Once-daily dolutegravir versus twice-daily raltegravir in antiretroviral-naive adults with HIV-1 infection (SPRING-2 study): 96 week results from a randomised, double-blind, non-inferiority trial

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Summary

Background: In the primary analysis of SPRING-2 at week 48, dolutegravir showed non-inferior efficacy to and similar tolerability to raltegravir in adults infected with HIV-1 and naive for antiretroviral treatment. We present the 96 week results.

Methods: SPRING-2 is an ongoing phase 3, randomised, double-blind, active-controlled, non-inferiority study in treatment-naive adults infected with HIV-1 that started in Oct 19, 2010. We present results for the safety cutoff date of Jan 30, 2013. Patients had to be aged 18 years or older and have HIV-1 RNA concentrations of 1000 copies per mL or more. Patients were randomly assigned (1:1) to receive either dolutegravir (50 mg once daily) or raltegravir (400 mg twice daily), plus investigator-selected tenofovir‐emtricitabine or abacavir‐lamivudine. Prespecified 96 week secondary endpoints included proportion of patients with HIV-1 RNA less than 50 copies per mL, CD4 cell count changes from baseline, safety, tolerability, and genotypic or phenotypic resistance. We used an intention-to-treat exposed population (received at least one dose of study drug) for the analyses. Sponsor staff were masked to treatment assignment until primary analysis at week 48; investigators, site staff , and patients were masked until week 96. This study is registered with ClinicalTrials.gov, NCT01227824.

Findings: Of 1035 patients screened, 827 were randomly assigned to study group, and 822 received at least one dose of the study drug (411 patients in each group). At week 96, 332 (81%) of 411 patients in the dolutegravir group and 314 (76%) of 411 patients in the raltegravir group had HIV-1 RNA less than 50 copies per mL (adjusted difference 4.5%, 95% CI ‐1.1% to 10.0%) confirming non-inferiority. Secondary analyses of efficacy such as per protocol (HIV RNA <50 copies per mL: 83% for dolutegravir and 80% for raltegravir) and treatment-related discontinuation equals failure (93% without failure for dolutegravir; 91% for raltegravir) supported non-inferiority. Virological non-response occurred less frequently in the dolutegravir group (22 [5%] patients for dolutegravir vs 43 [10%] patients for raltegravir). Median increases in CD4 cell count from baseline were similar between groups (276 cells per μL for dolutegravir and 264 cells per μL for raltegravir). Ten patients (2%) in each group discontinued because of adverse events, with few such events between weeks 48 and 96 (zero in the dolutegravir group and one in the raltegravir group). No study-related serious adverse events occurred between week 48 and week 96. At virological failure, no additional resistance to integrase inhibitors or nucleotide reverse transcriptase inhibitors was detected since week 48 or in any patient receiving dolutegravir.

Interpretation: At week 96, once-daily dolutegravir was non-inferior to twice-daily raltegravir in treatment-naive, patients with HIV-1. Once-daily dosing without requirement for a harmacokinetic booster makes dolutegravir-based therapy an attractive treatment option for HIV-1-infected treatment-naive patients.

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