Elvitegravir Study Highlights Value of Strong Background Regimen

September 19, 2007 By Tim Horn

Like all other promising experimental drugs, Gilead's integrase inhibitor elvitegravir needs to be combined with other active drugs to which HIV is sensitive. This has been a recurrent theme at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, with very important implications for HIV-positive people cobbling together drug regimens to treat drug-resistant HIV.

Encouraging preliminary week data from a Phase II study of elvitegravir were reported earlier this year at the 14th Conference on Retroviruses and Opportunistic Infections (CROI) in Los Angeles.

Gilead Study 0105 randomized 278 treatment-experienced patients to receive one of three doses of elvitegravir (20 mg, 50 mg or 125 mg), combined with 100 mg Norvir (ritonavir) for boosting purposes, twice daily, or an approved Norvir-boosted protease inhibitor (PI).

All patients combined their selected treatment with an optimized background regimen (OBR) consisting of approved nucleoside reverse transcriptase inhibitors (NRTIs) with or without Fuzeon (enfuvirtide). After eight weeks, patients in the elvitegravir groups were permitted to add Norvir-boosted Prezista (darunavir) or Aptivus (tipranavir) to their regimens.

There was significant treatment experience among the study participants—they entered the clinical trial with an average of 11 mutations in their HIV conferring drug resistance to available PIs.

According to the report at CROI, the average viral load drop after 16 weeks was 1.7 in the 125mg elvitegravir group—the most effective dose. The viral load reductions were similar after 24 weeks in the study.

At ICAAC, Andrew Zolopa, MD, of Stanford University reported that treatment responses varied according to the strength of the OBR. Twenty-six patients receiving 125mg elvitegravir used OBRs that didn't contain any active drugs and 28 had virus that was sensitive to at least one NRTI. Approximately one quarter of the patients in the 125mg elvitegravir group started Fuzeon (enfuvirtide) for the first time in the study.

Among those without any active agents in their OBR, the average viral load reduction after 24 weeks among those receiving 125mg elvitegravir was 0.7 log copies. When at least one active NRTI was included in the OBR, the average viral load reduction was 1.7 log copies after 24 weeks.

When Fuzeon was used—either with or without an active NRTI—a whopping 2.9-log reduction in viral load was seen after six months of treatment. Viral loads were also three times more likely to be undetectable (below 50 copies) after 16 weeks among those taking elvitigravir plus Fuzeon compared to those using Fuzeon for the first time in the control group.

In conclusion, the study's authors stress the obvious: that "OBR is critical to maintain suppression" of viral loads in treatment-experienced patients. Addition studies, evaluating 125mg elvitegravir in combination with the strongest OBR options available, are being planned.

Source:

Zolopa AR, Lampiris H, Blick G, et al. **The HIV integrase inhibitor elvitegravir (EVG/r) has potent and durable activity in treatment-experienced patients with active optimized background therapy (OBT)** [Abstract H-714]. 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, 2007.
