TÜRK KARACİĞER VAKFI
(www.tkcv.org)

AZERBAYCAN
TIP ÜNİVERSİTESİ

3 TÜRKİYE-AZERBAYCAN ORTAK HEPATOLOJİ KURSU
29-30 Eylül 2017, İstanbul

Renal Yetersizlik ve HCV Tedavisi

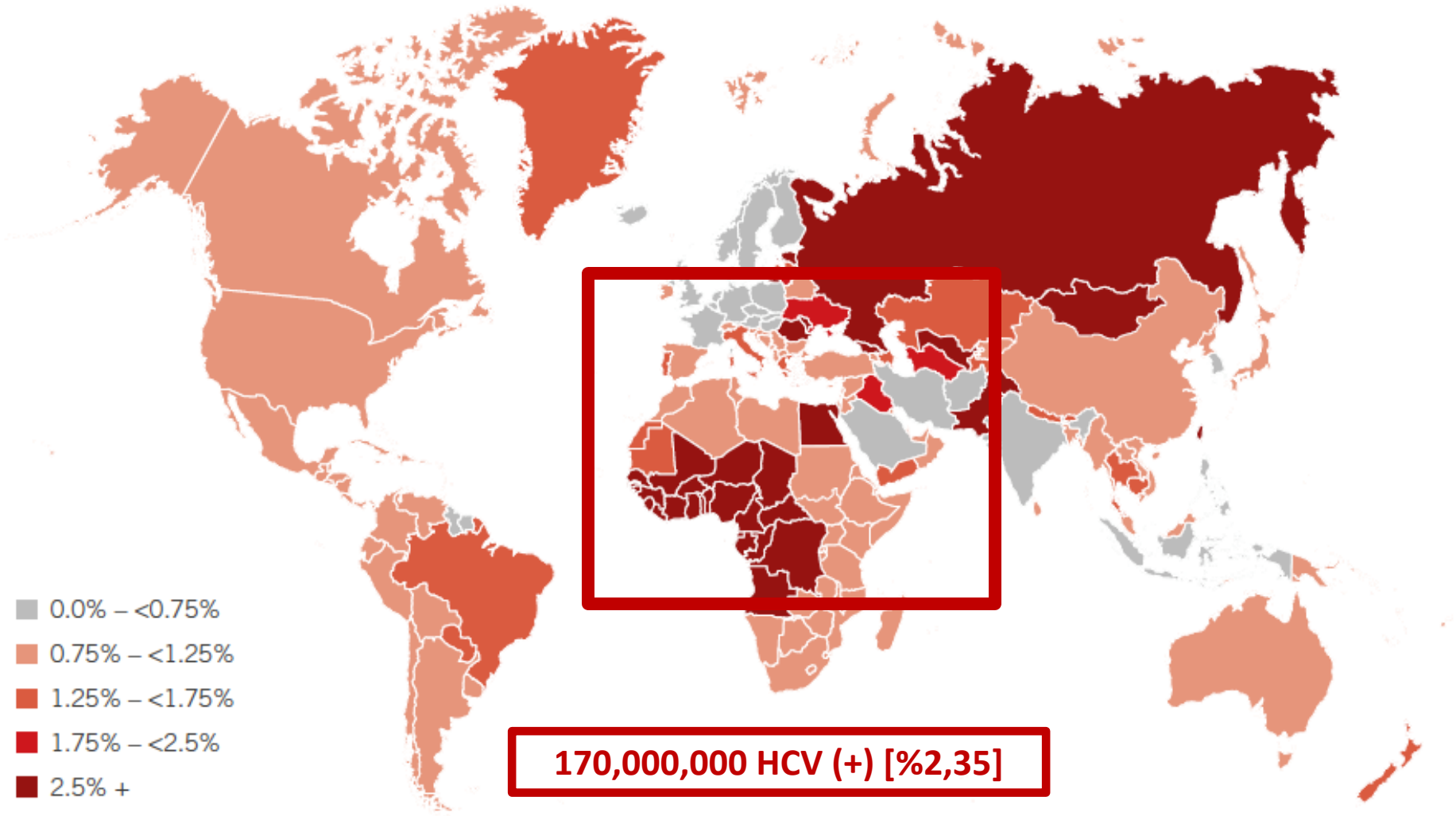
Prof. Dr. A. Sedat Boyacıoğlu

29 Eylül 2017

BAŞKENT ÜNİVERSİTESİ

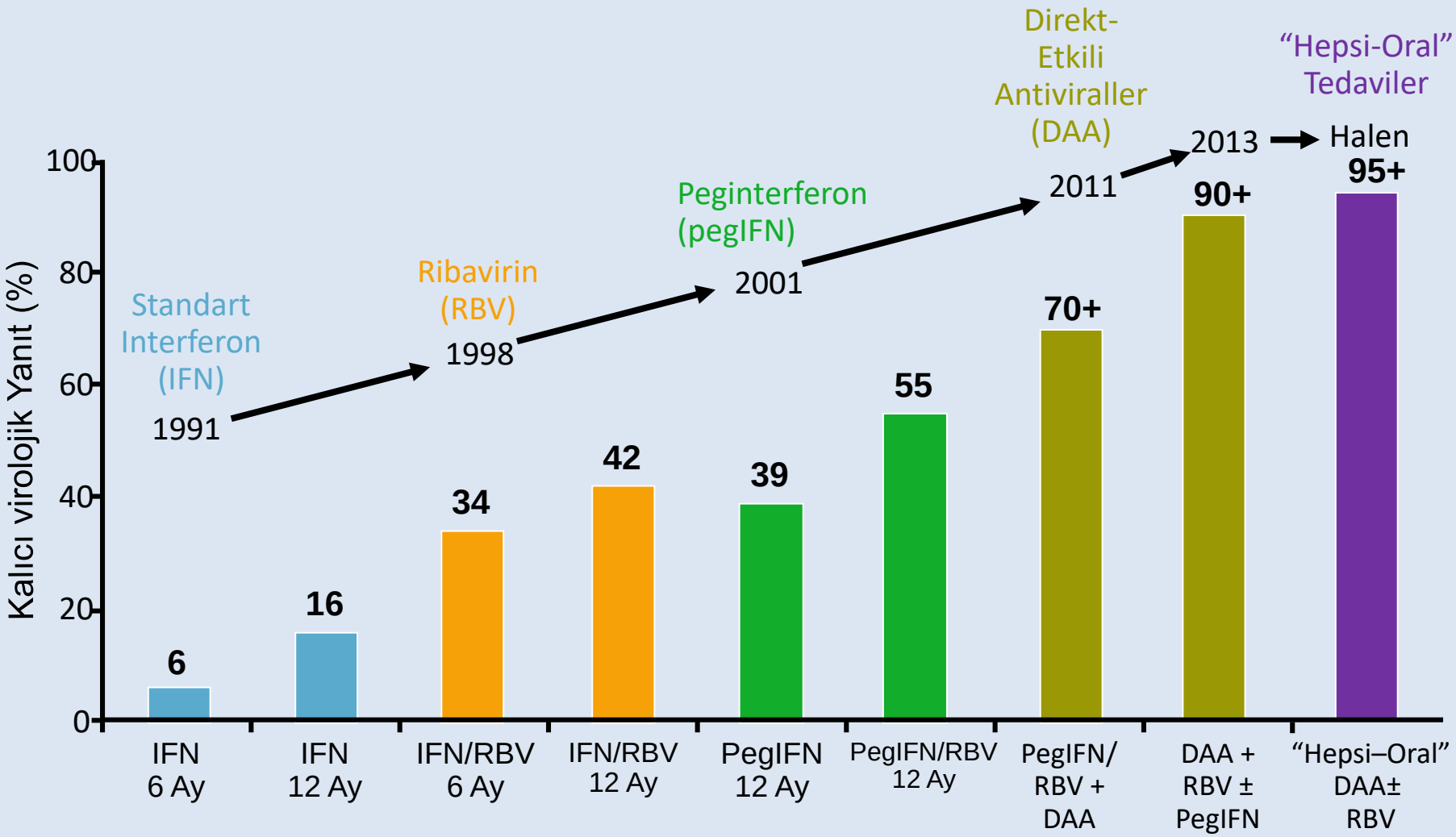
Vincent van Gogh

FIG. 1.1. Global prevalence of viraemic HCV (reported and extrapolated)



Estes GE et al. J Hepatol 2014;61(Suppl 1):S45-57(2).
Lavanchy D. Clin Microbiol Infect 2011;17(2):107–15.

HCV Tedavilerinin dünü ve bugünü



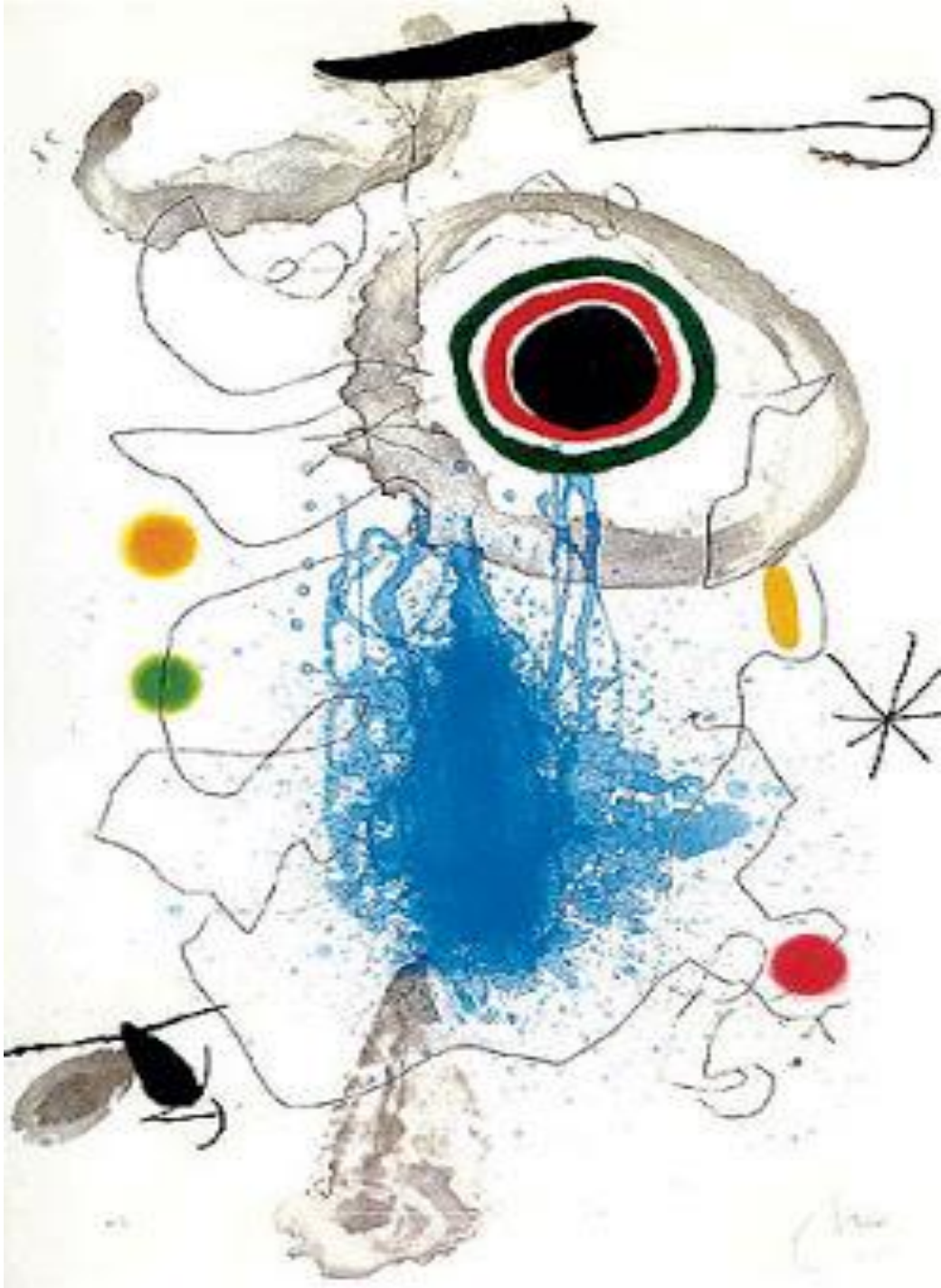
Türkiye’de ruhsatlı ve geri ödenen DAA’lar

- **Ombitasvir / Paritaprevir / Ritonavir(VIEKIRAX®)**
  +
  Dasabuvir (EXVIERA®) *

  * Türkiye’de güncellenen ürün bilgisine göre böbrek yetersizliği olan hastalarda da kullanılabilir

- **Sofosbuvir / Ledipasvir (HARVONİ®)**

Kronik Böbrek Hastalığı ve HCV



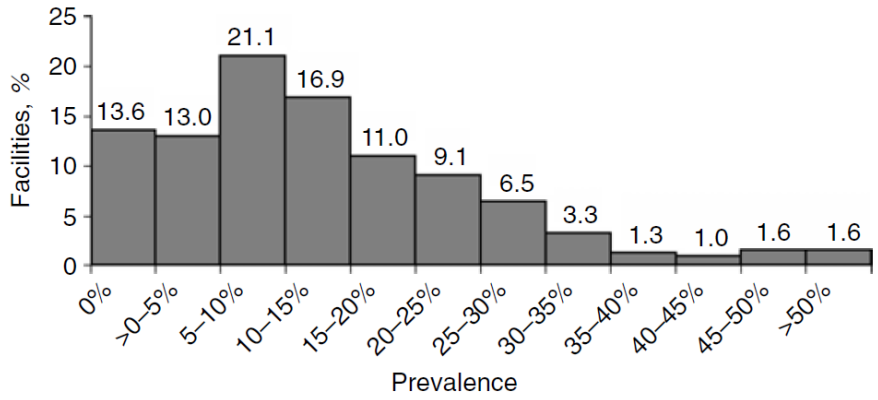
Joan Miró

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

Table 2. Prevalence and seroconversion rates, by country

Country	Unadjusted prevalence %	Adjusted prevalence[a] % (95% CI)	Unadjusted seroconversions/100 patient-years %	Adjusted seroconversions/100 patient-years[a] % (95% CI)
France	14.7	10.4 (9.7–11.2)	1.9	2.0 (1.4–2.8)
Germany	3.9	3.8 (3.3–4.4)	1.7	1.7 (1.2–2.5)
Italy	22.2	20.5 (19.4–21.7)	3.6	3.9 (2.9–5.2)
Japan	19.9	14.8 (14.0–15.6)	3.1	3.0 (2.3–3.9)
Spain	22.2	22.9 (21.7–24.1)	3.0	3.5 (2.5–4.8)
United Kingdom	2.7	2.6 (2.1–3.2)	1.1	1.2 (0.7–2.0)
United States	14.4	14.0 (13.6–14.5)	3.1	2.5 (2.1–2.9)

[a]Adjusted for the average of each of the following patient characteristics: age, gender, race, time on end-stage renal disease (ESRD), and alcohol or drug abuse in the past 12 months.



HCV prevalansı:
Ortalama %13.5
Ortanca: %10.5

HCV prevalansı %0-5 olan merkezler:
%26.6

Fissell R et al. Kidney International 2004;65:2335-42.

Table 1 | Prevalence of HCV infection in hemodialysis patients from various countries

Country	Prevalence of HCV (+)	Year(s) of testing	Reference
Brazil	17%	2002–2005	Santos and Souto[39]
Belgium	7%	2000	Jadoul *et al.*[38]
France	15%	1997–2001	Fissell *et al.*[40]
Germany	7%	1996–1997	Hinrichsen *et al.*[41]
India	12–42%	2001	Saha and Agarwal[42]
Iran	9%	2004	Shamshirsaz *et al.*[43]
Italy	22%	1997–2001	Fissell *et al.*[40]
Japan	20%	1997–2001	Fissell *et al.*[40]
New Zealand	5%	1992	Blackmore *et al.*[44]
Poland	42%	1992	Hruby *et al.*[45]
Saudi Arabia	68%	1994	Huraib *et al.*[46]
South Africa	21%	1994	Cassidy *et al.*[47]
Spain	22%	1997–2001	Fissell *et al.*[40]
Thailand	20%	1994	Luengrojanakul *et al.*[48]
The Netherlands	3%	1997	Schneeberger *et al.*[49]
Tunisia	20%	2001–2003	Hmaied *et al.*[50]
United States	14%	1997–2001	Fissell *et al.*[40]
United Kingdom	3%	1997–2001	Fissell *et al.*[40]

KDIGO Guidelines, 2008

TND: TÜRKİYE'DE NEFROLOJİ, DİYALİZ VE TRANSPLANTASYON KAYITLARI 1997

BAŞKENT ÜNİVERSİTESİ

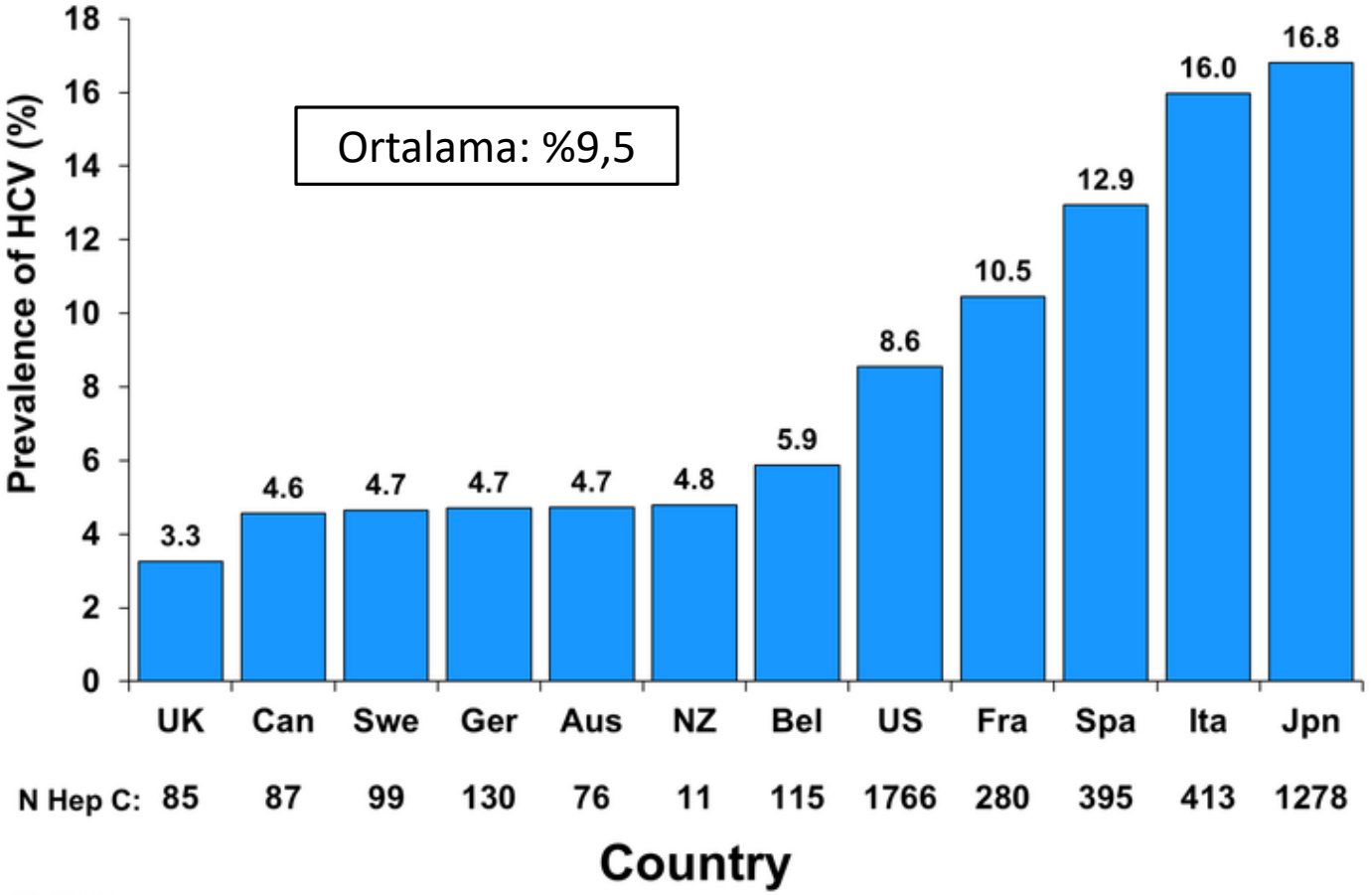
13. HEPATİT SEROLOJİSİ VE KARACİĞER HASTALIĞI

SEROLOJİ	N		
HBSAG (=/-):	563/75 15	TOPLAM: 7878	%7.1
HCV Ab (+/-):	3095/ 2093	TOPLAM: 5787	**%52.6**
İKİSİ POZİTİF	266		

Aynı dönemde Başkent Üniversitesi: %46

Figure 3

Prevalence of HCV Infection



DOPPS

Goodkin et al. *Am J Nephrol* 2013;38:405-412

TND: TÜRKİYE'DE NEFROLOJİ, DİYALİZ VE TRANSPLANTASYON KAYITLARI 2015

BAŞKENT ÜNİVERSİTESİ

	n	%
HBsAg (+)	3242	5.69
Anti-HCV (+)	3753	6.59
HBsAg (+), Anti-HCV (+)	649	1.14
HBsAg (-), Anti-HCV (-)	49307	86.58
Toplam / *Total*	56951	100.00

BÜ Ankara Diyaliz Merkezleri (2017): (12/456) %2,6

Kronik Böbrek Hastalığı ve HCV infeksiyonu

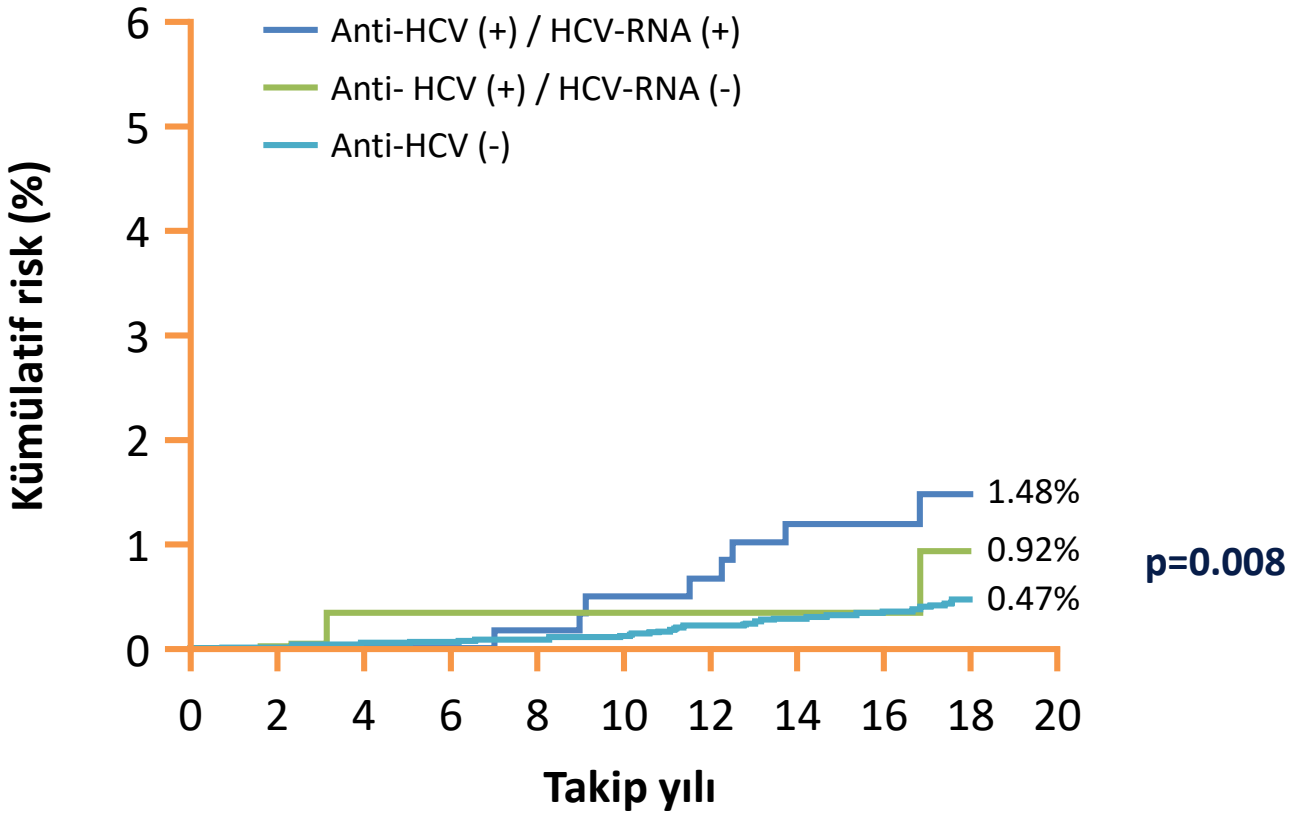
- Morbidite ve mortaliteyi artırıcı etkisi iyi bilinir.
- Kompanse KBH'nın son dönem böbrek hastalığına ilerlemesini hızlandırır.
- Böbrek transplantasyonlu hastalarda graft ve hasta sağ kalım sürelerini azaltır.
- Renal transplantasyon sonrasında de novo MPGN riski vardır.
- Renal transplant hastalarında HCC riskini artırır.

Fabrizi F et al. Am J Transplant 2005; 5:1402-61.
Fabrizi F et al. J Viral Hepat 2007; 14:697-703.
Hoffmann CJ et al. Transplantation 2008;86:784-90.
Fabrizi F et al. Dig Dis Sci 2015; 60:3801-13
Jadoul M, Martin P. Blood Purif 2017;43:206-9.

Chronic Hepatitis C Virus Infection Increases Mortality From Hepatic and Extrahepatic Diseases: A Community-Based Long-Term Prospective Study

BAŞKENT ÜNİVERSİTESİ

Çalışma başlangıcında Anti-HCV pozitifliği ve serum HCV RNA değerine göre kümülatif renal mortalite (nefrit, nefrotik sendrom ve nefrozis)



Lee MH, et al. J Inf Dis 2012:206:469–77.

Impact of hepatitis C on survival in dialysis patients: a link with cardiovascular mortality?

BAŞKENT ÜNİVERSİTESİ

Hemodiyaliz hastalarında HCV enfeksiyonunun etkisini değerlendiren gözlemsel çalışmaların meta-analizi

HCV (+) diyaliz hastalarında ölüm riski	Çalışma sayısı	Relatif risk (95% CI)
Tüm sebeplere bağlı ölüm	14	1.35 (1.25–1.47)
Karaciğere bağlı ölüm	4	3.82 (1.82–7.61)
Kardiyo-vasküler ölüm	3	1.26 (1.10–1.45)
Enfeksiyöz hastalığına bağlı ölüm	2	1.53 (1.11–2.12)

HCV enfekte hemodiyaliz hastalarında kardiyovasküler ve karaciğere bağlı ölümler en yaygın ölüm sebebidir

Fabrizi F, et al. Journal of Viral Hepatitis 2012; 19:601–607.

HCV (+) olan böbrek transplantasyonu adaylarının yönetimi: KDIGO önerileri (2017)

BAŞKENT ÜNİVERSİTESİ

- HCV (+) olan KBH'ları karaciğer fibrozisi açısından değerlendirilmelidir.
- Önce non-invazif karaciğer testleriyle değerlendirme önerilir.
- Kuşku varsa karaciğer biyopsisi düşünülmelidir.
- İleri fibrozisi olanlar KBH hastalarında portal hipertansiyon değerlendirmesi yapılmalıdır.

KDIGO 2017 CLINICAL PRACTICE GUIDELINE ON THE PREVENTION, DIAGNOSIS, EVALUATION AND TREATMENT OF HEPATITIS C IN CKD

Artificial Organs
21(5):355–358, Blackwell Science, Inc., Boston

Histopathological Impacts of Hepatitis Virus Infection in Hemodialysis Patients: Should Liver Biopsy Be Performed Before Renal Transplantation?

Mete Özdoğan, Orhan Özgür, Gürden Gür, Sedat Boyacioğlu, Yasemin Özderin, *Beyhan Demirhan, Hasan Telatar, and †Mehmet Haberal

*Department of Internal Medicine, Division of Gastroenterology; *Department of Pathology; and †Department of General Surgery, Baskent University, School of Medicine, Ankara, Turkey*

Abstract: To evaluate the histologic changes in the livers of renal transplant candidates who were infected with hepatitis viruses, we performed a percutaneous liver biopsy in each of 74 regular hemodialysis patients. Forty percent of them were seropositive for the antibody to hepatitis C virus (anti-HCV) whereas 29.7% had anti-HCV and antibody to hepatitis B surface antigen (anti-HBs) concomitantly. Seven (9.5%) were seropositive for only hepatitis B surface antigen HBsAg. Histopathological examination revealed that 30% of patients had chronic active hepatitis (CAH), 11% had chronic persistent hepatitis (CPH), and 3% displayed histopathological evidence of cirrhosis. Eleven of 22 patients with CAH were positive for only anti-HCV, and 2 of 22 were positive for only HBsAg. One patient had HBsAg and anti-HCV together, and 8 of 22 had anti-HBs and anti-HCV concomitantly. None of the anti-HBs positive patients exhibited abnormal histopathological changes. We found no statistically significant difference in histopathological findings between the HBsAg positive and anti-HCV positive patients. As 32 of 74 patients (43%) had some degree of chronic liver disease, we concluded that it is prudent to evaluate liver histology in HBsAg and anti-HCV seropositive renal transplant candidates before transplantation. **Key Words:** Liver disease—Renal transplantation—Hepatitis viruses.

Regular hemodialysis patients encounter hepatitis viruses more often than the normal population, and liver diseases caused by these viruses increase the morbidity and mortality rates in this group of patients (1,2). During the past 13 years, the incidence of hepatitis B virus (HBV) infection decreased from 3.0% to 0.2% among hemodialysis patients in the United States (1). This is attributed to serological screenings, vaccination programs, and meticulous infection control attempts (3). Although the prevalence of HBV infection is declining, it is not possible to claim the same thing for hepatitis C virus (HCV) infection (4,5). The course of liver disease is negatively affected by immunosuppressive therapy used after renal transplantation. In a study, histological worsening of liver disease was documented during the posttransplant period in 80% of HBsAg positive patients initially biopsied at the time of transplantation (6). Hepatitis virus infections seem to alter the mortality and morbidity of transplanted patients (7,8). Because interferon (IFN) therapy may cause irreversible renal allograft dysfunction (9), it is not recommended for patients with special risks, e.g., patients in a posttransplant situation or patients undergoing immunosuppressive therapy (10). Thus, problems must be solved before transplantation using IFN, which seems to be the only effective mode of therapy for chronic liver disease resulting from hepatitis virus infection.

In this study, we performed percutaneous liver biopsy (PLB) in regular hemodialysis patients (as candidates for renal transplantation) with hepatitis virus infection, and our goal was to investigate histopathologic changes in the liver.

Received November 1995; revised July 1996.
Address correspondence and reprint requests to Dr. Mete Özdoğan, Department of Internal Medicine, Division of Gastroenterology, Başkent University, School of Medicine, Fevzi Çakmak Cad. 10.Sok No:45, Bahçelievler, 06490 Ankara, Turkey.

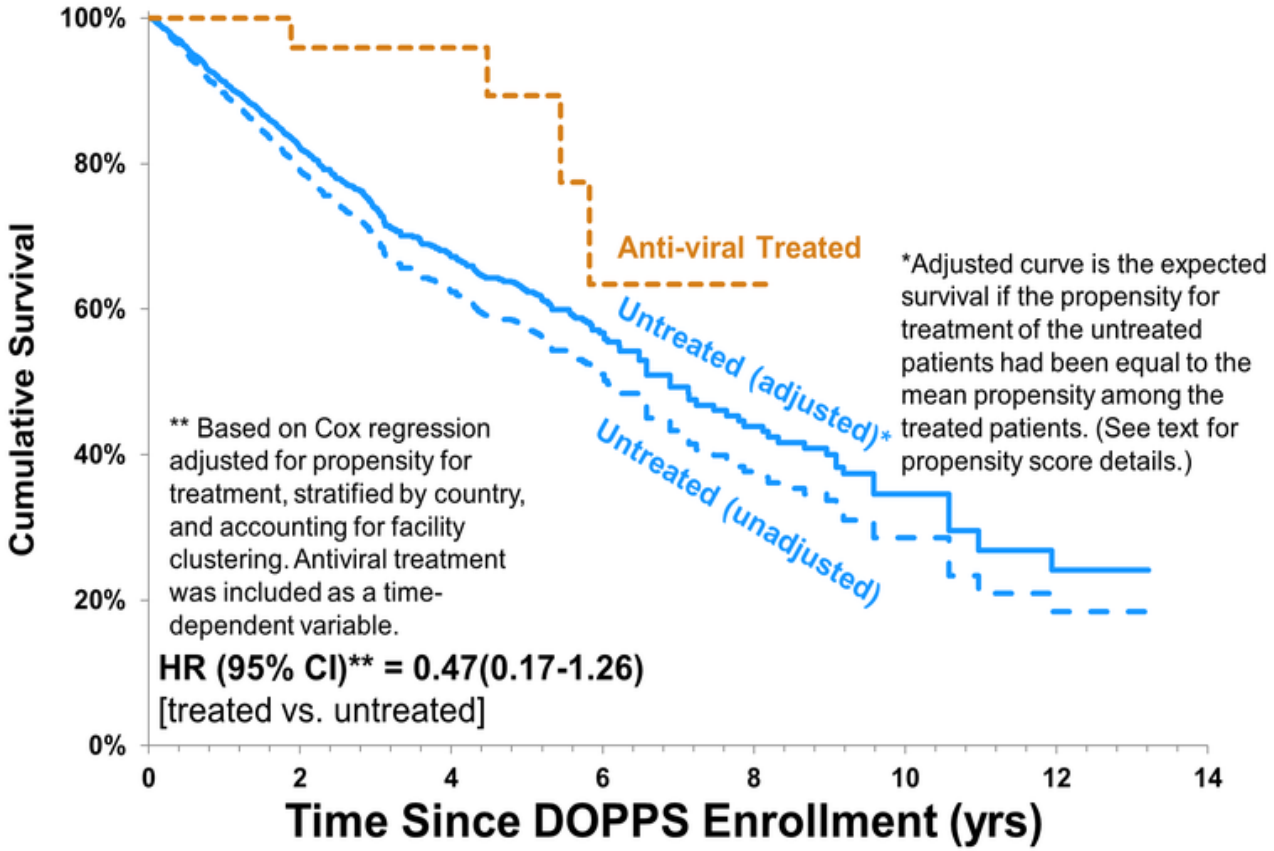
MATERIALS AND METHODS

Seventy-four maintenance hemodialysis patients who were candidates for renal transplantation were

DOPPS: Dialysis Outcomes and Practice Patterns Study

Figure 4

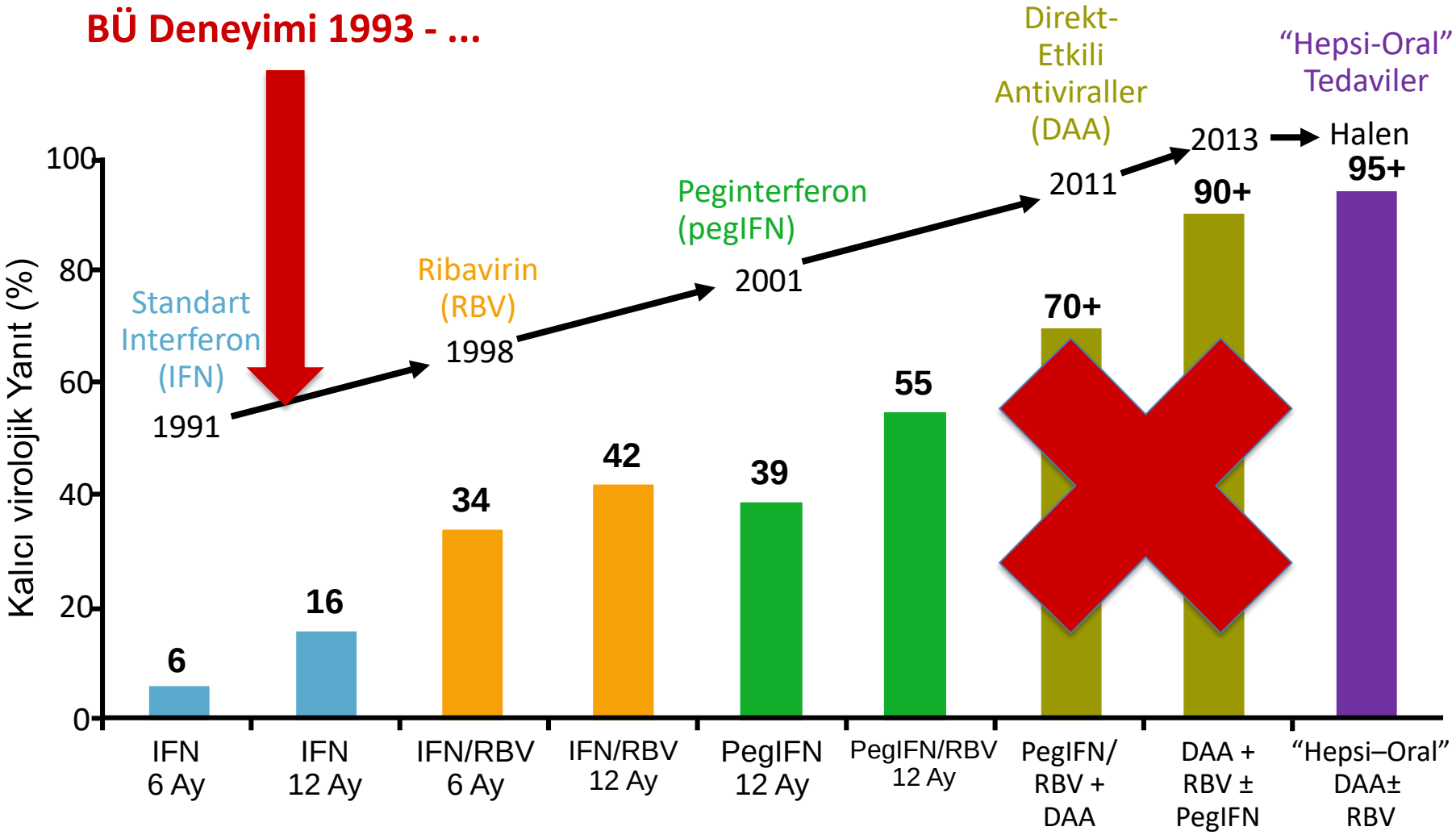
Survival of HCV+ Patients, by Treatment



DOPPS

Goodkin et al. *Am J Nephrol* 2013;38:405-412

HCV Tedavilerinin dünü ve bugünü



Kronik Böbrek Hastalığı ve HCV

- Geçmişte tek seçenek IFN'lar ± RBV idi.
- Bu tedavilerle
  - Valıcı viral yanıt: <%40
  - İntolerans %25

Russo GW, et al. Am J Gastroenterol 2003
Fabrizi F., et al. J Viral Hepat 2008
Fabrizi F. et al., *J MedVirol 2010*
Li CH et al. Gut 2008
Perico N. et al. Clin J Am Soc Nephrol 2009
Bruchfeld A. Et al., Ther Drug Monit 2002

Son yıllarda kullanılmaya başlanan oral DAA'lar diğer hasta gruplarında olduğu gibi kronik böbrek hastaları grubunda da çok etkilidir

DAA'lar ile öncü çalışmalar

- Çeşitli kombinasyonlarla ile yapılan çalışmalarda hemen her kombinasyonun etkin olduğu gösterilmişlerdir.
- Tolere edilebilir ve güvenli bulunmuşlardır.
- Ribavirin kullanıldığında daha yakın monitorizasyon gereklidir.
- Kalsinörin inhibitörleri başta olmak üzere immünsüpresif ilaç etkileşimlerine dikkat etmek gerekir.

Kamar N et al. Am j Transplat 2015; 16: 1474-9.
Lin Mg et al. PLoS ONE 11(7):e0158431-2016, DOI:10.1371/journal.pone.0158431.
Pockros PJ et al. Gastroenterology 2016;150:1590-8.
Sawinski D et al. Am J Transplant 2016;16:1588-95.
Beinhardt S et al. Transplant International 2016; 29: 999-1007.
Gentil MA et al. Transplant Proc 2016; 48:2944-6.
Fernandez I et al. J Hepatol 2017; 66:718-23.
Colombo M et al. Ann Int Med 2017;166(2):109-117.
Saxena V et al. Hepatology 2017; 66:1090-1101.

Kronik Böbrek Hastalığı ve HCV (HCV TARGET)

- Sofosbuvir temelli tedaviler eGFR <45 mL/dak olan kronik böbrek hastalarında kalıcı viral yanıt %80-85 olmuştur.
- Ancak:
  - Böbrek fonksiyonlarında kötüleşme
  - Anemide artış
  - Daha fazla yan etkiler
- Araştırmanın yazarları sofosbuvir içeren tedavilerde yakın hasta monitorizasyonu önermişlerdir.

Saxena V et al. Liver Int 2016;36:807-816.

TABLE 1. DAA AGENTS: DOSE, CLEARANCE, AND USE IN CKD AND ESRD PATIENTS

Medication	Clearance	Use in CKD Stages IV and V	Use in ESRD
Sofosbuvir	Renal: 81% GI: 15%	eGFR 15-29 mL/min: not recommended eGFR < 15 mL/min: not recommended	Limited data available;higher rates of anemia, worsening renal dysfunction, and increased adverse events[13]
Simeprevir	Renal: <1%	eGFR 15-29 mL/min: dose adjustment not required eGFR < 15 mL/min: not recommended	Limited data available
Daclatasvir	Renal: 7% GI: 88%	eGFR 15-29 mL/min: dose adjustment not required eGFR < 15 mL/min: dose adjustment not required	Limited data available; patient on dialysis; no serious adverse events[14]
Ledipasvir	Renal: 1% GI: 86%	eGFR 15-29 mL/min: dose adjustment not required eGFR < 15 mL/min: not recommended	Limited data available
Ombitasvir/Paritaprevir/ Ritonavir	Renal: <2% GI: 90%	eGFR 15-29 mL/min: dose adjustment not required eGFR < 15 mL/min: dose adjustment not required	Dialysis patients studied;safely used in patients with advanced CKD[15]
Dasabuvir			
Grazoprevir/Elbasvir	Renal: <1%	eGFR 15-29 mL/min: dose adjustment not required eGFR < 15 mL/min: dose adjustment not required	Dialysis population studied;minimal adverse events in patients with advanced CKD and ESRD on hemodialysis[16]
Sofosbuvir/Velpatasvir	Renal: 81% GI/Renal: 15%/0.4% GI: 94%	eGFR 15-29 mL/min: not recommended eGFR < 15 mL/min: not recommended	Limited data available; no dosage recommendation for patients with severe renal impairment[17]

Pedraza FE et al. Clin Liv Dis 2017; 9(3): 55-9.

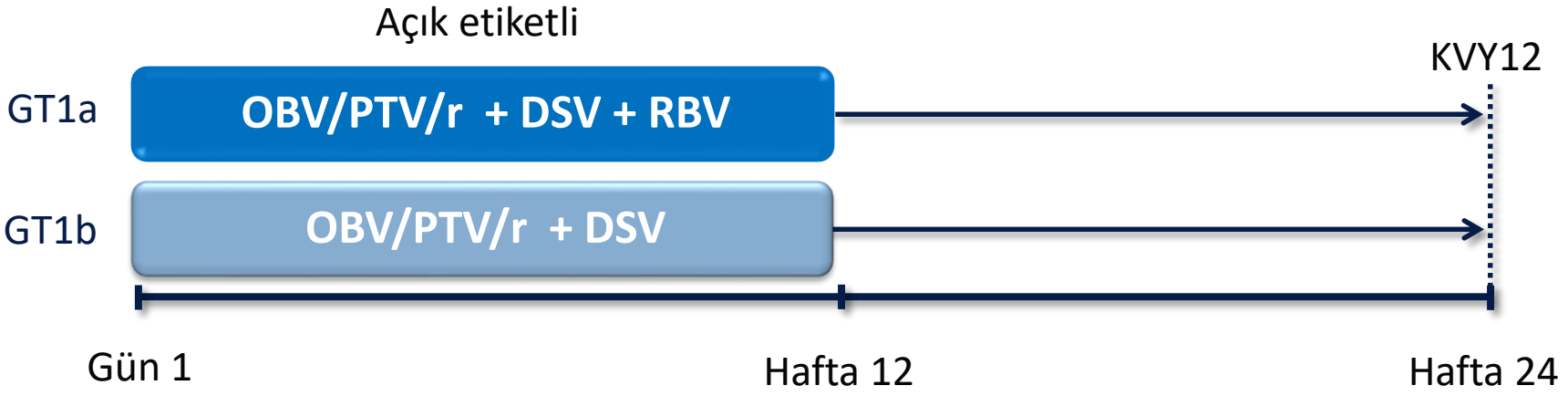
TABLE 2. INTERACTIONS OF DAAS WITH IMMUNOSUPPRESSIVE AGENTS

Medication	SOF/LDV	SOF	SMV	OMV/PTV/r/DSV	EBR/GZR
TAC	No changes in TAC levels	No changes in TAC levels	Decrease TAC levels Needs close monitoring of TAC levels	Increase TAC levels (ritonavir)	Increase TAC levels
CyA	No changes in CyA levels	No changes in CyA levels	Increase levels of both CyA and SMV	Increase CyA levels (ritonavir)	Increased levels of GZR, contraindicated to use together
SRL	No changes in SRL levels	No changes in SRL levels	Increase or decrease levels of SRL	Increase SRL levels (ritonavir)	Increase SRL levels

Abbreviations: CyA, cyclosporine; EBR/GZR, elbasvir/grazoprevir; LDV, ledipasvir; OMV/PTV/r/DSV, ombitasvir/paritaprevir/ritonavir/dasabuvir; SMV, simeprevir; SOF, sofosbuvir; SRL, sirolimus; TAC, tacrolimus.

Pedraza FE et al. Clin Liv Dis 2017; 9(3): 55-9.

RUBY-I: Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir +/- Ribavirin in Non-cirrhotic HCV Genotype 1 -infected Patients With Severe Renal Impairment or End-Stage Renal Disease

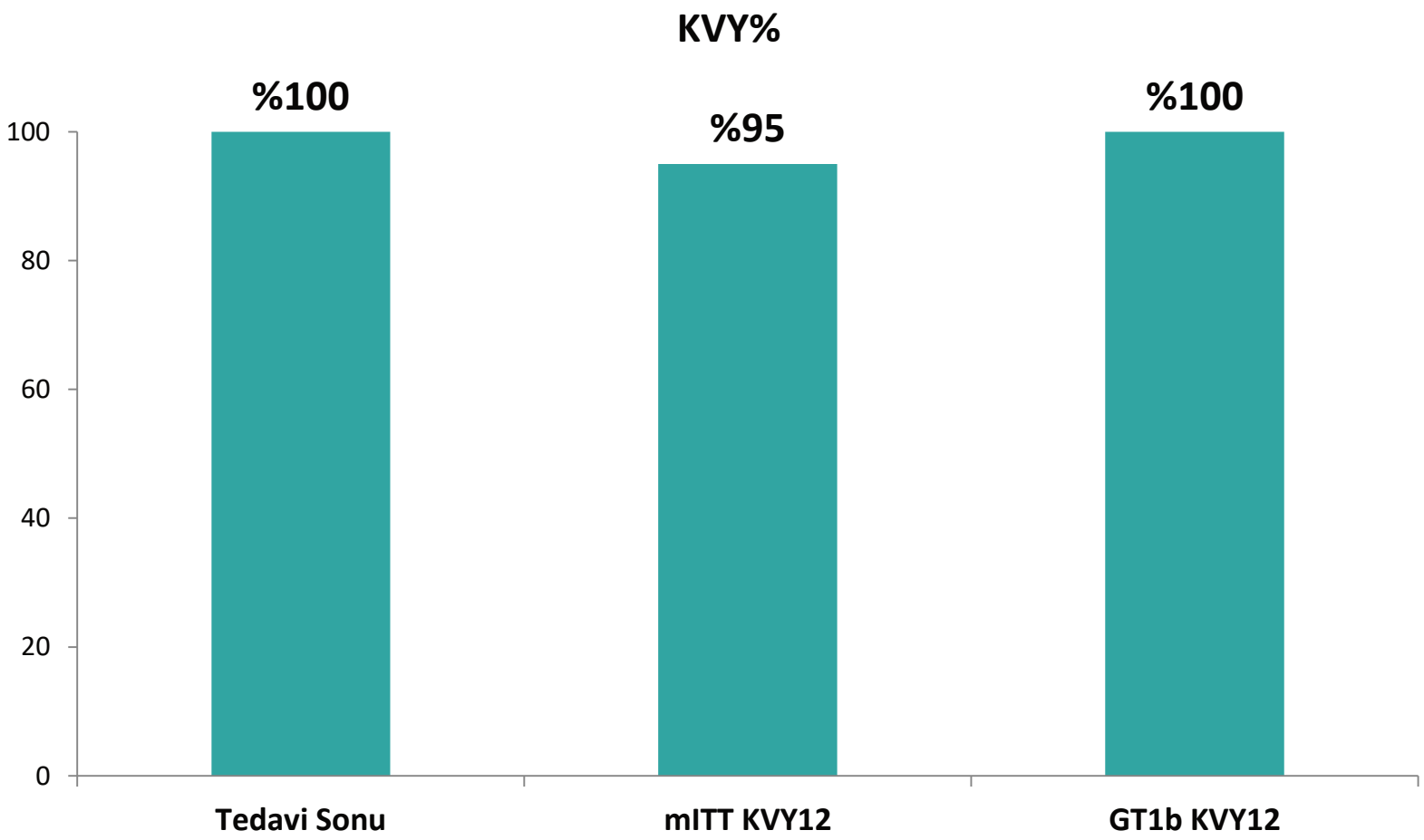


Başlangıç renal parametreler	N=20
KBY evresi; n (%)	
4 (eGFR 15–30 mL/dk/1.73m^2)	6 (30)
5 (eGFR <15 mL/dk/1.73m^2 veya diyaliz)	14 (70)
eGFR, mL/dk/1.73m^2; median (range)	10.9 (5.4–29.9)
Kreatinin, mg/dL; median (range)	6.2 (2.2–10.8)

* RBV = 200 mg QD.

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

RUBY-I: Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir +/- Ribavirin in Non-cirrhotic HCV Genotype 1 -infected Patients With Severe Renal Impairment or End-Stage Renal Disease



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

RUBY-I: Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir +/- Ribavirin in Non-cirrhotic HCV Genotype 1 -infected Patients With Severe Renal Impairment or End-Stage Renal Disease

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	GT1b OBV/PTV/r + DSV (N=7)	GT1a OBV/PTV/r + DSV + RBV (N=13)
Advers Olay, n (%)		
Anemi	0	9 (69)
Halsizlik	2 (29)	5 (58)
Diyare	1 (14)	4 (31)
Bulantı	0	5 (38)
Baş ağrısı	0	3 (23)
Periferal ödem	2 (29)	1 (8)

- AO'lar genel olarak hafif ya da orta derecede bulundu.
- Hiçbir hasta AO nedeniyle çalışmayı bırakmadı.
- Dört hastadan dokuzunda, biri ölüm, ciddi AO bildirildi. Bunların hiç biri ilaçlara veya RBV'ne bağlı bulunmadı.
- Dört hasta anemi için eritropoetin ihtiyacı duydu; hiç birine kan transfüsyonu yapılmadı.
- Karaciğer ve böbrek fonksiyonlarında klinik olarak anlamlı değişiklik yaşanmadı.

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

Efficacy of Direct-Acting Antiviral Combination for Patients With Hepatitis C Virus Genotype 1 Infection and Severe Renal Impairment or End-Stage Renal Disease

BAŞKENT ÜNİVERSİTESİ

Ombitasvir/Paritaprevir/Ritonavir

+

Dasabuvir

±

Ribavirin

tedavisi ile HCV virus genotip 1 enfeksiyonu olan son dönem böbrek hastarında %90 kalıcı viral yanıt sağlanmıştır (KVY12: GT1a %85 ve GT1b %100).

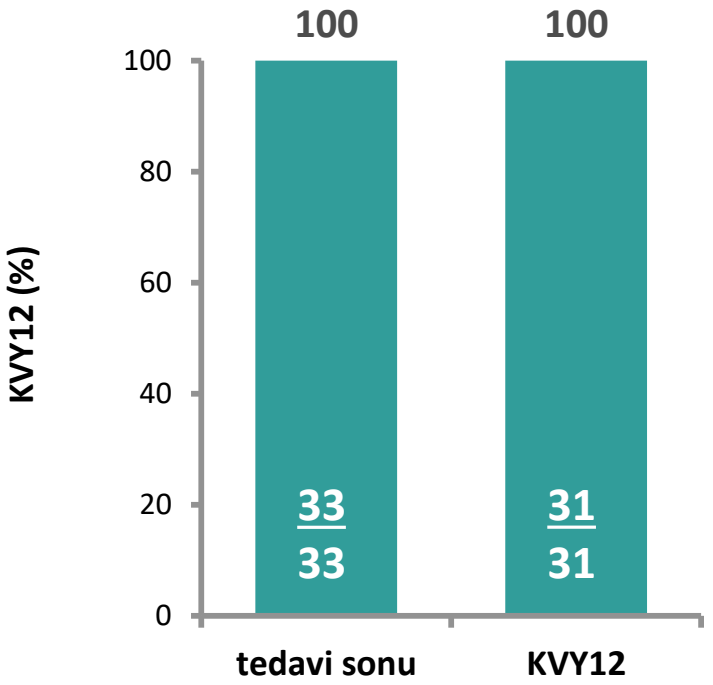
Pockros PJ et al. Gastroenterology 2016;150:1590-1598.

İspanya, Madrid Gerçek Yaşam Verileri: Non-sirotik veya kompanse sirotik KBY hastalarında V/E etkililiği

BAŞKENT ÜNİVERSİTESİ

- Bu çalışmada RUBY I'den farklı olarak, **kompanse sirotik** ve **tedavi deneyimli** hastalar da bulunmaktadır.
- Tedavi sonrası 12. haftaya ulaşan **tüm hastalarda kür elde etmiştir.**

n (%)	OBV/PTV/r + DSV ± RBV* (N=33)
Erkek, n (%)	23 (69)
Ortalama yaş (aralık)	57 (39–78)
HCV genotip, n (%)	
GT1a	6 (18)
GT1b	23 (70)
GT4	3 (9)
Mixed(1b ve 4)	1(3)
Child-Pugh A	13 (39)
Böbrek yetmezliği	
Evre 4 (CrCL 15–29 mL/dk)	7 (11)
Evre 5 (CrCl <15 ml/DK) veya diyaliz	26 (79)
Tedavi deneyimli (peg INF/RBV)	8 (25)

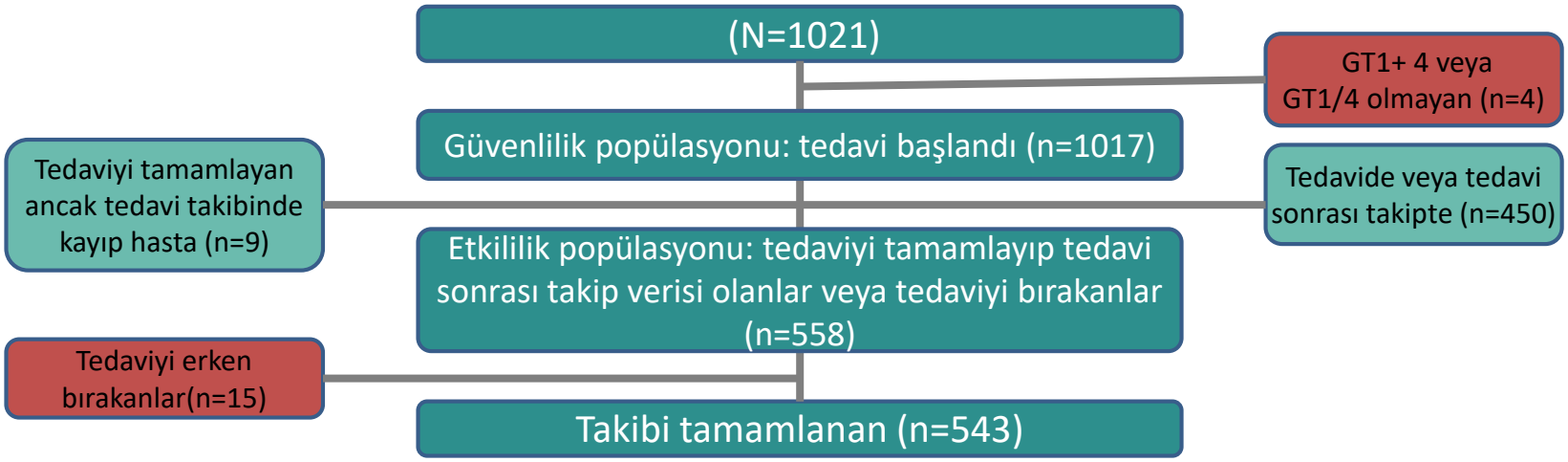


GT1a=F4 =OBV/PTV/r + DSV + RBV * 24 hafta
GT1a=F1-3=OBV/PTV/r + DSV + RBV * 12 hafta
GT1b=OBV/PTV/r + DSV 12 hafta
GT4=F1-3=OBV/PTV/r + RBV * 12 hafta
GT4=F4=OBV/PTV/r + RBV *

* 200 mg/gün

Muñoz Gomez R, *et al. EASL 2016*. P#105.

Almanya Gerçek Yaşam Verileri (254 Merkez)



	OBV/PTV/r + DSV + RBV (n=1017)
Erkek, n(%)	660 (65)
Yaş yıl, ortalama	54.3 ± 12.5
HCV Genotip, n(%)	
GT1	892 (88)
1a	261(26)
1b	614 (60)
diğer	17(2)
GT4	125(12)
Siroz, n/N(%)	228/1017(22)
Kompanse siroz (CP-A)	149/228(65)
Dekompanse (CP-A/C)	16/228
Veri mevcut değil	63/228

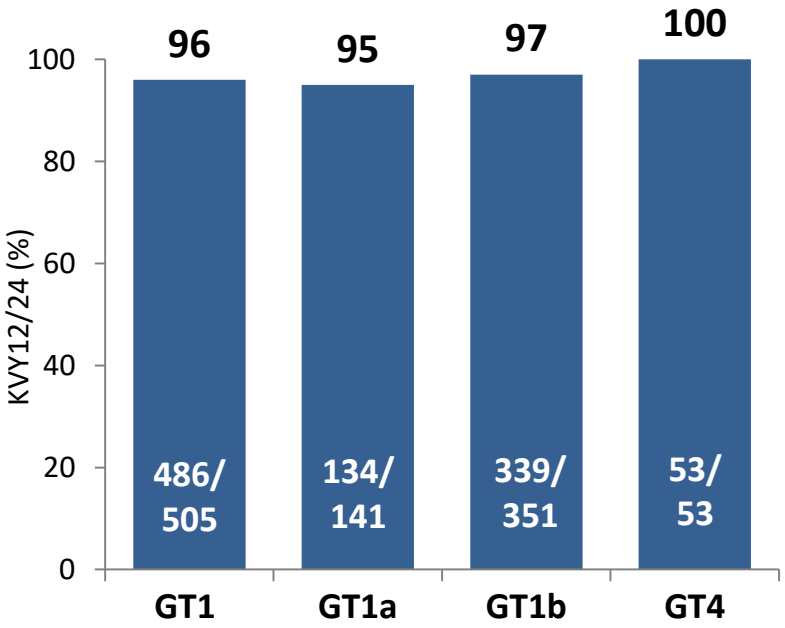
Hinrichsen H, et al. EASL 2016, GS07

Almanya Gerçek Yaşam Verileri – Genotip ve Renal Yetmezliğe Göre Kalıcı Virolojik Yanıt

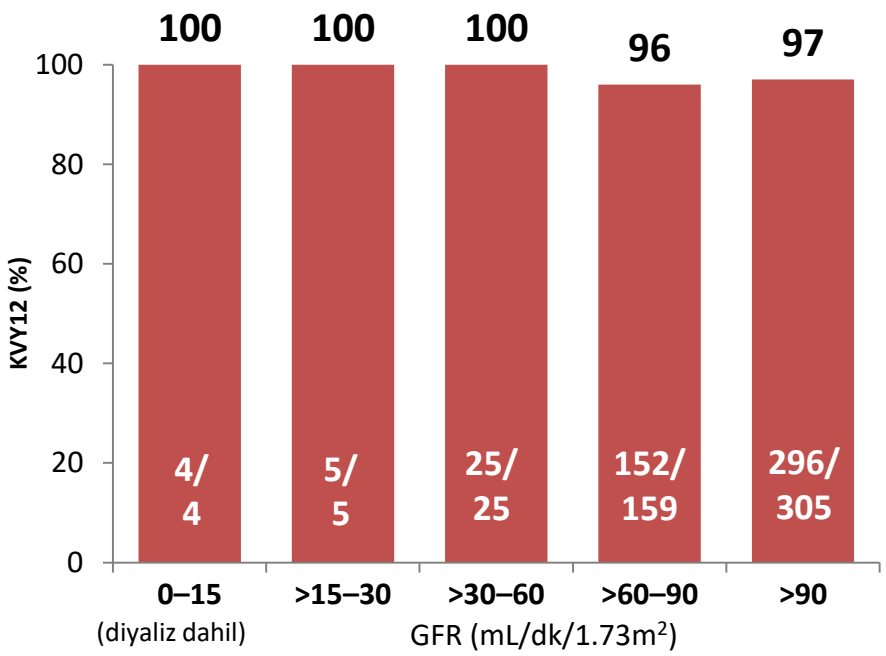
BAŞKENT ÜNİVERSİTESİ

- Çalışmaya dahil olan tüm genotip ve alt genotiplerde **yüksek KVY_{12} oranları** gözlemlenmiştir.
- **GFR<60 mL/dk** olan hastalarda **%100 KVY_{12}** elde edilmiştir.

Genotipe göre etkililik



Etkililik ve renal yetmezlik



Hinrichsen H, et al. EASL 2016, GS07

KBY'li Hastalarda DAA'le HCV Enfeksiyonu tedavisi: Başkent Üniversitesi Gerçek Yaşam Verileri

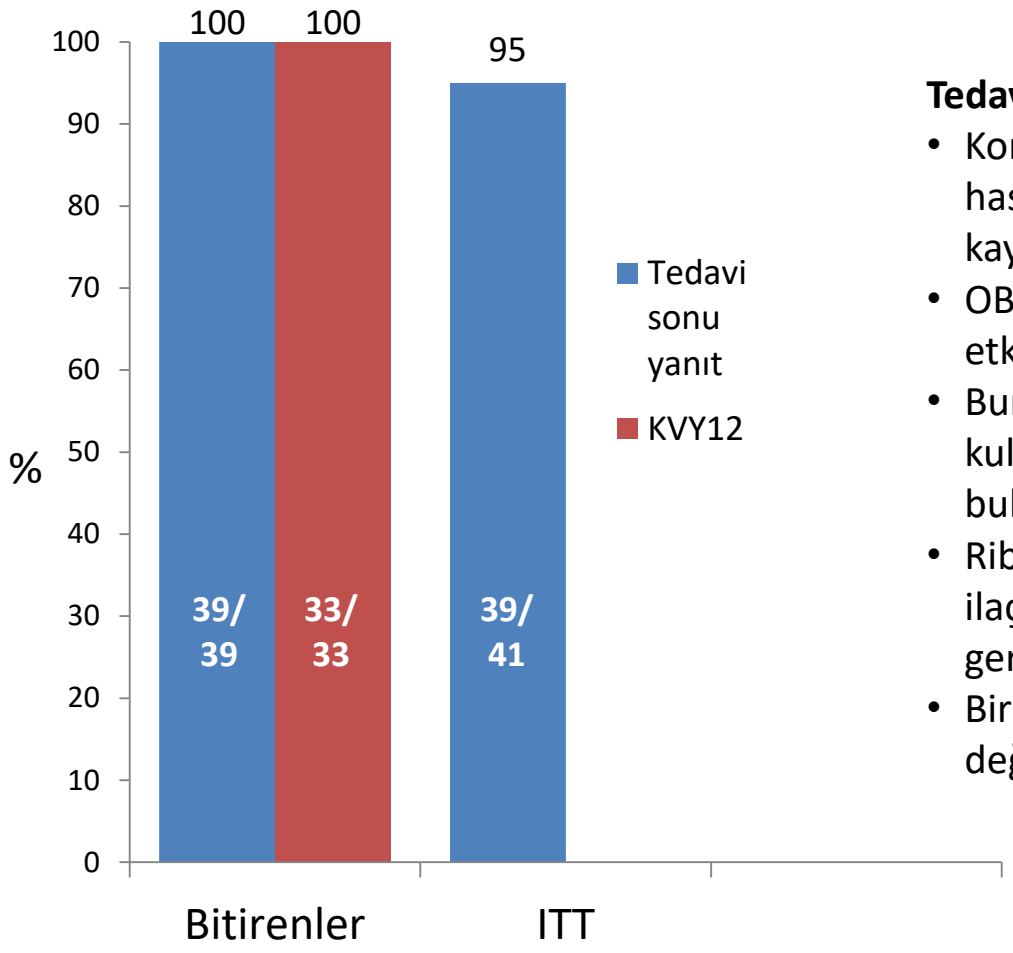
BAŞKENT ÜNİVERSİTESİ

Hasta sayısı **Toplam** **Tedaviyi bitiren** **Tedavi sonrası 12. hft**	 **41** 40 33
Yaş	55,5 (33-71)
Cinsiyet (E/K)	30/11
Nonsirotik/Sirotik	41/1 (Child A)
Tedavi deneyimli	15
Genotip **GT1a** **GT1b**	 11 30
Ortalama viral yük	1,7 x 10^7 IU/mL
Tedavi **GT1a** **GT1b**	 OBV/PTV/r + DSV + RBV x 12 hft OBV/PTV/r x DSV 12 hft

KBY'li Hastalarda DAA'le HCV Enfeksiyonu tedavisi: Başkent Üniversitesi Gerçek Yaşam Verileri

Başkent Üniversitesi Merkezleri	n
Ankara	17
Adana	11
Konya	5
İstanbul	8
TOPLAM	**41**

KBY'li Hastalarda DAA'le HCV Enfeksiyonu tedavisi: Başkent Üniversitesi Gerçek Yaşam Verileri



Tedaviyi Bırakma, Tolerans ve Yan Etki:

- Koroner *"bypass"* operasyon öyküsü olan bir hasta tedavinin 35. günü kardiyak nedenle kaybedildi [tedavinin 1. ayında HCV-RNA (-)].
- OBV/PTV/r + DSV + RBV alan bir hasta yan etkiler nedeniyle tedaviyi bıraktı.
- Bunların dışında en sık görülen yan etki ilaç kullanımını değiştirmeyi gerektirmeyen halsizlik, bulantı ve baş ağrısı idi.
- Ribavirin kullanan 3 hastada, anemi nedeniyle ilaç doz redüksiyonu ve kan ürünü transfüzyonu gerekti.
- Bir hastada tedavi süreci içinde SVO gelişti. İlaç değişikliği yapılmadı.

AASLD/EASL tedavi önerileri: Kompanse KBH

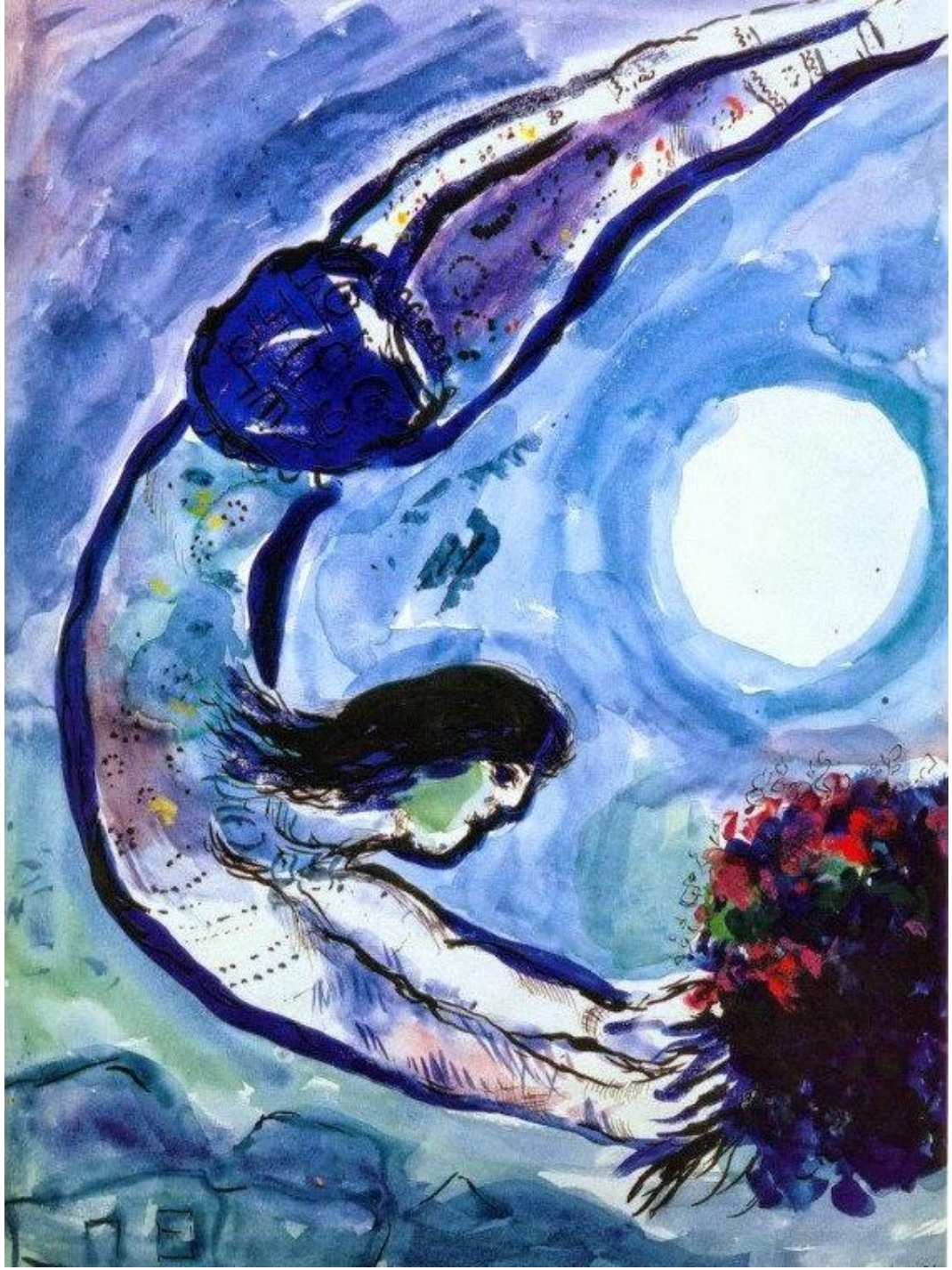
- Ruhsatlı herhangi bir DAA-temeli bir rejim
- Genel önerilere uyulacak
- Böbrek fonksiyonları yönünden yakın monitorizasyon

AASLD Recommendations for Testing, Managing, and Treating Hepatitis C, http://www.hcvguidelines.org/unique-populations/renal-impairment (21 Eylül 2017)
EASL Recommendations on Treatment of Hepatitis C 2016. J Hepatol (2016), http://dx.doi.org/10.1016/j.jhep.2016.09.001

AASLD/EASL tedavi önerileri: Dekompanse KBH

- **GT1a:**
  - **Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir + Ribavirin x 12 hafta**
  - Gazoprevir/Elbasvir ± Ribavirin x 12 hafta
  - Glecaprevir/Pibrentasvir x 8-16 hafta
- **GT1b:**
  - **Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir x 12 hafta**
  - Gazoprevir/Elbasvir x 12 hafta
  - Glecaprevir/Pibrentasvir x 8-16 hafta
- **GT4**
  - **Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir + Ribavirin x 12 hafta**
  - Gazoprevir/Elbasvir ± Ribavirin (12 Hafta)
  - Glecaprevir/Pibrentasvir x 8-16 hafta
- **GT2 , 3 , 5 , 6 (AASLD):**
  - Glecaprevir/Pibrentasvir (8-16 Hafta)
- **GT2 (EASL):**
  - Sofosbuvir and velpatasvir
  - Sofosbuvir and daclatasvir

AASLD Recommendations for Testing, Managing, and Treating Hepatitis C, http://www.hcvguidelines.org/unique-populations/renal-impairment (21 Eylül 2017)
EASL Recommendations on Treatment of Hepatitis C 2016. J Hepatol (2016), http://dx.doi.org/10.1016/j.jhep.2016.09.001

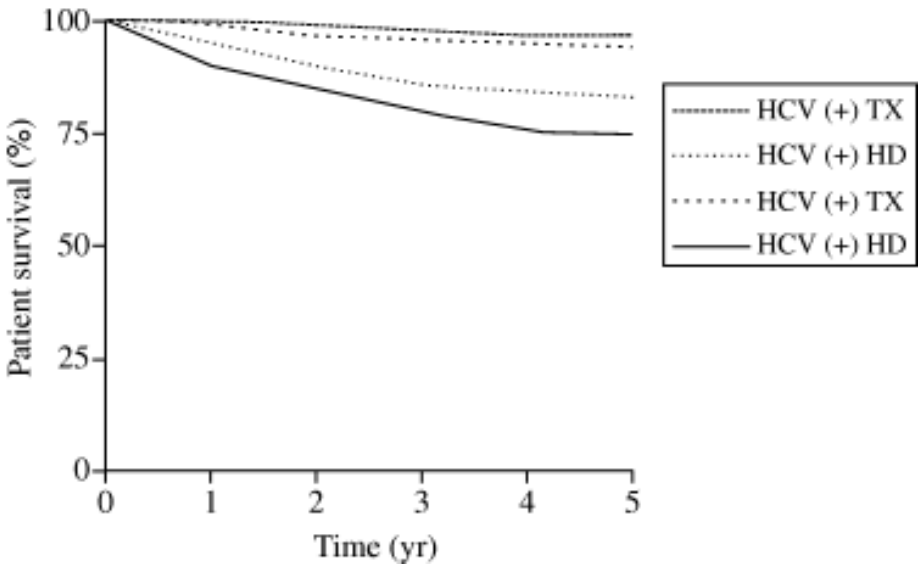


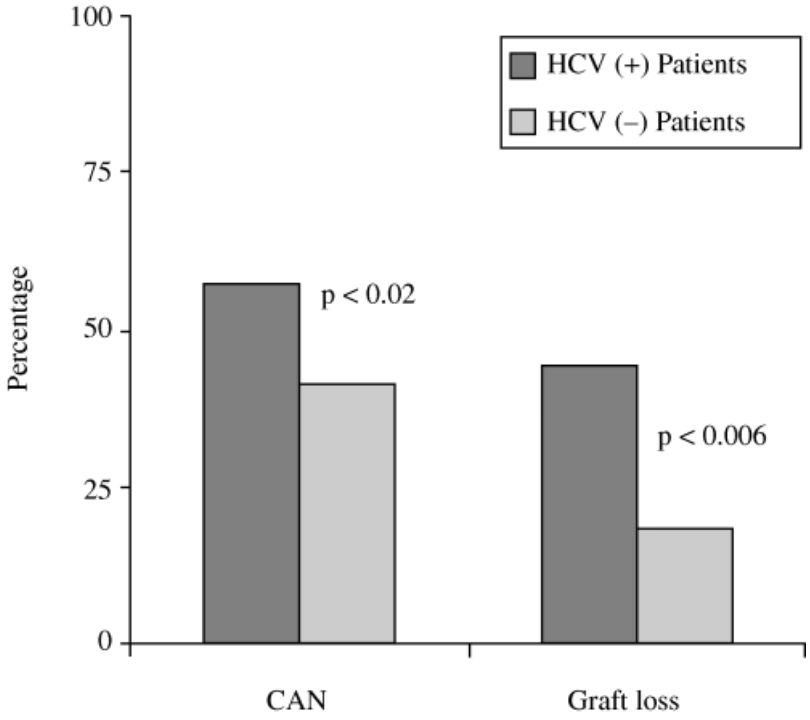
BAŞKENT ÜNİVERSİTESİ

Renal Transplatasyon ve HCV

Marc Chagall

Renal transplantation offers a better survival in HCV-infected ESRD patients





Sezer S et al. Clin Transplant 2004: 18: 619–623.
DOI: 10.1111/j.1399-0012.2004.00252.x

Impact of hepatitis B and C virus on kidney transplantation outcome

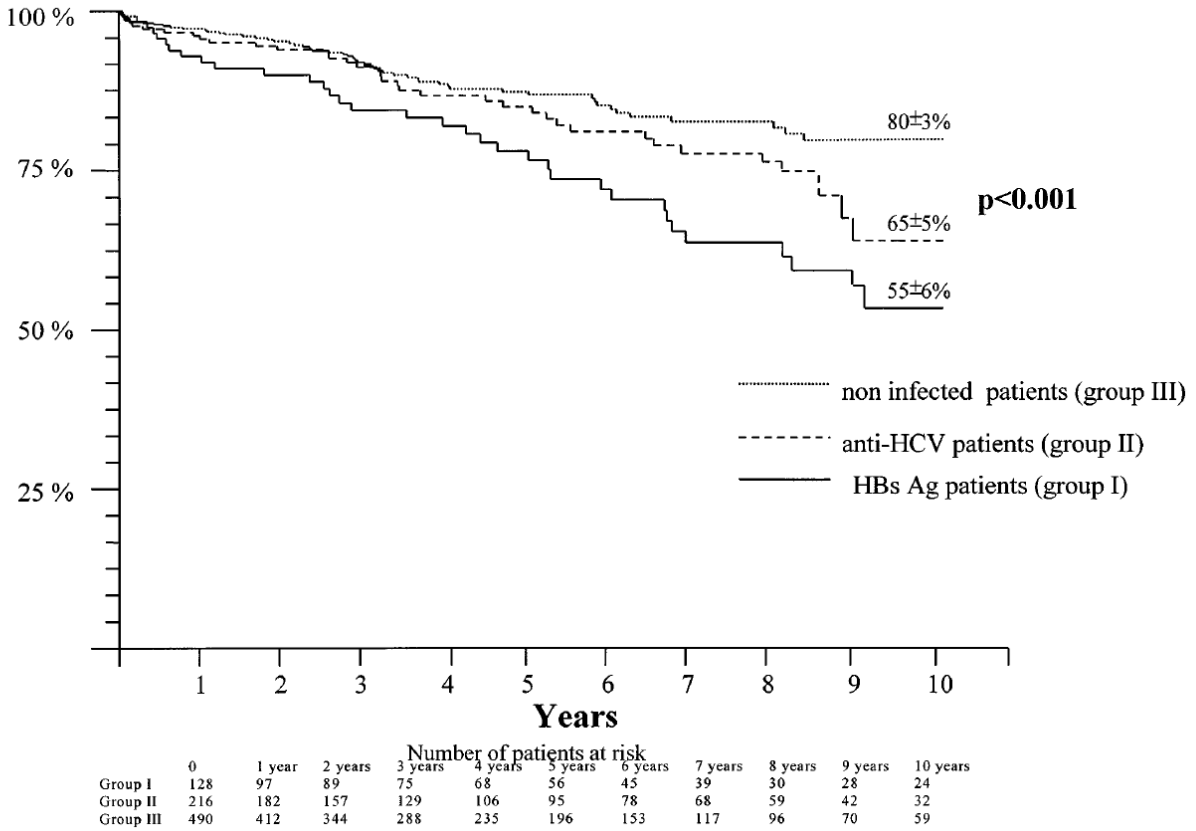


FIG. 1. Patient survivals at 10 years in HBsAg-positive patients, in anti-HCV–positive patients, and in noninfected patients.

Mathurin P. Hepatology 1999 Jan;29(1):257-63.

Impact of hepatitis B and C virus on kidney transplantation outcome

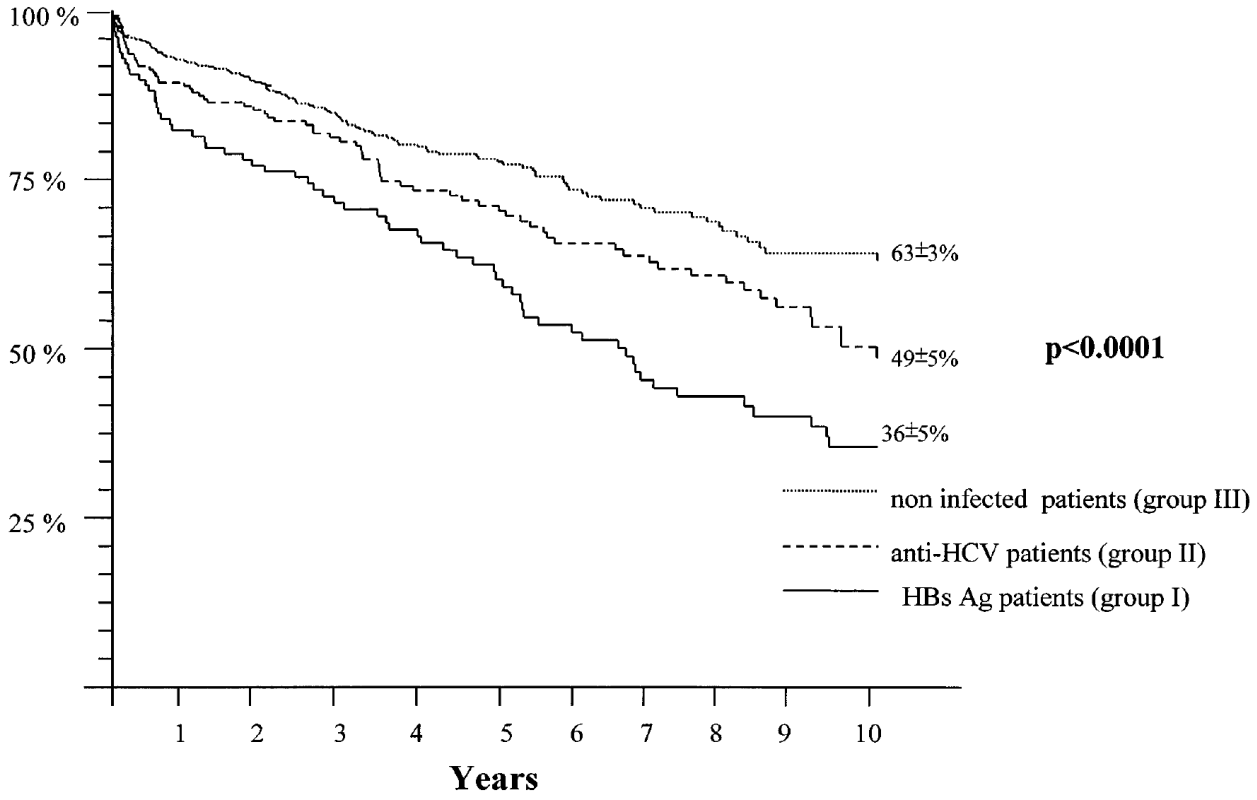


FIG. 2. Graft survivals at 10 years in HBsAg-positive patients, in anti-HCV–positive patients, and in non-infected patients.

Mathurin P. Hepatology 1999 Jan;29(1):257-63.

Nephrol Dial Transplant (1995) 10: 2104–2106

Nephrology
Dialysis
Transplantation

Original Article

Recombinant α-interferon in renal allograft recipients with chronic hepatitis C

O. Özgür, S. Boyacioğlu, H. Telatar and M. Haberal

Başkent University Hospital, Turkey

Abstract

Background. Although chronic hepatitis C infection is one of the factors that can lead to morbidity and mortality in renal allograft recipients, treatment procedures have not been well documented. Interferon treatment has been shown to be effective in the normalization of biochemical hepatitis C and in the clearing of hepatitis C virus RNA. However, little is known concerning the efficacy and safety of interferon treatment in renal allograft recipients with chronic hepatitis C. Interferon has also been accused of increasing renal allograft rejection.

Methods. Recombinant α-interferon in a dose of 4.5 million units three times per week was given to five renal-allograft recipients with chronic hepatitis C for 6 months. Besides biochemical investigations, liver histopathologies before and after the treatment course were also studied.

Results. Interferon treatment was effective in two of the patients, in another two cases renal function deteriorated during the treatment. In the last case ALT increased again after cessation of interferon therapy.

Conclusion. We conclude that interferon seems to be moderately effective in treating chronic hepatitis C in renal allograft recipients, but a risk of renal functional deterioration and rejection remains.

acquire HCV infection may develop chronic hepatitis and in nearly 20% of them progression to cirrhosis may be seen [4]. In immunosuppressed patients, persistent HCV infection may progress to chronic active hepatitis, to cirrhosis, or even to hepatocellular carcinoma [1–3].

Recently interferon therapy has been shown to be effective in the normalization of serum transaminase level with some amelioration of the histological activity of chronic hepatitis caused by HCV infection. Interferon was reported to be the most potent agent to stop HCV replication in many patients [5,6]. There is little information on the efficacy and safety of interferon treatment in renal transplant recipients with chronic hepatitis C. Interferon has been reported to induce steroid-resistant renal allograft rejection when used for the prevention of CMV infection shortly after renal transplantation [7]. Only a few studies report on the use of interferon treatment in renal allograft recipients with chronic hepatitis C, and the results seem to be poor [2,8,9].

We present here our results with recombinant interferon α (r-IFN-α) treatment in five renal allograft recipients with chronic hepatitis C.

Renal transplant hastalarında HCV tedavisi
Başkent Üniversitesi Ankara Hastanesi Deneyimi

BAŞKENT ÜNİVERSİTESİ

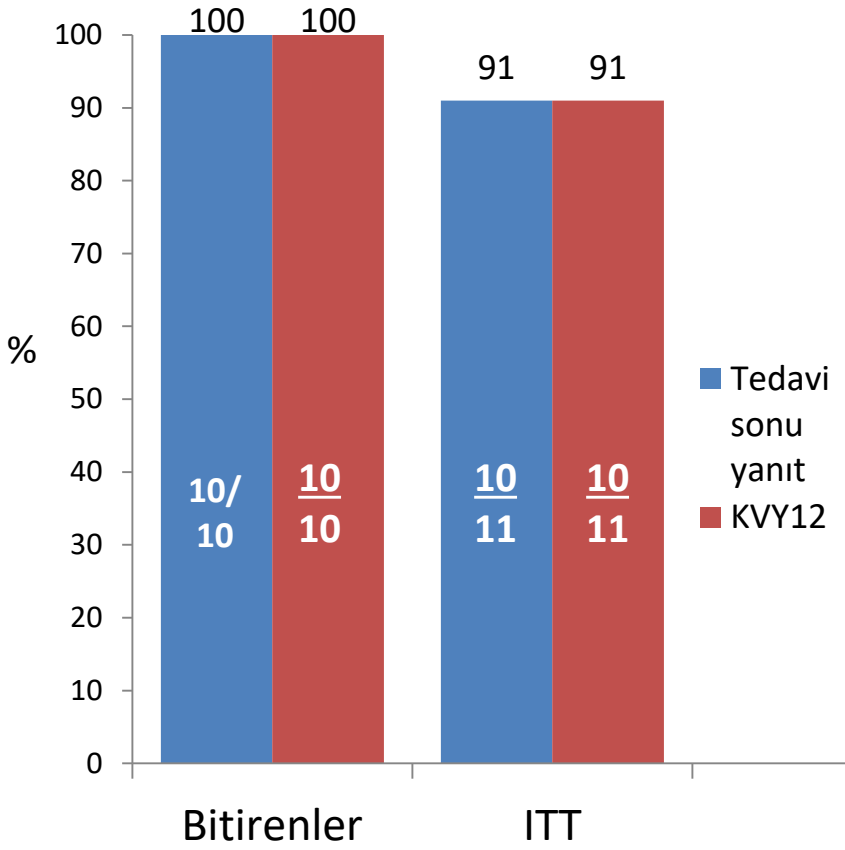
Hasta sayısı **Toplam** **Tedaviyi bitiren** **Tedavi sonrası 12. hafta**	 **11** 10 10
Yaş	51,3 (37-67)
Cinsiyet (E/K)	8/3
Nonsirotik/Sirotik	9/2 (Child A)
Tedavi deneyimli	6
Genotip **GT1a** **GT1b**	 3 8
Ortalama viral yük	2,8 x 10^6 IU/mL

Renal transplant hastalarında HCV tedavisi
Başkent Üniversitesi Ankara Hastanesi Deneyimi

BAŞKENT ÜNİVERSİTESİ

Tedavi (SUT kurallarına göre)	n
Paritaprevir/Ombitasvir/Ritonavir + Dasabuvir x 12 hft	7
Paritaprevir/Ombitasvir/Ritonavir + Dasabuvir + Ribavirin x 12 hft	1
Sofosbuvir + Ledipasvir (12 hafta)	1
Sofosbuvir + Ledipasvir (24 hafta)	1
Sofosbuvir + Ledipasvir + Ribavirin (12 hafta)	1

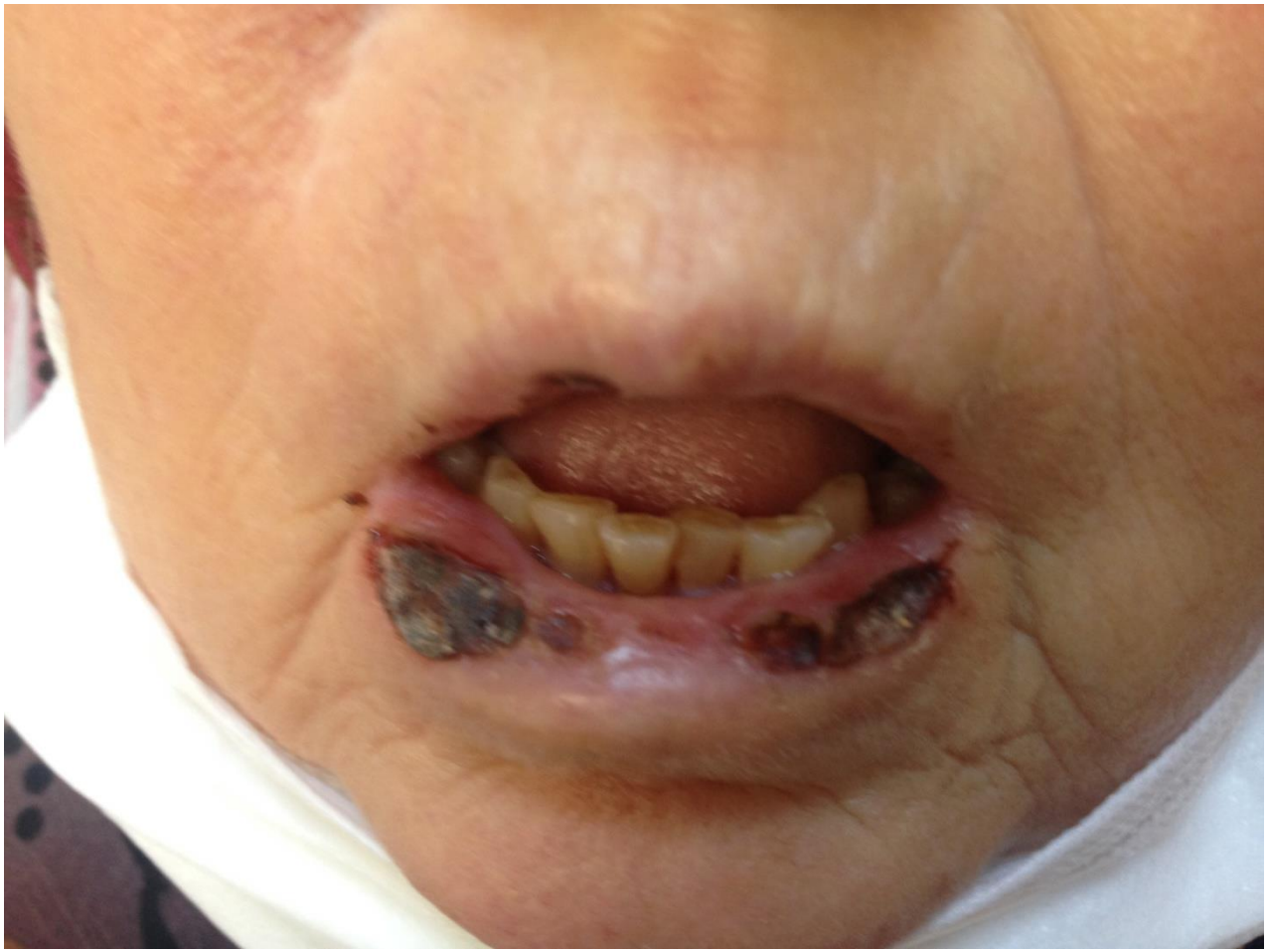
Renal transplant hastalarında HCV tedavisi Başkent Üniversitesi Ankara Hastanesi Deneyimi



Tedaviyi Bırakma, Tolerans ve Yan Etki:

- OBV/PTV/r + DSV alan bir hasta tedavinin 5. günü tekrarlayan cilt döküntüleri ve kreatinin klerensinin bozulması nedeniyle tedaviyi bıraktı.
- OBV/PTV/r + DSV alan bir hastada şiddetli mukozit ve glossit nedeniyle 10. haftada tedavi kesildi (HCV-RNA negatif)
- RBV alan 1 hastada anemi nedeniyle ilaç dozu razaltılması gerekti.
- Bir hastada tedaviden sonra kreatinin klerensinde azalma olması nedeniyle böbrek biyopsisi yapıldı ve kronik rejeksiyon saptandı.

P.A. (67. günde tedavi kesildi)



Sabırla dinlediğiniz için teşekkür ederim

Henri Toulouse-Lautrec