Rehberler Işığında HIV'de Tedavi Alternatifleri

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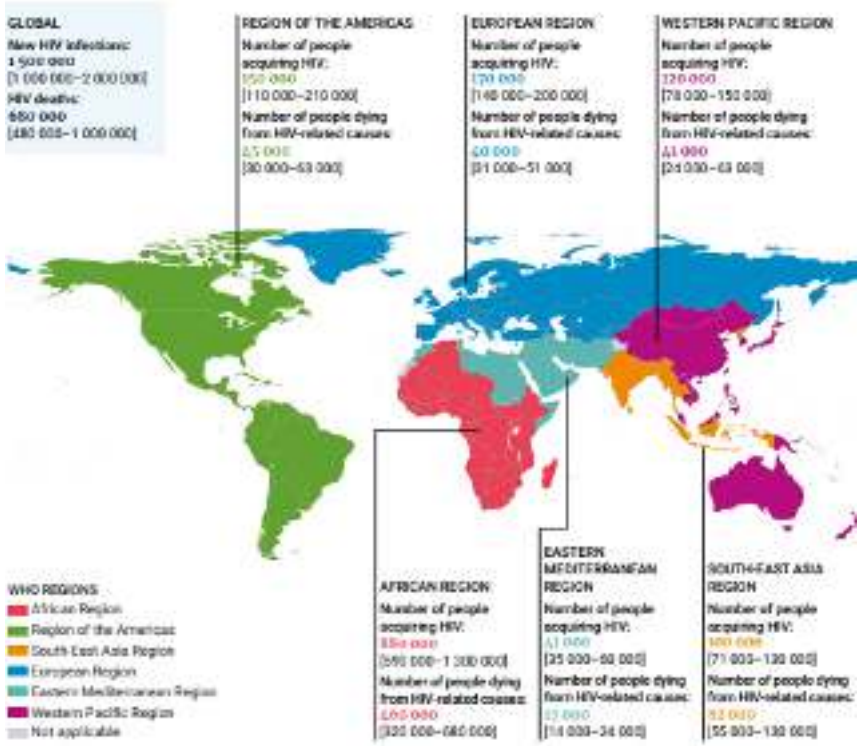
08.06.2022

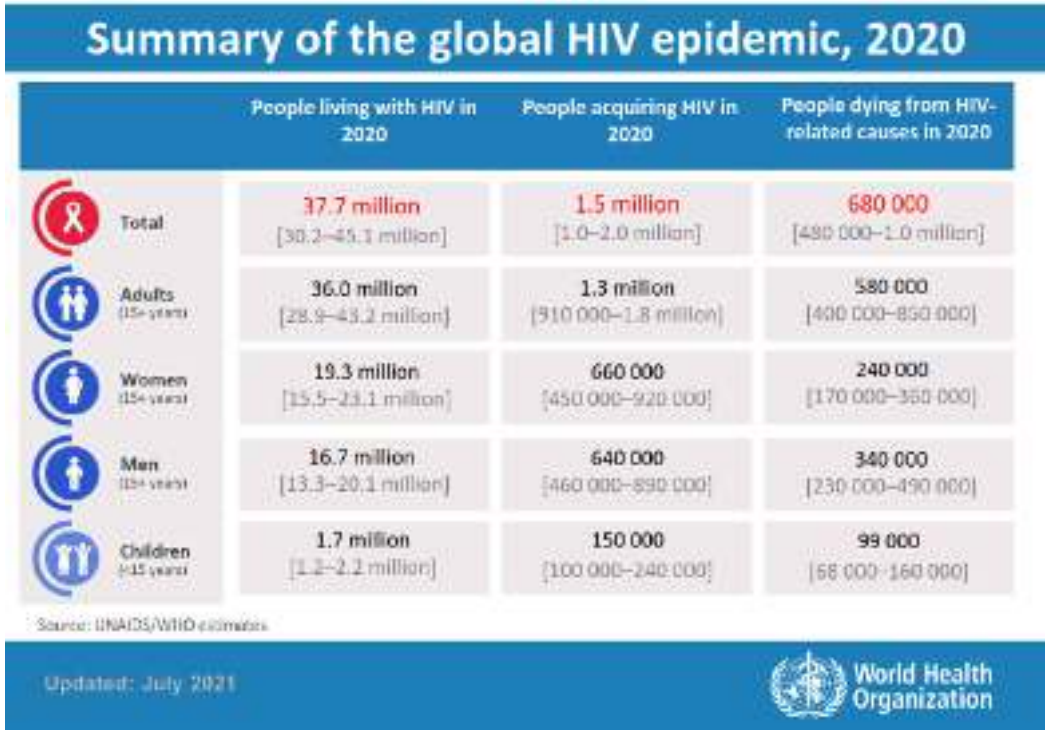
Sunum Planı

- Giriş
- Rehberler ve faydaları
- Tedavi hedefi
- Kime, ne zaman tedavi
- Tedavi öncesi değerlendirme
- Rehberlerde antiretroviral tedavi seçenekleri

Dünyada HIV Enfeksiyonu



37.7 milyon enfekte kişi



Summary of the global HIV epidemic, 2020

	People living with HIV in 2020	People acquiring HIV in 2020	People dying from HIV-related causes in 2020
Total	37.7 million [30.2–45.1 million]	1.5 million [1.0–2.0 million]	680 000 [480 000–1.0 million]
Adults (15+ years)	36.0 million [28.9–43.2 million]	1.3 million [910 000–1.8 million]	580 000 [400 000–850 000]
Women (15+ years)	19.3 million [15.5–23.1 million]	660 000 [450 000–920 000]	240 000 [170 000–360 000]
Men (15+ years)	16.7 million [13.3–20.1 million]	640 000 [460 000–890 000]	340 000 [230 000–490 000]
Children (<15 years)	1.7 million [1.2–2.2 million]	150 000 [100 000–240 000]	99 000 [68 000–160 000]

Source: UNAIDS/WHO estimates

Updated: July 2021

World Health Organization

79.3 milyon enfekte kişi

36.3 milyon ölüm

UNAIDS/WHO, 2021

https://www.unaids.org/en/resources/fact-sheet

Türkiye'de HIV Enfeksiyonu

- İlk HIV pozitif vaka bildirimi 1985 yılında
- Vaka sayısı 15 Kasım 2021 tarihinde 29,284 HIV(+) kişi ve 2052 AIDS

HIV / AIDS TOPLAM VAKA VE ÖLÜM SAYILARININ SON 5 YIL DAĞILIMI

YILLAR	HIV	AIDS	TOPLAM	ÖLÜM
2017	3146	126	3272	32
2018	3825	130	3955	31
2019	4015	134	4149	39
2020	2797	68	2865	37
2021	2021	53	2074	25

https://hsgm.saglik.gov.tr/tr/bulasici-hastaliklar/hiv-aids/hiv-aids-liste/hiv-aids-istatislik.html

CDC

MMWR

Weekly

Opportunistic Infections and Kaposi's Sarcoma among Haitians in the United States

Yıl 1981
ABD-Haitili
Göçmenler

CDC

MMWR

Weekly

September 24, 1982 / 31(37);507-508,513-514

Persons using assistive technology might not be able to fully access information in this file. For assistance, please send e-mail to: mmwrq@cdc.gov. Type 508 Accommodation and the title of the report in the subject line of e-mail.

Current Trends Update on Acquired Immune Deficiency Syndrome (AIDS) -- United States

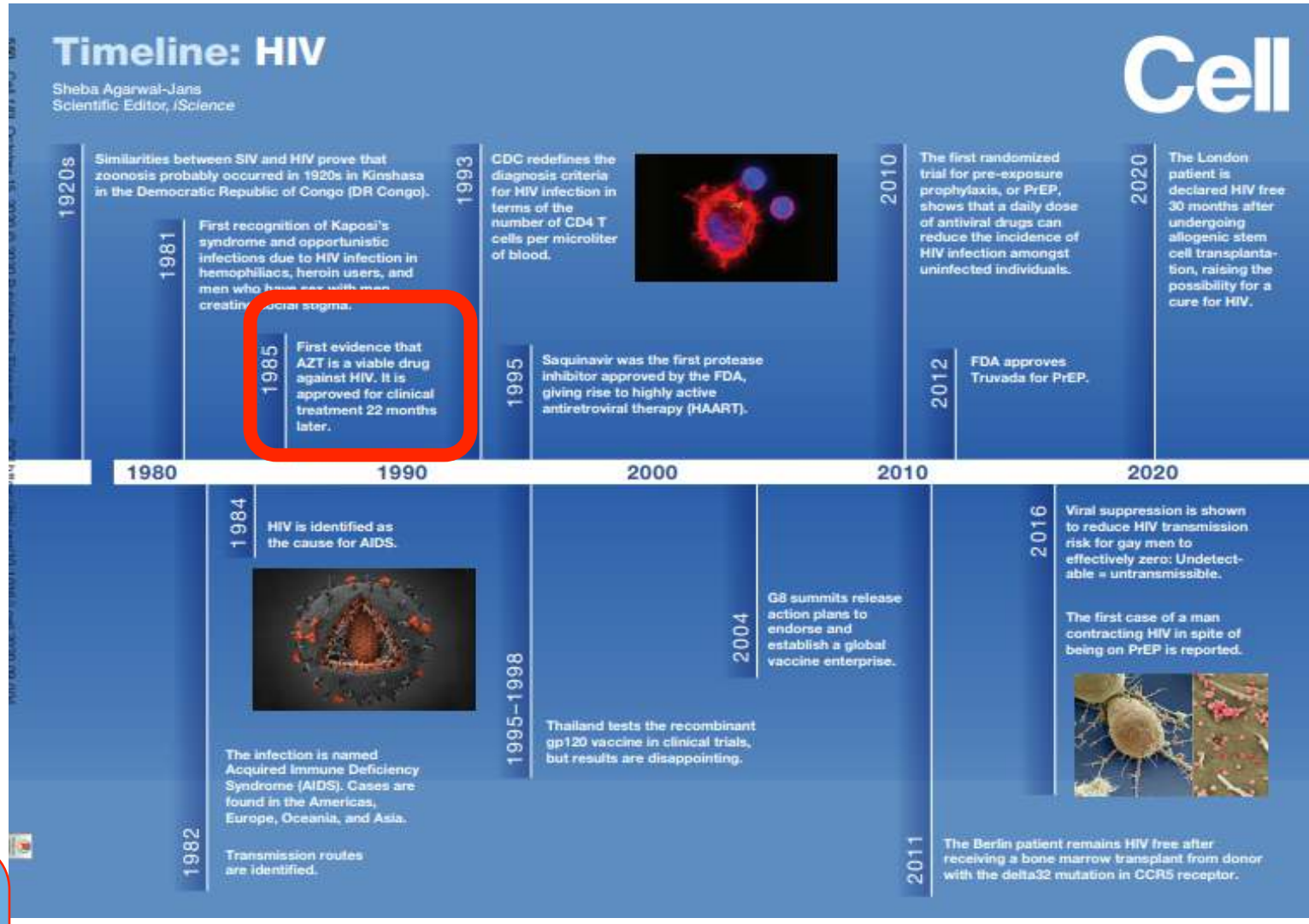
Between June 1, 1981, and September 15, 1982, CDC received reports of 593 cases of acq

Analysis of reported AIDS cases shows that 51% had Pneumocystis carinii pneumonia (PC (OOI) predictive of cellular immunodeficiency); 30% had KS without PCP (with or witho neither PCP nor KS. The overall mortality rate for cases of PCP without KS (47%) was m PCP and KS (68%) was more than three times as great. The mortality rate for OOI with n

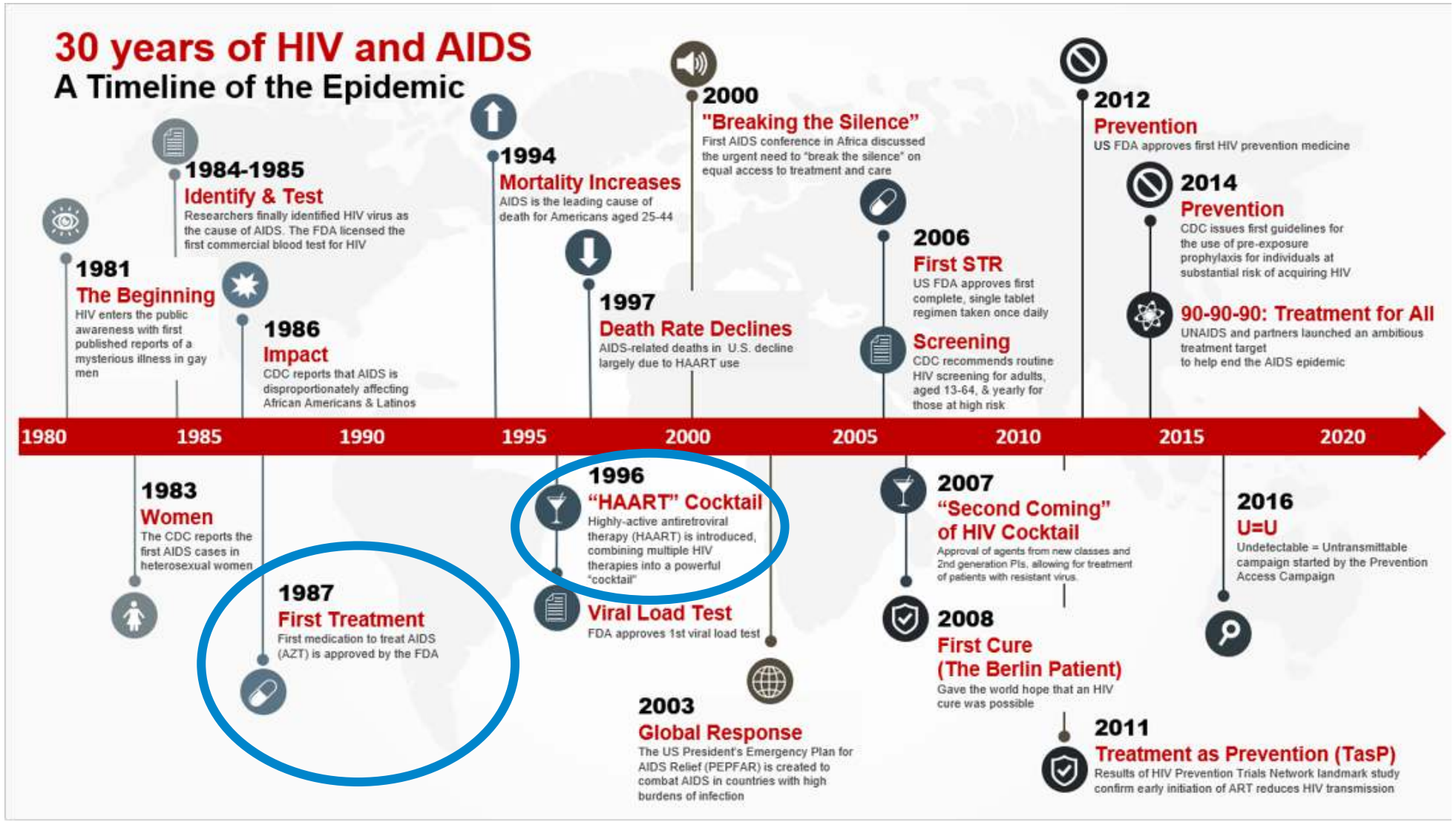
The incidence of AIDS by date of diagnosis (assuming an almost constant population at ri average of one to two cases are now diagnosed every day. Although the overall case morta over a year ago.

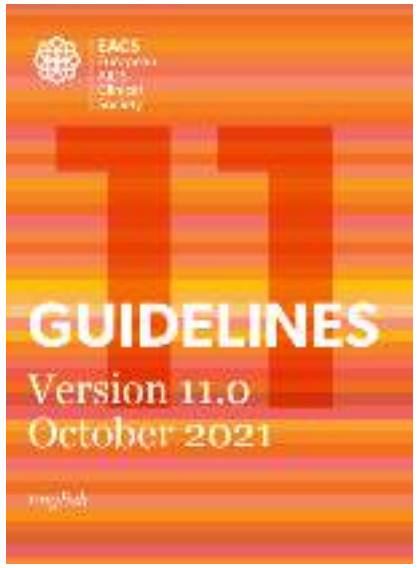
Almost 80% of reported AIDS cases in the United States were concentrated in six metrop distribution was not simply a reflection of population size in those areas; for example, the 1982, in New York City and San Francisco was roughly 10 times greater than that of the c District of Columbia, and CDC has received additional reports of 41 cases from 10 foreign

Yıl 1982
CDC → AIDS
Human
Immunodeficiency
Virus (HIV-1)



Agarwal-Jans S. Timeline: HIV. Cell. 2020 ;183(2):550.


30 years of HIV and AIDS
A Timeline of the Epidemic
1981
The Beginning
HIV enters the public awareness with first published reports of a mysterious illness in gay men
1983
Women
The CDC reports the first AIDS cases in heterosexual women
1984-1985
Identify & Test
Researchers finally identified HIV virus as the cause of AIDS. The FDA licensed the first commercial blood test for HIV
1986
Impact
CDC reports that AIDS is disproportionately affecting African Americans & Latinos
1987
First Treatment
First medication to treat AIDS (AZT) is approved by the FDA
1994
Mortality Increases
AIDS is the leading cause of death for Americans aged 25-44
1996
"HAART" Cocktail
Highly-active antiretroviral therapy (HAART) is introduced, combining multiple HIV therapies into a powerful "cocktail"
1997
Death Rate Declines
AIDS-related deaths in U.S. decline largely due to HAART use
Viral Load Test
FDA approves 1st viral load test
2000
"Breaking the Silence"
First AIDS conference in Africa discussed the urgent need to "break the silence" on equal access to treatment and care
2003
Global Response
The US President's Emergency Plan for AIDS Relief (PEPFAR) is created to combat AIDS in countries with high burdens of infection
2006
First STR
US FDA approves first complete, single tablet regimen taken once daily
Screening
CDC recommends routine HIV screening for adults, aged 13-64, & yearly for those at high risk
2007
"Second Coming" of HIV Cocktail
Approval of agents from new classes and 2nd generation PIs, allowing for treatment of patients with resistant virus.
2008
First Cure (The Berlin Patient)
Gave the world hope that an HIV cure was possible
2011
Treatment as Prevention (TasP)
Results of HIV Prevention Trials Network landmark study confirm early initiation of ART reduces HIV transmission
2012
Prevention
US FDA approves first HIV prevention medicine
2014
Prevention
CDC issues first guidelines for the use of pre-exposure prophylaxis for individuals at substantial risk of acquiring HIV
90-90-90: Treatment for All
UNAIDS and partners launched an ambitious treatment target to help end the AIDS epidemic
2016
U=U
Undetectable = Untransmittable campaign started by the Prevention Access Campaign
1980
1985
1990
1995
2000
2005
2010
2015
2020

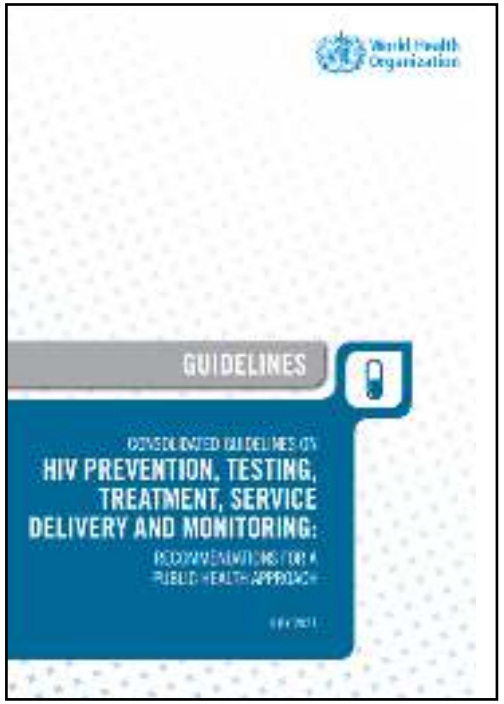

EACS
11
GUIDELINES
Version 11.0
October 2021


HIV/AIDS
Tanı Tedavi Rehberi
T.C. SAĞLIK BAKANLIĞI
HIV


HIV/AIDS
TANI İZLEM VE TEDAVİ
EL KİTABI
KLİMİK


Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV
Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)


AIDSinfo
Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

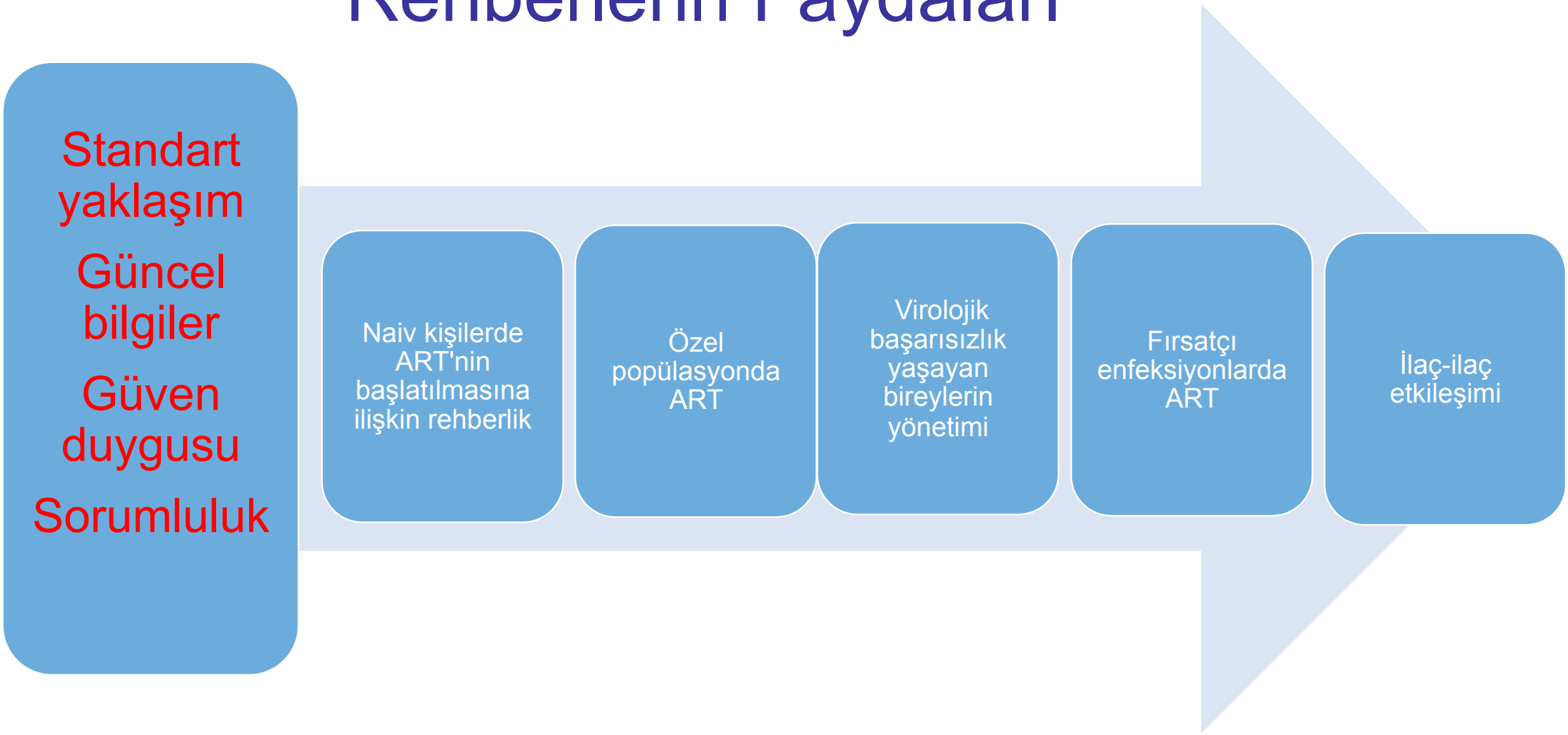

World Health Organization
GUIDELINES
HIV PREVENTION, TESTING, TREATMENT, SERVICE DELIVERY AND MONITORING:


BHIVA
British HIV Association


IAS

DERNEK	REHBER	SON GÜNCELLEME
Department of Health and Human Services (DHHS)	Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV	Haziran 2021
European AIDS Clinical Society (EACS)	Guidelines, Version 11.0	Ekim 2021
AIDS ve CYBH Derneği, EKMUD, HIV/ AIDS Korunma ve Eğitim Derneği, HIVEND, KLİMİK	HIV/AIDS Tanı İzlem ve Tedavi El Kitabı	Aralık 2021, sürüm 2.0

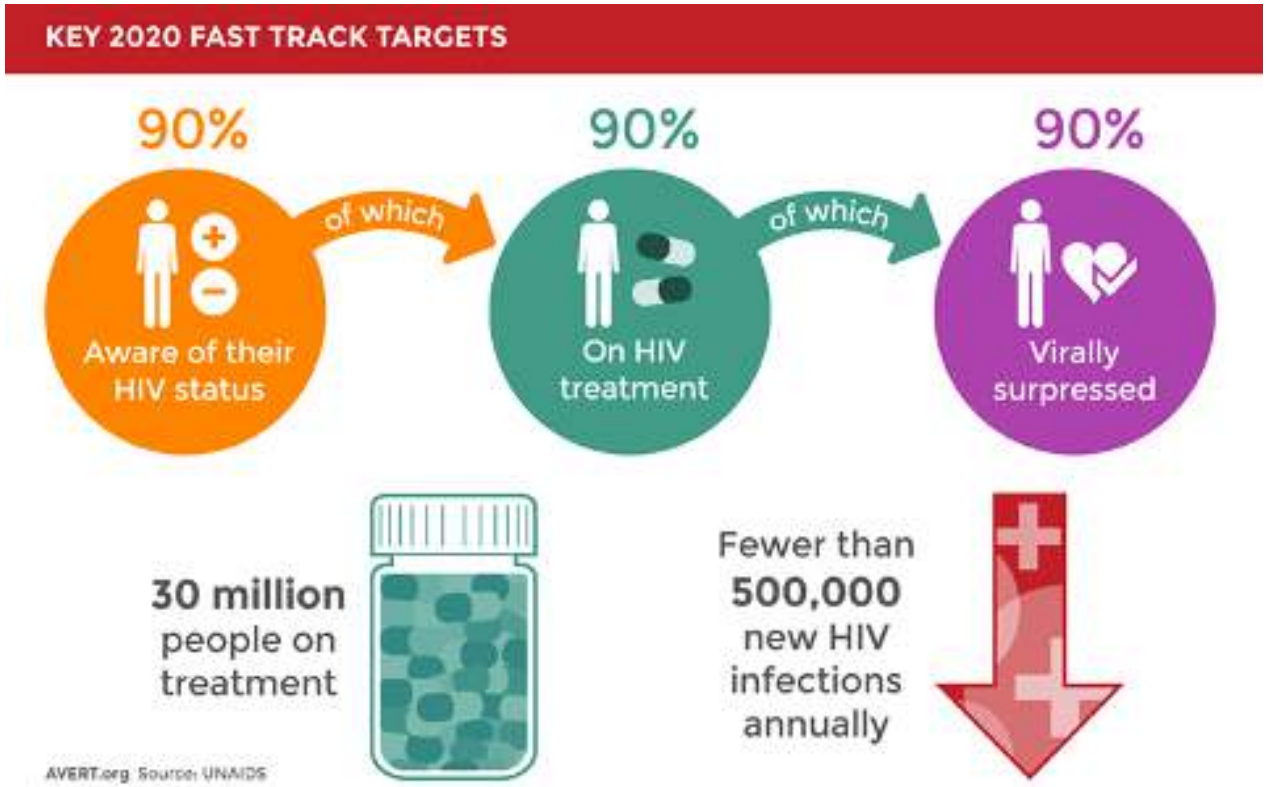
Rehberlerin Faydaları



Antiretroviral Tedavi Hedefi

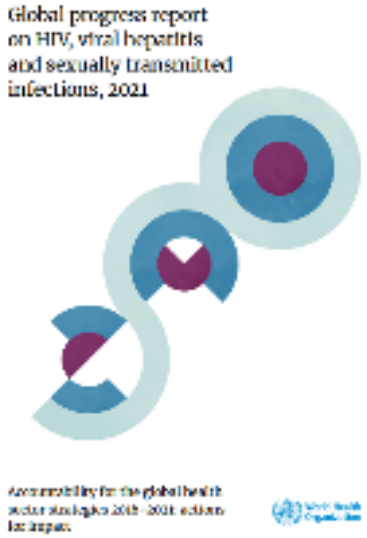
- HIV RNA - viral yükü maksimum seviye ve süre baskılamak
- İmmünolojik fonksiyonları korumak, iyileştirmek
- HIV ile ilişkili morbiditeyi azaltmak, yaşam süresini ve kalitesini arttırmak
- HIV bulaşını önlemek

DHHS,EACS,WHO,HIV/AIDS TANI TEDAVİ REHBERİ, BHIVA

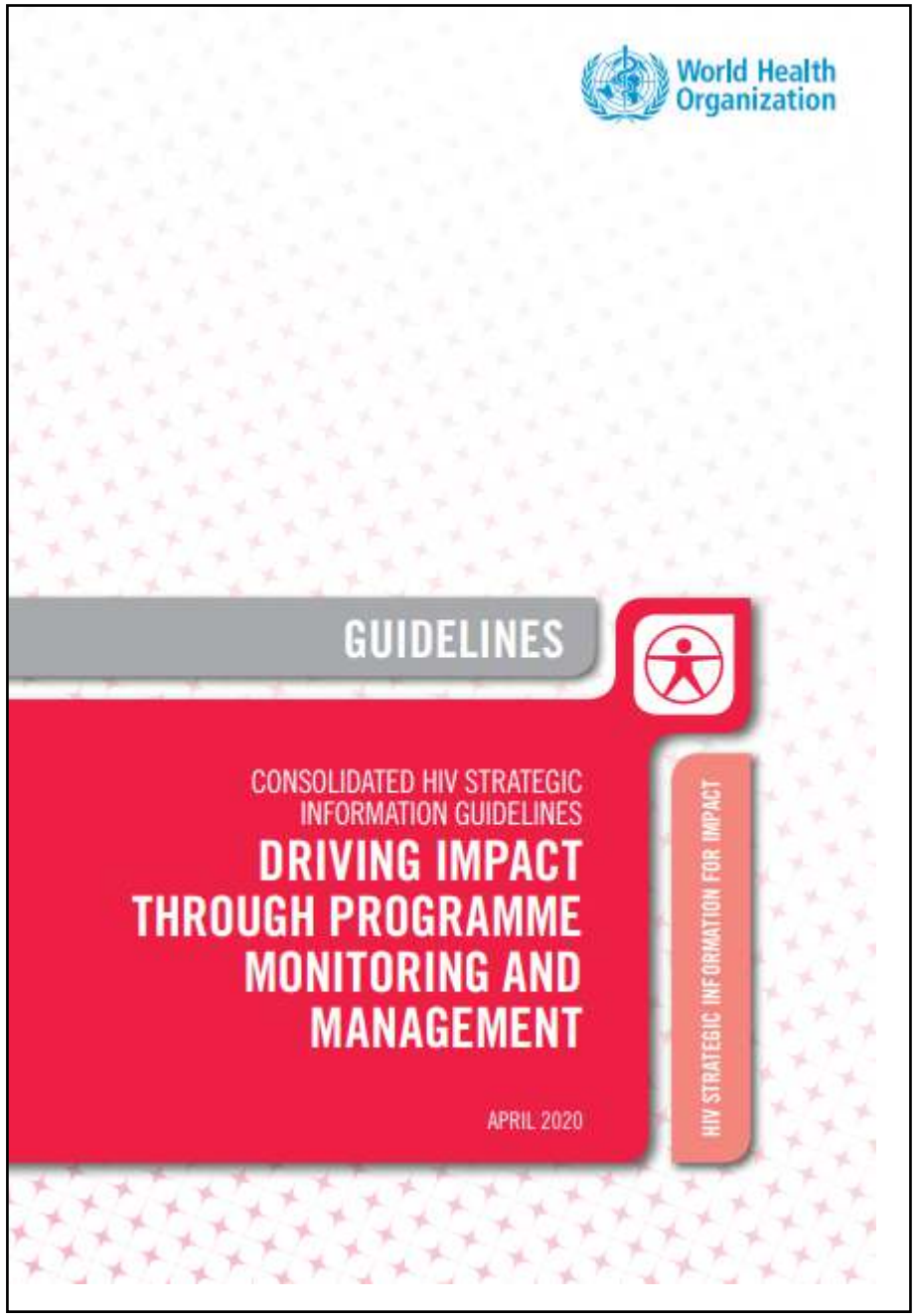


2020'nin sonunda

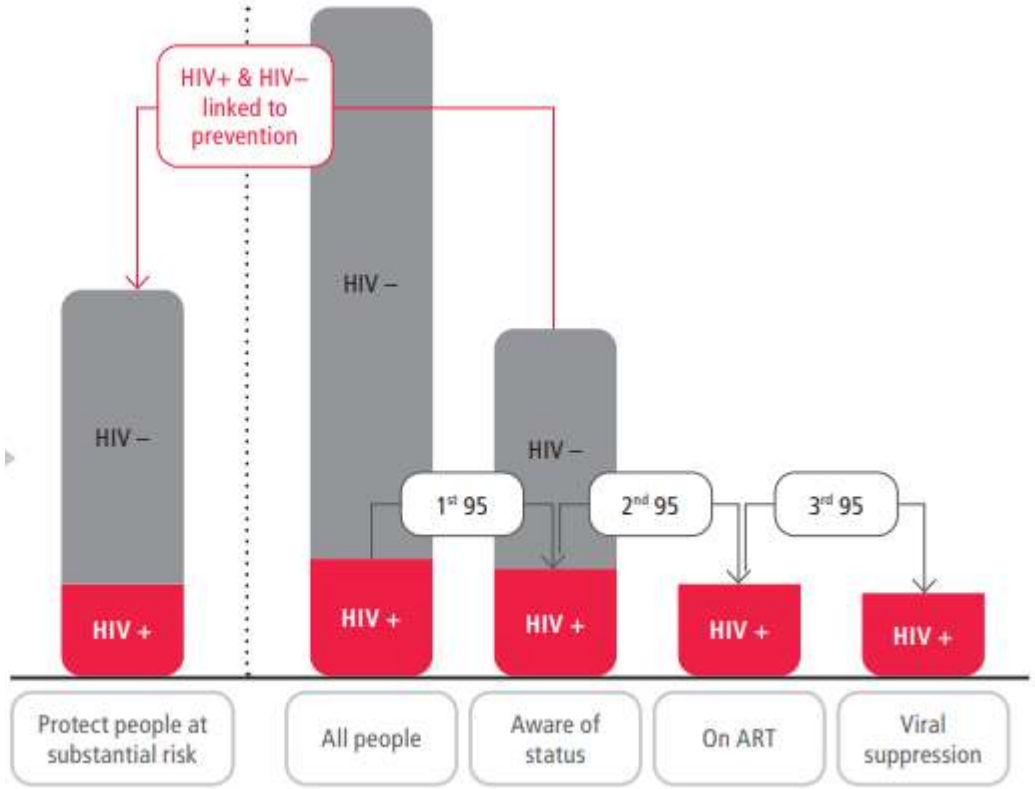
- %84'ü HIV durumunu biliyor
- %87 ART alıyor
- Tedavi görenlerin %90 viral baskılanma



UNAIDS DATA 2021
https://www.unaids.org/sites/default/files/media_asset/JC3032_AIDS_Data_book_2021_En.pdf



2030 Hedefi 95-95-95



https://apps.who.int/iris/handle/10665/331697

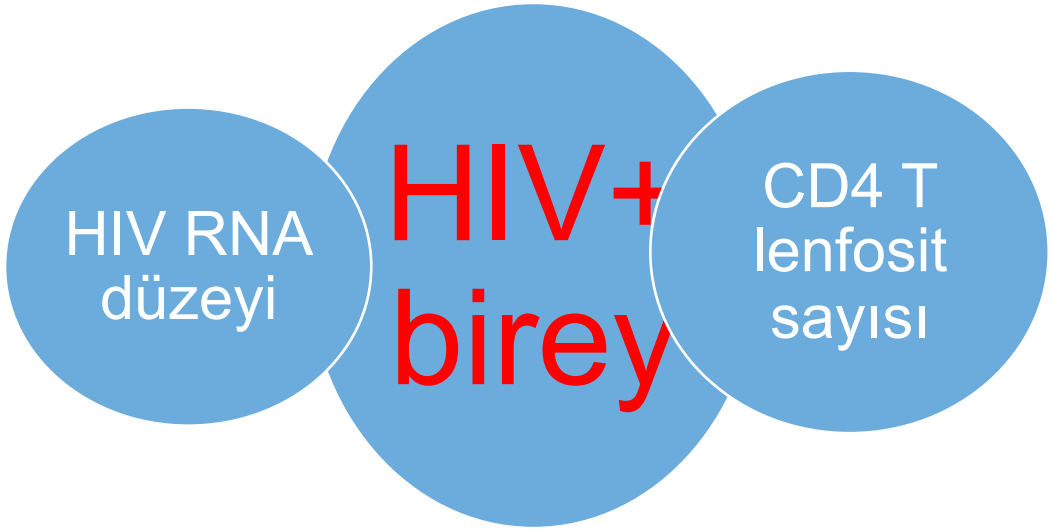
- Başarılı HAART ilişkili virolojik baskılama ile HIV bulaş riski dramatik ölçüde azalır

  Cohen MS et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. *N Engl J Med.* 2016;375(9):830-839.

- ART kullanan hastalarda yaşam beklentisi, HIV-negatif emsallerine benzer

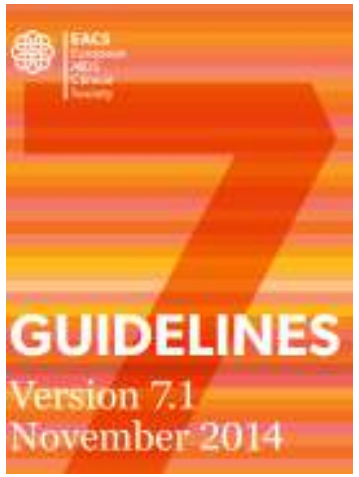
  May MT, et al. Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy. *AIDS.* 2014;28(8):1193-1202.

Kimleri Tedavi Edelim?



Recommendations for Initiation of ART in HIV-positive Persons without Prior ART Exposure[1]

Present condition/circumstance	Current CD4 count[4,5]	
	350-500	> 500
Asymptomatic HIV infection	C	C
To reduce transmission of HIV	C	C
Symptomatic HIV disease (CDC B or C conditions) incl. tuberculosis	R	R
Primary HIV infection	C	C
Pregnancy (before third trimester)	R	R
Conditions (likely or possibly) associated with HIV, other than CDC stage B or C disease:	R	R
• HIV associated kidney disease	R	R
• HIV-associated neurocognitive impairment	R	R
• Hodgkin's lymphoma	R	R
• HPV associated cancers	R	R
• Other non-AIDS-defining cancers requiring chemo- and/or radiotherapy	C	C
• Autoimmune disease – otherwise unexplained	C	C
• High risk for CVD (> 20% estimated 10-yr risk) or history of CVD	C	C
Chronic viral hepatitis:		
• HBV requiring anti-HBV treatment	R	R
• HBV not requiring anti-HBV treatment	R[6]	C
• HCV for which anti-HCV treatment is being considered or given	R[4]	C



ART is always recommended in any HIV-positive person with a current CD4 count below 350 cells/µL.

R use of ART is recommended
C use of ART should be considered and actively discussed with the HIV-positive person; under these circumstances, some experts would

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 27, 2015 VOL. 373 NO. 9

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

- Nisan 2009 - Aralık 2013, 35 ülke, 4685 hasta
- CD4+ T lenfosit sayısı >500 olan ve <350 ART başlama
- ART CD4+ T lenfosit sayısı >500 başlananlarda net faydalar

Ertelenen Tedavi

Hemen Başlanan Tedavi

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

- Sahra altı Afrika, Mart 2008 - Ocak 2015, 2056 hasta
- Erken ART başlanan hastalar, ertelenerek ART başlananlarla karşılaştırıldığında ölüm ve HIV ile ilişkili ciddi hastalık riski daha düşük

N Engl J Med. 2015;373(9):808-22.

4.4 When to start ART

Recommendations (2016)

ART should be initiated for all people living with HIV regardless of WHO clinical stage and at any CD4 cell count.

World Health Organization

The TEMPRANO and START trials had very similar estimates for the protective effect of ART among individuals with HIV who had CD4 counts >500 cells/mm^3, further supporting the Panel's recommendation that ART be initiated in all patients regardless of CD4 count.

ART is recommended in all adult PLWH, irrespective of CD4 counts[i]

EACS European AIDS Clinical Society

Asemptomatik, semptomatik, tüm HIV ile enfekte kişilere, HIV pozitifliği saptanır saptanmaz antiretroviral tedavi (ART) olabildiğince erken başlanmalıdır. Bu sayede, etkin viral

HIV/AIDS

Tanı Tedavi Rehberi

- We recommend that all people living with HIV should be on ART (Grade 1A).

BHIVA British HIV Association

4.5.1 Rapid ART initiation

Recommendation (2017)

7 gün içinde ART başlanması
WHO

Hızlı ART

Aynı gün/Acil ART

Initiation of Antiretroviral Therapy (Last updated December 18, 2019; last reviewed December 18, 2019)

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality (AI) and to prevent the transmission of HIV to others (AI).
• The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV (AII).

Mümkün olan en kısa sürede
WHO, BHIVA, DHHS, IAS
EACS, HIV/AIDS EL KİTABI

Acil ART / Hızlı ART Kimlere?

- Semptomatik Primer HIV Enfeksiyonu
- Hastanın aynı gün tedaviye başlama isteği ve klinik uygunluk
- Gebelik

WHO,BHIVA,DHHS,EACS

Circumstances where immediate treatment initiation should be advised

Acute infection
Severe or prolonged symptoms
Neurological disease
Age ≥ 50 years
CD4 count < 350 cells/μL
Pregnancy

- CD4 T lenfosit sayısı ne kadar düşükse ART o kadar acil başlanmalı
- AIDS tanımlayan hastalık
- HIV ile ilişkili nefropati (HIVAN)
- HBV/ HCV Koenfeksiyonu
- Akut/ yeni edinilmiş HIV enfeksiyonu
- Gebelik

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

Tedavi Öncesi Değerlendirme

Yüz yüze sonuç verme
Net, anlaşılır olma
Ölümcül değil, kronik bir hastalık vurgusu
Hasta hakları
Bulaş yolları
Tedavinin önemi

Tedavi Öncesi Değerlendirme

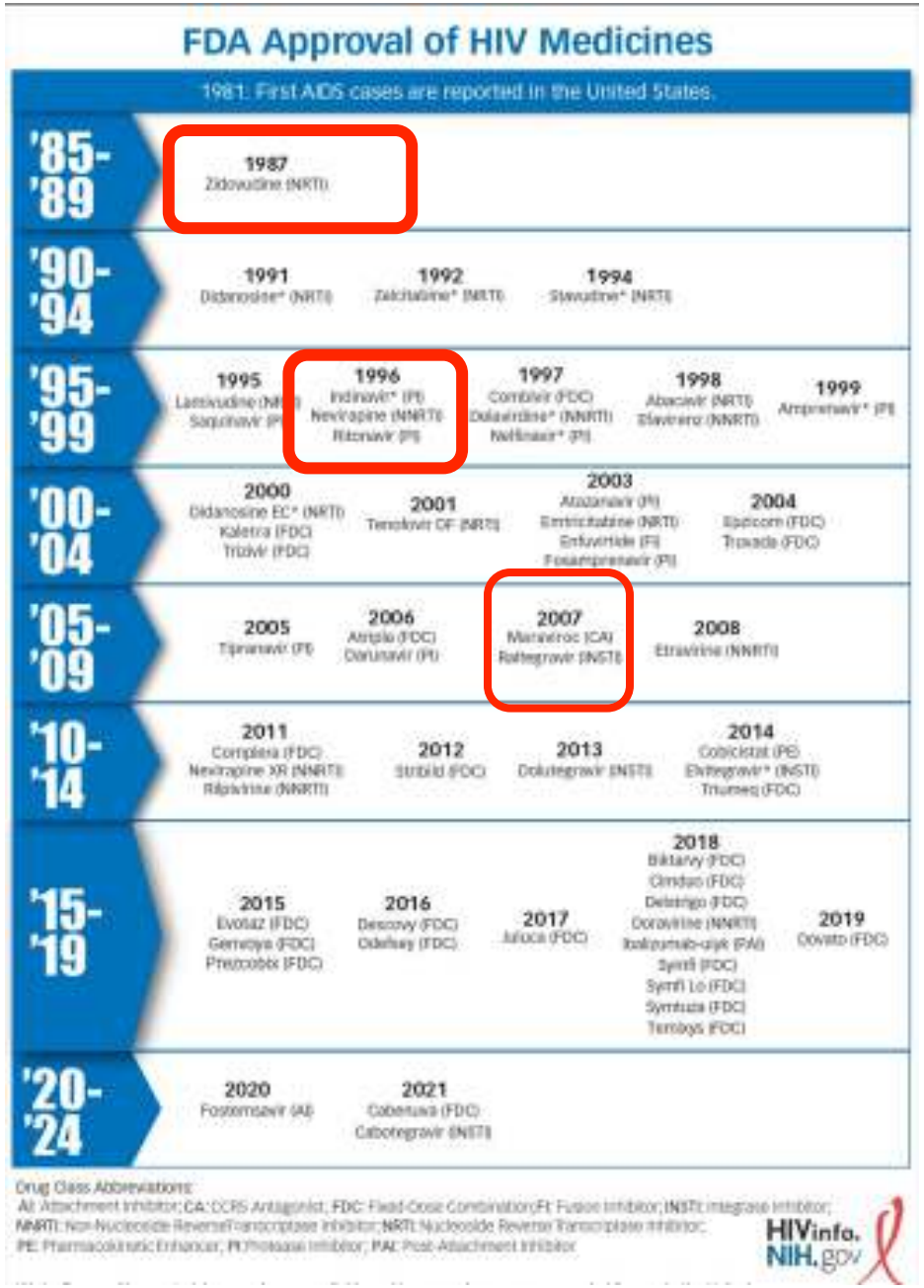
Anamnez
(aile öyküsü, ek hastalık, alışkanlıklar)
Fizik muayene
Laboratuvar testleri

Sosyal
Psikolojik
Medikal destek

HIV RNA
CD4 T lenfosit sayısı
Tam Kan Sayımı
Biyokimyasal testler
Serolojik testler
Gebelik testi
Ppd
Görüntülemeler
Genotipik direnç testi
HLA-B 5701

HIV Evresini belirleme
Uygun ART seçimi

DHHS,EACS, HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI 2021



1987 Monoterapi → 1996 HAART → 2007 Güncel ART

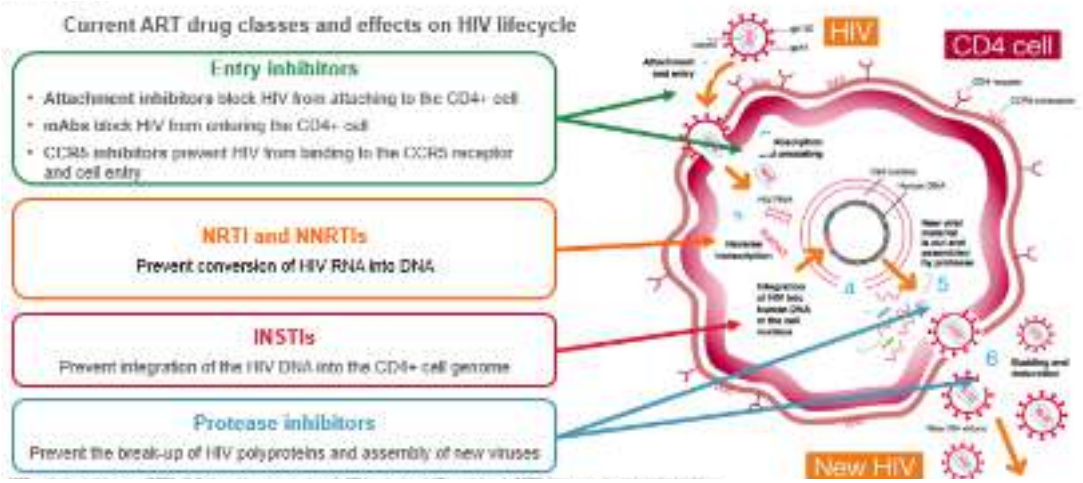
Chaudhuri S. et al.Innovation and trends in the development and approval of antiviral medicines: 1987-2017 and beyond. Antiviral Res. 2018;155:76-88.

Cihlar T. Et al. Current status and prospects of HIV treatment. Curr Opin Virol. 2016;18:50-6.

https://hivinfo.nih.gov/understanding-hiv/infographics/fda-approval-hiv-medicines

Antiretroviral İlaçlar (ART)

- Nükleozid veya nükleotid revers transkriptaz inhibitörleri (NRTI)
- Non-nükleozid revers transkriptaz inhibitörleri (NNRTI)
- Proteaz inhibitörleri (PI)
- İntegraz inhibitörleri (INSTI)
- Giriş inhibitörleri (Gİ) (Füzyon inhibitörleri - CD4 T lenfosit bağlanma sonrası inhibitörleri, gp120 bağlanma inhibitörleri, CCR5 reseptör antogonisti)



https://i-base.info/guides/art-in-pictures/the-hiv-lifecycle

Güncel Antiretroviral İlaçlar

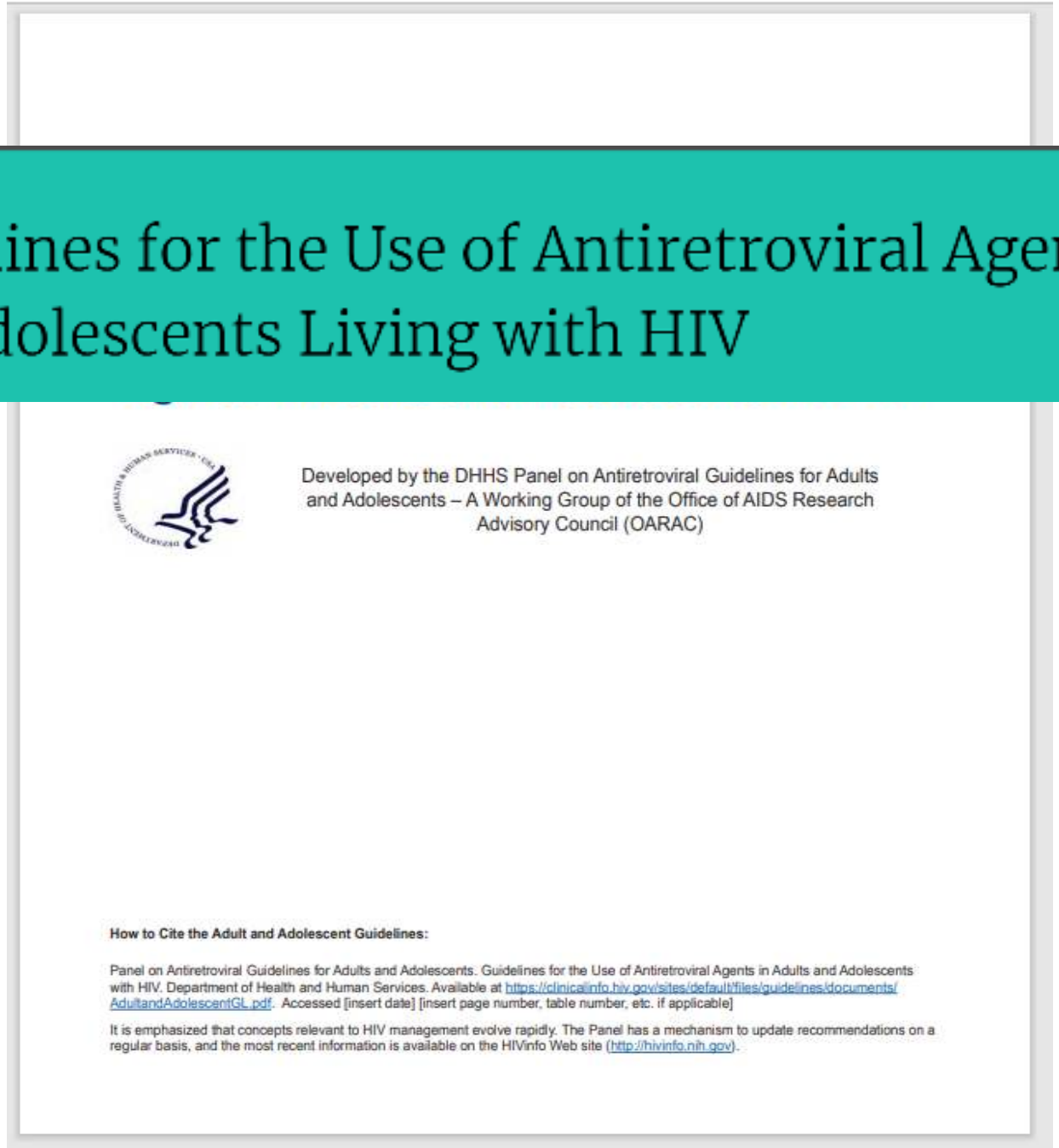
NRTI	NNRTI	Proteaz İnh.	İntegraz İnh.	Giriş İnh.	Güçlendiriciler
Abacavir (ABC)	Doravirin (DOR)	Atazanavir (ATV)	Biktegravir (BIC)	Enfuvirtid (ENF-T20) (füzyon inh.)	Ritonavir (r/RTV)
Didanosin (ddI)	Efavirenz (EFV)	Darunavir (DAR)	Dolutegravir (DTG)	İbalizumab (IBA) (CD4 bağlanma sonrası inh.)	Kobistat (c/COBI)
Emtristabin (FTC)	Etravirin (ETR)	Fosamprenavir (FPV)	Elvitegravir (EVG)	Maravirok (MVC) (CCR5 antogonisti)	
Lamivudin (3TC)	Nevirapin (NVP)	İndinavir (IDV)	Raltegravir (RAL)	Fostemsavir (FTR) (gp120 bağlanma inh.)	
Stavudin (d4T)	Rilpivirin (RPV)	Lopinavir (LPV)	Kabotegravir (CAB)		
Tenofovir (TAF/ TDF)		Nelfinavir (NLF)			
Zidovudin (ZDV)		Sakinavir (SQV)			

Virolojik süpresyon
ART ile HIV RNA seviyesinin ölçüm sınırlarının altına indirmek

Virolojik Başarısızlık
HIV RNA <200 kopya/ mL sağlanamaması veya sürdürülememesi

Tam olmayan Virolojik Yanıt
ART 24 haftaya tamamlandıktan sonra 2 ardışık HIV RNA ≥200 kopya/ mL

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV



Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Guidelines:

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Accessed [insert date] [insert page number, table number, etc. if applicable]

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the HIVinfo Web site (http://hivinfo.nih.gov).

CLINICAL INFO HIV.gov

Naiv Hastada ART Başlama Önerileri

Key Considerations and Recommendations

- An antiretroviral (ARV) regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) administered in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (also known as a booster; the two drugs used for this purpose are cobicistat and ritonavir).
- Data also support the use of the two-drug regimen, dolutegravir plus lamivudine, for initial treatment.
- Before initiating antiretroviral therapy (ART) in a person of childbearing potential, clinicians should discuss the person's intentions regarding pregnancy and a pregnancy test should be performed **(AIII)**. Clinicians should refer to the Perinatal Guidelines for recommendations on initial ARV regimen for an ART-naive person around the time of conception and during pregnancy.
- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies the following regimens as *Recommended Initial Regimens for Most People with HIV* (in alphabetical order):
  - Bictegravir/tenofovir alafenamide/emtricitabine **(AI)**[a]
  - Dolutegravir/abacavir/lamivudine—**only** for individuals who are HLA-B*5701 negative and without chronic hepatitis B virus (HBV) coinfection **(AI)**
  - Dolutegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF])[b] **(AI)**
  - Dolutegravir/lamivudine **(AI)**—except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or when ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
- To address individual patient characteristics and needs, the Panel also provides a list of Recommended Initial Regimens in Certain Clinical Situations (see Table 6 below).
- Given the many excellent options for initial therapy, selection of a regimen for a particular patient should be guided by such factors as virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance test results, comorbid conditions, access, and cost. Table 7 provides guidance on choosing an ARV regimen based on selected clinical case scenarios. Table 9 highlights the advantages and disadvantages of different components in a regimen.
- Patients without prior ART who wish to begin long-acting intramuscular cabotegravir (CAB) and rilpivirine (RPV) should first achieve viral suppression on another regimen before switching to oral, and then injectable, CAB and RPV (see Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression)

2 NRTI yanına INSTI
veya
Dolutegravir ve lamivudinden oluşan ikili tedavi

DHHS 2021

Naiv Hastada ART Başlama Önerileri

INSTI + 2 NRTI • BIC/TAF/FTC (AI) • DTG/ABC/3TC (AI) • DTG + TAF veya TDF+ FTC veya 3TC (AI)	**HLA-B*5701 negatif**
INSTI + NRTI • DTG/3TC (AI)	HIV RNA >500.000 kopya/mL olmayan HBsAg negatif Direnç tespit edilmemiş

DHHS 2021

Dual Tedavi

- ART sayesinde HIV ile yaşayan hastaların yaşam beklentisi artıyor
- ART ilişkili potansiyel komorbiditeler, kardiyovasküler hastalıklar, böbrek hastalıkları, kemik patolojileri ve diyabet dahil olmak üzere bir endişe kaynağı

Lerner AM et al. Comorbidities in Persons With HIV: The Lingering Challenge. JAMA. 2020;323(1):19-20.

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 28, Number 00, 2012
© Mary Ann Liebert, Inc.
DOI: 10.1089/aid.2011.0276

Lopinavir/Ritonavir Combined with Raltegravir or Tenofovir/Emtricitabine in Antiretroviral-Naive Subjects: 96-Week Results of the PROGRESS Study

Jacques Reynes[1], Roger Trinh[2], Federico Pulido[3], Ruth Soto-Malave[4], Joseph Gathe[5], Roula Gaspar[6], Min Tran[7], Linda Fredrick[7], Thomas Podsadecki[8], Michael Norton[7], and Angela Nitue[9]

HIV Clinical Trials

ISSN: 1528-4336 (Print) 1945-6771 (Online) Journal homepage: http://www.tandfonline.com/loi/yhct20

A Nucleoside- and Ritonavir-Sparing Regimen Containing Atazanavir Plus Raltegravir in Antiretroviral Treatment-Naïve HIV-Infected Patients: SPARTAN Study Results

Michael J. Kozal, Sergio Lupo, Edwin DeJesus, Jean-Michel Molina, Cheryl McDonald, Francois Raffi, Jorge Benetucci, Marco Mancini, Rong Yang, Victoria Wirtz, Lisa Percival, Jenny Zhang, Li Zhu, Dilek Arikan, Awny Farajallah, Bach-Yen Nguyen, Randi Leavitt, Donnie McGrath, Max Lataillade & for the SPARTAN Study Team

Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies

Josep M Llibre, Chien-Ching Hung, Cynthia Brinson, Francesco Castelli, Pierre-Marie Girard, Lesley P Kahl, Elizabeth A Blair, Kostas Angelis, Brian Wynne, Koh Vandermeulen, Mark Lindenwood, Kim Smith, Martin Gartland, Michael Aboud

CLINICAL SCIENCE

Efficacy of a nucleoside-sparing regimen of darunavir/ritonavir plus raltegravir in treatment-naive HIV-1-infected patients (ACTG A5262)

Tebas, Babafemi[4]; Zheng, Li[5]; Gallien, Sebastien[6]; Watkins, Roy R.[7]; Kuritzkes, Daniel R.[8]; Wilson, Cara C.[9]; Benitez, Baiba L.[10]; Acosta, Edward P.[11]; Bastow, Barbara[12]; Kim, Peter S.[13]; Eron, Joseph J. Jr[14]; ACTG A5262 Team

Author Information

AIDS: November 13, 2011 - Volume 25 - Issue 17 - p 2173-2182
doi: 10.1097/QAD.0b013e32834bcaa9

Lamivudin (3TC)-Dolutegravir (DTG) Dual Tedavisi

YAZAR ADI	ÇALIŞMA ADI	METOD	ÜLKE	HASTA SAYISI	DTG bazlı tedavi	TEDAVİ ŞEKLİ	ÇALIŞMAYA ALINMA KRİTERLERİ
Maggilo ve ark. 2017		prospektif	İtalya	94	DTG+ 3TC	İdame tedavisi	≥18 yaş, kullanılan ilaçlara direnç olmamalı, 6 ay yada daha
Borghetti ve ark. 2016		retrospektif	İtalya	36	DTG+ 3TC	İdame tedavisi	HIV RNA<50 kopya/ml (undetectable), daha önce en az bir
Borghetti ve ark. 2019		retrospektif	İtalya	587	DTG+ 3TC/ PI+3TC	İdame tedavisi	HIV RNA süprese hastalar,
Joly ve ark. 2018	LAMIDOL	prospektif	Fransa	104	DTG+ 3TC	İdame tedavisi	18 yaş, en az 2 yıldır HIV RNA<50 kopya/ml, yılda en az 3 d
Charpentier ve ark. 2017	DOLULAM	prospektif	Fransa	27	DTG+ 3TC	İdame tedavisi	en az 12 ay ART almak, >12 ay HIV RNA <50 kopya/ml, inte
Baldin ve ark. 2019		retrospektif	İtalya	221	DTG+ 3TC	İdame tedavisi	≥18 yaş,HIV RNA<50 kopya/ml
Ciccullo ve ark. 2018	kemik mineral çalışması	retrospektif	İtalya	20	DTG+ 3TC	İdame tedavisi	Virolojik süprese (HIV RNA<50 kopya/ml), tedavisi Dol+LA
Cahn ve ark. 2017	PADDLE	prospektif	Arjantin	20	DTG+ 3TC	Başlangıç tedavisi	≥18 yaş, naiv, HIV RNA 5000- ≤ 100.000 copy/ml, CD4>20
Tenorio ve ark. 2019	DOLAMA	retrospektif	İspanya	177	DTG+ 3TC	İdame tedavisi	≥18 yaş, en az 6 ay süre ile ART alan,HIV RNA<50 kopya/ml,
Cahn ve ark. 2018	GEMINI 1-2	randomize	21 ülke 192 merkez	719/722 (Dual/ Üçlü tdv)	DTG+ 3TC/ üçlü DTG+3TC+Emtristabin	Başlangıç tedavisi	≥18 yaş, HIV RNA ≤ 500.000kopya/ml
Nyaku ve ark. 2019			ABD		DTG+3TC	Başlangıç tedavisi	≥18 yaş, HIV RNA ≤ 500.000kopya/ml, CD4 sayısı önemli de
Taiwo ve ark. 2017	ASPIRE	prospektif	ABD		DTG+3TC	Başlangıç tedavisi	≥18 yaş, HIV RNA ≤ 500.000kopya/ml
Taiwo ve ark. 2019		randomize	ABD		DTG+3TC / üçlü tdv	İdame tedavisi	
Blanco ve ark 2018	DOLAM	randomize			DTG mono+ DTG dual		
van Wyk J ve ark 2020	TANGO			369 DTG+3TC/ 372 TAF	DTG+3TC/ TAFlı kombinasyon		
Gilman ve ark. 2019							
Boffito ve ark. 2019							
Girouard ve ark. 2016	cost effectivite çalışması	matematiksel mod	ABD				
Wandeler ve ark. 2019		meta-analiz	İsviçre	251 mono/ 1670 DTG bazlı dua	DTG mono/ DTG bazlı dual	İdame tedavisi	
Cruciani ve ark 2019		meta-analiz	İtalya		DTG bazlı üçlü/ nonDTG üçlü(naiv hasta)	Başlangıç tedavisi	
Baril ve ark.2016		derleme	Kanada				
Radford ve ark. 2019		metaanaliz	ABD		DTG bazlı dual/ klasik üçlü tedavi (naiv hasta)	Başlangıç tedavisi	
Boswell ve ar. 2018		derleme	Kanada		DTG bazlı dual tedavileri kapsayan derleme	İdame tedavisi	10 gözlemsel, 2 randomize çalışmayı içeriyor
Achhra ve ark. 2016		meta-analiz	Avustralya		tüm dual tdv/ üçlü tdv		
Scott ve ark. 2019		derleme	İsviçre		DTG+3TC		

3TC Aç karnına ya da gıda ile birlikte
İyi bir güvenlik profili
İlaç ilaç etkileşimi az
Maliyeti düşük

İki ilaç aynı anda alınabilir
Tek tablet formu

DTG Aç ya da tok gıda ile birlikte
Yüksek genetik bariyere sahip, potent
İlaç ilaç etkileşimi az

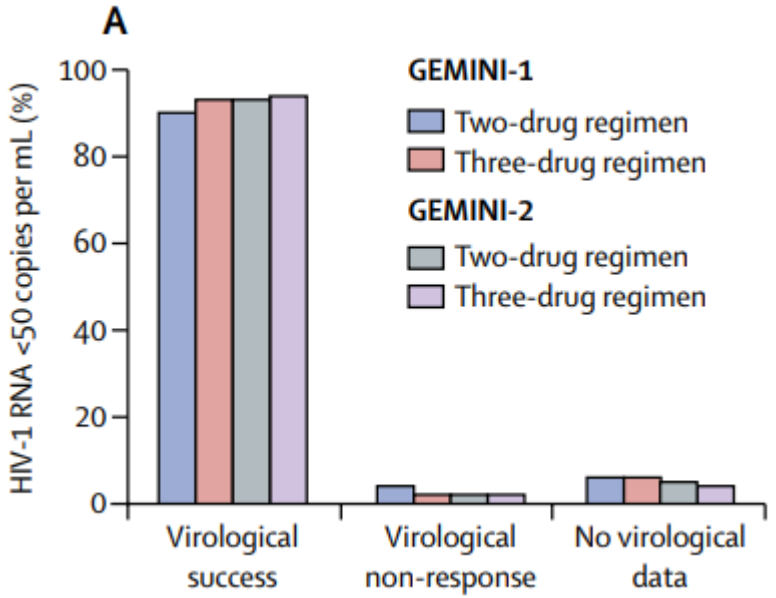
Perry CM et al. Drugs. 1997;53(4):657-80

Katlama et al. Expert Opin Investig Drugs. 2012;21(4):523-30

Soriano et al. Expert Opin Drug Saf. 2017;16(8): 923-932.

Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials

Pedro Cahn, Juan Sierra Madero, José Ramón Arribas, Andrea Antinori, Roberto Ortiz, Amanda E Clarke, Chien-Ching Hung, Jürgen K Rockstroh, Pierre-Marie Girard, Jörg Sievers, Choy Man, Alexander Currie, Mark Underwood, Allan R Tenorio, Keith Pappa, Brian Wynne, Anna Fettiplace, Martin Gartland, Michael Aboud, Kimberly Smith, and the GEMINI Study Team



21 ülke 192 merkez
2016 Temmuz-2017 Mart
1441 hasta
(719 dua l/ 722 üçlü)

- 3TC/DTG, naiv hastalarda 48 haftada üçlü rejime karşı düşük olmayan etkililiği ve benzer tolere edilebilirlik
- HIV-1 enfeksiyonu olan hastalarda başlangıç tedavisi olarak kullanımını desteklemekte

CLINICAL SCIENCE

Durable Efficacy of Dolutegravir Plus Lamivudine in Antiretroviral Treatment–Naive Adults With HIV-1 Infection: 96-Week Results From the GEMINI-1 and GEMINI-2 Randomized Clinical Trials

Pedro Cahn, MD,[a] Juan Sierra Madero, MD,[b] José R. Arribas, MD,[c] Andrea Antinori, MD,[d] Roberto Ortiz, MD,[e] Amanda E. Clarke, BM,[f,g] Chien-Ching Hung, MD,[h] Jürgen K. Rockstroh, MD,[i] Pierre-Marie Girard, MD,[j] Jörg Sievers, DPhil,[j] Choy Y. Man, BSc,[k] Rimgaile Urbaityte, MStat,[k] Daisy J. Brandon, BSc,[k] Mark Underwood, PhD,[k] Allan R. Tenorio, MD,[k] Keith A. Pappa, PharmD,[k] Brian Wynne, MD,[k] Martin Gartland, PhD,[k] Michael Aboud, MD,[k] Jean van Wyk, MBChB, MFPM,[k] and Kimberly Y. Smith, MD, MPH[k]

- 48 haftalık verilerle tutarlı olarak, tedaviyle ortaya çıkan direnç riskinde artış olmaksızın 3TC/TDF/DTG karşılaştırıldığında uzun süreli, daha düşük olmayan etkinlik
- HIV-1 ile enfekte kişilerde kullanımını desteklemekte

J Acquir Immune Defic Syndr. 2020 Mar 1;83(3): 310-318.

OPEN

Three-year durable efficacy of dolutegravir plus lamivudine in antiretroviral therapy – naive adults with HIV-1 infection

Pedro Cahn[a], Juan Sierra Madero[b], José R. Arribas[c], Andrea Antinori[d], Roberto Ortiz[e], Amanda E. Clarke[f], Chien-Ching Hung[g], Jürgen K. Rockstroh[h], Pierre-Marie Girard[i], Jörg Sievers[j], Choy Y. Man[k], Rimgaile Urbaityte[l], Daisy J. Brandon[l], Mark Underwood[k], Keith A. Pappa[k], Lloyd Curtis[l], Kimberly Y. Smith[k], Martin Gartland[k], Michael Aboud[j], Jean van Wyk[j] and Brian Wynne[k]

- Üç yıllık kalıcı etkinlik, uzun süreli tolere edilebilirlik ve yüksek direnç bariyeri,
- HIV-1 tedavisi için DTG + 3TC'nin birinci basamak kullanımını destekler

AIDS. 2022 Jan 1;36(1):39-48.

Belirli Klinik Durumlarda Önerilen Başlangıç Rejimleri

2 NRTI+ INSTI:

- TAF veya TDF /FTC/ EVG/c/
- TAF veya TDF + FTC veya 3TC + RAL

2 NRTI+ PI

- TAF veya TDF + FTC veya 3TC + DRV (c/r)
- TAF veya TDF + FTC veya 3TC + ATV(c/r)
- ABC/3TC+ DRV (c/r)

2 NRTI+ NNRTI

- TDF /3TC/DOR veya TAF/FTC +DOR
- TAF veya TDF+ FTC veya 3TC+ EFV
- TAF veya TDF/FTC/RPV

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Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/ mm^3	**Do Not Use the Following Regimens:** • RPV-based regimens • DRV/r plus RAL	A higher rate of virologic failure has been observed in those with low pretreatment CD4 counts.
	HIV RNA >100,000 copies/mL (also see next row if HIV RNA >500,000 copies/mL)	**Do Not Use the Following Regimens:** • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL	Higher rates of virologic failure have been observed in those with high pretreatment HIV RNA levels
	HIV RNA >500,000 copies/mL	**Do Not Use the Following Regimens:** • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL • DTG/3TC	For DTG/3TC, limited data are available in patients above this viral load threshold.
	HLA-B*5701 positive or result unknown	**Do not use ABC-containing regimens.**	ABC hypersensitivity, a potentially fatal reaction, is highly associated with the presence of the HLA-B*5701 allele.

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Tek tablet rejimleri

ART-Specific Characteristics	A one-pill, once-daily regimen is desired	**STR Options as Initial ART Include:** • BIC/TAF/FTC • DOR/TDF/3TC • DRV/c/TAF/FTC • DTG/ABC/3TC • DTG/3TC • EFV/TDF/FTC • EFV/TDF/3TC • EVG/c/TAF/FTC • EVG/c/TDF/FTC • RPV/TAF/FTC • RPV/TDF/FTC

Coformulated Combination Products as Single-Tablet Regimens		
Bictegravir/Tenofovir Alafenamide/Emtricitabine		
• Biktarvy	50 mg/25 mg/200 mg tablet	30 tablets
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine		
• Symtuza	800 mg/150 mg/10 mg/200 mg tablet	30 tablets
Dolutegravir/Abacavir/Lamivudine		
• Triumeq	50 mg/600 mg/300 mg tablet	
Dolutegravir/Lamivudine		
• Dovato	50 mg/300 mg tablet	
Dolutegravir/Rilpivirine		
• Juluca	50 mg/25 mg tablet	
Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine		
• Delstrigo	100 mg/300 mg/300 mg tablet	
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine		
• Generic	600 mg/300 mg/200 mg tablet	
• Atripla	600 mg/300 mg/200 mg tablet	
Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine		
• Symfi	600 mg/300 mg/150 mg tablet	
• Symfi Lo	400 mg/300 mg/150 mg tablet	
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine		
• Genvoya	150 mg/150 mg/10 mg/200 mg tablet	
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine		
• Stribild	150 mg/150 mg/300 mg/200 mg tablet	
Rilpivirine/Tenofovir Alafenamide/Emtricitabine		
• Odefsey	25 mg/25 mg/200 mg tablet	
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine		
• Complera	25 mg/300 mg/200 mg tablet	

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
ART-Specific Characteristics, *continued*	Food effects	**Regimens that Can be Taken Without Regard to Food:** • BIC-, DOR-, DTG-, or RAL-based regimens	Oral bioavailability of these regimens is not significantly affected by food.
		Regimens that Should be Taken with Food: • ATV/r- or ATV/c-based regimens • DRV/r- or DRV/c-based regimens • EVG/c/TAF/FTC[a] • EVG/c/TDF/FTC[a] • RPV-based regimens	Food improves absorption of these regimens. RPV-containing regimens should be taken with ≥390 calories of food.
		Regimens that Should be Taken on an Empty Stomach: • EFV-based regimens	Food increases EFV absorption and may increase CNS side effects.

Özel Durumlar

Kronik Böbrek Yetmezliği (GFR<60 ml/dk)	TDF, ATV kullanmaktan kaçın ABC kullanılabilir TAF GFR >30 ml/dk veya kronik diyaliz hastasında (çalışma EVG/c/TAF/FTC) kullanılabilir ABC, TAF veya TDF kullanamadığın durumlarda - DTG/3TC (HIV RNA <500,000 kopya/mL) - DRV/r + 3TC - DRV/r + RAL (CD4 sayısı 200 hücre/mm3 and HIV RNA >100,000 kopya/mL)

Özel durumlar

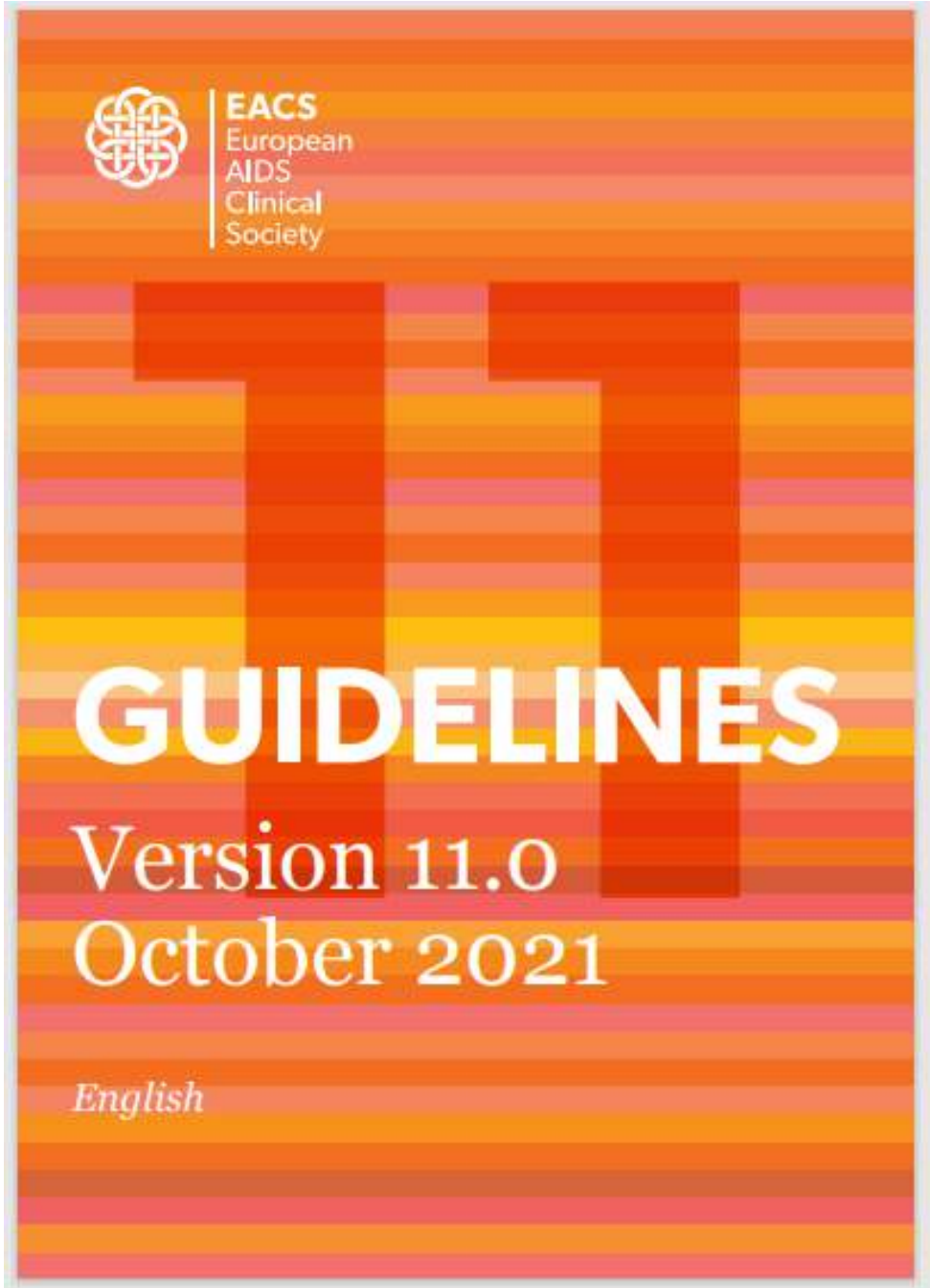
Kilo alımı	- INSTI (özellikle BIC ve DTG) NNRTI veya PI rejimlerinden daha fazla kilo alımı ile ilişkilendirilmiş - TDF den TAF geçişinde gözlemlenmiş
Osteoporoz	- TDF kullanmaktan kaçın - ABC kullanılabilir
Psikiyatrik rahatsızlık	- EFV ve RPV kaçın
Hiperlipidemi	- PI, ELV, EFV dislipidemi ile ilişkili - BIC, DOR, DTG, RAL ve RPV daha az lipid etkisine sahip - TDF'den TAF'a geçişte artan lipid değerleri

- DTG nöral tüp defekt prevalansı DTG dışı ART kullananlarla istatiksel olarak anlamlı değil (Botswana Tsepamo çalışmaları)
- DTG yerine RAL seçimine gerek yok
- RAL düşük genetik bariyerli ve tek doz tedavilerde yeri yok
- ELV düşük genetik bariyerli

- 3 ila 6 ay boyunca oral tedavide virolojik olarak baskılanmış
- Sık klinik izlemi kabul eden hastalar için
- Enjekte edilebilir cabotegravir ve rilpivirin kombinasyonu
- Uzun etkili bir ARV rejimi
- Başlangıç tedavisi olarak önerilmemekte

INSTI plus One NNRTI		
Cabenuva (CAB IM and RPV IM)	Cabenuva 600 mg/900 mg kit contains: • CAB 600 mg/3 mL vial and RPV 900 mg/3 mL vial Cabenuva 400 mg/600 mg kit contains: • CAB 400 mg/2mL vial and RPV 600 mg/2 mL vial	**Lead-in with Oral CAB and RPV:** • (CAB 30 mg and RPV 25 mg) PO once daily with a meal for 4 weeks **IM CAB and RPV:** • Loading dose: CAB 600 mg/3 mL IM × 1 dose and RPV 900 mg/3 mL IM × 1 dose • Continuation phase: CAB 400 mg/2 mL IM every 4 weeks and RPV 600 mg/2 mL IM every 4 weeks

- İlaçlara ileri düzeyde dirençli HIV enfeksiyonu olan ve viral yükü saptanabilir düzeyde devam eden hastalarda sadece çalışma kapsamında elde edilecek ilaçlar önerilmekte
- İslatravir (NRTI), lenakapavir (kapsid inhibitörü) ve leronlimab (CCR5 antagonisti) araştırma aşamasında olan ilaçlar arasında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Version 11.0
October 2021
English

Naiv Hastada ART Başlama Önerileri

Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
TAF/FTC or TDF/XTC + RAL qd or bid	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR	

Regimen	Main requirements
Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC or TDF/FTC or TDF/3TC + DTG	
TAF/FTC/BIC	
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid	
1 NRTI + INSTI	
3TC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL

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Alternative regimens	
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner
TAF/FTC or TDF/XTC + RPV or TAF/FTC/RPV or TDF/FTC/RPV	CD4 count > 200 cells/μL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food
2 NRTIs + PI/r or PI/c	
TAF/FTC or TDF/XTC + DRV/c or DRV/r or TAF/FTC/DRV/c	With food

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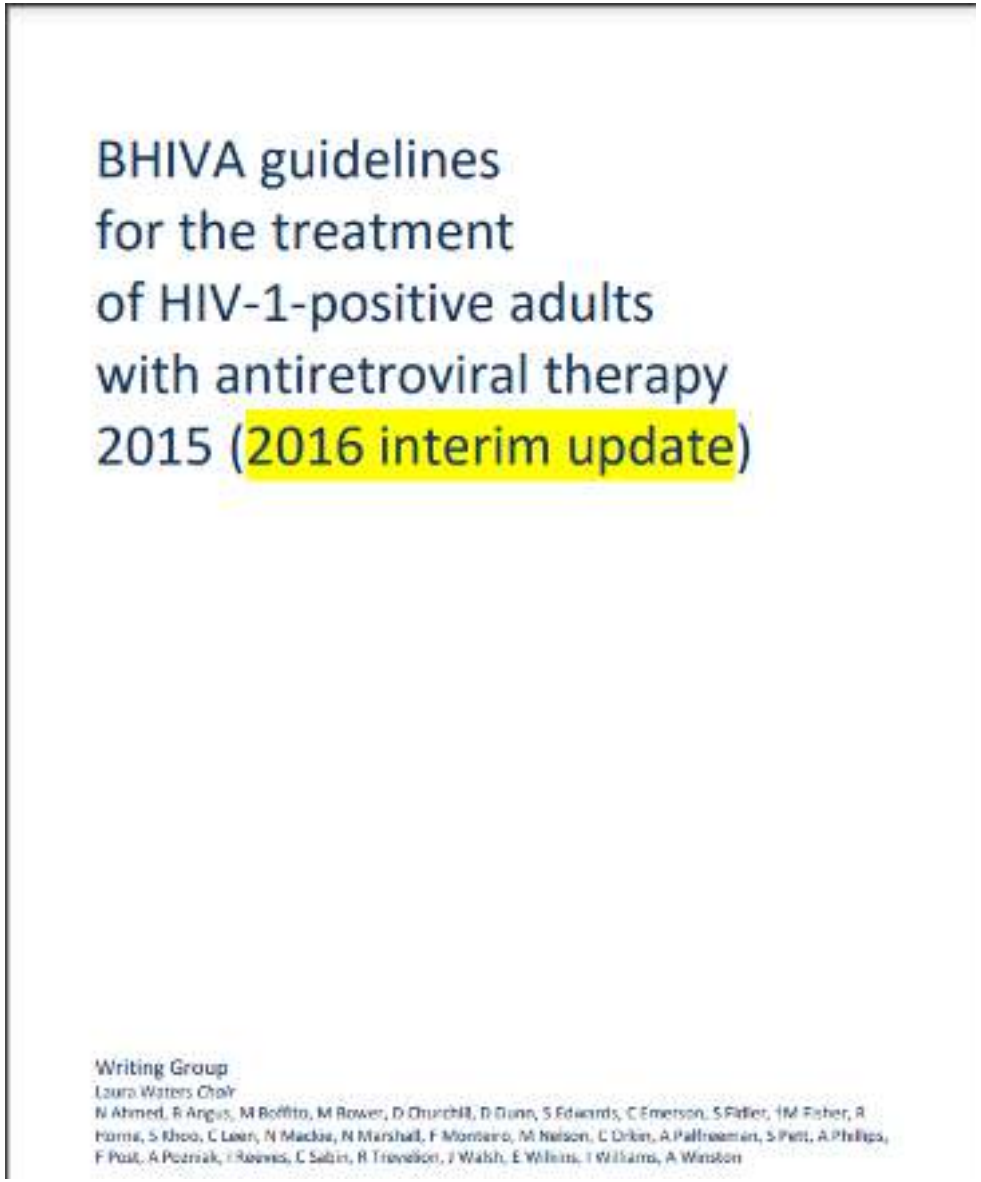
- INSI ve TAF kilo alma ilişkisi olabilir
- TDF böbrek, kemik toksisitesi
- EFV suisid girişim, mental rahatsızlık öyküsü olanlarda kullanılmaması



Antiretroviral treatment for adults living with HIV-1 2022 - consultation open until Thursday 9 June 2022

Table 5.1 Recommendations for choice of first-line ART

Recommended as initial treatment for most people living with HIV (Grade 1A)	
Tenofovir-DX/emtricitabine or tenofovir-AF/emtricitabine with dolutegravir	
Abacavir/lamivudine/dolutegravir	HLA B*5701 negative and estimated 10-year risk of CVD less than 10%
Tenofovir-AF/emtricitabine/bictegravir	
Dolutegravir/lamivudine	No baseline lamivudine resistance Baseline viral load less than 500,000 copies/mL Baseline CD4 count greater than 200 cells/mm^3 No active hepatitis B infection and if at risk of hepatitis B, hepatitis B virus immune
Recommended as initial treatment in certain clinical situations (Grade 2A)	
Tenofovir-DX/emtricitabine or tenofovir-AF/emtricitabine with raltegravir	Baseline viral load less than 100,000 copies/mL
Tenofovir-DX/emtricitabine or tenofovir-AF/emtricitabine with darunavir/ritonavir or darunavir/cobicistat	
Tenofovir-DF/lamivudine/doravirine or tenofovir-DX/emtricitabine or tenofovir-AF/emtricitabine with doravirine	
Tenofovir-DX/emtricitabine or tenofovir-AF/emtricitabine or abacavir/lamivudine with efavirenz	May be a first-line choice in pregnancy and for people on TB treatment but not recommended outside these scenarios

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HIV/AIDS

TANI İZLEM VE TEDAVİ

EL KİTABI

Türkiye'de bulunan Antiretroviral İlaçlar

ARV İlaç Sınıfı	ARV İlaç, İçerdiği İlaç Miktarı	Ticari Preparat
NRTI	TDF/FTC, 300/200 mg	Hivent film tablet
		Sidatria film tablet
		Truvada film tablet
	ABC, 300 mg	Ziagen film tablet
	3TC, 150 mg	Epivir tablet
	ZDV, 250 mg	Retrovir 250 mg kapsül
	ZDV, 200 mg	Retrovir 200 mg flakon
	ZDV, 50 mg / 200 ml	Retrovir süspansiyon
NNRTI	EFV, 600 mg	Stocrin tablet
	RPV, 25 mg	Edurant tablet
	NVP, 200 mg	Viramune tablet
PI	DRV, 400 mg ve 600 mg	Prezista tablet
	LPV/r, 200/50 mg	Kaletra tablet
	RTV, 100 mg	Norvir tablet
INSTI	RAL, 400 mg	Isentress tablet
	TDF/FTC/EVG/c 300/200/150/150 mg	Stribild tablet
	TAF/FTC/EVG/c 10/200/150/150 mg	Genvoya tablet
	DTG, 50 mg ve DTG, 25 mg	Tivicay tablet
	ABC/3TC/DTG 600/300/50 mg	Triumeq tablet
	TAF/FTC/BIC 25/200/500 mg	Biktarvy tablet
CCR5 antagonisti	Maraviroc 150/300mg tablet	Celsentri

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI 2021

Tablo 4.1. Daha önce ART almamış, erişkin HIV pozitif bireyler için birinci basamak ART rejimi

A) Önerilen rejimler†‡

Rejim	Doz	Uyarı	Gıda Gereksinimi
ABC/3TC/DTG[a,b]	ABC/3TC/DTG 600/300/50 mg Günde 1 tablet	» Al/Ca/Mg içeren antasit ve multivitaminler ile eş zamanlı alınmamalıdır (en az 2 saat önce veya 6 saat sonra alınabilir). » Rifampisin ile birlikte kullanılacaksa DTG 50 mg günde iki kez önerilir.	Yok
DTG+3TC[a,b]	DTG+3TC 50+2x150 mg Günde 3 tablet	» HIV RNA >500.000 kopya/mL olanlarda ve HBV koenfeksiyonu olanlarda kullanılmaz. » Genotipik direnç sonucu yoksa tercih edilmez. » Al/Ca/Mg içeren antasitler ve multivitaminler ile eş zamanlı alınmamalıdır (en az 2 saat önce veya 6 saat sonra alınabilir). » Rifampisin ile birlikte kullanılacaksa DTG 50 mg günde iki kez önerilir.	Yok
TAF/FTC/BIC[c]	TAF/FTC/BIC 25/200/50 mg Günde 1 tablet	Ağır karaciğer yetmezliğinde kullanılmamalıdır.	Yok
TAF/FTC[c] veya TDF/FTC[c] + DTG	TAF/FTC 25/200 mg Günde 1 tablet TDF/FTC 300/200 mg Günde 1 tablet DTG 50 mg Günde 1 tablet	» Al/Ca/Mg içeren antasit ve multivitaminler ile eş zamanlı alınmamalıdır (en az 2 saat önce veya 6 saat sonra alınabilir). » Rifampisin ile birlikte kullanılacaksa DTG 50 mg günde iki kez önerilir.	Yok
TDF/3TC/DOR[c] veya TDF/FTC + DOR[c]	TDF/FTC/DOR 300/200/100 mg Günde 1 tablet TDF/FTC 300/200 mg Günde 1 tablet + DOR 100 mg Günde 1 tablet	18 yaşından büyüklerde kullanılır, CYP3A4 üzerinden metabolize olan ilaçlara dikkat	Yok
TAF/FTC[c] veya TDF/FTC[c] + RAL	TAF/FTC 25/200 mg Günde 1 tablet veya TDF/FTC 300/200 mg Günde 1 tablet RAL 400 mg Günde iki defa 1 tablet veya RAL 600 mg Günde bir defa 2 tablet	» Al/Mg içeren antasitlerle eş zamanlı alınması önerilmez. » Rifampisin ile birlikte kullanılacaksa RAL 400 veya 800 mg günde iki kez alınmalıdır.	Yok

B) Alternatif rejimler (önerilen rejimdeki ilaçlardan hiçbiri kullanılamıyorsa, temin edilemiyorsa veya uygun değilse)

Rejim	Doz	Uyarı	Gıda Gereksinimi
TAF/FTC[c] veya TDF/FTC[c] + ATV/c[a,b] veya ATV/r[a,b]	TAF/FTC 10/200 mg Günde 1 tablet veya TDF/FTC 300/200 mg Günde 1 tablet ATV/c 300/150 mg Günde 1 tablet veya ATV 300 mg Günde 1 tablet ve RTV 100 mg Günde 1 tablet		Yemekle
TAF/FTC[c] veya TDF/FTC[c] + DRV/c[d] veya DRV/r[d]	TAF/FTC 10/200 mg Günde 1 tablet veya TDF/FTC 300/200 mg Günde 1 tablet ve DRV/c 800/150 mg Günde 1 tablet veya DRV 800 mg Günde 1 tablet ve RTV 100 mg Günde 1 tablet	Sülfonamit alerjisi olan hastalar izlenmelidir.	Yemekle
TDF/FTC + EFV[c,f]	TDF/FTC 300/200 mg Günde 1 tablet ve EFV 600 mg Günde 1 tablet	Yatmadan önce veya akşam yemeğinden 2 saat önce	Aç karna
TAF/FTC/EVG/c[c] veya TDF/FTC/EVG/c[c,e]	TAF/FTC/EVG/c 10/200/150/150 mg Günde 1 tablet veya TDF/FTC/EVG/c 300/200/150/150 mg Günde 1 tablet	Al/Ca/Mg içeren antasitler ve multivitaminler ile eş zamanlı alınmamalıdır (en az 2 saat önce veya 6 saat sonra alınabilir).	Yemekle
TAF/FTC/RPV[c] veya TDF/FTC/RPV[c]	TAF/FTC/RPV 25/200/25 mg Günde 1 tablet veya TDF/FTC/RPV 300/200/25 mg Günde 1 tablet	CD4 T lenfositi sayısı >200 hücre/mm³ ve HIV RNA düzeyi <100.000 kopya/mL ise kullanılabilir. PPI kontrendikedir. H2 antagonistleri, RPV'den12 saat önce ve 4 saat sonra alınabilir.	Yemekle
RAL[b] + DRV/c[d] veya DRV/r[d]	RAL 400 mg, Günde iki defa1 tablet DRV/c 800/150 mg Günde 1 tablet veya DRV 400 mg Günde 2 tablet ve RTV 100 mg Günde 1 tablet	» CD4 T lenfositi sayısı >200 hücre/mm³ ve HIV RNA düzeyi <100.000 kopya/mL ise önerilmez. » Al veya Mg içeren antasitlerle birlikte kullanılması önerilmez.	Yemekle

Naiv Hastada Birinci Basamak Tedavi

Rejim	Uyarı	Gıda Gereksinimi
ABC/3TC/DTG	• Al/Ca/Mg içeren antiasit ve*** multivitaminler ile eş zamanlı alınmamalı • Rifampisin ile DTG günde 2 kez	yok
DTG+3TC	• HIV RNA >500.000 kopya/mL olanlarda ve HBV koenfeksiyonu olanlarda kullanılmaz. • Genotipik direnç sonucu yoksa tercih edilmez	yok
TAF/FTC/BIC	• Ağır karaciğer yetmezliğinde kullanılmamalıdır	yok
TAF/FTC veya TDF/FTC+DTG	***	yok
TDF/3TC/DOR veya TDF/FTC+DOR	• 18 yaş üzerinde kullanım	yok
TAF/FTC veya TDF/FTC+RAL	• Al/Mg içeren antiasit ve multivitaminler ile eş zamanlı alınmamalı	yok

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI 2021

Alternatif Rejimler

Rejim	Uyarı	Gıda Gereksinimi
TAF/FTC veya TDF/FTC+ ATV/c veya ATV/r		yemekle
TAF/FTC veya TDF/FTC+ DRV/c veya DRV/r	Sülfanamid alerjisi olan hastalar izlenmeli	yemekle
TDF/FTC+ EFV	Yatmadan önce ya da akşam yemeğinden 2 saat önce	aç karnına
TAF/FTC/EVC/c veya TDF/FTC/EVG/c	Al/Ca/Mg içeren antiasit ve multivitaminler ile eş zamanlı alınmamalı	yemekle
TAF/FTC/RPV veya TDF/FTC/RPV	CD4 T lenfositi sayısı >200 hücre/mm3 ve HIV RNA düzeyi < 100.000kopya/mL ise kullanılır PPI kontrendike H2antagonistleri RPV'den 12 saat önce ya da 4 saat sonra	yemekle
RAL+DRV/c veya DRV/r	CD4 T lenfositi sayısı >200 hücre/mm3 ve HIV RNA düzeyi < 100.000kopya/mL ise kullanılır Al/Mg içeren antiasitler ile eş zamanlı alınmamalı	yemekle

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI 2021

Antiretroviral Tedavi Değişikliği Nedenleri

Gereksiz tedavi değişikliğinden kaçın!

Virolojik başarısızlık

Hasta isteği
Yan etki
Toksisite
Basitleştirme
İlaç ilaç etkileşimi
Gebelik
Maliyet

African Health Sciences
Makerere Medical School

- Ocak 2016-Nisan 2021
- Herhangi bir üçlü ART kullanmış
- En az 6 ay süre ile HIV RNA 100IU/ml altı ya da negatif olan
- CD4 T lenfosit sayısı 200 hücre/mm3den fazla
- En az 6 ay 3TC+DTG alan hastalar
- 63 hasta çalışmaya alındı

Evaluation of Treatment Efficacy after Switching to Dolutegravir-Lamivudine Dual Therapy in People Living with HIV

Abstract

Background: People living with HIV need to use antiretroviral therapy throughout their lives.

Objectives: Studies on the efficacy and safety of dual therapy are limited in Turkey. We sought to evaluate the treatment efficacy and side effects among pat... combination of dolutegravir (DTG) and lamivudine (3TC) as a main...

Methods: This retrospective, single-centre study included individu... who were older than 18 years of age, living with HIV, switc... antiretroviral therapy regimen to DTG-3TC dual therapy, and follow...

Results: The study included 63 patients living with HIV. The ... (interquartile range (IQR): 36-51 years). The median follow-up unc... was 10.4 months (7.1-16.0 months). In the course of dual therapy, ... serious adverse effects that would necessitate a therapy switch, but ... in two patients. Two patients lost their lives, with one dying from s... respiratory failure associated with the underlying chronic obstructiv...

Conclusion: The DTG-3TC dual-therapy regimen is a promising an... be used as a treatment of choice for eligible patients.

Table 3. Reasons for and frequencies of switching to dual therapy.

Reasons for switch	n (%)*
Osteopenia	32 (43.2)
Osteoporosis	10 (13.5)
Renal dysfunction	13 (17.6)
Drug hypersensitivity	1 (1.4)
Adverse gastrointestinal effects	2 (2.7)
Drug-drug interactions	3 (4.1)
Hyperlipidemia	3 (4.1)
Simplification	8 (10.8)
Outdated cART	2 (2.7)

ART Değişikliğinde Öneriler

Önerilir

- 2NRTI+NNRTI rejiminde başarısız olanlar
- NRTI/NRTI + DTG
- NRTI/NRTI + PI/r (alternatif)
- PI/r + INSTI
- DTG + MVC
- 2NRTI + PI/r rejiminde başarısız olanlar
- NRTI/NRTI + DTG
- DRV (2x600) / r (2x100) + DTG
- DTG + MVC
- 2NRTI + INSTI rejiminde başarısız olanlar NRTI/ NRTI + PI
- NRTI/NRTI + DTG (2x50mg)
- PI/r + DTG (2x50mg)

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

Managing Patients with Virologic Failure

If virologic failure is suspected or confirmed, a thorough assessment of whether one or more of the above factors could have been the cause(s) of failure is indicated. Often, the causes of virologic failure can be identified, but in some cases, they are not obvious. Distinguishing among the causes of virologic failure is important, because the approaches to subsequent therapy may differ, depending on the cause. Potential causes of virologic failure should be explored in depth. Once virologic failure is confirmed, steps should be taken to improve virologic outcomes. These approaches are outlined below.

Key Factors to Consider When Designing a New Antiretroviral Regimen

- When designing a new ARV regimen for a patient with virologic failure, the expected potency of the new agent(s) is critical in predicting virologic efficacy. A fully active drug is one that is expected to have uncompromised activity after considering the patient's ART history and current and previous resistance test results, and whether an ARV drug with a new mechanistic action is available.[8,16-25]
- A new ARV regimen can include two fully active drugs if at least one has a high resistance barrier, such as the second-generation integrase strand transfer inhibitor (INSTI) dolutegravir (DTG) or the boosted-protease inhibitor (PI) darunavir (DRV) **(AI)**. Bictegravir (BIC), which is available only in a combination pill with emtricitabine/tenofovir alafenamide (FTC/TAF), also has a high resistance barrier; however, no data exist on its efficacy in this setting. If one of these drugs is fully active, they can be combined with two NRTIs if at least one is also fully active. Alternatively, if both the second-generation INSTI and boosted PI are fully active, they can be used in combination and be highly effective in those with virologic failure, without NRTIs. If no fully active drug with a high resistance barrier is available, then every effort should be made to include three fully active drugs in the regimen **(AI)**. See the clinical scenarios below for further guidance on the number of fully active drugs a regimen should contain.
- Despite the presence of some drug-resistance mutations, some ARV drugs in the regimen may still have

DHHS

TAF/FTC ile kombinasyon bulunan BIC yüksek direnç bariyerine sahip; bununla birlikte, yeterli veri yok

Strategies not recommended

a. Monotherapy with a PI/b
b. Monotherapy with DTG
c. Dual or triple NRTIs combinations

EACS

Hepatit B/ HIV Koenfeksiyonu

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B/HIV Virus Coinfection (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations

- Before initiation of antiretroviral therapy (ART), all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication **(AIII)**.
- Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) have activity against both HIV and HBV, an ART regimen for patients with both HIV and HBV should be include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen **(AI)**.
- If TDF or TAF cannot safely be used, the alternative recommended HBV therapy is entecavir in addition to a fully suppressive ARV regimen **(BI)**. Entecavir has activity against HIV; its use for HBV treatment without ART in patients with dual infection may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to patients with HBV/HIV-coinfection **(AII)**. Peginterferon alfa monotherapy may also be considered in certain patients **(CII)**.
- Other HBV treatment regimens, including adefovir alone or in combination with 3TC or FTC and telbivudine, **are not recommended** for patients with HBV/HIV coinfection **(CII)**.
- Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against stopping these medications and be carefully monitored during interruptions in HBV treatment **(AII)**.
- If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression **(AIII)**.
- HBV reactivation has been observed in persons with HBV infection during interferon-free HCV treatment. For that reason, all patients initiating HCV therapy should be tested for HBV. Persons with HCV/HIV coinfection and active HBV infection (determined by a positive HBsAg test) should receive ART that includes two agents with anti-HBV activity prior to initiating HCV therapy **(AIII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Hepatit B serolojisi
İzole AntiHBc pzotifliği olanlarda HBV DNA
Hepatit B aşı programı
AntiHBs kontrol, 100IU/ml altında rapel
TDF ya da TAF, 3TC ya da FTC ile kombinasyonları
Telbuvidin, adefovir önerilmez
Entekavir etkin ART ile

DHHS,EACS, HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

Hepatit C / HIV Koenfeksiyonu

Hepatitis C Virus/HIV Coinfection

(Last updated August 16, 2021; reviewed August 16, 2021)

Panel's Recommendations
• All people with HIV should be screened for hepatitis C virus (HCV) infection **(AIII).** Patients at high risk of HCV infection should be screened annually and whenever incident HCV infection is suspected **(AIII).**
• Antiretroviral therapy (ART) may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most persons with HCV/HIV coinfection, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury. Therefore, ART should be initiated in all patients with HCV/HIV coinfection, regardless of CD4 T lymphocyte cell count **(AI).**
• Initial ART regimens that are 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 regimens should be selected with special consideration for potential drug-drug interactions and overlapping toxicities **(AIII)** (see discussion in the text below and in Table 18).
• All patients with HCV/HIV coinfection should be evaluated for HCV therapy, which includes assessing their liver fibrosis stage to guide the duration of therapy and predict subsequent risk of hepatocellular carcinoma and liver disease complications **(AIII).**
• 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 Immunoglobulin G). 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 HCV treatment with direct-acting antivirals. Accordingly, before initiating HCV therapy, persons with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes two agents with anti-HBV activity **(AIII).**

HCV serolojisi
HCV RNA
ART CD4 T lenfosit sayısından bağımsız başlanmalı
HCV tedavisi sırasında Hepatit B reaktive olabilir!
HCV tedavisinde ilaç ilaç etkileşimi

DHHS,EACS, HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

DEA'lar	ATV/c	ATV/r	DRVc	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	BIC	DTG	EVG/c	RAL	ABC	FTC	TDF	TAF
DCV	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔
EBR/GZR	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔
GLE/PIB	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
PTV/r/ OMB/ DSV	↑	↑	↑	↓	↑	↓	↓↑	↓↑	↑	↑	↑	↔	↑	↔	↔	↔	↔	↑
SMP	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔
SOF/LDV	↑	↑	↑	↑	↑	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔
SOF/VEL	↔	↑	↔	↑	↑	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔
SOF/ VEL/ VOX	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔
SOF	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔

Tablo işaretleri

↑ *DEA düzeyinde yükselme*

↓ *DEA düzeyinde azalma*

↑ *ARV düzeyinde yükselme*

↓ *ARV düzeyinde azalma*

↔ *Klinik olarak anlamlı etkileşim yok*

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

Tüberküloz / HIV Koenfeksiyonunda ART

- TB/HIV koenfeksiyonu olan tüm kişiler, CD4 sayısından bağımsız olarak ART'ye başlamalı
- ART, CD4 sayısından bağımsız olarak mümkün olan en kısa sürede (TB tedavisine başladıktan sonraki iki hafta içinde) başlatılmalı
- Düşük CD4 sayısı seviyelerinde - erken ART başlayan kişilerde IRIS- BYYS (bağışıklığın yeniden yapılanmasına bağlı yangı sendromu) dikkat
- ART ile 4 hafta süreyle profilaktik prednizon

	Initiation of ART
General recommendation	As soon as possible within 2 weeks after starting treatment for the opportunistic infection
Tuberculosis **- TB meningitis**	As soon as possible within two weeks of starting TB treatment, regardless of CD4 count ART should be delayed for 4 weeks, but can be initiated within the first 2 weeks in PLWH with TB meningitis and CD4 < 50 (100) cells/μL
Cryptococcal meningitis	Defer initiation of ART for at least 4 weeks (WHO recommends a delay of 4-6 weeks and some specialists recommend a delay of 6-10 weeks in severe cryptococcal meningitis)

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Tüberküloz / HIV Koenfeksiyonunda ART

- All patients with HIV and active TB who are not on antiretroviral therapy (ART) should be started on ART as described below.
  - **CD4 T lymphocyte (CD4) cell counts <50 cells/mm³:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment **(AI)**.
  - **CD4 counts ≥50 cells/mm³:** Initiate ART within 8 weeks of starting TB treatment **(AI)**.
  - **During pregnancy, regardless of CD4 count:** Initiate ART as early as feasible, for treatment of the person with HIV and to prevent HIV transmission to the infant **(AIII)**.
  - **With TB meningitis:** When initiating ART early, patients should be closely monitored, as high rates of adverse events and deaths have been reported in a randomized trial **(AI)**.
  - For patients with active TB who are receiving ART, the ARV regimen should be assessed with particular attention to potential drug-drug interactions between ARVs and TB drugs. Rifamycin antibiotics (rifabutin, rifampin, and rifapentine), in particular, have considerable potential for drug-drug interactions. The ARV regimen may need to be modified to permit use of the optimal TB treatment regimen (see Tables 24a through 24e for drug interaction data and dosing recommendations). **(AII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

DHHS

- CD4 T lenfosit sayısı <50/ mm3 ise TB tedavisinden 2 hafta sonra ART
- CD4 T lenfosit sayısı ≥50/ mm3 ise TB tedavisinden 8 hafta sonrasına kadar ART ertelenebilir (özellikle ilaç etkileşim durumunda)
- ART ile 4 hafta süreyle profilaktik prednizon (14 gün boyunca 40 mg, ardından 14 gün boyunca 20 mg)

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

Recommended regimens with rifampicin	
2 NRTIs + NNRTI	
TDF/XTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bedtime or 2 hours before dinner
Alternative regimens with rifampicin	
2 NRTIs + INSTI	
TDF/XTC + DTG bid	
TDF/XTC + RAL bid	
ABC/3TC + RAL bid	HBsAg negative HLA-B*57:01 negative
Other combinations with rifabutin	
2 NRTIs + PI/r	
TDF/XTC + DRV/r, ATV/r or LPV/r	With food
ABC/3TC + DRV/r, ATV/r, or LPV/r	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL With food

EACS

Birinci Seçenek ART	**TDF/FTC+ EFV veya TDF/ 3TC+EFV ABC/3TC+EFV**
Alternatif ART (rifampisin ile)	TDF/FTC veya TDF/3TC +DTG (günde 2 kez) TDF/FTC veya TDF/3TC +RAL (günde 2 kez) ABC/3TC+RAL (günde 2 kez)
Alternatif ART (rifabutin ile)	TDF/FTC veya TDF/3TC +DRV/r, ATV/r, LPV/r ABC/3TC+ +DRV/r, ATV/r, LPV/r

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

Tablo 6.4. Rifampisin-rifabutinin antiretroviral tedavi ile kullanımı		
	Rifampisin	**Rifabutin**
NRTI		
TDF	Her iki ilaç da standart dozda	Her iki ilaç da standart dozda
TAF[a]	TAF günde iki kez	TAF düzeyinin azalması beklenmektedir. TAF-rifampisin çalışmaları göz önüne alınarak TAF günde iki kez önerilebilir
NNRTI		
EFV	Her iki ilaç da standart dozda	Rifabutin 450 mg/gün EFV standart dozda
PI		
LPV/r	Çift doz LPV/r ya da RTV 2 x 400 mg	Rifabutin 150 mg/gün
DRV/r	Önerilmemekte	Rifabutin 150 mg/gün
ATV/R	Önerilmemekte	Rifabutin 150 mg/gün
INSTI		
DTG	DTG 2 x 50 mg	Her iki ilaç da standart dozda
EVG/c	Önerilmemekte	Rifabutin 150 mg/gün (haftada üç kez
RAL	RAL 2 x 800 mg veya 2x400 mg	Her iki ilaç da standart dozda
BIC	Önerilmemekte	Önerilmemekte
CCR5 inhibitörü		
MVC	Çift doz MVC günde iki kez	Her iki ilaç da standart dozda
FI		
ENF (T20)	Her iki ilaç da standart dozda	Her iki ilaç da standart dozda

[a] *Rifampisin varlığında TAF'ın günde bir kez kullanımı ile ilgili yeterli veri yok*

Karaciğer Fonksiyon Bozukluğunda ART

NRTIs	
ABC	Child-Pugh Class A: 200 mg bid (use oral solution) Child-Pugh Class B or C: contraindicated
FTC	No dosage adjustment
3TC	No dosage adjustment
TAF	No dosage adjustment
TAF/FTC	No dosage adjustment
TDF	No dosage adjustment
TDF/FTC	No dosage adjustment
ZDV	Reduce dose by 50% or double the interval between doses if Child-Pugh Class C
NNRTIs	
EFV	No dosage adjustment; use with caution in persons with hepatic impairment
TDF/FTC/EFV	
ETV	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
NVP	Child-Pugh Class B or C: contraindicated
RPV	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
TAF/FTC/RPV	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
TDF/FTC/RPV	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
TDF/3TC/DOR	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
DOR	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data

PIs	
ATV	Child-Pugh Class A: no dose adjustment
	Child-Pugh Class B: 300 mg qd (unboosted)
	Child-Pugh Class C: not recommended
ATV/c	Child-Pugh Class A: no dosage adjustment
	Child-Pugh Class B or C: not recommended
COBI	Refer to recommendations for the primary PI
DRV	Child-Pugh Class A or B: no dosage adjustment
	Child-Pugh Class C: not recommended
DRV/c	Child-Pugh Class A or B: no dosage adjustment
	Child-Pugh Class C: not recommended
TAF/FTC/DRV/c	Child-Pugh Class A or B: no dosage adjustment
	Child-Pugh Class C: not recommended
LPV/r	No dosage recommendation; use with caution in persons with hepatic impairment
RTV	Refer to recommendations for the primary PI
AI	
FTR	No dosage adjustment
FI	
ENF	No dosage adjustment
EI	
Ibalizumab	No dosage adjustment
CCR5 Inhibitor	
MVC	No dosage recommendations. Concentrations will likely be increased in persons with hepatic impairment
INSTI	
RAL	No dosage adjustment
EVG	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
DTG	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
BIC	Child-Pugh Class A or B: no dosage adjustment
	Child-Pugh Class C: no data, not recommended
TAF/FTC/EVG/c	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
TDF/FTC/EVG/c	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
ABC/3TC/DTG	Use separate compounds and refer to those adjustments
TAF/FTC/BIC	Child-Pugh Class A or B: no dosage adjustment
	Child-Pugh Class C: no data
CAB	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data

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Böbrek Fonksiyon Bozukluğunda ART

	eGFR[i] (mL/min)				Haemodialysis[ix]
	≥ 50	30-49	10-29	< 10	
NRTIs					
Individual agents					
ABC[iii]	300 mg q12h or 600 mg q24h	No dose adjustment required			
FTC[v]	200 mg q24h		200 mg q72h	200 mg q96h	200 mg q24h[v]
3TC[v]	300 mg q24h	150 mg q24h	100 mg q24h[vi]	50-25 mg q24h[vi]	50-25 mg q24h[vi, vii]
TDF[viii]	300[viii] mg q24h	300[viii] mg q48h	Not recommended (300[viii] mg q72-96h, if no alternative	Not recommended (300[viii] mg q7d, if no alternative)	300[viii] mg q7d[ix]
TAF[iii,x]	25[x] mg q24h			No data	25 mg q24h[ix]
ZDV	300 mg q12h	No dose adjustment required		100 mg q8h	100 mg q8h[ix]
Combinations					
ABC[iii]**/3TC**[v]	600/300 mg q24h	Use individual drugs			
ZDV/3TC	300/150 mg q12h				
ABC/3TC/ZDV	300/150/300 mg q12h				
TAF[iii]**/FTC**[v]	25[x]/200 mg q24h		Use individual drugs[xv]		25/200 mg q24[ix]
TDF[viii]**/FTC**[v]	300[viii]/200 mg q24h	300[viii]/200 mg q48h	Use individual drugs		
NNRTIs					
EFV	600 mg q24h	No dose adjustment required			
ETV	200 mg q12h	No dose adjustment required			
NVP	200 mg q12h	No dose adjustment required			Additional 200 mg[ix]
RPV	25 mg q24h	No dose adjustment required			
TAF[iii]**/FTC**[v]**/RPV**	25[x]/200/25 mg q24h		Use individual drugs[xv]		25/200/25 mg q24h[ix]
TDF[viii]**/FTC**[v]**/RPV**	300[viii]/200/25 mg q24h	Use individual drugs			
DOR	100 mg q24h	No dose adjustment required; < 10: no PK data			
TDF[viii]**/3TC**[v]**/DOR**	300[viii]/300/100 mg q24h	Use individual drugs			
PIs[xvii]					
ATV/c	300/150 mg q24h Do not initiate if eGFR < 70 mL/min if used with TDF *	No dose adjustment required[xviii]			Not recommended
ATV/r	300/100 mg q24h	No dose adjustment required[xviii]			Not recommended
DRV/r	800/100 mg q24h 600/100 mg q12h	No dose adjustment required[xviii]			
DRV/c	800/150 mg q24h Do not initiate if eGFR < 70 mL/min if used with TDF *	No dose adjustment required[xviii]			Not evaluated
TAF[iii]**/FTC**[v]**/DRV/c**	10/200/800/150 mg q24h		Use individual drugs		
LPV/r	400/100 mg q12h	No dose adjustment required[xviii]			

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	eGFR[ii] (mL/min)				Haemodialysis[iii]
	≥ 50	30-49	10-29	< 10	
RAL	1 x 400 mg tablet q12h or 2 x 600 mg tablets q24h	No dose adjustment required[xxii]			
DTG	50 mg q24h	No dose adjustment required[xxii]			
3TC[v]/DTG	300/50 mg q24h	Use individual drugs			
ABC[iv]/3TC[v]/DTG	600/300/50 mg q24h	Use individual drugs[xxiii]			
RPV/DTG	25/50 mg q24h	No dose adjustment required[xxii]			
TAF[ix]/FTC[v]/BIC	25/200/50 mg q24h	No dose adjustment required[xxvii]	Not recommended if eGFR > 15 - < 30 mL/min or if eGFR < 15 mL/min without chronic HD as safety not established[xxvii]	No adjustment if on HD, however, use should generally be avoided and only used if potential benefits outweigh potential risks[xxvii]	
TAF[ix]/FTC[v]/EVG/c	10/200/150/150 mg q24h		Not recommended[xxii]	10/200/150/150 mg q24h[iv]	
TDF[xiv]/FTC[v]/EVG/c	300[xxiii]/200/150/150 mg q24h Do not initiate if eGFR < 70 mL/min	Not recommended			
CAB	30 mg q24h	No dose adjustment required[xxiii]			
CAB LA RPV LA	400/600 mg 1x/4 w 600/900 mg 1x/8 w	No dose adjustment required[xxiii]			
MVC: co-administered without CYP3A4 inhibitors[xiv]	300 mg q12h	No dose adjustment required[xxiii]			
MVC: co-administered with CYP3A4 inhibitors[xiv]	If eGFR < 80 mL/min 150 mg q24h[xxiv]				
Ibalizumab	2000 mg loading dose followed by 800 mg every 2 weeks. No dose adjustment required				
FTR	600 mg q12h	No dose adjustment required			

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Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Persons with Renal Insufficiency	Dosing in Persons with Hepatic Impairment
Some FDC products are not recommended in persons with different degrees of renal insufficiency. The recommendations for individual FDCs based on CrCl level are outlined below. • *CrCl <70 mL/min:* **Initiation of Stribild is not recommended.** • *CrCl <50 mL/min:* **FDCs not recommended:** Atripla, Cimduo, Complera, Delstrigo, Temyxis, Truvada, Symfi, Symfi-Lo • *CrCl <30 mL/min:* **FDCs not recommended:** Dovato, Epzicom, Triumeq • *CrCl <30 mL/min* ***and*** *not on HD:* **FDCs not recommended:** Biktarvy, Descovy, Genvoya, Odefsey, and Symtuza. The component drugs in some of the FDC products listed above may be prescribed as individual formulations with dose adjustment based on CrCl level as indicated below in this table.			
NRTIs			
Abacavir (ABC) *Ziagen*	ABC 300 mg PO twice daily *or* ABC 600 mg PO once daily	No dose adjustment necessary.	*Child-Pugh Class A:* ABC 200 mg PO twice daily (use oral solution) *Child-Pugh Class B or C:* **Contraindicated**

Appendix B, Table 11. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency
(Last updated June 3, 2021; last reviewed June 3, 2021) (Page 1 of 10)

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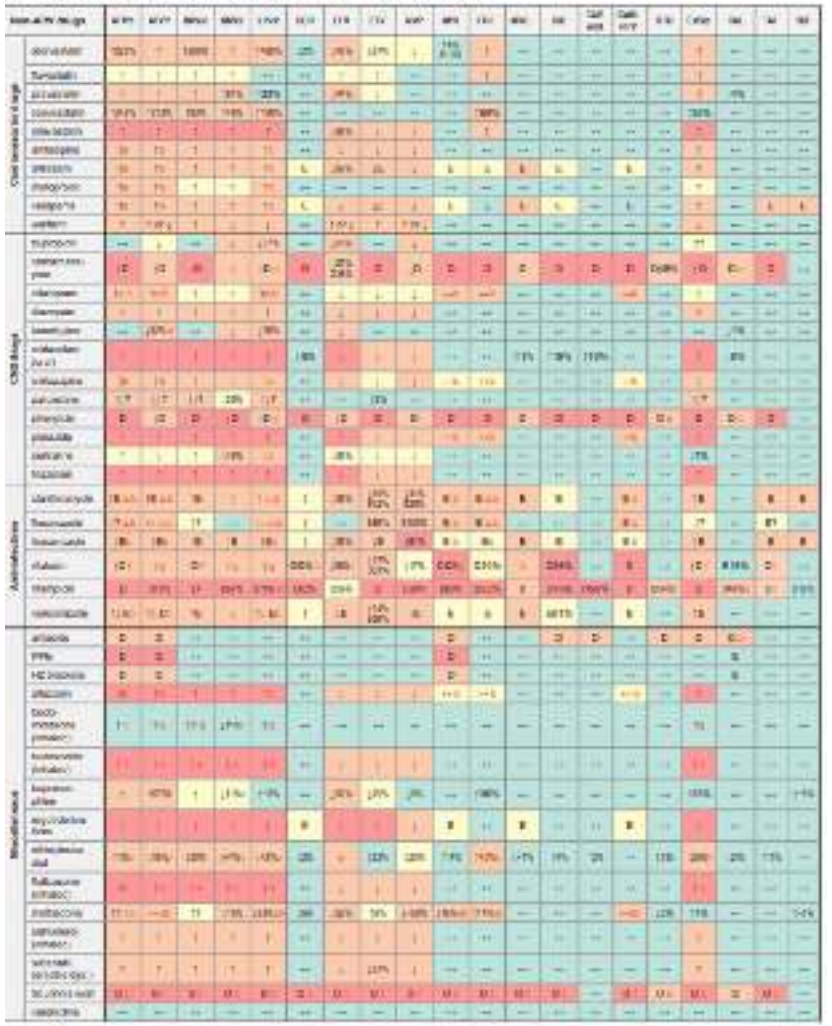
Tablo 4.7. Antiretroviral ilaçlar ile kardiyovasküler sistem, gastrointestinal sistem ilaçları ve antidiyabetik ilaçlar arasındaki etkileşimler

		PI		NNRTI				INSTI					NRTI					Diğer	
		DRV/r	LPV/r	EFV	ETV	NVP	RPV	ISL	DTG	EVG/c	RAL	BIC	CBG	ABC	FTC	3TC	TAF/TDF	ZDV	MVC	FTR
Statinler	Atorvastatin	↑	↑%490 ↑	↓%43 ↑	↓%33 ↑	↑	–	–	–	↑	–	–	–	–	–	–	–	–	–	↑
	Fluvastatin	–	–	–	↑	↑	–	–	–	↑	–	–	–	–	–	–	–	–	–	↑
	Pravastatin	↓%51 ↑	–	↓%44 ↑	↑	–	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
	Rosuvastatin	↓%23 ↑	↑%107 ↑	–	–	–	–	–	–	↑%38 ↑	–	–	–	–	–	–	–	–	–	↑
	Simvastatin	↑	↑	↓%58 ↑	↑	↑	–	–	–	↑	–	–	–	–	–	–	–	–	–	↑
ARBL	İrbesartan	↑	↑	↑	↑	–	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
	Losartan																			
	Valsartan	↑	↑	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	↑
Beta Blokörler	Atenolol	–	– *	–	–	–	–	–	–	–	–	↑	–	–	–	–	–	–	–	–
	Bisoprolol	↑	↑ *	↑	↑	↑	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
	Karvedilol	↑↑	↑↑ *	↑↑	↑↑	–	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
	Metoprolol	↑	↑ *	–	–	–	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
	Propranolol	↑	↑ *	–	–	–	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
Kalsiyum Kanal Blokörleri	Amlodipin Felodipin Lerkanidipin Nifedipin	↑	↑ *	↑	↑	↑	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
	Diltiazem	↑	↑ *	↓%69 ↑	↑↑	↑	↑	–	–	↑	–	↑	–	–	–	–	–	–	↑	↑
	Verapamil	↑	↑ *	↑	↑↑	↑	↑	–	–	↑	–	↑	–	–	–	–	↑ D	–	↑	↑
Diüretikler	Furosemid	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	↑ D	–	–	–
	İndapamid	↑	↑	↑	↑	↑	–	–	–	↑	–	–	–	–	–	–	–	–	–	–
Diğer	Amiodaron	↑	↑	–	–	–	–	–	–	–	–	↑	–	–	–	–	–	–	–	↑
	Propafenon	↑	↑	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	Digoksin	↑%36 ↑	↑	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	İvabradin	↑	↑	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

A, tenofovir alafenamit; D, tenofovir disoproksil fumarat. ARBL, anjiyotensin reseptör blokerleri
*QT aralığında uzama
Hidroklorotiyazit, spironolakton, klortalidon, eprosartan, telmisartan, olmesartan, kandesartan ve ACE inhibitörleri ile antiretroviral ilaçlar arasında etkileşim beklenmemektedir.

HIV/AIDS TANI İZLEM VE TEDAVİ EL KİTABI

Drug-drug Interactions between ARVs and non-ARVs



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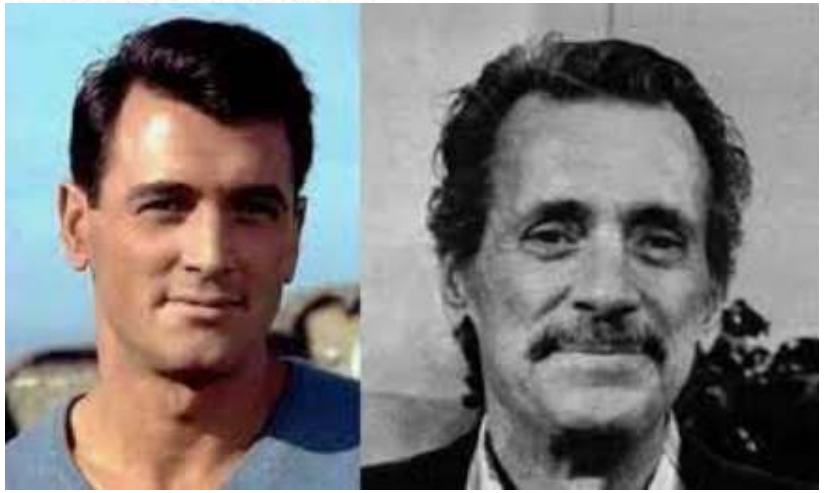
Özet

- Tedaviye başlama kararı hasta ile birlikte alınmalı
- Mümkün olan en kısa sürede ART başlamalı
- Naiv hastada 2NRTI+ INSTI ya da 3TC+DTG
- Hastaların özel durumları, koenfeksiyonları değerlendirilerek alternatif ART seçilmeli
- Ömür boyu ART kullanmanın önemi anlatılmalı

Seksenli Yıllar - Üstünde dantel örtüsü olma.



HIV+

Teşekkür ederim……..