

CCR5 Inhibitor - Maraviroc

Pfizer Protocol A4001027: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of a Novel CCR5 Antagonist, UK-427,857, In Combination with Optimized Background Therapy Versus Optimized Background Therapy Alone for the Treatment of Antiretroviral-Experienced HIV-1 Infected Subjects.

Purpose: The primary objective is to confirm the hypothesis that UK-427,857 added to Optimized Background Therapy (OBT) provides an additional reduction in plasma HIV-1 RNA compared to OBT alone, as measured by the difference between each of the two UK-427,857 regimens versus the placebo regimen in the mean changes from baseline in plasma HIV-1 RNA at week 48. The secondary objectives include assessments of safety and tolerability of UK-427,857 when added to OBT versus OBT alone.

About the study: This will involve approximately 90 centers to achieve a total randomized subject population of 500 subjects. This is a 48-week, randomized, double blind, superiority study designed to compare the safety and antiviral activity of UK-427,857 at two different doses versus placebo, each in combination with optimized background therapy. Subjects must be infected with CCR5-tropic HIV-1 and have had at least 6 months of prior treatment with at least one agent (two for protease inhibitors) from 3 of the 4 antiretroviral drug classes or multi-class resistance and treatment failure to an existing regimen. Subjects will be randomized into one of the three treatment groups:

UK-427,857 150 mg QD

UK-427,857 150 mg BID

Placebo

Required:

- HIV-1 RNA levels $\geq 5,000$ copies/mL
- Stable pre-study antiretroviral regimen, or on no antiretroviral agents, for at least 4 weeks.
- Documented genotypic or phenotypic resistance to three of the four antiretroviral drug classes

Or

Antiretroviral-class experience ≥ 6 months with at least three of the following:

- a) One nucleoside or nucleotide reverse transcriptase inhibitor
- b) One non-nucleoside reverse transcriptase inhibitor
- c) Two protease inhibitors (excluding low-dose ritonavir)
- d) Enfuvirtide

Not Allowed:

- Suspected or documented active, untreated HIV-1 related opportunistic infection or other condition requiring acute therapy (eg, hepatitis C virus infection) at the time of randomization, patients on a stable (.1 month) secondary OI prophylaxis regimen or chronic treatment are eligible for the study
- Previous therapy with a potentially myelosuppressive, neurotoxic, hepatotoxic, and/or cytotoxic agent within 30 days prior to randomization, or expected need for such therapy during the study period.
- Documented acute hepatitis or pancreatitis within 30 days prior to randomization
- Cirrhosis of the liver; AST and/or ALT greater than 5 times the upper limit of normal; total bilirubin greater than 5 times the upper limit of normal
- Platelet count $\leq 50,000$ cells/mm³
- Contraindicated medications (interferon for the ongoing treatment of Hepatitis C infection is permitted)

Study Location:

Orange County Center for Special Immunology

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