High Prevalence of Previously Undocumented Baseline M184V/I Does Not Affect Virologic Outcome in Virologically-Suppressed Patients Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) from a Boosted Protease Inhibitor-based Regimen

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Background

- Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is approved by the US FDA and EMA for treatment of HIV-1 infection (treatment-naive and virologically-suppressed patients).
- Five Phase 3 studies of 1440 participants demonstrated safety and efficacy without development of resistance to B/F/TAF through 48 weeks.

M184V/I is the most common NRTI substitution in patients with virologic failure to 3TC or FTC.
- Occurs in up to 64% of patients after failure.
- Confers resistance to 3TC and FTC and decreases susceptibility to ABC, but increases susceptibility to TDF.
- May not preclude response to triple therapy regimens containing FTC and tenofovir (TFV) in either prodrug form (TFV-D4T or TFV-IDV).
- May be under-reported by the Genotypic Archive assay.
- Virologic response to therapy may be re-evaluated, random biological fluctuation, or clinical outcomes are conflicting.

Methods

Figure 1. Study 1987 Design

Results

Table 2. Baseline Resistance Frequencies and Virologic Suppression at Last On-treatment Visit through Week 48

Table 3. Proportion of Participants with Blips and Virologic Suppression at Last On-treatment Visit through Week 48

Table 4. Proportion of Participants with Blips and Virologic Suppression at Last On-treatment Visit through Week 48

Table 5. Proportion of Participants with Blips and Virologic Suppression at Last On-treatment Visit through Week 48

Results (cont’d)

- Presence of proviral M184V/I was associated with longer time since ART initiation compared to wild-type M184.
- But some participants with M184V/I initiated ART as few as 3 years ago.

Conclusions

- Unexpectedly high levels of preexisting M184V/I not detected at screening.
- 15% of participants with any baseline genotypic data had archived M184V/I by retrospective proviral DNA genotype.
- 6% of participants with wild-type M184 by historical genotype had archived M184V/I.
- 21% of participants without historical genotypes had archived M184V/I.
- Both historical and proviral genotypes may help detect M184V/I but sensitivity is limited.
- Characteristics associated with archived M184V/I:
  - Participants with M184V/I were older and had longer ART durations.
  - Mean ARV duration was 15 years, but some participants with M184V/I initiated ARV as few as 3 years ago.
  - M184V/I often detected with other resistance mutations (38% with other NRTI-R [16/42] and 52% with NRTI-R [22/42]).
  - B/F/TAF maintained high levels of HIV-1 RNA suppression, regardless of M184V/I.
  - 98% of all participants overall.
  - 95% of participants with preexisting M184V/I.
  - No treatment-emergent resistance in the B/F/TAF group.
  - Viral blips were infrequent with B/F/TAF group (5.2%).
  - Similar with or without M184V/I.
  - Participants on boosted PIs had more blips with B/F/TAF group.
  - Presence of blips did not alter suppression at Week 48.

A triple therapy regimen of B/F/TAF may be an effective treatment option for suppressed patients with or without evidence of preexisting M184V/I.

Acknowledgments

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References

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Figure 2. Baseline Genotypic Data Sources and M184V/I Detection in the B/F/TAF Group

Figure 3. Virologic Suppression at Last On-treatment Visit through Week 48 Stratified by M184V/I Detection

Figure 4. Virologic Profiles of Participants with Proviral M184V/I and HIV-1 RNA 250 c/mL, at Week 48 (n=2)

Figure 5. Proportion of Participants with Blips

Figure 6. Viral Load at Blip (46 Blips in 38 Participants)