

November 1, 2004

Public Relations

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Phase II Clinical Study with New HIV Drug (Oral CCR5 Antagonist) Completed

Ono Pharmaceutical Co., Ltd. announced that a Phase II clinical study with a new HIV drug (development code: ONO-4128/873140) has been completed; and the results of the study will be presented at the 44th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) held from October 30 to November 2, 2004 in the US. This agent was licensed by Ono Pharmaceutical to GlaxoSmithKline (GSK) in December 2002.

In the study, ONO-4128/873140 was administered to 40 adult HIV patients as monotherapy for a short period of time to examine its antiviral effect, safety, pharmacokinetics and CCR5 receptor occupancy. Forty adult HIV patients were equally divided into 4 dose groups: once daily dose of 200 mg, twice daily dose of 200 mg, once daily dose of 400 mg, and twice daily dose of 600 mg. The investigational drug or placebo was administered to the 10 patients of each group (8 and 2 patients, respectively) for 10 days to observe the patients until Day 24. The antiviral effect was evaluated with decrease in number of copies of HIV RNA in plasma. Number of copies of HIV RNA in plasma decreased to approx. 1/3 at a dose of 200 mg QD, to approx. 1/17 at a dose of 200 mg BID, to approx. 1/11 at a dose of 400 mg QD, and to approx. 1/46 at a dose of 600 mg BID while almost no changes were observed in the placebo group.

In terms of safety, some mild gastrointestinal complaints were observed upon initiation of treatment, but resolved within a few days; no clinically significant abnormalities were confirmed on ECG or in laboratory parameters.

In addition, it was clarified that the receptor occupancy rate was 90% or higher in all treatment groups, and dose-dependently decreased after administration completion.

These findings demonstrate a high antiviral effect and safety of ONO-4128/873140, and supports future evaluation in clinical studies. GSK is scheduled to commence the next phase of clinical study by the end of 2004.

(Reference)

Profile of the compound

[ONO-4128/873140: CCR5 antagonist]

- The human CCR5 receptor is believed to be the predominant co-receptor used by HIV to enter human cells. ONO-4128/873140 appears to block the entry of HIV through a new mechanism of action that is different from marketed HIV drugs.
- In addition, since the CCR5 receptor exists on the surface of human immune cells, the possibility of viral resistance being developed by mutant HIV might be lower.
- ONO-4128/873140 appears to be well-tolerated based on preliminary data from a Phase I clinical study in healthy adult subjects and a Phase IIa clinical study in adult HIV patients. Because it was confirmed that ONO-4128/873140 binds to the CCR5 receptor for an extended period of time, an oral formulation with fewer administrations and lower dosage is being considered for the development program.