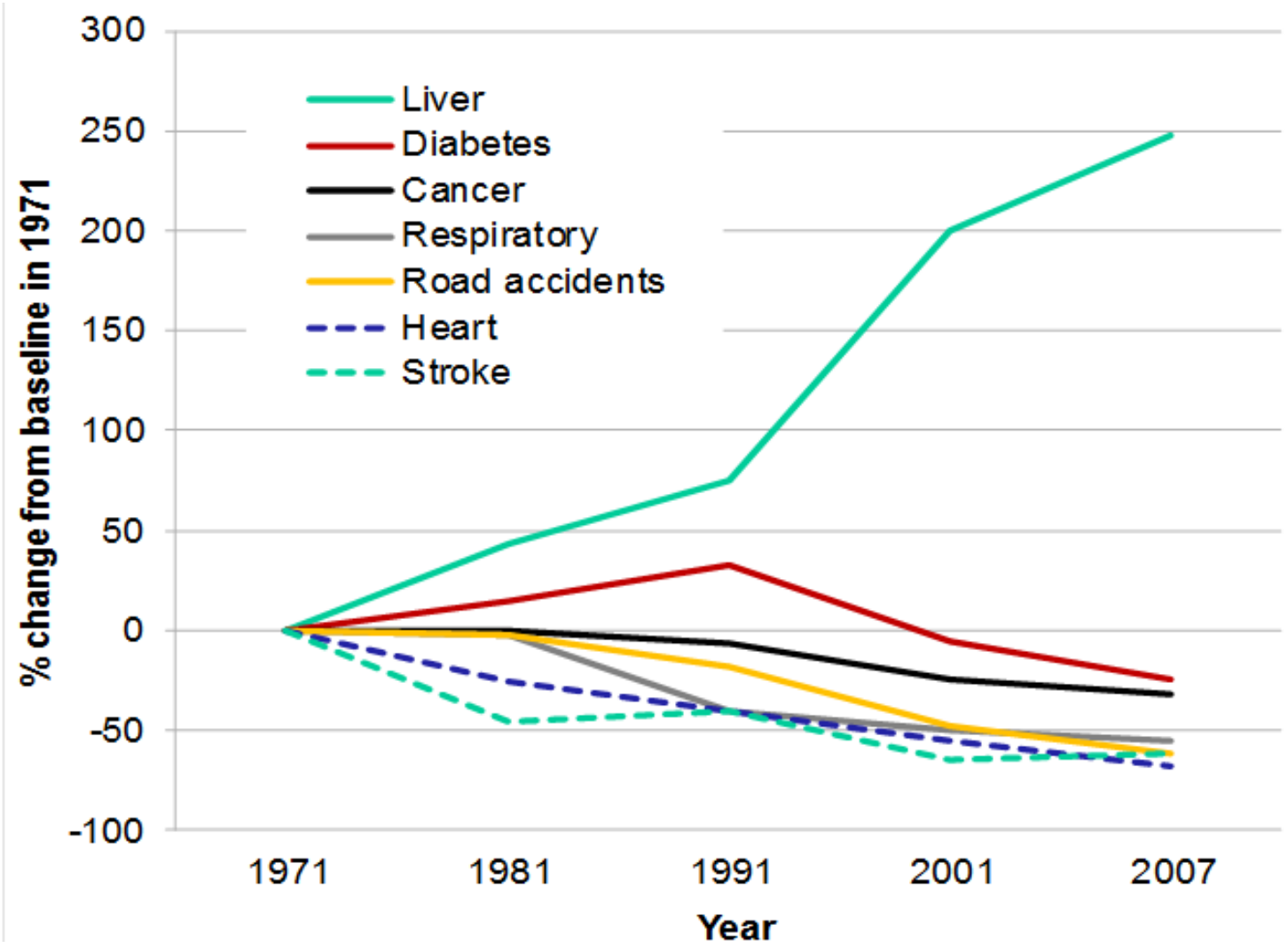
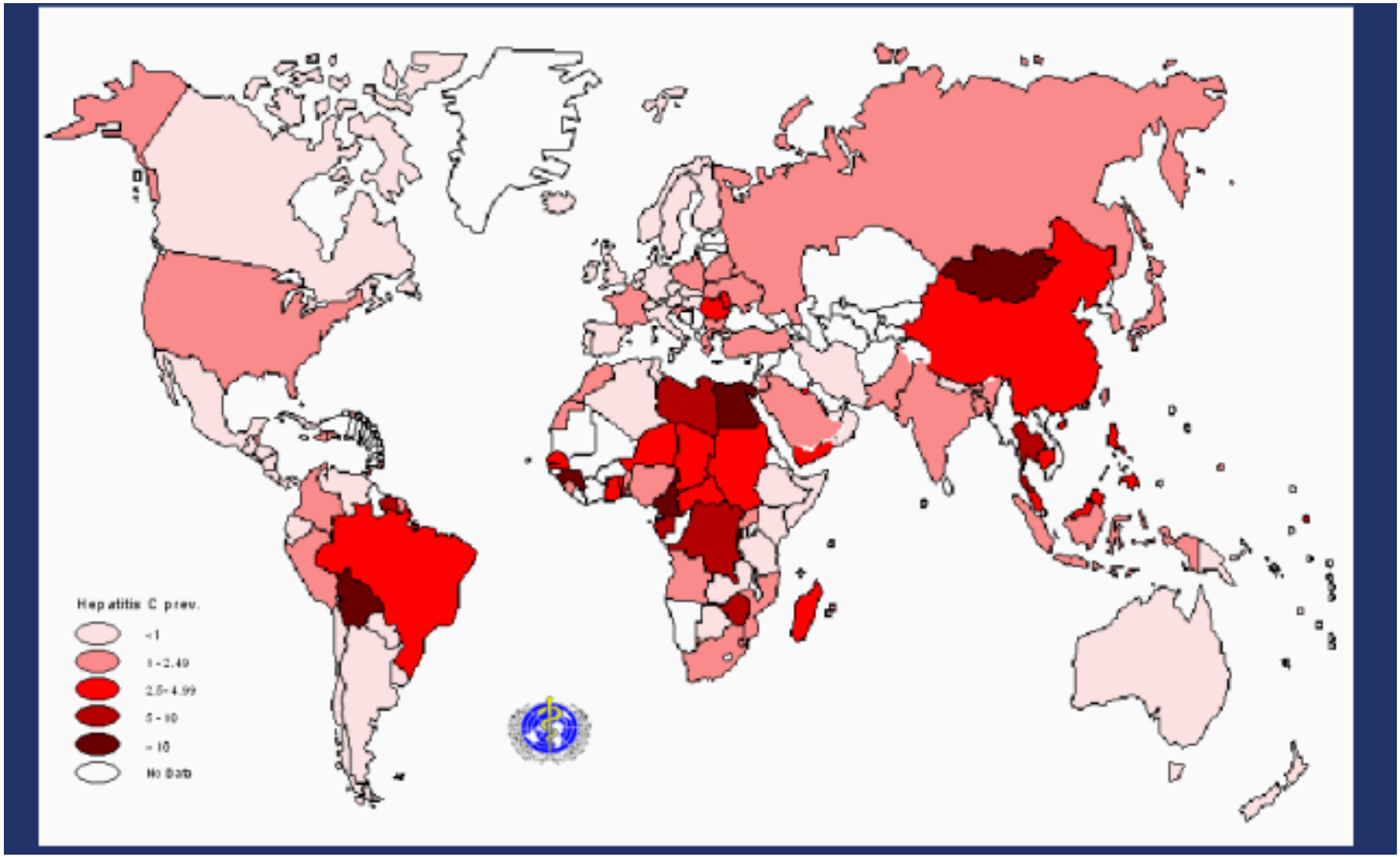
Kronik HCV güncel tedavisi & Evliya Çelebi E.A.H. Gastroenteroloji verileri

Dr.Süleyman Coşgun



İngilterede yapılan bir araştırmaya göre karaciğer kaynaklı mortalide artışı 1971–2007

Tüm dünyada HCV – 250 million



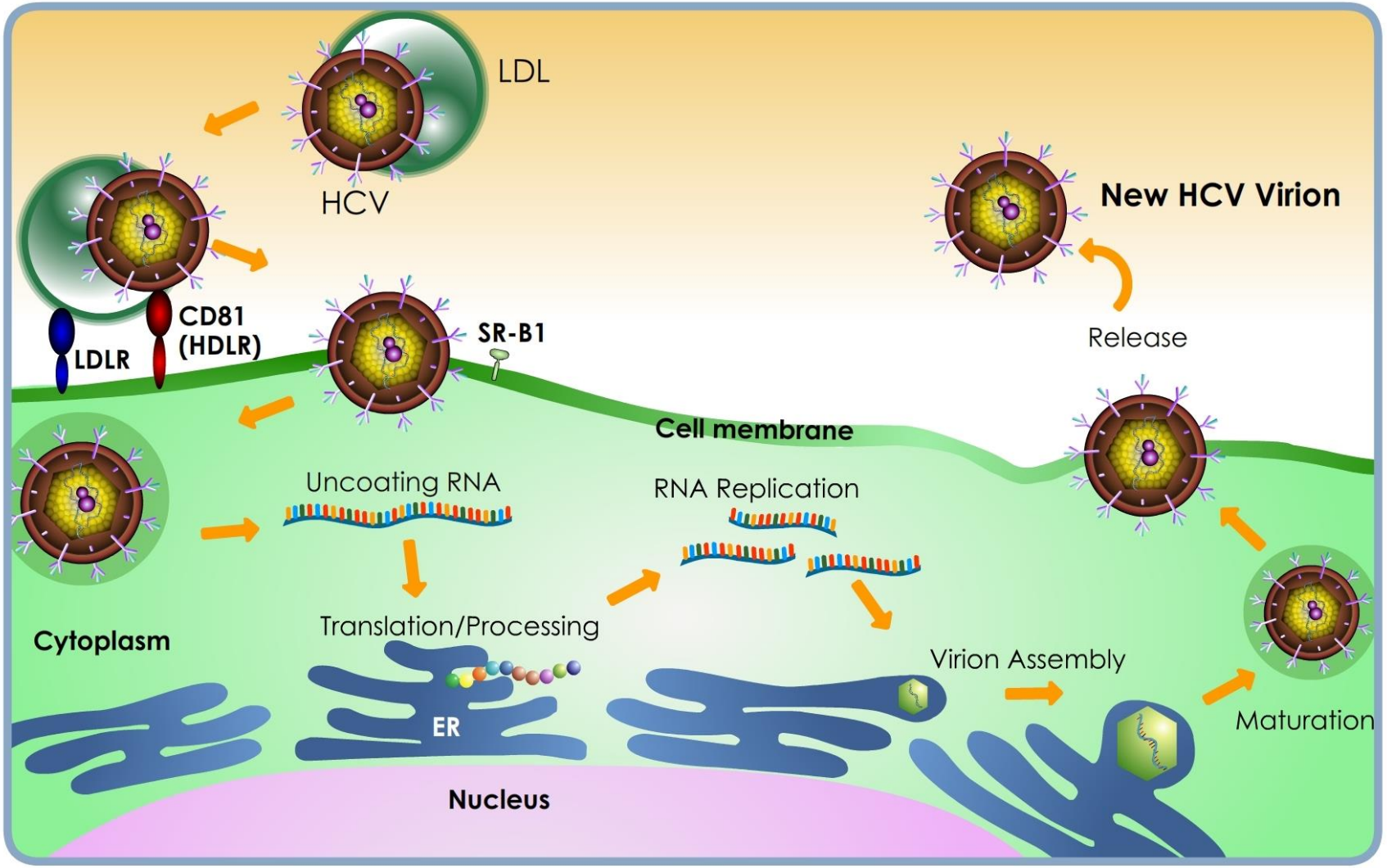
World Health Organization. Hepatitis C. Fact sheet Number 164, revised October 2000.

Bulaş yolları

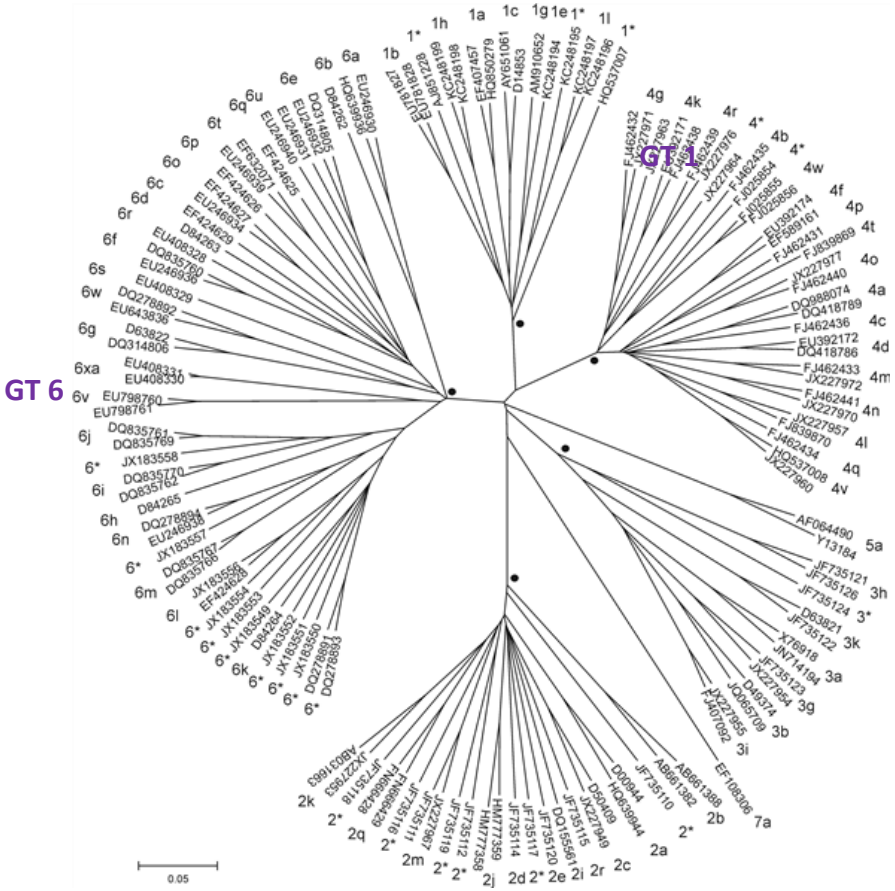
- Kan ve kan ürünü transfüzyonu
- Enfekte iğne(kaynatma)
- Dövme/ piercing
- Uyuşturucu bağımlısı
- Perinatal geçiş
- Girişimler
  - Diş
  - Hemodiyaliz
- Cinsel temas?

Alternatif bulaş yolları

HCV yaşam döngüsü

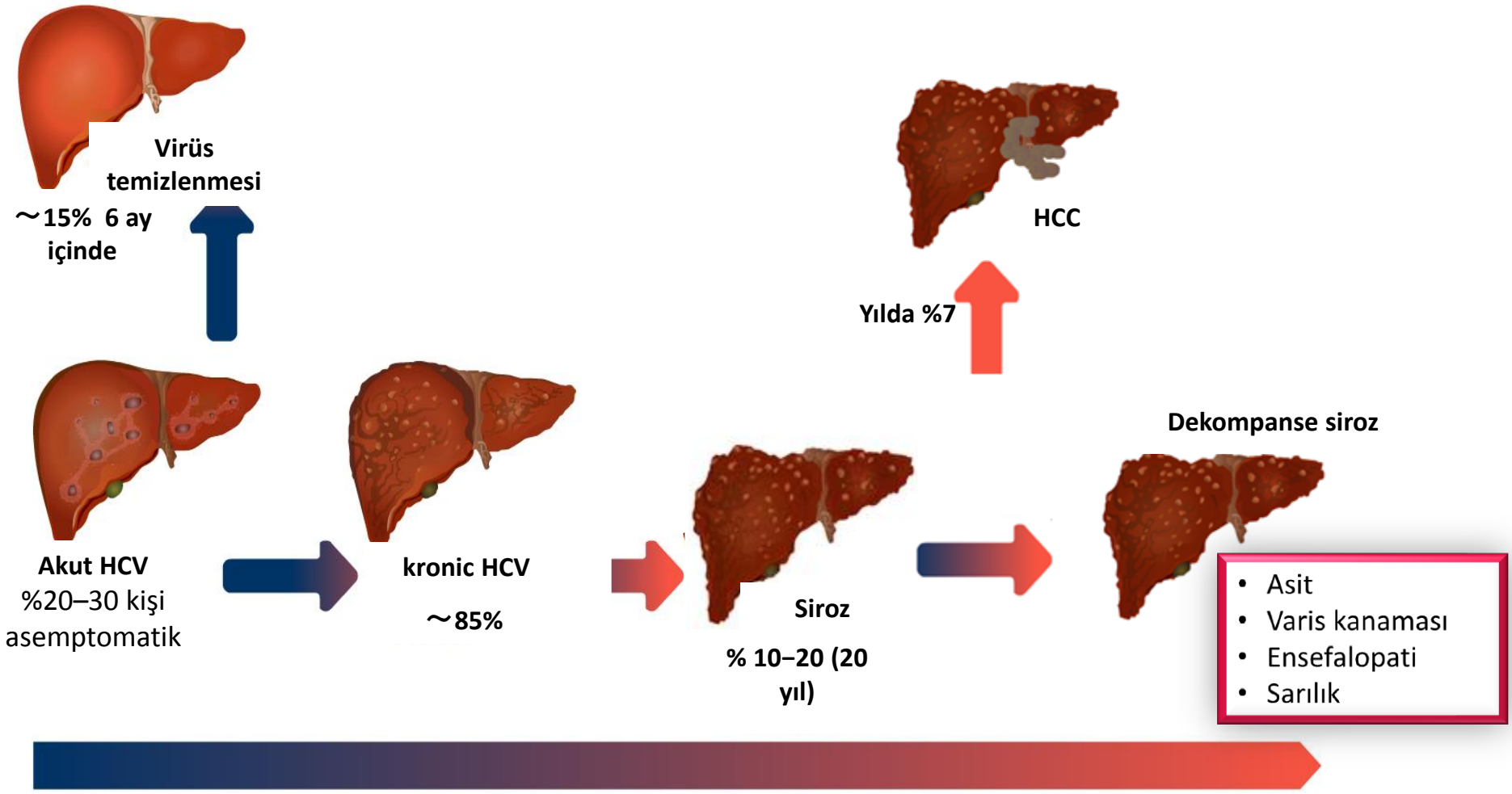


Genotip

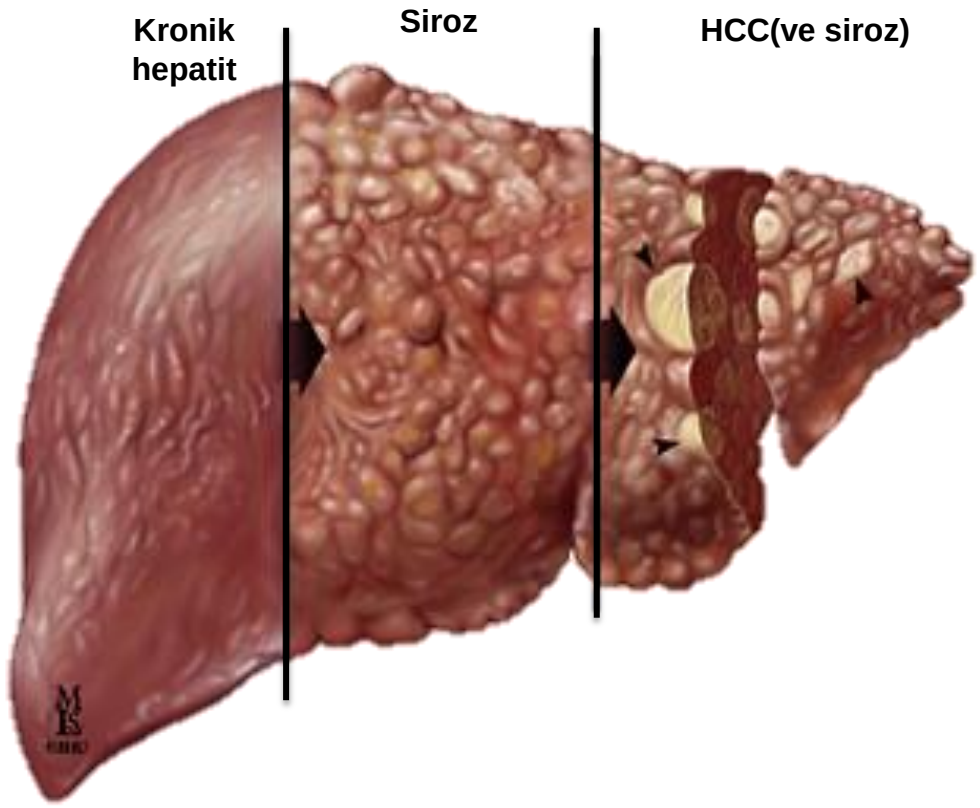


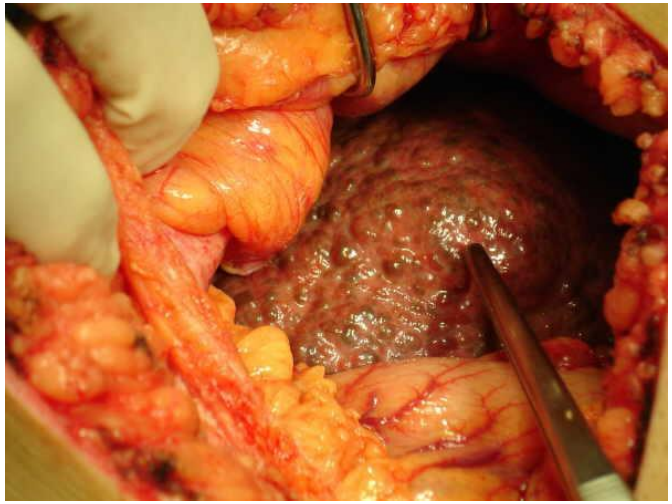
adapted from Los Alamos National Laboratory HCV sequence database, http://hcv.lanl.gov

HCV seyir ve prognoz

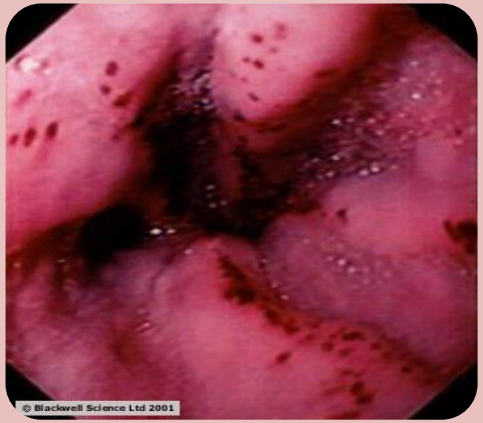


Kronik viral hepatit– Hastalık seyri

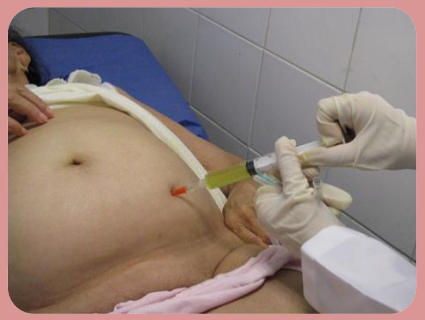




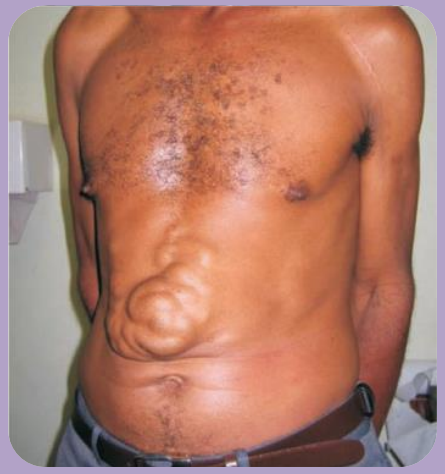
İleri karaciğer yetmezliği komplikasyonları



Varis

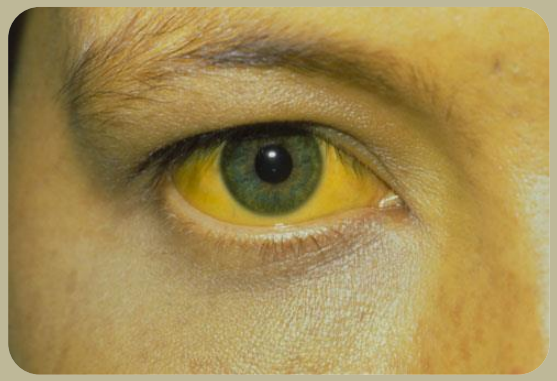


Ascites



Kaput medusa

Sarılık



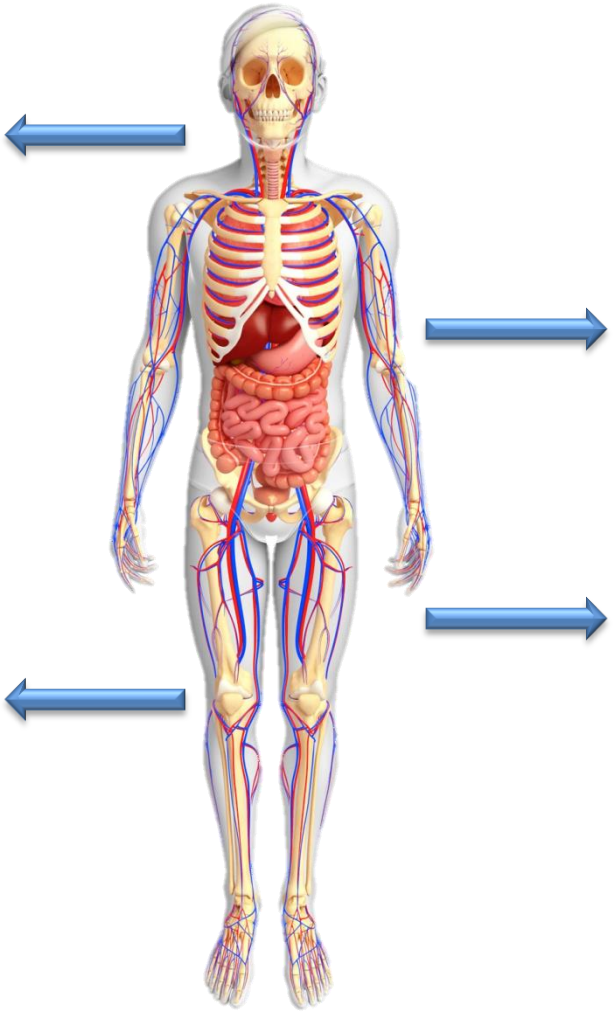
HCV ve ekstrahepatik bulgular

Hematolojik
- Mix cryglobulinemi
- Aplastik anemi
- Trombositopeni
- Non-Hodgkin b-cell lenfoma

Dermatolojik
- Porfiria kutanea tarda
- Liken planus
- Kutanöz nekrotizan vaskülit

Renal
- Glomerülonefrit
- Nefrotik sendrom

Endokrin
- Hipotiroidi
- DM



Oküler
- Korneal Ülser
- Üveit

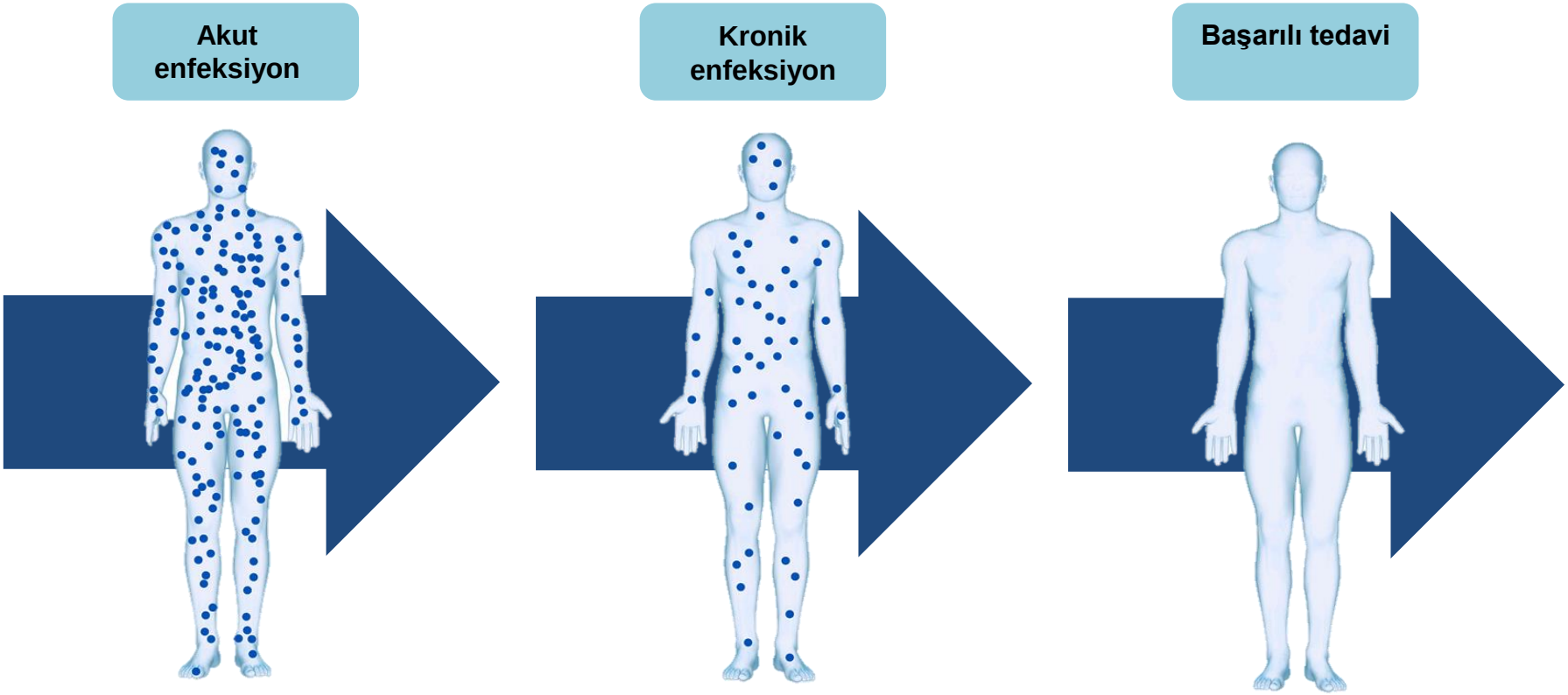
Vasküler
- Nekrotizan vaskülit
- PAN

Nöromusküler
- Güçsüzlük, miyalji
- Periferal nöropati
- Artrit, artralji

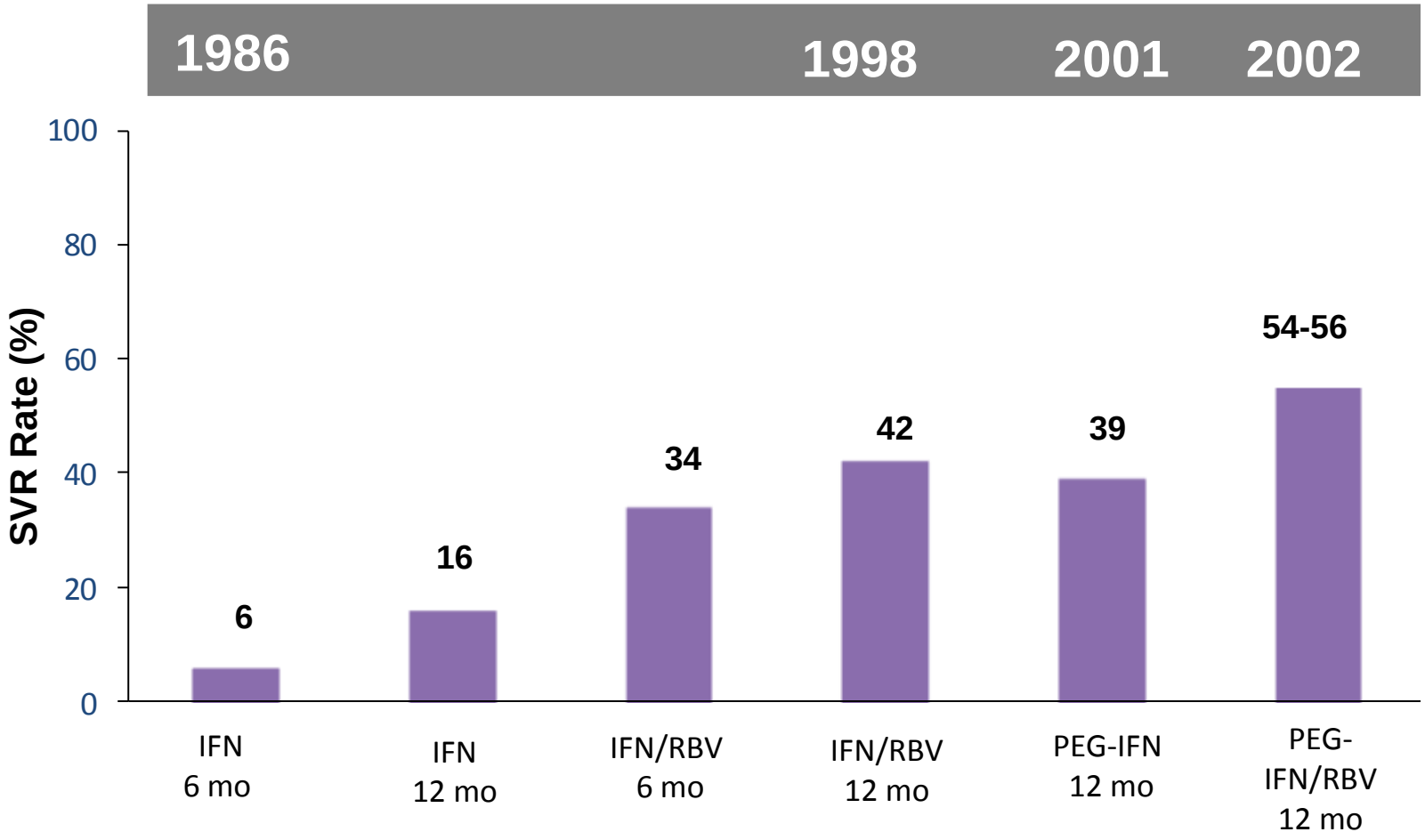
Otoimmün fenomen
- CREST ssendromu

Nöropsikiyatrik
- Depresyon

HIV ve HBV enfeksiyonunun aksine Kronik HCV enfeksiyonunda kür elde edilebilir(siroz ise komplikasyonlar açısından takibe devam)



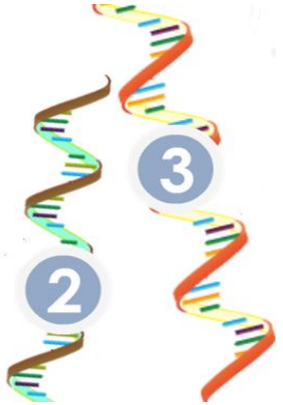
SVR GT1


1986
1998
2001
2002
SVR Rate (%)
100
80
60
40
20
0
6
16
34
42
39
54-56
IFN 6 mo
IFN 12 mo
IFN/RBV 6 mo
IFN/RBV 12 mo
PEG-IFN 12 mo
PEG-IFN/RBV 12 mo

HCV genotipi-tedavi başarısı

Genotip 1/4
PEG-IFN/RBV:
∼50%

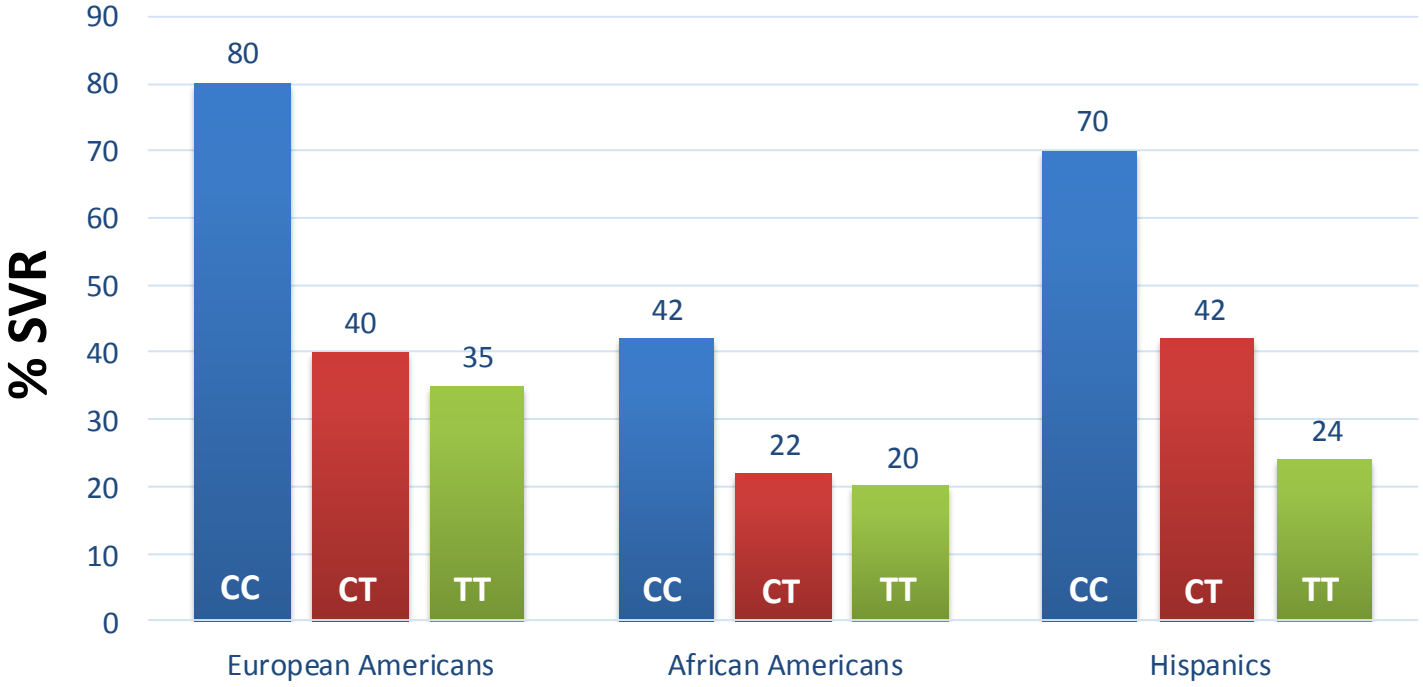
Genotip 2
PEG-IFN/RBV: ∼80%

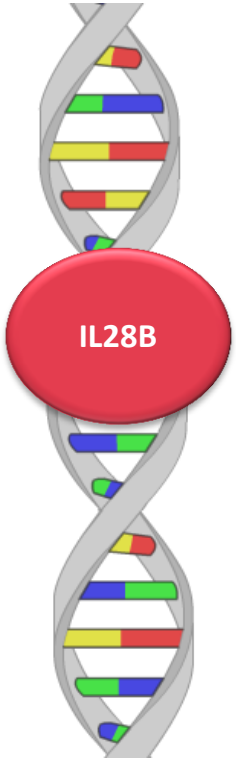


Genotip 3
PEG-IFN/RBV: ∼
70%

Haplotipleme

- IL28B gen haplotiplemesi ve İNF bazlı rejimde SVR prediksiyonu





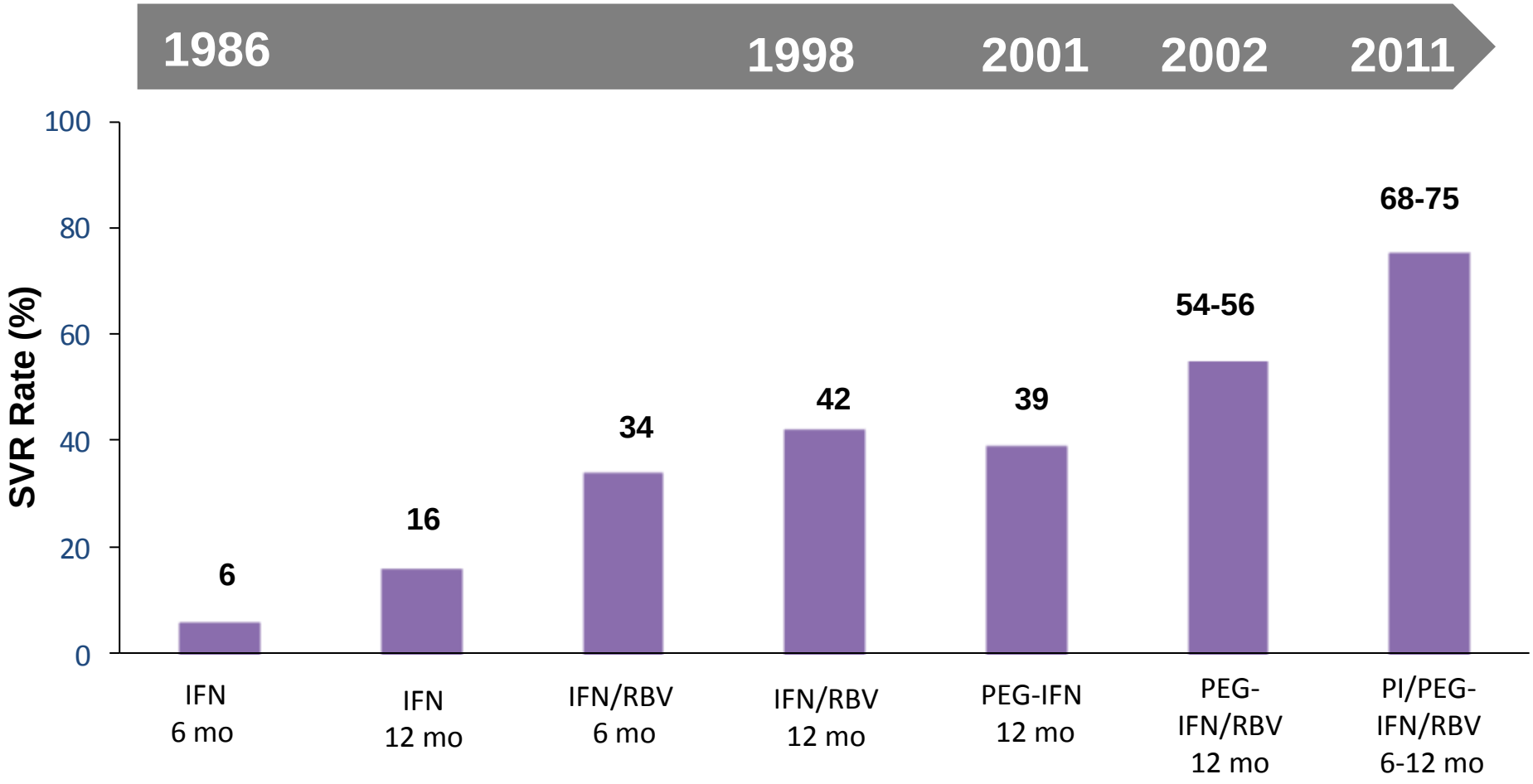
Ge et al. *Nature*. 2009

Proteaz inhibitörleri

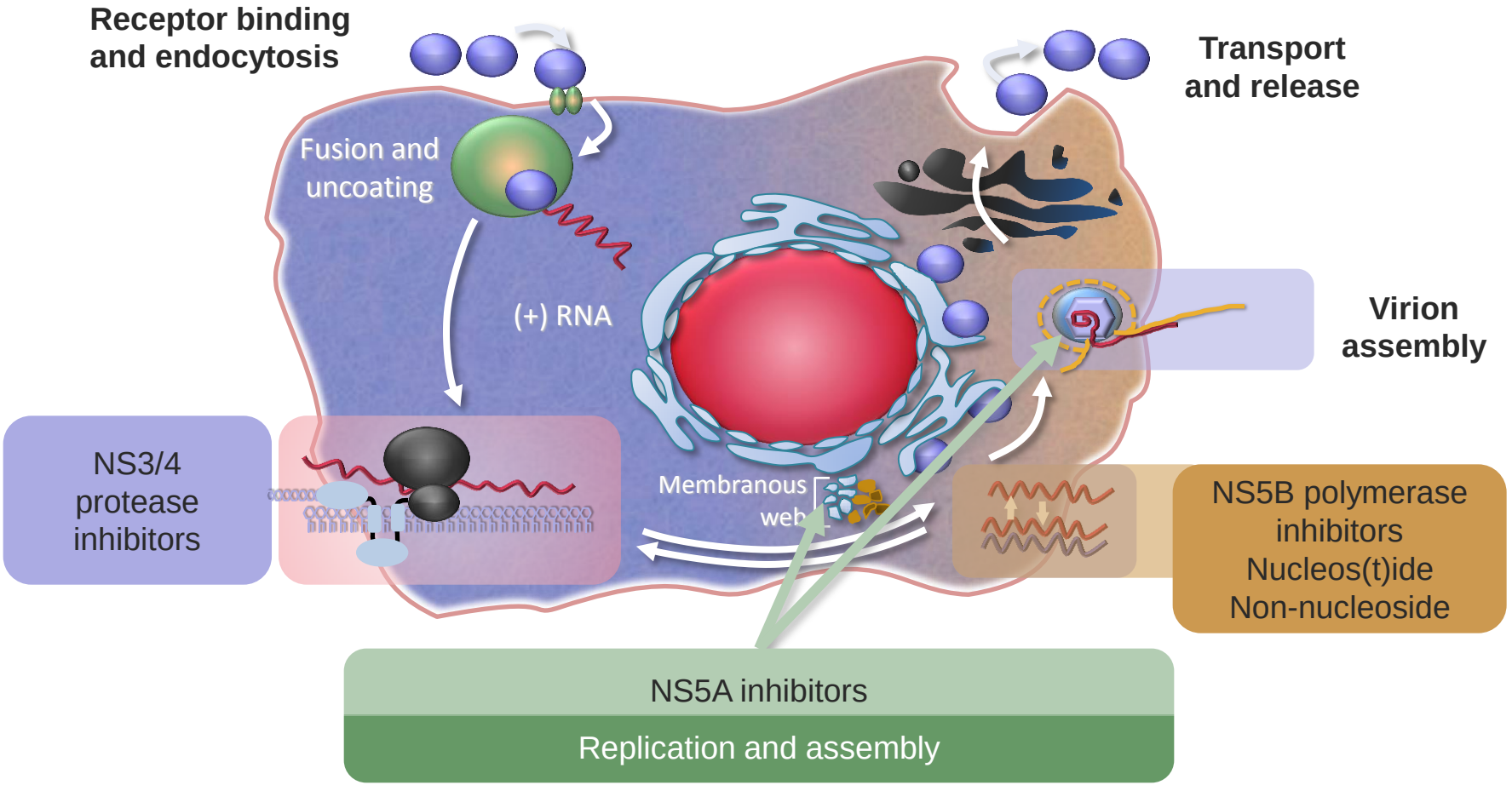
- 1. jenerasyon
  - HCV replikasyonunu inhibe eden onaylanmış ilk ilaçlar
  - anti-HCV ilaçlardan «direct acting antivirals (DAAs)»

  Denenlerin ilkleri

Proteaz ilavesi ile SVR



HCV yaşam döngüsünde «Direct-Acting Antivirals (DAAs)» ilaçların hedefi



- HCV replikasyon mekanizmalarının ortaya çıkarılması ilave DAA sınıflarının geliştirilmesine yol açmıştır.

DAA Sınıf özellikleri

NS3/4A Protease Inhibitors (PI)
- High potency
- Multi-genotypic coverage
- Intermediate to high barrier to resistance

NS5B Nucleoside Inhibitors (NI)
- Intermediate potency
- Pan-genotypic coverage
- High barrier to resistance

NS5A Inhibitors
- High potency
- Multi-genotypic coverage
- Low to intermediate barrier to resistance

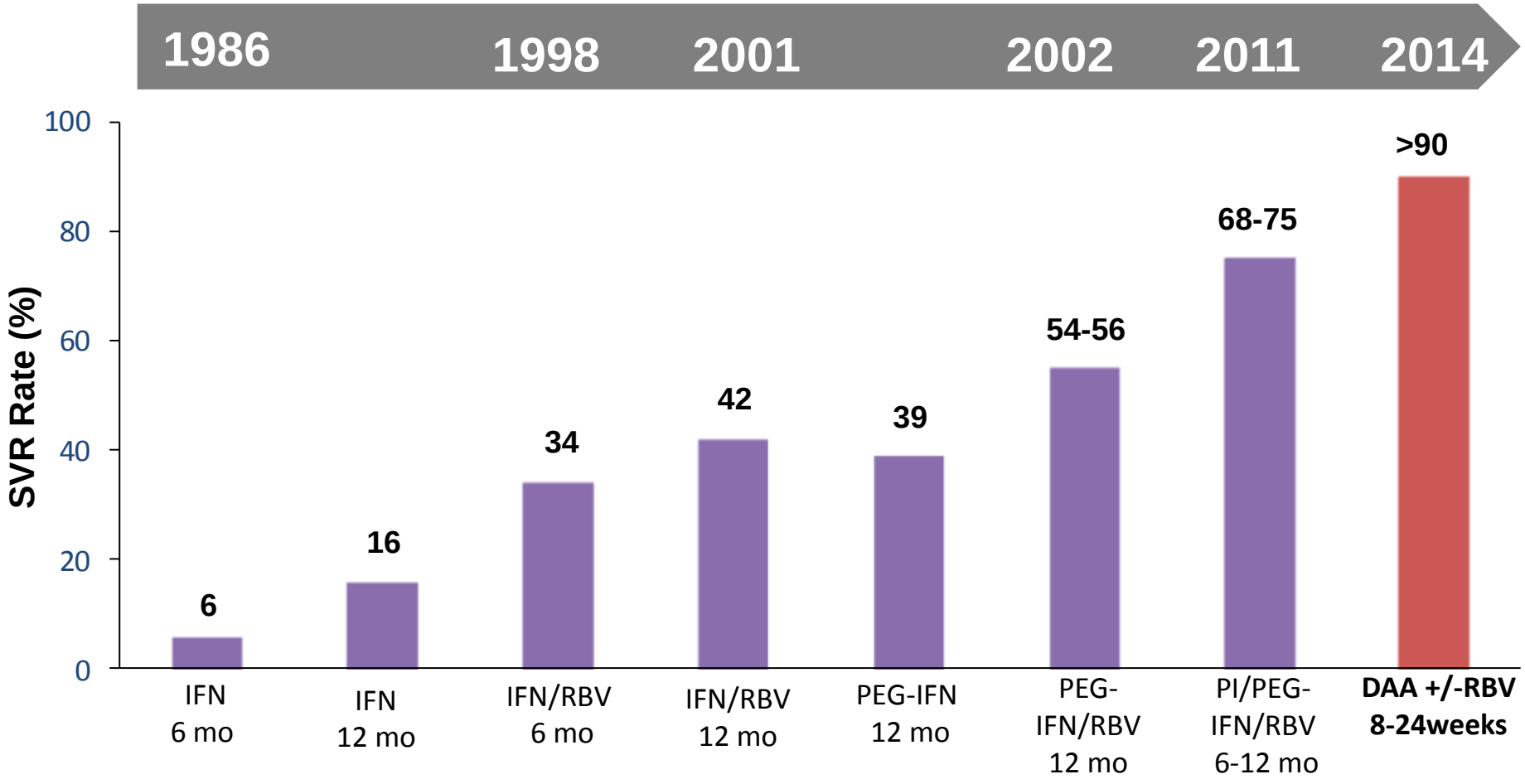
NS5B Non-Nucleoside Inhibitors (NNI)
- Intermediate potency
- Limited-genotypic coverage
- Low barrier to resistance

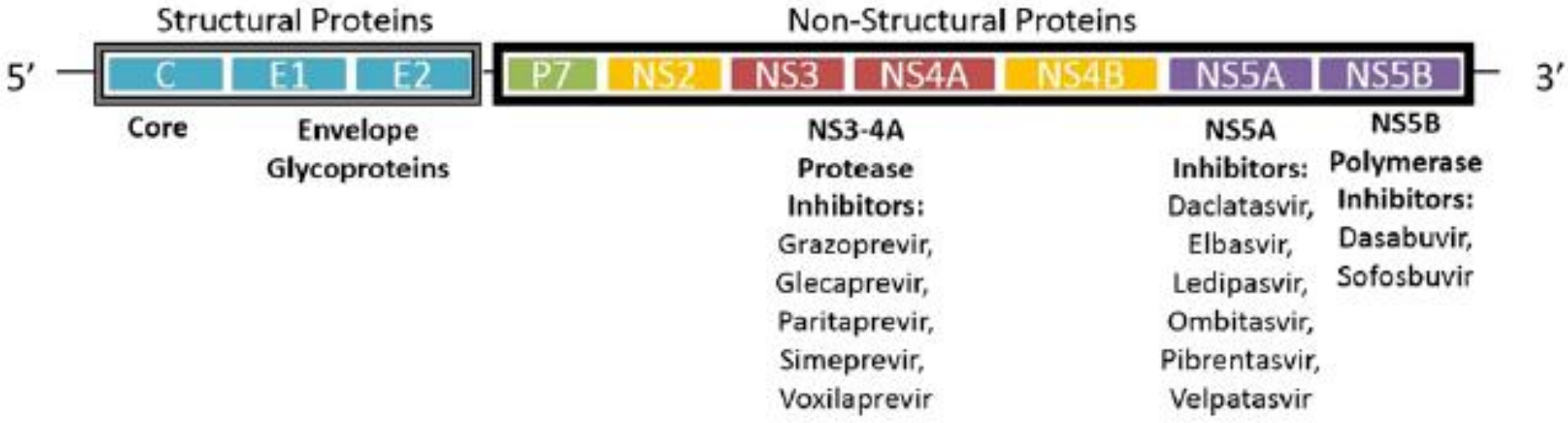
Source: J Viral Hepat, 2012 Blackwell publishing

İdeal tedavi

- **Etkinlik**
  - Hastalığın evresinden ve virüse ve bireye özgü farklardan bağımsız yüksek etkin olmalı(ileri evre siroz, ırk, cins, hastanın genetiği, BMI, HCV genotipi)
- **Güvenlik**
  - Tolere edilebilir ilaç
  - Minimal yan etki
  - İleri evrede bile güvenli, komorbid durumlarda(KBY) kullanışlı
- **Basit**
  - Oral tedavi
  - Kısa süre
  - Günlük tablet sayısı
  - Minimal ilaç-ilaç etkileşimi
  - Her genotipe etkili tek bir rejim

İnterferonlu ve interferonsuz rejimlerde SVR

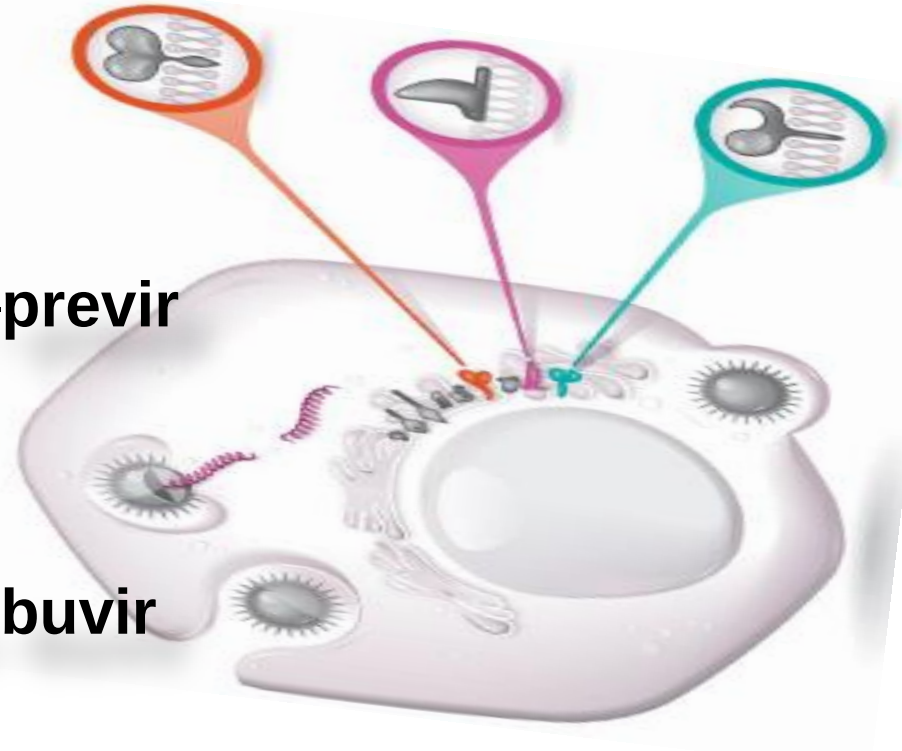




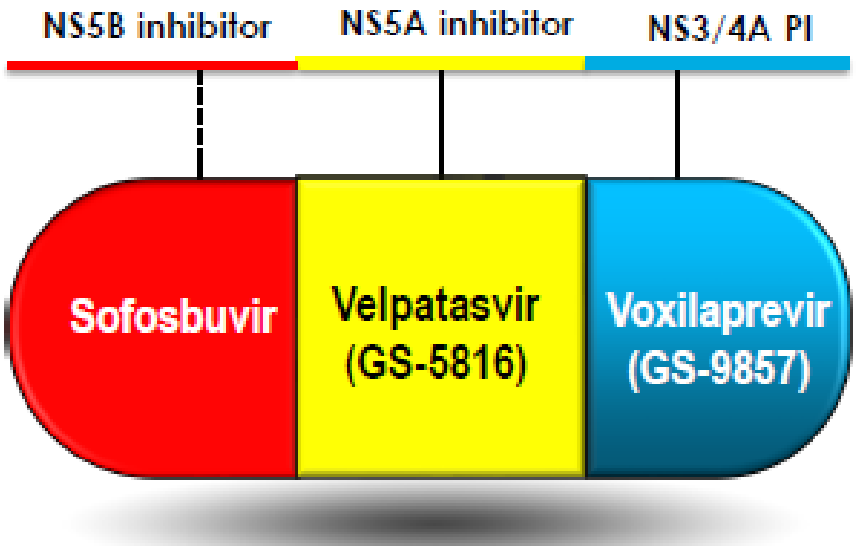
NS3/4A proteaz inhibitörleri sonu –**previr**

NS5A inhibitörleri sonu -**asvir**

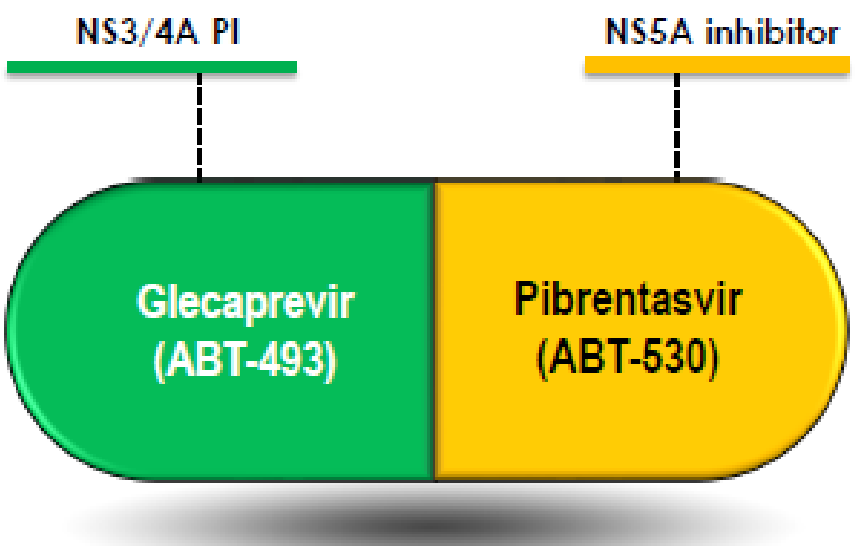
NS5B polimeraz inhibitörleri sonu -**buvir**



Yeni onaylı ilaçlar



1 tablet/gün yemekle
Vosevi



3 tablet/gün yemekle
Mavyret

ilaçlar

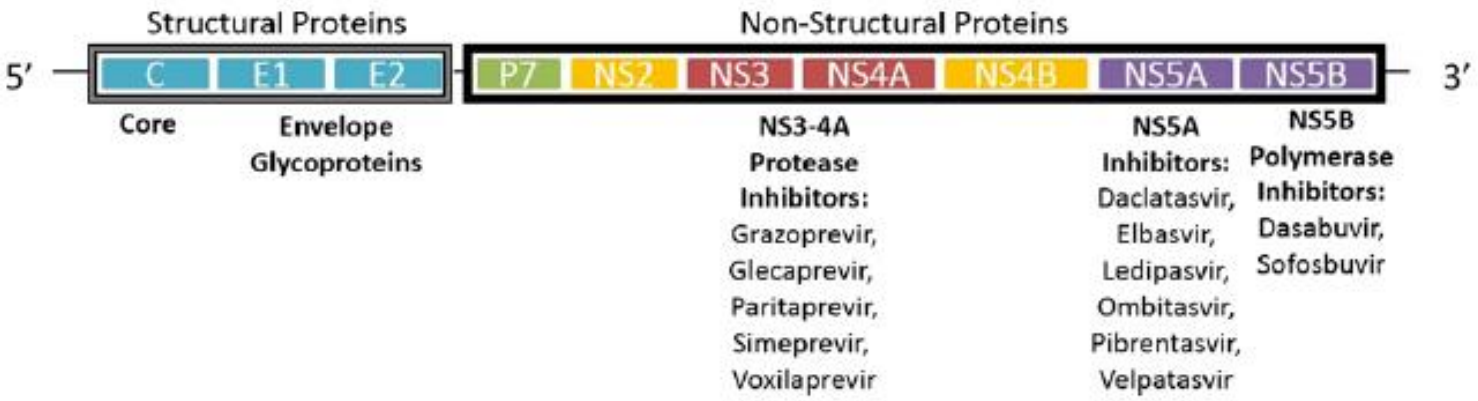
- Sofosbuvir (aç veya tok)

400mg/gün

%80 atılım böbrek, %15 feçes

GFR<30? Diyaliz hastası?

Amiodaron!!!

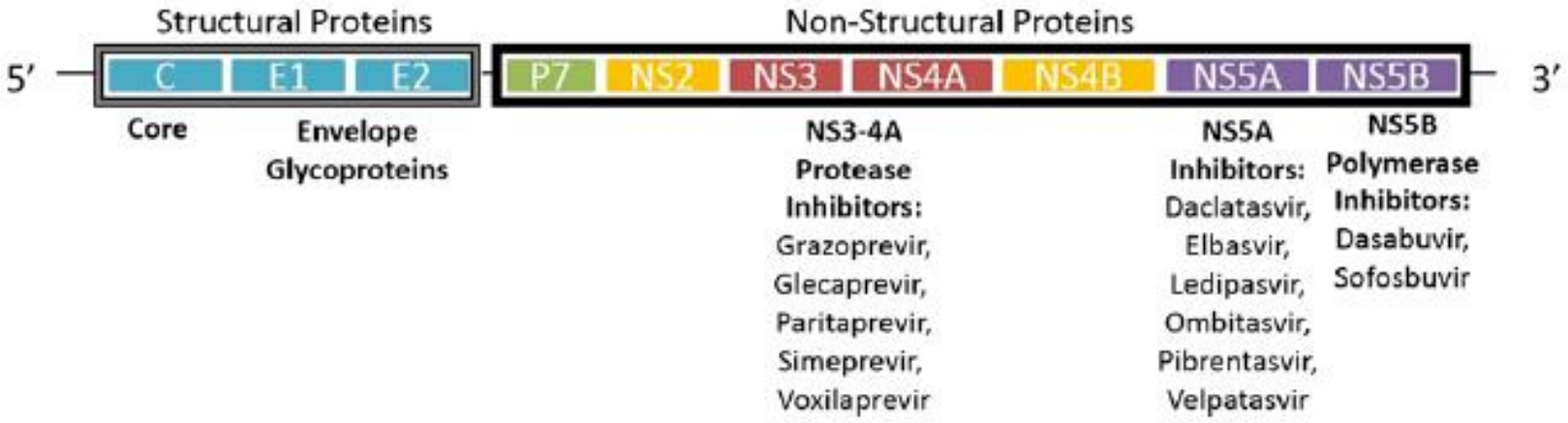


- Sofosbuvir+ledipasvir 400mg+90mg (aç veya tok)

Ledipasvir safra ile atılım

GFR ve Diyaliz!!!

En yaygın yan etki halsizlik ve baş ağrısı

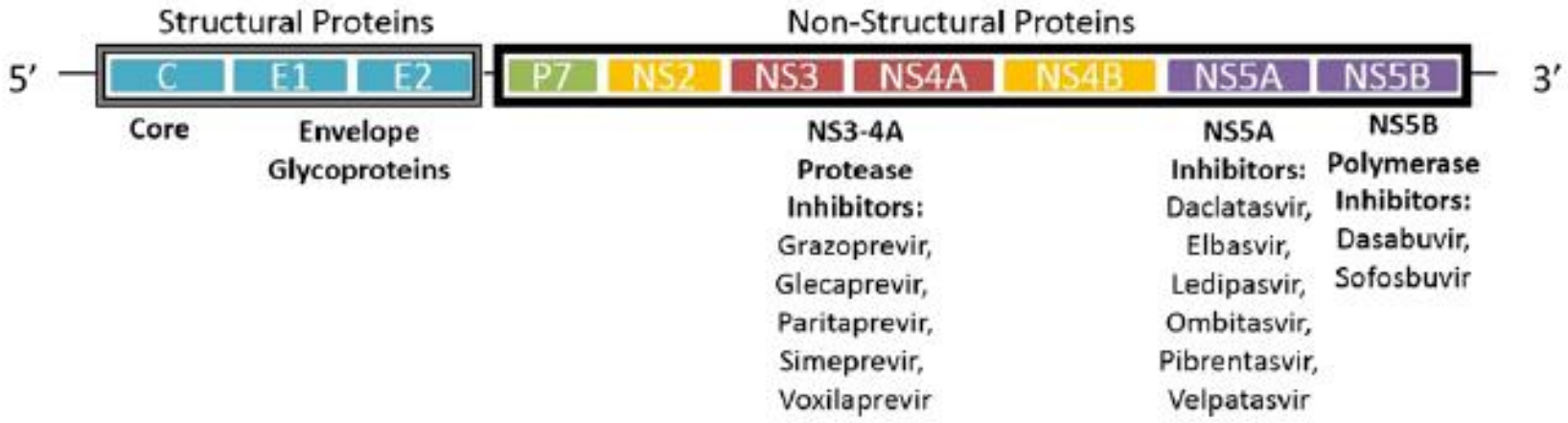


- Sofosbuvir+velpatasvir 400mg+100mg(aç veya tok)

Velpatasvir major ekskresyonu biliyer

Baş ağrısı, halsizlik, bulantı en yaygın yan etkisi

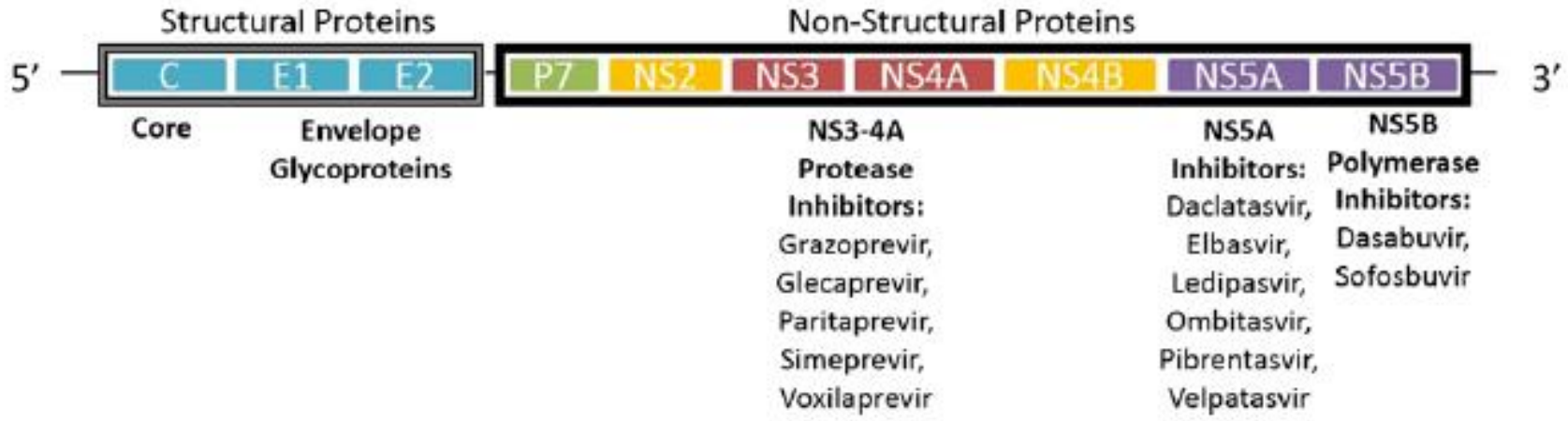
GFR ve Diyaliz!!!



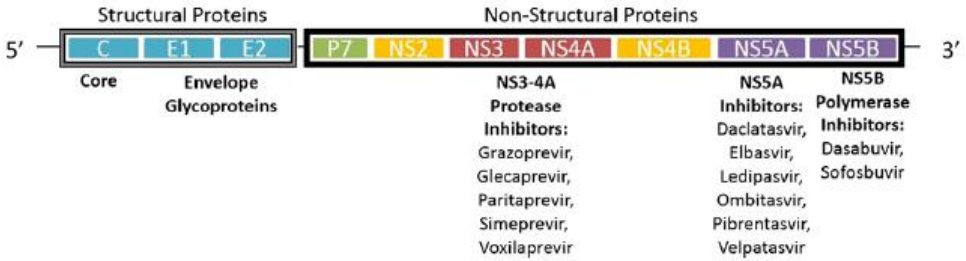
- Sofosbuvir+velpatasvir+voxilaprevir (400mg+100mg+100mg) 1x1 yemekle birlikte

Voxilaprevir büyük oranda biliyer ekskrese

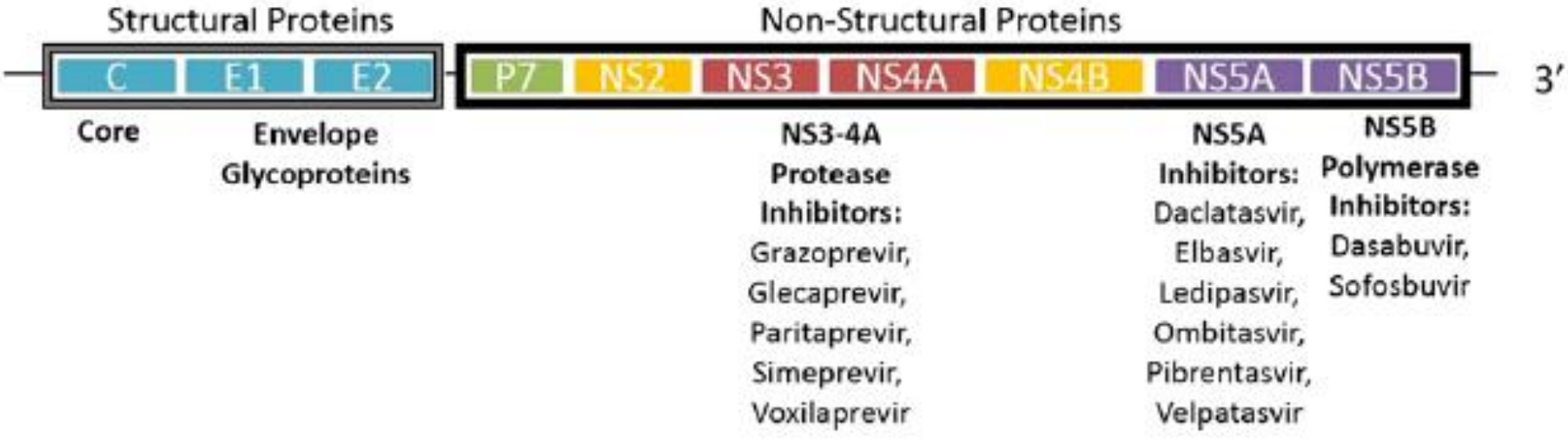
Child A da verilebilir, B de önerilmez, C de kontraindike



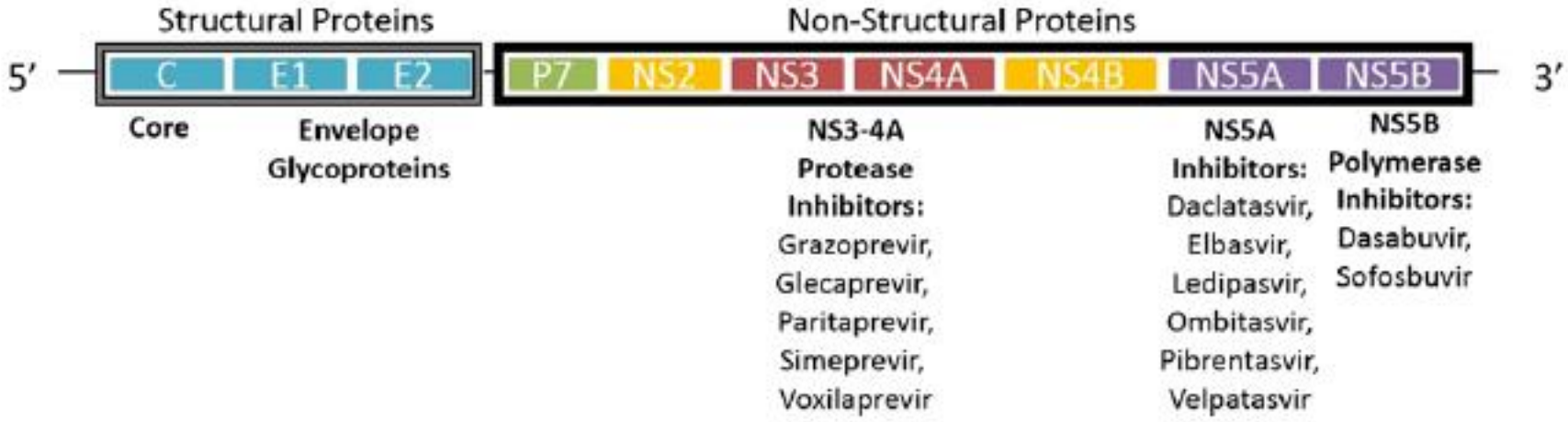
- Ritonavir+paritaprevir+Ombitasvir(50mg+75mg+12,5mg) 1x2 yemekle birlikte
- +dasabuvir250mg2x1
- Genotip 1
- Paritaprevir fekal
- Ombitasvir fekal
- Dasabuvir hepatobiliyer
- En yaygın yan etkiler yorgunluk ve bulantı
- Child B ve C de önerilmiyor
- KBY ve diyaliz hastalarında kullanılabiliyor
- İlaç etkileşimi dikkat!!!



- Grazoprevir+elbasvir (100mg+50mg) 1x1 aç veya tok
- biliyer ve fekal ekskresyon
- Child B ve C de önerilmez
- Hafif-orta-ağır renal yetmezlikte doz ayarlama önerilmez
- Yorgunluk ve başağrısı



- Glecaprevir+pibrentasvir(100mg+40mg)
- 1x3 yemekle birlikte
- Major eliminasyon biliyer
- Child B ve C de kontrendike
- En sık yan etki baş ağrısı ve yorgunluk



Non-sirotik veya kompanse sirotik

Genotype	Pangenotypic regimens			Genotype-specific regimens		
	SOF/ VEL	GLE/PIB	SOF/ VEL/ VOX	SOF/ LDV	GZR/ EBR	OBV/ PTV/r + DSV
Genotype 1a	Yes	Yes	No*	Yes[a]	Yes[b]	No
Genotype 1b	Yes	Yes	No*	Yes	Yes	Yes
Genotype 2	Yes	Yes	No*	No	No	No
Genotype 3	Yes[c]	Yes	Yes[d]	No	No	No
Genotype 4	Yes	Yes	No*	Yes[a]	Yes[e]	No
Genotype 5	Yes	Yes	No*	Yes[a]	No	No
Genotype 6	Yes	Yes	No*	Yes[a]	No	No

- * Triple combination therapy efficacious but not useful due to the efficacy of double combination regimens. a Treatment-naïve patients without cirrhosis or with compensated (Child-Pugh A) cirrhosis. b Treatment-naïve and treatment-experienced patients without cirrhosis or with compensated (Child-Pugh A) cirrhosis with an HCV RNA level ≤800,000IU/ ml (5.9 Log10 IU/ml). c Treatment-naïve and treatment-experienced patients without cirrhosis. d Treatment-naïve and treatment-experienced patients with compensated (Child-Pugh A) cirrhosis. e Treatment-naïve patients without cirrhosis or with compensated (Child-Pugh A) cirrhosis with an HCV RNA level ≤800,000 IU/ml (5.9 Log10 IU/ml).

Tedavi naif veya deneyimli non sirotik

Patients	Prior treatment experience	SOF/VEL	GLE/PIB	SOF/VEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
Genotype 1a	Treatment-naïve	12 wk	8 wk	No	8-12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	8 wk	No	No	12 wk (HCV RNA ≤800,000 IU/ml)	No
Genotype 1b	Treatment-naïve	12 wk	8 wk	No	8-12 wk	8 wk (F0-F2) 12 wk (F3)	8 wk (F0-F2) 12 wk (F3)
	Treatment-experienced	12 wk	8 wk	No	12 wk	12 wk	12 wk
Genotype 2	Treatment-naïve	12 wk	8 wk	No	No	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 3	Treatment-naïve	12 wk	8 wk	No	No	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 4	Treatment-naïve	12 wk	8 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 5	Treatment-naïve	12 wk	8 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 6	Treatment-naïve	12 wk	8 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No

%98 %98 %98 %97 %99 %100 %100 %99 %99 %99 %98 %98 %95 %100 %100 %99 %95 %97 %100 %97 %100 %96

Tedavi naif veya deneymili kompanse sirotik

Patients	Prior treatment experience	SOF/VEL	GLE/PIB	SOF/VEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
Genotype 1a	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	12 wk	No	No	12 wk (HCV RNA ≤800,000 IU/ml)	No
Genotype 1b	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk	12 wk
	Treatment-experienced	12 wk	12 wk	No	12 wk	12 wk	12 wk
Genotype 2	Treatment-naïve	12 wk	12 wk	No	No	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 3	Treatment-naïve	No	12 wk	12 wk	No	No	No
	Treatment-experienced	No	16 wk	12 wk	No	No	No
Genotype 4	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 5	Treatment-naïve	12 wk	12 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 6	Treatment-naïve	12 wk	12 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No

Nakil gerektiren veya gerektirmeyen ileri karaciğer hastası

- Tedavi edilmemiş hastada nakil sonrası nüks
- Nakil öncesi tedavi nüksü önler ve nakile kadar karaciğeri stabilize edebilir
- Canlıda nakil zamanı öngörülür
- Kadavra bekleyen hastada ise ne zaman organ bulunacağı bilinemez, belki daha tam eradikasyon sağlanamadan organ bulunup nakile çağrılabilir

Nakil gerektiren veya gerektirmeyen ileri karaciğer hastası

- Nakil listesinden çıkarılıp tedavi başlanırsa bu süreçte hastalık ilerleyebilir, HCC gelişip hasta kaybedilebilir, nakil bu süreçte ertelenmeyip önce nakil sonra HCV tedavisi daha uygun olur.
- Proteaz inhibitörleri dekompanse sirozda önerilmez, daha önce dekompansasyon atağı yaşayan hastada da önerilmez

Patients with decompensated (Child-Pugh B or C) cirrhosis should be treated in experienced centres with easy access to liver transplantation and close monitoring during therapy is required, with the possibility of stopping therapy with evidence of worsening decompensation during treatment (**A1**).

Patients with decompensated (Child-Pugh B or C) cirrhosis, without HCC, awaiting liver transplantation with a MELD score <18–20 should be treated prior to liver transplantation. Treatment should be initiated as soon as possible in order to complete a full treatment course before transplantation and assess the effect of SVR on liver function, because significant improvement in liver function may lead to delisting in selected cases (**A1**).

Protease inhibitors-containing regimens are contraindicated in patients with decompensated (Child-Pugh B or C) cirrhosis (**A1**).

Patients with decompensated (Child-Pugh B or C) cirrhosis, without HCC, awaiting liver transplantation with a MELD score <18–20 can be treated with sofosbuvir and ledipasvir (genotypes 1, 4, 5 and 6), or with sofosbuvir and velpatasvir (all genotypes), with daily weight-based ribavirin (1,000 or 1,200 mg in patients <75 kg or ≥75 kg, respectively) for 12 weeks (**A1**).

In patients with decompensated (Child-Pugh B or C) cirrhosis without HCC awaiting liver transplantation with a MELD score <18–20 treated with sofosbuvir and ledipasvir with ribavirin, or with sofosbuvir and velpatasvir with ribavirin, ribavirin can be started at the dose of 600 mg daily and the dose subsequently adjusted depending on tolerance (**B1**).

Patients with decompensated (Child-Pugh B or C) cirrhosis with contraindications to the use of ribavirin or with poor tolerance to ribavirin on treatment should receive the fixed-dose combination of sofosbuvir and ledipasvir (genotypes 1, 4, 5 or 6), or the fixed-dose combination of sofosbuvir and velpatasvir (all genotypes), for 24 weeks without ribavirin (**A1**).

The higher risk of adverse events reported in patients with decompensated cirrhosis awaiting liver transplantation necessitates appropriately frequent clinical and laboratory assessments during and after HCV therapy (**B1**).

Patients with decompensated cirrhosis without HCC awaiting liver transplantation with a MELD score ≥18–20 should be transplanted first, without antiviral treatment. HCV infection should be treated after liver transplantation (**B1**).

Patients with decompensated cirrhosis without HCC awaiting liver transplantation with a MELD score ≥18–20 can be treated before transplantation if the waiting time on the transplant list exceeds 6 months, depending on the local situation (**B2**).

Treatment-Naive Genotype 1a Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[a] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL	8 weeks	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg), with weight-based ribavirin	12 weeks	I, A
Daily simeprevir (150 mg) plus sofosbuvir (400 mg)	12 weeks	I, A
Daily daclatasvir (60 mg)[c] plus sofosbuvir (400 mg)	12 weeks	I, B
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for patients with baseline NS5A RASs[a] for elbasvir	16 weeks	IIa, B

Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis[a]		
RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[b] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[c]	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for patients with baseline NS5A RASs[b] for elbasvir	16 weeks	IIa, B

Treatment-Naive Patients Genotype 1b Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL	8 weeks	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg)	12 weeks	I, A
Daily simeprevir (150 mg) plus sofosbuvir (400 mg)	12 weeks	I, A
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	12 weeks	I, B

Treatment-Naive Genotype 1b Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg)[c]	12 weeks	I, A

Treatment-Naive Genotype 2 Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	12 weeks	IIa, B

Treatment-Naive Genotype 2 Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/ pibrentasvir (120 mg)[b]	12 weeks	I, B
ALTERNATIVE	**DURATION**	**RATING**
Daily daclatasvir (60 mg)[c] plus sofosbuvir (400 mg)	16 to 24 weeks	IIa, B

Treatment-Naive Genotype 3 Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	12 weeks	I, A

Treatment-Naive Genotype 3 Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)[c]	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) when Y93H is present	12 weeks	IIa, B
Daily daclatasvir (60 mg)[d] plus sofosbuvir (400 mg) with or without weight-based ribavirin[c]	24 weeks	IIa, B

Treatment-Naive Genotype 4 Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	IIa, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, B
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) and weight-based ribavirin	12 weeks	I, A

Treatment-Naive Genotype 4 Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	12 weeks	I, B
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	IIa, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, B
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) and weight-based ribavirin[c]	12 weeks	I, A

Treatment-Naive Genotype 5 or 6 Patients With and Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/ pibrentasvir (120 mg)[b]	8 weeks (no cirrhosis)	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/ pibrentasvir (120 mg)[b]	12 weeks (cirrhosis)	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, B

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1, 4, 5, or 6 Infection and Are Ribavirin Eligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	I, A[b]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[c]	12 weeks	I, A[d]
Genotype 1 or 4 infection only: Daily daclatasvir (60 mg)[e] plus sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	I, B

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1, 4, 5, or 6 Infection and Are Ribavirin Ineligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	24 weeks	I, A[b]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	24 weeks	I, A[c]
Genotype 1 or 4 infection only: Daily daclatasvir (60 mg)[d] plus sofosbuvir (400 mg)	24 weeks	II, C

Patients With Decompensated Cirrhosis[a] and Genotype 1, 4, 5, or 6 Infection in Whom Prior Sofosbuvir- or NS5A-Based Treatment Failed

RECOMMENDED	DURATION	RATING
Prior sofosbuvir-based treatment failure only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg; increase as tolerated)	24 weeks	II, C[b]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[c]	24 weeks	II, C[d]

Patients With Decompensated Cirrhosis[a] Who Have Genotype 2 or 3 Infection and Are Ribavirin Eligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin	12 weeks	I, A
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	II, B

Patients With Decompensated Cirrhosis[a] Who Have Genotype 2 or 3 Infection and Are Ribavirin Ineligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	24 weeks	I, A
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	24 weeks	II, C

Patients With Decompensated Cirrhosis[a] and Genotype 2 or 3 Infection in Whom Prior Sofosbuvir- or NS5A-Based Treatment Failed

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[b]	24 weeks	II, C

Evliya Çelebi

- 28E
- 57K
- ----------
- 30TD
- 55Naif
- ---------
- Genotip3 2hasta
- Genotip4 1 hasta

- 49 non sirotik
- 21 kompanse
- 15 dekompanse

- 42bx+
- 43bx-
- ----------
- 6 6/6
- 3 5/6
- 9 4/6
- 11 3/6
- 9 2/6
- 4 1/6

- 24 SOF/LDV
- 5 SOF/LDV/RBV
- 2 SOF/RBV
- 37 OBV/PTV/r+DSV
- 16 OBV/PTV/r+DSV/RBV
- 1 DSV/RBV

- 24 SOF/LDV
- 5 SOF/LDV/RBV
- 2 SOF/RBV
- 37 OBV/PTV/r+DSV
- 16 OBV/PTV/r+DSV/RBV
- 1 DSV/RBV

~ %100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