Gelecek İçin Sözümüz Var

Genvoya Gerçek Yaşam Verileri

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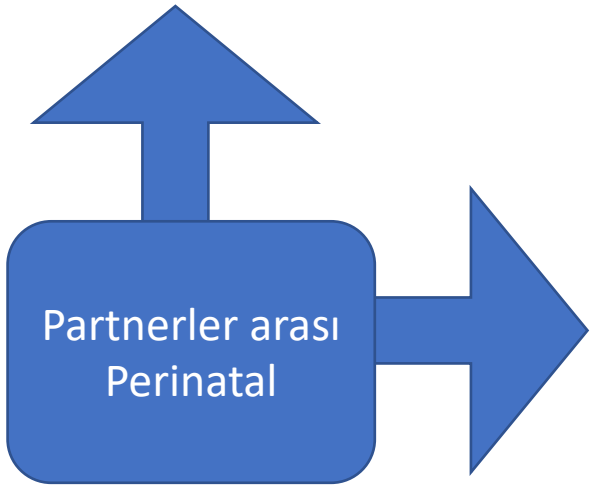
Treatment Goals (Last updated January 28, 2016; last reviewed January 28, 2016)

- Maximally and durably suppress plasma HIV RNA;
- Restore and preserve immunologic function;
- Reduce HIV-associated morbidity and prolong the duration and quality of survival; and
- Prevent HIV transmission.



Part II ART of PLWH

This section provides an overview of the important aspects of the management of PLWH starting or established on ART. Recommendations are based on a range of evidence, in particular it is weighted towards randomised controlled clinical trials. Other data have been taken into account, including cohort studies, and where evidence is limited, the panel has reached a consensus around best clinical practice. The ART section is wide ranging and, with the change in starting therapy independently of CD4 count, there is an important section on readiness to start. Treatment recommendations are based on drugs licensed in Europe and range from initial therapy through to switching with or without virological failure. Two important areas of ART are highlighted: pregnancy and TB. Details on the use of PrEP, which is being rolled out across Europe, are also included.

Assessing PLWH's Readiness to Start and Maintain ART[ix]

Goal: to help persons start and/or maintain ART	
Starting ART is recommended for all PLWH regardless of CD4 count to reduce the morbidity and mortality associated with HIV infection, and to prevent HIV transmission (START trial, HPTN 052, PARTNER Study) [1-3]. Evidence is accumulating that starting ART on the same day after establishing a diagnosis of HIV infection is feasible and acceptable to PLWH. Nevertheless, assessment of the readiness to start ART is essential to enable PLWH to express their preference and not feel pressured to start ART immediately, unless clinically indicated Given the need for lifelong treatment, successful ART requires a person's readiness to start and adhere to the regimen in a sustained manner. The trajectory from problem awareness to maintenance on ART can be divided into five stages. Knowing a person's stage, health care providers use appropriate techniques to assist them to start and maintain ART	Identify the person's stage of readiness using WEMS[i] techniques, and start discussion with an open question/invitation: "I would like to talk about HIV medicines." <wait> "What do you think about them?" Based on the person's response, identify his/her stage of readiness and intervene accordingly[ii] Immediate (i.e. same day) start of ART should be considered, especially in the following situations: - In the setting of primary HIV infection, especially in case of clinical signs and symptoms of meningoencephalitis (within hours). In this situation, the clinician may start ART immediately after a positive screening HIV test and before obtaining confirmatory HIV test results such as a HIV-VL - The wish of a PLWH to start ART immediately - In a setting where loss-to-follow-up is more likely if ART is not started the same day

Lancet. 2009 Jan 3;373(9657):48-57. doi: 10.1016/S0140-6736(08)61697-9. Epub 2008 Nov 27.

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model.

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Abstract

BACKGROUND: Roughly 3 million people worldwide were receiving antiretroviral therapy (ART) at the end of 2007, but an estimated 6.7 million were still in need of treatment and a further 2.7 million became infected with HIV in 2007. Prevention efforts might reduce HIV incidence but are unlikely to eliminate this disease. We investigated a theoretical strategy of universal voluntary HIV testing and immediate treatment with ART, and examined the conditions under which the HIV epidemic could be driven towards elimination.

METHODS: We used mathematical models to explore the effect on the case reproduction [illegible]erm dynamics of the HIV epidemic (deterministic transmission model) of testing all people in o[illegible] older) for HIV every year and starting people on ART immediately after they are diagnose[illegible] as the test case for a generalised epidemic, and assumed that all HIV transmission was h[illegible]

FINDINGS: The studied strategy could greatly accelerate the transition from the present e[illegible] HIV are not receiving ART, to an elimination phase, in which most are on ART, within 5 ye[illegible] to less than one case per 1000 people per year by 2016, or within 10 years of full impleme[illegible] prevalence of HIV to less than 1% within 50 years. We estimate that in 2032, the yearly c[illegible] strategy would both be US$1.7 billion; however, after this time, the cost of the present str[illegible] of the theoretical strategy would decrease.

INTERPRETATION: Universal voluntary HIV testing and immediate ART, c[illegible] major effect on severe generalised HIV/AIDS epidemics. This approach merit[illegible] consultation.

(TasP)

ART HIV insidansını

[illegible]ine

PLOS | ONE

[illegible]AART Coverage Is Associated with [illegible]eases in HIV/AIDS Morbidity, Mortality [illegible]mission: The "HIV Treatment as [illegible]perience in a Canadian Setting

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Ab[illegible]

Backgro[illegible] [illegible]ere has been renewed call for the global expansion of highly active antiretroviral therapy (HAART) under the framework [illegible] HIV treatment as prevention (TasP). However, population-level sustainability of this strategy has not been characterized.

Methods: We used population-level longitudinal data from province-wide registries including plasma viral load, CD4 count, drug resistance, HAART use, HIV diagnoses, AIDS incidence, and HIV-related mortality. We fitted two Poisson regression models over the study period, to relate estimated HIV incidence and the number of individuals on HAART and the percentage of virologically suppressed individuals.

Results: HAART coverage, median pre-HAART CD4 count, and HAART adherence increased over time and were associated with increasing virological suppression and decreasing drug resistance. AIDS incidence decreased from 6.9 to 1.4 per 100,000 population (80% decrease, $p = 0.0330$) and HIV-related mortality decreased from 6.5 to 1.3 per 100,000 population (80% decrease, $p = 0.0115$). New HIV diagnoses declined from 702 to 238 cases (66% decrease; $p = 0.0004$) with a consequent estimated decline in HIV incident cases from 632 to 368 cases per year (42% decrease; $p = 0.0003$). Finally, our models suggested that for each increase of 100 individuals on HAART, the estimated HIV incidence decreased 1.2% and for every 1% increase in the number of individuals suppressed on HAART, the estimated HIV incidence also decreased by 1%.

Conclusions: Our results show that HAART expansion between 1996 and 2012 in BC was associated with a sustained and profound population-level decrease in morbidity, mortality and HIV transmission. Our findings support the long-term effectiveness and sustainability of HIV treatment as prevention within an adequately resourced environment with no financial barriers to diagnosis, medical care or antiretroviral drugs. The 2013 Consolidated World Health Organization Antiretroviral Therapy Guidelines offer a unique opportunity to further evaluate TasP in other settings, particularly within generalized epidemics, and resource-limited setting, as advocated by UNAIDS.

Initiating Antiretroviral Therapy

ART is recommended for all individuals with HIV to reduce the morbidity and mortality associated with HIV infection **(AI)** and to prevent HIV transmission to sexual partners and infants **(AI)**. ART should be initiated as soon as possible after HIV diagnosis **(AII)**. When initiating ART, it is important to educate patients about the goals and benefits of ART and to identify and address barriers to care engagement and treatment adherence **(AIII)**. Patients should also understand that currently available ART does not cure HIV. To improve and maintain immunologic function and maintain viral suppression, ART should be continued indefinitely without interruption. Initiating ART early is particularly important for patients with AIDS-defining conditions, those with acute or recent HIV infection, and individuals who are pregnant; delaying therapy in these subpopulations has been associated with high risks of morbidity, mortality, and HIV transmission.

Immediate Antiretroviral Therapy Initiation on the Day of HIV Diagnosis

Since individuals may fail to engage in care between the initial HIV diagnosis (or first clinic visit) and the time ART is prescribed, some groups have proposed rapid ART initiation on the same day of HIV diagnosis as a strategy to increase ART uptake and engagement in care and to accelerate the time to ART-mediated viral suppression which people with newly diagnosed H randomized controlled

- Viral baskılanma süresini hızlandırmak (Bulaş süresini kısaltmak)
- ART alımını ve tedaviye katılımı artırmak

AIDSinfo

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.

INSTI plus 2 NRTIs:

Note: For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.

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

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:

Note: For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.

- EVG/c/(TAF or TDF)[a]/FTC **(BI)**

Boosted PI plus 2 NRTIs:

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

NNRTI plus 2 NRTIs:

- DOR/TDF[a]/3TC **(BI)** or DOR plus TAF[a]/FTC **(BIII)**
- EFV plus (TAF or TDF)[a] 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)/FTC **(BI)—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[a] **(CI)**

EACS European AIDS Clinical Society

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk)
TAF/FTC or TDF/FTC or TDF/3TC + DTG		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) III Weight increase
TAF/FTC/BIC		
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)
1 NRTI + INSTI		
DTG + 3TC	HBsAg negative HIV-VL < 500,000 copies/mL CD4 count > 200 cells/µL	
2 NRTIs + NNRTI		
TAF/FTC or TDF/FTC or TDF/3TC + DOR TDF/3TC/DOR		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) V (DOR: HIV-2)
TAF/FTC or TDF/FTC or TDF/3TC + RPV TAF/FTC/RPV TDF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on proton pump inhibitor With food	II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VI (RPV: HIV-2)
2 NRTIs + PI/r or PI/c		
TAF/FTC or TDF/FTC or TDF/3TC + DRV/c or DRV/r TAF/FTC/DRV/c	With food	II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VII (DRV/r: cardiovascular risk)
Alternative regimens		
2 NRTIs + INSTI		
ABC/3TC + RAL qd or bid	HBsAg negative HLA-B*57:01 negative	I (ABC: HLA-B*57:01, cardiovascular risk) IV (RAL: dosing)
TDF/FTC/EVG/c TAF/FTC/EVG/c	With food	II (TDF: prodrug types. Renal and bone toxicity) VIII (EVG/c: use in renal impairment)
2 NRTIs + NNRTI		
ABC/3TC +EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bed time or 2 hours before dinner	I (ABC: HLA-B*57:01, cardiovascular risk) IX (EFV: suicidality. HIV-2 or HIV-1 group 0)
TAF/FTC or TDF/FTC or TDF/3TC + EFV TDF/FTC/EFV	At bed time or 2 hours before dinner	II TDF: prodrug types. Renal and bone toxicity. TAF dosing) IX (EFV: suicidality. HIV-2 or HIV-1 group 0)
2 NRTIs + PI/r or PI/c		
ABC/3TC + ATV/c or ATV/r	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL Not on proton pump inhibitor With food	I (ABC: HLA-B*57:01, cardiovascular risk) X (ATV/b & renal toxicity)
ABC/3TC + DRV/c or DRV/r	HLA-B*57:01 negative HBsAg negative With food	I (ABC: HLA-B*57:01, cardiovascular risk) VII (DRV/r and cardiovascular risk)
TAF/FTC or TDF/FTC or TDF/3TC + ATV/c or ATV/r	Not on proton pump inhibitor With food	II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) X (ATV/b: renal toxicity)
Other combinations		
RAL 400 mg bid + DRV/c or DRV/r	HBsAg negative HIV-VL < 100,000 copies/mL	VII (DRV/r: cardiovascular risk)

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

A) Önerilen rejimler†‡

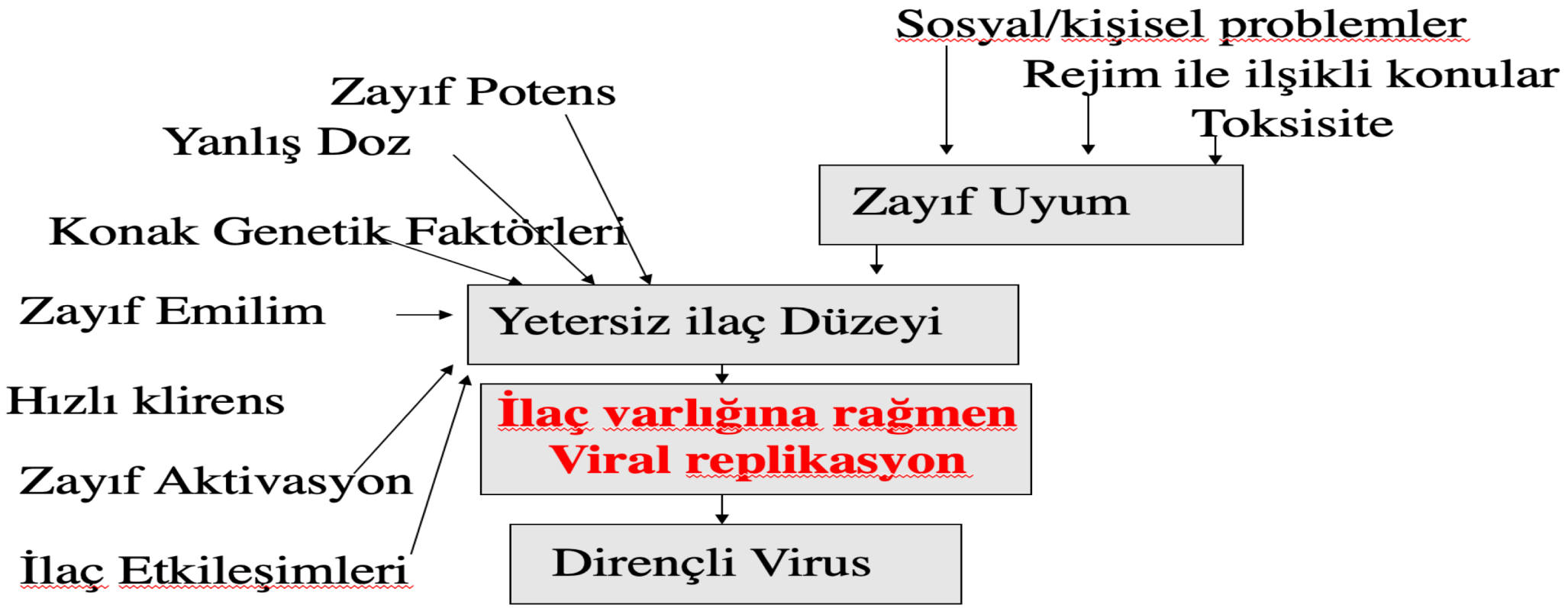
Rejim	Doz	Uyarı	Gıda Gereksinimi
2 Nükleozit analoğu revers transkriptaz inhibitörü + İntegraz inhibitörü			
ABC/3TC/DTG[1,2]	ABC/3TC/DTG 600/300/50 mg Günde 1 tablet	» Al/Ca/Mg içeren antasit ve multivitaminler ile eş zamanlı alınmamalıdır (en az 2 saat önce veya 6 saat sonra alınabilir). » Rifampisin ile birlikte kullanılacaksa DTG 50 mg günde iki kez önerilir.	Yok
TAF/FTC/BIC[3]	TAF/FTC/BIC 25/200/50 mg Günde 1 tablet	Ağır karaciğer yetmezliğinde kullanılmamalıdır.	Yok
TAF/FTC[3] veya TDF/FTC[3] + 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
TAF/FTC/EVG/c[3] veya TDF/FTC/EVG/c[3,4]	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 antasit ve multivitaminler ile eş zamanlı alınmamalıdır (en az 2 saat önce veya 6 saat sonra alınabilir).	Yemekle
TAF/FTC[3] veya TDF/FTC[3] + 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
2 Nükleozit analoğu revers transkriptaz inhibitörü + Nonnükleozit revers transkriptaz inhibitörü			
TAF/FTC/RPV[3] veya TDF/FTC/RPV[3]	TAF/FTC/RPV 25/200/25mg 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
2 Nükleozit analoğu revers transkriptaz inhibitörü + Güçlendirilmiş proteaz inhibitörü			
TAF/FTC[3] veya TDF/FTC[3] + DRV/c(v) veya DRV/r(v)	TAF/FTC 10/200 mg Günde 1 tablet veya TDF/FTC 300/200 mg Günde 1 tablet 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

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

Rejim	Doz	Uyarı	Gıda Gereksinimi
2 Nükleozit analoğu revers transkriptaz inhibitörü + İntegraz inhibitörü			
ABC/3TC[1,2] + RAL	ABC/3TC 600/300 mg Günde1 tablet RAL 400 mg Günde iki defa 1 tablet	» Al/Mg içeren antasitlerle eş zamanlı alınması önerilmez. » Rifampisin ile birlikte kullanılacaksa RAL 400 veya 800 mg günde iki kez alınmalıdır.	Yok
2 Nükleozit analoğu revers transkriptaz inhibitörü + Nonükleozit revers transkriptaz inhibitörü			
ABC/3TC[1,2] + EFV[6]	ABC/3TC 600/300 mg Günde 1 tablet EFV 600 mg Günde 1 tablet	HIV RNA düzeyi <100.000 kopya/mL ise kullanılabilir.	Yatmadan önce veya akşam yemeğinden 2 saat önce
TDF/FTC/EFV[3,6]	TDF/FTC/EFV 300/200/600 mg Günde 1 tablet		Yatmadan önce veya akşam yemeğinden 2 saat önce
2 Nükleozit analoğu revers transkriptaz inhibitörü + Güçlendirilmiş proteaz inhibitörü			
TAF/FTC[3] veya TDF/FTC[3] + ATV/c[7,8] veya ATV/r[7,8]	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
ABC/3TC[1,2] + ATV/c[7,8] veya ATV/r[7,8]	ABC/3TC 600/300 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	HIV RNA düzeyi <100.000 kopya/mL ise.	Yemekle

After initiation of effective ART, viral load reduction to below limits of assay detection usually occurs within the first 12 to 24 weeks of therapy. Predictors of virologic success include the following:

- Low baseline viremia;
- High potency of the ARV regimen;
- Tolerability of the regimen;
- Convenience of the regimen; and
- Excellent adherence to the regimen.



In Vitro «Forgiveness» Çalışmaları: BIC+FTC+TAF vs DTG+3TC

Vahşi Tip HIV-1 (HIV IIIb suşu) ile Yapılan Analiz: Viral Alevlenme

B/F/TAF vs DTG+3 ... *tro* ortamda, 3 ardışık doza

Table 1. Drug Concentrations for Cell Culture Equivalents

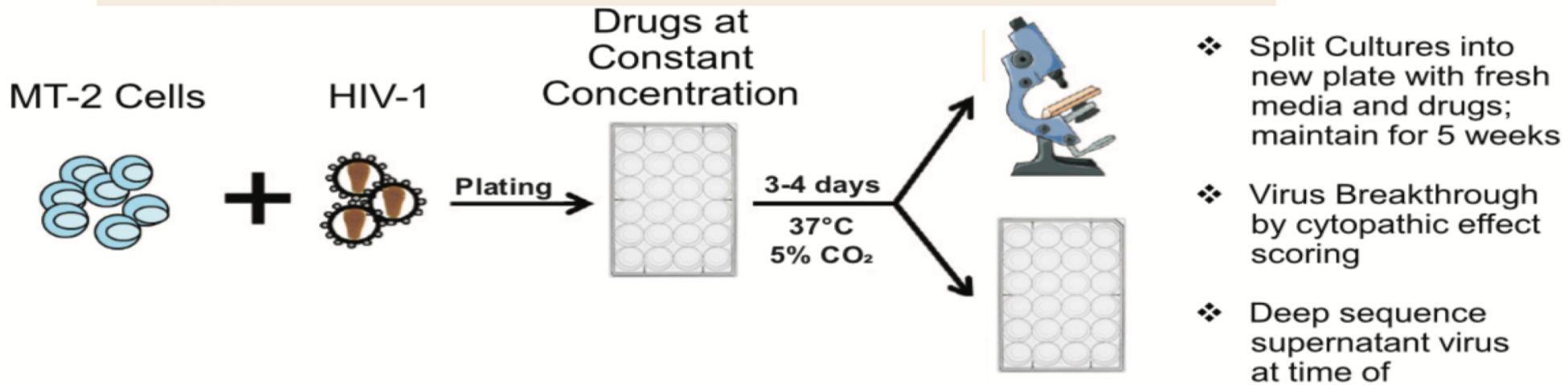
	BIC + FTC + TAF			DTG + 3TC	
	BIC	FTC	TAF	DTG	3TC
Clinical Dose (mg)	50	200	25	50	300
Molecular Weight (g/mol)	449.4	247.2	534.5	419.4	229.3
Clinical C_{min} (µg/mL)[a]	2.61	0.096	0.008	1.11	0.042
Clinical C_{min} (nM)	5808	388	15	2515	265
Human Serum Shift[b]	43.6	1.0	1.0	27.5	1.0
Cell Culture Equivalent C_{min} (nM)[c]	133	388	15	91	265
$t_{½}$ (hr)[d]	17	37	116	14	17.5

a. C_{min} values are median values from United States prescribing information (USPI)
b. BIC and DTG data generated in-house by standard equilibrium dialysis shift in human serum versus cell culture media[15]
c. C_{min} / Human Serum Shift
d. $t_{1/2}$ for FTC, TAF, and 3TC represent intracellular half-life of the active di- or tri- phosphate metabolite[18-20]; $t_{1/2}$ values for BIC and DTG from USPI

Figure 2. ... **ogy**

Drugs: B

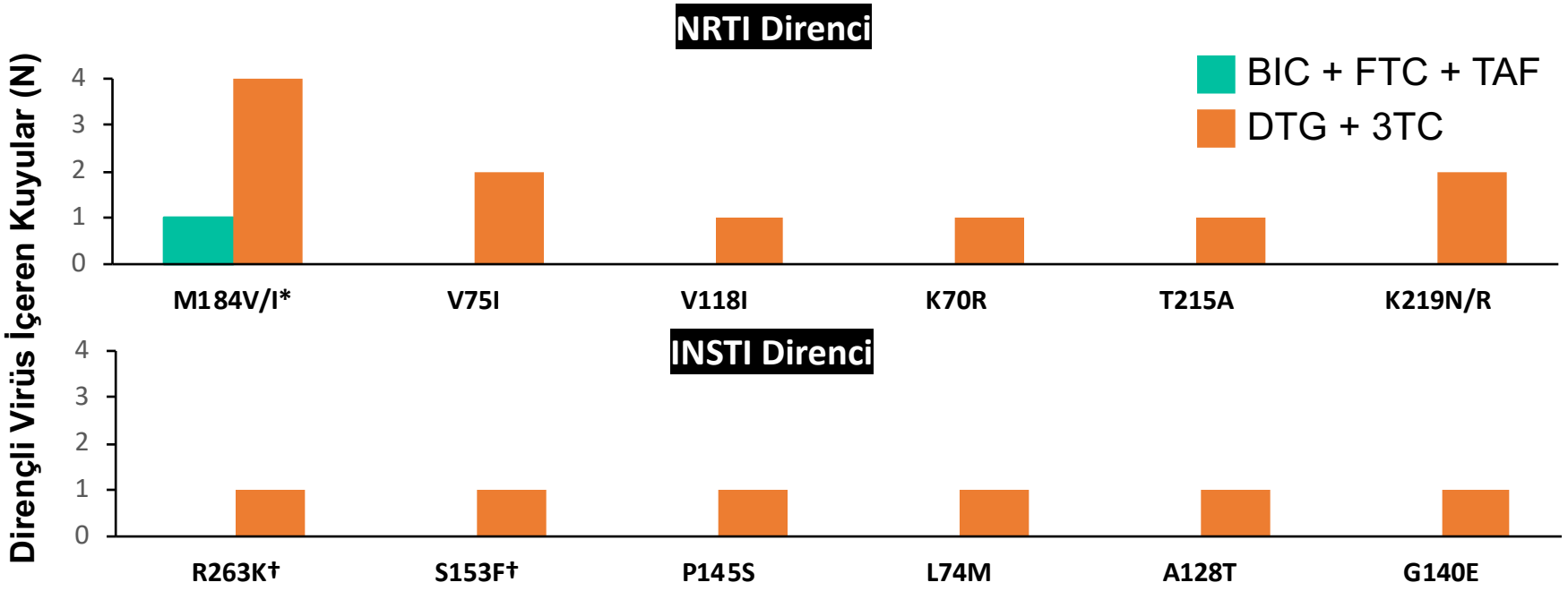
- Viral Bre



Mulato A, et al. IAS 2019. Mexico City, Mexico. TUPEA103; Mulato A, et al. European Meeting on HIV and Hepatitis. Rome, Italy. Poster # 50

Vahşi Tip HIV-1 (HIV IIIb suşu) ile Yapılan Analiz: Direnç Gelişimi

B/F/TAF vs DTG+3TC'in "affediciliğinin" (viral alevlenme/sıçrama ve direnç gelişimi düzeyi), *in vitro* ortamda, 3 ardışık doza kadar atlanan sub-optimal tedavi uyumu koşullarında simüle edilmesi



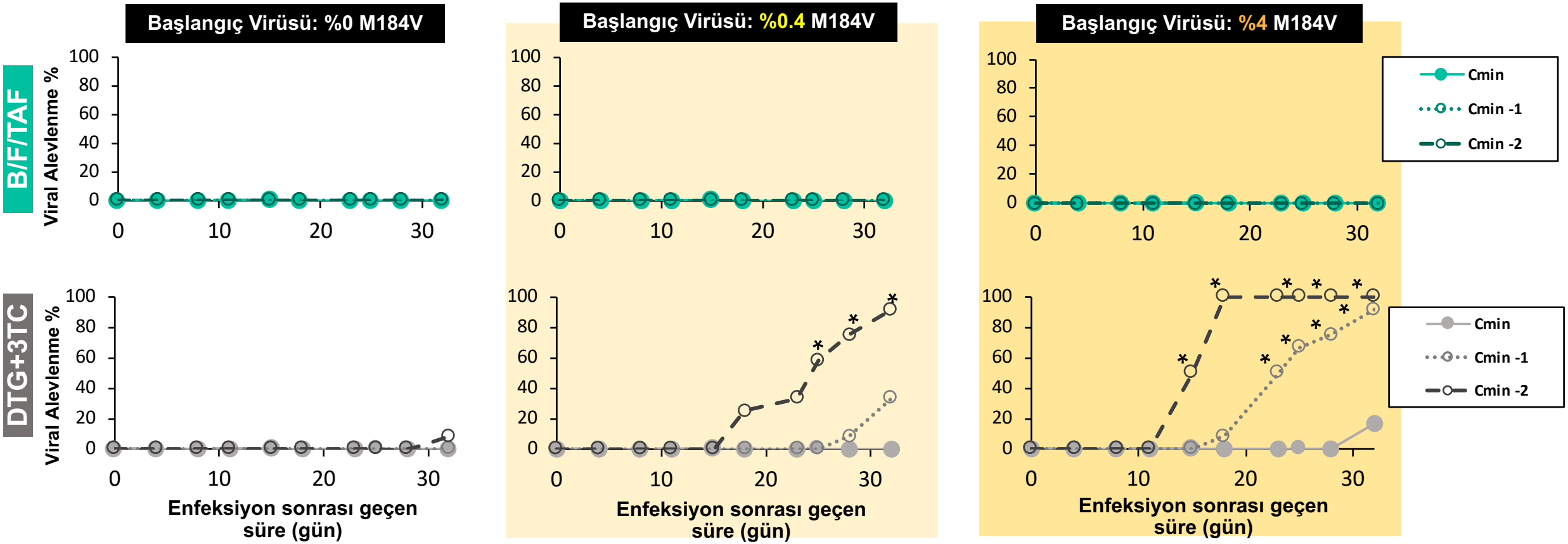
- BIC+FTC+TAF'a kıyasla DTG+3TC'de daha fazla direnç (1/144)
- BIC+FTC+TAF: M184V/I bir kere, 3 dozun atlandığı deneyde gelişmiştir.

Vahşi tip HIV'de DTG+3TC'ye kıyasla **BIC+FTC+TAF ile *in vitro* ilaç direnci gelişimi daha az görülmüştür**

* M184V ve M184I yüksek düzeyde FTC ve 3TC direncine ve TAF duyarlılığında artışa yol açar
† R263K ve S153F DTG tarafından daha önce seçilime uğramıştır ve DTG'ye duyarlılığın azalmasına neden olabilir. IN'deki R263K'lı kuyuda T215A ve K219R de bulunmuştur.
Mulato A, et al. IAS 2019. Mexico City, Mexico. TUPEA103

İnokulumda Önceden Olan M184V ile Yapılan Analiz (HIV-1 xxLAI suşu):Viral Alevlenme

B/F/TAF vs DTG+3TC'in "affediciliğinin" (viral alevlenme/sıçrama ve direnç gelişimi düzeyi), *in vitro* ortamda, 3 ardışık doza kadar atlanan sub-optimal tedavi uyumu koşulları altında simüle edilmesi



İnokulumda önceden M184V olduğu veya olmadığı durumlarda, DTG+3TC'ye kıyasla BIC+FTC+TAF ile daha az *in vitro* viral alevlenme görülmüştür

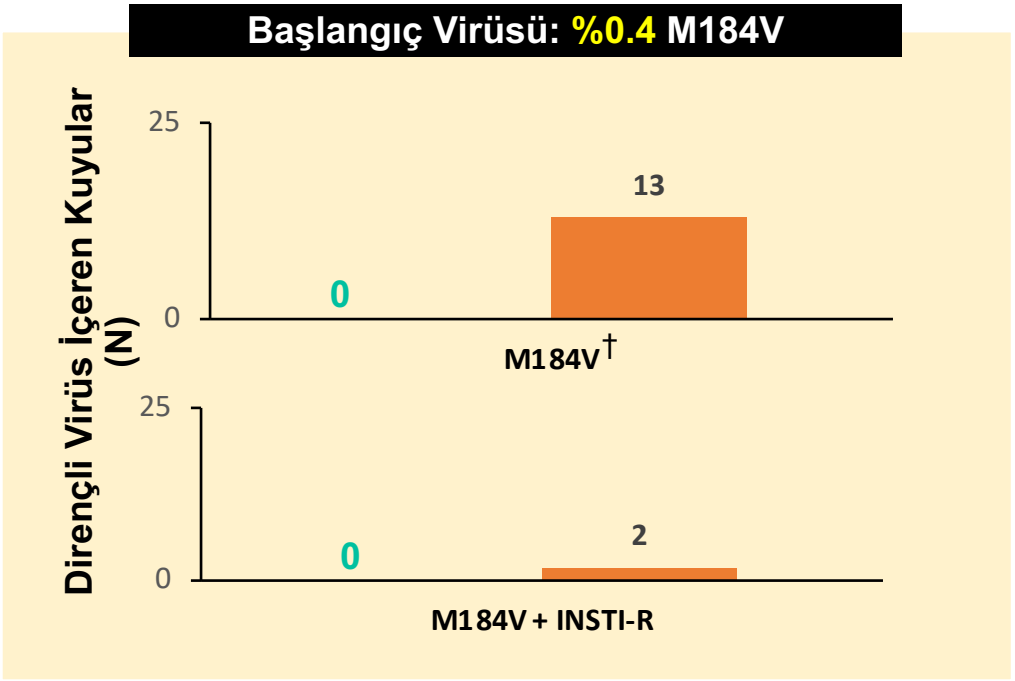
* P-değeri < 0.05 (Fisher's Exact testi, B+F+TAF ve DTG+3TC karşılaştırması)
Mulato A, et al. IAS 2019. Mexico City, Mexico. TUPEA103

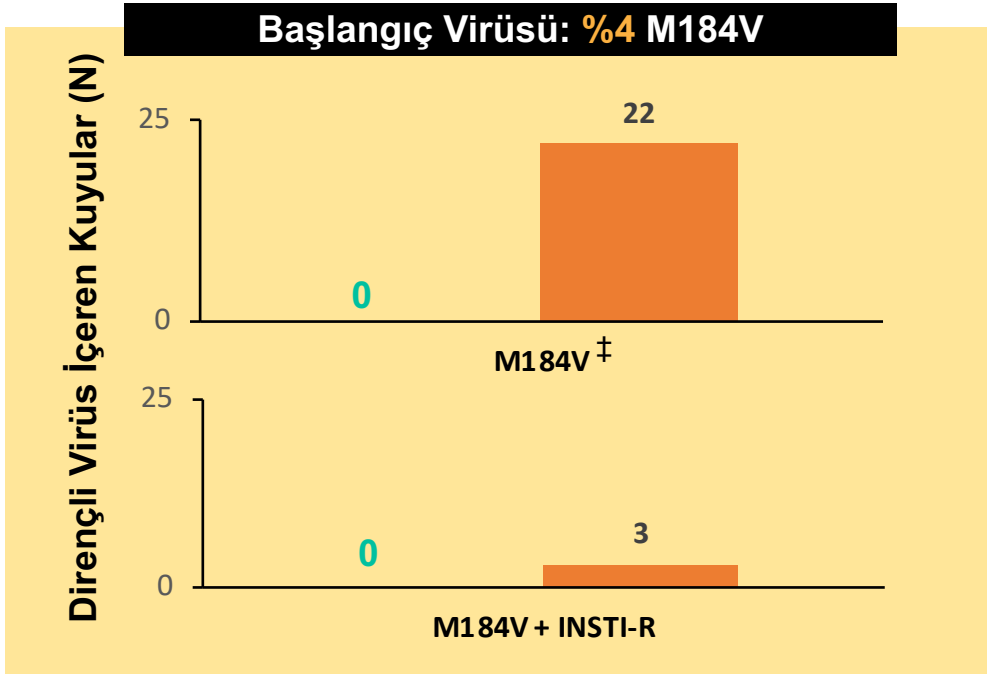
İnokulumda Önceden Var Olan M184V ile Yapılan Analiz (HIV-1 xxLAI suşu): Direnç Gelişimi

B/F/TAF vs DTG+3TC'in "affediciliğinin" (viral alevlenme/sıçrama ve direnç gelişimi düzeyi), *in vitro* ortamda, 3 ardışık doza kadar atlanan sub-optimal tedavi uyumu koşulları altında simüle edilmesi

Direnç Gelişimi

• BIC+FTC+TAF ile karşılaştırıldığında, **DTG+3TC** ile direnç görülen daha fazla sayıda kuyu dirençli virüse sahipti (%56 vs. %0)





İnokulumda önceden M184V'nin olduğu durumda, DTG+3TC'ye kıyasla BIC+FTC+TAF ilaç direnci gelişimini önlemede daha iyi bulunmuştur.

* P-value < 0.05 (Fisher's Exact testi, B+F+TAF ve DTG+3TC karşılaştırması); † Alevlenmelerin 1'i M184V/I, geri kalan hepsi M184/V ile; ‡ Alevlenmelerin 1'i D67N, geri kalan hepsi M184V ile.
Mulato A, et al. IAS 2019. Mexico City, Mexico. Poster TUPEB244

Prevalence of NRTI or NNRTI DRMs by ARV-class, ARV and HIVDB mutation score

Number of patients receiving first-line regimen containing NRTIs

4019

NRTI-resistance mutations with an HIVDB score ≥30 (assoicated with intermediate or high-level resistance to one or more NRTIs)

K65R, D67d, T69i, K70R, L74I/V, Y115F, Q151L/M, M184I/V, T215F/Y

Partitioning sequences in order of the most prevalent NRTI-resistance mutations

Prevalence of NRTI-resistance mutations (minimum prevalence ≥0.5)

Mutation	No. Patients	%Patients
M184V	2759	68.8
None	985	24.5
K70R	449	11.2
T215Y	347	8.7
K65R	314	7.8
T215F	284	7.1
M184I	121	3.0
Q151M	108	2.7
L74V	98	2.4
Y115F	76	1.9
L74I	68	1.7

Fig. 5: Pretreatment HIV drug resistance mutations by country [13]

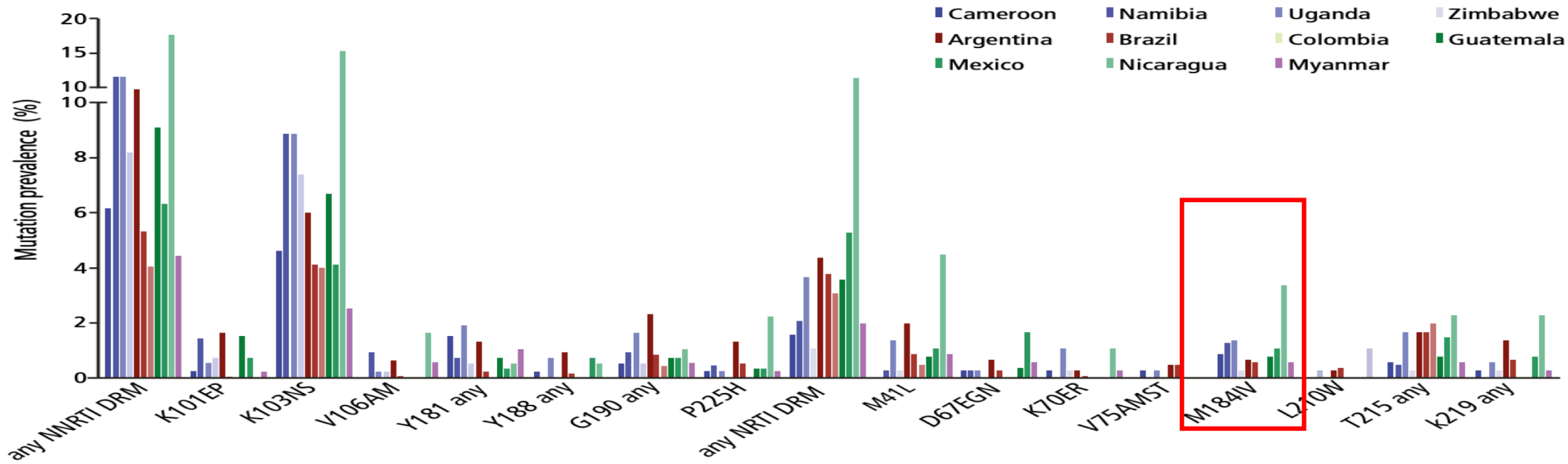
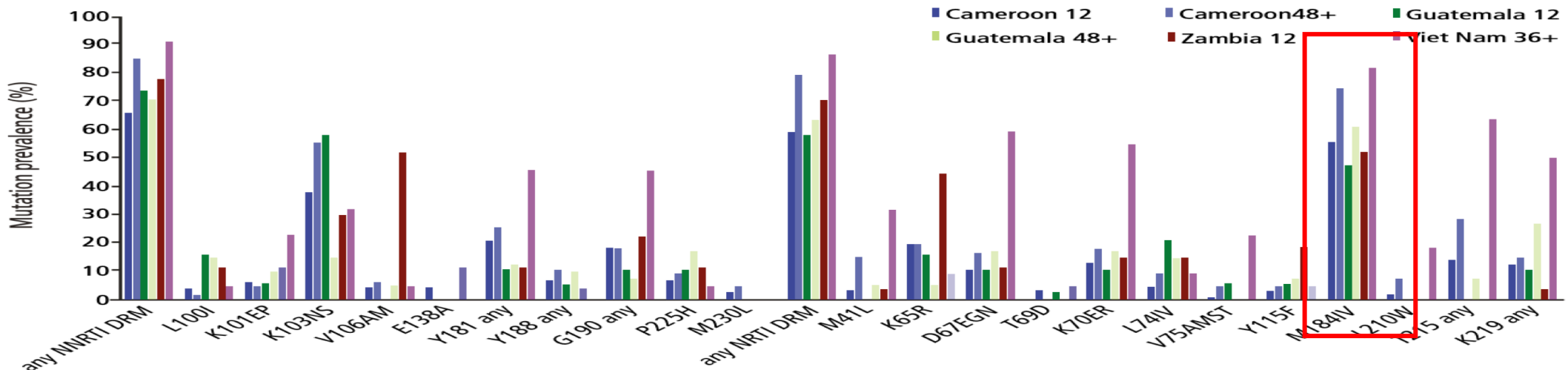


Fig. 14: Acquired HIV drug resistance mutations by country[25]



Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study

*The TenoRes Study Group**

Lancet Infect Dis 2016; 16: 565–75
Published Online

Summary

Background Antiretroviral therapy (ART) is crucial for controlling HIV-1 infection through wide-scale treatment as prevention and pre-exposure prophylaxis (PrEP). Potent tenofovir disoproxil fumarate-containing regimens are increasingly used to treat and prevent HIV, although few data exist for frequency and risk factors of acquired drug

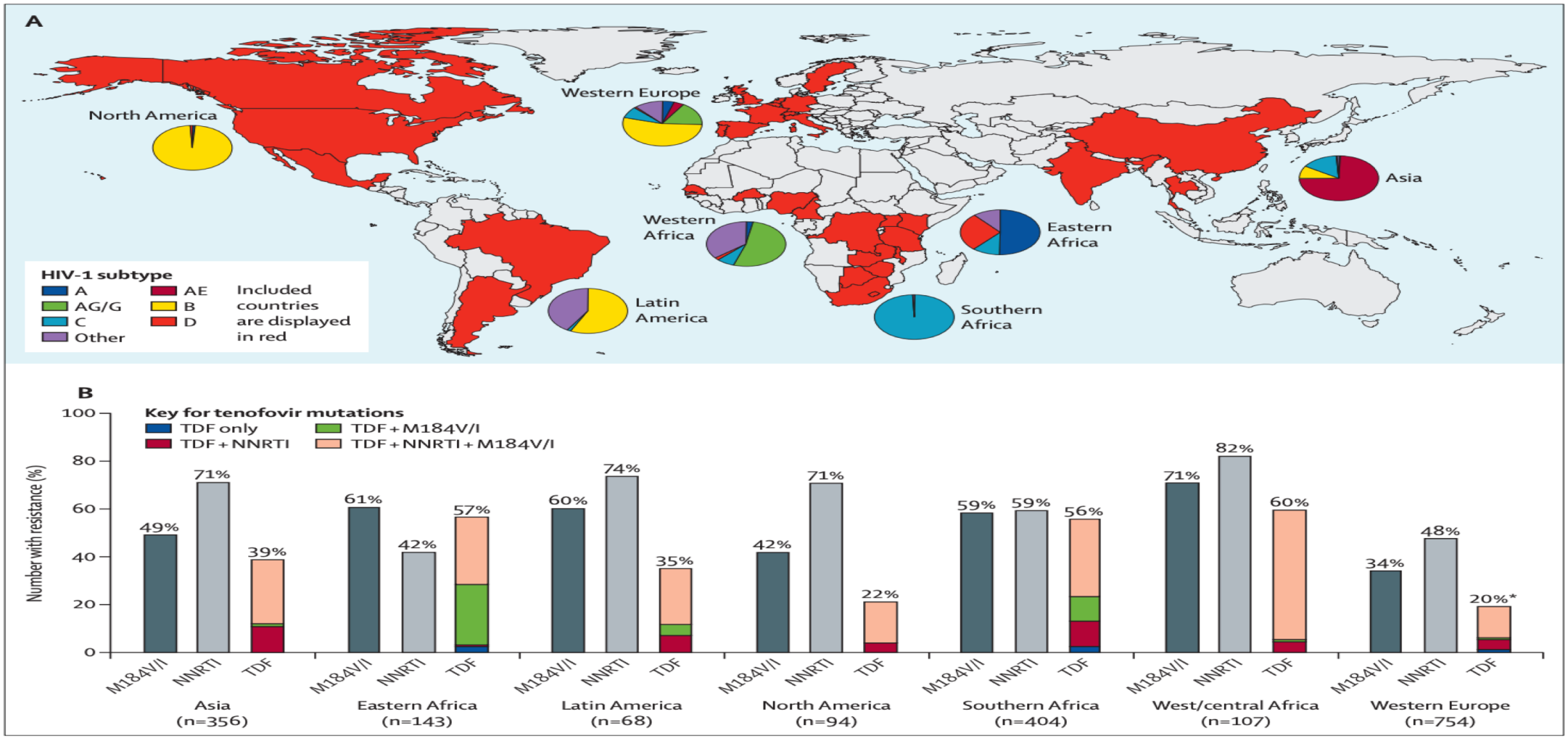


Figure 1: **(A) Countries contributing data to resistance analysis and HIV-1 subtype distribution, (B) prevalence of drug resistance by mutation and by region**
NNRTI=non-nucleotide reverse-transcriptase inhibitor. TDF=tenofovir disoproxil fumarate. *24% (n=462) of participants had tenofovir resistance when genotypes from viral load >1000 copies HIV-1 RNA per mL were considered.

Tanı konulduğu gün tedavi

HIV enf. ciddi bir durum olduğu mesajını verir, uyumu arttırır

bulaş süresi kısalır, oluşabilecek yeni enfeksiyonlar azalır

Rehberlere göre hızlı ART başlarken !!

HIV Pozitif Bireylerin Çoğu İçin Önerilen Başlangıç Tedavi Rejimleri	
INSTI + 2 NRTIs	B/F/TAF **(AI)**
	DTG/3TC/ABC **(AI) (HLA-B*5701 negatif ise)**
	DTG + (TAF veya TDF) + (FTC veya 3TC) **(AI)**
	RAL + (TAF veya TDF) + (FTC veya 3TC) **TDF/[FTC or 3TC]=BI** **TAF/FTC= BII**
INSTI + 1 NRTI	DTG/3TC (AI) **HIV-1 RNA > 500.000 kopya/ml** **HBV ko-enfeksiyonu olan veya** **reverse transcriptase için genotipik test sonucu veya HBV test sonucu gelmeden tedavi başlanacak kişiler haricinde**

BFTAF, **direnç testi sonucu bilinmeyen** veya **hızlı tedavi planlanan hastalarda** önerilen tedaviler arasındadır

DTG/3TC, **direnç testinde RT duyarlılığının gösterildiği hastalarda** supresyonun devamı için etkilidir

Tanı konulduğu gün tedavi

HIV enf. ciddi bir durum olduğu mesajını verir, uyumu arttırır

bulaş süresi kısalır, oluşabilecek yeni enfeksiyonlar azalır

İlaç uyumu

Gelecek İçin Sözümüz Var

Genvoya Gerçek Yaşam Verileri

Uzm. Dr. Esra Zerdali

Biktarvy PK ve Ruhsat Çalışmaları

Doç. Dr. Dilek Yıldız Sevgi

MUTATIONS IN THE INTEGRASE GENE ASSOCIATED WITH RESISTANCE TO INTEGRASE STRAND TRANSFER INHIBITORS[z]

Dolutegravir[aa]

	F	E	G	**Q**	N	R
	121	138	140	**148**	155	263
	Y	A K	A S	**H** **K** **R**	H	K

Elvitegravir[bb]

	T	E	T	F	S	Q	N	R
	66	**92**	97	**121**	**147**	**148**	**155**	263
	I A K	**Q** G	A	**Y**	**G**	**H** **K** **R**	**H**	K

Raltegravir[cc]

	L	E	T	F	E	G	Y	Q	N	R
	74	92	97	**121**	138	140	**143**	**148**	**155**	263
	M	Q	A	**Y**	A K	A S	**R** **H** **C**	**H** **K** **R**	**H**	K

MARVEL on RT mutations at position 184

HIVdb Algorithm: Comments & Scores

- M184V/I cause high-level resistance to 3TC and FTC and low-level resistance to ddI and ABC. However, M184V/I are not contraindications to continued treatment with 3TC or FTC because they increase susceptibility to AZT, TDF and d4T and are associated with clinically significant reductions in HIV-1 replication. In combination with K101E or E138K, M184I synergistically reduces RPV susceptibility.

Mutation	3TC	FTC	ABC	AZT	D4T	DDI	TDF
M184I	60	60	15	-10	-10	10	-10
M184V	60	60	15	-10	-10	10	-10

Footnote: Mutation scores on the left are derived from published literature linking mutations and ARVs (the complete details can be found in the HIVdb Release Notes).

NRTI direnç mutasyonları

- En sık görülen NRTI mutasyonu M184V/I
  - 3TC ve FTC tarafından seçilir ve bu ilaçlara yüksek düzeyde (>200 kat) azalmış duyarlılığa neden olur
  - Ayrıca abakavire de düşük düzeyde dirence neden olur
  - 3TC veya FTC içeren rejimlerde M184I daha önce ortaya çıkar (M184V'den)
    - Ancak birkaç haftada çoğu hastada M184V üstün gelir
  - M184V/I mutasyonunda, 3TC ve FTC'ye görülen yüksek fenotipik dirence rağmen tedaviye bu ajanlarla devam edilebilir
    - Bu mutasyonlar virolojik fitnessi azaltmaya devam ettiği ve AZT ve TDF'e duyarlılığı artırdığı için