TENOFOVIR (TDF) IS EFFECTIVE IN LAMIVUDINE (LAM)-RESISTANT CHRONIC HEPATITIS B PATIENTS WHO HARBOUR rtA194T AT BASELINE

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1. Background
- Tenofovir (TDF) is a potent oral nucleotide analogue of adenosine.
- TDF has demonstrated safety and efficacy in pivotal studies for the treatment of chronic hepatitis B.1
- No signature resistance mutations have been identified in patients receiving 3 years of continuous TDF therapy.2
- Antiviral-treatment mutations associated with virologic breakthrough on TDF therapy have not been fully characterized.
- Of the 950 consecutive treatment-experienced adult patients with chronic hepatitis B tested, rtA194T was found in association with rtL180M + rtM204V/I in all 10/12 (83%) patients.
- After detection of LAM-resistant mutation, salvage therapy was started in 9/12 (75%) patients.
- rtA194T detected in 12 TDF-naïve HBV patients with lamivudine-resistant CHB.
- rtA194T is a potent oral nucleotide analogue of adenosine.

2. Aim
- To determine the effect of rtA194T on treatment response to TDF 300 mg daily alone or in combination with other antiviral agents in patients with lamivudine-resistant HBV.

3. Patients and Methods
- Adult HRV patients receiving oral antiviral therapy at University Health Network Liver Clinics (Toronto, Canada) were monitored for genotypic antiviral resistance.
- Routine bloodwork, HBV serology and HBV DNA levels were measured every 3 months on treatment.
- Resistance testing was performed on all patients who developed virologic breakthrough.
- Genotyping and detection of resistance mutations were performed using a line probe assay.
- Antiviral-resistance mutations associated with virologic breakthrough on TDF therapy have not been fully characterized.
- No signature resistance mutations have been identified in patients receiving 3 years of continuous TDF therapy.2
- Tenofovir (TDF) is a potent oral nucleotide analogue of adenosine.

4. Results
Patient Treatment Duration (Months) Baseline HBV DNA (log IU/mL) Last HBV DNA (log IU/mL) Last ALT ALT U/L (U/L)
3 LAM + ADV 30 3.6 <12 30
4 LAM + TDF 26 6.1 UND 13
5 LAM + TDF 21 6.4 UND 35
6 TDF alone 13 4.3 <12 55
8 FTC + TDF 27 5.9 UND 24
9 TDF alone 18 4.5 3.4 log10 277
10 LAM + TDF 24 4.3 UND 27
11 TDF alone 8 4.5 <12 24
12 LAM + TDF 9 7.3 <12 21

5. Summary
- Of the 950 consecutive treatment-experienced adult patients with chronic hepatitis B tested for antiviral resistance, 12 (1.2%) were found to harbour rtA194T.
- rtA194T was found in association with rtL180M + rtM204V/I in all 10/12 (83%) patients.
- After detection of LAM-resistant mutation, salvage therapy was started in 9/12 (75%) patients.

6. Conclusions
- rtA194T was detected in 12 TDF-naïve HBV patients with lamivudine-resistant CHB.
- rtA194T is a potent oral nucleotide analogue of adenosine.
- TDF alone or in combination used as salvage therapy in 10 patients.
- Mean treatment of 19.5 months.
- HBV DNA <12 IU/mL or undetectable in 7 (84%) patients.
- Patient underwent treatment for hepatocellular carcinoma and was admitted non-compliant with TDF.
- ALT normalized in 6 (75%) patients.

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References
5. Qi et al. Susceptibility of A914T examined in other studies yielded contradictory results.5