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ANTIVIRAL ACTIVITY, SAFETY AND PHARMACOKINETICS OF IDX899, A NOVEL HIV-1 NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR WITH HIGH BARRIER TO RESISTANCE, IN TREATMENT-NAÏVE HIV-1-INFECTED PATIENTS

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BACKGROUND: In vitro data indicate that IDX899, a second generation non-nucleoside reverse transcriptase inhibitor (NNRTI), has potent activity against wild-type and NNRTI-resistant HIV-1 with a higher genetic barrier to resistance than efavirenz. Favourable clinical safety and pharmacokinetics (PK) in healthy patients supported the current study which assessed antiviral activity, safety and PK in HIV-1-infected patients naïve to antiretroviral therapy.

METHODS: Ten treatment-naïve patients with HIV-1 RNA viral load $\geq 5,000$ copies/ml and a CD4+ T-cell count ≥ 200 cells/mm³ were enrolled and randomized (8:2) to receive 800 mg of IDX899 or placebo once a day (QD) for 7 days. HIV-1 RNA levels were measured using the Roche Cobas TaqMan® HIV-1 assay and IDX899 plasma levels were quantitated using a validated LC/MS-MS methodology. As potent antiviral activity was demonstrated at 800 mg, sequential cohorts evaluating 400 mg, 200 mg or lower doses are being enrolled.

RESULTS: At the time of abstract submission, patients in the 800 mg cohort have completed dosing and all patients in the 400 mg cohort have initiated or completed therapy. The median changes in HIV-1 plasma RNA from baseline to day 8 were $-1.95 \log_{10}$ copies/ml and median CD4+ T-cell count increased by 52.0 cells/ml in the 800 mg cohort. The median changes in HIV-1 plasma RNA from baseline to day 8 were $+0.08 \log_{10}$ copies/ml and median CD4+ T-cell count decreased by 14 cells/ μ l in the placebo cohort. There were no treatment discontinuations, treatment emergent serious adverse events or dose-limiting toxicities. No discernable patterns in adverse events, laboratory abnormalities or ECG abnormalities were observed within or between treatment groups. Results from the 400 mg and 200 mg cohorts will be available for presentation.

CONCLUSIONS: IDX899, dosed at 800 mg QD for 7 days was well tolerated and demonstrated potent HIV-1 antiviral activity. Our results support further evaluation of IDX899 at lower doses as well as longer studies of combination therapy to assess durability of antiviral response and long-term safety.

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