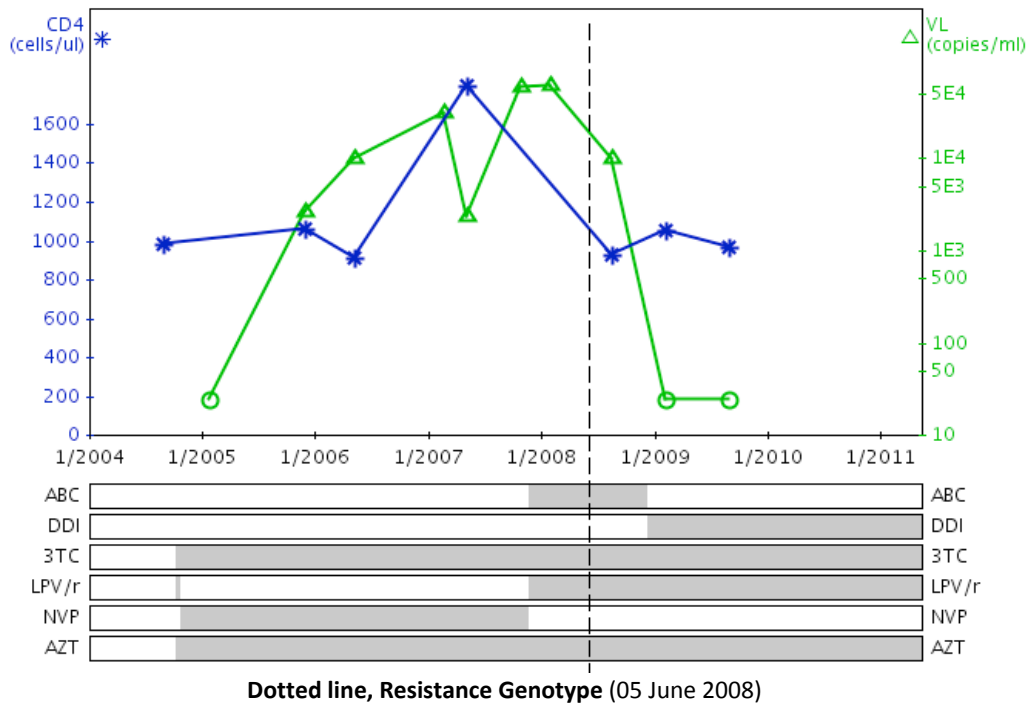


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Example: SATuRN RegaDB Drug Resistance & Clinical Management Report.



Dotted line, Resistance Genotype (05 June 2008)

Subtype Result: HIV-1 Subtype C (Rega Subtyping tool v2.0)

Algorithm interpretation: HIV Stanford HIV Drug Resistance DB 6.0.5

Drug	Mutations	Description	Level	GSS
Zidovudine (AZT)	67N 70R 184V 219Q	Intermediate resistance	4	0.5
Zalcitabine	N/A	N/A	N/A	N/A
Didanosine (DDI)	67N 184V	Potential low-level resistance	2	1.0
Lamivudine (3TC)	184V	High-level resistance	5	0.0
Stavudine	67N 70R 184V 219Q	Low-level resistance	3	0.5
Abacavir (ABC)	67N 184V	Low-level resistance	3	0.5
Emtricitabine	184V	High-level resistance	5	0.0
Tenofovir	67N 70R 184V	Susceptible	1	1.0
Nevirapine (NVP)	103N 138Q	High-level resistance	5	0.0
Delavirdine	103N 138Q	High-level resistance	5	0.0
Efavirenz	103N 138Q	High-level resistance	5	0.0
Etravirine	103N 138Q	Low-level resistance	3	0.5
saquinavir/r		Susceptible	1	1.0
indinavir/r		Susceptible	1	1.0
Nelfinavir		Susceptible	1	1.0
fosamprenavir/r		Susceptible	1	1.0
lopinavir/r (LPV/r)		Susceptible	1	1.0
atazanavir/r		Susceptible	1	1.0
tipranavir/r		Susceptible	1	1.0
darunavir/r		Susceptible	1	1.0

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Representative clinical chart and interpretation of resistance. This paediatric patient had resistance mutations directed against three of the four antiretroviral drugs he/she was receiving. Fortunately, the pattern did not include any PI (LPV/r) mutations that would exclude the use of this class of drugs. The patient exhibited high-level resistance to Lamivudine (3TC), intermediate resistance to Zidovudine (AZT) and low-level resistance to Abacavir (ABC). His/her HIV population had the characteristic 3TC resistance mutation, M184V, in addition to three TAMs, 67N, 70R and 219Q.

The patient's last six VLs prior to resistance genotyping ranged between 1,000 and 50,000 copies/mL of plasma. The presence of multiple TAMs and relatively low level of viral replication (ie. for a paediatric patient) suggest that, although the child appeared to be taking his/her antiretroviral drugs, adherence may have been suboptimal, or that the drug dosage was not appropriate.

As would be expected, the CD4 T cell count decreased during virological failure.

Infectious Disease (I.D.) Specialist Comments: The presence of multiple TAMs limits this patient's options for a subsequent regimen. In the absence of a novel drug class, such as an entry inhibitor or integrase inhibitor, an augmented standard second-line regimen is suggested. This is achieved by adding 3TC to a NRTI-combination of AZT and ddI in order to 'cripple' the virus and make it hyper-susceptible to AZT. This augmented backbone is combined with the protease inhibitor, lopinavir/ritonavir. Special attention should be paid to adherence issues that might have compromised the first regimen, with special attention to family support structures, the use of any concomitant medication or alternative remedies, and drug dosage. Ongoing adherence support should be provided because of the high pill burden and side-effect profile of this combination of drugs.

Clinical Outcome: Complete viral suppression was achieved by switching to an augmented second-line regimen. If this viral suppression is sustained, simplification of the regimen can be considered with removal of 3TC or ddI, depending on the clinical picture and side-effect profile of the child.