

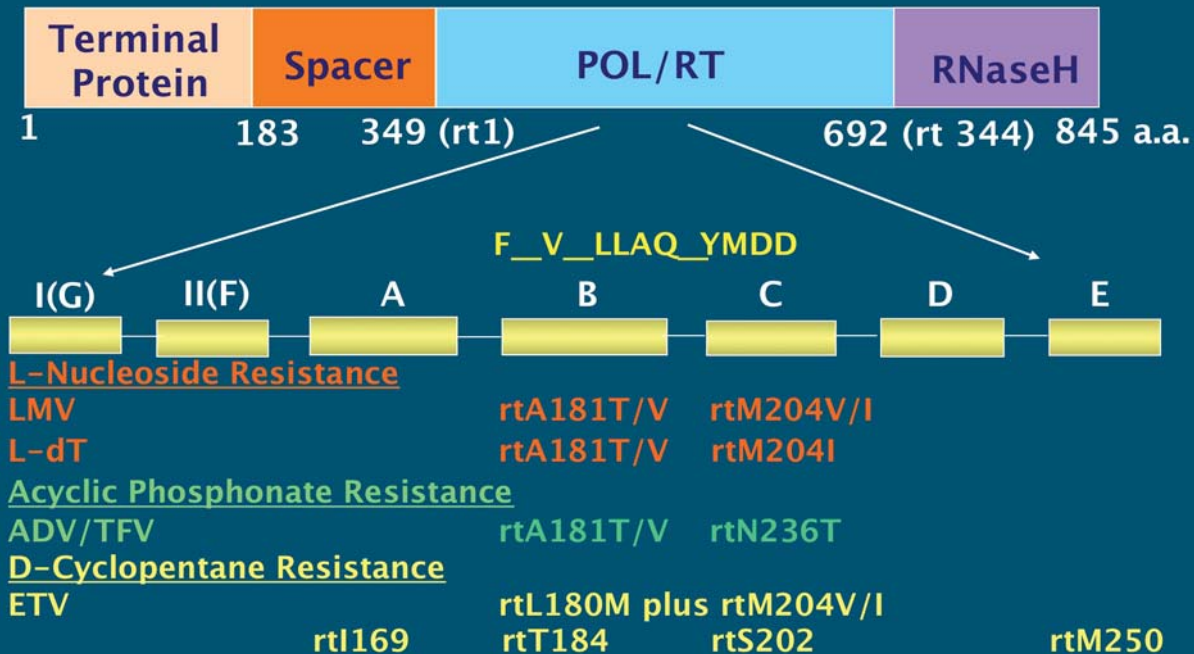
Hepatitis B Antiviral Drug Resistance: Navigating the Way Forward

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Antiviral Drug Resistance and Hepatitis B

Primary Resistance Substitutions

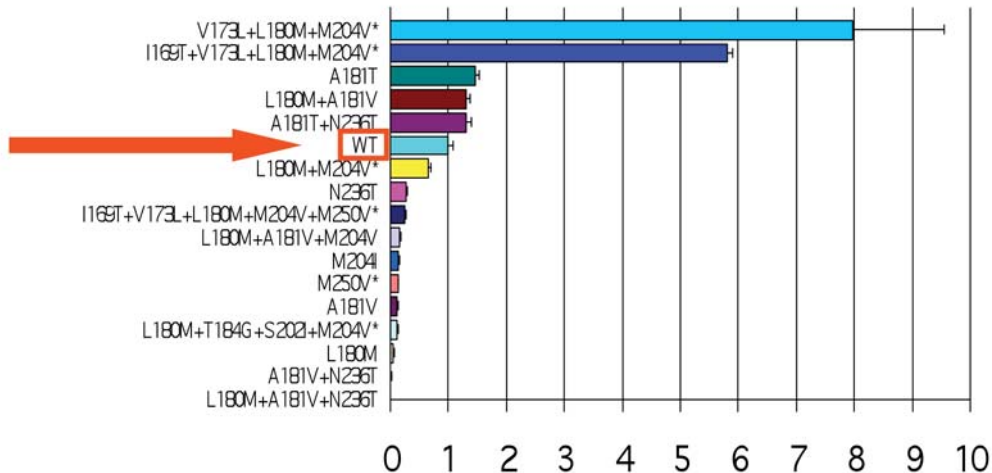


Pathways of Antiviral Resistance in Chronic Hepatitis B

Pathway	Mutation	Associated Resistance
L-nucleoside	rtM204V/I	Lamivudine Emtricitabine Telbivudine
Acyclic phosphonate	rtN236T	Adefovir Tenofovir
“Shared”	rtA181T/V	L- nucleosides (see above) Acyclic phosphonates (see above)
naïve entecavir resistance	rtL180M + rtM204V with one of rtT184, S202 or M250	Entecavir
Multi-drug resistance	Complex patterns e.g. rtA181T + rtN236T + rtM250L	Multi-drug

Compensatory Substitutions

Relative replication yield of HBV mutants



Multi-Drug Resistance (MDR)

Sequential addition of resistance mutations to the same viral genome

Promoted with sequential monotherapy, especially by using drugs with similar (structural) characteristics

Role of compensatory mutations
virus replication competence (fitness)

Need for drug-resistance testing
(Pol sequencing) to determine and monitor therapy:

- **rtA181T** ("Shared" Pathway)
- **rtA181T+rtN236T**
- **rtA181T+rtI233V+rtN236T+rtM250L**

Resistance Rates Through 6 Years Among Nucleos(t)ide-Naïve Patients



[§] Patients with HBV DNA ≥ 400 copies/mL at Week 72 could add FTC to TDF;

* Cumulative probabilities of resistance taken; † Naïve HBeAg (+); † Naïve HBeAg(-); N/A not available.