OLGU SUNUMU

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Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

Türkiye EKMUD İstanbul Günleri, Haziran 2022

Olgu

- 30 yaş kadın
- 18 haftalık gebe (ilk gebelik)
- İstanbul'da yaşıyor
- Aktif şikayeti yok
- Tarama sırasında HIV enfeksiyonu saptanmış
- Enfeksiyon Hastalıkları polikliniği: Kasım 2015

Olgu

- Özgeçmiş: Talasemi minör
- Kullandığı ilaçlar: demir desteği
- Sigara: 15 paket/yıl
- Alkol: sosyal içici
- Madde kullanımı: bonzai ve ekstazi kullanımı, gebelik öncesi
- Soygeçmiş: özellik yok

LABORATUVAR

- HIV RNA:5900 IU/ml
- CD4:565 hücre/mm^3 (%24)

- Partner taraması: negatif
- Danışmanlık

LABORATUVAR

- HBsAg: -
- Anti HBcIgG: -
- Anti HBs: -
- Anti HCV: -
- Anti HAV IgG: -
- VDRL: -
- TPHA: -
- Toxo IgM: -
- Toxo IgG: -
- CMV IgM: + (1,27)
- CMV IgG: +
- CMV Avitide: yüksek
- Kızamık IgG: -
- Varicella IgG: +

LABORATUVAR

- Tam kan sayımı
- CRP
- Karaciğer fonksiyonları
- Böbrek fonksiyonları
- Lipid profili
- Tiroid fonksiyonları
- İdrar

NORMAL

WBC	10600	**HDL**	56 mg/dl
PNL	%66	**LDL**	84 mg/dl
HB	12 g/dl	**Kolesterol**	166 mg/dl
PLT	293000	**Trigliserid**	128 mg/dl
CRP	0,5 mg/dl	**TSH**	2.05 IU/ml
AST	18 IU/ml	**T3**	3.51 pg/ml
ALT	11 IU/ml	**T4**	0,95 ng/dl
BUN	8 mg/dl		
KRE	0.51 mg/dl		
K	3.4 mEq/L		
Na	134 mEq/L		
AKŞ	72 mg/dl		

Tedavi

- **TDF/FTC 1X1**
- **LPV/r 2X2**

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Criteria for starting ART in pregnant women (see different scenarios)	Same as for non pregnant
Objective of treatment in pregnant women	Full plasma HIV-VL suppression at least by third trimester and specifically at time of delivery
Resistance testing	Same as for non pregnant women, i.e. before starting ART and in case of virological failure
SCENARIO	
1. Women planning to be pregnant while already on ART	1. Maintain ART, unless taking some contra-indicated regimen during pregnancy (ddI + d4T, triple NRTI combinations)
2. Women becoming pregnant while already on ART	2. Maintain ART, unless taking some contra-indicated regimen during pregnancy (ddI + d4T, triple NRTI combinations)
3. Women becoming pregnant while treatment-naïve	3. Starting ART as soon as possible and not later than beginning of 2nd trimester is highly recommended
4. Women whose follow-up starts after week 28 of pregnancy	4. Start ART immediately and consider adding INSTI to obtain rapid HIV-VL decline in case of high HIV-VL
5. Women whose HIV-VL is not undetectable at third trimester	5. Perform resistance testing and consider adding INSTI to obtain rapid HIV-VL decline
Antiretroviral regimen in pregnancy	Same as non pregnant
	NVP not to be initiated but continuation is possible if started before pregnancy
	EFV can be started if other options are not available or suitable. Continuation of EFV is possible if already started before pregnancy
	Among PI/r, prefer LPV/r or ATV/r
	If RAL, DRV/r: could be continued
Drugs contra-indicated during pregnancy	ddI + d4T, triple NRTI combinations
iv ZDV during labour	Not necessary if HIV-VL < 50 copies/mL
Single dose NVP during labour	Not recommended
Caesarean section	Only if HIV-VL > 50 copies/mL at week 34-36

DHHS, Mart 2014

Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 1 of 2)

These recommendations are for pregnant women who have never received antiretroviral therapy (ART) previously (i.e., ARV-naive) and are predicated on lack of evidence of resistance to regimen components. See Table 7 for more information on specific drugs and dosing in pregnancy. Within each drug class, regimens are listed alphabetically, and the order does not indicate a ranking of preference. It is recommended that women who become pregnant while on a stable ARV regimen with viral suppression remain on that same regimen.

Drug	Comments
Preferred Regimens	
Regimens with clinical trial data in adults demonstrating optimal efficacy and durability with acceptable toxicity and ease of use, PK data available in pregnancy, and no evidence to date of teratogenic effects or established adverse outcomes for mother/fetus/newborn. To minimize the risk of resistance, a PI regimen is preferred for women who may stop ART during the postpartum period.	
Preferred Two-NRTI Backbone	
ABC/3TC	Available as FDC, can be administered once daily, but potential HSR. ABC **should not be used** in patients who test positive for HLA-B*5701
TDF/FTC or 3TC	TDF/FTC available as FDC. Either TDF/FTC or 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.
ZDV/3TC	Available as FDC. NRTI combination with most experience for use in pregnancy but has disadvantages of requirement for twice-daily administration and increased potential for
PI Regimens	
ATV/r + a Preferred Two-NRTI Backbone	Once-daily administration.
LPV/r + a Preferred Two-NRTI Backbone	Twice-daily administration. Once-daily LPV/r is not recommended for use in pregnant women.
NNRTI Regimen	
EFV + a Preferred Two-NRTI Backbone **Note:** May be initiated after the first 8 weeks of pregnancy	Concern because of birth defects seen in primate study, risk in humans is unclear (see Teratogenicity and Table 7). Postpartum contraception must be ensured. Preferred regimen in women requiring co-administration of drugs with significant interactions with PIs.

Takip

- 1.ay kontrolü: Aralık 2015
- 24.hafta
- HIV RNA: negatif

- 4.ay kontrolü: Mart 2016
- 36.hafta
- HIV RNA: negatif

DOĞUM

- 38. hafta, Mart 2016
- Planlı c/s ile
- Viral yük negatif olduğundan gebeye zidovudin verilmedi
- Yenidoğan sağlıklı
- Emzirme önerilmedi
- Pediatri takibi, Marmara Üniversitesi
- 6 aylık takibinde bakılan virolojik testler negatif

Takip

- Doğumdan 4 ay sonra
- HIV RNA: 1049 IU/ml
- CD4: 508 hücre/ mm^3
- İlaç kullanımı uyumsuz

- Takibi terk
- Madde kullanımı
- Cezaevi

- 3 yıl sonra başvuru, Ağustos 2019
- HIV RNA: 10955 IU/ml
- CD4: 219 hücre/ mm^3
- HIV ilaç direnci

- 11 haftalık gebe

TEDAVİ

- 12.hafta, Eylül 2019
- **TDF/FTC 1X1**
- **Raltegravir 2X 400mg**

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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)

HIV ilaç direnci

Sequence Quality Assessment

PR153045607590199, RT35701051401752101233

Drug Resistance Interpretation: PR

PI Major Resistance Mutations:None

PI Accessory Resistance Mutations:None

Other Mutations:K14R, I15V, L19I, K20R, E35D, M36I, R41K, R57K, I62V, L63T, E65D, T74S, L89M

Protease Inhibitors

atazanavir/r (ATV/r)	Susceptible
darunavir/r (DRV/r)	Susceptible
fosamprenavir/r (FPV/r)	Susceptible
indinavir/r (IDV/r)	Susceptible
lopinavir/r (LPV/r)	Susceptible
nelfinavir (NFV)	Susceptible
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Susceptible

Drug Resistance Interpretation: RT

NRTI Resistance Mutations:None

NNRTI Resistance Mutations:**E138A**

Other Mutations:P19V, K20Q, V21G, V35T, T39G, D123E, I135T, K173E, Q174H, V179I, R211K, F214L

Nucleoside Reverse Transcriptase Inhibitors

abacavir (ABC)	Susceptible
zidovudine (AZT)	Susceptible
stavudine (D4T)	Susceptible
didanosine (DDI)	Susceptible
emtricitabine (FTC)	Susceptible
lamivudine (3TC)	Susceptible
tenofovir (TDF)	Susceptible

Non-nucleoside Reverse Transcriptase Inhibitors

doravirine (DOR)	Susceptible
efavirenz (EFV)	Susceptible
etravirine (ETR)	Potential Low-Level Resistance
nevirapine (NVP)	Susceptible
rilpivirine (RPV)	Low-Level Resistance

RT Comments

- **E138A** is a common polymorphic accessory mutation weakly selected in patients receiving ETR and RPV. It reduces ETR and RPV susceptibility ~2-fold. It has a weight of 1.5 in the Tibotec ETR genotypic susceptibility score.

Mutation Scoring: RT

NNRTI	DOR	EFV	ETR	NVP	RPV
E138A	0	0	10	0	15
Total	0	0	10	0	15

TAKİP

- 2.ay kontrolü, 20.hafta
- HIVRNA: <70 IU/ml

- 28. hafta
- HIV RNA: 6272 IU/ml
- Sağlık sigortasında sorunlar

- 34. hafta
- HIV RNA: negatif
- CD4:431 hücre/ mm^3

- 36.hafta
- HIV RNA: negatif

Doğum

- 38. hafta, Mart 2020
- Planlı c/s ile
- Yenidoğan sağlıklı
- Pediatri takibi
- Emzirme önerilmiyor
- Hastadan öğrenildiği kadarıyla bebeğe bulaş yok?

SONUÇ

- Gebelikte tarama
- HIV bulaş riski yüksek gebelerde tarama tekrar edilmeli
- Gebeye HIV ve diğer CYBE bulaşı hakkında bilgilendirme yapılmalı
- Güncel rehberler eşliğinde hastaya en uygun tedavi seçilmeli
- Viral süpresyonu sağlamak için tedaviye en hızlı şekilde başlanmalı
- Olası yan etkiler ve toksisite riski açısından hasta ile birlikte karar verilmeli

SONUÇ

- Hastanın takibe uyumunun kötü olduğu durumlarda gebelikte daha yakın izlem !!
- Farklı tarihlerde iki farklı tedavi ile başarılı hasta yönetimi
- Etkin tedavi ile bebeğe bulaş önlendi

} Multidisipliner yaklaşım İşbirliği

TEŞEKKÜRLER