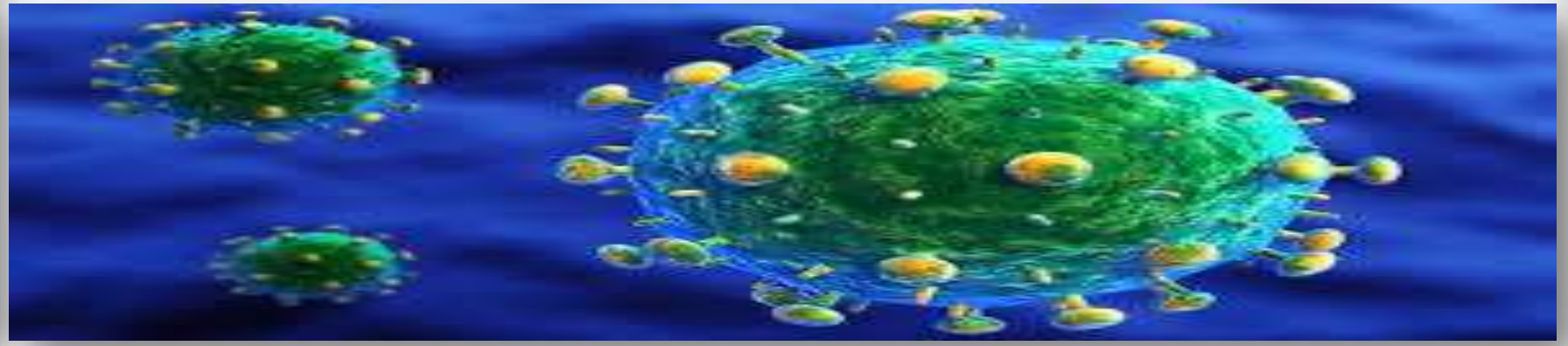
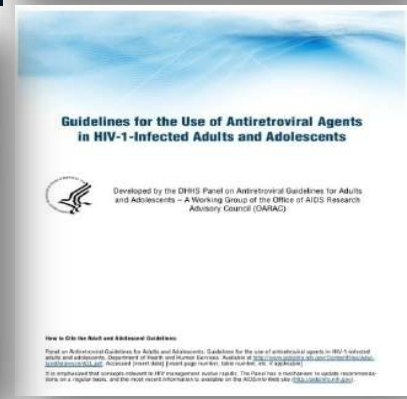


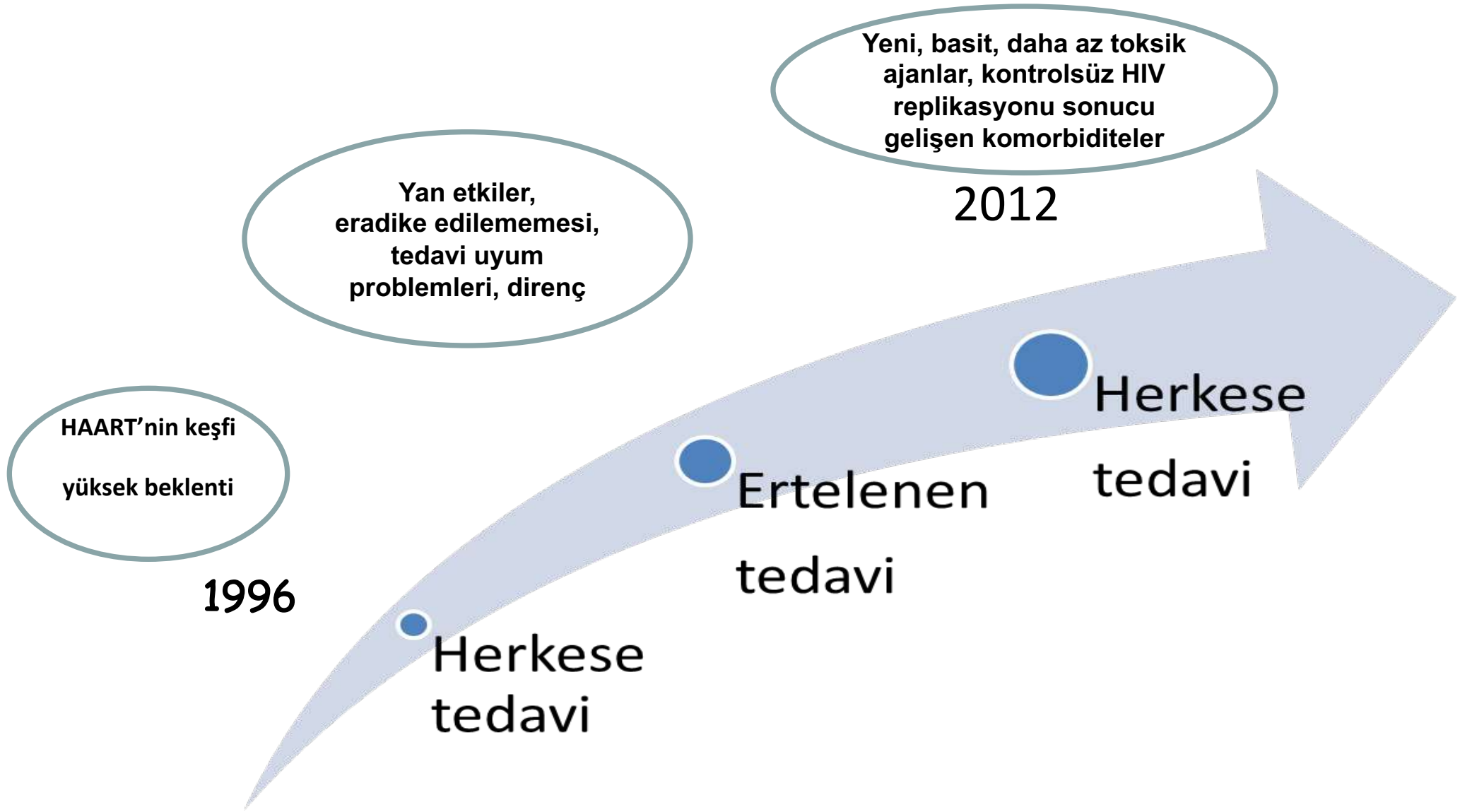


Antiretroviral Tedavi ve Fırsatçı Enfeksiyonların İzleminde Güncel Rehberlerde Neler Değişti ?

Asuman İnan

Haydarpaşa Numune Eğitim ve Araştırma Hastanesi

11 Mart 2022


Yeni, basit, daha az toksik ajanlar, kontrolsüz HIV replikasyonu sonucu gelişen komorbiditeler
2012
Yan etkiler, eradike edilememesi, tedavi uyum problemleri, direnç
HAART'nin keşfi
yüksek beklenti
1996
Herkese tedavi
Ertelenen tedavi
Herkese tedavi

Rehberler


EACS
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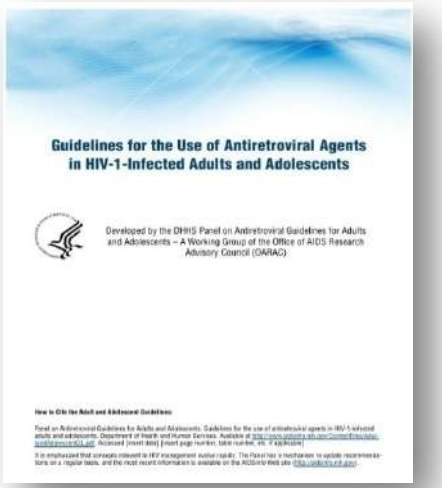
11
GUIDELINES
Version 11.0
October 2021
English

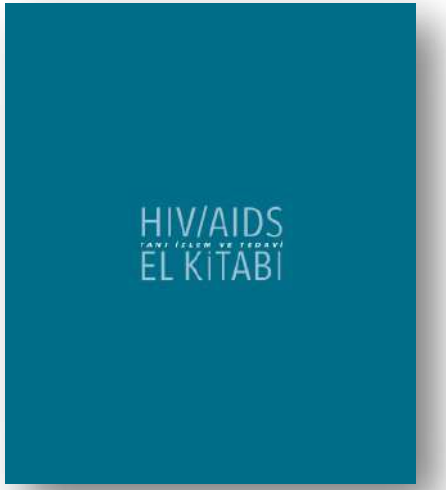

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents
Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)


HIV / AIDS TANI
TEDAVİ REHBERİ


British HIV Association
BHIVA


International AIDS Society
Stronger Together


World Health Organization


HIV/AIDS
EL KİTABI

Değişmesinler

HIV/AIDS

TANI İZLEM VE TEDAVİ

EL KİTABI

Tablo 4.2. Daha önce antiretroviral kullanmamış, erişkin HIV pozitif bireylerde birinci basamak antiretroviral tedavi rejimi için Türkiye'de bulunan antiretroviral ilaçlar

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
		Truvent 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

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[g,h] veya ATV/r[g,h]	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[e] veya DRV/r[e]	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,d]	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'den 12 saat önce ve 4 saat sonra alınabilir.	Yemekle
RAL[b] + DRV/c[e] veya DRV/r[e]	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

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HIV TREATMENT

ART Naif HIV ile Yaşayan Bireylerde Başlangıç Kombinasyon Rejimi

SADECE 2 KATEGORİ

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	

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

ART Naif HIV ile Yaşayan Bireylerde Başlangıç Kombinasyon Rejimi

Regimen	Main requirements	Additional guidance (see footnotes)
Recommended regimens		
2 NRTIs + INSTI		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk) II (Weight increase (DTG))
TAF/FTC/BIC		II (Weight increase (BIC, TAF))
TAF/FTC or TDF/XTC + DTG		II (Weight increase (DTG, TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing)
TAF/FTC or TDF/XTC + RAL qd or bid		II (Weight increase (RAL, TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)
1 NRTI + INSTI		
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure	II (Weight increase (DTG)) V (3TC/DTG not after PrEP failure)
2 NRTIs + NNRTI		
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR		II (Weight increase (TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VI (DOR: caveats, HIV-2)

YENİ

ART Naif HIV ile Yaşayan Bireylerde Başlangıç Kombinasyon Rejimi

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

~~ABC/3TC + RAL qd or bid~~ ~~TDF/FTC/EVG/c~~
~~TAF/FTC/EVG/c~~
~~ABC/3TC +EFV~~
~~ABC/3TC + ATV/c or ATV/r~~
~~ABC/3TC + DRV/c or DRV/r~~
~~TAF/FTC or TDF/FTC or TDF/3TC + ATV/c or ATV/r~~
~~RAL 400 mg bid + DRV/c or DRV/r~~

ART Naif HIV ile Yaşayan Bireylerde Başlangıç Kombinasyon Rejimi

Eğer kişi PrEP kullanırken HIV ile infekte olmuşsa, kullanılan ikili ajana direnç bariyeri yüksek bir 3. ajan (DRV/b, DTG veya BIC) eklenmelidir.

1 NRTI + INSTI		
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure	II (Weight increase (DTG)) V (3TC/DTG not after PrEP failure)

Virolojik Baskılanma Sağlanmış Kişilerde İlaç Değiştirme Stratejileri

Dual therapies

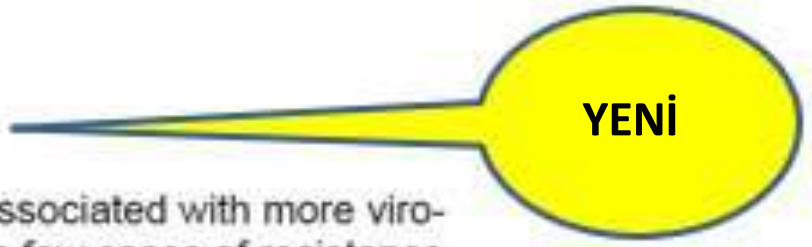
In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months these dual therapy strategies should only be given if there is

a) no historical resistance and

b) HBV immunity or if non-immune concomitant HBV Vaccination

Dual therapies supported by large randomized clinical trials or meta-analyses:

DTG + RPV
XTC + DTG
XTC + DRV/b
Long-acting CAB + RPV bi-monthly injections



In clinical trials, these strategies have not been associated with more virological rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and CAB + RPV

Virolojik Baskılanma Sağlanmış Kişilerde İlaç Değiştirme Stratejileri

Dual therapies

In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months these dual therapy strategies should only be given if there is

a) no historical resistance and

b) HBV immunity or if non-immune concomitant HBV Vaccination

Dual therapies supported by large randomized clinical trials or meta-analyses:

DTG + RPV
XTC + DTG
XTC + DRV/b
Long-acting CAB + RPV bi-monthly injections

~~3TC+ATV/R~~

In clinical trials, these strategies have not been associated with more virological rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and CAB + RPV

Virolojik Başarısızlık

Direnç mutasyonlarının varlığında tedavi önerileri için yeni ifadeler dahil olmak üzere bölüm güncellendi

In case of demonstrated resistance mutations	General recommendations:
	Use at least 2 and preferably 3 active drugs in the new regimen (including active drugs from previously used classes) based on resistance mutations present in current and earlier genotypic analyses
	* If genotype shows only limited NRTI mutation(s) e.g. M184V and/or 1-2 TAMs[iii]: new regimen can include 2 NRTIs (3TC or FTC plus another NRTI with at most low level resistance) and either 1 active PI/b (i.e. DRV/b) or BIC or DTG (RAL, EVG/c or NNRTI not recommended) * If genotype shows multiclass resistance (i.e. ≥ 2 classes): new regimen will usually use - at least 1 fully active PI/b (i.e. DRV/b) or 1 fully active 2nd generation INSTI (BIC, DTG) - plus 1 or 2 drugs remaining fully active despite resistance to other drugs from the class (i.e. 1 or 2 NRTIs and/or DOR) - and/or from a class not used previously i.e. INSTI, NNRTI, PI/b, assessed by genotypic testing * When a 2-3 drugs active regimen cannot be constructed with NRTI, NNRTI, PI/b and INSTI, a drug with a new mechanism of action such as fostemsavir or ibalizumab can be added to obtain such a 2-3 drugs active regimen

En az 2 tercihan 3 aktif ilaç kullanın

Sadece sınırlı NRTI mutasyonu varsa (M184 V ve/veya 1-2 TAM): yeni rejim 2 NRTI ve 1 aktif PI /b (DRV/r vb) veya BIC veya DTG içermelidir (RAL, EVG/c veya NRTI önerilmez)

Çok sınıfa direnç varsa

En az 1 tam aktif PI/b veya 1 tam aktif 2. sınıf INSTI (BIC, DTG)

+

Sınıfına direnç olsa bile aktif 1 veya 2 ilaç (1 veya 2 NRTI ve /veya DOR)

ve/veya

Daha önce kullanılmamış bir sınıftan 1 veya 2 ilaç (INSTI, NNRTI, PI/b)

HIV ile Yaşayan Gebe veya Gebelik düşünen Kadınlarda Tedavi

“ART kararı kişi ile birlikte verilmeli ve tolerabilite, olası uyum sorunları göz önüne alınarak bireyselleştirilmeli, ayrıca ART kullanımından kaynaklanabilecek olası riskler veya gebelikte değişebilecek farmakokinetik özellikler değerlendirilmelidir. «

HIV ile Yaşayan Gebe veya Gebelik düşünen Kadınlarda Tedavi

Recommended regimens	
2 NRTIs + INSTI (PREFERRED)	
ABC/3TC + DTG or ABC/3TC/DTG	DTG to be discussed with women considering to become pregnant or if to be used in first 6 weeks of pregnancy HLA-B*57:01 negative HBsAg negative
TDF/XTC or TAF/FTC + DTG	DTG to be discussed with women considering to become pregnant or if to be used in first 6 weeks of pregnancy. TAF/FTC not recommended in first 14 weeks of pregnancy
TDF/XTC or TAF/FTC + RAL 400 mg bid	TAF/FTC not recommended in first 14 weeks of pregnancy
2 NRTIs + PI/r	
TDF/XTC or TAF/FTC + DRV/r 600 mg/100 mg bid	With food TAF/FTC not recommended in first 14 weeks of pregnancy

YENİ

YENİ

YENİ

YENİ

- DTG gebeliğin ilk 6 haftasında kullanım için veya gebe kalmak isteyen kadınlarda kullanım için tartışılabilir
- TAF artık önerilen rejimler arasında (14 haftalık gebelikten sonra)

HIV ile Yaşayan Gebe veya Gebelik Planlayan Kadınlarda Tedavi

Alternative regimens	
2 NRTIs + INSTI	
ABC/3TC + RAL 400 mg bid	HBsAg negative HLA-B*57:01 negative
2 NRTIs + NNRTI	
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bedtime or 2 hours before dinner
TDF/XTC or TAF/FTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner TAF/FTC not recommended in first 14 weeks of pregnancy
TDF/XTC or TAF/FTC + RPV or TDF/FTC/RPV or TAF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food TAF/FTC not recommended in first 14 weeks of pregnancy
2 NRTIs + PI/r	
ABC/3TC + DRV/r 600 mg/100 mg bid	HLA-B*57:01 negative HBsAg negative With food

~~ATV, ZDV~~

~~LPV/r artık alternatiflerden de kaldırıldı~~

Temas Öncesi Proflaksi (PrEP)

Tüm bölüm güncellendi

The following procedures are recommended:

- Documented negative fourth generation
starting PrEP. In case of suspicion of a
on plasma should also be performed, p
generation HIV test should be repeated
months. In stable long-term users who
an interim third generation test that can
clinic is acceptable
- PrEP should be changed to triple-drug
of early clinical signs of HIV seroconv
test which may necessitate referral for
ART initiation page 12
- PrEP may continue during pregnancy and breastfeeding if the risk of acquiring HIV persists

- 4.kuşak HIV testi TÖP başlanmadan önce bakılmalı, 1. ayda her 3 ayda bir tekrar edlmelidir
- Akut HIV infeksiyonundan şüpheleniliyorsa HIV RNA bakılmalıdır.

- Risk varsa gebelik ve emzirme döneminde de TÖP'e devam edilebilir

YENİ

Pre-exposure Prophylaxis (PrEP)

Tüm bölüm güncellendi

3. PrEP regimen

- TDF/FTC 300*/200 mg 1
  should be taken for 7 da
  days after the last expos
- A trial with daily TAF/FT
  non inferiority to daily TD
  groups
- For men only, PrEP may
  FTC 2-24 hours before e
  doses of TDF/FTC, 24 and 48 hours after the first drug intake; no data for TAF/FTC so far). There are no efficacy data with on demand PrEP with TDF/FTC in women

- **TDF/FTC 1 tablet /gün erkek ve kadınlarda temas öncesi 7 gün ve son temastan sonra 7 gün**
- **TAF/ETC ESE ve transgender kadınlarda etkili**
- **İsteğe bağlı TÖP: temastan 1 gün önce 2 doz, temastan sonra 24 ve 48. saatlerde birer doz sadece erkekler için öneriliyor**

YENİ

Fırsatçı İnfeksiyonlarda ART Ne Zaman Başlanmalıdır ?

	Initiation of ART	Comments
General recommendation	As soon as possible within 2 weeks after starting treatment for the opportunistic infection	
Tuberculosis	As soon as possible within two weeks of starting TB treatment, regardless of CD4 count	For details, see ART in TB/HIV Co-infection section, page 20
- TB meningitis	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	Corticosteroids are recommended as adjuvant treatment for TB meningitis

- ART, fırsatçı infeksiyon tedavisi başlandıktan sonraki 2 hafta içerisinde mümkün olduğu kadar erken başlanmalıdır
- Tüberkülozda: CD4 sayısından bağımsız olarak TB tedavisi başlandıktan sonraki 2 hafta içerisinde başlanmalıdır
- Tüberküloz menenjitte: ART 4 hafta sonrasına ertelenmelidir, CD4< 50(100) h/µl ise ilk 2 hafta içerisinde başlanabilir

Fırsatçı İnfeksiyonlarda ART Ne Zaman Başlanmalıdır ?

	Initiation of ART	Comments
General recommendation	As soon as possible within 2 weeks after starting treatment for the opportunistic infection	
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)	Corticosteroids are not recommended as adjuvant treatment

- Kriptokok menenjitinde ART en az 4 hafta sonrasına (DSÖ 4-6 hafta, bazı uzmanlar 6-10 hafta öneriyor) ertelenmelidir

CD4 count threshold / indication			
CD4 count < 200 cells/µL, CD4 percentage < 14%, recurrent oral thrush, or relevant concomitant immunosuppression*			
Prophylaxis against *Pneumocystis jirovecii* Pneumonia (PcP) & *Toxoplasma gondii* infection **Stop:** if CD4 count > 100 cells/µL and HIV-VL undetectable over 3 months * e.g. use of corticosteroids > 20 mg prednisone equivalent per day for > 2 weeks, cancer chemotherapy, biological agents such as rituximab and others. Decisions on installation and discontinuation in these situations have to be taken individually			
	Drug	**Dose**	**Comments**
Positive or negative serology for Toxoplasmosis	**trimethoprim-sulfamethoxazole (TMP-SMX)**	400/80 mg qd po or 800/160 mg qd po or 800/160 mg x 3/week po	
Negative serology for toxoplasmosis	**pentamidine**	300 mg in 6 mL sterile water x 1 inhalation/month	Does not prevent the rare extrapulmonary manifestations of *P. jirovecii*
Negative serology for toxoplasmosis	**dapsone**	100 mg qd po	Check for G6PD-deficiency
Negative serology for toxoplasmosis	**atovaquone suspension**	1500 mg qd (with food)	
Positive serology for toxoplasmosis	**dapsone** **+ pyrimethamine** **+ folinic acid**	200 mg/week po 75 mg/week po 25-30 mg/week po	Check for G6PD-deficiency
Positive serology for toxoplasmosis	**atovaquone suspension** **+/- pyrimethamine** **+ folinic acid**	1500 mg qd po (with food) 75 mg/week po 25-30 mg/week po	
Positive cryptococcal serum antigen and CD4 count < 100 cells/µL	**fluconazole**	800 mg qd po for 2 weeks followed by 400 mg qd po for 8 weeks	Asymptomatic individual and cryptococcal meningitis, pulmonary or other site infection ruled out

YENİ

- Kriptokok antijeni pozitif ve CD4<100 h/µl ise flukonazol ile proflaksi
- (CD4 sayısı<100 h/µl serum kriptokok antijeni ile tarama)

Pneumocystis jirovecii Pnömonisi

Sekonder Proflaksi

- CD4>100 h /µl ve HIV viral yük 3 ay üzerinde saptanamaz düzeyde ise kesilebilir

Tedavi

- «Orta- ciddi PJP'de standart tedaviye kaspofungin ve diğer ekinokandinlerin eklenmesi: düşünülebilir ama zorunlu değil « olarak değiştirildi.

Tüberküloz 1

Tam duyarlı TB

- Alternatif kısa rejim: rifapentine ulaşılabiliyorsa
- rifapentin izoniyazid pirazinamid ve moksifloksasin 2 ay,
- sonrasında rifapentin izoniyazid ve moksifloksasin ile 2 ay

Tüberküloz 2

- Dirençli TB teksti DSÖ 2020 kılavuzu ile uyumlu olarak değiştirildi
- XDR-TB tanımı
- MDR-XDR için tüm oral rejimler
- ve seçilmiş MDR-XDR gruplarda daha kısa (6-12 ay) rejimler

Drug choices	
Each empiric regimen should be reassessed and modified if needed once drug sensitivity results become available	
Group A: **Include all three drugs**	• **levofloxacin** or **moxifloxacin** • **bedaquiline** • **linezolid**
Group B: **Add one or both drugs**	• **clofazimine** • **cycloserine** or **terizidone**
Group C: **Add to complete the regimen and when drugs from Groups A and B cannot be used**	• **ethambutol** • **delamanide** • **pyrazinamide** • **amikacin** (or **streptomycin** – only if susceptible) • **imipenem–cilastatin** or **meropenem** with **amoxicillin/clavulanic acid** • **ethionamide** or **prothionamide** • **para-aminosalicylic acid**

Diagnosis of Multidrug Resistant TB (MDR-TB) / Extensively Drug-Resistant TB (XDR-TB)

MDR/XDR-TB should be suspected in case of:

- Previous TB treatment
- Contact with MDR/XDR-TB index case
- Birth, travel or work in an area endemic for MDR-TB
- History of poor adherence
- No clinical improvement on standard therapy and/or sputum smear positive after 2 months of TB therapy or culture positive at 3 months
- Homelessness/hostel living and, in some countries, recent/current incarceration
- In areas with very high MDR/XDR-TB prevalence

MDR-TB: Resistance to **isoniazid** AND **rifampicin**
XDR-TB: Resistance to **isoniazid** AND **rifampicin** AND **fluoroquinolones** AND at least one of the following injectable drugs:
kanamycin, **capreomycin** or **amikacin**
XDR-TB 2021 update: Resistance to **isoniazid** AND **rifampicin** AND **fluoroquinolones** AND at least one additional **Group A** drug, see below

Rapid detection

Gene Xpert or similar technology has the advantage of rapid detection of rifampicin resistance. Drug susceptibility testing is important for optimising treatment

Treatment of resistant TB

Isoniazid-resistant TB
- **rifampicin/rifabutin + pyrazinamide + ethambutol + fluoroquinolone** for 6 months, WHO 2020 recommendations

Rifampicin-resistant (RR) and MDR/XDR-TB
- Treatment of MDR/XDR-TB is a specialist area. WHO has recently published new Guidelines

Shorter 9-12 months all oral regimen
Can be used in PLWH with confirmed RR/MDR-TB who have not been exposed to treatment with second-line TB drugs, used in this regimen, for more than 1 month, and in whom resistance to fluoroquinolones has been excluded.
Intensive phase: 4 months (can be extended to 6 months if positive sputum smear at the end of 4 months):
bedaquiline (used for 6 months) + **levo-/ moxifloxacin** + **ethionamide** + **ethambutol** + **isoniazid** (high-dose) + **pyrazinamide** + **clofazimine**
Continuation phase: 5 months:
levo-/ moxifloxacin + **clofazimine** + **ethambutol** + **pyrazinamide**
Treatment compliance is crucial. If needed, each dose of MDR/XDR-TB regimen should be given as DOT throughout the whole treatment period

Surgery
Surgical resection may be part of the management for selected persons with focal pulmonary MDR-/XDR-TB

Drug choices	
Each empiric regimen should be reassessed and modified if needed once drug sensitivity results become available	
Group A: **Include all three drugs**	• **levofloxacin** or **moxifloxacin** • **bedaquiline** • **linezolid**
Group B: **Add one or both drugs**	• **clofazimine** • **cycloserine** or **terizidone**
Group C: **Add to complete the regimen and when drugs from Groups A and B cannot be used**	• **ethambutol** • **delamanide** • **pyrazinamide** • **amikacin** (or **streptomycin** – only if susceptible) • **imipenem–cilastatin** or **meropenem** with **amoxicillin/clavulanic acid** • **ethionamide** or **prothionamide** • **para-aminosalicylic acid**

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)

January 20, 2022

Early (Acute and Recent) HIV Infection

- In the previous version of the guidelines, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) suggested that an HIV RNA level of <10,000 copies/mL in a person suspected to have acute HIV may represent a false-positive test result. The section was updated to revise this threshold. The Panel noted that given the improved sensitivity and specificity of current HIV RNA tests in the presence of compatible symptoms or exposure history, even a low HIV RNA concentration (e.g., <3,000 copies/mL) in the setting of a negative or indeterminate HIV antibody test result may represent acute HIV. The Panel noted that, in rare cases, an HIV RNA <3,000 copies/mL may represent a false-positive quantitative test result. In that case, repeat testing should be done to confirm the diagnosis.

- HIV antikor testi negatif veya indeterminant olarak gelen, uygun semptomları ve temas öyküsü bulunan hastalarda düşük HIVRNA düzeyleri bile (örn HIV RNA< 3000 k /ml) akut HIV infeksiyonu ile uyumludur.

Bostwana Tsepamo Doğum Sonuçları Sürveyans Çalışması

- Mayıs 2018: Planlanmamış analizde dolutegravir kullanırken hamile kalan kadınlardan doğan infantlarda NTD prevalansı yüksek bulunmuştu[1]
  - Konsepsiyonda DTG içeren - DTG içermeyen ART : %0.94 vs %0.12 (**prevalans farkı: %0.82**; % 95CI: 0.24-2.3)
- Daha fazla veri birikince DTG ile NTD prevalansı azaldı ve konsepsiyonda DTG içermeyen ART'den anlamlı farkı kalmadı

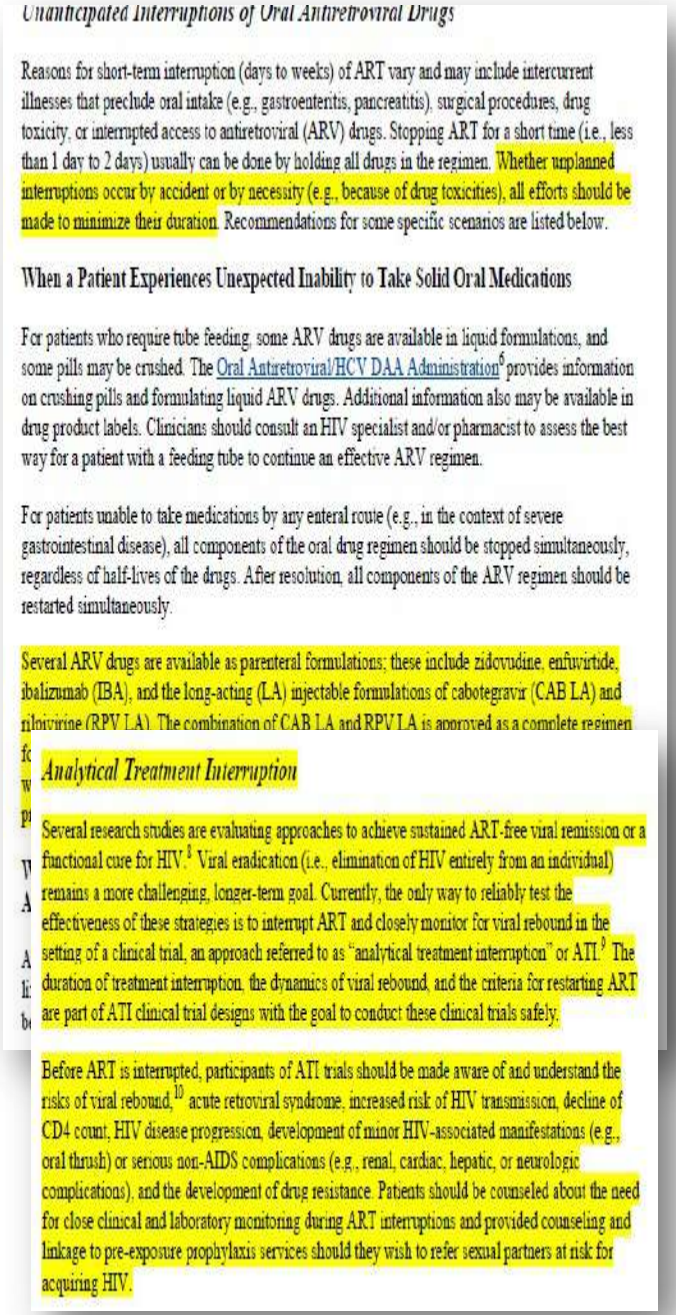
Data Through March 2021[2]	Conception			Pregnancy	HIV Negative (n = 144,967)
	DTG (n = 5860)	Non-DTG (n = 22,475)	EFV (n = 13,217)	DTG (n = 5535)	
Total NTDs per exposures, n/N	9/5860	22/22,475	8/13,217	3/5535	97/144,967
NTD prevalence, % (95% CI)	0.15 (0.08-0.29)	0.10 (0.06-0.15)	0.06 (0.03-0.12)	0.05 (0.02-0.16)	0.07 (0.05-0.08)
Prevalence diff. for DTG at conception, % (95% CI)	Ref	0.06 (-0.03 to 0.20)	0.09 (-0 to 0.23)	0.10 (-0.03 to 0.24)	0.09 (0.01-0.23)

1. Zash. NEJM. 2018; 379:979. 2. Zash. IAS 2021. Abstr. PE02B52.

Discontinuation or Interruption of Antiretroviral Therapy

- This section has been updated to include discussions regarding discontinuation or interruption of long-acting antiretroviral drugs, including ibalizumab and the intramuscular formulations of cabotegravir and rilpivirine. The section also includes discussions regarding steps to take before and during ART interruption for people with HIV who participate in clinical trials that involve analytical treatment interruptions.

- ART'nin gastroenterit, pankreatit, cerrahi gibi nedenlerle 1-2 gün kesilmesi sorun yaratmaz
- Planlanmamış ara vermelerde (ilaç toksisitesi gibi ART mümkün olan en kısa süre kesilmelidir.)
- Hayatı tehdit eden bir toksisite yaşanırsa tüm ilaçlar kesilmeli ve tamamen farklı bir kombinasyonla devam edilmelidir.



Unanticipated Interruptions of Oral Antiretroviral Drugs

Reasons for short-term interruption (days to weeks) of ART vary and may include intercurrent illnesses that preclude oral intake (e.g., gastroenteritis, pancreatitis), surgical procedures, drug toxicity, or interrupted access to antiretroviral (ARV) drugs. Stopping ART for a short time (i.e., less than 1 day to 2 days) usually can be done by holding all drugs in the regimen. Whether unplanned interruptions occur by accident or by necessity (e.g., because of drug toxicities), all efforts should be made to minimize their duration. Recommendations for some specific scenarios are listed below.

When a Patient Experiences Unexpected Inability to Take Solid Oral Medications

For patients who require tube feeding, some ARV drugs are available in liquid formulations, and some pills may be crushed. The Oral Antiretroviral/HCV DAA Administration[6] provides information on crushing pills and formulating liquid ARV drugs. Additional information also may be available in drug product labels. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way for a patient with a feeding tube to continue an effective ARV regimen.

For patients unable to take medications by any enteral route (e.g., in the context of severe gastrointestinal disease), all components of the oral drug regimen should be stopped simultaneously, regardless of half-lives of the drugs. After resolution, all components of the ARV regimen should be restarted simultaneously.

Several ARV drugs are available as parenteral formulations; these include zidovudine, enfuvirtide, ibalizumab (IBA), and the long-acting (LA) injectable formulations of cabotegravir (CAB LA) and rilpivirine (RPV LA). The combination of CAB LA and RPV LA is approved as a complete regimen

Analytical Treatment Interruption

Several research studies are evaluating approaches to achieve sustained ART-free viral remission or a functional cure for HIV.[8] Viral eradication (i.e., elimination of HIV entirely from an individual) remains a more challenging, longer-term goal. Currently, the only way to reliably test the effectiveness of these strategies is to interrupt ART and closely monitor for viral rebound in the setting of a clinical trial, an approach referred to as "analytical treatment interruption" or ATI.[9] The duration of treatment interruption, the dynamics of viral rebound, and the criteria for restarting ART are part of ATI clinical trial designs with the goal to conduct these clinical trials safely.

Before ART is interrupted, participants of ATI trials should be made aware of and understand the risks of viral rebound,[10] acute retroviral syndrome, increased risk of HIV transmission, decline of CD4 count, HIV disease progression, development of minor HIV-associated manifestations (e.g., oral thrush) or serious non-AIDS complications (e.g., renal, cardiac, hepatic, or neurologic complications), and the development of drug resistance. Patients should be counseled about the need for close clinical and laboratory monitoring during ART interruptions and provided counseling and linkage to pre-exposure prophylaxis services should they wish to refer sexual partners at risk for acquiring HIV.

June 3, 2021

What to Start

- Since the release of the last guidelines, updated data from the Botswana Tsepamo study have shown that the prevalence of neural tube defects (NTD) associated with dolutegravir (DTG) use during conception is much lower than previously reported. Based on these new data, the Panel now recommends that a DTG-based regimen can be prescribed for most people with HIV who are of childbearing potential. Before initiating a DTG-based regimen, clinicians should discuss the risks and benefits of using DTG with persons of childbearing potential, to allow them to make an informed decision. Table 6b has been removed from this section.
- Raltegravir (RAL)-based regimens as initial antiretroviral therapy (ART) have been moved from the category of "Recommended Initial Regimens for Most People with HIV" to "Recommended Initial Regimen in Certain Clinical Situations" **(BI)**. The reasons for this change are as follows:
  - Updated Tsepamo data show a lower prevalence of NTD associated with DTG use during conception, which means choosing RAL over DTG is no longer necessary.
  - RAL has a lower barrier to resistance than DTG and bictegravir (BIC).
  - RAL-based regimens have a higher pill burden than other integrase strand transfer inhibitor (INSTI)–based regimens and are not available as part of a single-tablet regimen.

- Bostwana Tsepamo çalışmasının yeni sonuçları konsepsiyon sırasında Dolutegravir kullanılmasının nöral tüp defektlerine yol açma riskinin önceden belirlenenden düşük olduğunu gösterdi, bu nedenle kılavuzdan tablo 6b kaldırıldı.
- Raltegravir çoğu kişiye önerilen sınıfından, belirli klinik durumlarda önerilen kategorisine alındı

Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of ART during pregnancy should be guided by recommendations from the Perinatal Guidelines.

INSTI plus 2 NRTIs:

- BIC/TAF/FTC **(AI)**[c]
- DTG/ABC/3TC **(AI)—if HLA-B*5701 negative**
- DTG plus (TAF or TDF)[a] plus (FTC or 3TC) **(AI)**

INSTI plus 1 NRTI:

- DTG/3TC **(AI)**, except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

Recommended Initial Regimens in Certain Clinical Situations

These regimens are effective and tolerable but have some disadvantages when compared with the regimens listed above or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred (see Table 7 for examples).

INSTI plus 2 NRTIs:

- EVG/c/(TAF or TDF)[c]/FTC **(BI)**[b]
- RAL plus (TAF or TDF)[c] plus (FTC or 3TC) **(BI for TDF/[FTC or 3TC], BII for TAF/FTC)**

Boosted PI plus 2 NRTIs:

- In general, boosted DRV is preferred over boosted ATV
- (DRV/c[b] or DRV/r) plus (TAF or TDF)[c] plus (FTC or 3TC) **(AI)**
- (ATV/c[b] or ATV/r) plus (TAF or TDF)[c] plus (FTC or 3TC) **(BI)**
- (DRV/c[b] or DRV/r) plus ABC/3TC —**if HLA-B*5701 negative (BII)**

NNRTI plus 2 NRTIs:

- DOR/TDF[c]/3TC **(BI)** or DOR plus TAF[c]/FTC **(BIII)**
- EFV plus (TAF or TDF)[c] plus (FTC or 3TC)
  - EFV 600 mg plus TDF plus (FTC or 3TC) **(BI)**
  - EFV 400 mg/TDF/3TC **(BI)**
  - EFV 600 mg plus TAF/FTC **(BII)**
- RPV/(TAF or TDF)[c]/FTC (**BII for TAF and BI for TDF)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3**

Regimens to Consider when ABC, TAF, and TDF Cannot be Used or Are Not Optimal:

- DTG/3TC **(AI)**, except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available
- DRV/r plus RAL twice a day **(CI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3**
- DRV/r once daily plus 3TC **(CI)**

Virologic Failure

- For patients with virologic failure, the Panel's recommendation of "A new regimen should include at least two, and preferably three, fully active agents **(AI)**" has been changed to "A new regimen can include two fully active drugs if at least one with a high resistance barrier is included (e.g., DTG or boosted darunavir) **(AI)**." This change is prompted by accumulating clinical trial data showing that in these patients, a new regimen containing two fully antiretroviral (ARV) drugs can effectively achieve viral suppression, provided that one of the two drugs has a high barrier to resistance.
- Clinical trial data on the use of fostemsavir for patients with multidrug-resistant HIV has been added.

- Virolojik yetersizlik saptanan hastalarda» yeni rejim en az 2 , tercihen 3 aktif ilaç içermeli» önerisi,
- «yeni rejim biri yüksek direnç bariyerli (dolutegravir ya da güçlendiricili darunavir vb) iki tam aktif ilaç içermeli» olarak değiştirildi

Poor CD4 Recovery and Persistent Inflammation

- This section has been revised to include updates on studies describing mechanisms for declining CD4 counts despite suppressive ART and a review of the status of experimental interventional strategies to reduce persistent inflammation. It also includes an explanation for why monitoring levels of inflammation is not currently recommended in clinical practice.

- ART ile viral yükün baskılanmasına rağmen CD4 sayısı düşen hastalar ile ilgili çalışmalar gözden geçirildi ve klinik pratikte inflamasyon düzeylerinin monitorize edilmesinin gerekli olmadığı açıklandı.

Tuberculosis/HIV Coinfection

- The key update to this section includes recommendations for ARV regimens that can be used if a 3-month regimen of weekly isoniazid and rifapentine is prescribed for the treatment of latent tuberculosis infection. The Panel noted that DTG 50 mg once daily may be used with once-weekly rifapentine, provided the patient does not require twice-daily DTG dosing (e.g., in those with certain INSTI-associated resistance mutations or with clinically suspected INSTI resistance).

Latent TB

- 3 ay haftada 1 INH ve Rifapentin
- 4 ay günlük Rifampin
- 3 ay günlük INH ve Rifampin

Key Considerations and Recommendations

- Selection of tuberculosis (TB)-preventive treatment for individuals with HIV and latent tuberculosis infection (LTBI) should be based on the individual's antiretroviral (ARV) regimen as noted below.
  - With daily isoniazid alone for 6 or 9 months, any ARV regimen can be used **(AIII)**.
  - With once-weekly isoniazid plus rifapentine for 3 months:
    - Efavirenz (EFV) 600 mg once daily or raltegravir 400 mg twice daily (in combination with either abacavir/lamivudine [ABC/3TC] or tenofovir disoproxil fumarate/emtricitabine [TDF/FTC]) can be used **(AII)**.
    - Dolutegravir (DTG) 50 mg once daily may be used for those in whom once-daily DTG is appropriate **(BII)**. This 3-month regimen **is not recommended** for patients who require twice-daily DTG therapy (e.g., those with certain integrase strand transfer inhibitors [INSTI]-associated resistance substitutions or clinically suspected INSTI resistance) **(AIII)**.
  - With once-daily isoniazid and rifapentine for 1 month:
    - EFV 600 mg once daily (in combination with either ABC/3TC or TDF/FTC) can be used without dose adjustment **(AI)**.
  - If rifampin or rifapentine is used to treat LTBI, clinicians should review Tables 24a through 24e to assess the potential for drug-drug interactions among different ARV drugs and the rifamycins **(AII)**.
- 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)**.

Recommendations for the Use of Antiretroviral Drugs During Pregnancy *and* Interventions to Reduce Perinatal HIV Transmission in the United States

Developed by the HHS Panel on Treatment of
HIV During Pregnancy and Prevention of Perinatal Transmission—
A Working Group of the Office of AIDS Research Advisory Council (OARAC)

Preferred Dual-NRTI Backbones	
ABC/3TC	Available as an FDC. Can be administered once daily. ABC **should not be used** in patients who test positive for HLA-B*5701 because of the risk of developing a hypersensitivity reaction. ABC/3TC administered with ATV/r or EFV is not recommended if pretreatment HIV RNA is >100,000 copies/mL.
TAF/FTC ***or*** **TAF plus 3TC**	TAF/FTC is available as an FDC. Either coformulated TAF/FTC or separate doses of TAF and 3TC can be administered once daily. When combined with DTG, the efficacy and toxicity of TAF/FTC and TDF/FTC for treatment of pregnant patients are similar, but TAF/FTC is associated with fewer adverse birth outcomes and slightly higher gestational weight gain.
TDF/FTC ***or*** **TDF/3TC**	TDF/FTC is available as an FDC. Either coformulated TDF/FTC or separate doses of TDF and 3TC can be administered once daily. TDF has potential renal toxicity; thus, TDF-based, dual-NRTI combinations should be used with caution in patients with renal insufficiency.

Preferred INSTI Regimens	
DTG/ABC/3TC (FDC) *or* DTG plus a *Preferred* Dual-NRTI Backbone[a]	Administered once daily. The use of DTG/ABC/3TC requires HLA-B*5701 testing before starting therapy because this FDC contains ABC. INSTI-based regimens may be particularly useful when drug interactions or the potential for preterm delivery with a PI-based regimen are a concern. In nonpregnant adults, DTG is associated with lower rates of INSTI resistance than RAL; like RAL, DTG has been shown to rapidly decrease viral load in ARV-naive pregnant women who present to care later in pregnancy. DTG is the only *Preferred* agent recommended for the treatment of acute HIV infection during pregnancy. Either DTG or RAL is the *Preferred* agent for patients who present to care late in pregnancy. However, DTG is the only *Preferred* drug for pregnant patients with acute HIV (see Acute HIV Infection). Specific timing and/or fasting recommendations apply if DTG is taken with calcium or iron (e.g., in prenatal vitamins; see Table 11). The use of DTG at conception has been associated with a small increase in the risk of NTDs, but this was not seen when DTG was started during pregnancy. However, in the most recent data from Botswana, there was no longer a significant difference in NTDs with the use of DTG-containing compared to non-DTG containing ARV regimens at conception. This information should be discussed with patients to ensure informed decision-making. For more information, see Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 5, Teratogenicity, and Appendix C: Antiretroviral Counseling Guide for Health Care Providers.
RAL plus a *Preferred* Dual-NRTI Backbone	PK data are available for RAL in pregnancy when using the twice-daily formulation (400 mg twice daily), but data are not available for the once-daily 1,200 mg (2 × 600 mg) extended-release formulation "raltegravir HD." Twice-daily dosing is required in pregnancy. RAL has been shown to produce rapid viral load decline to undetectable levels in women who present for initial therapy late in pregnancy and thus is a *Preferred* ARV option in this setting. However, RAL is an *Alternative* ARV for persons diagnosed with acute HIV during pregnancy (see Acute HIV Infection). INSTI-based regimens may be particularly useful when drug interactions or the potential for preterm delivery with PI-based regimens are a concern. Specific timing and/or fasting recommendations apply if RAL is taken with calcium or iron (e.g., in prenatal vitamins; see Table 11).

Preferred PI Regimens	
ATV/r plus a *Preferred* Dual-NRTI Backbone	Once-daily administration. Extensive experience with use in pregnancy. Maternal hyperbilirubinemia; no clinically significant neonatal hyperbilirubinemia or kernicterus reported, but neonatal bilirubin monitoring is recommended. Cannot be administered with PPIs. Specific timing recommended for dosing with H2 blockers (see Table 11).
DRV/r plus a *Preferred* Dual-NRTI Backbone	Must be used twice daily in pregnancy.

- ATV/r, DRV/r tercih edilen PI'leri

Alternative Dual-NRTI Backbones	
ZDV/3TC	Available as an FDC. Although not recommended for initial therapy in nonpregnant adults, ZDV/3TC is the NRTI combination with most experience for use in pregnancy. It has the disadvantages of requiring twice-daily administration and having the potential for hematologic toxicities and other toxicities.
Alternative NNRTI Regimens	
EFV/TDF/FTC (FDC) _or_ EFV/TDF/3TC (FDC) _or_ EFV plus a _Preferred_ Dual-NRTI Backbone	Birth defects have been reported in primate studies of EFV, but no evidence has been found of an increased risk of birth defects in human studies and extensive experience in pregnancy; cautionary text remains in the package insert (see Teratogenicity, Efavirenz, and Table 11). These regimens are useful for patients who require treatment with drugs that have significant interactions with _Preferred_ agents or who need the convenience of a coformulated, single-tablet, once-daily regimen and are not eligible for DTG or RPV. Screening for antenatal and postpartum depression is recommended. Higher rate of adverse events than some _Preferred_ drugs.
RPV/TDF/FTC (FDC) _or_ RPV/TAF/FTC (FDC) RPV (oral) plus a _Preferred_ Dual-NRTI Backbone	RPV **is not recommended** in patients with pretreatment HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm^3. Do not use with PPIs. PK data are available for pregnant individuals, but there is relatively little experience with use in pregnancy. PK data suggest lower drug levels and risk of viral rebound in the second and third trimesters; if used, consider monitoring viral load more frequently. Should be taken with food. Available in a coformulated, single-tablet, once-daily regimen.

Insufficient Data in Pregnancy to Recommend for Initial Regimens in People Who Are ART-Naive	
These drugs are approved for use in adults but lack adequate pregnancy-specific PK or safety data.	
BIC/TAF/FTC (FDC)	Limited data on the use of BIC in pregnancy.
DOR	No data on the use of DOR in pregnancy.
IBA	No data on the use of IBA in pregnancy.

Gebelik Tedavi: DHHS Kılavuzu Aralık 2021

İki NRTI

ABC/3TC veya

TDF/FTC veya TDF/3TC

TAF/FTC

+

İntegraz inhibitorü

Dolutegravir (gebelik boyunca ve gebelik deneyenlerde tercih edilen ajan)

Raltegravir (günde 2 kez) veya

veya

Proteaz inhibitörü

Darunavir/ritonavir (günde 2 kez)

veya

Atazanavir/ritonavir

Biktegravir (yetersiz veri) Elvitegravir/kobi (FK sorunlar) DRV/kobi (FK sorunlar) ATV/kobi (FK sorunlar)

DOR (yetersiz veri)

2-ilaç rejimleri önerilmez

DHHS Perinatal Guidelines. 2021.

21 Ocak 2021'de, Uzun Etkili KAB+ RPV, FDA Tarafından Onaylandı

- FDA endikasyonu :
  - Stabil bir ART rejimi ile virolojik olarak baskılanan yetişkinlerde tam bir rejim olarak
  - KAB ve RPV'e bilinen ya da şüphe edilen direnç veya tedavi başarısızlığı öyküsü olmayan hastalarda
- Tolerabiliteyi sağlamak için başlangıçta yaklaşık 1 ay oral rejim
- Başlangıç oral tedavinin son gününde
  - KAB 600 mg + RPV 900 mg gluteal enjektabl başlanır ve ayda 1 enjeksiyonlar ile devam edilir

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212888s000lbl.pdf.

DHHS Açıklaması: Uzun Etkili KAB +RPV

- Oral ART ile en az 3 aydır viral baskılanmanın dökümante edildiği hastalarda KAB ve RPV İM enjeksiyonlar optimizasyon stratejisi olarak kullanılabilir) **(AI)**,
  - Herhangi bir ilaca direnç olmamalıdır
  - Daha önce virolojik başarısızlık olmamalıdır
  - Aktif HBV infeksiyonu olmamalıdır (oral HBV tedavisi alanlar dışında)
  - Gebelik ve gebelik planı olmamalıdır
  - Oral ya da İM KAB veya RPV ile belirgin ilaç ilaç etkileşimi olan tedavi alanlar kullanmalıdır

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/hhs-adults-and-adolescents-antiretroviral-guidelines-panel

Hızlı Tedavi: Kılavuz Önerileri

Guideline	Recommendation for Rapid ART	Recommendation on Rapid ART in Patients With OIs
EACS[1]	**Whether rapid, possibly same-day ART start is proposed** to newly diagnosed persons or postponed until complementary assessments **depends on the setting and medical circumstances, medical indications to start ART more urgently and risk of loss from care**	In persons with OIs, ART initiation may have to be deferred; **initiate ART as soon as possible and within 2 wk after starting treatment for the OI**
DHHS	**Initiate ART immediately (or as soon as possible)** after HIV diagnosis 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	**When no effective therapy exists for the OI, initiate ART without delay[2]**; *Pneumocystis jirovecii*: ART should be initiated in patients, when possible, within 2 wk of *Pneumocystis jirovecii* diagnosis[3]
IAS-USA[4]	**Start ART as soon as possible,** including immediately after diagnosis, **if patient is ready**	**Initiation of ART is recommended within 2 wk of initiation of treatment for most OIs**

1. EACS Guidelines. v11 October 2021. 2. DHHS ART Guidelines. August 2021.
3. DHHS OI Guidelines. Augost 2021 4. Saag. JAMA. 2020;324:1651.

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Bizde Neler Değişti

- Maske
- Mesafe
- Yorgunluk
- Üstüne kırgınlık

"Umutsuz durum yoktur. Umutsuz insanlar vardır. Ben hiçbir zaman umudumu yitirmedim."

M. Atatürk