Olgu sunumu

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Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

Olgu

- 55 y 
- 2016 yılında bir aydır devam eden ishal ve yaygın LAP ->HIV Ag/Ab pozitif
- Heteroseksüel?
- Evli-> eşi negatif

Olgu

- Üniversite mezunu
- Ticaret ile uğraşıyor
- Eşlik eden hastalık yok
- Kullandığı ilaç yok
- Sigara: 40 paket/yıl, aktif içici günde yarım paket
- Alkol : sosyal (ayda 1-2 kez)

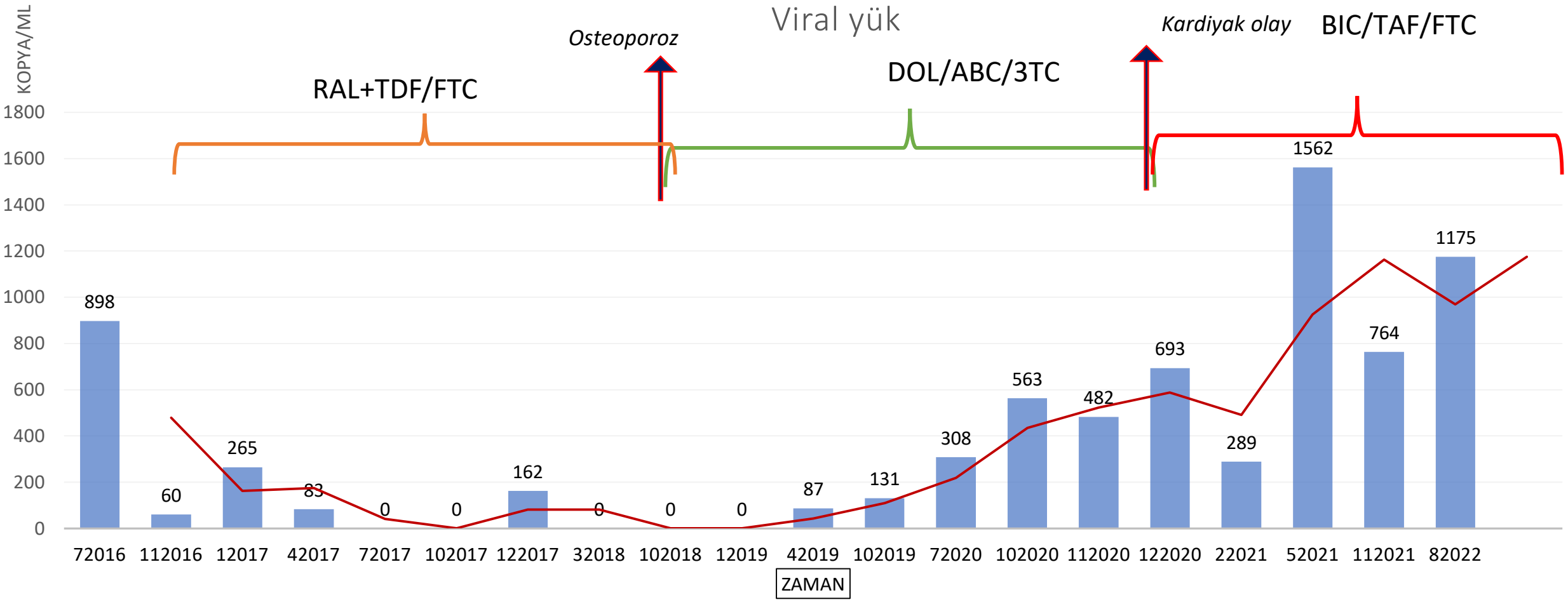
Olgu

- Fizik bakı: servikal ve aksiller LAP, diğer sistem bakıları olağan
- 30.05.2016- viral yük 7.637.772 kopya/ml
- 30.05.2016- CD4 + T hücre sayısı: (%11) 264 hücre/mm^3, CD4/CD8:0,19
- HBsAg (-), Anti HBc total (-), Anti HBs (-), Anti HCV(-), Anti HAV total (+)
- Anti-T.pallidum IgM, IgG (-)

Olgu

- Toksoplazma IgM(-), IgG(-), CMV IgM(-), CMV IgG(+)
- KCFT, BFT normal
- Direnç testi gönderiliyor
- 13.06.2016'da RAL+ TDF/FTC başlanıyor
- 1. ayda viral yük: 898 kopya/ml CD4+ T hücre: (%23) 782/mm^3

Takip


Viral yük
KOPYA/ML
RAL+TDF/FTC
Osteoporoz
DOL/ABC/3TC
Kardiyak olay
BIC/TAF/FTC
1800
1600
1400
1200
1000
800
600
400
200
0
898
60
265
83
0
0
162
0
0
0
87
131
308
563
482
693
289
1562
764
1175
72016
112016
12017
42017
72017
102017
122017
32018
102018
12019
42019
102019
72020
102020
112020
122020
22021
52021
112021
82022
ZAMAN

Olgu

- 20.12.2023 tedavisi kesilerek 1 hafta sonra direnç testi istendi.

- 27.12.2023 ->viral yük :474.000 kopya/ml

Metot

- Plazma örneğinden RNA ekstraksiyonu Qiagen EZ1 otomatize cihazı ile viral nükleik asit ekstraksiyon kiti kullanılarak ticari kit önerileri doğrultusunda yapıldı.
- Antiretroviral direnç analizi in-house metot ile pol gen bölgesine spesifik primerler kullanılarak gerçekleştirildi.
- Proteaz bölgesi 1-99. Kodon, reverse transkriptaz bölgesinin 1-258. Kodonları ve integraz bölgesinin 1-288.
- Kodonları spesifik primerler ile çoğaltıldı ve amplifikasyon izlenen örnekler Sanger dizi analizi metodu ile sekans analizine alındı.

Stanford University

HIV DRUG RESISTANCE DATABASE

A curated public database to represent, store and analyze HIV drug resistance data.

HIV-1 Sequence Analysis Report

Generated at 04.02.2023 21:04:17

1. 142-23 NECAHA62 (24.01.2023) IZMIR TEPECIK

Sequence summary

Sequence includes PR:	codons 1 - 99
Sequence includes RT:	codons 1 - 262 (missing: 263-560)
Subtype:	⊟ B (6.56%)

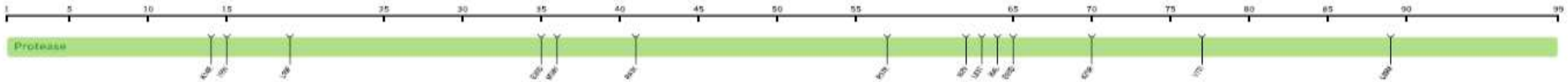
- **AB873942: Japan (2009); B (6.56%); best match**
- AY455778: Brazil (1999); B + F (CRF29_BF, 6.74%)
- EU581824: Paraguay (2002); B + F (CRF17_BF, 6.74%)
- KJ704787: United States (1983); B (6.74%)
- JF804813: Brazil (2005); B (6.83%)
- KY658687: Argentina (2012); B (6.83%)
- AF408629: Argentina (1997); B + F (CRF12_BF, 7.02%)
- EU581828: Peru (2002); B + F (CRF17_BF, 7.02%)

- FJ213780: Uruguay (2005); B + F (CRF38_BF, 7.02%)
- DQ085874: Brazil (1999); B + F (CRF28_BF, 7.11%)

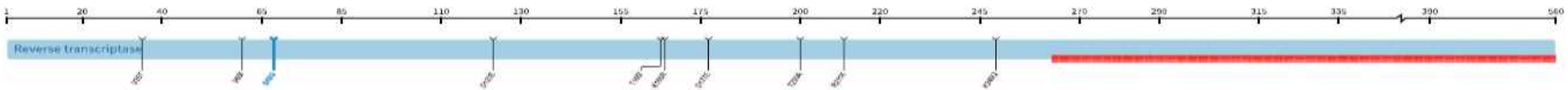
PR SDRMs: None
RT SDRMs: None

Sequence quality assessment

Protease (PR)



Reverse transcriptase (RT)



- **Note**: 298 positions were not sequenced or aligned: RT 263-560. Of them, 2 are at drug-resistance positions: RT 318, 348.

Drug resistance interpretation: PR

HIVDB 9.4 (2022-12-07)

PI Major Mutations: None
PI Accessory Mutations: None
PR Other Mutations: K14R • I15V • L19F • E35D • M36V • R41K • R57K • I62V • L63T • I64L • E65D • K70R • V77I • L89M

K14R, I15V, L19F, E35D, M36V, R41K, R57K, I62V, L63T, I64L, E65D,K70R, V77I, 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

Mutation scoring: PR	HIVDB 9.4 (2022-12-07)

No drug resistance mutations were found for PI.

Drug resistance interpretation: RT	HIVDB 9.4 (2022-12-07)

NRTI Mutations:	S68G
NNRTI Mutations:	None
RT Other Mutations:	V35T • V60I • D123E • T165I • K166R • D177E • T200A • R211K • K249Q

NRTI: S68G, NNRTI: yok
Diğer; V35T, V60I, D123E, T165I, K166R, D177E, T200A, R211K, K249Q

Nucleoside Reverse Transcriptase Inhibitors		Non-nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	Susceptible	**doravirine (DOR)**	Susceptible
zidovudine (AZT)	Susceptible	**efavirenz (EFV)**	Susceptible
stavudine (D4T)	Susceptible	**etravirine (ETR)**	Susceptible
didanosine (DDI)	Susceptible	**nevirapine (NVP)**	Susceptible
emtricitabine (FTC)	Susceptible	**rilpivirine (RPV)**	Susceptible
lamivudine (3TC)	Susceptible		
tenofovir (TDF)	Susceptible		

RT comments

NRTI

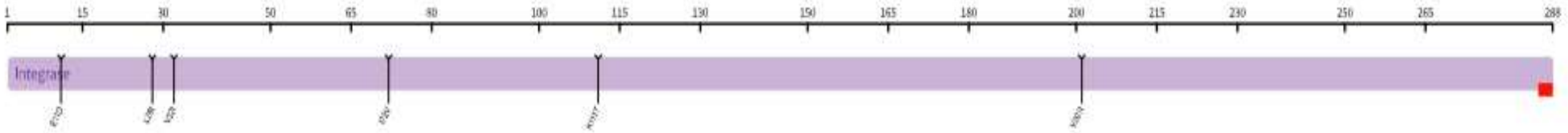
- **S68G** is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.

Mutation scoring: RT HIVDB 9.4 (2022-12-07)

No drug resistance mutations were found for NRTI.

No drug resistance mutations were found for NNRTI.

Integrase (IN)



- **Severe warning**: This sequence may also have nucleotides belonging to RT. Reason to exclude RT: Alignment of gene HIV1RT was discarded since the length of alignment was too short (< 50).
- **Warning**: 3 positions were not sequenced or aligned: IN 286-288. However, none is at drug-resistance position.

Drug resistance interpretation: IN	HIVDB 9.4 (2022-12-07)

INSTI Major Mutations:	None
INSTI Accessory Mutations:	None
IN Other Mutations:	E11D • L28I • V32I • I72V • K111T • V201I

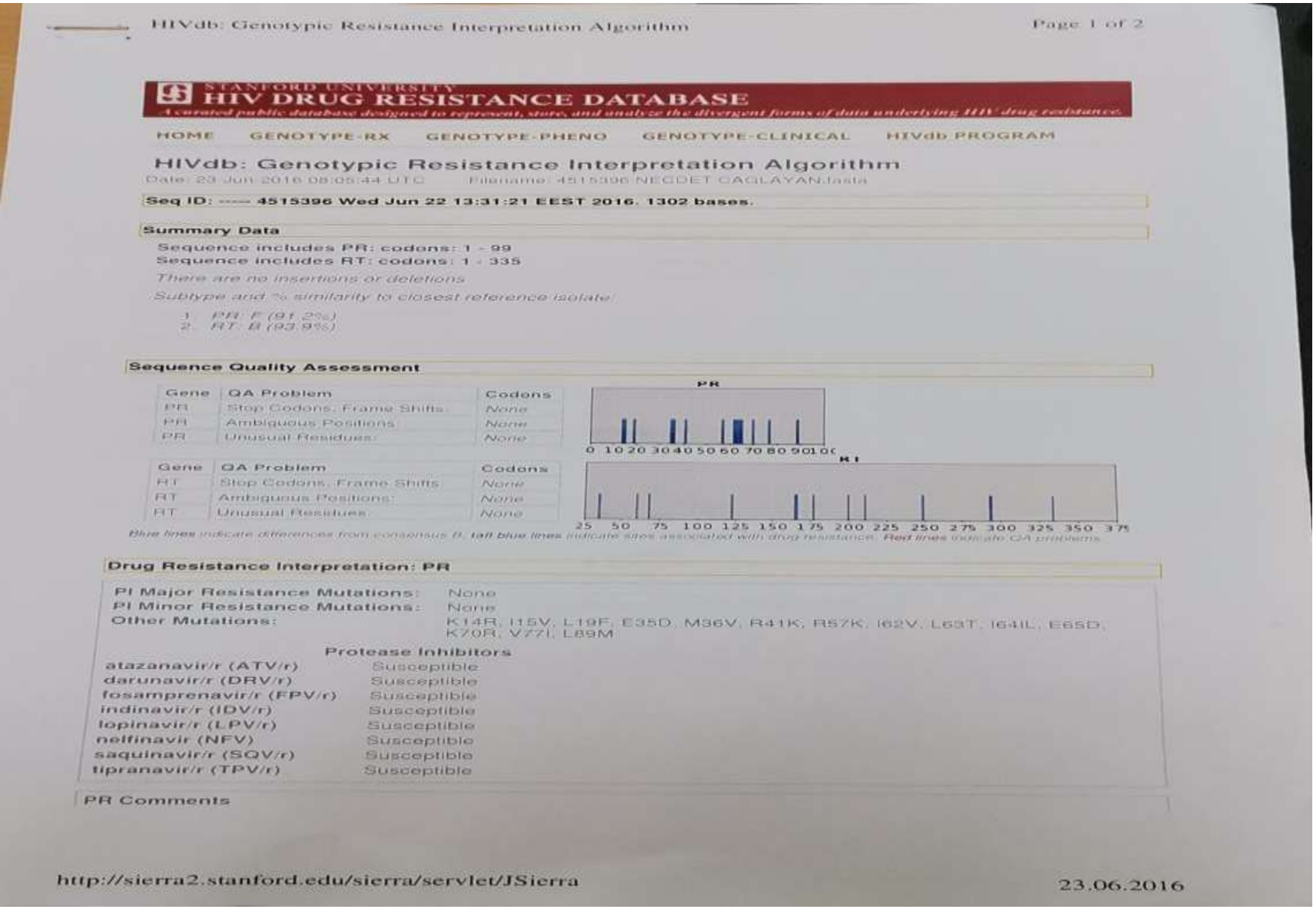
INSTI: Majör veya minör mutasyon yok
Diğer mutasyonlar:E11D, L28I, V32I, I72V, K111T, V201I

Integrase Strand Transfer Inhibitors	
bictegravir (BIC)	Susceptible
cabotegravir (CAB)	Susceptible
dolutegravir (DTG)	Susceptible
elvitegravir (EVG)	Susceptible
raltegravir (RAL)	Susceptible

Mutation scoring: IN HIVDB 9.4 (2022-12-07)

No drug resistance mutations were found for INSTI.

Tedavi öncesi 2016'daki direnç testi



HIVdb: Genotypic Resistance Interpretation Algorithm Page 1 of 2

STANFORD UNIVERSITY
HIV DRUG RESISTANCE DATABASE
A curated public database designed to represent, store, and analyze the divergent forms of data underlying HIV drug resistance.

HOME GENOTYPE-RX GENOTYPE-PHENO GENOTYPE-CLINICAL HIVdb PROGRAM

HIVdb: Genotypic Resistance Interpretation Algorithm

Date: 23 Jun 2016 08:05:44 UTC Filename: 4515396 NECDET CAGLAYAN.fasta

Seq ID: ---- 4515396 Wed Jun 22 13:31:21 EEST 2016. 1302 bases.

Summary Data

Sequence includes PR: codons: 1 - 99
Sequence includes RT: codons: 1 - 335
There are no insertions or deletions
Subtype and % similarity to closest reference isolate
1. *PR: F (91.2%)*
2. *RT: B (93.9%)*

Sequence Quality Assessment

Gene	QA Problem	Codons
PR	Stop Codons, Frame Shifts:	None
PR	Ambiguous Positions:	None
PR	Unusual Residues:	None

PR

0 10 20 30 40 50 60 70 80 90 10

Gene	QA Problem	Codons
RT	Stop Codons, Frame Shifts:	None
RT	Ambiguous Positions:	None
RT	Unusual Residues:	None

RT

25 50 75 100 125 150 175 200 225 250 275 300 325 350 375

Blue lines indicate differences from consensus B, tall blue lines indicate sites associated with drug resistance, Red lines indicate QA problems.

Drug Resistance Interpretation: PR

PI Major Resistance Mutations: None
PI Minor Resistance Mutations: None
Other Mutations: K14R, I15V, L19F, E35D, M36V, R41K, R57K, I62V, L63T, I64IL, E65D, K70R, V77I, L89M

Protease Inhibitors

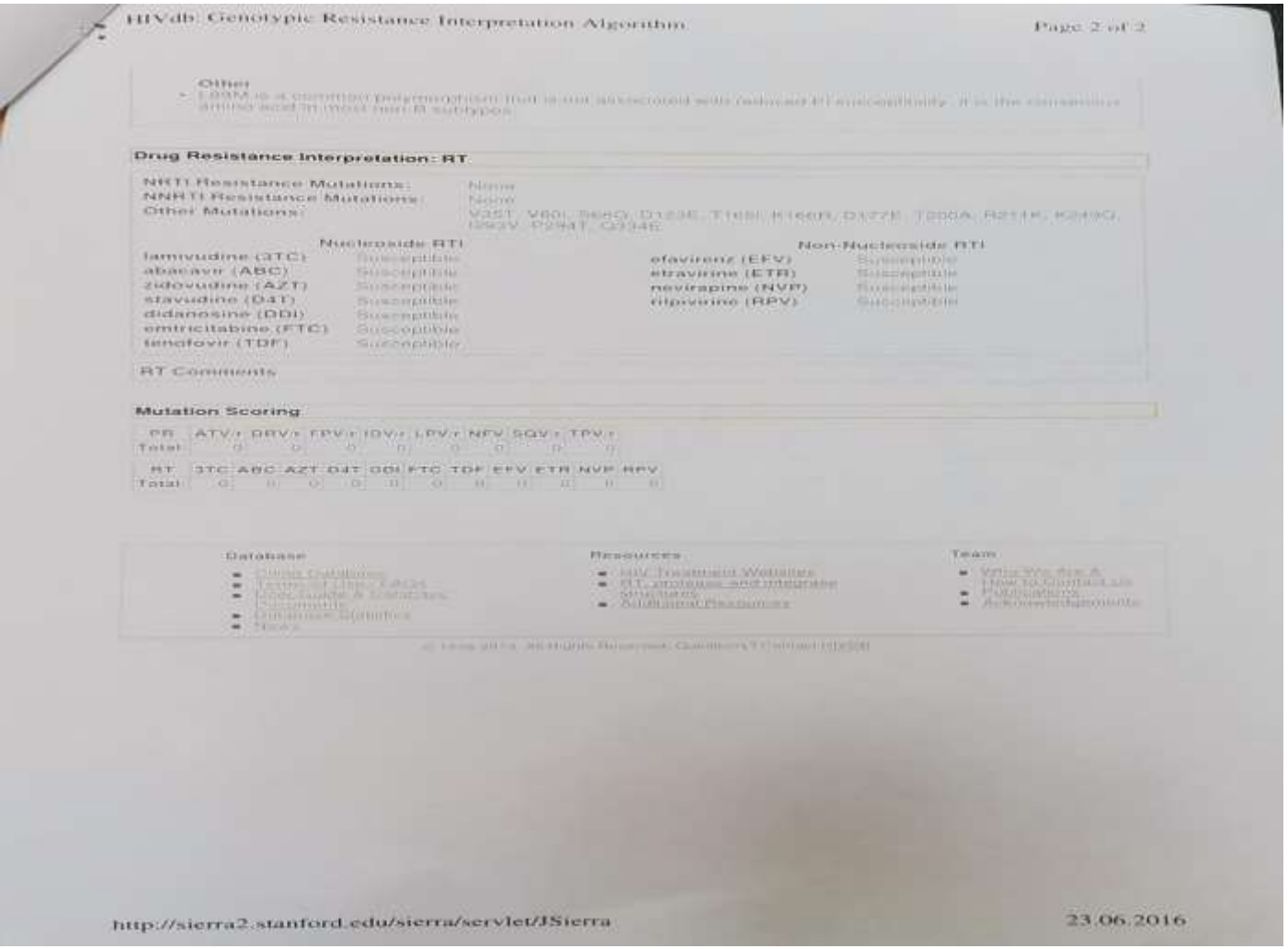
atazanavir/r (ATV/r)	Susceptible
darunavir/r (DRV/r)	Susceptible
fosamprenavir/r (FPV/r)	Susceptible
indinavir/r (IDV/r)	Susceptible
lopinavir/r (LPV/r)	Susceptible
nelfinavir (NFV)	Susceptible
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Susceptible

PR Comments

http://sierra2.stanford.edu/sierra/servlet/JSierra 23.06.2016

PI: Majör ve minör mutasyon yok
Diğer mutasyonlar:K14R, I15V, L19F, E35D, M36V, R41K, R57K, I62V, L63T, I64IL, E65D, K70R, V77I, L89M*
***PI duyarlılığı ile ilgili değil, B dışındaki alt tiplerde sıklıkla görülür.**

Tedavi öncesi 2016’daki direnç testi



HIVdb: Genotypic Resistance Interpretation Algorithm — Page 2 of 2

Other

Drug Resistance Interpretation: RT

NRTI Resistance Mutations:	None
NNRTI Resistance Mutations:	None
Other Mutations:	V35T, V60I, S68G, D123E, T165I, K166R, D177E, T200A, R211K, K249Q, I293V, P294T, Q334E

Nucleoside RTI		Non-Nucleoside RTI	
lamivudine (3TC)	Susceptible	efavirenz (EFV)	Susceptible
abacavir (ABC)	Susceptible	etravirine (ETR)	Susceptible
zidovudine (AZT)	Susceptible	nevirapine (NVP)	Susceptible
stavudine (D4T)	Susceptible	rilpivirine (RPV)	Susceptible
didanosine (DDI)	Susceptible		
emtricitabine (FTC)	Susceptible		
tenofovir (TDF)	Susceptible		

RT Comments

Mutation Scoring

	ATV/r	DRV/r	FPV/r	IDV/r	LPV/r	NFV	SQV/r	TPV/r
PR Total	0	0	0	0	0	0	0	0

	3TC	ABC	AZT	D4T	DDI	FTC	TDF	EFV	ETR	NVP	RPV
RT Total	0	0	0	0	0	0	0	0	0	0	0

Database — Resources — Team

http://sierra2.stanford.edu/sierra/servlet/JSierra 23.06.2016

NRTI,NNRT ; Majör ve Minör mutasyon yok

Diğer mutasyonlar; V35T, V60I, S68G, D123E, T165I, K166R, D177E,T200A, R211K, K249Q, I293V, P294T, Q334E

- Tedaviyi nasıl planlayalım?

Tedavi ve virolojik yanıt

- 07.02.2023-> DOL+DAR/r

Tarih	Viral yük k/ml	CD4 + T hücre%	CD4/CD8
Ağustos 2022	1175	35	1,18
Aralık 2022	2640		
→ Şubat 2023	3762	28,7	0,86
Nisan 2023	66		
Ağustos 2023	<45	38,5	1,31
Kasım 2023	240		
Ocak 2024	<45	37	1,30
Ağustos 2024	<45		
Ocak 2025	<45	36	1,23