Six Abacavir/Lamivudine (ABC/3TC) Clinical Trials Show Robust Virologic Responses in ART-Naïve Patients for Baseline (BL) Viral Loads (VL) of ≥100,000 c/mL and <100,000 c/mL

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Background

A. A5202 Study

- The Phase IIIB, randomized, partially blinded, 4-arm equivalence study (ABC/3TC vs. TDF/FTC) vs. HEAT was conducted in ART-naïve patients with BL HIV-1 RNA ≥100,000 c/mL.
- The primary efficacy endpoint was time to viral failure (VF; defined as HIV-1 RNA ≥50 c/mL).
- Subjects were randomized into one of four treatment arms: ABC/3TC, TDF/FTC, EFV (hepatitis B core antigen (HBcAg) negative), or HEAT.
- Safety data were collected in all arms.

B. A5202 endpoints are different from HEAT (and most other HIV studies) although when these endpoints are compared, the results are quite similar.

C. A larger sample size has more power to declare a small difference to be statistically significant than a smaller sample size for the same endpoint.

Methods

- We present the results from 6 clinical trials using ABC/3TC-containing regimens using different regimens to assess the impact of baseline viral load and adherence on treatment outcomes.
- The safety and efficacy of ABC/3TC were evaluated in 6 clinical trials of up to 48 weeks.
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Results

1. Figure 1: Proportion of Patients with HIV-1 RNA <50 c/mL at 48 weeks.

2. Figure 2: Proportion of Patients with HIV-1 RNA <400 c/mL at 48 weeks.

3. Table 1: Summary of Key Details of Clinical Studies Included in Analysis

4. Table 2: Baseline and demographic characteristics of subjects from studies included in analysis

5. Table 3: Number (%) of subjects meeting primary safety endpoint defined in A5202 for the high baseline VL stratum at 48 weeks. Incidences shown.

6. Table 4: HEAT Study: Number (%) of subjects meeting primary safety endpoint defined in A5202 for the high baseline VL stratum at 48 weeks. Incidences shown.

Discussion

The differences in results in the high-viral-load strata between A5202 and our analyses of GlaxoSmithKline studies may be attributed to a number of factors, some of which are discussed below:

1. The Phase IIIB, randomized, partially blinded, 4-arm equivalence study (ABC/3TC vs. TDF/FTC) vs. HEAT was conducted in ART-naïve patients with BL HIV-1 RNA ≥100,000 c/mL.

2. The primary efficacy endpoint was time to viral failure (VF; defined as HIV-1 RNA ≥50 c/mL).

3. Subjects were randomized into one of four treatment arms: ABC/3TC, TDF/FTC, EFV (hepatitis B core antigen (HBcAg) negative), or HEAT.

4. Safety data were collected in all arms.

5. A5202 endpoints are different from HEAT (and most other HIV studies) although when these endpoints are compared, the results are quite similar.

6. A larger sample size has more power to declare a small difference to be statistically significant than a smaller sample size for the same endpoint.

7. A larger study does NOT mean that a larger difference will be observed.

Conclusions

The results from these 6 clinical trials using ABC/3TC-containing regimens using different regimens to assess the impact of baseline viral load and adherence on treatment outcomes are quite similar.

Efficacy Summary

- In all 6 clinical trials, ABC/3TC performed similarly to TDF/FTC in both viral load strata (Figures 1 and 2).
- Multiple analysis of ABC/3TC regimens have been presented previously in A5202.
- Results for the 6-arm equivalence study (ABC/3TC vs. TDF/FTC) vs. EFV were presented previously in A5202.
- Results for the 6-arm equivalence study (ABC/3TC vs. TDF/FTC) vs. HEAT were presented previously in A5202.

Safety Summary

- In all 6 clinical trials, ABC/3TC performed similarly to TDF/FTC in both viral load strata (Figures 1 and 2).
- Multiple analysis of ABC/3TC regimens have been presented previously in A5202.
- Results for the 6-arm equivalence study (ABC/3TC vs. TDF/FTC) vs. EFV were presented previously in A5202.
- Results for the 6-arm equivalence study (ABC/3TC vs. TDF/FTC) vs. HEAT were presented previously in A5202.

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References

1. Pappa K, Hernandez J, Ha B, et al. Abacavir/lamivudine (ABC/3TC) shows robust virologic responses in ART-naïve patients for Baseline (BL) Viral Loads (VL) of ≥100,000 c/mL and <100,000 c/mL. Presented at the XVII International AIDS Conference, 3–8 August 2008, Mexico City. Late-blower abstract THAB0303.