HIV ve GEBELİK

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V. HIV/AIDS Mezuniyet Sonrası Eğitim Kursu
İstanbul

Sunum Planı

- Anneden çocuğa HIV bulaş oranları
- HIV ile yaşayan bireylerde gebeliğin planlanması
- HIV ile yaşayan bireylerde konsepsiyon
- Antiretroviral tedavi seçimi
- Gebeliğin izlemi
- Doğum
- Emzirme
- Yenidoğan profilaksisi

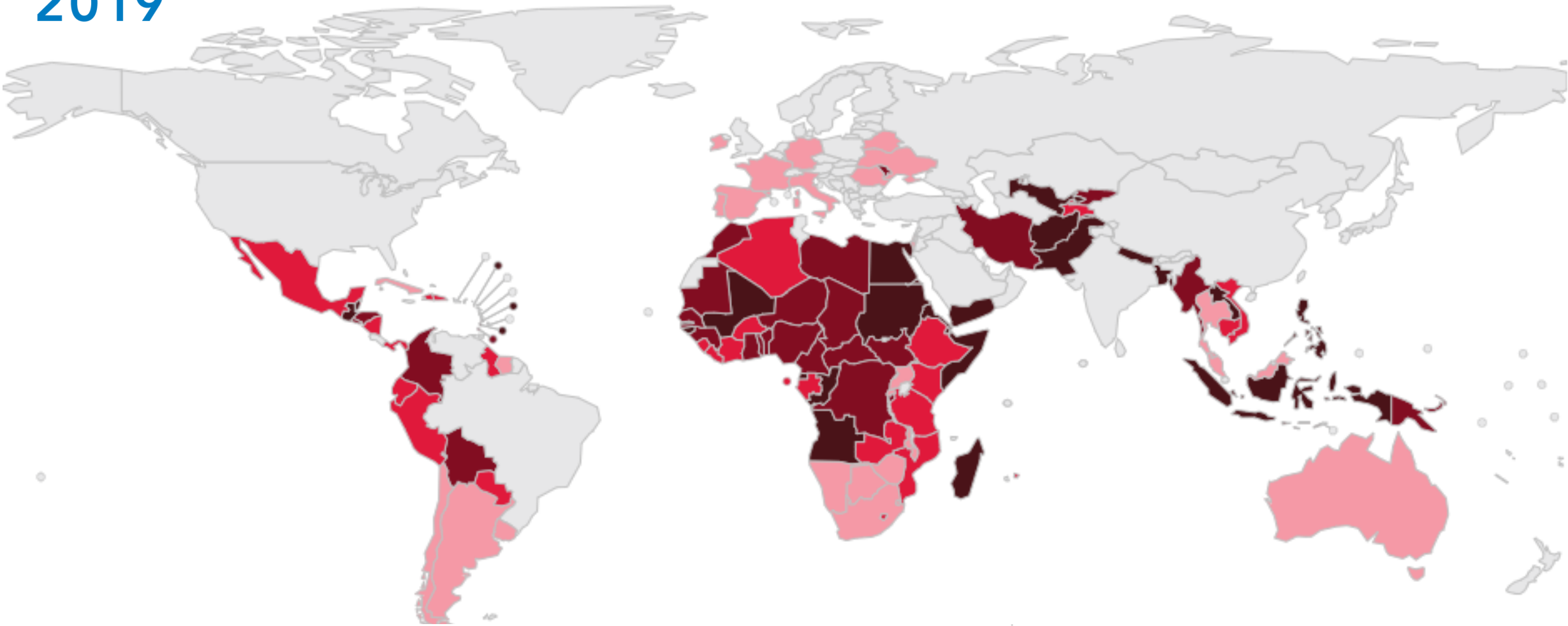
UNAIDS DATA 2019

Regional HIV and AIDS statistics and features | 2018

	Adults and children living with HIV	Adults and children newly infected with HIV	Adult and child deaths due to AIDS
Eastern and southern Africa	20.6 million [18.2 million–23.2 million]	800 000 [620 000–1.0 million]	310 000 [230 000–400 000]
Western and central Africa	5.0 million [4.0 million–6.3 million]	280 000 [180 000–420 000]	160 000 [110 00–230 000]
Middle East and North Africa	240 000 [160 000–390 000]	20 000 [8500–40 000]	8400 [4800–14 000]
Asia and the Pacific	5.9 million [5.1 million–7.1 million]	310 000 [270 000–380 000]	200 000 [160 000–290 000]
Latin America	1.9 million [1.6 million–2.4 million]	100 000 [79 000–130 000]	35 000 [25 000–46 000]
Caribbean	340 000 [290 000–390 000]	16 000 [11 000–24 000]	6700 [5100–9100]
Eastern Europe and central Asia	1.7 million [1.5 million–1.9 million]	150 000 [140 000–160 000]	38 000 [28 000–48 000]
Western and central Europe and North America	2.2 million [1.9 million–2.4 million]	68 000 [58 000–77 000]	13 000 [9400–16 000]
TOTAL	37.9 million [32.7 million–44.0 million]	1.7 million [1.4 million–2.3 million]	770 000 [570 000–1.1 million]

UNAIDS DATA 2019

MOTHER-TO-CHILD TRANSMISSION RATE



Period
2010 - 2018

2018

27.7+
15.43 - 27.7
9.78 - 15.43
< 9.78
No data

HIV ile Yaşayan bireylerde Gebeliğin Planlanması

Gebeliğin Planlanması

- Doğurganlık çağındaki her HIV ile yaşayan birey
  - Gebelik isteği
    - İnfertilite açısından eşlerin incelenmesi
    - 400 µg folik asit iceren multivitamin
- Doğum kontrol yöntemleri
    - Oral kontraseptif-ART etkileşimine dikkat

Drug-drug Interactions between Contraceptives and ARVs

Contraceptives		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	MVC	BIC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF
Es	ethinylestradiol (COC, TS, VR)	↑1%a	↓19%b	↓30%	↓44%a	↓42%a	↓2%	c	↑22%	↓20%	↑14%	↓<1%	↑4%	↑3%	↓25%d	↓2%	↔	↑11%	↔	↑11%	↔
Progestins	desogestrel (COC)	↑	↑e,b	↑	↑f	↑f	↔	↓g	↓	↓	↔	↔	↔	↔	↑d,e	↔	↔	↔	↔	↔	↔
	desogestrel (POP)	↑	↑	↑	↑	↑	↔	↓g	↓	↓	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	drospirenone (COC)	↑130%	↑e,b	↑58%f	↑f	↑f	↔	↓g	↓	↓	↔	↔	↔	↔	↑d,e	↔	↔	↔	↔	↔	↔
	etonogestrel (IP)	↑	↑	↑	↑	↑52%	↔	↓63%g	↓	↓	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	etonogestrel (VR)	↑	↑~80%h	↑	↑h	↑h	↔	↓~79%g	↓	↓	↔	↔	↔	↔	↑h	↔	↔	↔	↔	↔	↔
	gestodene (COC)	↑	↑e,b	↑	↑f	↑f	↔	↓g	↓	↓	↔	↔	↔	↔	↑d,e	↔	↔	↔	↔	↔	↔
	levonorgestrel (COC)	↓8%	↑e,b	↑	↑f	↑f	↑21%	↓g	↓	↑	↔	↓2%	↔	↔	↑	↔	↔	↔	↔	↔	↔
	levonorgestrel (IP)	↑	↑	↑	↑	↑	↔	↓57%g	↓	↑14%	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	levonorgestrel (IUD)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	levonorgestrel (POP)	↑	↑	↑	↑	↑	↔	↓g	↓	↑	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	medroxy-progesterone (POI)	↔	↔	↔	↔	↑~70%	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	norelgestromin (TS)	↑	↑e,b	↑	↑f	↑83%f	↔	↓g	↓	↓	↔	↔	↔	↔	↑d,e	↔	↔	↔	↔	↔	↔
	norethisterone (COC)	↑	↑e,i	↑	↓14%f	↓17%f	↔	↓g	↓5%	↓19%	↓11%	↔	↔	↔	↑d,e	↔	↔	↔	↔	↔	↔
	norethisterone (POI)	↔	↔	↔	↔	↔	↔	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	norethisterone (POP)	↑	↑50%	↑	↑50%	↑50%	↔	↓g	↓	↓	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	norgestimate (COC)	↑	↑85% e,b	↑	↑f	↑f	↔	↓64%g	↓	↓	↔	↔	↑8%	↓2%	↑126% d,e	↑14%	↔	↔	↔	↔	↔
	norgestrel (COC)	↑	↑e,b	↑	↑f	↑f	↔	↓g	↓	↑	↔	↔	↔	↔	↑d,e	↔	↔	↔	↔	↔	↔
Other	levonorgestrel (EC)	↑j	↑j	↑j	↑j	↑j	↔	↓58%k	↔	↔	↔	↔	↔	↔	↑j	↔	↔	↔	↔	↔	↔
	mifepristone	↑j	↑j	↑j	↑j	↑j	E j	↓	↓	↓	E j	E j	E j	↔	↑j	↔	↔	↔	↔	↔	↔
	ulipristal	↑j	↑j	↑j	↑j	↑j	↔	↓l	↓l	↓l	↔	↔	↔	↔	↑j	↔	↔	↔	↔	↔	↔

Colour legend

No clinically significant interaction expected

These drugs should not be co-administered

b Unboosted ATV increased ethinylestradiol AUC by 48%. Use no more than 30 µg of ethinylestradiol if co-administered with unboosted ATV

Planlı gebeliklerde zamanlama

- Maksimum sürdürülebilir viral baskılanma sonrası konsepsiyon
  - Partnerin korunması
  - Perinatal geçiş riskini en aza indirmek için
- Cinsel yolla bulaşan hastalıkların tedavisi sonrası

Panel's Recommendations

- Discuss reproductive desires with all women of childbearing age on an ongoing basis throughout the course of their care **(AIII)**.
- Provide information about effective and appropriate contraceptive methods to reduce the likelihood of unplanned pregnancy **(AI)**.
- During preconception counseling, provide information on safe sex and encourage the elimination of alcohol, tobacco, and other drugs of abuse; if elimination is not feasible, clinicians should provide appropriate treatment (e.g., methadone or buprenorphine) or counsel patients on how to manage health risks (e.g., use of a syringe services program) **(AII)**.
- Women with HIV should attain maximum viral suppression before attempting conception for their own health, to prevent sexual HIV transmission to partners without HIV **(AI)**, and to minimize the risk of perinatal HIV transmission to the infant **(AI)**.
- When selecting or evaluating an antiretroviral (ARV) regimen for women of childbearing age with HIV, consider a regimen's effectiveness, a woman's hepatitis B status, the teratogenic potential of the drugs in the ARV regimen, and the possible adverse outcomes for the mother and fetus **(AII)**. See Teratogenicity and Recommendations for Use of Antiretroviral Drugs During Pregnancy for more information. The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission emphasizes the importance of counseling and informed decision-making regarding all ARV regimens for people with HIV **(AIII)**.
- HIV infection does not preclude the use of any contraceptive method; however, drug-drug interactions between hormonal contraceptives and antiretrovirals should be considered **(AII)**.

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

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Preconception Counseling and Care for Women of Childbearing Age Living with HIV (Last updated December 24, 2019; last reviewed December 24, 2019)

HIV ile yaşayan bireylerde konsepsiyon

B = B U = U

BELİRLENEMEYEN UNDETECTABLE

BULAŞTIRMAYAN UNTRANSMITTABLE

- Partner Çalışması (2010 – 2014)

  1166 serodiskordan viral suprese çift (Heteroseksüel ve MSM)

  58,000 kondomsuz ilişki

  HIV bulaşı yok

Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner Is using suppressive antiretroviral therapy. *JAMA*. 2016;316(2):171-181. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27404185.

OPEN

Natural conception in HIV-serodiscordant couples with the infected partner in suppressive antiretroviral therapy

A prospective cohort study

Jorge Del Romero, MD[a], María Begoña Baza, MD[a,*], Isabel Río, PhD[b], Adrián Jerónimo, MD[a], Mar Vera, MD[a], Victoria Hernando, PhD[b,c], Carmen Rodríguez, PhD[a], Jesús Castilla, MD, PhD[c,d]

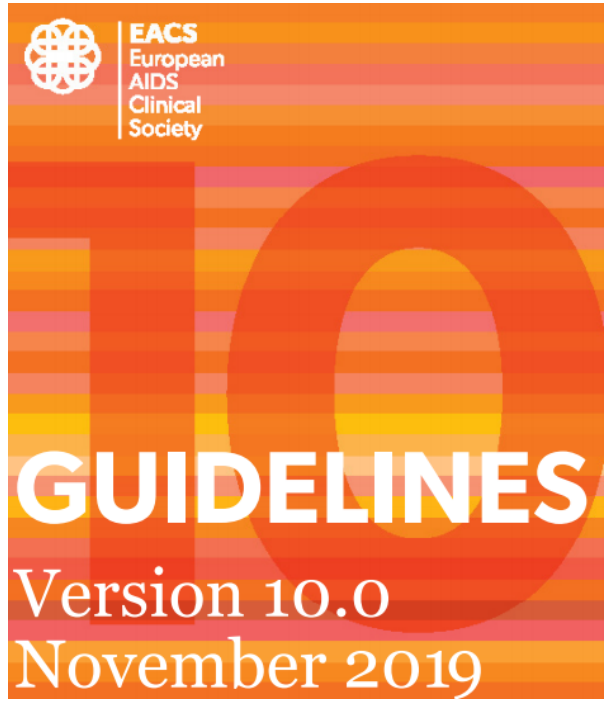
- 2002-2013
- 161 serodiskordan çift (133 ünde erkek +)
  - ART uyumu >%95
  - Son 6 ayda optimal viral baskılanma ve erkekse semende viral yük negatif
  - Genitoüriner enfeksiyonu olmayan
- 144 doğal yolla gebelik, 107 bebek
- HIV bulaşı yok

Del Romero J, Baza MB, Rio I, et al. Natural conception in HIV-serodiscordant couples with the infected partner in suppressive antiretroviral therapy: a prospective cohort study. *Medicine (Baltimore)*. 2016;95(30):e4398. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27472733.

Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection *and* Interventions to Reduce Perinatal HIV Transmission in the United States

January 17, 2020

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



Reproductive Options for Couples When One or Both Partners are Living with HIV (Last updated December 24, 2019; last reviewed December 24, 2019)

People with HIV who take ART as prescribed and who achieve and maintain an undetectable viral load have effectively no risk of transmitting HIV through sex. This is commonly known as Undetectable = Untransmittable or U=U. For more information, see the Prevention IS Care Resources from CDC.

For couples with differing HIV statuses where the partner with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom allows for conception with effectively no risk of sexual transmission to the partner without HIV. It is not known how frequently viral load testing should be conducted when a patient is relying on treatment and viral suppression as a prevention strategy.[1] There is currently not enough evidence to determine the optimal schedule for viral load testing in people with HIV who rely on this prevention strategy. Consider monitoring the viral load more frequently in these individuals than the current treatment guidelines recommend.

https://aidsinfo.nih.gov/guidelines on 2/2/2020

HIV ile yaşayan bireylerde konsepsiyon

- Ovulasyon takibi (takip kiti)
- Ovulasyon döneminde kondomsuz cinsel ilişki önerilebilir*
  - En az 3 ay arayla bakılan 2 Viral yükün negatif olması şartıyla
  - Tedavi uyumu önemli

- HIV negatif eşler için ek bilgilendirme yapılmalı
  - PrEP
  - Konsepsiyon yöntemleri

Reproductive Options for Couples When One or Both Partners are Living with HIV (Last updated December 24, 2019; last reviewed December 24, 2019)
https://aidsinfo.nih.gov/guidelines on 2/2/2020

HIV ile yaşayan bireylerde konsepsiyon

- **Kadın (+) erkek (-) ise ;**

Spermin peri ovulatuvar donemde vajinaya enjektor ile boşaltılması

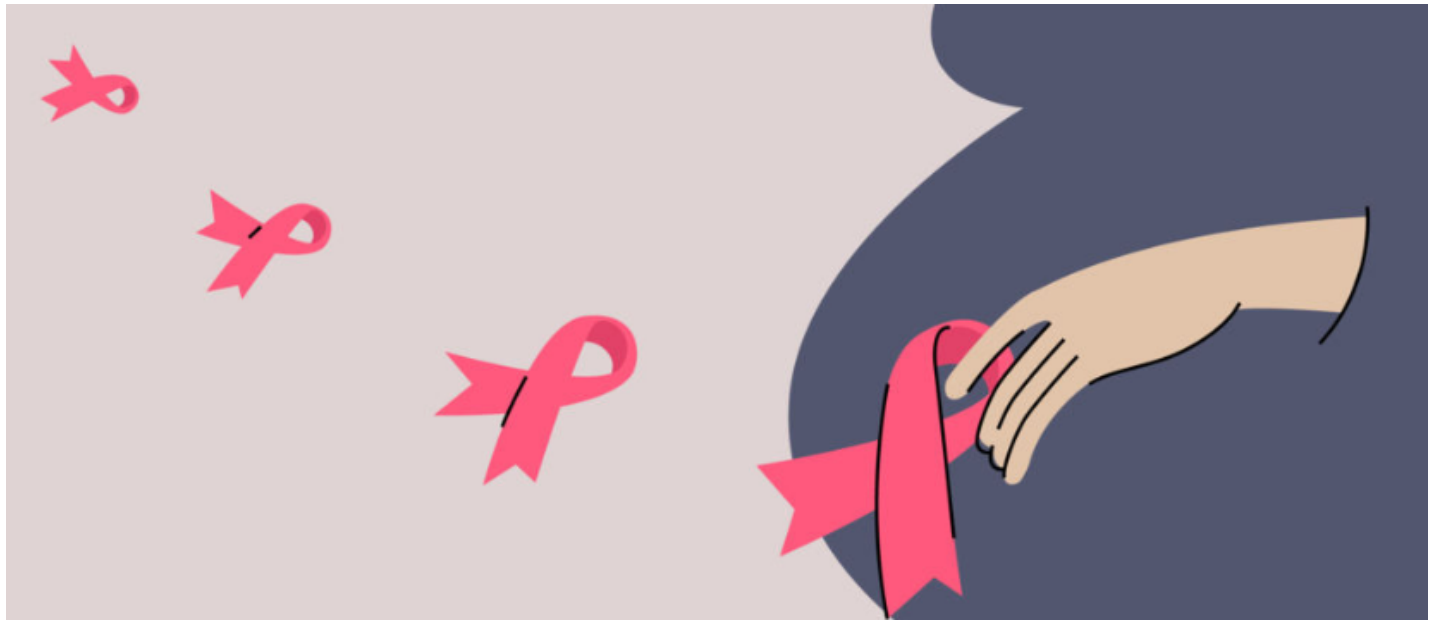
HIV ile yaşayan bireylerde konsepsiyon

- **Erkek (+) kadın (-) yada viral yük baskılanmamış ise;**

- TDF/FTC ile temas öncesi proflaksi (hamilelikten bir ay önce başlanıp bir ay sonraya kadar)

- *Donör spermi kullanımı*
- *Semen yıkama ile hem intrauterin inseminasyon hem de invitro fertilizasyonn birlikte kullanımı*

Antiretroviral Tedavi Seçimi



Gebelikte hemen ART başlanmalı

- ART, viral yüke gör doğumun planlaması ve mzirmenin önlenmesi ile risk <%1

1. Senaryo:
Gebelik planlayan HIV tespit edilen hasta

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Table 1. Antiretroviral drugs not recommended in women who wish to conceive

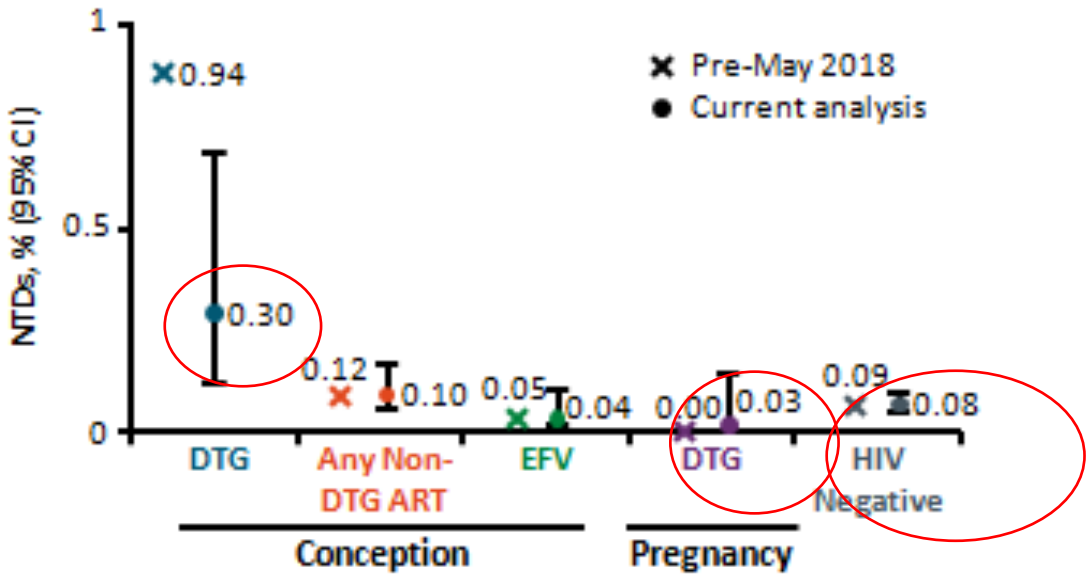
DRUG	Reason
INSTI	
DTG	Higher risk of neural tube defects if used preconception. Should be switched to another drug

N Engl J Med. 2019 Aug 29;381(9):827-840. doi: 10.1056/NEJMoa1905230. Epub 2019 Jul 22.

Neural-Tube Defects and Antiretroviral Treatment Regimens in Botswana.

Zash R[1], Holmes L[1], Diseko M[1], Jacobson DL[1], Brummel S[1], Mayondi G[1], Isaacson A[1], Davey S[1], Mabuta J[1], Mmalane M[1], Gaolathe T[1], Essex M[1], Lockman S[1], Makhema J[1], Shapiro RL[1].

- Ağustos 2014-Mart 2019
- 119.033 gebe incelenmiş
- Gebeler folik asit kullanmamış
- Konsepsiyon sırasında DTG
  - 1683 hastanın 5 bebeğinde NTD
  - Diğer rejimlerine göre NTD anlamlı olarak fazla



Outcome	Consepsion sırasında			DTG Hamilelikte (n = 3840)	HIV Negatif (n = 89,372)
	DTG (n = 1683)	Non-DTG (n = 14,792)	EFV (n = 7959)		
NTDs per exposures, n/N	5/1683	15/14792	3/7959	1/3840	70/89372
▪ Prevalence difference, % (95% CI)	Reference	0.20 (0.01-0.59)	0.26 (0.07-0.66)	0.27 (0.06-0.67)	0.22 (0.05-0.62)
NTDs per exposures since May 2018, n/N	1/1275	1/3492	0/2172	1/1028	9/23,315

Botswana sürveyans çalışması

- Propektif sürveyans çalışması (Ekim 2018 - Mart 2019)
- Tsepamo tarafından kapsanmayan 22 merkez

Outcome	HIV Positive			HIV Negative (n = 2328)
	DTG (n = 152)	Any Non-DTG ART (n = 381)	EFV (n = 261)	
NTDs, n (%) [95% CI]	1 (0.66) [0.02 to 3.69]	0 (0) [0 to 0.79]	0 (0) [0 to 1.15]	2 (0.09) [0.01 to 0.31]
Prevalence difference, % (95% CI)	Reference	0.66 (-0.73 to 4.16)	0.66 (-1.25 to 4.16)	0.58 (-0.10 to 4.10)

Raesima. IAS 2019.

Brezilya Kohortu-NTD

- Retrospektif kohortu (2017-2018)
- Gebe kaldıklarında DTG kullanan 384 kadın
- NTD saptanmamış

Pereira. IAS 2019

THE ANTIRETROVIRAL PREGNANCY REGISTRY

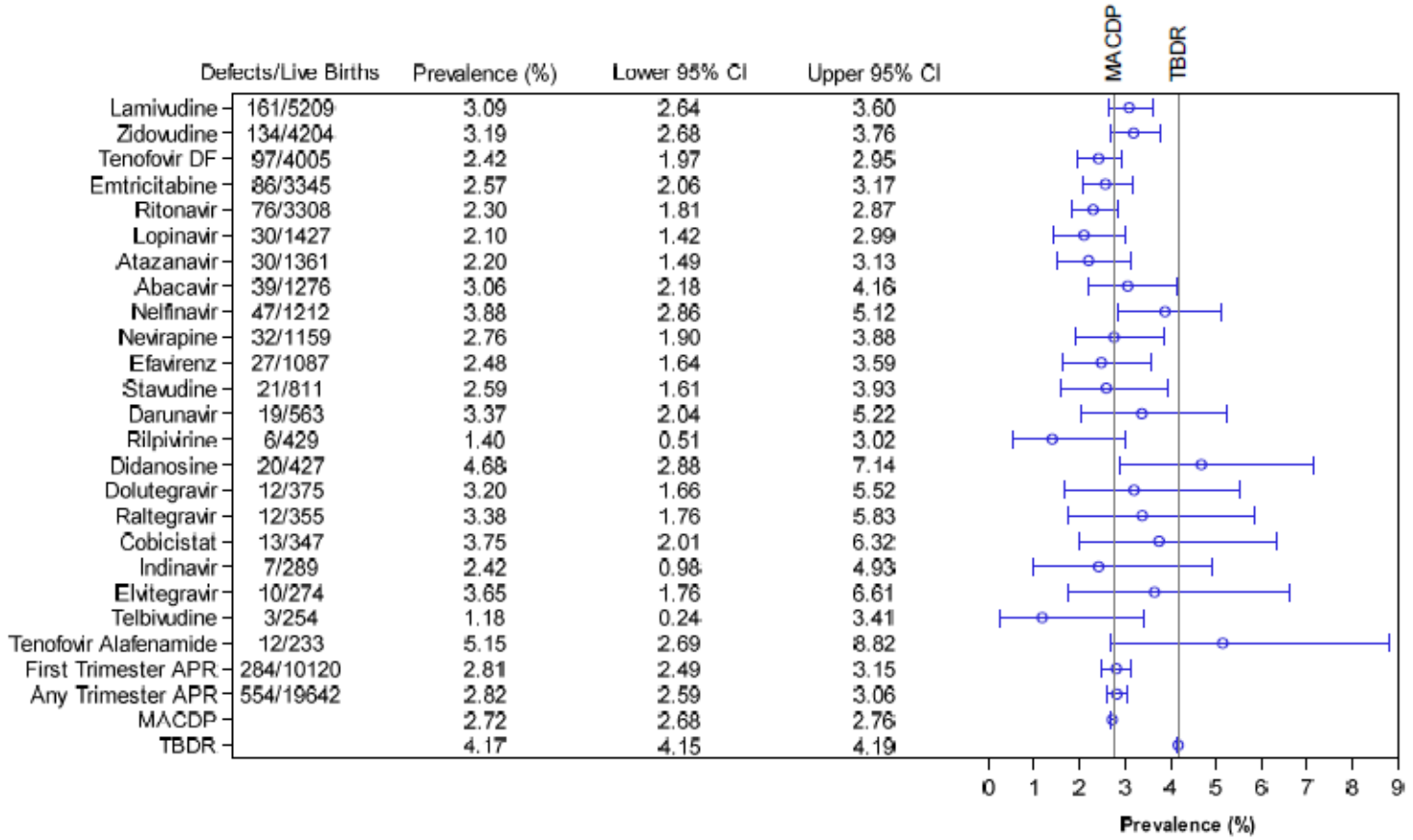
THE ANTIRETROVIRAL PREGNANCY REGISTRY INTERIM REPORT

1 JANUARY 1989 THROUGH 31 JULY 2019

(Issued: December 2019)

- **1 Ocak 1989- 31Temmuz 2019**
- 20.759 HIV+gebelik
- Doğum kusur oranı nüfusa dayalı gözlem verileri ile karşılaştırılmış
- İlk trimestr de ART alan gebelerde 100 canlı doğumda 2.8 doğumsal anomali (diğer sistemlerle anlamlı farklılık yok)
- Diğer trimestrlerde benzer
- Konsepsiyon sırasında maruziyette risk ⬆

Figure 1: Summary of Birth Defects among First Trimester Exposures, Prospective Registry Cases Closed with Outcome through 31 July 2019



MACDP = Metropolitan Atlanta Congenital Defects Program (reference 5); TBDR = Texas Birth Defects Registry (reference 7).

Interim Report July 2019, www.APRegistry.com.

THE ANTIRETROVIRAL PREGNANCY REGISTRY

THE ANTIRETROVIRAL PREGNANCY REGISTRY INTERIM REPORT

1 JANUARY 1989 THROUGH 31 JULY 2019

(Issued: December 2019)

Birth Defect Outcomes of Pregnant Women Exposed to Integrase Inhibitors
Prospective Registry Cases with Follow-up Closed through 31 July 2019

	Total Outcomes N	Live Births	Defect Cases	CNS Defect Cases [1, 2]	NT Defect Cases [1]	Encephalocele Defect Cases [2]
Any InSTI Exposure [3]	1710	1566	54	5	1	0
Periconception	969	846	27	3	1	0
Later First Trimester	143	134	3	1	0	0
Second/Third Trimester	596	584	24	1	0	0
Any Bictegravir Exposure [3]	17	15	0	0	0	0
Periconception	11	9	0	0	0	0
Later First Trimester	2	2	0	0	0	0
Second/Third Trimester	4	4	0	0	0	0
Any Dolutegravir Exposure [3]	667	614	21	4	1	0
Periconception	357	312	10	2	1	0
Later First Trimester	67	63	2	1	0	0
Second/Third Trimester	243	239	9	1	0	0
Any Elvitegravir Exposure [3]	377	340	11	1	0	0
Periconception	286	251	10	1	0	0
Later First Trimester	23	23	0	0	0	0
Second/Third Trimester	68	66	1	0	0	0
Any Raltegravir Exposure [3]	755	698	27	1	0	0
Periconception	331	289	10	0	0	0
Later First Trimester	75	66	2	1	0	0
Second/Third Trimester	346	340	15	0	0	0

http://www.apregistry.com/InterimReport.aspx

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- DTG
  - Gebelikte önerilen(>8hf)
  - Gebelik planlayanlarda alternatif

- Dolutegravir konsepsiyon yada 1. trimestirin erken döneminde kullanılmamalı

Appendix D: Dolutegravir Counseling Guide for Health Care Providers (Last updated December 12, 2019; last reviewed December 12, 2019)

This counseling guide represents the most recent guidance by the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (the Panel) based on all currently available data. It replaces all prior statements regarding the safety of dolutegravir (DTG) in pregnant women and women who are trying to conceive.

Use of Dolutegravir in Pregnant Women and Women Who Are Trying to Conceive[a]

In 2018, preliminary data from a study in Botswana identified an increased risk of infant neural tube defects (NTDs) in women who were taking DTG when they became pregnant. This observation led numerous organizations, including the Panel, to advise avoiding the use DTG in women who are trying to conceive or who are already in the first trimester[b] of pregnancy. In July 2019, the results from an analysis of NTDs in a larger number of pregnancies were published. The updated data showed that the risk of infant NTDs is lower than previously reported in preliminary data, but there was still a small but significant increase in the risk of infant NTDs among women who were taking DTG when they became pregnant compared to women who conceived on a regimen that did not contain DTG. An increased risk of infant NTDs has not been found in women who initiate DTG during pregnancy.

Because updated data indicate that the increased risk of NTDs associated with the use of DTG is small, and because DTG has the advantages of once-daily dosing, being generally well tolerated, and producing rapid, durable viral load suppression, which is important for the prevention of perinatal HIV transmission, **the Panel now recommends DTG as a *Preferred* antiretroviral (ARV) drug throughout pregnancy, and as an *Alternative* ARV drug in women who are trying to conceive**. The Panel strongly recommends that use of DTG be accompanied by appropriate counseling to allow patients and their health care providers to make joint decisions about treatment. This counseling guide summarizes considerations that should be addressed when counseling pregnant women and women who are trying to conceive about the use of DTG. For more information, see Updated Guidance about the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 4, Table 5, and Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy.

DHHS 2020

ART Regimen Component	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[a]	New ARV Regimen for Pregnant Women Whose Current Regimen is Not Well Tolerated and/or is Not Fully Suppressive[a]	ART for Nonpregnant Women Who Are Trying to Conceive[a,b]
INSTIs Used in combination with a dual-NRTI backbone[c]					
DTG[d]	Preferred	Continue	Preferred	Preferred	Alternative
RAL	Preferred	Continue	Preferred	Preferred	Preferred
BIC	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
EVG/c[e]	Not recommended	Consider switching, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
PIs Used in combination with a dual-NRTI backbone[c]					
ATV/r	Preferred	Continue	Preferred	Preferred	Preferred
DRV/r	Preferred	Continue	Preferred	Preferred	Preferred
LPV/r	Alternative	Continue	Alternative	Alternative	Alternative
ATV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
DRV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
NNRTIs Used in combination with a dual-NRTI backbone[c]					
EFV	Alternative	Continue	Alternative	Alternative	Alternative
RPV[f]	Alternative	Continue	Alternative	Alternative	Alternative
DOR	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
ETR[g]	Not recommended	Continue	Not recommended, except in special circumstances	Not recommended, except in special circumstances	Not recommended, except in special circumstances

2. Senaryo:
ART naive gebe

ART naive gebe

- Hızla ART başlanmalı
- Hızlı viral süpresyon
- İlaç seçiminde;
  - Teratojenite
  - Gebelik fizyolojisine uygun ilaç dağılımı
  - Komorbiditeler
  - Koenfeksiyonlar-Hepatit B

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Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	Initiate after 8 weeks of pregnancy HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, may delay starting ART) II (DTG: neural tube defects risk during periconception)
TDF/FTC or TDF/3TC + DTG	Initiate after 8 weeks of pregnancy	III (Tenofovir salts) II (DTG: neural tube defects risk during periconception)
TDF/FTC or TDF/3TC + RAL 400 mg bid		III (Tenofovir salts) IV (RAL in pregnancy, bid dosing)
2 NRTIs + PI/r		
TDF/FTC or TDF/3TC + DRV/r 600 mg/100 mg bid	With food	III (Tenofovir salts) V (DRV dosing) VI (COBI boosting)

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Alternative regimens		
2 NRTIs + INSTI		
ABC/3TC + RAL 400 mg bid	HBsAg negative HLA-B*57:01 negative	I (ABC: HLA-B*57:01, may delay starting ART) IV (RAL in pregnancy, bid dosing)
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, may delay starting ART) VII (EFV HIV-2 & group O)
TDF/FTC or TDF/3TC + EFV TDF/FTC/EFV	At bed time or 2 hours before dinner	III (Tenofovir salts) VII (EFV HIV-2 & group O)
TDF/FTC or TDF/3TC + RPV TDF/FTC/RPV	CD4 count > 200 cells/μL HIV-VL <100,000 copies/mL Not on proton pump inhibitor With food	II (Tenofovir salts) VIII (RPV exposure during 2nd and 3rd trimester, HIV-2) IX (Interactions)
2 NRTIs + PI/r		
ABC/3TC + ATV/r	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL Not on proton pump inhibitor H2 blockers timing recommended With food	I (ABC: HLA-B*57:01, may delay starting ART) VI (COBI boosting) IX (Interactions) X (Maternal hyperbilirubinemia)
TDF/FTC or TDF/3TC + ATV/r	Not on proton pump inhibitor H2 blockers timing recommended With food	VI (COBI boosting) IX (Interactions) X (Maternal hyperbilirubinemia)
ABC/3TC + DRV/r 600 mg/100 mg bid	HLA-B*57:01 negative and HBsAg negative With food	I (ABC: HLA-B*57:01, may delay starting ART) V (DRV dosing) VI (COBI boosting)
Other drugs not recommended as initial therapy for PLWH but with evidence of safety during pregnancy		
AZT		XI (access) XII (toxicity)
LPV/r	Dose increase recommended in third trimester of pregnancy	XI (access) XIII(toxicity)

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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.
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, because this FDC contains ABC. INSTI-based regimens may be 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 *Preferred* for the treatment of pregnant women with acute HIV infection and for women who present to care late in pregnancy. There are specific timing and/or fasting recommendations if DTG is taken with calcium or iron (e.g., in prenatal vitamins; see Table 8). The use of DTG at conception and in very early pregnancy has been associated with a small but statistically significant increase in the risk of NTDs; this information should be discussed with patients to ensure informed decision-making. For more information, see Updated Guidance About the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 5. Teratogenicity
RAL plus a Preferred Dual-NRTI Backbone	PK data are available for RAL use in pregnancy, and experience with use in pregnancy is increasing. RAL has been shown to produce rapid viral load decline to undetectable levels in women who present for initial therapy late in pregnancy. INSTI-based regimens may be useful when drug interactions or the potential for preterm delivery with PI-based regimens are a concern. Twice-daily dosing required. There are specific timing and/or fasting recommendations if RAL is taken with calcium or iron (e.g., in prenatal vitamins; see Table 8).
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 8).
DRV/r plus a Preferred Dual-NRTI Backbone	Better tolerated than LPV/r. Experience with use in pregnancy is increasing. Must be used twice daily in pregnancy.

3. Senaryo:
ART alırken gebe kalan hasta

ART alırken gebe kalan hasta

- Teratojenite

- Aynı ART'ye devam edelim mi?

- Viral yük ve CD4 düzeyleri bakılmalı
- İlaç uyumu ve tolerasyonu değerlendirilmeli

DHHS 2020

ART Regimen Component	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[a]	New ARV Regimen for Pregnant Women Whose Current Regimen is Not Well Tolerated and/or is Not Fully Suppressive[a]	ART for Nonpregnant Women Who Are Trying to Conceive[a,b]
INSTIs Used in combination with a dual-NRTI backbone[c]					
DTG[d]	Preferred	Continue	Preferred	Preferred	Alternative
RAL	Preferred	Continue	Preferred	Preferred	Preferred
BIC	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
EVG/c[e]	Not recommended	Consider switching, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
PIs Used in combination with a dual-NRTI backbone[c]					
ATV/r	Preferred	Continue	Preferred	Preferred	Preferred
DRV/r	Preferred	Continue	Preferred	Preferred	Preferred
LPV/r	Alternative	Continue	Alternative	Alternative	Alternative
ATV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
DRV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
NNRTIs Used in combination with a dual-NRTI backbone[c]					
EFV	Alternative	Continue	Alternative	Alternative	Alternative
RPV[f]	Alternative	Continue	Alternative	Alternative	Alternative
DOR	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
ETR[g]	Not recommended	Continue	Not recommended, except in special circumstances	Not recommended, except in special circumstances	Not recommended, except in special circumstances

4. Senaryo:
ART alan 2. yada 3. trimestirde HIV RNA

ART alan 2. yada 3. trimestr de HIV RNA↑

- Direnç testi istenmeli
- İntegraz inhibitörü ile değiştirilmeli ya da eklenmeli (DTG/RAL)

DHHS 2020

ART Regimen Component	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[a]	New ARV Regimen for Pregnant Women Whose Current Regimen is Not Well Tolerated and/or is Not Fully Suppressive[a]	ART for Nonpregnant Women Who Are Trying to Conceive[a,b]
INSTIs Used in combination with a dual-NRTI backbone[c]					
DTG[d]	Preferred	Continue	Preferred	Preferred	Alternative
RAL	Preferred	Continue	Preferred	Preferred	Preferred
BIC	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
EVG/c[e]	Not recommended	Consider switching, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
PIs Used in combination with a dual-NRTI backbone[c]					
ATV/r	Preferred	Continue	Preferred	Preferred	Preferred
DRV/r	Preferred	Continue	Preferred	Preferred	Preferred
LPV/r	Alternative	Continue	Alternative	Alternative	Alternative
ATV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
DRV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
NNRTIs Used in combination with a dual-NRTI backbone[c]					
EFV	Alternative	Continue	Alternative	Alternative	Alternative
RPV[f]	Alternative	Continue	Alternative	Alternative	Alternative
DOR	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
ETR[g]	Not recommended	Continue	Not recommended, except in special circumstances	Not recommended, except in special circumstances	Not recommended, except in special circumstances

Gebelikte İzlem

Gebelikte izlem-CD4

- İlk vizitte
- >2 yıl ART , CD4> 300/mm3, viral baskılanma … tekrar bakma
- <2 yıl ART, CD4 < 300/mm3, ölçülebilir viral yük….. 3-6 ayda bir ölçüm

Gebelikte izlem-HIV RNA

- İlk vizitte
- ART başlandıktan ya da değiştirildikten 2-4 hafta sonra
- RNA saptanamaz düzeye gelene kadar aylık
- Sonra her 3 ayda bir
- En son 34- 36. gebelik haftasında (doğum şekli ve yenidoğanda tdv)

Gebelikte izlem-Diğer

- OGTT;
  - 24-28. haftalarda
  - PI temelli rejimlerde daha erken
- İlaç yan etkilerinin izlemi;
  - RAL….. transaminaz artışı
  - TDF….. renal fonksiyon takibi
  - PI…….. hepatik disfonksiyon
  - NRTI….hepatosteatoz ve laktik asidoz

DOĞUM

Doğum-EACS 2019

- **34-36. haftada VY>50 kopya/ml ;**
  - 38. hf elektif sezeryan
  - Doğum sırasında iv zidovudin
    - 2mg/kg yükleme, 1mg /kg /saat doğuma kadar
    - Yükleme planlı seeryandan 3 saat önce, değilse yukleme dozu ardından sezeryan
- **Doğum anında HIV pozitif saptandı ise;**
  - Sezeryan planlanmalı
  - IV Zidovudin
  - PEP yenidoğana verilmeli

Doğum- DHHS 2020

- 38. hf HIV RNA > 1000 kopya/ml ya da bilinmiyorsa…… sezeryan+IV zidovudin
- VY 50 ile 1000 kopya/ml arasında…… IV zidovudin???

Emzirme

EACS 2019

- **Emzirme önerilmez**
  - Yüksek gelir duzeyi olan ülkelerde…… mama ile beslenme
  - Laktasyon supresyonu (cabergoline)
- **Emzirmeyi tercih eden anne/bebek multidisipliner takip**
  - Aylık viral yuk takibi
  - Sütte ilac duzeyi takibi
  - Anne VY >50 kopya/ml ise…..emzirme kesilerek cabergoline başlanmalı
  - İnfanta PrEP önerisi icin kanıt yok
  - Emzirme kesildikten sonra infant rutin takip altına alınmalı

DHHS 2020

- **Emzirme önerilmez**, emzirenlerde infant PrEP ?
- Emzirme döneminde HIV RNA >50 kopya/ml risk yüksek
- HIV RNA <50 kopya/ml…..risk devam ediyor

- Botswana' lı emziren 500 anneden 2 bebeğe HIV bulaşı
  - 1. ve 3. ayda plazma ve anne sütünde HIV RNA <50 kopya/ml

Shapiro RL, *N Engl J Med. 2010;362(24):2282-2294.*

- Tanzanya'da 186 anne izlenmiş, viral suprese annelerin hiçbirinde geçiş saptanmamış *

Luoga E, No HIV transmission from virally suppressed mothers during breastfeeding in rural Tanzania. *J Acquir Immune Defic Syndr. 2018;79(1):e17-e20.*

Yenidoğan Profilaksisi

Yenidoğan Profilaksisi

- Bütün HIV’ e maruz kalan infantlar, post partum ART almalı

- ART profilaksisi mümkün olduğunca erken verilmeli (doğumu takiben 6-12 saat içinde)

Yenidoğan profilaksi-DHHS 2020

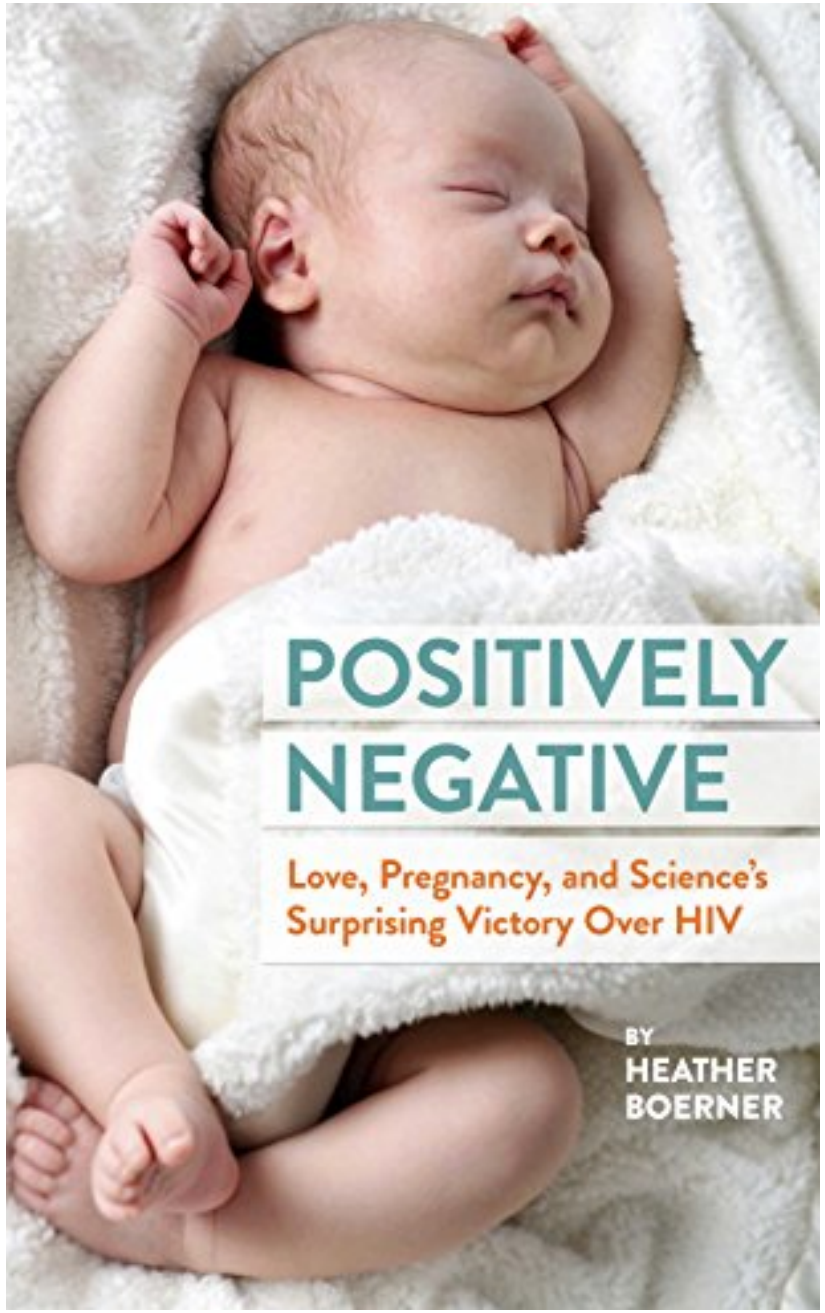
DÜŞÜK RİSK	**Anne gebelikte ART almış** **Viral supresyon sağlanmış** **Uyum sorunu yok**	**4 hafta zidovudin**
YÜKSEK RİSK	Anne ART almamış Sadece doğumda almış Viral supresyon sağlanamamış Gebelikte akut HIV infeksiyonu Emzirme	6 hf ZDV+2-6 hf 3TC+NVP 6 hf ZDV+2-6 hf 3TC+RAL 6 hf ZDV+ilk hf 3 doz NVP

Bebeğin HIV takibi

- 4 kez HIV-RNA PCR
  Doğumdan sonraki ilk 48 saat
  2-3. haftada
  1-2. ayda
  4-6. ayda

- 6 aylıktan sonra yapılmış 2 virolojik test negatif……enfeksiyonu dışlar

Teşekkürler




It is my baby's right
to be born HIV-negative