Dolutegravir versus raltegravir in antiretroviral-experienced, integrase-inhibitor-naive adults with HIV: week 48 results from the randomised, double-blind, non-inferiority SAILING study

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Summary

Background: Dolutegravir (GSK1349572), a once-daily HIV integrase inhibitor, has shown potent antiviral response and a favorable safety profile. We evaluated safety, efficacy, and emergent resistance in antiretroviral-experienced, integrase-inhibitor-naive adults with HIV-1 with at least two-class drug resistance.

Methods: ING111762 (SAILING) is a 48 week, phase 3, randomised, double-blind, active-controlled, non-inferiority study that began in October, 2010. Eligible patients had two consecutive plasma HIV-1 RNA assessments of 400 copies per mL or higher (unless >1000 copies per mL at screening), resistance to two or more classes of antiretroviral drugs, and had one to two fully active drugs for background therapy. Participants were randomly assigned (1:1) to once-daily dolutegravir 50 mg or twice-daily raltegravir 400 mg, with investigator-selected background therapy. Matching placebo was given, and study sites were masked to treatment assignment. The primary endpoint was the proportion of patients with plasma HIV-1 RNA less than 50 copies per mL at week 48, evaluated in all participants randomly assigned to treatment groups who received at least one dose of study drug, excluding participants at one site with violations of good clinical practice. Non-inferiority was prespecified with a 12% margin; if non-inferiority was established, then superiority would be tested per a prespecifi ed sequential testing procedure. A key prespecified secondary endpoint was the proportion of patients with treatment-emergent integrase-inhibitor resistance. The trial is registered at ClinicalTrials.gov, NCT01231516.

Findings: Analysis included 715 patients (354 dolutegravir; 361 raltegravir). At week 48, 251 (71%) patients on dolutegravir had HIV-1 RNA less than 50 copies per mL versus 230 (64%) patients on raltegravir (adjusted difference 7.4%, 95% CI 0.7 to 14.2); superiority of dolutegravir versus raltegravir was then concluded (p=0.03). Significantly fewer patients had virological failure with treatment-emergent integrase-inhibitor resistance on dolutegravir (four vs 17 patients; adjusted difference ‑3.7%, 95% CI ‑6.1 to ‑1.2; p=0.003). Adverse event frequencies were similar across groups; the most commonly reported events for dolutegravir versus raltegravir were diarrhea (71 [20%] vs 64 [18%] patients), upper respiratory tract infection (38 [11%] vs 29 [8%]), and headache (33 [9%] vs 31 [9%]). Safety events leading to discontinuation were infrequent in both groups (nine [3%] dolutegravir, 14 [4%] raltegravir).

Interpretation: Once-daily dolutegravir, in combination with up to two other antiretroviral drugs, is well tolerated with greater virological eff ect compared with twice-daily raltegravir in this treatment-experienced patient group.

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