Cabotegravir plus rilpivirine, once a day, after induction with cabotegravir plus nucleoside reverse transcriptase inhibitors in antiretroviral-naive adults with HIV-1 infection (LATTE): a randomised, phase 2b, dose-ranging trial.

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BACKGROUND:
In phase 1 trials, the HIV-1 integrase strand transfer inhibitor cabotegravir (GSK1265744) was well tolerated, both alone, and in combination with the non-nucleoside reverse transcriptase inhibitor rilpivirine. We assessed cabotegravir plus rilpivirine, as a two-drug oral antiretroviral regimen, for the maintenance of viral suppression in antiretroviral-naive HIV-1-infected individuals.

METHODS:
In the phase 2b Long-Acting antireTroviral Treatment Enabling (LATTE) trial, a multicentre study done in Canada and the USA, antiretroviral-naive HIV-1-infected adults (aged ≥18 years) were randomly allocated in a 1:1:1:1 ratio to oral cabotegravir 10 mg once a day, 30 mg once a day, 60 mg once a day, or oral efavirenz 600 mg once a day with dual nucleoside reverse transcriptase inhibitors (NRTIs) for 24 weeks of induction. Patients who were virologically suppressed by week 24 received a two-drug maintenance regimen consisting of their randomly allocated cabotegravir dose plus oral rilpivirine 25 mg or continued efavirenz plus NRTIs for an additional 72 weeks. Patients and investigators were masked to doses of cabotegravir received for 96 weeks, but not to the assignment of cabotegravir or efavirenz. The primary endpoint was the proportion of patients with fewer than 50 copies per mL of HIV-1 RNA (US Food and Drug Administration snapshot algorithm) at week 48. Analysis was by intention to treat. This study is registered with ClinicalTrials.gov, NCT01641809.

FINDINGS:
Of 243 patients randomly allocated and treated, 156 (86%) of 181 patients in the cabotegravir groups (52 [87%] of 60, 51 [85%] of 60, and 53 [87%] of 61 patients in the 10 mg, 30 mg, and 60 mg groups, respectively) and 46 (74%) of 62 in the efavirenz group had fewer than 50 copies per mL of HIV-1 RNA after induction therapy. After patients in the cabotegravir groups were changed over from dual NRTIs to rilpivirine at week 24, 149 (82%; 95% CI 77-88) patients in the cabotegravir groups (48 [80%; 70-90], 48 [80%; 70-90], and 53 [87%; 78-95] patients in the 10 mg, 30 mg, and 60 mg groups, respectively) versus 44 (71%; 60-82) in the efavirenz group were virologically suppressed at week 48, and 137 (76%; 69-82) in the efavirenz group were virologically suppressed at week 96. Treatment-related adverse events were reported by 93 (51%) cabotegravir-treated patients (28 [47%], 32 [53%], and 33 [54%] patients in the 10 mg, 30 mg, and 60 mg groups, respectively) and 42 (68%) efavirenz-treated patients. Six (3%) patients in the cabotegravir groups (one [2%], one [2%], and four [7%] patients in the 10 mg, 30 mg, and 60 mg groups, respectively) withdrew because of treatment-emergent adverse events compared with nine (15%) in the efavirenz group.
INTERPRETATION:
Cabotegravir plus dual NRTI therapy had potent antiviral activity during the induction phase. As a two-drug maintenance therapy, cabotegravir plus rilpivirine provided antiviral activity similar to efavirenz plus dual NRTIs until the end of week 96. Combined efficacy and safety results lend support to our selection of oral cabotegravir 30 mg once a day for further assessment. LATTE precedes studies of the assessment of longacting injectable formulations of both drugs as a two-drug regimen for the treatment of HIV-1 infection.

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