

Stanford HIV Database

Use and Utility



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Objectives

- Discuss Stanford HIV Database utility via a case discussion
- Review the Stanford HIV Database in Real time

No Disclosures

Stanford University
HIV DRUG RESISTANCE DATABASE
A curated public database to represent, store and analyze HIV drug resistance data.

HOME GENOTYPE-RX GENOTYPE-PHENO GENOTYPE-CLINICAL HIVDB PROGRAM ABOUT HIVDB SUPPORT HIVDB!

HIVDB Algorithm Version 9.0
Mar 1, 2021

SIERRA
release notes / web service
Mar 1, 2021

Stanford Coronavirus Antiviral Research Database
Antivirals, investigational agents, repurposed drugs, monoclonal antibodies, interferons, and lead compounds (Apr 2020)

Reference Library: Dolutegravir Resistance
A body of literatures reviewed, annotated and searchable
June 24, 2020

HIVdb-NGS (Beta)
release notes
Oct 24, 2019

HIVDB released on February 3, 2021
Query / Download

Genotype-treatment
ARV selection data comprising 189,227 protease, 199,615 RT and 26,998 integrase HIV-1 virus sequences from 213,273 persons; 1,075 protease, 838 RT and 340 integrase HIV-2 virus sequences from 1,134 persons.

Genotype-phenotype
Drug susceptibility data comprising 25,434 PI, 19,922 NRTI, 11,554 NNRTI and 4,982 INI susceptibility results from HIV-1 virus isolates

HIVdb Program

Drug Resistance Summaries (Download PDF)

PIs NRTIs NNRTIs INSTIs

HIVdb NGS Program

<https://hivdb.stanford.edu/>

Stanford HIV Drug Resistance Database

OBJECTIVES

- To collect, analyse, and make available the diverse forms of data underlying HIV drug resistance knowledge
- To provide a resource for care providers treating patients with HIV infection and scientists studying **HIV treatment**



<https://hivdb.stanford.edu/about/faq/>

The Stanford University HIV Drug Resistance Database provides helpful guidance for interpreting genotypic resistance test results

<https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/drug-resistance-testing?view=full>

Major Mutations



Stanford University

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HIVdb version 8.8 (last updated on 2019-02-13)

NRTI Resistance Notes (PI · NRTI · NNRTI · INSTI)

Notes last updated on 2016-05-31

Major Nucleoside RT Inhibitor (NRTI) Resistance Mutations

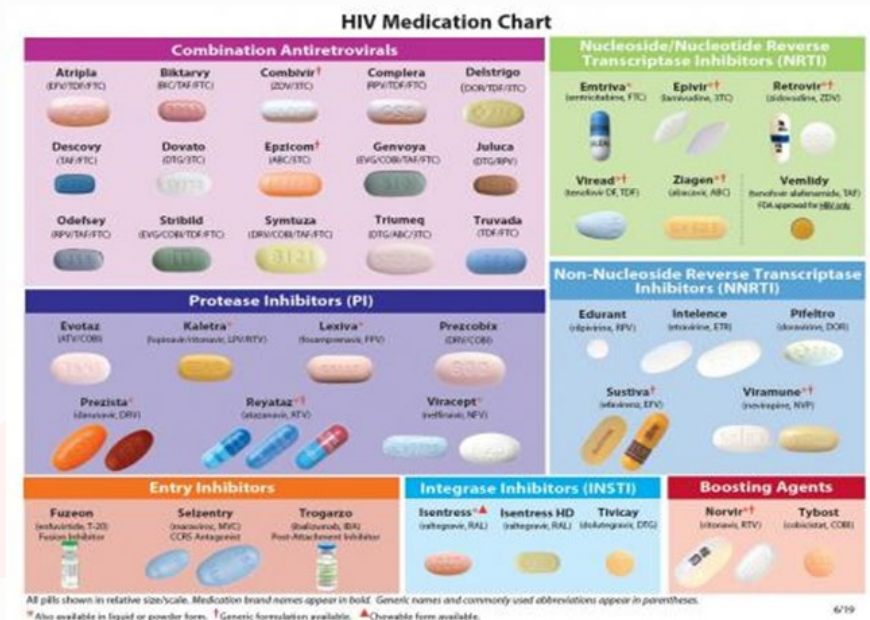
	Discriminatory Mutations					Thymidine Analog Mutations (TAMs)						MDR Mutations	
	184	65	70	74	115	41	67	70	210	215	219	69	151
Consensus	M	K	K	L	Y	M	D	K	L	T	K	T	Q
3TC	VI	R										Ins	M
FTC	VI	R										Ins	M
ABC	VI	R	E	VI	F	L			W	FY		Ins	M
DDI	VI	R	E	VI		L			W	FY		Ins	M
TDF	***	R	E		F	L		R	W	FY		Ins	M
D4T	***	R	E			L	N	R	W	FY	QE	Ins	M
ZDV	***	***	*	*		L	N	R	W	FY	QE	Ins	M

https://hivdb.stanford.edu/pages/download/resistanceMutations_handout.pdf

<https://www.iasusa.org/sites/default/files/2017-drug-resistance-mutations-hiv-1-figure.pdf>

Clinical Case

- 38 yo AAM entering care
 - He is unaware of what ARVs he has “been on” in the past
 - Reports taking several types of pills over the years with many SEs
 - Points to: AZT, CBV, TDF, Truvada, Kaletra, DTG, Descovy, Evotaz
- Archive genotype demonstrates:
 - 36I, 62V, 219Q, 138A, 179D
 - 190A, 318F, 101Q, 143C, 230R
- HIV-VL: 98,000
- CD4: 86 / 4.1%
- eGFR: 61



Stanford HIV Drug Resistance Database

Drug display options

By default, results will be shown for checked ARVs. Use checkboxes for additional ARVs. (select all ARVs, revert to default)

NRTI: ABC AZT FTC 3TC TDF D4T DDI NNRTI: DOR EFV ETR NVP RPV

INSTI: BIC CAB DTG EVG RAL PI: ATV/r DRV/r LPV/r FPV/r IDV/r NFV SQV/r TPV/r

Input mutations Input sequences

Reverse Transcriptase **Protease** **Integrase**

Input mutation(s)

Select mutations:

40	41	44	62
---	---	---	---
65	67	68	69
---	---	---	---
70	74	75	77
---	---	---	---
90	98	100	101
---	---	---	---
103	106	108	115
---	---	---	---
116	118	138	151
---	---	---	---
179	181	184	188
---	---	---	---
190	210	215	219
---	---	---	---
221	225	227	230
---	---	---	---
234	236	238	318
---	---	---	---
348			

Select mutations:

10	11	13	20
---	---	---	---
23	24	30	32
---	---	---	---
33	35	36	43
---	---	---	---
46	47	48	50
---	---	---	---
53	54	58	63
---	---	---	---
71	73	74	76
---	---	---	---
77	82	83	84
---	---	---	---
85	88	89	90
---	---	---	---
93			

Select mutations:

51	66	74	92
---	---	---	---
95	97	114	118
---	---	---	---
121	128	138	140
---	---	---	---
143	145	146	147
---	---	---	---
148	151	153	155
---	---	---	---
157	163	230	263
---	---	---	---

Keep input mutations when browsing back

Reset Analyze

Nucleoside Reverse Transcriptase Inhibitors

abacavir (ABC)	Potential Low-Level Resistance
zidovudine (AZT)	Low-Level Resistance
stavudine (D4T)	Low-Level Resistance
didanosine (DDI)	Potential Low-Level Resistance
emtricitabine (FTC)	Susceptible
lamivudine (3TC)	Susceptible
tenofovir (TDF)	Potential Low-Level Resistance

Non-nucleoside Reverse Transcriptase Inhibitors

efavirenz (EFV)	High-Level Resistance
etravirine (ETR)	Intermediate Resistance
nevirapine (NVP)	High-Level Resistance
rilpivirine (RPV)	Intermediate Resistance

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

NRTI	ABC	AZT	D4T	DDI	FTC	3TC	TDF
<u>A62V</u>	5	5	5	5	5	5	5
<u>K219Q</u>	5	10	10	5	0	0	5
Total	10	15	15	10	5	5	10

NNRTI	EFV	ETR	NVP	RPV
<u>V179D</u>	10	10	10	10
<u>G190A</u>	45	10	60	15
<u>Y318F</u>	10	0	30	0
<u>E138A</u>	0	10	0	15
Total	65	30	100	40

<https://hivdb.stanford.edu>

Integrase Strand Transfer Inhibitors

bictegravir (BIC)	Low-Level Resistance
dolutegravir (DTG)	Intermediate Resistance
elvitegravir (EVG)	Intermediate Resistance
raltegravir (RAL)	High-Level Resistance

INSTI	BIC	DTG	EVG	RAL
<u>Y143C</u>	5	5	10	60
<u>S230R</u>	10	20	20	20
<u>Y143C + S230R</u>	5	5	5	0
Total	20	30	35	80

Dosage Considerations

- There is evidence for intermediate **DTG** resistance. If **DTG** is used, it should be administered twice daily.

Genotypic Score	https://hivdb.stanford.edu/
0 – 9	Susceptible
10 – 14	Potential Low-Level Resistance
15 – 29	Low-Level Resistance
30 – 59	Intermediate Resistance
≥ 60	High-Level Resistance



<https://www.collegetransitions.com/bl-og/should-i-use-the-common-app-additional-information-section/>

Clinic's Course

- CCC consulted: had concerns about missing data
- Recommended: Descovy™ + Prezcoibix™
- 12-week labs (missed 4-week follow up appointment)
 - HIV-VL 26,000 Initial: 98,000
 - CD4: 132 / 6% Initial: 86 / 4.1%
 - CD4 lab circled with note: GOOD 😊
 - Plan: staff stressed adherence & follow-up as scheduled in 3-mnths



<https://nccc.ucsf.edu/>

Onsite Chart Review

- Staff stated: Archived Genotype was performed so all other resistance testing was archived as deemed no longer needed
- Asked for all records:
 - 3-days until records pulled from storage
 - Client asked to present for resistance testing (Genotype)
- From old records
 - 36I, 62V, 63P/S, 65R, 184I/V, 219Q, 138A, 179D, 190A, 230L, 318F, 101Q, 103R, 143C, 230R, 74M, 151I
- No additional mutations from genotype testing that week
- Reminder: Archive genotype
 - 36I, 62V, 219Q, 138A, 179D, 190A, 318F, 101Q, 143C, 230R

Real Time

<https://hivdb.stanford.edu/hivdb/by-mutations/>

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Conclusion

- Reminder: Decision made prior to newer ARV availability
- Initial regimen
 - Descovy + Prezcoibix: TDF (60), FTC (95), DRV (0)
 - Result: Monotherapy
- Changed ARVs:
 - AZT (-10: close monitoring), Prezcoibix™ (0) + DTG (30: twice day)
- Follow-up: HIV-VL: <40, CD4: 201/12%, eGFR: 70

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Newer ARVs not available at the time of this case.

Thank you

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