HIV Koenfeksiyonları (HBV ve HCV)

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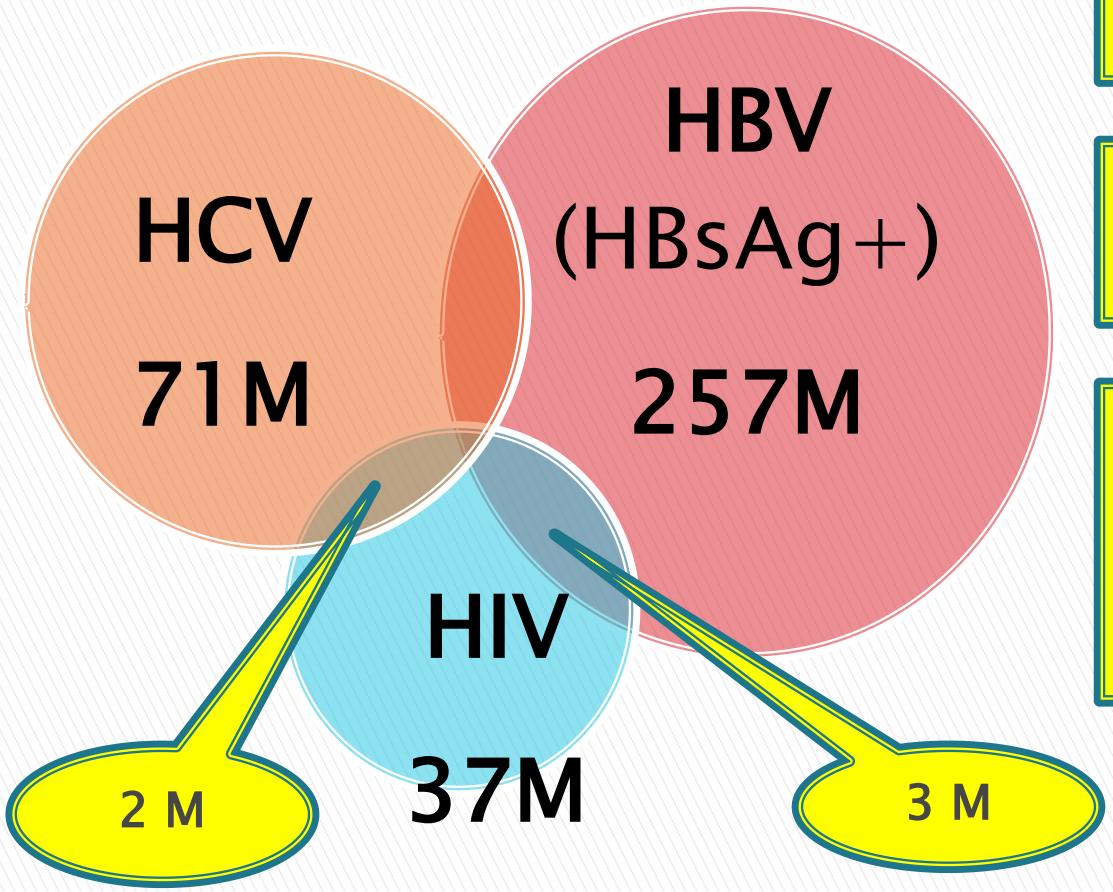
Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi

HBV-HCV-HIV: Epidemiyoloji (DSÖ 2015)



Asya'da HCC: %80 HBV

HCC'nin %30-50'si siroz olmadan, doğrudan HBV ile ilişkili

Tanı Oranları

HBV'nin %9
HCV'nin %20
HIV'in %70

1 Bosch FX, et al. Clin Liver Dis. 2005;9:191-211
2 Mitchell AE, et al. Hepatology. 2010;51:729-733.
3 WHO guideline on HBV and HCV testing Feb2017
4 Who Global Hepatitis Report 2017

Serological Profiles of HBV Among HIV-Infected Patients in Istanbul, Turkey

Hayat Kumbasar Karaosmanoglu, Ozlem Altuntas Aydin, Bilgul Mete, Alper Gunduz, Bahadır Ceylan, Mucahit Yemisen, Nuray Uzun, Resat Ozaras, Fehmi Tabak

ACTHIV-IST (ACTion against HIV in Istanbul) study group, Istanbul, Turkey

ŞEEAH- Enfeksiyon Kliniği (912 hasta)

HBV Serolojisi	N	%
HBsAg (+)	56	6.1
İzole Anti-HBc Total	63	6.9

A multicentre observational retrospective study has been conducted by ACTHIV-IST study group, including 4 centres following-up HIV patients in Istanbul. Patients followed-up between January 2006-November 2012 were enrolled in this study. Demographic and laboratory data were collected retrospectively from the patients' files and transferred to an HIV data base system. Serological profiles of HBV were classified into four groups; current HBV infection, isolated anti-HBc, past infection and vaccinated.

RESULTS

A total of 567 HIV/AIDS patients were i… study. Mean age was 38.5 years ± 11.2… 81.5% were male. Four hundred twen… tested for all HBV markers such as H… and anti-HBs. Serological profiles o… shown in table 1: 8.4% had current H… had been vaccinated and 16.8 % had past inf…

Kronik HBV enf %8.4

	(86.1%/13.9%)	(81.9%/18.1%)	(86.2%/13.8%)	
Transmission routes				
Homo/bisexual	8 (22.2%)	18 (25.0%)	22 (37.9%)	0.16
contact	22 (61.1%)	41 (56.9)	31 (53.4%)	0.76
Heterosexual contact	0	2 (2.8%)	1 (1.7%)	NA
Injecting drug use	0	0	0	NA
Blood products	0	0	0	NA
Maternal	0	2 (2.8%)	0	NA
Unknown	1	2	0	NA
Miscelaneous				
HCV coinfection (anti-HCV +, HCV RNA +)	0	2 (2.9%)	1 (1.7%)	0.60
CD4 cell counts				0.032
< 200/mm³	8 (22.9%)	32 (45.1%)	15 (27.3%)	1 vs 2: p=0.026
> 200/mm³	27 (77.1%)	39 (54.9%)	40 (72.7%)	1 vs 3: p=0.64
				2 vs 3: p=0.040
…RNA	5.13 0.98	4.98 1.17	4.60 1.76	0.51
	159.1 423.0	28.4 21.6	31.2 25.9	0.004
				1 vs 2: p=0.005
				1 vs 3: p=0.009
				2 vs 3: p=0.99

Table 1. Serological profiles of HBV infection in patients infected with HIV

HBV infection status	n	%
No HBV infection [HBsAg (-), anti-HBc IgG (-), anti-HBs (-)]	223	52.0
Current HBV infection [HBsAg (+), anti-HBc IgG (+), anti-HBs (-)]	36	8.4
Past infection [HBsAg (-), anti-HBc IgG (+), anti-HBs (+)]	72	16.8
Isolated anti-HBc seropositivity [HBsAg (-), anti-HBc IgG (+), anti-HBs (-)]	58	13.5
Vaccinated [HBsAg (-), anti-HBc IgG (-), anti-HBs (+)]	40	9.3
Total	429	100.

DISCUSSION

Current HBV infection and isolated anti-HBc prevalences are high among our HIV-infected patients. Parameters associated with current HBV infection were lower CD4 counts and increased ALT levels. Occult HBV infection was identified in 10.3% of patients with isolated anti-HBc tested for HBV DNA.

In conclusion, serological profiles of HBV must be assesed among HIV-infected patients and HBV vaccination must be offered in those without HBV markers. Determination of HBV DNA should be performed in patients with isolated anti-HBc to rule out the presence of occult infection.

Hepat Mon. 2014 Aug 16;14(8):e18128. doi: 10.5812/hepatmon.18128. eCollection 2014.

Low Prevalence of Hepatitis C Virus Infection Among HIV-Positive Patients: Data From a Large-Scale Cohort Study in Istanbul, Turkey.

Aydin OA[1], Yemisen M[2], Karaosmanoglu HK[1], Sargin F[3], Gunduz A[4], Ceylan B[5], Mete B[2], Ozgunes N[3], Sevgi DY[4], Ozaras R[2], Tabak F[2].

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ŞEEAH- Enfeksiyon Kliniği

HIV (+) 912 hasta

HIV/HCV %0.7

A

BA ciency virus (HIV) and hepatitis C virus (HCV) varies in different countries. This may be attributable to common transmission routes as well as social, economic, and cultural factors.

OBJECTIVES: The purpose of this study was to investigate the prevalence and risk factors of HCV infection among HIV-positive patients in Istanbul, Turkey.

PATIENTS AND METHODS: Since January 2006 to November 201 949 HIV-positive patients that were enrolled in this study by ACTHIV-IST (Action Against HIV in Istanbul) Study Group, which consists of five centers to follow up HIV-positive patients in Istanbul. Epidemiologic and clinical data were collected retrospectively from medical records and were transferred to an HIV database system.

RESULTS: Among 949 patients, 84% were men and the mean age was 37.92 ± 11.54 years (range, 17-79). The most frequent route of transmission was heterosexual intercourse (48.8%), followed by men having sex with men (30.5%). Only nine patients (0.9%) had history of injection drug use (IDU). The prevalence of HIV/HCV coinfection 4.4% (4:9) in patients with HIV/HCV coinfection (three of them were not Turkish citizens), whereas this ra IV infection ($P < 0.01$). Genotypes 1b, 2a/2c, and 3 were determined in five, one, and two patients, n one patient. History of residence in a foreign country ($P < 0.01$) and imprisonment ($P < 0.01$) were a /HCV coinfection.

HIV/HCV koenfeksiyonu %0.9

CONCLUSIONS: Prevalence of HIV/HCV coinfection is urkey. The extremely rare prevalence of IDU might have a role in this low prevalence.

KEYWORDS: Hepatitis C Virus; Human Immunodeficiency Virus; Prevalence; Turkey

HIV ⟷ HBV etkileşimi

HIV ⟹ HBV etkisi

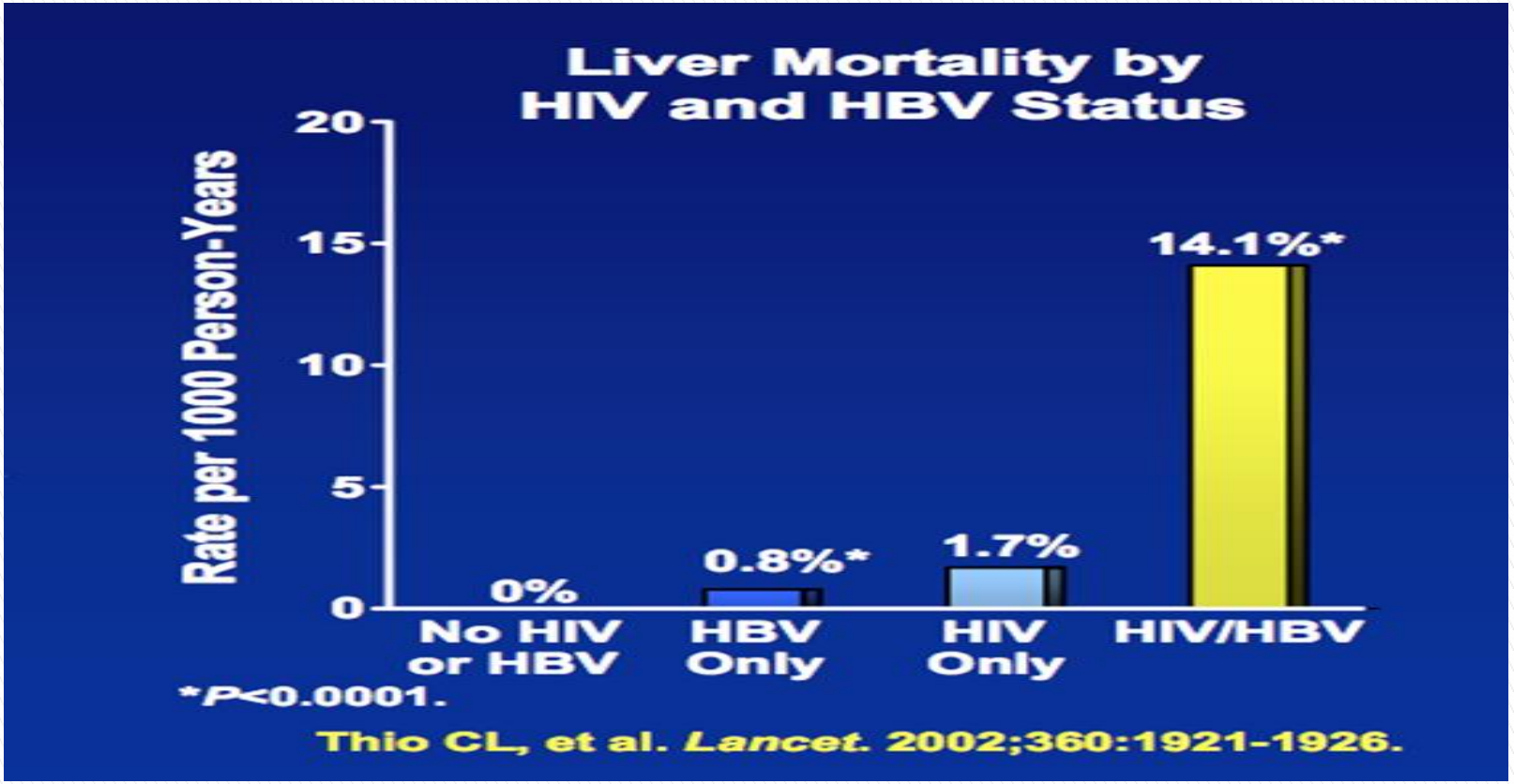
- Düşük spontan HBV klirensi
- Fibröz oluşma hızı ⇧
- Karaciğer ile ilşkili ölüm oranları ⇧

HBV ⟹ HIV etkisi

- HIV hastalığının seyrı hızlanmakta ???
- ART'nin cevabı azalmakta ???

1. Rouet F et al. J Med Virol 2004;74:34–40.
2. Hernandez MD, et al. Curr Opin HIV AIDS 2011;6:478–82.
3. Stabinski L, et al. Antivir Ther 2011;16:405–11.
4. Kaplan JE, et al. MMWR Recomm Rep 2009;58:1–207
5. Bonacini M, et al. AIDS 2004;18:2039–45.
6. Nikolopoulos GK, et al. Clin Infect Dis 2009;48:1763–71.
7. Agwale SM, et al. J Clin Virol 2004;31(Suppl. 1):S3–6.
8. Attia KA, et al. World J Hepatol 2012;4:218–23.
9. Sagoe KW, et al. JMed Virol 2012;84:6–10.
10. Wandeler G, et al. J Infect Dis 2013;208:1454-1458

HIV'İN HBV ÜZERİNDEKİ ETKİLERİ



HIV/Viral Hepatit tarama prosedürleri

- **Tarama:**

- HbsAg, Anti-HBs, Anti-HBc total
  Anti-HCV, Ant-HDV, Anti- HAV total

- **HBsAg :neg + Anti-HBc neg + AntiHBs neg ise; (CD4>200)**

- Aşılama, son aşıdan bir ay sonra Anti-HBs titresi
- Anti-HBs titresi, <10 IU ise → Çift doz aşı (40 µg)-0,1,6,12 aylarda

- **İzole anti-HBc pozitifliği;**

- Okült HBV enfeksiyon varlığı
- HBV DNA araştır
- Hepatit B aşısı ?

EACS Guidelines 2017

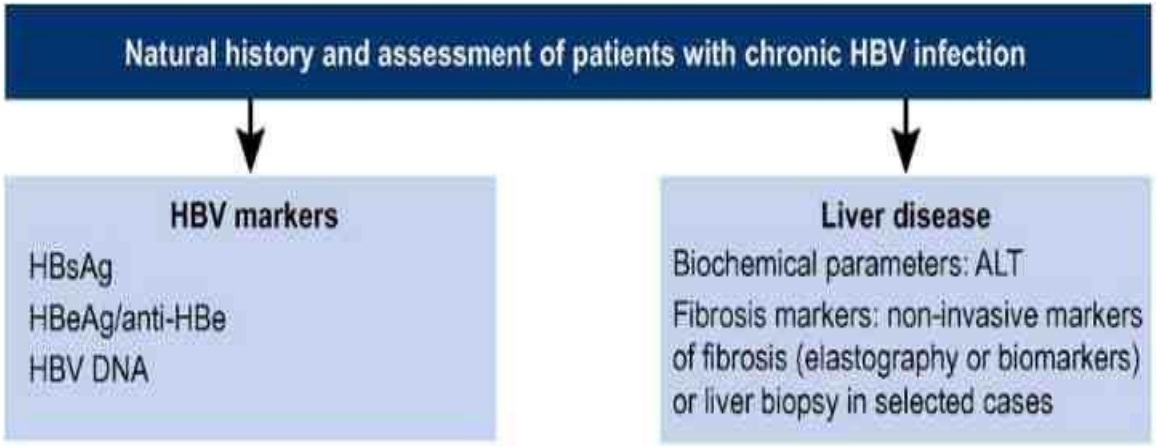
HIV'de hepatit B aşı şemaları: prospektif & RKÇ

Ref.	Yıl	n	Doz (ug)	Şema	Cevap	Öngörücüler
Standart doz						
Rey et al 1	2000	20	3 x 20	0,1,2 mo., IM	55.0%	CD4 > 500 cells/µL
Ungulkraiwit et al 2	2007	65	3 x 20	0,1,6 mo., IM	46.0%	Higher CD4; young age
Paitoonpong et al 3	2008	28	3 x 20	0,1,6 mo., IM	71.4%	Higher CD4; use of efavirenz
Irungu et al 4	2013	310	3 x 20	0,1-3,6 mo. IM	64.2%	CD4 > 500 cells/µL; female
Alternatif stratejiler						
Fonseca et al 5	2005	94 98	3 x 20 3 x 40	0,1,6 mo., IM	34.0% 47.0%	CD4 > 500 cells/µL HIV VL < 10,000 copies/mL
Cornejo-Juárez 6	2006	39 40	3 x 10 3 x 40	0,1,6 mo., IM	61.5% 60.0%	CD4 ≥ 200 cells/µL
Potsch et al 7	2010	47	3 x 40	0,1-2,6 mo. IM	89.0%	HIV VL < 80 copies/mL
Launay et al 8	2011	145 148 144	3 x 20 4 x 40 4 x 40	0,1,6 mo. IM 0,1,2,6 mo. IM 0,1,2,6 mo. ID	65.0% 82.0% 77.0%	HIV VL < 80 copies/mL Young age Four-doses

1) Vaccine 2000; 18: 11 ... 3) Scand J Infect Dis 2008; 40: 54. 4) J Infect Dis 2013; 207: 402.
2) 5) Vaccine 2005; 23: 2902-29 ... AIDS Res Ther 2006; 3: 9. 7) Vaccine 2010; 28: 1447. 8) JAMA 2011; 305: 1432.

Alıntı:Sun HY, et al. World J Gastroent ... 14;20:14598

EASL 2017
Kronik HBV enfeksiyonu:değerlendirme



	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10^7 IU/ml	10^4-10^7 IU/ml	<2,000 IU/ml°°	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

*Persistently or intermittently > traditional cut-off values (ULN 40 IU/ml).

EASL 2017 Clinical Practice Guidelines on the Management of Hepatitis B Virus Infection. Journal of Hepatology (... 18 2017).

Hepatit B aşısı antikor oluşturmuyor???

TDF, duyarlı HIV (+) bireylerde HBV enfeksiyonlarını önlüyor (Amsterdam)

Kaplan–Meier: HBV free-survival (MSM)

2;942 HIV(+) hasta, retrospektif

871 ‘HBV-duyarlı’

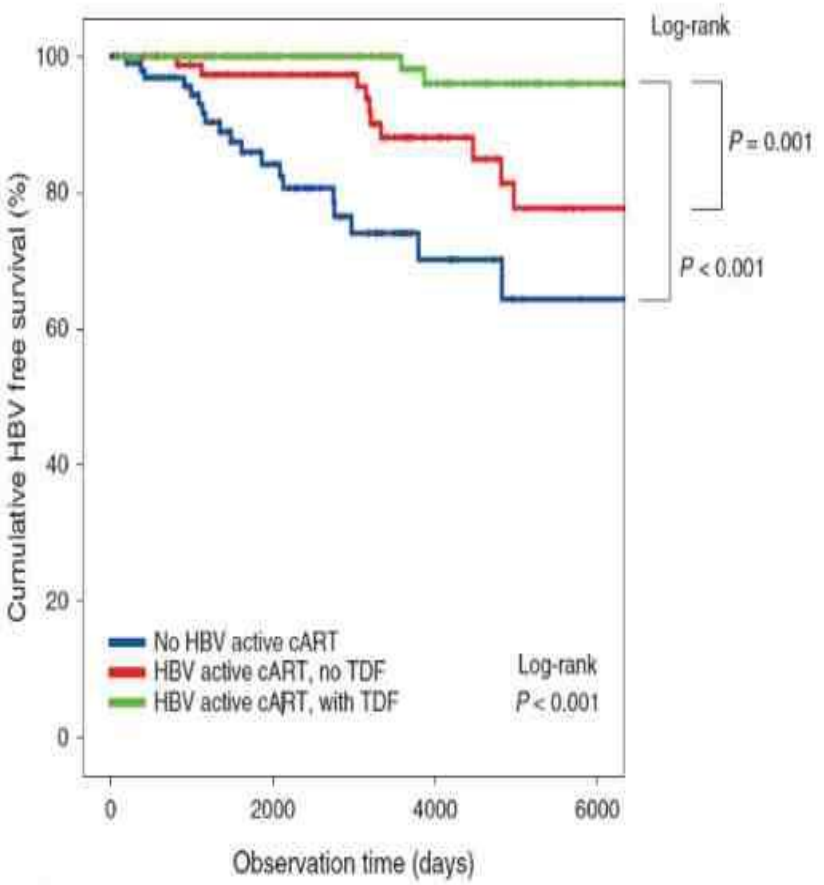
- **33’ü HBV ile enfekte olmuş**

ESE’lerde en düşük insidans, **TDF** içeren ART kullanan hastalarda saptanmış.

TDF ⇒ **0.14**/100 hasta yıl

LAM ⇒ 1.36

HBV’siz ⇒ **2.85**



Numbers in observation

No HBV active cART	106	49	18	7
HBV active cART, no TDF	81	63	32	14
HBV active cART, with TDF	194	53	42	14

Heuft M et al. AIDS 2014; 28:999–1005

TDF veya 3TC duyarlı HIV (+) bireylerde HBV enfeksiyonlarını önlüyor (Tokyo)

354 HIV+ MSM, non HBV vaccinated and negative for HBsAg, HBsAb, and HBcAb at baseline

ART	Observation period (PY)	HBV incident infection	Hazard ratio (95% CI)	P
No ART	446	30†	1	–
ART with 3TC or TDF*	1047	7	0.113 (0.049–2.61)	<.001
3TC - ART	814	7†	–	–
TDF-ART	233	0	–	–
Other ART	114	6†	0.924 (0.381–2.239)	.861

*All participants who took FTC received TDF/FTC, therefore, such treatment status was categorized into TDF-ART

†rtM204V/L mutation detected in 2 patients with no ART-other ART and 3 patients with 3TC-ART

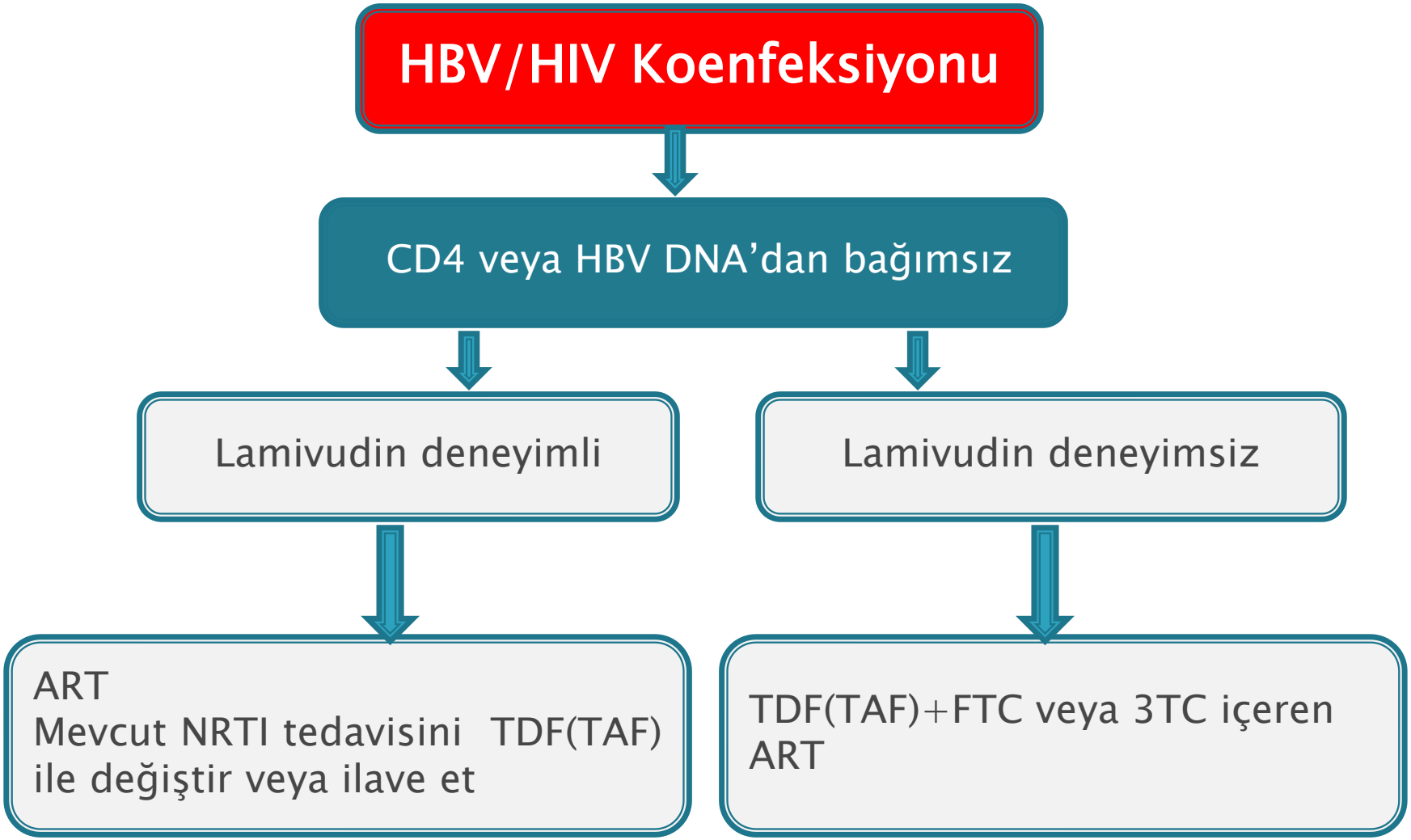
Gatanaga H et al. Clin Infect Dis 2013;56:1812–1819

HIV ile enfekte kişilerde HBV tedavisi

Rehber	Öneri
IAS-USA 2016	TDF veya TAF, 3TC veya FTC içeren ART
DHHS 2017	TDF/FTC, TAF/FTC, veya TDF +3TC, içeren ART
EACS 2017	TDF veya TAF bazlı ART
EASL 2017	TDF- veya TAF-bazlı ART

1. Gunthard HF, et al. JAMA 2016; 316: 191-120
2. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0
3. EASL HBV Guidelines 2017
4. EACS Guidelines 2017

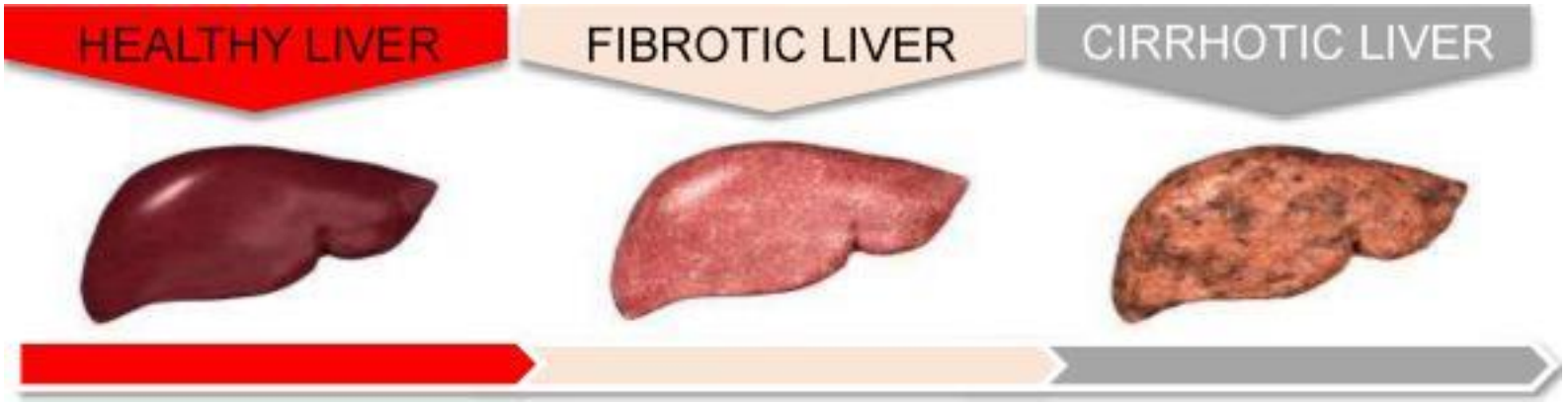
Yeni Rehberler 2017



CrCL>60 ml: TDF veya TAF
CrCl 30-59:TAF

EACS 2017, DHHS 2017, WHO 2016

HIV/HCV koenfeksiyonu: Çifte bela



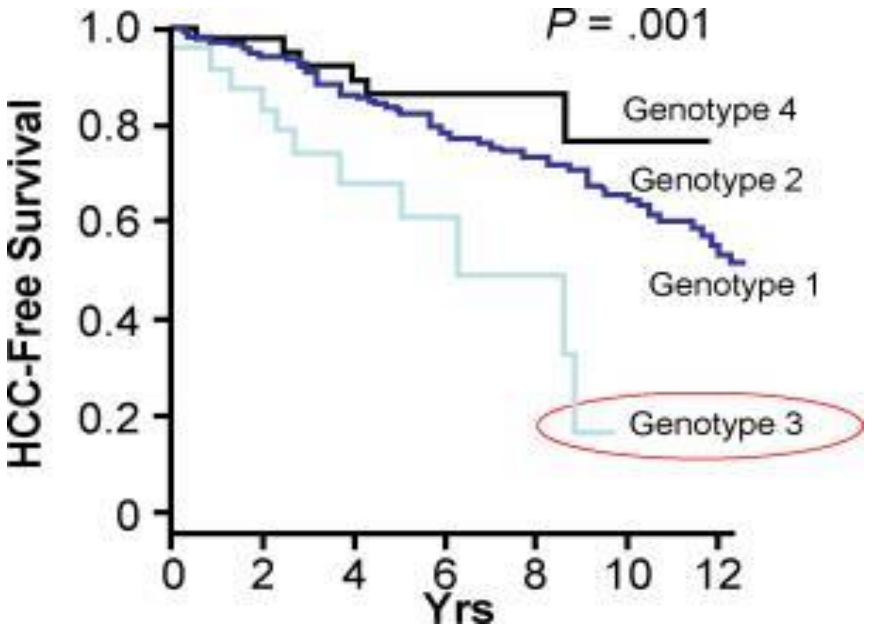
- HIV (+) kişilerde → Hepatit C'nin kronikleşme riski %90

- Fibröz oranı (2-5) kat daha fazla
- Siroz (2-3 kat)
- Karaciğer yetmezliği (16 kat)
- Hepatoselüler kanser (6 kat)

Genotip 3 ve karaciğer fibrozu/HSK

DEA'lara en dirençli genotip

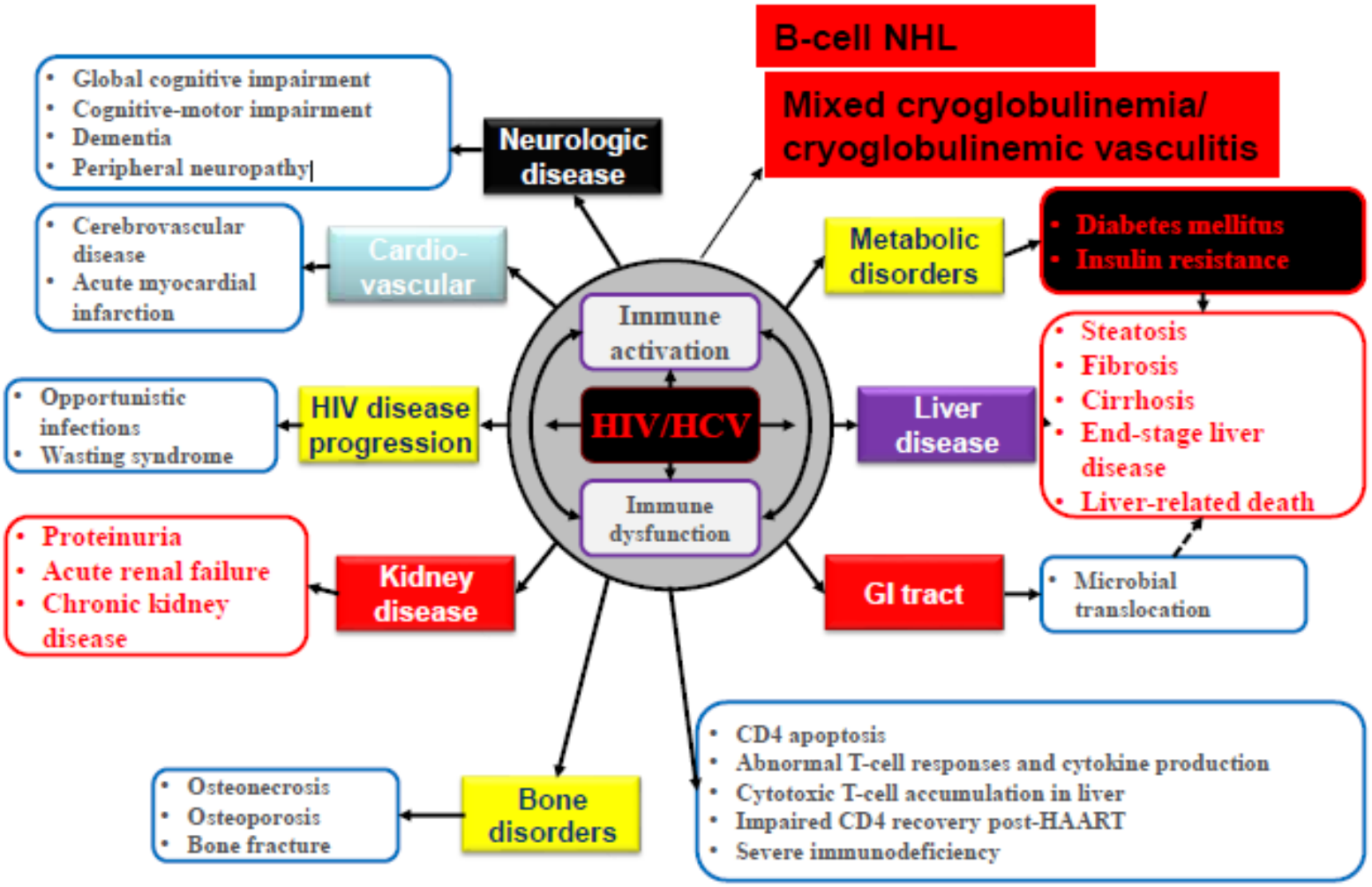
HCC-Free Survival by Genotype[2]



Genotype	1	251	207	166	85	56
Genotype	2	33	27	24	8	3
Genotype	3	25	20	10	3	1
Genotype	4	44	37	25	6	3

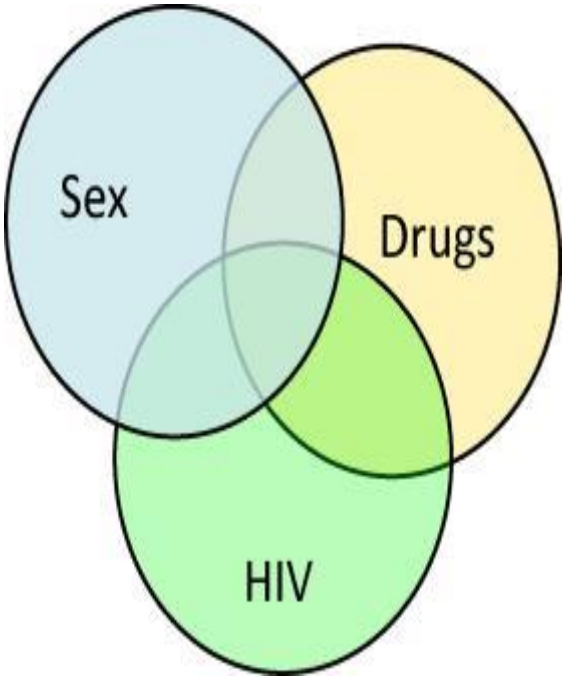
1. Messina JP, et al. Hepatology. 2015;61:77-87.
2. Nkontchou G, et al. J Viral Hepat. 2011;18:e516-e522.

HIV/HCV koenfeksiyonu: ekstrahepatik etkiler (%40-70)



AOperskalski EA and Kovacs A. Curr HIV/AIDS Rep. 2011;8:12-22.

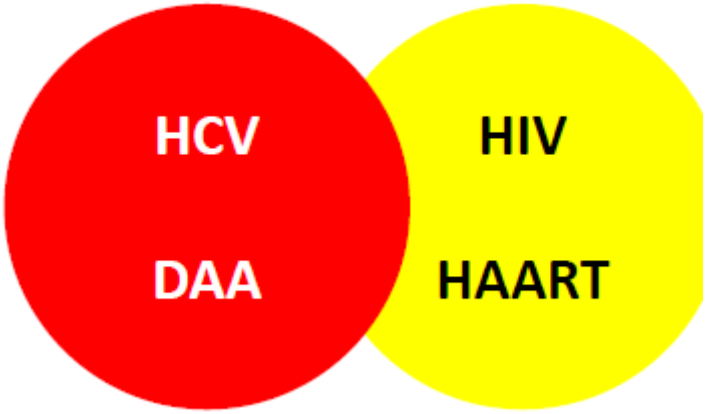
HCV enfeksiyonu= ESE'lerde CYBE



1. Terrault NA, et al. Hepatology. 2013;57:881-899. 2. Thomas SL, et al. Int J Epidemiol. 1998;27:108-117. 3. Larsen C, et al. PLoS One. 2011;6:1-9. 4. Shepard CW, et al. Lancet Infect Dis. 2005;5:558-567.

HIV-HCV

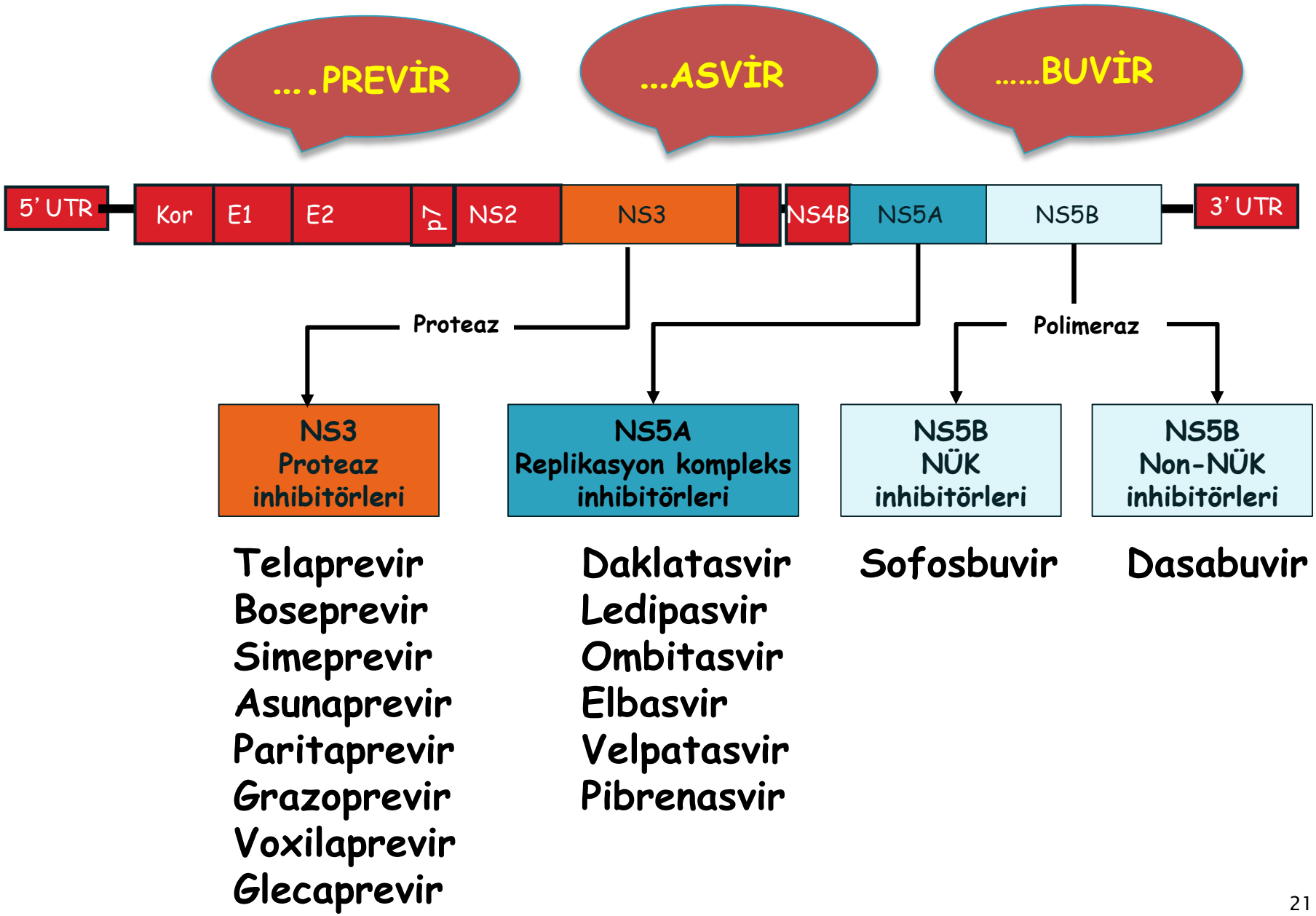
- >%90 kalıcı virolojik cevap
- Daha az toksisite
- Yönetilebilen ilaç-ilaç etkileşimleri



HCV- DEA

Rejim	Genotipler
Grazoprevir/elbasvir	1, 4
Ombitasvir/paritaprevir/ritonavir	4
Ombitasvir/paritaprevir/ritona vir + dasabuvir	1
Sofosbuvir + daclatasvir *	1, 3
Sofosbuvir/ledipasvir	1,4, 5, 6
Simeprevir + sofosbuvir	1
Sofosbuvir/velpatasvir *	1,2, 3, 4, 5,6
Sofosbuvir/velpatasvir/voxilaprevir*	1,2, 3, 4, 5,6
Glecaprevir/pibrentasvir*	1,2, 3, 4, 5,6

HCV'de doğrudan etkili antiviraller



DEA:İlaç etkileşimleri-1

www.hiv-druginteractions.org

www.hep-druginteractions.org

	DCV	EBR/ GZR	GLP/ PIB	LED/ SOF	OBV/ PTV/r	OBV/ PTV/r +DSV	SMV	SOF	SOF/ VEL	SOF/ VEL/ VOX	RBV
HIV Drugs											
Entry/Integrase Inhibitors											
Dolutegravir	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆
Elvitegravir/cobi /FTC/TAF	■	●	◆	◆	●	●	●	◆	◆	◆	◆
Elvitegravir/cobi/FTC/TDF	■	●	◆	■	●	●	●	◆	■	■	◆
Maraviroc	◆	◆	◆	◆	■	■	◆	◆	◆	◆	◆
Raltegravir	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆
NNRTIs											
Delavirdine	■	◆	◆	◆	■	■	●	◆	◆	◆	◆
Efavirenz	■	●	●	■	●	●	●	◆	●	●	◆
Etravirine	■	●	●	◆	●	●	●	◆	●	●	◆
Nevirapine	■	●	●	◆	●	●	●	◆	●	●	◆
Rilpivirine	◆	◆	◆	◆	■	■	◆	◆	◆	◆	◆

DEA:İlaç etkileşimleri-2

www.hiv-druginteractions.org

www.hep-druginteractions.org

	DCV	EBR/ GZR	GLP/ PIB	LED/ SOF	OBV/ PTV/r	OBV/ PTV/r +DSV	SMV	SOF	SOF/ VEL	SOF/ VEL/ VOX	RBV
NRTIs											
Abacavir	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	■
Didanosine	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	●
Emtricitabine (FTC)	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	■
FTC + Tenofovir alafenamide	◆	◆	◆	◆	■	■	◆	◆	◆	■	◆
Lamivudine	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	■
Stavudine	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	■
Tenofovir-DF (TDF)	◆	◆	◆	■	◆	◆	◆	◆	■	■	■
Zidovudine	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	●
Protease Inhibitors											
Atazanavir	■	●	●	◆	■	■	●	◆	◆	●	■
Cobicistat (with ATV or DRV)	■	●	■	■	●	●	●	◆	◆	■	◆
Darunavir	◆	●	●	◆	■	■	●	◆	◆	■	◆
Fosamprenavir	■	●	●	◆	■	■	●	◆	◆	●	◆
Indinavir	■	●	●	◆	●	●	●	◆	◆	●	◆
Lopinavir	◆	●	●	■	●	●	●	◆	◆	●	◆
Nelfinavir	◆	●	●	◆	■	■	●	●	◆	●	◆
Ritonavir	■	●	●	◆	●	●	●	◆	◆	■	◆
Saquinavir	■	●	●	◆	●	●	●	◆	◆	●	◆
Tipranavir	■	●	●	●	●	●	●	●	●	●	◆

HCV

HIV

HBV