Three Years of Tenofovir Disoproxil Fumarate (TDF) Treatment in HBeAg-Positive Patients (HBeAg+) With Chronic Hepatitis B (Study 103)

E J Heathcote1, E Gane2, R deMan3, S S Lee4, R Flisiak5, M Manns6, K Tchernev7, O Kurdas8, M Shiffman9, P Marcellin10, J Sorbel11, J Anderson11, E Mondou11, and F Rousseau11

1University of Toronto, Ontario Canada; 2Middlemore Hospital, Auckland New Zealand; 3Erasmus MC, University Medical Center Rotterdam, The Netherlands; 4University of Calgary, Calgary AB Canada; 5Medical University of Bialystok, Bialystok Poland; 6Medical School of Hannover (MHH), Hannover, Germany; 7Medical University, Sofia Bulgaria; 8Haydarpapa Numune Hospital, Istanbul Turkey; 9Virginia Commonwealth University, Richmond VA; 10Hospital Beaumarches, Clinice France; 11Gilead Sciences, Durham NC

Background

- TDF treatment in HBeAg-positive patients beyond Week 48 showed:

  - Both stable and viremic patients on ADV can effectively switch to TDF and achieve or maintain viral suppression (HBV DNA <400 copies/mL).
  - TDF treatment in HBeAg-positive patients beyond Week 48 showed:

Results

Figure 3. ALT (U/L) Over Time

Table 1. Baseline Characteristics of Patients Entering Year 3 Similar to Patients Randomized

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TDF-TDF</th>
<th>ADV-TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ALT (U/L)</td>
<td>142 kmol/mol</td>
<td>159 kmol/mol</td>
</tr>
<tr>
<td>5% - 95%</td>
<td>30% - 70%</td>
<td>35% - 70%</td>
</tr>
<tr>
<td>Mean (95% CI) ALT (U/L)</td>
<td>200</td>
<td>250</td>
</tr>
</tbody>
</table>

Methods

Methods

Objective

- Evaluate the safety and efficacy of up to 3 years of TDF therapy

Key Eligibility Criteria

- HBeAg-positive patients
- Age 18-69 years
- Compensated liver disease
- HBV DNA > 10,000 copies/mL
- No ongoing NAAs were excluded for risks after discontinuation.
- HBV DNA and laboratory data every 12 weeks
- HBeAg and HBsAg every 12 weeks
- Resistance surveillance: patients with HBV DNA > 400 copies/mL (92% of patients had HBV DNA <400 copies/mL at week 144)

Assessments During Year 3

- HBV DNA and laboratory data every 12 weeks
- HBV DNA and HCV seroconversion
- Resistance surveillance: patients with HBV DNA > 400 copies/mL (92% of patients had HBV DNA <400 copies/mL at week 144)

Statistical Methods

Long-Term Evaluation, TDF only analysis (LTE-TDF)

- Patients discontinuing the study early and missing data due to death, safety, tolerability, or efficacy; loss to follow-up; or for any other reason who were failures for the endpoint or had an ongoing AE at the last on-study visit were considered failures.
- Patients missing data at random or who discontinued for administrative reasons with HBV DNA >400 copies/mL, with no ongoing NAAs were excluded for risks after discontinuation.
- Patients with HBeAg loss who discontinued the study for any endpoint and met the endpoint criteria at the last on-study visit had the last value carried forward (LOCF) was included in the analysis as a success.
- Patients who added emtricitabine were considered failures at all time points following the addition of emtricitabine

Open-Label Extension, TDF only analysis (OLE-TDF)

- Includes only those patients who entered the open-label extension
- Employed an intent-to-treat missing/failure approach
- Patients who added emtricitabine were considered failures at all time points following the addition of emtricitabine

On-Treatment Analysis (observed data, missing/excluded)

- Includes patients with missing data from both the numerator and denominator at each applicable time point for the analyses of HBV DNA, ALT, and HBeAg loss and seroconversion

Conclusions

At Year 3, 80% of patients remained on treatment demonstrating:

- durable and potent antiviral activity, i.e., 93% of patients had HBV DNA <400 copies/mL
- an 8% cumulative probability of HBsAg loss
- no resistance to TDF
- a favorable tolerability profile

Acknowledgements

Special thanks to all participating investigators and patients in studies GS-US-174-0102 and GS-US-174-0103