;26:666–674.

Low recurrence rate of hepatocellular carcinoma following ledipasvir and sofosbuvir treatment in a real-world chronic hepatitis C patients cohort

Ramazan Idilman[1] | Mehmet Demir[2] | Murat Aladag[3] | Cihan Erol[4] | Bilger Cavus[5] | Raim Iliaz[5] | Hayrettin Koklu[6] | Yilmaz Cakaloglu[7] | Memduh Sahin[8] | Galip Ersoz[9] | İftihar Koksal[10] | Zeki Karasu[9] | Meric Ozgenel[11] | İlker Turan[9] | Feyza Gunduz[12] | Huseyin Ataseven[13] | Meral Akdogan[14] | Murat Kiyici[15] | Aydın Seref Koksal[16] | Sila Akhan[17] | Fulya Gunsar[9] | Fehmi Tabak[18] | Sabahattin Kaymakoglu[5] | Ulus S Akarca[9] | Early Access Program (EAP) Study Group[a]

- 175 hastanın 156'sı SOF/LDV, 19'u SOF/LDV + RBV
- Ortalama takip süresi 22.1 ay
- KVY12: %86 (İTT) - %98.3 (PP)
- Tedavi deneyim durumu ve Child Pugh sınıfları arasında KVY12 açısından anlamlı fark yok (CP-A %93.4, CP-B %82.1, CP-C %79.9 ve karaciğer nakli olanlarda %91.7)

TABLE 1 Baseline characteristics of all HCV-positive patients

n (%)	200
Age (y, median, range)	62 (27-84)
Gender (M/F)	92/108 (46/54)
Median serum HCV RNA level (log_{10} IU/mL)	5.94
Median serum ALT level (range, U/L)	65 (41-106)
HCV genotype*	
Genotype 1b	162 (84.4)
Genotype 1	20 (10.4)
Genotype 1a	7 (3.6)
Genotype 4	3 (1.6)
Antiviral treatment experience	116 (58)
Median Child-Pugh class	8 (5-14)
Child-Pugh class A/B/C	66/74/60 (33/37/30)
Median MELD score	16 (6-29)
Liver transplant recipients	48 (24%)

Original article

European Journal of Gastroenterology & Hepatology

2019 Apr;31(4):534-539.

Effectiveness of fixed-dose combination of paritaprevir, ritonavir, ombitasvir, and dasabuvir in patients with chronic hepatitis C virus infection and chronic kidney diseases: real-life experiences

Necati Örmeci[a], Orhan Sezgin[c], Rıdvan Karaali[d], Bilgehan Aygen[e], Dilara Turan[a], Serkan Yaras[c], İlknur Erdem[d], Orhan Yıldız[e], Fatih Karakaya[a], Kenan Ateş[b] and Özgün Ö. Asiller[a]

Table 1. Characteristics of patients

	n (%)
Sex (female–male count)	44 (58.66)–31 (41.33)
Genotype 1a	7 (9.33)
Genotype 1b	58 (77.33)
Genotype 4	10 (13.33)
Number of treatments experienced	9 (12)
PEG-α2a	7 (9.33)
PEG-α2b	1 (1.33)
IFN-2a	1 (1.33)
Number of treatments naive	66 (88)
CKD stage [GFR (ml/min/1.73 m^2)]	
Stage 2 (60–89)	12 (16)
Stage 3a (45–59)	1 (1.3)
Stage 3b (30–44)	1 (1.3)
Stage 4 (15–29)	13 (17.3)
Stage 5 (< 15)	49 (65.3)
Liver cirrhosis (CPT-A)	7 (9.3)
Kidney transplantation	4 (5.3)
Hemodialysis	53 (70.6)

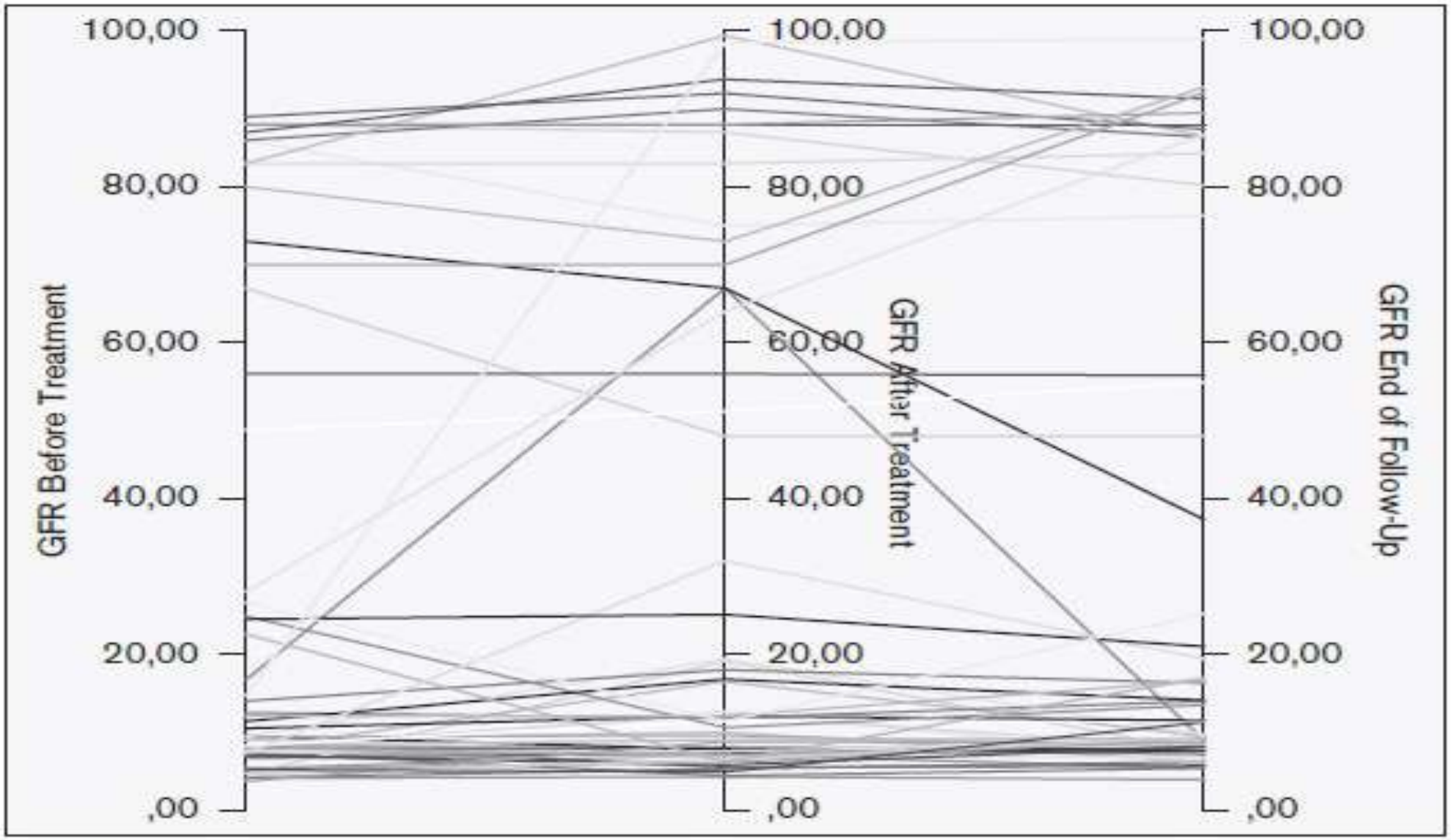

Fig. 2. There were no significant differences among glomerular filtration rates (GFRs) at baseline, end of treatment, and follow-up ($P = 0.22$, 0.69, 0.17, respectively).

KLİMİK-VHÇG

- Türkiye’de KHC’li hastalarda DEA tedavi sonuçlarının değerlendirildiği gerçek yaşam verisi çalışmaları -

- 1799 hasta -

- **34 merkez 1414 hasta**
  - **Sofosbuvirli kombinasyon tedavisi: 552**
  - **PTV-RTV+OBV ± DSV ± RBV tedavisi: 862**
- **GLE/PIB çalışması: 16 merkez, 385 hasta**

ORIGINAL ARTICLE

LIVER

Real-world efficacy, safety, and clinical outcomes of ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin combination therapy in patients with hepatitis C virus genotype 1 or 4 infection: The Turkey experience experience

*Bilgehan Aygen[1], Neşe Demirtürk[2], Orhan Yıldız[1], Mustafa Kemal Çelen[3], İlhami Çelik[4], Şener Barut[5], Onur Ural[6], Ayşe Batırel[7], Reşit Mıstık[8], Funda Şimşek[9], Ali Asan[10], Gülden Ersöz[11], Nesrin Türker[12], Hüseyin Bilgin[13], Sami Kınıklı[14], Faruk Karakeçili[15], Gökmen Zararsız[16], The Study Group for Viral Hepatitis of the Turkish Society of Clinical Microbiology and Infectious Diseases**

Turk J Gastroenterol 2020; 31(4): 305-17

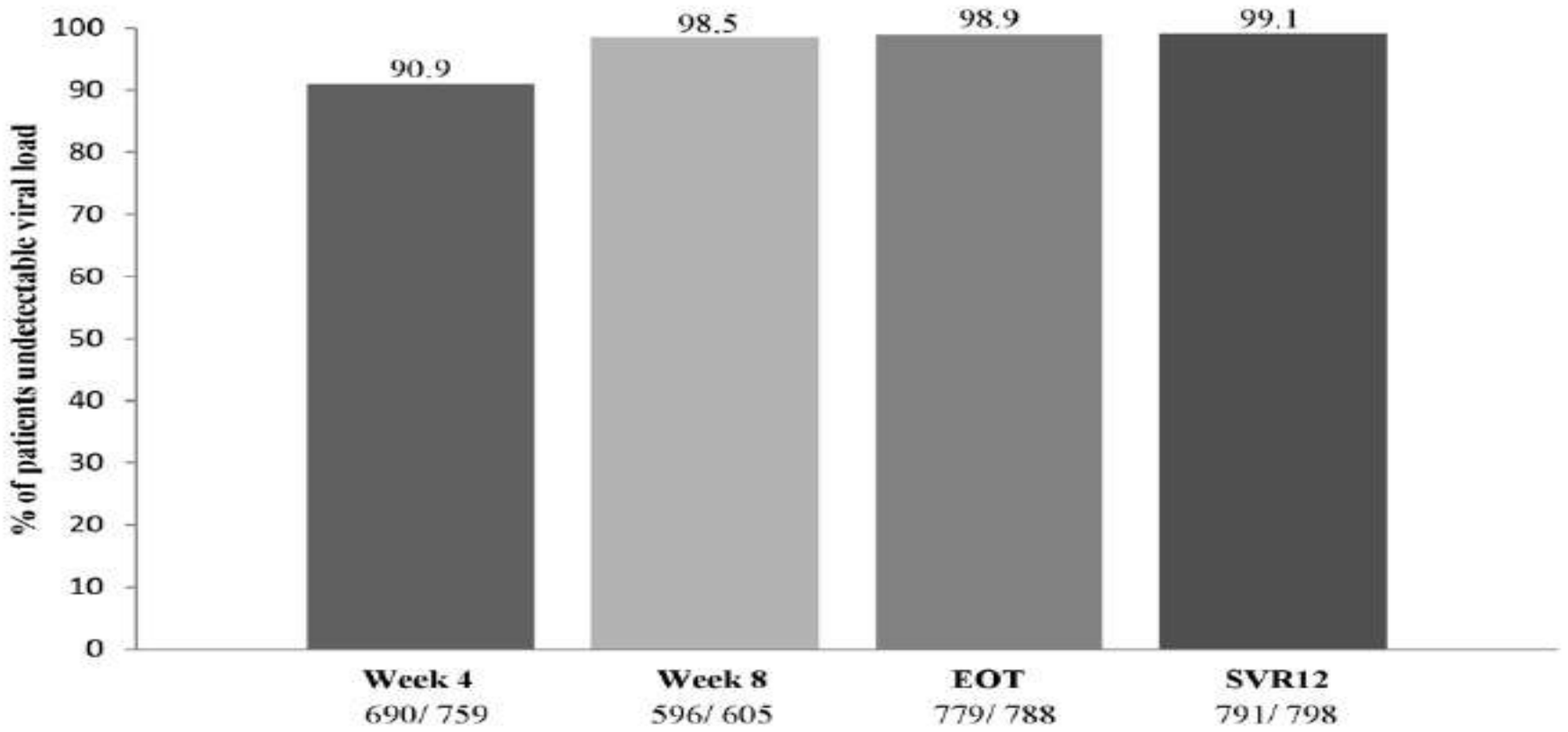

Figure 2. Efficacy of ombitasvir paritaprevir ritonavir ± dasabuvir ± ribavirin at different time points during treatment and 12 weeks after treatment.

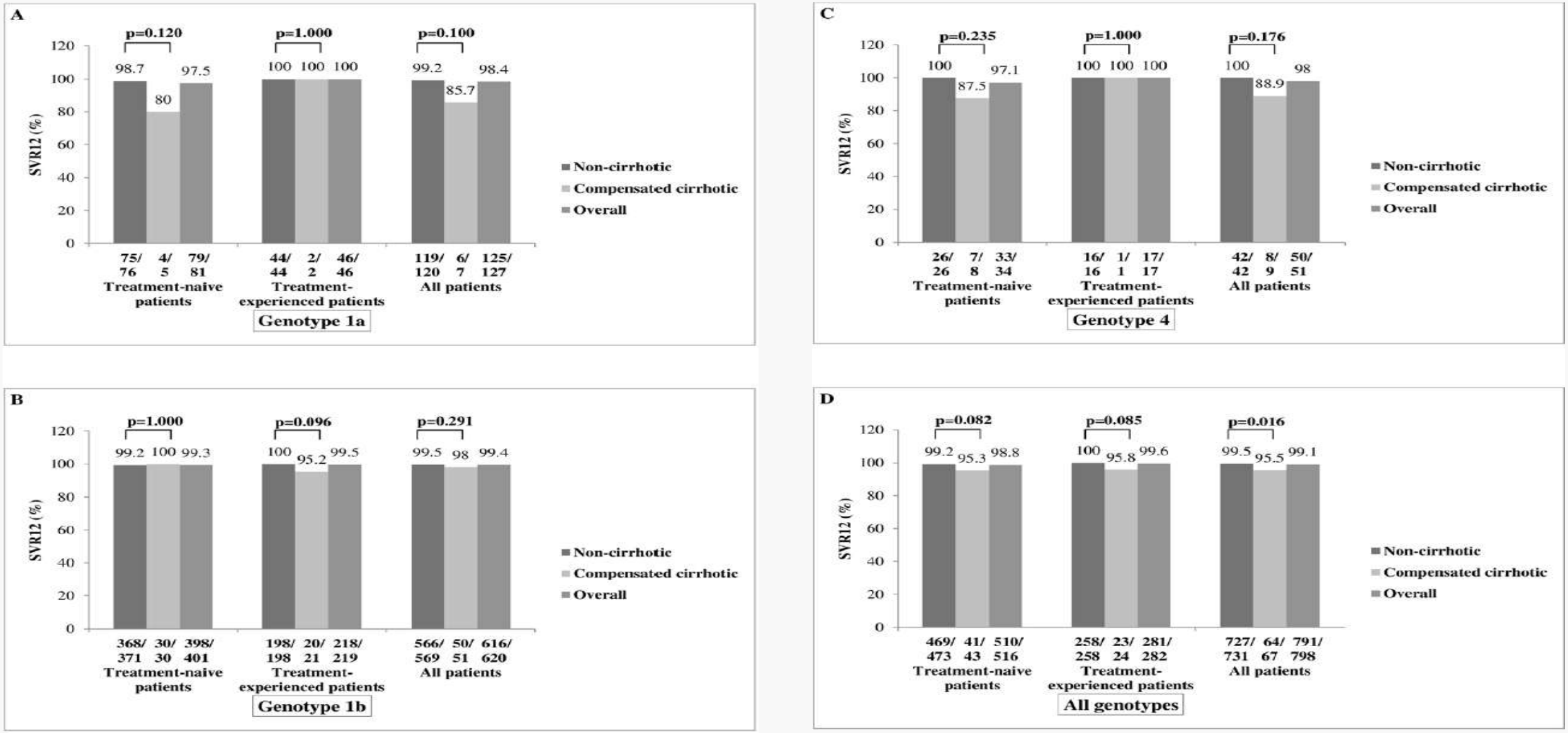

Figure 3. Rates of virological response to ombitasvir paritaprevir ritonavir dasabuvir ribavirin.

ORIGINAL ARTICLE

Infect Dis Clin Microbiol 2019; 1(2): 97-106

Ombitasvir/ Paritaprevir/ Ritonavir + Ribavirin Combination Therapy in Hepatitis C Virus Infected Patients with Genotype 4 in Real-life Practice: A Multicentre Experience

Bilgehan Aygen[1], Neşe Demirtürk[2], Orhan Yıldız[1], İlhami Çelik[3], Deniz Kamalak Güzel[3], Gülden Ersöz[4], Ayşe Batırel[5], Bahar Örmen[6], Faruk Karakeçili[7], Pınar Korkmaz[8], Nazan Tuna[9], Alper Şener[10], Rıza Aytaç Çetinkaya[11], Emine Türkoğlu[2], Güliz Evik[4], Nesrin Türker[6], Umut Devrim Binay[7], Ercan Yenilmez[11], Gökmen Zararsız[12]

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ABSTRACT

Objective: Objective: Ombitasvir/paritaprevir/ritonavir (OMV/PTV/r) + ribavirin (RBV) combination improved the efficacy, safety, and tolerability of the treatment of chronic hepatitis C virus (HCV) genotype 4 infection. We described the effectiveness and safety of OMV/PTV/r + RBV therapy in patients with genotype 4 infection.

Materials and Methods: In this prospective cohort study, HCV genotype 4-infected patients treated with OMV/PTV/r + RBV (n=55) who were registered in a national database were included. Study patients were treatment-naïve or interferon plus RBV-experienced with or without compensated cirrhosis. Demographic, clinical and virological data were analyzed. Details of clinical and laboratory adverse events (AEs) were recorded.

Results: The mean age of the patients was 55.2, and 52.7% were male. The majority of patients were non-cirrhotic (81.8%), and 69.1% were treatment-naïve. The HCV RNA level was below 800.000 IU/mL in 16 of the cases. Seventy-eight percent of the patients had an underlying disease. SVR12 rate was 98% in all patients. One patient had virological failure. HCV RNA was undetectable at treatment week 4 in 77.6%, at treatment week 8 in 100%, and at end of treatment in 98%. The SVR12 rates were 100% and 88.9% for those without or with compensated cirrhosis (p= 0.176). Rates of AEs and AEs-associated treatment discontinuation were 69.1% and 3.6% in the patients, respectively.

Conclusion: The OBV/PTV/r + RBV combination was found to have high efficacy and safety profile in the patients with chronic HCV genotype 4 infection.

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DOI: 10.36519/idcm.2019.19014

ORIGINAL ARTICLE

LIVER

Real-World Data from Turkey: Is Sofosbuvir/Ledipasvir With or Without Ribavirin Treatment for Chronic Hepatitis C Really Effective?

Neşe Demirtürk[1], Bilgehan Aygen[2], İlhami Çelik[3], Reşit Mıstık[4], Sıla Akhan[5], Şener Barut[6], Onur Ural[7], Ayşe Batırel[8], Funda Şimşek[9], Gülden Ersöz[10], Dilara İnan[11], Sami Kınıklı[12], Nesrin Türker[13], Hüseyin Bilgin[14], Yunus Gürbüz[15], Necla Tülek[16], Hüseyin Tarakçı[17], Orhan Yıldız[2], Emine Türkoğlu[1], Deniz Kamalak Güzel[3], Sümeyra Şimşek[18], Nazan Tuna[19], Nazlım Aktuğ Demir[7], Atahan Çağatay[20], Rıza Aytaç Çetinkaya[21], Faruk Karakeçili[22], İsmail Necati Hakyemez[23], Günay Tuncer Ertem[24], Bahar Örmen[13], Pınar Korkmaz[25], Uluhan Sili[26], Ziya Kuruüzüm[27], Alper Şener[28], Selcan Arslan Özel[29], Sinan Öztürk[30], Kaya Suer[31], Mustafa Kemal Çelen[32], Petek Konya[1], Ali Asan[33], Neşe Saltoğlu[34], Nurhan Doğan[35]

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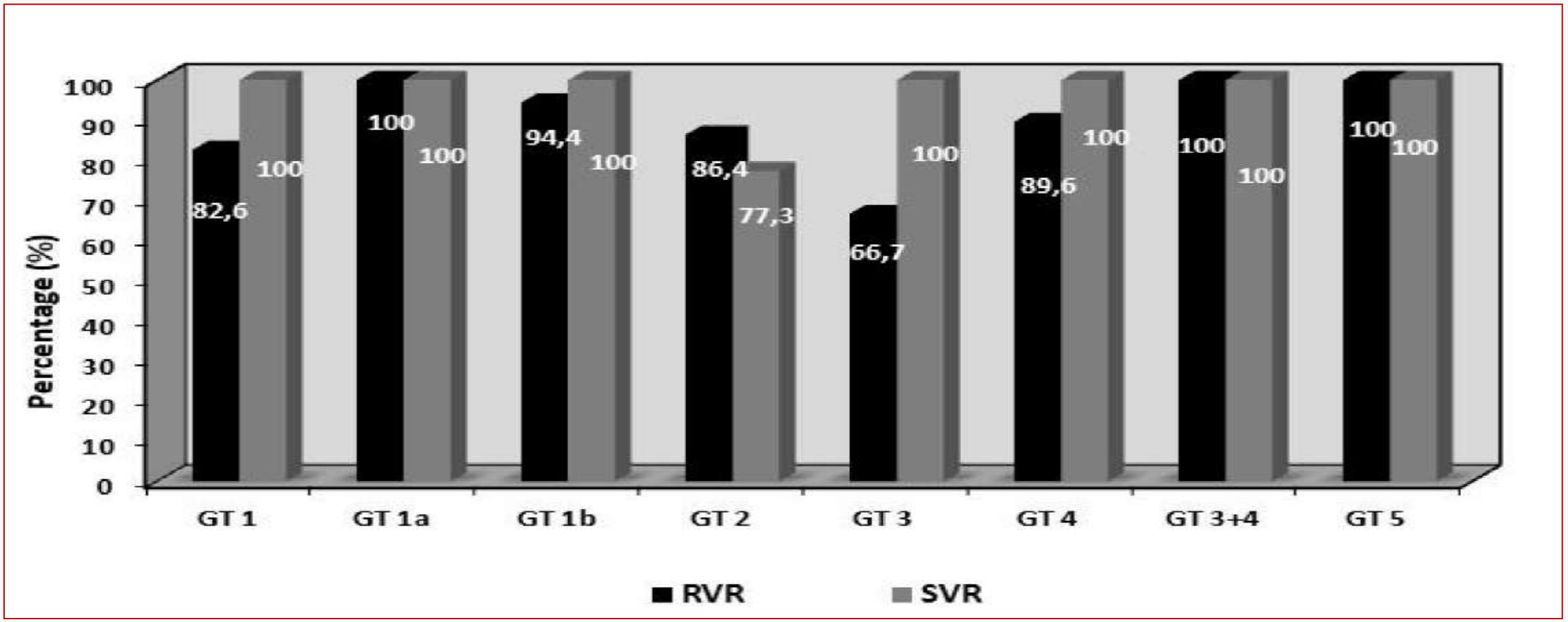
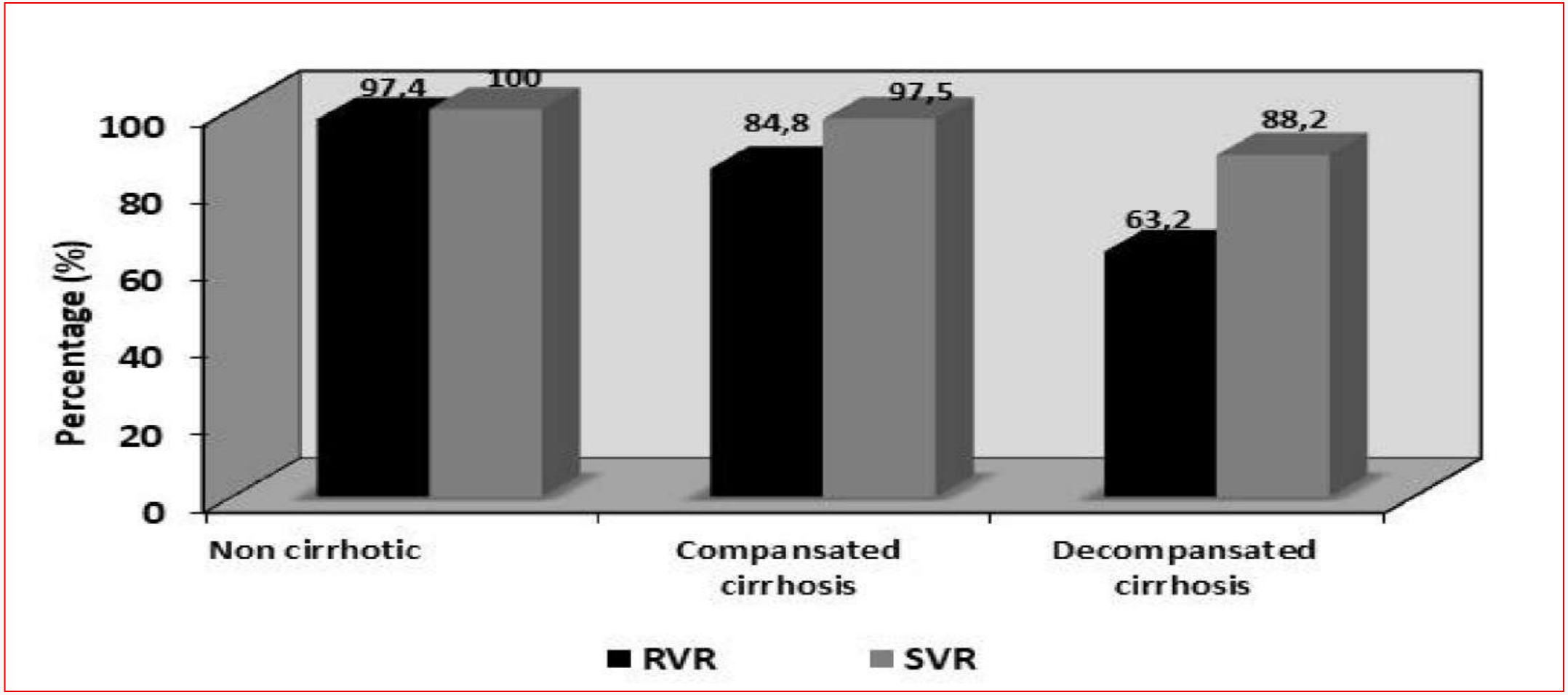


Figure 1: Virological responses according to genotypes



Virological responses according to cirrhosis

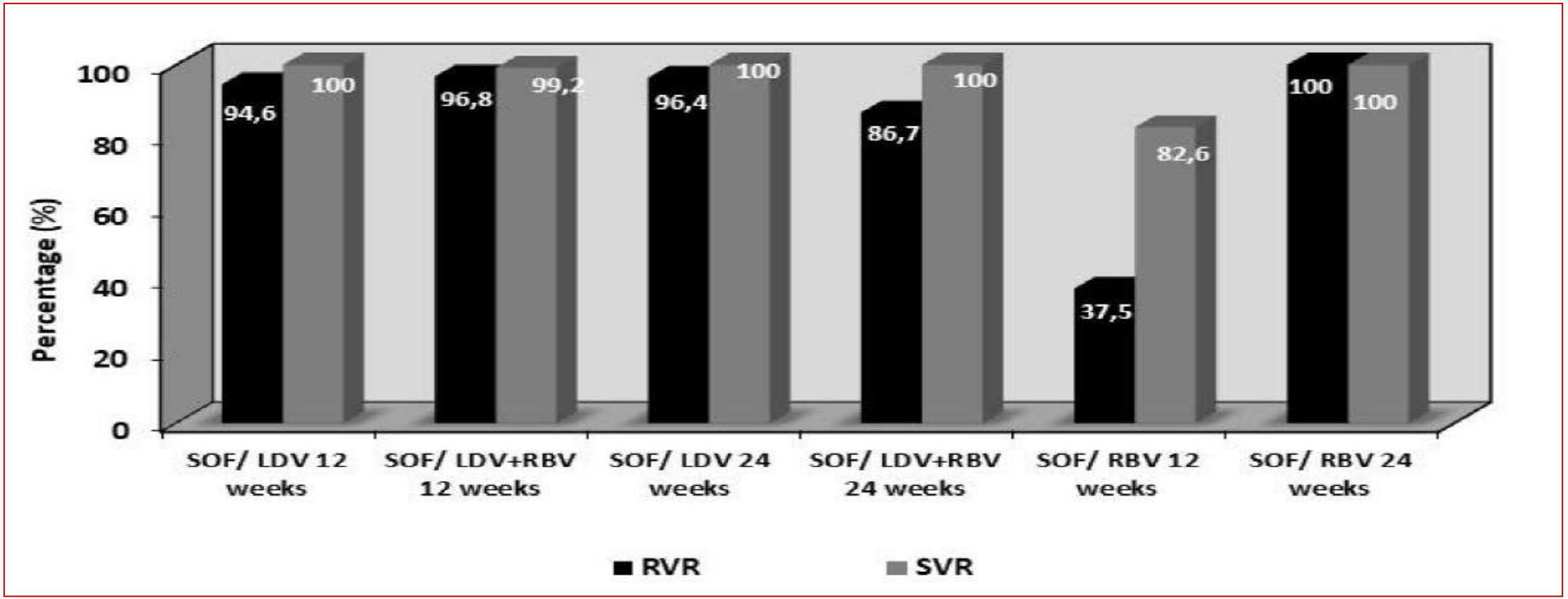


Figure 3. Virological responses according to treatment options

KLİMİK – VHÇG: GLE/PIB tedavisi gerçek yaşam verileri

- **16 merkez, 385 hasta (260 erkek, 125 kadın), yaş ortalaması 48 yıl**
  - **Tedavi naiv: 363 hasta**
  - **Tedavi deneyimli: 22 hasta**
    - İFN+RBV tedavisi: 15
    - PTV-RTV/OBV±DSV±RBV tedavisi: 4
    - SOF+RBV: 2
    - SOF/LDV: 1

HCV genotip dağılımı

- Genotip 1: 224
  - GT 1a: 63, **GT 1b: 148**, GT 1a+1b: 3, alt tipleme yapılmayan: 10
- Genotip 2: 35
  - GT 2b: 5, alt tipleme yapılmayan: 30
- Genotip 3: 100
  - GT 3a: 6, alt tipleme yapılmayan: 94
- Genotip 4: 23
  - GT 4a: 33, GT 4c: 2, GT 4d: 2 alt tipleme yapılmayan: 16
- Genotip 6: 2
- Genotip 1b+6: 1

Hastaların APRI skorları ve risk faktörleri

APRI skorları

- Skor 1: 114
- Skor 2: 105
- **Skor 3: 134**
- Skor 4: 16
- Skor 5: 16

Risk faktörleri

- Damar içi madde kullanımı: 87
  - **GT 3: 39**, GT 1: 32, GT 2: 8, GT 4: 6, GT 6: 2
- Hemodiyaliz uygulaması: 21
- Ek olarak 7 hastada HBV ko-infeksiyon

Virolojik yanıt sonuçları

- Erken virolojik yanıt: **%93.8** (255/272)
  - Test yapılan 272, test yapılmayan 113
- Tedavi sonu virolojik yanıt: **%99.1** (320/323)
  - Test yapılan 323, test yapılmayan 62
- Kalıcı virolojik yanıt: **%100** (188/188)
  - Test yapılan 272, test yapılmayan 113

Kontrol vizitlerine başvuru sayıları

- Birinci ay kontrolüne (birinci vizit) gelenler: 272/385
- Tedavi sonu kontrolüne (ikinci vizit) gelenler: 323/385
- Tedavi bittikten 12 ay hafta sonra kontrole (üçüncü vizit) gelenler: 188/385

COVID-19 PANDEMİSİNİN ETKİLERİ!

- Birinci vizite gelmeyen hastalar: 113
- Birinci ve ikinci vizite gelmeyen hastalar: 34
- Birinci, ikinci ve üçüncü vizite gelmeyen hastalar: 34
- Birinci vizite gelen, ikinci ve üçüncü vizite gelmeyen hastalar: 28
- Birinci ve ikinci vizite gelen, üçüncü vizite gelmeyen hastalar: 95

İstenmeyen etkiler

- 354 hastada yan etki yok, 31 (%8.1) hastada var
  - Sık görülen yan etkiler:
    - Kaşıntı: 10 hasta
    - Halsizlik, yorgunluk: 9 hasta
    - Baş ağrısı: 4 hasta
    - Bulantı-kusma: 4 hasta
    - Halüsinasyon: 3 hasta
    - Öksürük: 2 hasta
    - Mide ağrısı/dispepsi: 2 hasta
    - Uykusuzluk: 2 hasta
    - İştahsızlık, baş dönmesi, balgam çıkarma, kabus görme, miyalji, bacaklarda şişlik, döküntü ve osteoartrit gibi yan etkiler birer hasta

Yan etkiler nedeniyle tedavi kesilme zorunluluğu olan hasta yok!

GLE/PIB diğer Türkiye gerçek yaşam verileri

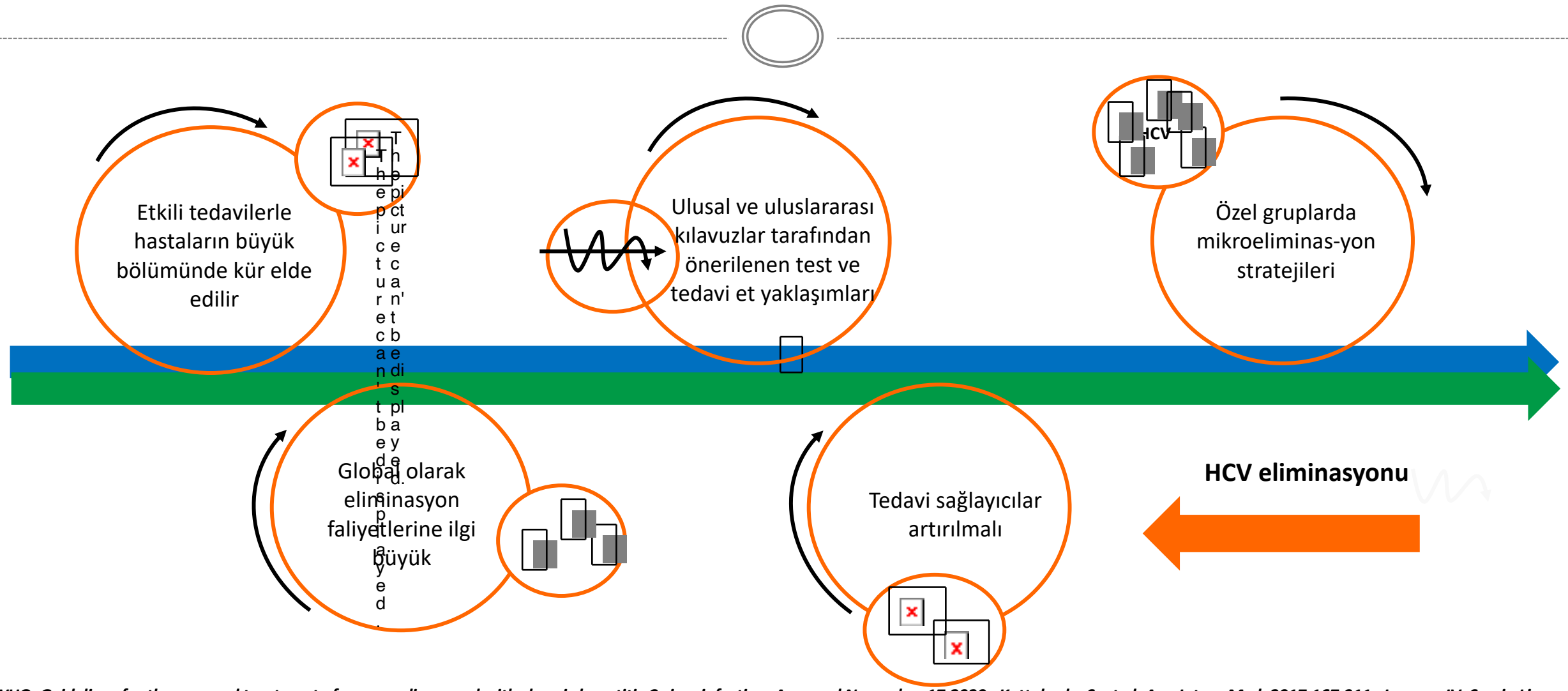
Konya Eğitim ve Araştırma Hastanesi Mart 2019-Ocak 2020[1]	Genotip 2 ve 3 ile infekte, "non" sirotik 127 hasta	Tedavi süresi 8 hafta	KVY oranı %99.2 (126/127)	Tedavi kesilmesine neden olan yan etki yok
Süleyman Demirel Üniversitesi 2018-2019[2]	68 olgu (genotip 1b: 42, genotip 1 a : 15, genotip 3: 6, genotip 2: 3, genotip 4 : 2hasta	16 hasta GLE/PIB	KVY oranı %100 (16/16)	Tedavi kesilmesine neden olan yan etki yok
Tepecik Eğitim ve Araştırma Hastanesi 2019-2021[3]	"Non" sirotik 25 olgu (genotip 1b: 15, genotip 3: 5, genotip 1a: 3	Tedavi süresi 8 hafta	KVY oranı %96 (24/25)	Yan etki yok
Dicle Üniversitesi Tıp Fakültesi 2022[4]	Genotip 1 (%89'u genotip 1b) ile infekte, 19 hasta (%63 tedavi deneyimli)	GLE/PIB	KVY oranı %100 (19/19)	Yan etki yok

1. Arch Curr Med Res 2021;2(2):06-11.
2. KLİMİK 2021 Kongresi Poster-280.
3. BUHASDER 2021 Kongresi Poster-89.
4. Anadolu Gastroentroloji Günleri 2022;SS-53.

- **Hastaların çoğunda tedavi ile kür elde edilebilir**

  …kür sürecin son aşamasıdır!

Eliminasyon adımları



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Idilman *et al. BMC Health Services Research* (2020) 20:249
https://doi.org/10.1186/s12913-020-5019-8

BMC Health Services Research

RESEARCH ARTICLE Open Access

A micro-elimination approach to addressing hepatitis C in Turkey

Ramazan Idilman[1], Homie Razavi[2], Sarah Robbins-Scott[2], Ulus Salih Akarca[3], Necati Örmeci[1], Sabahattin Kaymakoglu[4], Bilgehan Aygen[5], Nurdan Tozun[6], Rahmet Güner[7], Hurrem Bodur[8] and Jeffrey V. Lazarus[9,10*]

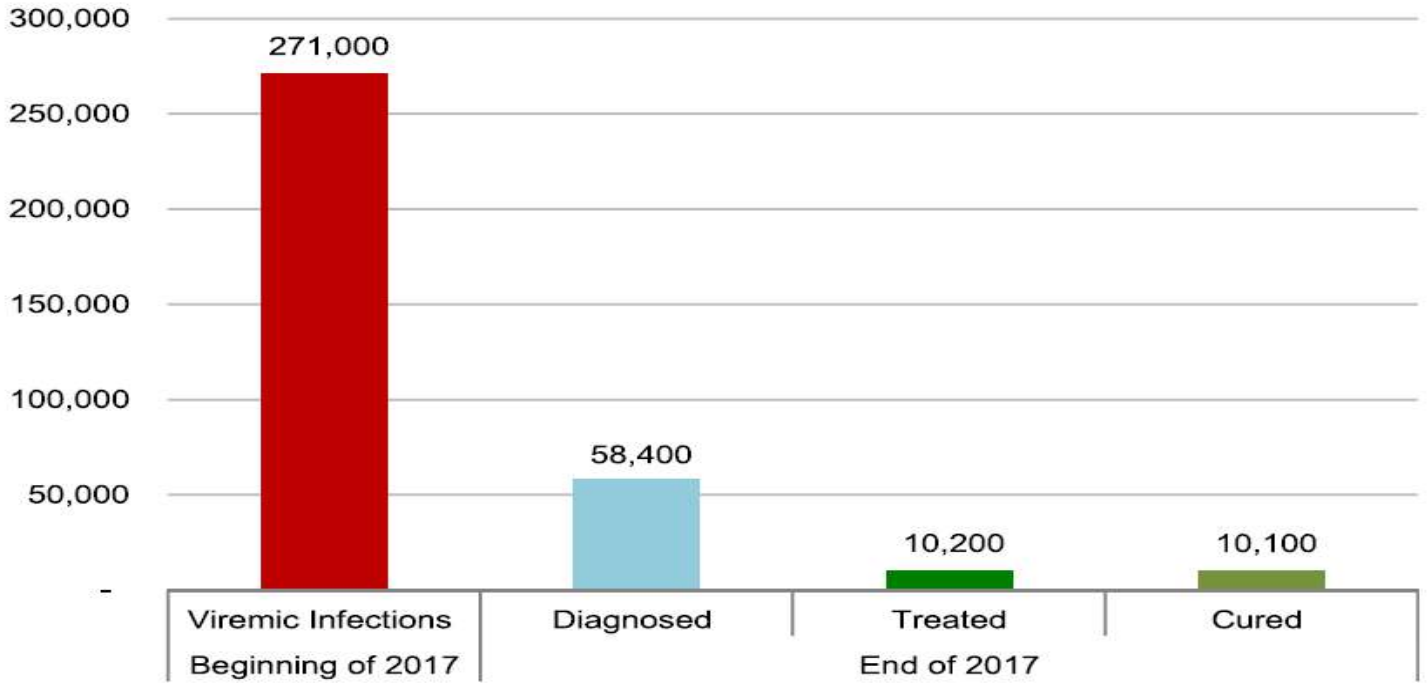
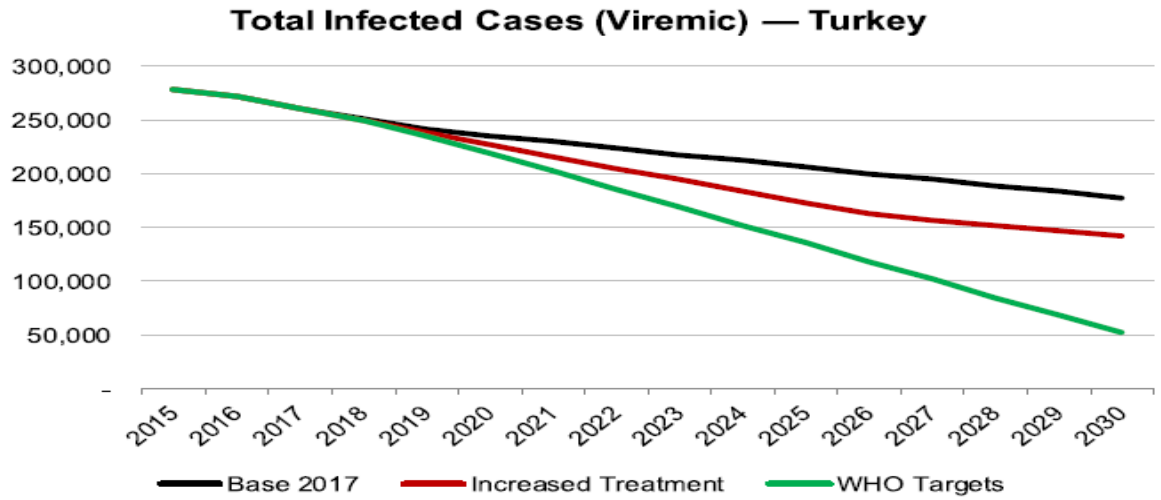
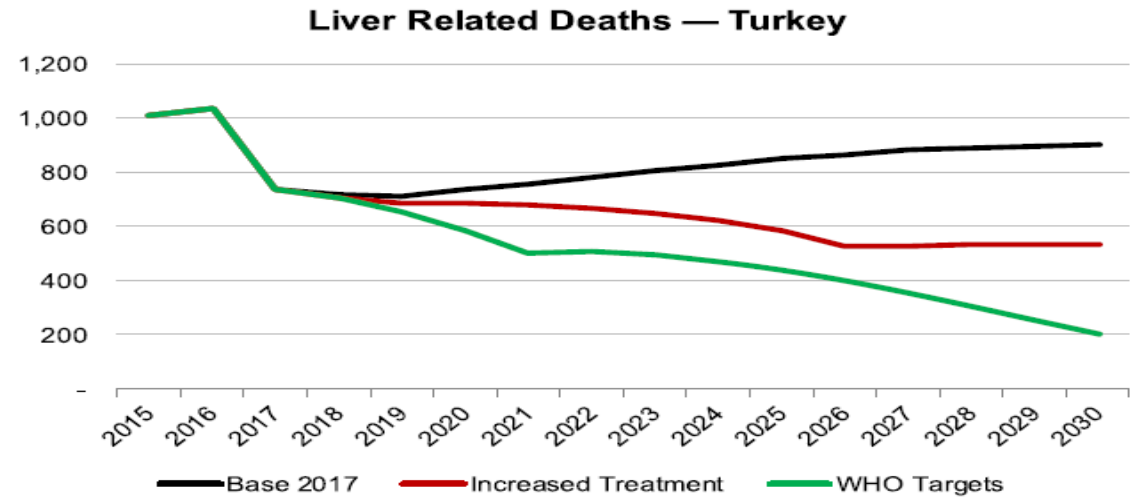
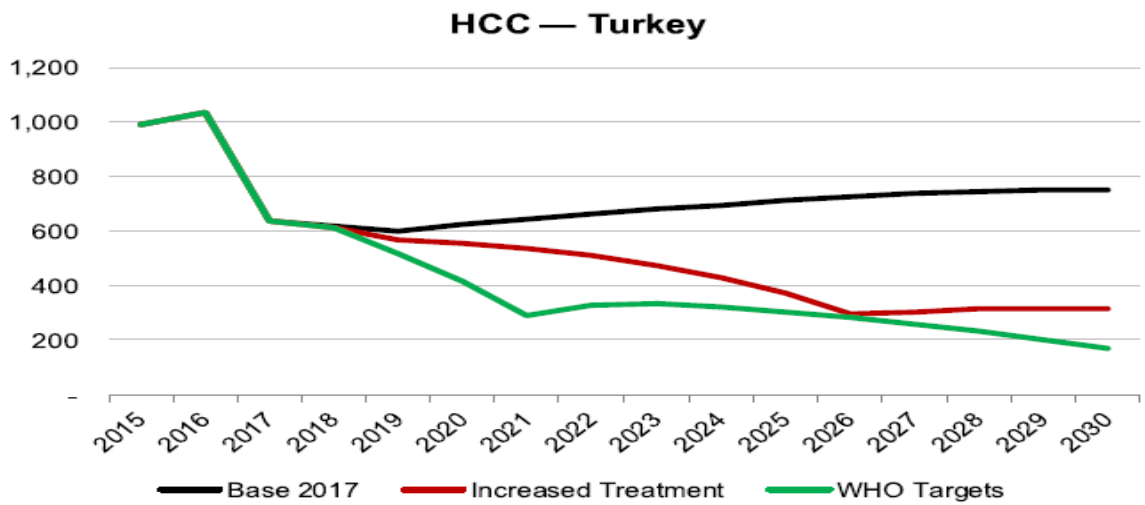


Fig. 1 The hepatitis C cascade of care, including the total number of viremic infections, the number of diagnosed patients, and the number of patients treated and cured, in Turkey in 2017







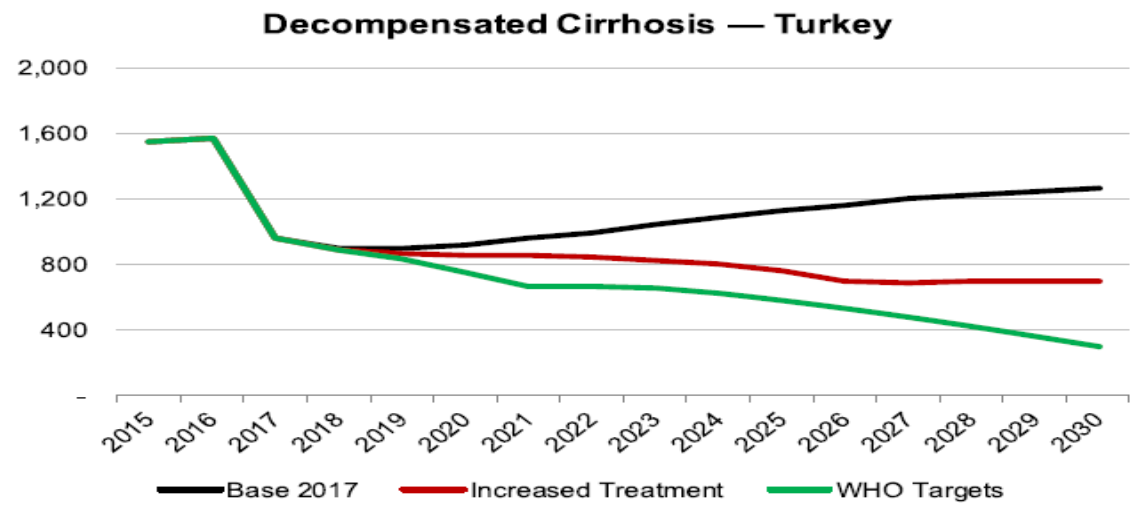


Fig. 2 Total infected cases, liver-related deaths, prevalent HCC and prevalent decompensated cirrhosis in Turkey, 2015–2030

Research Article
Viral Hepatitis

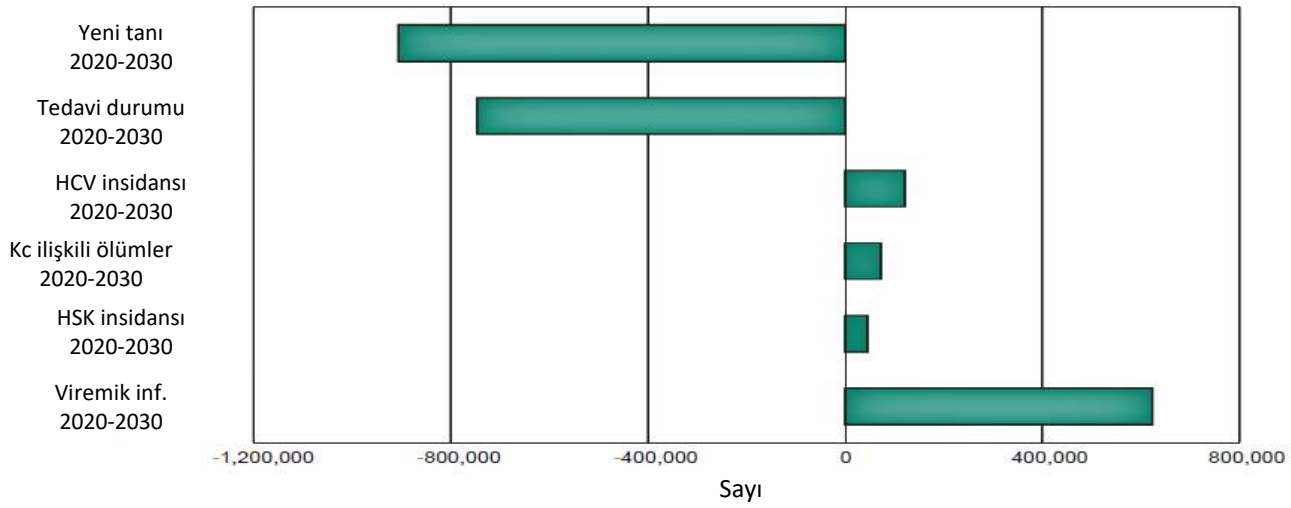
JOURNAL OF HEPATOLOGY
Journal of Hepatology 2021 vol. 74 | 31–36

Impact of COVID-19 on global HCV elimination efforts

Sarah Blach[1,*], Loreta A. Kondili[2], Alessio Aghemo[3,4], Zongzhen Cai[1], Ellen Dugan[1], Chris Estes[1], Ivane Gamkrelidze[1], Siya Ma[1], Jean-Michel Pawlotsky[5,6], Devin Razavi-Shearer[1], Homie Razavi[1], Imam Waked[7], Stefan Zeuzem[8], Antonio Craxi[9]

- COVID-19 pandemisi birçok hepatit eliminasyon programının yavaşlamasına veya tamamen durmasına neden olmuştur
- Hepatit tanı ve tedavisinde bir yıllık bir gecikme, 2030'a kadar küresel olarak HCV ile ilişkili
  - 44.800 ek karaciğer kanseri ve 72.300 ek ölümle sonuçlanabilir

HCV programlamasında bir yıllık gecikmenin küresel etkisi

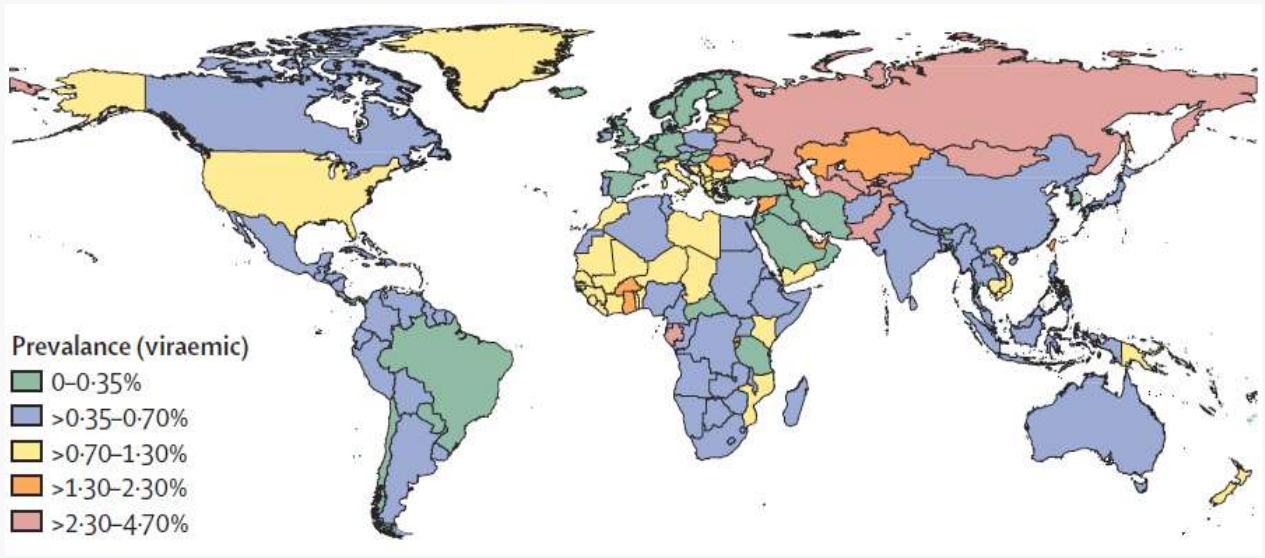


Değişen HCV epidemiyolojisi ve eliminasyon?

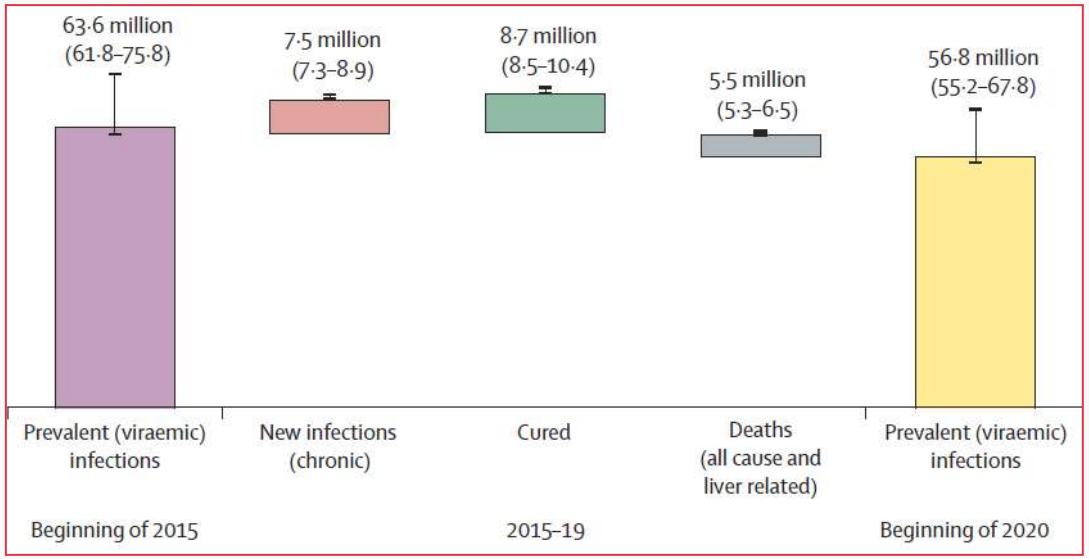
Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study

*The Polaris Observatory HCV Collaborators**

Lancet Gastroenterol Hepatol 2022; 7: 396–415



Ülkeler ve bölgelerde viremik HCV infeksiyonu prevalansı



2015-2020 arasında viremik HCV infeksiyonunun prevalansındaki değişim

Tedavi

Feld JJ, et al. NEJM 2015;373:2599. Foster. GR, et al. NEJM 2015:373;2608. Zeuzem S, et al. NEJM 2018;378:354. Puoti M, et al. J Hepatol 2018;69:293. Bourliere M. NEJM 2017;376:2134. Bourliere M, et al. Lancet Gastroenterol Hepatol 2018;3:559. Wyles D, et al. J Hepatol 2018;68:S23.