Once-daily '572 as part of initial therapy for HIV

The investigational integrase inhibitor '572 can be taken once daily and does not need to be boosted with ritonavir (Norvir) or any other drug. '572 is being tested as part of the initial therapy for HIV infection in several hundred people in a trial called Spring. Preliminary results are very promising.

Study details

In Spring, participants were randomly assigned to receive one of three doses of '572 (10, 25 or 50 mg) taken once daily or efavirenz 600 mg also taken once daily. All participants also received two nukes. Spring has a complex design and is planned to continue for at least 48 weeks. So far results for the first 16 weeks have been released.

The average profile of the 205 volunteers enrolled at the start of the study was as follows:

- 14% females, 86% males
- age – 37 years
- CD4+ count – 324 cells
- viral load – 29,000 copies/ml
- 21% of participants had a viral load greater than 100,000 copies/ml
- 67% of participants took a combination of tenofovir and FTC (Truvada)
- 33% of participants took a combination of abacavir and 3TC (Kivexa)

Results—16 weeks later

All doses of ‘572 performed well, achieving viral suppression more rapidly than efavirenz. This is not surprising, as integrase inhibitors as a class rapidly suppress HIV levels.

At 16 weeks, the proportion of participants in each dose group whose viral load was less than 50 copies/ml was as follows:

- 10 mg – 96%
- 25 mg – 92%
- 50 mg – 90%

These differences were not statistically significant.

The proportion of efavirenz users at week 16 who had a viral load less than 50 copies/ml was 60%. This difference was statistically significant.

One reason for the inability of efavirenz users to achieve undetectable viral loads by week 16 is that 30% were not able to suppress HIV by that time. In contrast, at week 16 only 10% of ‘572 users had not suppressed their viral load.

Lack of virologic suppression occurred as follows when analysed by the nuke regimen used:

- Truvada + ‘572 – 3 people
- Truvada + efavirenz – 11 people
- Kivexa + ‘572 – 4 people
- Kivexa + efavirenz – 4 people

Changes in CD4+ cell counts
In general, increases in CD4+ cell counts were greater by week 16 in users of ‘572 than in efavirenz users. Here is the combined analysis of ‘572 dose groups:

- ‘572 – 165 extra CD4+ cells
- efavirenz – 116 extra CD4+ cells

**Side effects**

About 8% of efavirenz users left the study prematurely because of severe side effects. Only 2% of people exposed to ‘572 left the study for such reasons.

The following proportion of participants reported the following side effects, which were graded as moderate to life-threatening among all ‘572 users:

- gastrointestinal – 2%
- psychiatric – 0%
- skin disorders – 0%
- general side effects – 1%

The proportion of efavirenz users who experienced the same intensity of side effects was as follows:

- gastrointestinal – 4%
- psychiatric – 6%
- skin disorders – 4%
- general side effects – 2%

While no serious side effects occurred among ‘572 users, one person taking efavirenz attempted to commit suicide.

One person left the study prematurely because of indigestion arising from ‘572. Four people left the study prematurely because of efavirenz-related side effects, such as:

- attempted suicide
- abnormal dreams
- drug intolerance
- hypersensitivity

Increased levels of so-called bad cholesterol (LDL-c) are associated with an increased risk for cardiovascular disease. In this study, changes in LDL associated with each drug were as follows:

- ‘572: +0.066 mmol/l
- efavirenz: +0.436 mmol/l

In summary, all doses of ‘572 showed potent anti-HIV activity with shorter times to undetectable viral load than efavirenz. The 50-mg once-daily dose of ‘572 has been selected for Phase III study, the final stage of large clinical trials before regulatory approval.

**REFERENCE:**

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