Sustained Antiretroviral Effect of Raltegravir at Week 156 in the BENCHMRK Studies, and Exploratory Analysis of Late Outcomes based on Early Virologic Responses

J. J. Erin, D. A. Cooper, R. T. Steigbigel, B. Clotet, H. Wan, A. Melbort, P. Sklar, B. Y. Nguyen, and H. Tepper for the BENCHMRK-1 and 2 Study Groups

1. University of North Carolina, USA; 2. University of New South Wales, Sydney, Australia; 3. SUNY at Stony Brook, USA; 4. University of Barcelona, Spain; 5. Merck Research Laboratories, North Wales, PA, USA

Abstract

In exploratory analyses to examine correlation of early virologic response with baseline prognostic factors, rapid viral decay (vRNA < 50 cp/mL between wk 2-12) was significantly associated with longer time to virologic failure. Patients with higher baseline HIV RNA level (log 10), lower CD4% and CD8%, higher baseline percentage of patients not suppressed >400 copies/mL and more advanced baseline disease characteristics (RNA, CD4) were more likely to fail treatment. In patients failing ART with triple-class resistance:

- RAL 400 mg b.i.d. or o.d. vs. PBO, compared to PRO plus OBT had potential, superior to an all-oral antiretroviral and immune-logic efficacy sustained through Week 156.
- 50% in RAL group sustained vRNA < 50 cp/mL.
- 12% in PRO plus OBT was generally well tolerated as compared to PRO plus OBT.

Few discontinuations due to adverse events.

For an efficacious antiretroviral, patient could be categorized by univariate, non-suppressor suppression, low level viremia, and intercurrent non-suppressor based on viRNA, evaluated as follows:

- Patients with low level virome at U/L/10,000: >400 at least once had more advanced baseline disease characteristics (AIDS, CD4) compared with the continuous suppression (CS, < 50 cp/mL).

In exploratory analyses to examine correlation of early virologic response with baseline prognostic factors (including rapid viral decay), i.e., viRNA < 50 cp/mL, at least one peak over 2-12.

Univariate and multivariate correlation with viRNA, CD4 count, and virologic failure.

In multivariate analysis, rapid viral decay showed the strongest association.

In exploratory analyses of wk. 156 outcomes based on viRNA, virome with the lowest virome demonstrated:

- Patients with 156 virologic and immune-logic outcomes:
  - 75% < 50 cp/mL, 75% < 100 cp/mL.
  - CD4 increase from BL: 226 cells/mm²

- Significantly shorter time to loss of virologic response (T50VR < 400 cp/mL) compared to CS group.

4. new knowledge points:

- In HIV infected, treatment-experienced patients failing ART with triple-class resistance:
  - RAL 400 mg b.i.d. or o.d. vs. PBO, compared to PRO plus OBT had potential, superior to an all-oral antiretroviral and immune-logic efficacy sustained through Week 156.
  - 50% in RAL group sustained vRNA < 50 cp/mL.
  - 12% in PRO plus OBT was generally well tolerated as compared to PRO plus OBT.

Few discontinuations due to adverse events.

For an efficacious antiretroviral, patient could be categorized by univariate, non-suppressor suppression, low level viremia, and intercurrent non-suppressor based on viRNA, evaluated as follows:

- Patients with low level virome at U/L/10,000: >400 at least once had more advanced baseline disease characteristics (AIDS, CD4) compared with the continuous suppression (CS, < 50 cp/mL).

In exploratory analyses to examine correlation of early virologic response with baseline prognostic factors, rapid viral decay (vRNA < 50 cp/mL between wk 2-12) was significantly associated with longer time to virologic failure. Patients with higher baseline HIV RNA level (log 10), lower CD4% and CD8%, higher baseline percentage of patients not suppressed >400 copies/mL and more advanced baseline disease characteristics (RNA, CD4) were more likely to fail treatment. In patients failing ART with triple-class resistance:

- RAL 400 mg b.i.d. or o.d. vs. PBO, compared to PRO plus OBT had potential, superior to an all-oral antiretroviral and immune-logic efficacy sustained through Week 156.
- 50% in RAL group sustained vRNA < 50 cp/mL.
- 12% in PRO plus OBT was generally well tolerated as compared to PRO plus OBT.

Few discontinuations due to adverse events.

For an efficacious antiretroviral, patient could be categorized by univariate, non-suppressor suppression, low level viremia, and intercurrent non-suppressor based on viRNA, evaluated as follows:

- Patients with low level virome at U/L/10,000: >400 at least once had more advanced baseline disease characteristics (AIDS, CD4) compared with the continuous suppression (CS, < 50 cp/mL).

In exploratory analyses to examine correlation of early virologic response with baseline prognostic factors (including rapid viral decay), i.e., viRNA < 50 cp/mL, at least one peak over 2-12.

Univariate and multivariate correlation with viRNA, CD4 count, and virologic failure.

In multivariate analysis, rapid viral decay showed the strongest association.

In exploratory analyses of wk. 156 outcomes based on viRNA, virome with the lowest virome demonstrated:

- Patients with 156 virologic and immune-logic outcomes:
  - 75% < 50 cp/mL, 75% < 100 cp/mL.
  - CD4 increase from BL: 226 cells/mm²

- Significantly shorter time to loss of virologic response (T50VR < 400 cp/mL) compared to CS group.