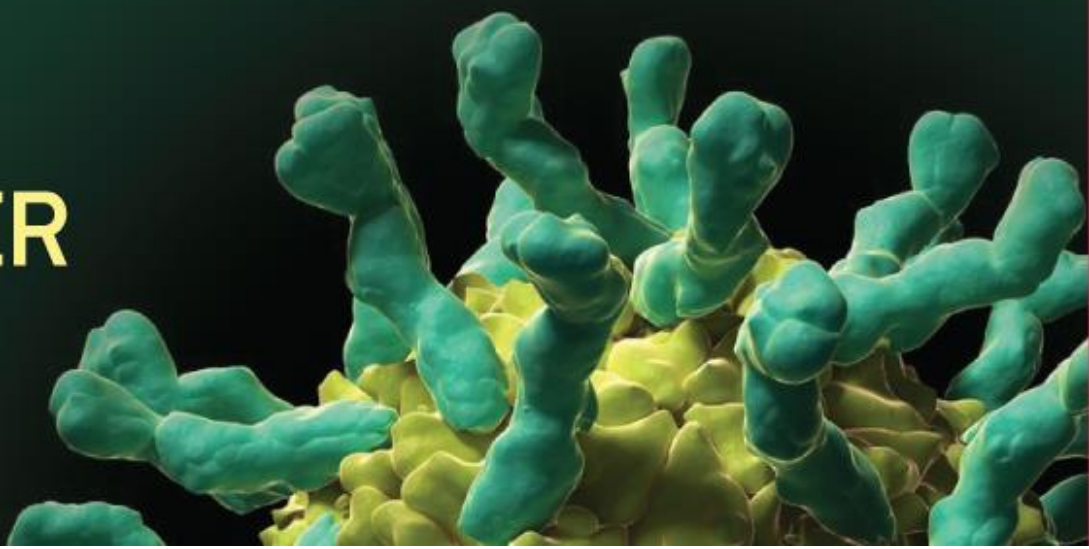
KLİMİK HEPATİT AKADEMİSİ 2017

TEMEL BİLGİLER

19-22 OCAK 2017
Sheraton Bursa Hotel / Bursa



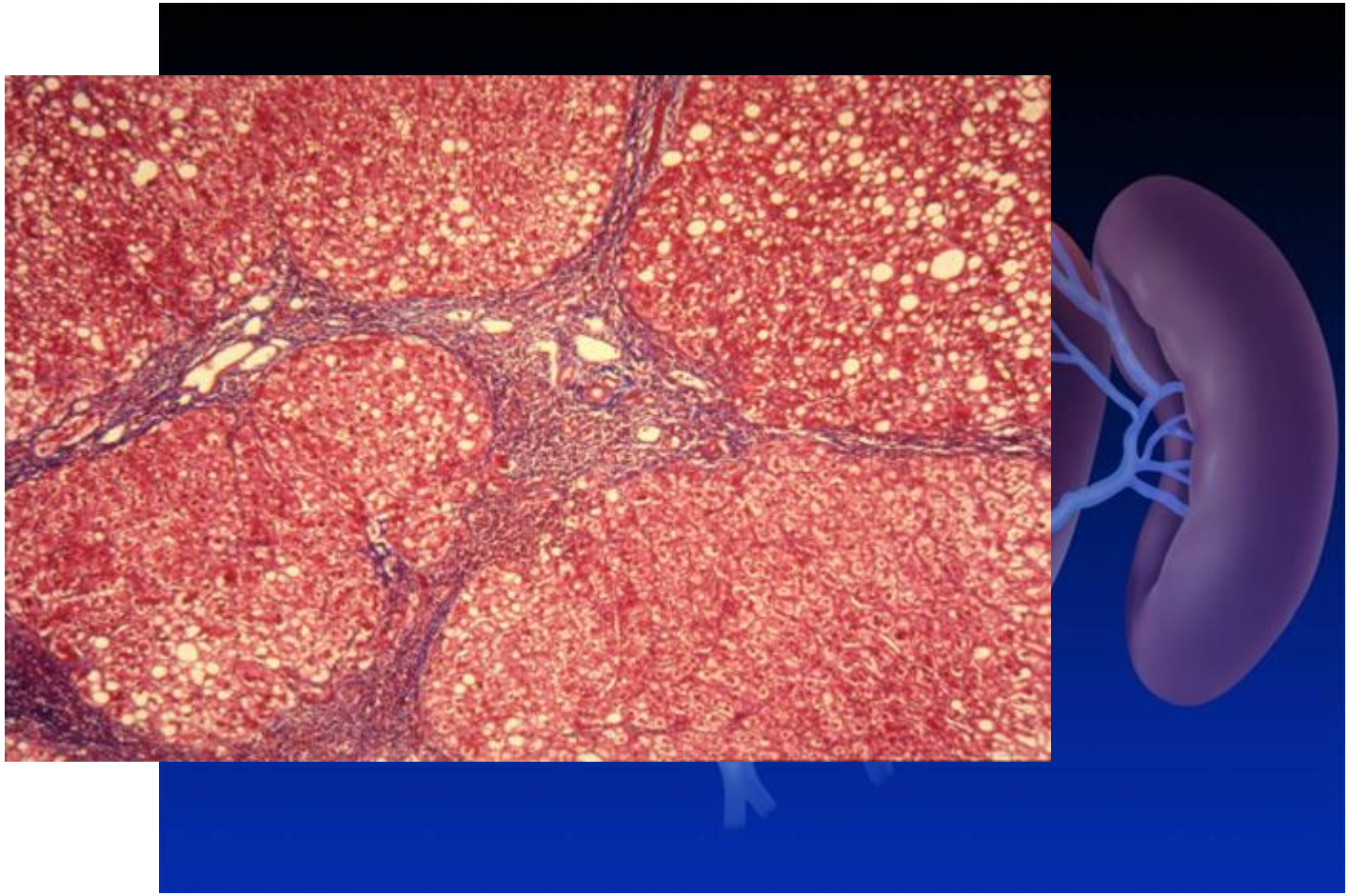
HCV yönetiminde özel hasta grupları (Sirotik Hasta, Diyaliz hastası)

Ulus Salih AKARCA

SİROZ HASTALARI HEPATİT C TEDAVİSİNE NİÇİN DAHA KÖTÜ CEVAP VERİR?

- İlacın ulaşmasında bozukluk

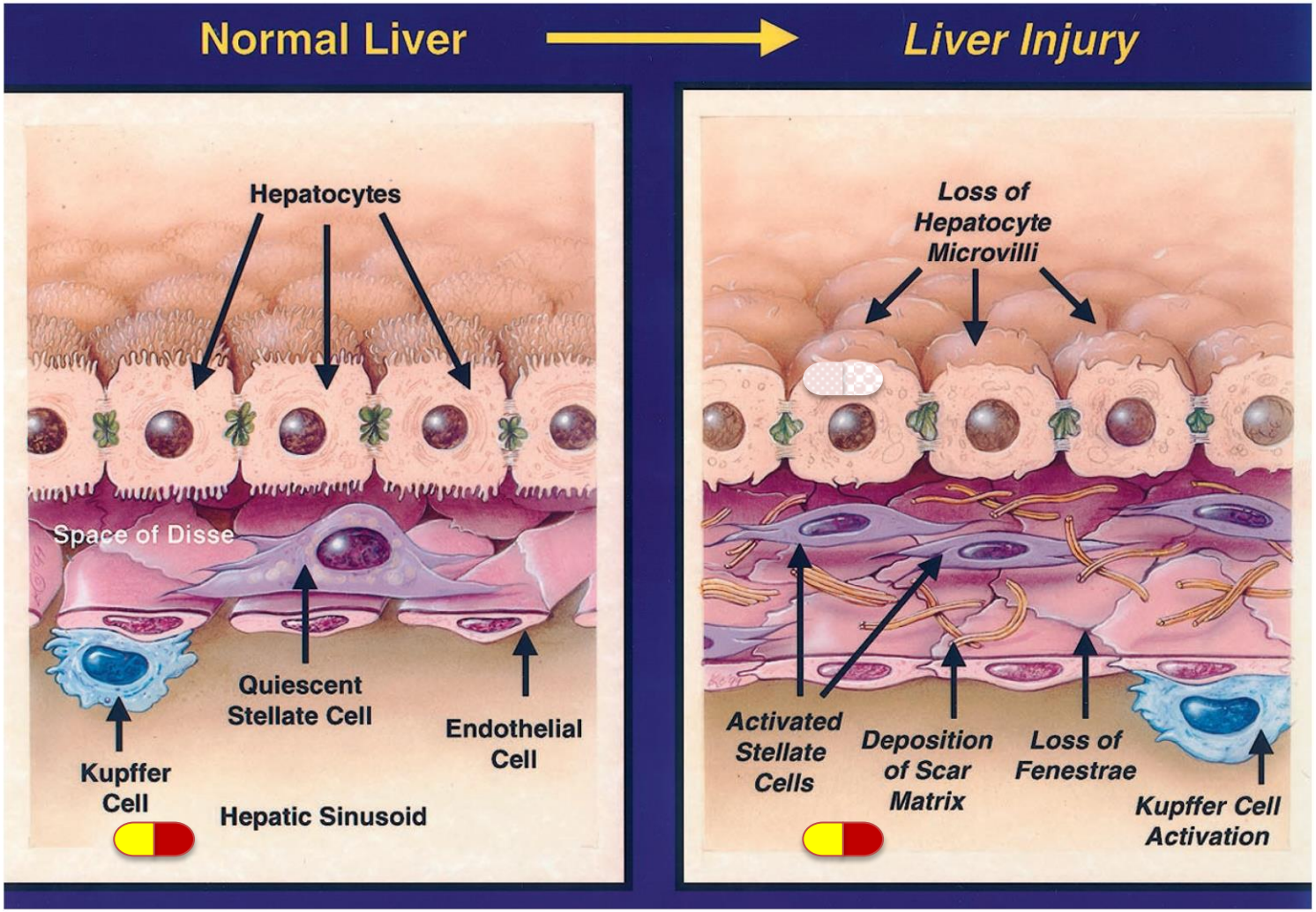
SİROZ HASTALARI HEPATİT C TEDAVİSİNE NİÇİN DAHA KÖTÜ CEVAP VERİR?



SİROZ HASTALARI HEPATİT C TEDAVİSİNE NİÇİN DAHA KÖTÜ CEVAP VERİR?

- İlaç uptake ve metabolizmasındaki bozukluk

SİROZ HASTALARI HEPATİT C TEDAVİSİNE NİÇİN DAHA KÖTÜ CEVAP VERİR?



SİROZ HASTALARI HEPATİT C TEDAVİSİNE NİÇİN DAHA KÖTÜ CEVAP VERİR?

- İlaç toksisitesi
  - Yan etkiye tolerans azalmıştır.
  - Proteaz inhibitörlerinin karaciğer toksisitesi riski artar.
  - Trombositopeni ve hipoalbuminemi toksisite riskini artırır.
  - Hipoalbuminemi PGE2 inhibisyonunda yetersizlik yaparak infeksiyon riskini artırır.

SİROZ HASTALARI HEPATİT C TEDAVİSİNE NİÇİN DAHA KÖTÜ CEVAP VERİR?

- İmmün fonksiyon bozulur
  - Malnutrisyon immün cevabı bozar.
  - TGF-β ↑ İFN sinyalini bozar.
  - NK hücre kitlesinin azalması innate immün cevabı, antifibrotik etkiyi, adaptif immün cevap için gerekli uyarıyı bozar
  - Artmış safra asiti düzeyi immün cevabı, İFN yolaklarını bozar
  - Artmış oksidatif stres
  - Vit D düzeyinde azalma

SİROZ HASTALARI HEPATİT C TEDAVİSİNE NİÇİN DAHA KÖTÜ CEVAP VERİR?

- Bütün bunlara rağmen DEA ilaçlar kompanse siroz hastalarında yüksek etkinlik ve emniyetle kullanılmaktadır.

AASLD kompanse siroz hastalarında tedavi önerileri

G1b-tedavi deneyimsiz

- [Elbasvir + Grazoprevir] 12 hafta
- [Ledipasvir + Sofosbuvir] 12 hafta
- [Paritaprevir+Ritonavir+Ombitasvir]+ Dasabuvir 12 hafta
- [Sofosbuvir + Velpatasvir] 12 hafta

A L T E R N A T İ F

- Sofosbuvir + Simeprevir ± RBV olmamak kaydıyla) 24 hafta (Q80K
- Sofosbuvir + Daclatasvir ± RBV 24 hafta

G1b tedavi deneyimli

- [Elbasvir + Grazoprevir] 12 hafta
- [Ledipasvir + Sofosbuvir] + RBV 12 hafta
- [Paritaprevir+Ritonavir+Ombitasvir]+ Dasabuvir 12 hafta
- [Sofosbuvir + Velpatasvir] 12 hafta

A L T E R N A T İ F

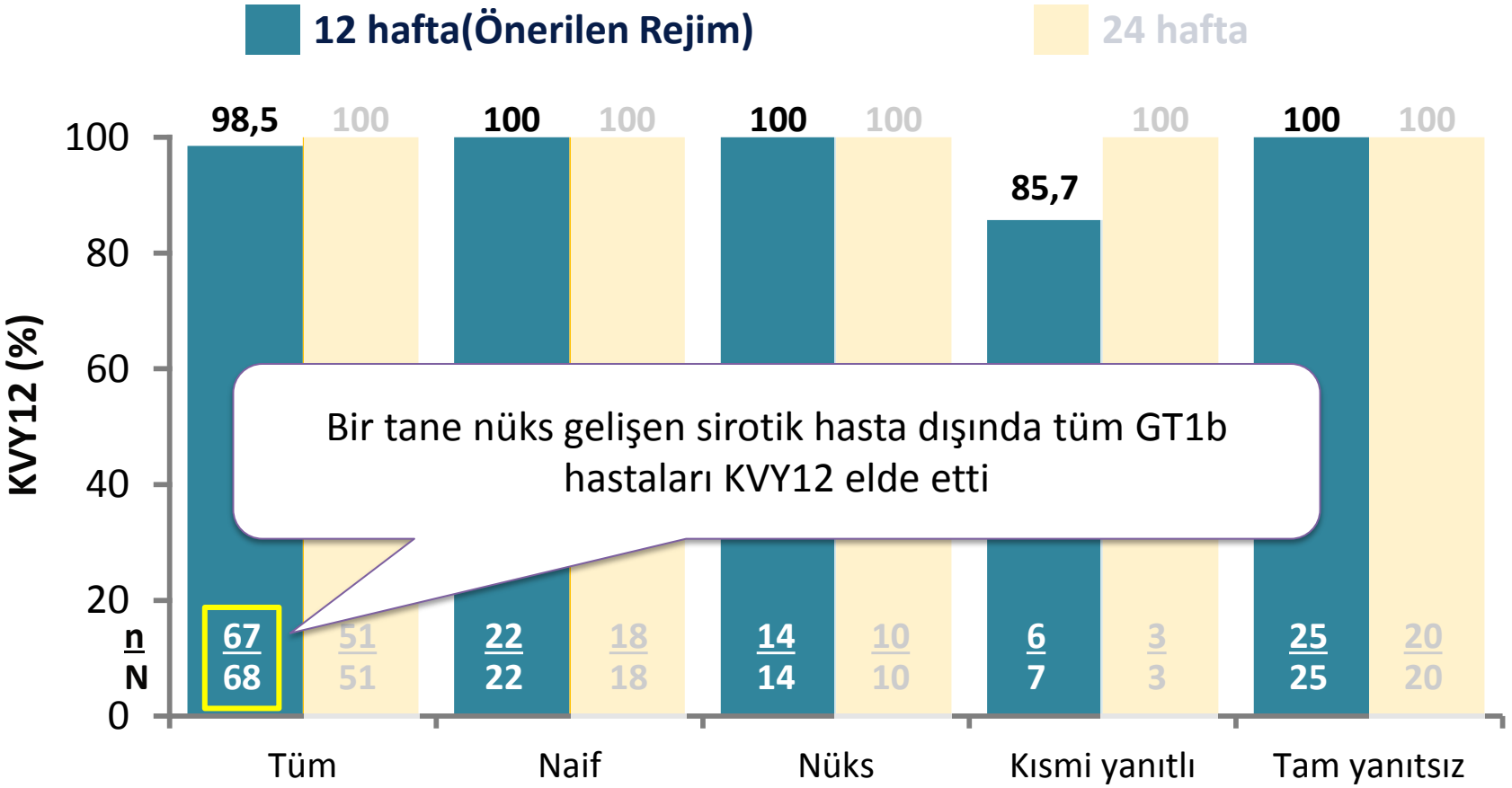
- Ledipasvir + Sofosbuvir 24 hafta
- Sofosbuvir + Simeprevir ± RBV olmamak kaydıyla) 24 hafta (Q80K
- Sofosbuvir + Daclatasvir ± RBV 24 hafta

G1b hastalarda Viekirax+Exviera

- TURQOISE II
  - Viekirax + Exviera + Ribavirin
    - 12 hafta
    - 24 hafta
- TURQOISE III
  - Viekirax + Exviera
    - 12 hafta

HCV GT1b Sirotik Hastalarda Viekirax/Exviera

68 GT1b hastası 12 hafta Viekirax/ Exviera + RBV alarak %99 KVY 12 oranı elde etti



- Viekirax KÜB (Erişim tarihi Kasım 2015);
- Poordad F, *et al. N Engl J Med.* 2014;**370**:1973–1982

Viekriax/Exviera GT1b Advers Olaylar

Birleştirilmiş Analiz:*

	Non-sirotik		Sirotik	
Adevers Olay, n (%)	RBV'siz 12 hafta (n=301)	+ RBV, 12 hafta (n=572)	+ RBV, 12 hafta (n=68)	+ RBV, 24 hafta (n=51)
Baş ağrısı	70 (23.3)		17 (25.0)	
Halsizlik	62 (20.6)		19 (27.9)	
Bulantı	15 (5.0)		10 (14.7)	
Asteni	18 (6.0)	85 (14.9)	15 (22.1)	10 (19.6)
Kaşıntı	19 (6.3)	79 (13.8)	14 (20.6)	11 (21.6)
Diyare	24 (8.0)	46 (8.0)	9 (13.2)	8 (15.7)
Insomnia	11 (3.7)	62 (10.8)	5 (7.4)	7 (13.7)
Öksürük	12 (4.0)	44 (7.7)	11 (16.2)	10 (19.6)
Döküntü	8 (2.7)	43 (7.5)	7 (10.3)	9 (17.6)
Sersemlik	12 (4.0)	41 (7.2)	7 (10.3)	3 (5.9)
Anemi	1 (0.3)	39 (6.8)	8 (11.8)	8 (15.7)
Üst karın ağrısı	8 (2.7)	31 (5.4)	7 (10.3)	5 (9.8)
Dispne	4 (1.3)	32 (5.6)	3 (4.4)	8 (15.7)
Artralji	10 (3.3)	22 (3.8)	4 (5.9)	6 (11.8)
Depresyon	10 (3.3)	13 (2.3)	1 (1.5)	6 (11.8)
Hiperbilirubinemi	3 (1.0)	14 (2.4)	9 (13.2)	0

Önerilen rejim

Önerilen rejim

* Veriler SAPPHIRE-I, SAPPHIRE-II, PEARL-II, PEARL-III ve TURQUOISE-II çalışmalarından.

Colombo M, *et al. Hepatology* 2014; **60**(Suppl):1131A.

Viekriax/Exviera GT1b Laboratuar Anomalileri

Birleştirilmiş Analiz:*

	Non-sirotik		Sirotik	
Olay, n (%)	Viekirax /Exviera, 12 hafta (n=301)	Viekirax/ Exviera + RBV, 12 hafta (n=572)	Viekirax/ Exviera + RBV, 12 hafta (n=68)	Viekirax/ Exviera + RBV, 24 hafta (n=51)
Total bilirubin				
Grade 3 (>3X–10X ULN)	1 (0.3)		7 (10.3)	
Grade 4 (>10X ULN)	0	1 (0.2)†	0	0
Hemoglobin				
Grade 3/4 (<8.0–6.5 g/dL)	0	2 (0.4)†	0	0
ALT				
Grade 3/4 (>5X ULN)	0	6 (1.1)†	1 (1.5)	0
AST				
Grade 3/4 (>5X ULN)	1 (0.3)	2 (0.4)‡	0	0

Önerilen rejim

Önerilen rejim

Viekirax/ Exviera ± RBV ile tedavi edilen hiç bir GT1b hastasının hemoglobin düzeyi <8 g/dL olmadı

* Veriler PEARL-II, PEARL-III VE TURQUOISE-II çalışmalarından;

Colombo M, *et al. Hepatology* 2014; **60**(Suppl):1131A.

TURQUOISE-III: GT1b, Tedavi Naif veya Deneyimli* Sirotik Hastalar

Feld JJ, *et al.* Journal of Hepatology 2016 vol. 64 j 301–307.

G1a-tedavi deneyimsiz

- [Elbasvir + Grazoprevir] 12 hafta (bazal NS5A direnci olmamak kaydıyla)
- [Ledipasvir + Sofosbuvir] 12 hafta
- [Sofosbuvir + Velpatasvir] 12 hafta

A L T E R N A T İ F

- [Paritaprevir+Ritonavir+Ombitasvir]+ Dasabuvir + RBV 24 hafta
- Sofosbuvir + Simeprevir ± RBV 24 hafta (Q80K olmamak kaydıyla)
- Sofosbuvir + Daclatasvir ± RBV 24 hafta
- [Elbasvir + Grazoprevir] + RBV 16 hafta (bazal NS5A direnci bakılamıyorsa veya varsa)

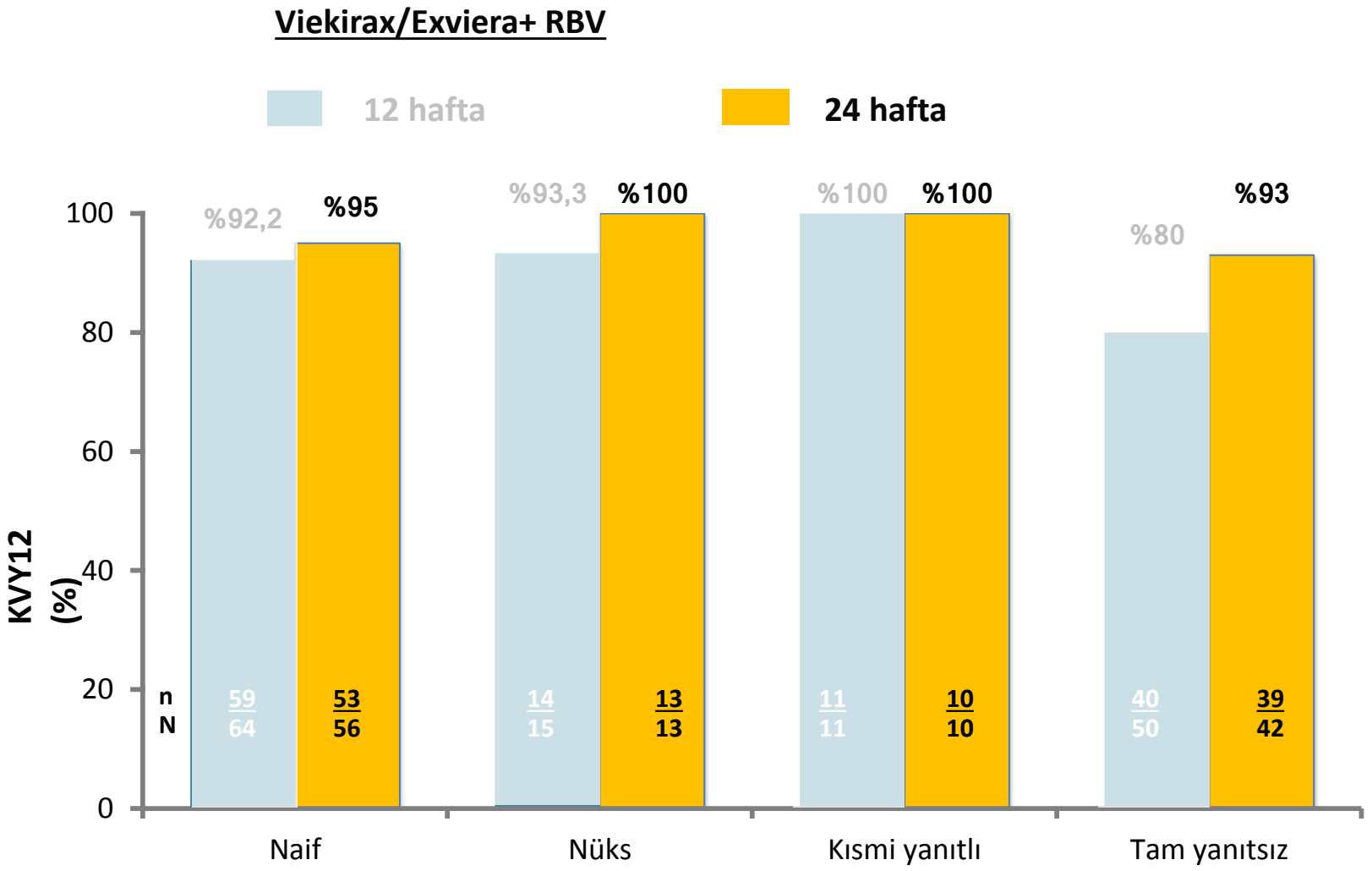
G1a tedavi deneyimli

- [Elbasvir + Grazoprevir] 12 hafta (bazal NS5A direnci olmamak kaydıyla)
- Ledipasvir + Sofosbuvir +RBV 12 hafta
- Sofosbuvir + Velpatasvir 12 hafta

ALTERNATİF

- [Paritaprevir+Ritonavir+Ombitasvir]+ Dasabuvir + RBV 24 hafta
- Ledipasvir + Sofosbuvir 24 hafta
- [Elbasvir + Grazoprevir] + RBV 16 hafta (bazal NS5A direnci bakılamıyorsa veya varsa)
- Sofosbuvir + Simeprevir ± RBV 24 hafta (Q80K olmamak kaydıyla)
- Sofosbuvir + Daclatasvir ± RBV 24 hafta

HCV GT1a Kompanse Sirotik Hastalarda Viekirax/Exviera TURQUOISE-II



P/R:PegINF/RBV

Poordad F, *et al. N Engl J Med* 2014; **370:**1973–1982; ViekiraxKÜB);
Colombo M, *et al. Hepatology* 2014; **60**(Suppl)**:**1132A.

Sirozlar için FDA uyarısı

- In October 2015, the FDA released a warning regarding the use of the PrOD or PrO (without dasabuvir) in patients with cirrhosis. (This statement is based on our review of the limited data available from the FDA and will be updated if and when more data become available.) PrOD and PrO are contraindicated inpatients with Child Turcotte Pugh (CTP) class B or C hepatic impairment (decompensated liver disease). The manufacturer's pharmacovigilance program reported rapid onset of liver injury and in some cases hepatic decompensation in patients with cirrhosis, including CTP class A compensated cirrhosis and decompensated cirrhosis, who were receiving PrOD or PrO. The liver injury and decompensating events occurred largely during the first 4 weeks of therapy and primarily involved a rapid increase in total and direct bilirubin, often associated with a concomitant increase in liver enzyme levels. In most cases, early recognition and prompt discontinuation of PrOD or PrO resulted in resolution of injury, although some patients, including at least 2 patients with CTP class A compensated cirrhosis, died or required liver transplantation. Although cirrhosis carries a 2% to 4% annual risk of hepatic decompensation, the rapid onset of hepatic decompensation and in many cases its resolution with discontinuation of treatment with PrOD or PrO is suggestive of drug-induced liver injury. Although PrOD and PrO are contraindicated in patients with CTP class B or C cirrhosis and decompensated liver disease, predictors of these events in patients with CTP class A cirrhosis are currently unclear.
- For patients with CTP class A cirrhosis, the unlikely but real possibility of drug-induced liver injury should be discussed with the patient. If the decision is made to initiate treatment with PrOD or PrO, close monitoring of total and direct bilirubin and transaminase levels every 1 week or 2 weeks for the first 4 weeks is recommended to ensure early detection of drug-induced liver injury. Also, educating patients about the importance of reporting systemic symptoms such as jaundice, weakness, and fatigue is strongly recommended. The regimen should be discontinued immediately if drug-induced liver injury is suspected. If a patient is already taking PrOD or PrO and is tolerating the regimen, laboratory monitoring as above without discontinuation is recommended unless there are signs or symptoms of liver injury. If heightened monitoring cannot be provided in the first 4 weeks of therapy with PrOD or PrO in patients with cirrhosis, the use of these regimens is not recommended.

Sirozlar için FDA uyarısı

- In October 2015, the FDA released a warning regarding the use of the PrOD or PrO (without dasabuvir) in patients with cirrhosis. (This statement is based on our review of the limited data available from the FDA and will be updated if and when more data become available.) **PrOD and PrO are contraindicated inpatients with Child Turcotte Pugh (CTP) class B or C hepatic impairment (decompensated liver disease). The manufacturer's pharmacovigilance program reported rapid onset of liver injury and in some cases hepatic decompensation in patients with cirrhosis, including CTP class A compensated cirrhosis and decompensated cirrhosis, who were receiving PrOD or PrO.** The liver injury and decompensating events occurred largely during the first 4 weeks of therapy and primarily involved a rapid increase in total and direct bilirubin, often associated with a concomitant increase in liver enzyme levels. In most cases, early recognition and prompt discontinuation of PrOD or PrO resulted in resolution of injury, although some patients, including at least 2 patients with CTP class A compensated cirrhosis, died or required liver transplantation. Although cirrhosis carries a 2% to 4% annual risk of hepatic decompensation, the rapid onset of hepatic decompensation and in many cases its resolution with discontinuation of treatment with PrOD or PrO is suggestive of drug-induced liver injury. Although PrOD and PrO are contraindicated in patients with CTP class B or C cirrhosis and decompensated liver disease, predictors of these events in patients with CTP class A cirrhosis are currently unclear.
- For patients with CTP class A cirrhosis, the unlikely but real possibility of drug-induced liver injury should be discussed with the patient. If the decision is made to initiate treatment with PrOD or PrO, close monitoring of total and direct bilirubin and transaminase levels every 1 week or 2 weeks for the first 4 weeks is recommended to ensure early detection of drug-induced liver injury. Also, educating patients about the importance of reporting systemic symptoms such as jaundice, weakness, and fatigue is strongly recommended. The regimen should be discontinued immediately if drug-induced liver injury is suspected. If a patient is already taking PrOD or PrO and is tolerating the regimen, laboratory monitoring as above without discontinuation is recommended unless there are signs or symptoms of liver injury. If heightened monitoring cannot be provided in the first 4 weeks of therapy with PrOD or PrO in patients with cirrhosis, the use of these regimens is not recommended.

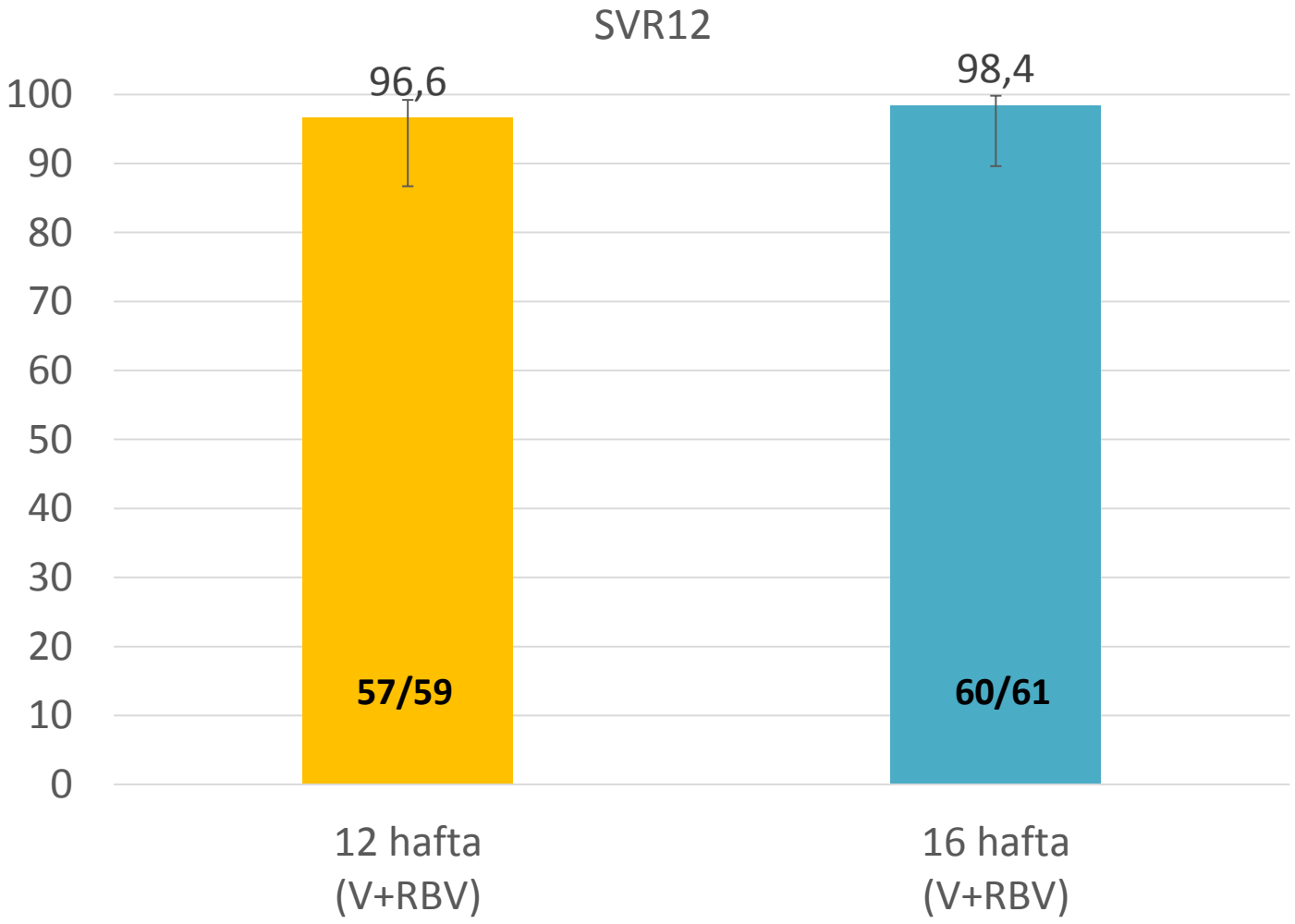
Sirozlar için FDA uyarısı

- In October 2015, the FDA released a warning regarding the use of the PrOD or PrO (without dasabuvir) in patients with cirrhosis. (This statement is based on our review of the limited data available from the FDA and will be updated if and when more data become available.) **PrOD and PrO are contraindicated inpatients with Child Turcotte Pugh (CTP) class B or C hepatic impairment (decompensated liver disease). The manufacturer's pharmacovigilance program reported rapid onset of liver injury and in some cases hepatic decompensation in patients with cirrhosis, including CTP class A compensated cirrhosis and decompensated cirrhosis, who were receiving PrOD or PrO.** The liver injury and decompensating events occurred largely during the first 4 weeks of therapy and primarily involved a rapid increase in total and direct bilirubin, often associated with a concomitant increase in liver enzyme levels. In most cases, early recognition and prompt discontinuation of PrOD or PrO resulted in resolution of injury, although some patients, including at least 2 patients with CTP class A compensated cirrhosis, died or required liver transplantation. Although cirrhosis carries a 2% to 4% annual risk of hepatic decompensation, the rapid onset of hepatic decompensation and in many cases its resolution with discontinuation of treatment with PrOD or PrO is suggestive of drug-induced liver injury. Although PrOD and PrO are contraindicated in patients with CTP class B or C cirrhosis and decompensated liver disease, predictors of these events in patients with CTP class A cirrhosis are currently unclear.
- **For patients with CTP class A cirrhosis, the unlikely but real possibility of drug-induced liver injury should be discussed with the patient. If the decision is made to initiate treatment with PrOD or PrO, close monitoring of total and direct bilirubin and transaminase levels every 1 week or 2 weeks for the first 4 weeks is recommended to ensure early detection of drug-induced liver injury.** Also, educating patients about the importance of reporting systemic symptoms such as jaundice, weakness, and fatigue is strongly recommended. The regimen should be discontinued immediately if drug-induced liver injury is suspected. If a patient is already taking PrOD or PrO and is tolerating the regimen, laboratory monitoring as above without discontinuation is recommended unless there are signs or symptoms of liver injury. If heightened monitoring cannot be provided in the first 4 weeks of therapy with PrOD or PrO in patients with cirrhosis, the use of these regimens is not recommended.

AASLD
G4-tedavi deneyimsiz

- [Paritaprevir+Ritonavir+Ombitasvir]+ RBV 12 hafta
- [Sofosbuvir + Velpatasvir] 12 hafta
- [Elbasvir + Grazoprevir] 12 hafta
- [Ledipasvir + Sofosbuvir] 12 hafta

HCV GT 4 Kompanse Sirotik Hastalarda Viekirax
AGATE-I



Asselah T et al. The Lancet Gastroenterology & Hepatology 2016;1:25-35.

Kronik Böbrek Yetmezliği

Hepatit C ve böbrek yetmezliği

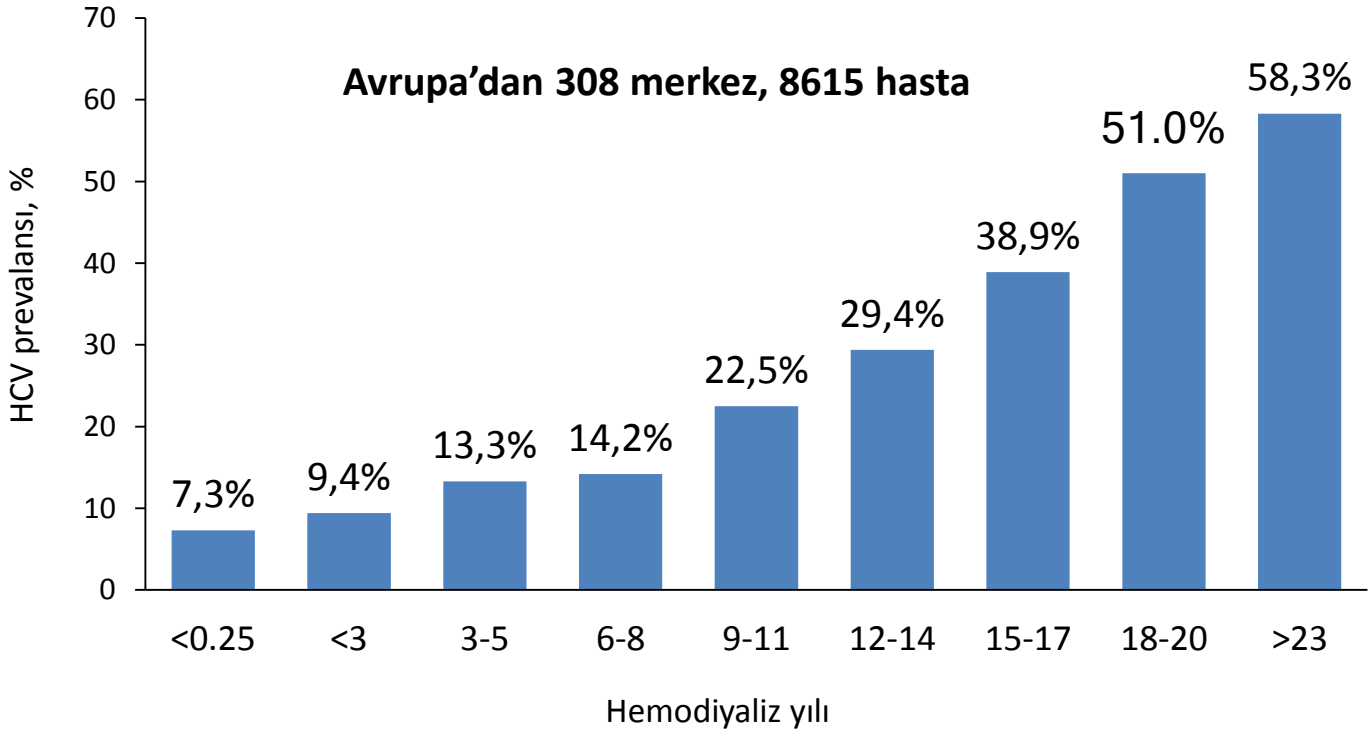
- Hepatit C'de böbrek bozukluğu riski artmaktadır.
- Hepatit C, böbrek kaynaklı ve diğer birçok sebebe bağlı ölüm riskini artırmaktadır.
- Hemodiyaliz hastalarında yüksek HCV infeksiyonu riski vardır.
- Hemodiyaliz hastalarındaki HCV infeksiyonu mortaliteyi artırmaktadır.
- Hepatit C ile infekte hemodiyaliz hastaları diğer hastaların infeksiyonu bakımından kaynaktır.

Böbrek hastalığında hepatit C prevalansı artar

Patterns of hepatitis C prevalence and seroconversion in hemodialysis units from three continents: The DOPPS

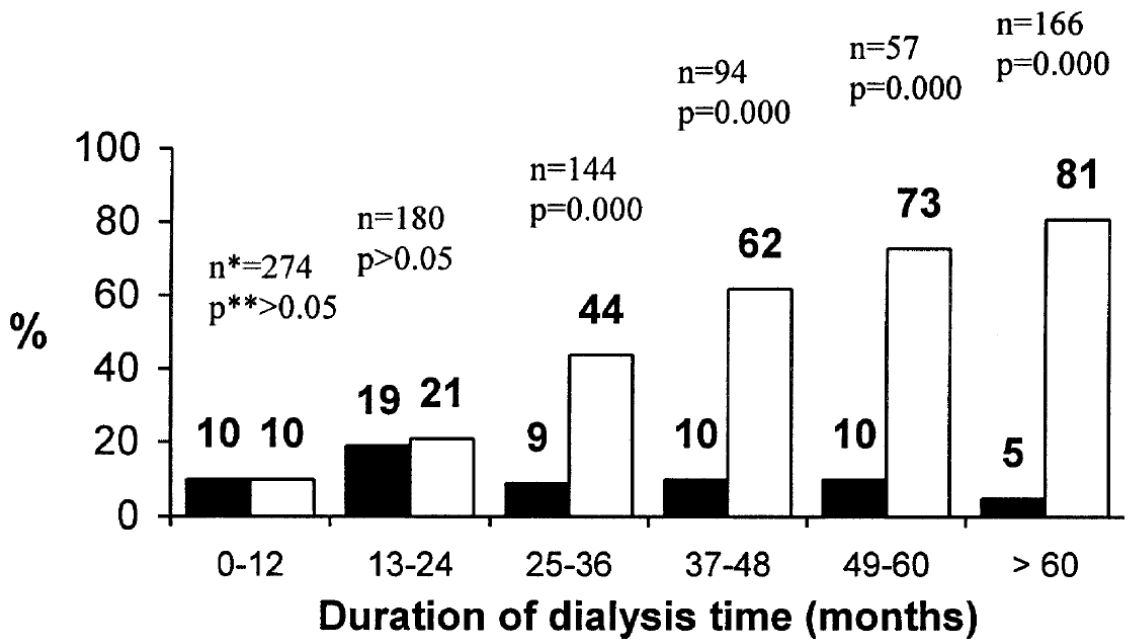
RACHEL B. FISSELL, JENNIFER L. BRAGG-GRESHAM, JOHN D. WOODS, MICHEL JADOUL, BRENDA GILLESPIE, SARA A. HEDDERWICK, HUGH C. RAYNER, ROGER N. GREENWOOD, TAKASHI AKIBA, and ERIC W. YOUNG

Kidney International, Vol. 65 (2004), pp. 2335–2342

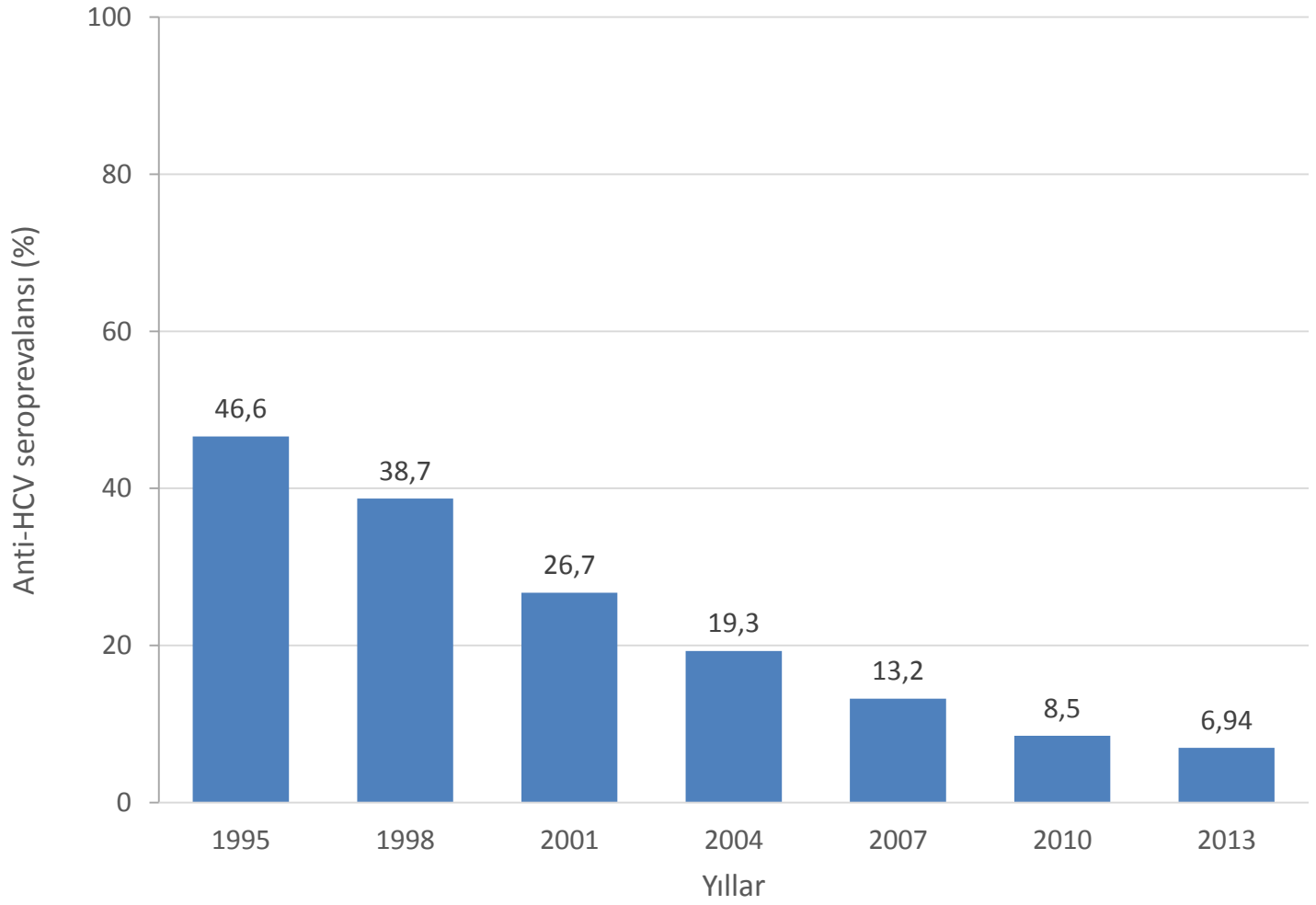


Böbrek hastalığında hepatit C prevalansı artar

Akpolat T; Turkish Multicentre CAPD Study Group (TULIP). CAPD: a control strategy to prevent spread of HCV infection in end-stage renal disease. PeritDial Int. 2001 Jan-Feb;21(1):77-9



Hemodiyaliz hastalarında anti-HCV pozitifliği oranı



Hemodiyaliz hastalarında hepatit C tedavisi

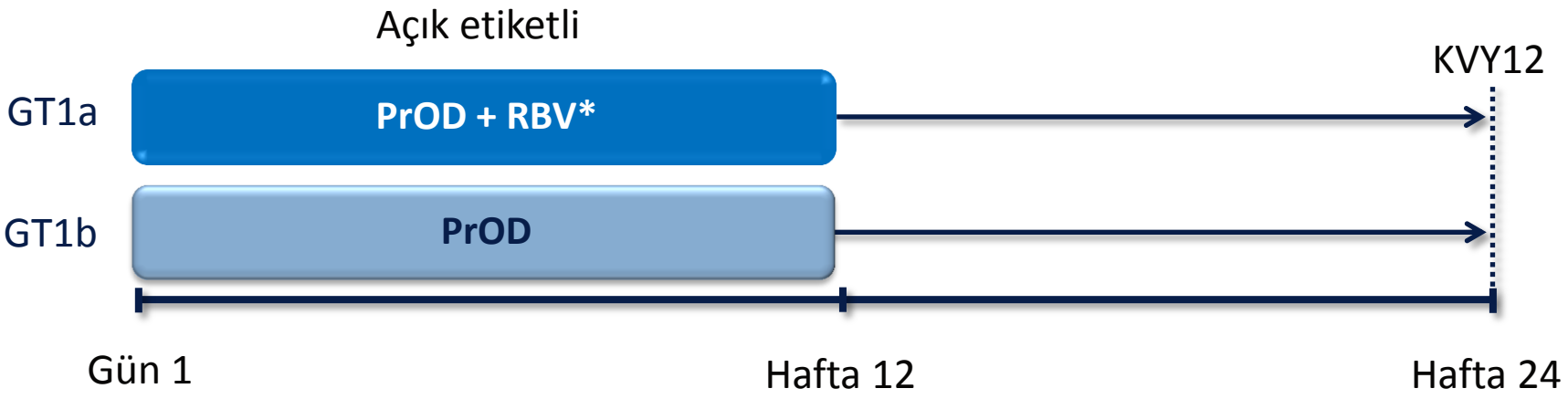
- Her hasta tedavi açısından değerlendirilmelidir.
- Yakın gelecekte nakil olasılığı görünmüyorsa tedavi mutlaka verilmelidir.
  - Mortaliteyi azaltmak
  - Bulaşı engellemek
- Nakil olacaklarda tedavi, nakil sonrasına ertelenebilir.

AASLD tavsiyesi

- For patients with genotype 1a, or 1b, or 4 infection and CrCl below 30 mL/min, for whom treatment has been elected before kidney transplantation, daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100mg) for 12 weeks
- For patients with genotype 1b infection and CrCl below 30 mL/min for whom the urgency to treat is high and treatment has been elected before kidney transplantation, daily fixed dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) for 12 weeks
- For patients with HCV genotype 2, 3, 5, or 6 infection and CrCl below 30 mL/min for whom the urgency to treat is high and treatment has been elected before kidney transplantation, PEG-IFN and dose-adjusted ribavirin** (200 mg daily)

Türkiye ürün bilgisine göre V/E kreatinin klirensi 15ml/dk altında olan hastalarda kullanılmamalıdır.

RUBY-I: GT1, Tedavi naif, Non-sirotik, Ciddi böbrek yetmezliği veya ESRD



Başlangıç renal parametreler	PrOD± RBV N=20
KBY evresi; n (%)	
4 (eGFR 15-30 mL/dk/1.73m^2)	6 (30)
5 (eGFR <15 mL/dk/1.73m^2 veya diyaliz)	14 (70)
eGFR, mL/dk/1.73m^2; median (range)	10.9 (5.4–29.9)
Kreatinin, mg/dL; median (range)	6.2 (2.2–10.8)

* RBV = 200 mg QD.

*Türkiye ürün bilgisine göre V/E kreatinin klirensi 15ml/dk altında olan hastalarda kullanılmamalıdır.

Pockros P, *et al. Hepatology* 2015; **62**(suppl):716–717A.

RUBY-I: Renal Yetmezliği Olan Hastalarda PrOD Etkililik Sonuçları

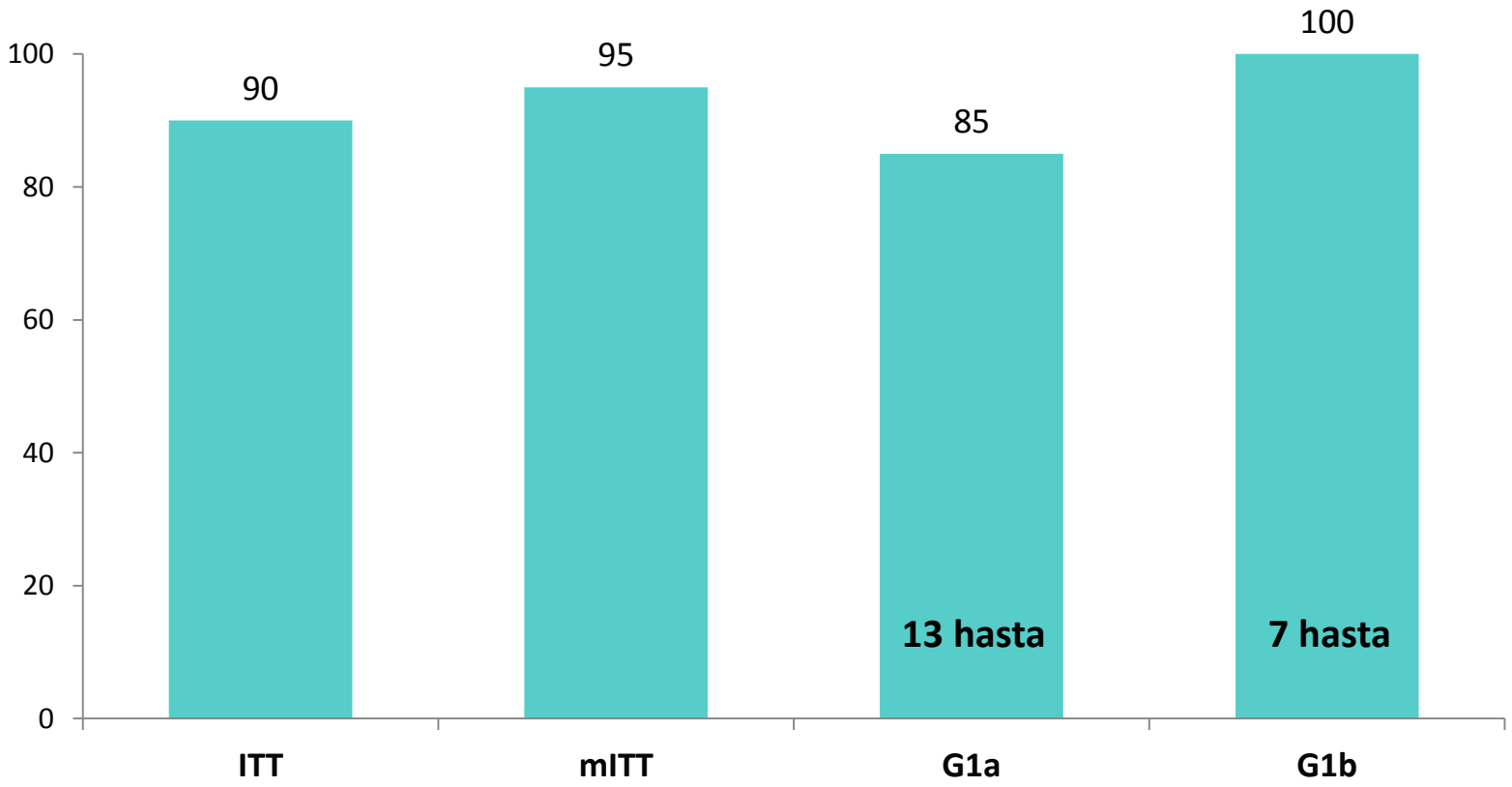
Hasta	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
GT*	1a	1a	1a	1a	1b	1a	1a	1a	1a	1a	1b	1a	1a	1a	1b	1b	1b	1b	1b	1a
KRY evresi	4	4	5	5	5	5	5	4	5	5	5	5	4	4	5	4	5	5	5	5
H1																				
H2																				
H4																				
H8																				
H12																				
TSH4										*										
TSH12																				
TSH24																				

HCV RNA: ≥25 IU/mL <25 IU/mL Tespit edilemeyen

H: Hafta, **TSH**: Tedavi sonrasında hafta, **KRY:** Kronik renal yetmezlik
* İlaca bağlı olmayan ölüm

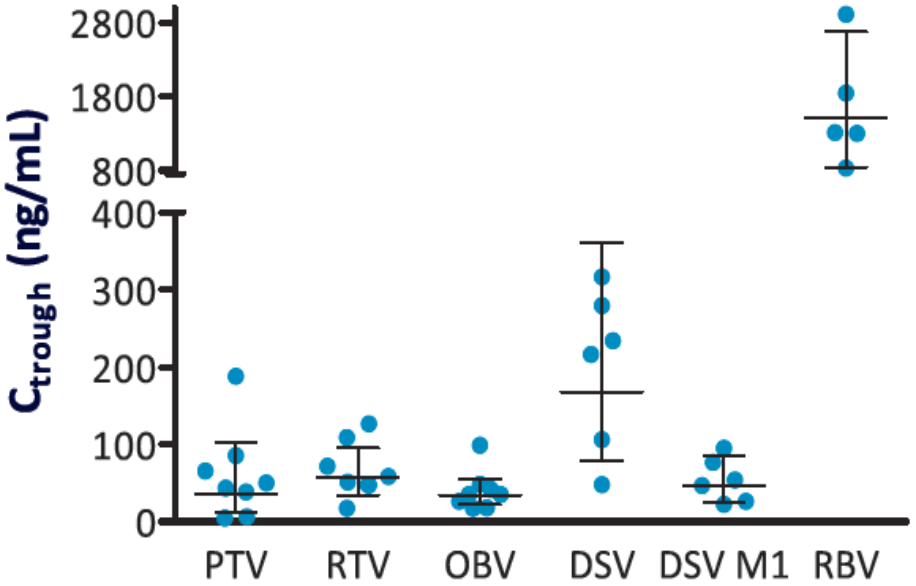
Pockros P., *et al.* #1039 *AASLD 2015*

RUBY-I: Renal Yetmezliği Olan Hastalarda PrOD Etkililik Sonuçları



- Pockros P., *et al.* #1039 *AASLD 2015*

RUBY-1 - Farmakokinetik veri



	PTV	RTV	OBV	DSV	DSV M1	RBV
RUBY-I N	8	8	8	6	6	5
Mean C_{trough}	36	57	35	168	47	1500
CV	97%	54%	65%	52%	53%	49%
Phase 3 Studies N	1277	1277	1277	1253	1253	897
C_{trough} range	16–36	40–57	24–33	175–269	55–75	2060–2330

CV= coefficient of variance; DSV M1 = dasabuvir metabolit.

Çalışma ilaçlarının konsantrasyonu KBY olmayan faz III çalışmalarındaki hastalarla karşılaştırılabilir düzeydedir

*Türkiye ürün bilgisine göre V/E kreatinin klirensi 15ml/dk altında olan hastalarda kullanılmamalıdır.

Pockros P, *et al. Hepatology* 2015; **62**(suppl):716–717A.

Hasta No	Yaş	Cinsiyet	Başlangıç ALT	Genotip	Başlangıç HCV-RNA IU/ml	1. hafta HCV-RNA	1. ay HCV-RNA	1. ay ALT	Yan etki	Ek hastalık	HCV RNA 3. Ay
1	62	Kadın	22	1B	993231	54	Negatif	20	Yok	Hemofili B	Negatif
2	60	Kadın	6	1B	47000	51	Negatif	5	Yok		Negatif
3	48	Erkek	20	1B	19400	Negatif	Negatif	21	Kaşıntı		Negatif
4	53	Erkek	20	1B	914	Negatif	Negatif	20	Yok		Negatif
5	64	Kadın	16	1B	297000	641	Negatif	22	Yok		Negatif
6	42	Erkek	40	1B	250634	-	Negatif	19	Kaşıntı		Negatif
7	37	Erkek	12	1B	10415	-	Negatif	16	Yok	KC-S Child A	Negatif
8	58	Kadın	37	1A	88493	-	16	6	Yok		Negatif
9	56	Kadın	72	1B	307592	-	Negatif	11	Yok	Tip2DM	Negatif

Hasta No	Yaş	Cinsiyet	Başlangıç ALT	Genotip	Başlangıç HCV-RNA IU/ml	1. hafta HCV-RNA	1. ay HCV-RNA	1. ay ALT	Yan etki	Ek hastalık	HCV RNA 3. Ay
10	37	Kadın	28	1A	810385	-	<12	15	yok	Böbrek nakilli + KBY	Sonuçlanmadı
11	60	Kadın	23	1B	66036	-			yok		Sonuçlanmadı
12	37	Kadın	34	1	110686	-			yok	Böbrek nakilli + KBY	Sonuçlanmadı
13	43	Erkek	15	1A	529800	104		9	yok	Child A KCS	Sonuçlanmadı
14	46	Erkek	50	1A	3106349	-	13	19	yok		Sonuçlanmadı
15	42	Kadın	23	1A	672162	-	Negatif	7	Anemi	+RBV	Sonuçlanmadı
16	46	Erkek	17	1B	208879	-	Negatif	10	yok	Böbrek nakilli + KBY	Sonuçlanmadı
17	35	Erkek	11	1A+1B	292759	-	Negatif	34	yok	KBY	Sonuçlanmadı
18	70	Erkek	36	1B	614923	-		7	yok	KAH + KOAH + HT	Sonuçlanmadı

SONUÇ

- Viekirax/Exviera
  - Kompanse siroz hastalarında
    - G1b → 12 hafta ribavirinsiz
    - G1a → 24 hafta ribavirinli
  - Orta-ağır kronik böbrek hastalarında (Türkiye ürün bilgisine göre GFR<15 ml/dk kullanılmamalıdır) ve hemodiyaliz hastalarında emniyet ve başarıyla kullanılabilir.