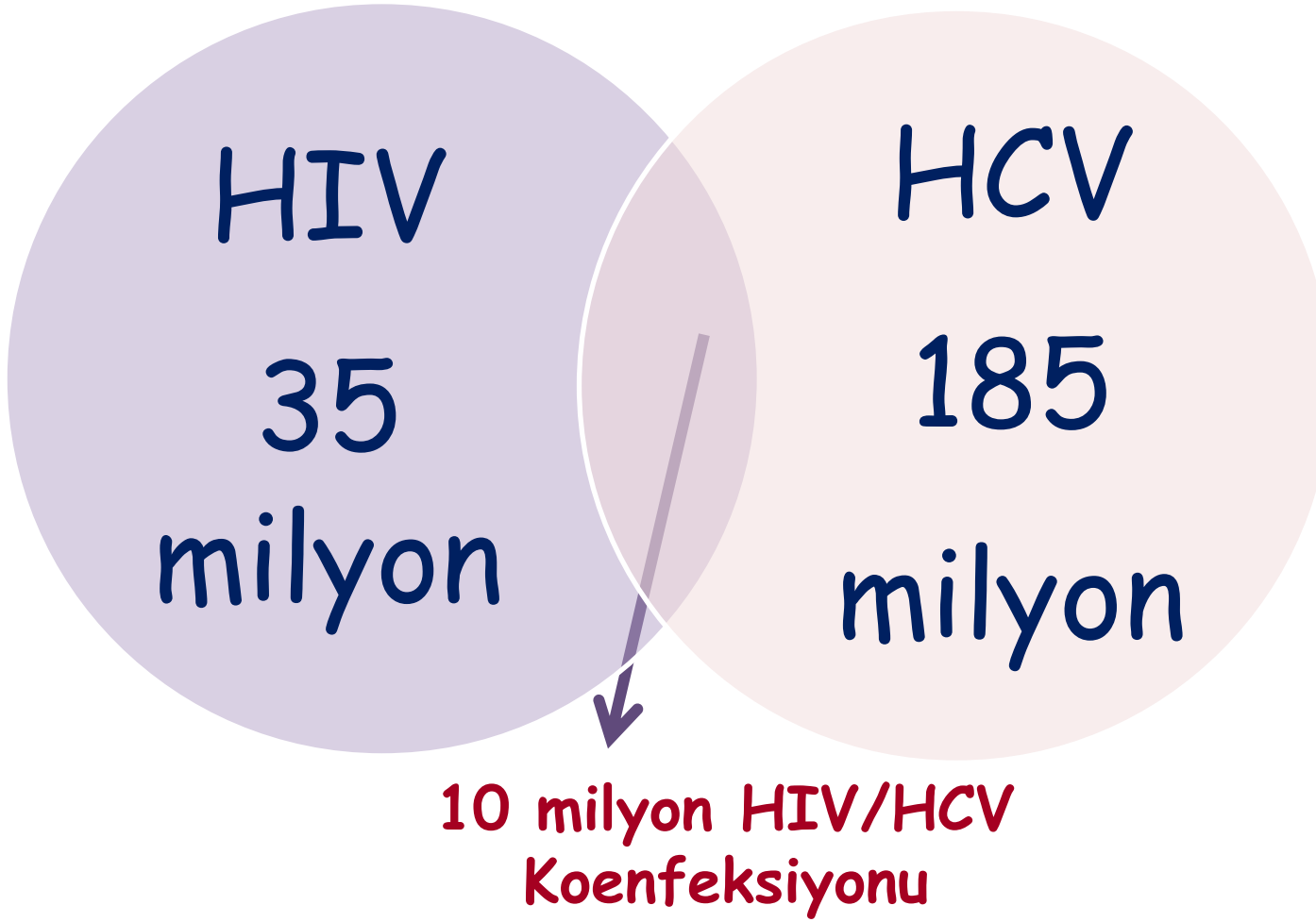
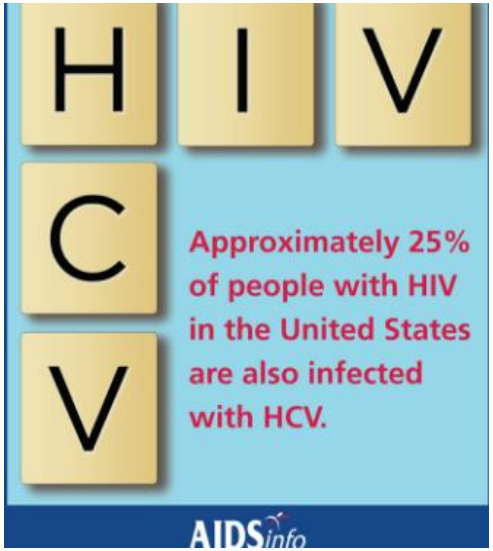
Olgu Sunumu 3
HIV-Pozitif Kronik Hepatit C Olgusu

Doç Dr Aysel Kocagül Çelikbaş
Ankara Numune Eğitim ve Araştırma Hastanesi

HIV ve HCV Bulaş yolları

Epidemiyoloji





Epidemiyoloji

Haziran 2016

HIV enfekte hastaların

- ~%25'i HCV ile koenfekte
- HIV+ ve İV ilaç kullananların %75'i HCV ile koenfekte
- MSM HIV pozitiflerde koenfeksiyon %0.4-18

HIV'in HCV Üzerine Etkileri

- Akut HCV infeksiyonunda spontan klirens oranı düşük
- Kronik HCV enfeksiyonunda progresyon hızlı, siroza ilerleme 3 kat daha yüksek
- Mortalite riski daha fazla

Risk faktörleri

- İleri yaş
- Alkol
- DM
- Yüksek VKİ
- Yüksek aminotransferaz düzeyi
- **Düşük CD4 hücre sayısı**
- **HIV viremisi**

HIV ve HCV Koenfeksiyonu Klinik Seyir

Volume 58, Issue 6
15 March 2014

VIRAL HEPATITIS INVITED ARTICLE

Camilla S. Graham, Section Editor

HIV/Hepatitis C Virus–Coinfected Patients and Cirrhosis: How to Diagnose It and What to Do Next?

Valérie Martel-Laferrière,[1] Michael Wong,[2] and Douglas T. Dieterich[3]

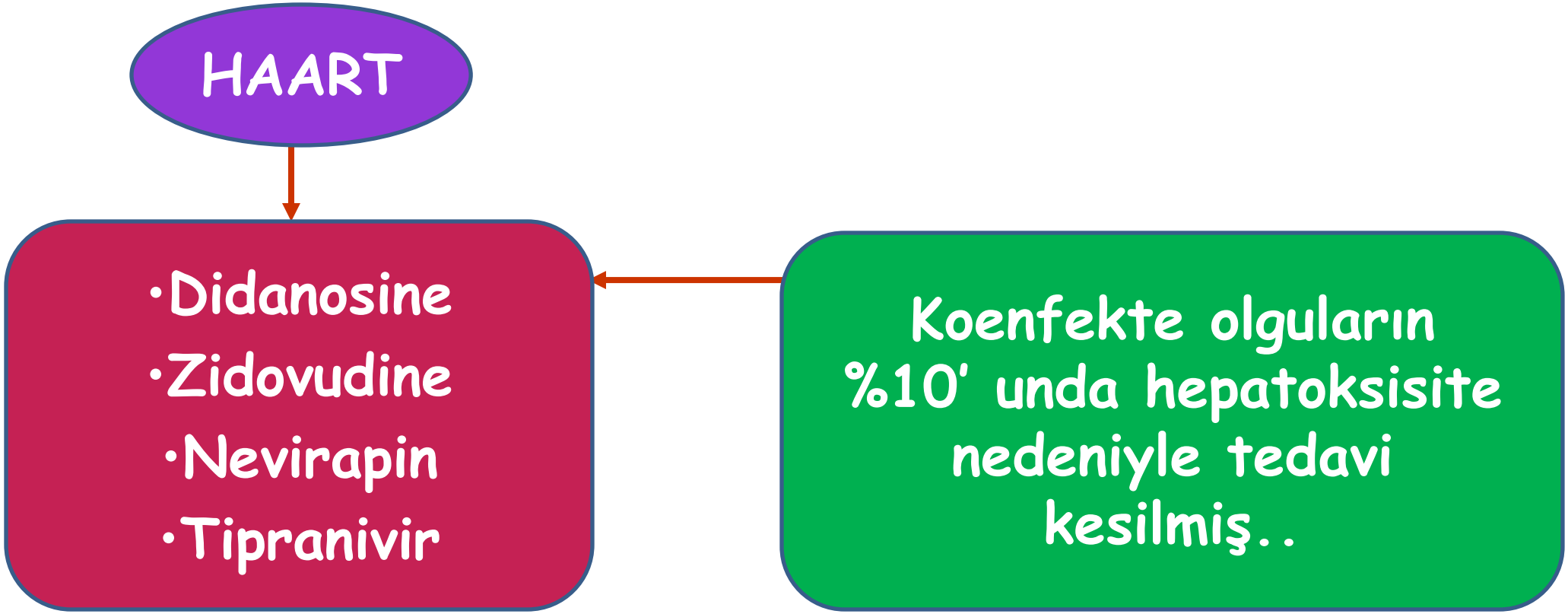
Hepatosellüler karsinom ve siroz riski daha yüksek

HCV MONOENFEKSİYONU
20-30 YIL

HCV/HIV KOENFEKSİYONU
10-20 YIL

HCV'nin HIV Seyrine Etkisi

- HCV'nin HIV seyrine belirgin etkisi yok



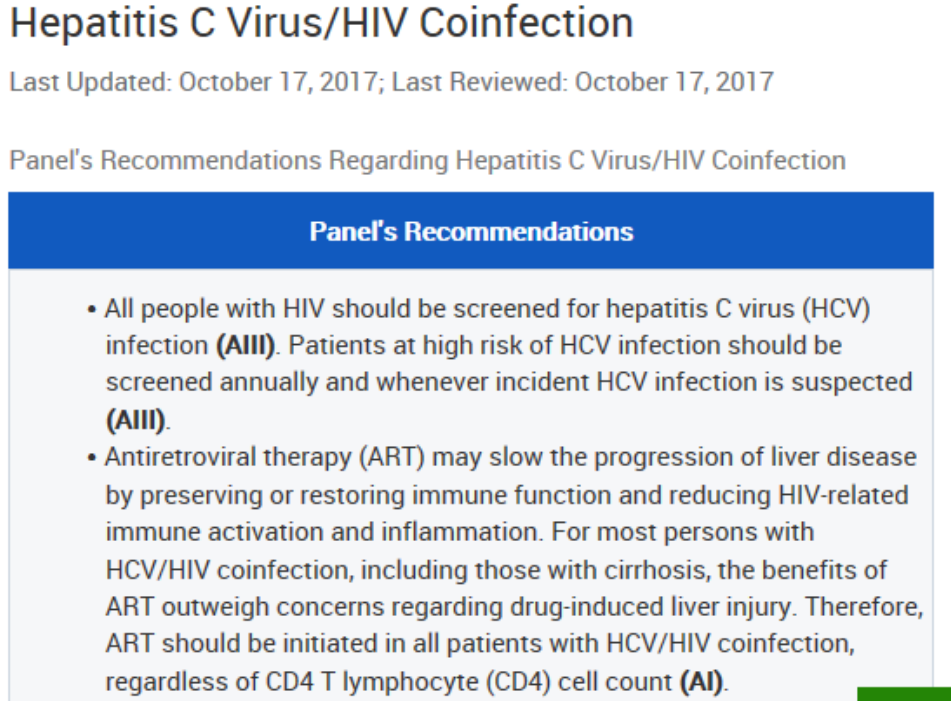
Koenfekte Olgularda Tanı ve Tedavi Yaklaşımı EACS / 2018

HIV+ olguların tümünde

- HIV pozitifliği saptandığı anda Anti HCV taranmalı
- Yüksek riskli olduğu düşünülen seronegatif bireyler her yıl veya gereğinde HCV açısından taranmalı
- Risk faktörü olan ve/veya açıklanamayan ALT yüksekliklerinde anti HCV negatif olsa da HCV RNA istenmelidir

- Tüm koinfekte hastalar tedavi açısından değerlendirilmelidir

- **Koenfeksiyonda ART ve HCV tedavi ve takibi monoinfeksiyonda olduğu gibidir**



- HIV pozitif her hasta HCV açısından taranmalı (AIII)
- Hastalar HCV açısından yüksek riskli olduğundan yılda bir kez yada şüphe olduğu anda taranmalı (AIII)
- Antiretroviral tedavi (ART), bağışıklık fonksiyonunu koruyarak veya düzelterek HIV ile ilişkili immün aktivasyonu ve inflamasyonu azaltarak karaciğer hastalığının ilerlemesini yavaşlatabilir
- Sirozlu olanlar da dahil olmak üzere, HCV / HIV koenfeksiyonu olan çoğu olgu için, ART'ın faydaları ilaca bağlı karaciğer hasarı ile ilgili endişelerden ağır basmaktadır. Bu nedenle, HCV / HIV ile koenfekte olan tüm olgulara CD4 T lenfosit (CD4) hücre sayısına bakılmaksızın ART başlatılmalıdır (AI)

- Initial ART regimens recommended for most patients with HCV/HIV coinfection are the same as those recommended for individuals without HCV infection. However, when treatment for both HIV and HCV is indicated, the ART and HCV treatment regimen should be selected with special consideration for potential drug-drug interactions and overlapping toxicities (see discussion in the text below and in Table 12).
- In patients with lower CD4 counts (e.g., <200 cells/mm³), ART should be initiated promptly **(AI)** and HCV therapy may be delayed until the patient is stable on HIV treatment **(CIII)**.
- All patients with HCV/HIV coinfection should be evaluated for HCV therapy and have their liver fibrosis stage assessed to inform the length of their therapy, ribavirin need (a concern with some regimens), and subsequent risk of hepatocellular carcinoma and liver disease complications.

- Başlangıç ART rejimi HIV mono enfekte olgularla aynı
- HCV tedavisi de planlanacağı zaman ilaç ilaç etkileşimleri gözönüne alınarak tedavi modifikasyonu yapılabilir
- CD4 sayısı düşük olan olgularda (<200 h/mm³) ART hemen başlanıp, Hasta stabil olana kadar HCV tedavisi ertelenebilir
- HCV/HIV koenfekte tüm hastalar Fibrozis evresi , ribavirin gerekliliği, siroz, HCC ve tedavi gerekliliği açısından değerlendirilmelidir

- Persons with chronic HCV/HIV coinfection should be screened for active and prior hepatitis B virus (HBV) infection by testing for the presence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B surface (HBsAb) and core (HBcAb total or IgG). Persons who are not immune to HBV infection (HBsAb-negative) should receive anti-HBV vaccination **(AIII)**.
- HBV reactivation has been observed in persons with HBV infection during interferon-free HCV treatment. Accordingly, persons with HCV/HIV coinfection and active HBV infection (HBsAg-positive) should receive ART that includes two agents with anti-HBV activity prior to initiating HCV therapy **(AIII)**.

- HCV/HIV koenfekte olguların tümü aktif veya geçirilmiş HBV enfeksiyonu açısından test edilmeli, HBs Ag, Anti HBs, Anti HBc total veya Ig G bakılmalıdır. Anti HBs negatif tüm olgular aşılanmalıdır
- DAA tedaviler sırasında HBV alevlenmesi olabileceğinden HBs Ag pozitif tüm olguların ART rejiminde HBV ye etkili en az iki ajanın bulunmasına dikkat edilmelidir.

Yeni Tesbit HIV Pozitif Olguya Yaklaşım

- Anti HAV Ig G
- HBs Ag
- Anti HBc
- Anti HBs
- Anti HCV

Hepatit A ve B markerları negatif

Aşı

Anti HCV +

HCV RNA

Olgu

- 43 yaşında erkek hasta
- 2012 yılında cerrahi bir operasyon planlanıyor
- Preoperatif tetkikleri sırasında Anti HIV pozitifliği saptanması üzerine operasyondan vazgeçilerek hasta kliniğimize yönlendiriliyor

Öykü:Uzun süre Fransa'da yaşamış

Korunmasız cinsel temas

IV ilaç kullanımı

Olgu - Laboratuvar

- BK: **3500**
- HB 11 g/dl
- Trombosit :**125000**
- AKŞ: 90 mg/dl
- Üre: 33mg/dl
- Kreatinin: 0.7mg/dl
- **ALT: 45 U/L**
- **AST: 50 U/L**

- T. Protein: 6.1 g/dl
- Albumin: 3.4 g/dl
- T. Bil: normal
- D. Bil: normal
- PT: 21 sn
- **INR: 1.89**
- Fib: 184
- AFP: 2.3

- Anti HAV Ig G: Pozitif
- HBs Ag: Negatif
- Anti HBs: Negatif
- TORCH Ig M: Negatif

  Ig G: Pozitif
- VDRL: Negatif
- **Anti HCV: Pozitif**

Hızla ART Başlanması Gereken Durumlar

- Akut/erken infeksiyon (akut retroviral sendrom)
- **HIV/hepatitis B–C koinfeksiyonu**
- AIDS tanımlayıcı hastalık, HIV-ilişikili demans ve AIDS-ilişkili malignite
- Fırsatçı infeksiyonlar
- Düşük CD4 sayısı (<200 /mm^3)
- HIV ilişkili nefropati (HIVAN)
- Gebelik

http://www.eacsociety.org/files/guidelines_8.2-english.pdf
https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

Olgu

HIV RNA: 3.2X 10^6 k/ml

CD4:360 hücre/mm^3

ART: Tenofovir Emtristabin

Lopinavir/Ritonovir

10. ayda HIV RNA negatif

Olgu

- **HCV RNA: 10^7**
- **HCV genotip 3**
- **Biyopsi:** HAİ: 8/18, Fibrozis 4 /6
- **Batın Ultrasonografisi:** Karaciğer 18cm. hafif heterojen, dalak büyüklüğü sınırda

Genotip 3 Dünyada Durum

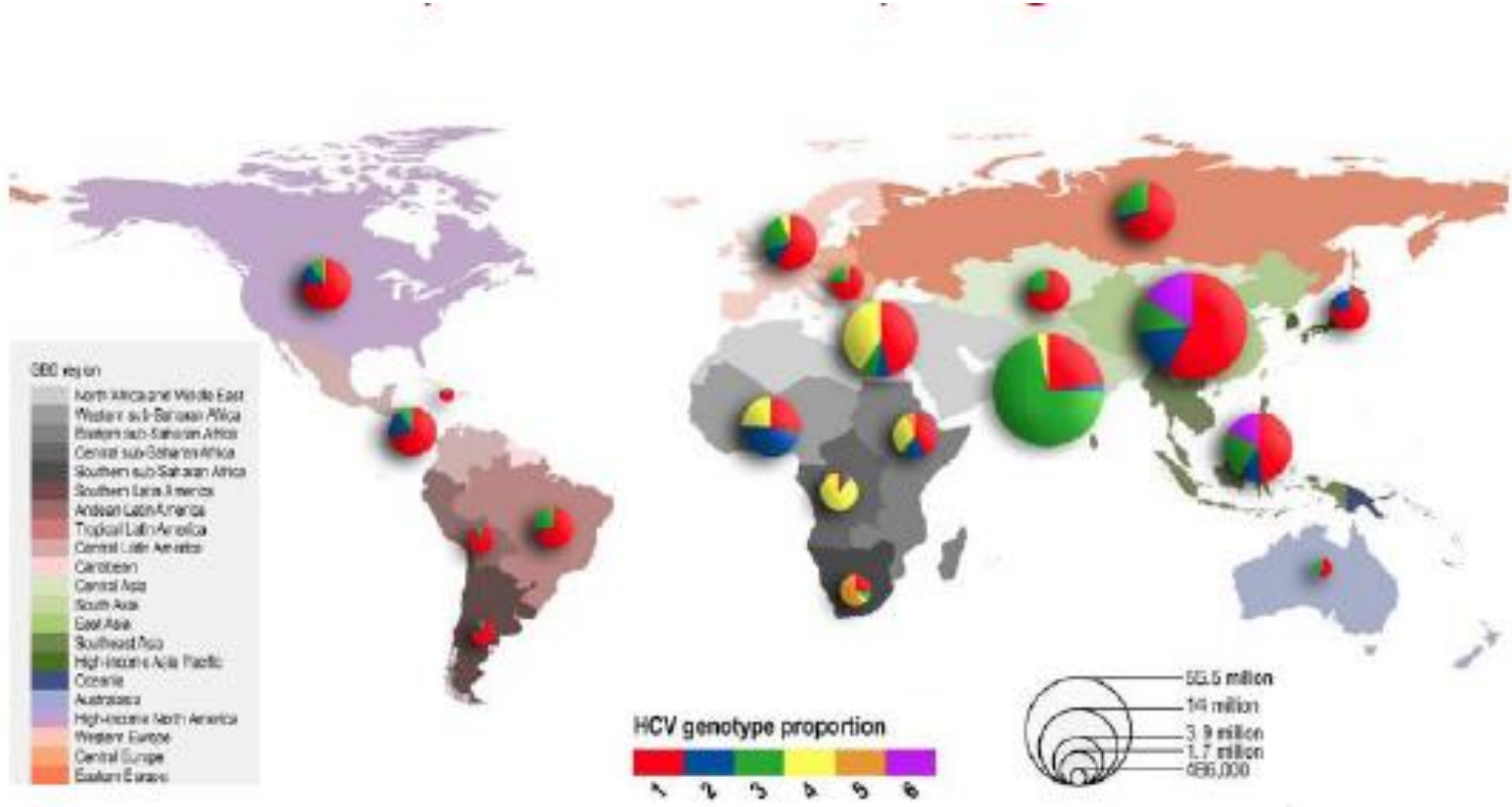


Fig. 1. Relative prevalence of each HCV genotype by GBD region. Size of pie charts is proportional to the number of seroprevalent cases as estimated by Hanafiah et al.[2]

Genotip 3 ülkemizde durum

Tablo II. *Ülkemizde Değişik Bölgelerde Yapılan HCV Genotiplendirme Çalışmaları*

Bölge	Yıl	Örnek sayısı	Yöntem	Genotipler										Araştırıcı
				1	1a	1b	2	2a	3	3a	4	4a	Diğer	
Mersin	2013	236	LiPA	3.8	1.7	84.7	2.1	-	-	4.2	-	0.8	0.4[a], 2.1[b]	Tezcan ve ark.[25]
Kayseri	2012	375	RT	2.4	2.4	57.6	3.2	-	1.1	-	32	-	1.3[b]	Kayman ve ark.[24]
Gaziantep	2011	51	DA	-	9.8	78.4	-	7.8	-	2.0	-	-	-	Karslıgil ve ark.[23]
Zonguldak	2010	39	LiPA	-	2.6	97.4	-	-	-	-	-	-	-	Aktaş ve ark.[22]
Afyon	2010	30	DA		20	63.3						13.3	3.3[c]	Kalaycı ve ark.[21]
Sivas	2010	178	LiPA	-	9.0	88.2	-	1.1	1.7	-	-	-	-	Çelik ve ark.[20]
Istanbul	2010	52	LiPA		1.9	76.9	3.8			9.6	1.9			Küçüköztaş ve ark[19]
Manisa	2009	100	DA	-	2.0	90	-	2.0	-	-	-	5	-	Şanlıdağ ve ark.[18]
Diyarbakır	2009	74	LiPA	4.1		87.8	2.7		2.7	2.7				Özbek ve ark.[17]
GD Anadolu	2007	30	DA	-	22.7	72.8	-	-	-	4.5	-	-	-	Çil ve ark.[16]
Konya	2007	80	DA	-	-	100	-	-	-	-	-	-	-	Ural ve ark.[15]
İzmir	2008	345	RFLP/DA	-	10	87	0.9	-	1.4	-	0.6	-	-	Altuğlu ve ark.[10]
İç Anadolu	2004	365	RFLP	-	11	84	3	-	1.0	-	1	-	-	Bozdayı ve ark.[7]
İzmir	1995	89	RFLP		19.1	75.3	3.4				2.2			Abacıoğlu ve ark.[6]

GD: Güneydoğu; LiPA: Line probe assay; RT: Real-time; DA: Dizi analizi; RFLP: Restriction fragment length polymorphism; a: Genotip 6; b: Karışık tip; c: Genotip 1c

Mikrobiyol Bul 2014; 48(3): 484-490

6.2.13.E-2- Kronik Hepatit C tedavisi (Değişik: 06/8/2010-27664/8 md.)

- Erişkin Genotip 2 ve 3 hastalarda ribavirin dozu en fazla 800 mg olacak şekilde verilir
- Bu hastalarda gerek interferonun gerekse ribavirinin tedavi süresi en fazla 24 haftadır
- Genotip 2 ve 3 hastaların tedavisinde 12 hafta sonundaki HCV RNA azalması koşulu aranmaz

OLGU

Hasta 62 kg

Tedavinin

Pegileinterferon alfa 2b 1,5µg/kg

Ribavirin 2 x 400 mg

1. ayında HCV RNA negatif (HVY +)

3. ayda HCV RNA negatif (EVY +)

4. ay: Beyaz küre:1900/mm^3

Nötrofil: 1000/mm^3

Hb: 8,5 gr

Trombositopeni 90000/mm^3

OLGU

- Ribavirin ve interferon doz ayarı
- 15 günde bir kontrol ile tedavi 6 aya tamamlandı
- Tedavi sonu yanıt (TSY +)

- Tedavi sonrası 3. ayda HCV RNA 10^5 k/ml
- 2 yıl süreyle HCV RNA +
- AST ve ALT yüksek

Kalıcı Viral Yanıt Oranı

Liver INTERNATIONAL
OFFICIAL JOURNAL OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE LIVER

Liver International ISSN 1478-3223

REVIEW ARTICLE

Treatment of hepatitis C virus genotype 3-infection

Stanislas Pol, Anaïs Vallet-Pichard and Marion Corouge

Université Paris Descartes, APHP, Unité d'Hépatologie, Hôpital Cochin, INSERM U-1016, Institut Cochin, Paris, France

Keywords
cirrhosis – combination therapy – direct-acting antiviral – hepatitis C virus – polymerase inhibitor – protease inhibitor – replication complex inhibitor

Abbreviations
DAAs, direct-acting antiviral drugs; EVR, early virological response; HCV, hepatitis C virus; PEG-IFN, pegylated interferon; RBV, ribavirin; RVR, rapid viral response; SOC, standard of care; SVR, sustained virological response.

Correspondence:
Pr. Stanislas Pol, MD, PhD, Unité d'Hépatologie, Hôpital Cochin, 7 rue du faubourg Saint Jacques, 75679 Paris Cedex 14, France
Tel: +33 1 58 41 30 01
Fax: +33 1 58 41 30 15

Abstract
The treatment of hepatitis C virus (HCV) infection with pegylated interferon (PEG-IFN) alfa and ribavirin (800 mg daily) (RBV) is the standard of care (SOC) for hepatitis C virus genotype 3-infection leading to a sustained virological response (SVR) in around 65% of patients. A better understanding of the HCV life-cycle has recently resulted in the development of several potential direct-acting antiviral drugs (DAAs) targeting viral proteins (NS3/4A protease, NS5B nucleos(t)idic and non-nucleos(t)idic polymerase, NS5A viral replication complex). First generation protease inhibitors in combination with PEG-IFN/RBV are not efficient in genotype 3-infected patients. The combination of PEG-IFN/RBV with Daclatasvir, a NS5A inhibitor for 12–24 weeks results in a SVR in around 75% while the triple combination of PEG-IFN/RBV with the oral nucleotidic polymerase inhibitor Sofosbuvir (GS-7977) for 12 weeks in naïve patients results in a SVR in more than 95%. The results of the first oral combination of Sofosbuvir and RBV for 12 weeks in genotype 3-infected patients have been rather disappointing with a slightly lower SVR than after 24 weeks of PEG-IFN: around 60%, and only 30% in patients with cirrhosis. Extending treatment from 12 to 16 weeks in treatment experienced patients doubled the SVR rate and an 80% SVR rate is

Clinical Infectious Diseases

SUPPLEMENT ARTICLE

Management of Hepatitis C/HIV Coinfection in the Era of Highly Effective Hepatitis C Virus Direct-Acting Antiviral Therapy

David L. Wyles,[1] Mark S. Sulkowski,[2] and Douglas Dieterich[3]

[1]Divisions of Infectious Diseases, Department of Medicine, University of California, San Diego; [2]Johns Hopkins University School of Medicine, Baltimore, Maryland; and [3]Division of Liver Disease, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York

The increased life expectancy of persons infected with human immunodeficiency virus (HIV) treated with antiretroviral therapy (ART) has resulted in renewed attention to non-HIV-related diseases exacerbated by HIV infection. Coinfection with hepatitis C virus (HCV) is a particular area of con we discuss the epidemiology of HCV infect the efficacy of emerging HCV treatment str vith HIV/HCV coinfection suggest that HC oral HCV regimens have shown high rates sci- plinary approach to HCV treatment i ure, practitioners also need to be mindful

Keywords. HCV; hepatitis C; HIV

Kür şansı yüksek

Ancak reinfeksiyon riski de yüksek

Hastalar eğitilmeli

07.10.2016 TARİHLİ SUT
4.2.13.3.2.A.2 Tedavi deneyimli Genotip 3 Kronik Hepatit C hastalarında yeniden tedavi

- 4.2.13.3.2.A.2 -Genotip 3 hastalarda yeniden tedavi;

a) Nonsirotik hastalarda:

Sofosbuvir+ Ribavirin ile tedavi süresi toplam 24 haftadır

b) Sirotik hastalarda (Child A) :

1- Sofosbuvir + Ribavirin ile tedavi süresi toplam 24 haftadır

2- Sofosbuvir + Ledipasvir ile tedavi süresi ribavirin ile birlikte toplam 24 haftadır

OLGU

Tedavi deneyimli nonsirotik

- HCV RNA: 905000 IU/ml
- AST: 59 U/L
- ALT: 52 U/L
- Üre: 30 mg/dl
- Kreatinin: 1.09 mg/dl

14 Ekim 2016'da 6 ay süreli Sofusbuvir + Ribavirin tedavisi başlandı

İLAÇ ETKİLEŞİMLERİ

Selected HIV Drugs	HCV DAA Drugs					
	NS5A Inhibitor	NS5B Inhibitor	Coformulated NS5A/NS5B Inhibitor	Coformulated NS5A Inhibitor/ NS3A/4A Protease Inhibitor	Coformulated NS5A/NS3A/4A Protease Inhibitor plus NS5B Inhibitor	NS3A/4A Protease Inhibitor[a]
	Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir[b]	Simeprevir
Nucleoside Reverse Transcriptase Inhibitors						
3TC	✓	✓	✓	✓	✓	✓
ABC	✓	✓	✓	✓	✓	✓
FTC	✓	✓	✓	✓	✓	✓
TDF	✓	✓	✓ Monitor for TDF toxicity.	✓	✓	✓
TAF	✓	✓	✓	✓	✓	✓

DHSS 2018

İLAÇ ETKİLEŞİMLERİ

Selected HIV Drugs	HCV DAA Drugs					
	NS5A Inhibitor	NS5B Inhibitor	Coformulated NS5A/NS5B Inhibitor	Coformulated NS5A Inhibitor/ NS3A/4A Protease Inhibitor	Coformulated NS5A/NS3A/4A Protease Inhibitor plus NS5B Inhibitor	NS3A/4A Protease Inhibitor[3]
	Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir	Simeprevir
HIV Protease Inhibitors, continued						
ATV/r or ATV/c	✓ ↓ DCV dose to 30 mg/day	✓	✓ If PI/r (or ATV/c, DRV/c) is used with TDF, ↑TDF concentrations are expected. If coadministration necessary, monitor for TDF-associated toxicities (see footnote[c]).	×	✓ Take ATV 300 mg in the morning at same time as ombitasvir/ paritaprevir/r plus dasubuvir; discontinue RTV or COBI in HIV regimen until HCV therapy completed.	×
DRV/r or DRV/c	✓	✓		×	×	×
FPV or FPV/r	✓	✓		×	×	×
LPV/r	✓	✓		×	×	×
SQV/r	✓ ↓ DCV dose to 30 mg/day			×	×	×
TPV/r	?	×	×	×	×	×
Non-Nucleoside Reverse Transcriptase Inhibitors						
EFV	✓ ↑ DCV dose to 90 mg/day	✓	✓ If used with TDF, monitor for TDF toxicity.	×	×	×
ETR	↑ DCV dose to 90 mg/day	✓		×	×	×
NVP	↑ DCV dose to 90 mg/day	✓		×	×	×
RPV	✓	✓		✓	×	✓

DHSS 2018

İLAÇ ETKİLEŞİMLERİ

Selected HIV Drugs	HCV DAA Drugs					
	NS5A Inhibitor	NS5B Inhibitor	Coformulated NS5A/NS5B Inhibitor	Coformulated NS5A Inhibitor/ NS3A/4A Protease Inhibitor	Coformulated NS5A/NS3A/4A Protease Inhibitor plus NS5B Inhibitor	NS3A/4A Protease Inhibitor[a]
	Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir	Simeprevir
Integrase Strand Transfer Inhibitor						
DTG	✓	✓	✓ If used with TDF, monitor for TDF toxicity.	✓	✓	✓
EVG/c/TDF/FTC	✓ ↓ DCV dose to 30 mg/day	✓	×	×	×	×
EVG/c/TAF/FTC	✓ ↓ DCV dose to 30 mg/day	✓	✓	×	×	×
EVG (plus PI/r without COBI)	✓ ↓ DCV dose to 30 mg/day for all PI/r, except TPV/r — do not coadminister	Refer to Recommendations for individual ritonavir-boosted PI.				
RAL	✓	✓	✓	✓	✓	✓
CCR5 Antagonist						
MVC	✓	✓	✓	?	×	✓

DHSS 2018

Kronik Hepatit C Virusu İnfeksiyonunun Yönetimi: Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Derneği Viral Hepatit Çalışma Grubu Uzlaşı Raporu-2017 Güncellemesi

Management of Chronic Hep... Study Group for Viral Hepati... Infectious Diseases-2017 Up...

Tenofovir Emtristabin

Lopinavir/Ritonovir

Tablo 5. Kronik Hepatit C Tedavisinde Kullanılan Doğrudan Etkili Antiviral İlaçlarla Antiretroviral İlaçlar Arasındaki Etkileşimler*

		SOF	SOF/LDV	SOF/VEL	PTV-RTV/OBV+DSV	GRZ/EBV	DCV	SMV
NRTI'ler	Abakavir							
	Emtrisitabin							
	Lamivudin							
	Tenofovir							
NNRTI'ler	Efavirenz							
	Etravirin							
	Nevirapin							
	Rilpivirin		†	†				
Proteaz inhibitörleri	Atazanavir; atazanavir/RTV; atazanavir/kobisistat		†	†	‡			
	Darunavir/RTV; darunavir/kobisistat		†	†	‡			
	Lopinavir/RTV		†	†				
Füzyon/İntegraz inhibitörleri	Dolutegravir							
	Elvitegravir/kobisistat/emtrisitabin/tenofovir disoproksil fumarat		†	†				
	Elvitegravir/kobisistat/emtrisitabin/tenofovir alafenamid							
	Maravirok							
	Raltegravir							

Klinik olarak anlamlı etkileşim yok.

Etkileşim potansiyeli var. Doz ayarlanması, zamanlama değişimi veya ek monitörizasyon gerekebilir.

Bu ilaçlar birlikte kullanılmamalıdır.

HIV ve HCV Koenfeksiyonu DAA…

SOFOSBUVİR

- HCV NS5B nükleotid polimeraz inhibitörü

- P-glikoproteinin bir substratı
- Sitokrom P450 enzim sistemi tarafından metobolize edilmez
- Birçok ART rejimi ile birlikte kullanımı uygun
- P-glikoprotein indikatörleri (tipranavir) sofosbuvir kan düzeyini düşürür

HIV ve HCV Koenfeksiyonu
DAA…

SOFOSBUVİR

- TDF birlikte kullanıldığında TDF ↑
- Ritonovir veya kobisistat ile birlikte kullanılırsa TDF ↑↑

- TDF maruziyetlerindeki artışları önlemek için alternatif HCV veya ART tercih edilebilir
- Böbrek yetmezliği ve hasarı açısından hastalar dikkatli takip edilmeli

OLGU

ART: Tenofovir emtristabin + Lopinovir/ritonovir

HCV tedavisi: Sofusbuvir + Ribavirin

Tedavinin 1. ayında HCV RNA negatifleşti

İlaç modifikasyonunu gerektiren yan etki saptanmadı

12.04.2017 de tedavi tamamlandı. TSY alındı.

17.04.2018 tarihli HCV RNA negatif

HIV RNA: negatif

Halen kullandığı ART:

Tenofovir alafenamid + emtristabin + cobistat + elvitagravir (Genvoya)

Takipleri devam ediyor.

Güncel Rehberler HCV genotip 3 tedavisinde ne öneriyor ?

EASL 2018

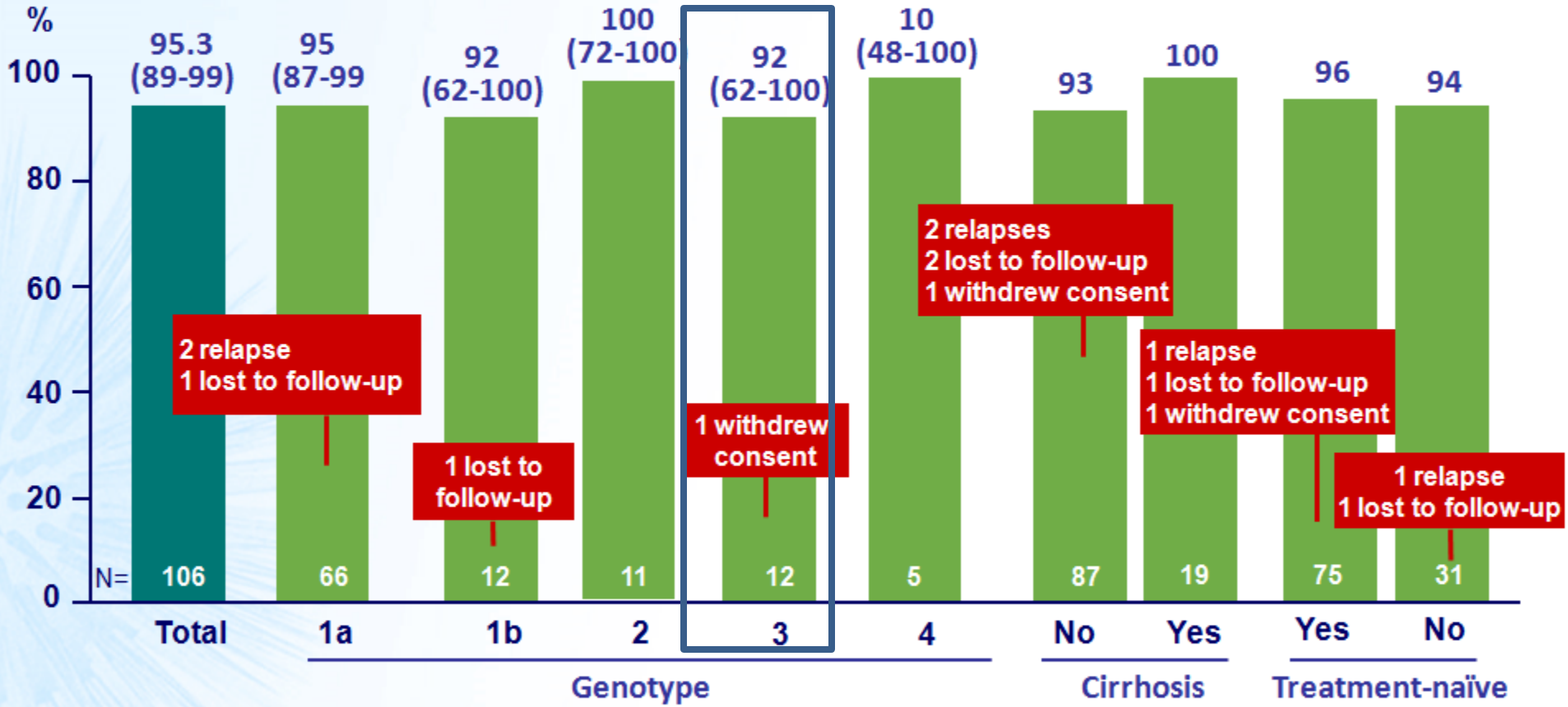
- Sofosbuvir/velpatasvir 12 hafta
- Glecaprevir/pibrentasvir 8 hafta

  (sirozlu olgularda 12 hafta)
- Sofosbuvir/velpatasvir/voxilaprevir 12 hafta

ASTRAL-5 trial

ASTRAL-5 study: SOF/VEL in HIV coinfection

SVR_{12} overall, by genotype and by cirrhosis or prior treatment, % (95% CI), ITT



- **No impact of baseline NS5A RAVs:** all 13 patients with baseline NS5A RASs (cutoff 15%) achieved SVR_{12}

Wyles D, Clin Infect Dis 2017 ; 65 :6-12

ASTRAL-5 study: SOF/VEL in HIV coinfection

HCV-trials.com

- **Summary**
  - SOF/VEL for 12 weeks resulted in overall 95% SVR_{12} in HIV coinfected patients
    - 100% SVR_{12} in patients with cirrhosis
    - 96% SVR ... in patients with prior failure to HCV therapy

Tedavi tenofovir bazlı ART rejimi alanlar dahil güvenli

HIV/ HCV konefekte hastalarda 12 hafta KVY %95

Wyles D, Clin Infect Dis 2017 ; 65 :6-12

Efficacy and Safety of Glecaprevir/Pibrentasvir in Patients Co-infected with Hepatitis C Virus and Human Immunodeficiency Virus-1: The EXPEDITION-2 Study

Jürgen K Rockstroh[1], **Karine Lacombe**[2], Rolando M. Viani[3], Chloe Orkin[4], David Wyles[5], Anne F Luetkemeyer[6], Ruth Soto-Malave[7], Robert Flisiak[8], Sanjay Bhagani[9], Kenneth E. Sherman[10], Tatiana Shimonova[11], Peter Ruane[12], Joseph Sasadeusz[13], Jihad Slim[14], Zhenzhen Zhang[3], Teresa I. Ng[3], Abhishek Gulati[3], Roger Trinh[3], Mark Sulkowski[15]

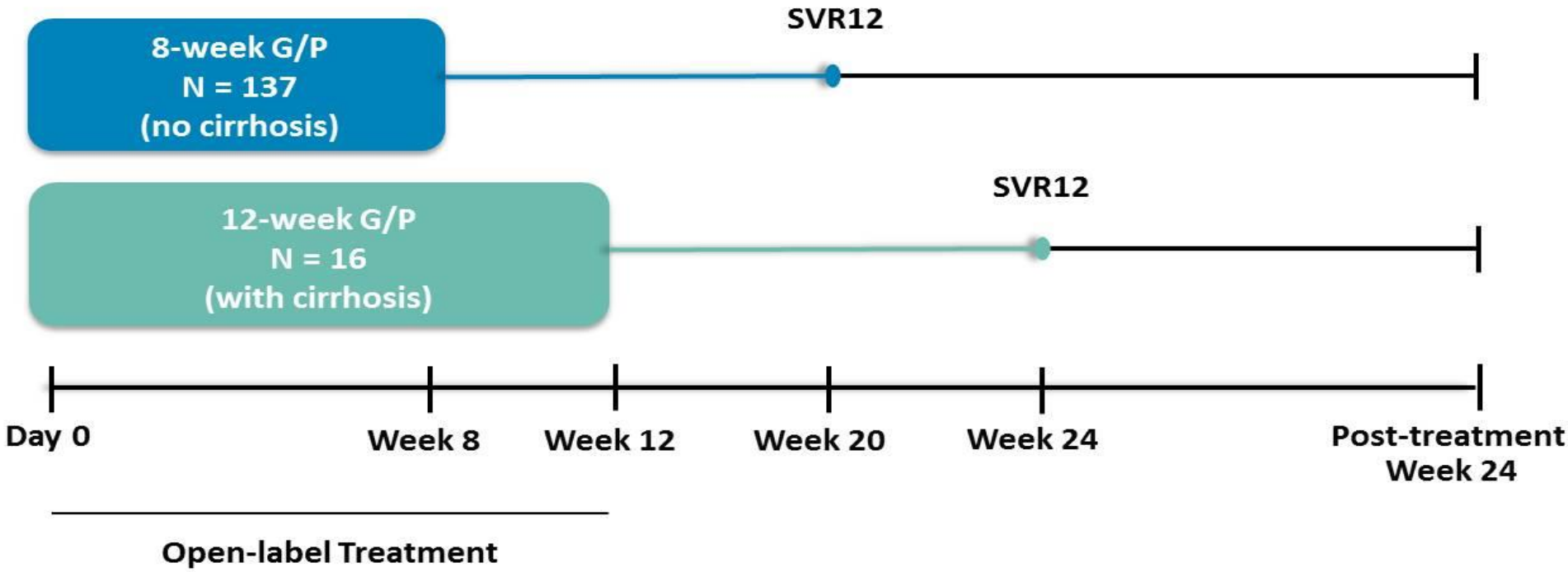
1. Universitätsklinikum Bonn, Bonn, Germany; 2. Inserm UMR-S1136, Université Pierre et Marie Curie, Hôpital Saint-Antoine, APHP, Paris; 3. AbbVie Inc., North Chicago, Illinois, USA; 4. The Royal London Hospital, London, UK; 5. Denver Health Medical Center, Denver, Colorado, United States; 6. Zuckerberg San Francisco General, San Francisco, CA, USA; 7. Innovative Care P.S.C., Bayamon, Puerto Rico; 8. Klinika Chorób Zakaźnych i Hepatologii UM w Białymstoku, Białystok, Poland; 9. Royal Free London Foundation Trust, London, UK; 10. University of Cincinnati, Cincinnati, OH 11 . State budgetary Healthcare Institution Infectious Clinical Hospital #2 of Moscow City Healthcare Department, Moscow, Russia; 12. Ruane Medical & Liver Health Institute, Los Angeles, California, United States; 13. Royal Melbourne Hospital, Parkville,Victoria, Australia; 14. St. Michael's Medical Center, Newark, NJ, United States; 15. Johns Hopkins University School of Medicine,Baltimore, Maryland, USA

IAS
• Paris, France•
24 July 2017

abbvie

EXPEDITION-2 Study Design

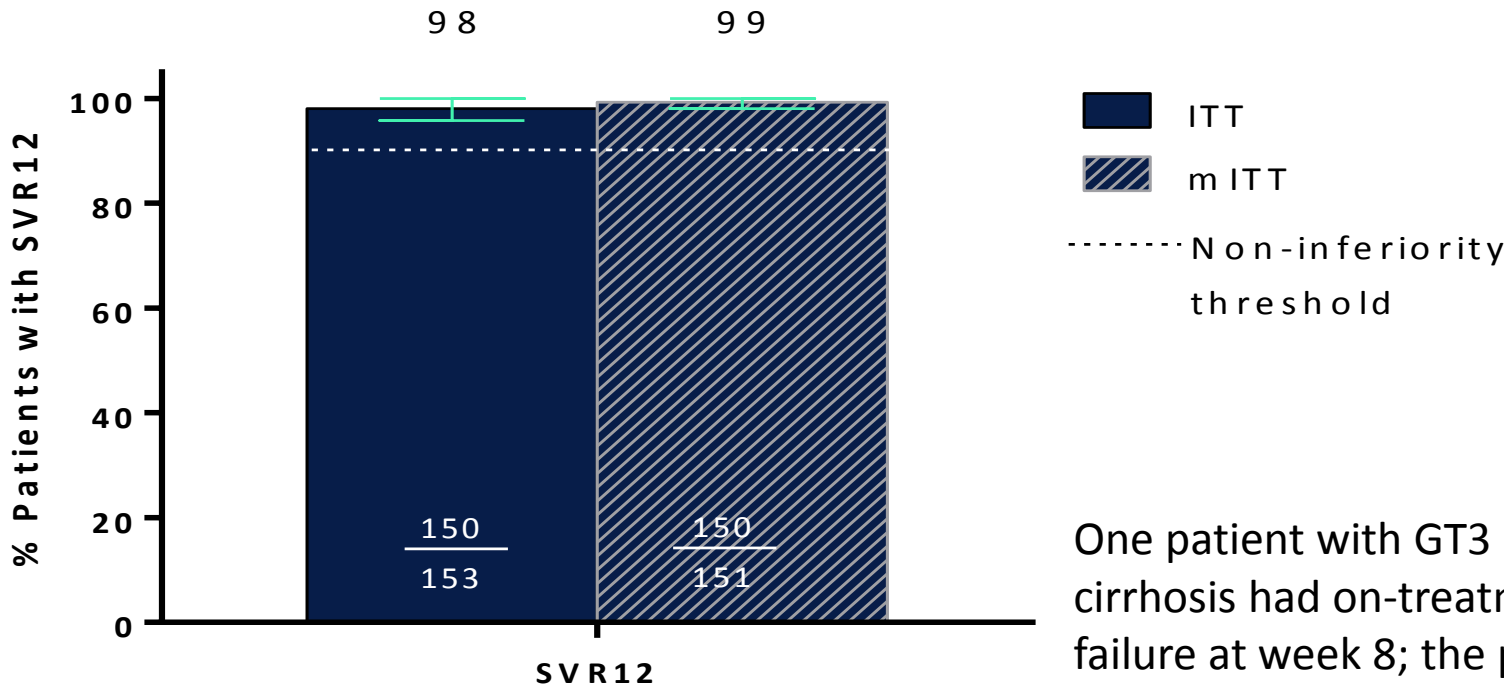
A phase 3, multicenter global study evaluating 8- or 12-week treatment with G/P in HCV/HIV-1 co-infected adults without or with compensated cirrhosis, respectively



Patients were enrolled in Australia, Belarus, France, Germany, Poland, Puerto Rico, Russian Federation, United Kingdom and United States

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg.

Efficacy Expedition 2



One patient with GT3 infection and cirrhosis had on-treatment virologic failure at week 8; the patient was 85% compliant with treatment

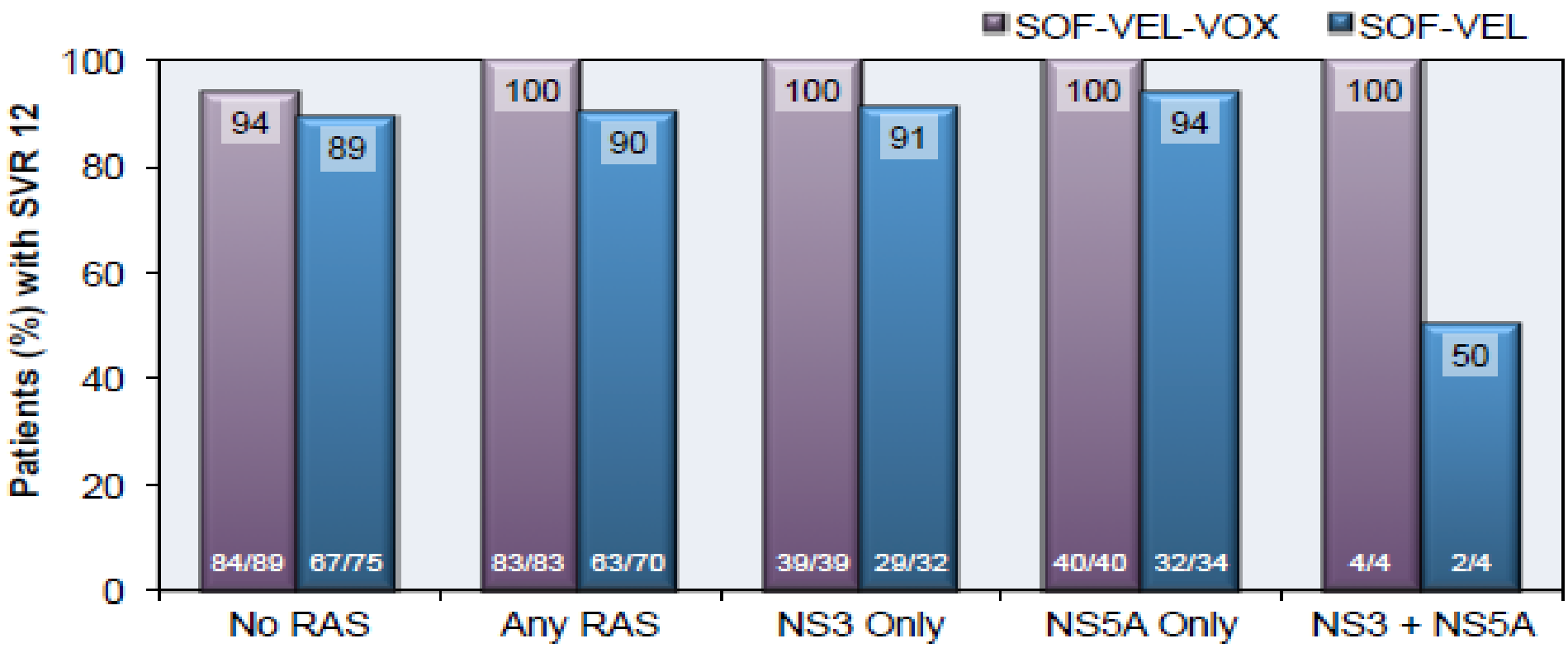
Breakthrough	1
Relapse	0
Missing Data	1*
Discontinued	1

*Patient returned at post-treatm

Sirozu olmayan koenfekte hastalarda G/P rejimi 8-hafta kullanılabilir

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 POLARIS-4: Results

POLARIS-4: Overall SVR by Baseline RAS



N=22 patients had NS5B RASs – all went on to achieve SVR12.
No treatment-emergent RASs noted in the viral relapser on SOF/VEL/VOX. In SOF/VEL group, 10/15 developed Y93H or Y93C.

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Treatment-Naive Genotype 3 Without Cirrhosis

Recommended and alternative regimens listed alphabetically for: **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

[a] This is a 3-tablet coformulation. Please refer to the prescribing information.

[b] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Treatment-Naive Genotype 3 With Compensated Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for:

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

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] This is a 3-tablet coformulation. Please refer to the prescribing information.
[c] RAS testing for Y93H is recommended for cirrhotic patients. If present, ribavirin should be included in the regimen or sofosbuvir/velpatasvir/voxilaprevir should be considered.
[d] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.


İLGİNİZ İÇİN TEŞEKKÜR EDERİM