IAC: Vicriviroc Shows Promise

August 17, 2006 By Tim Horn

August 17, 2006 (AIDSmeds)—The AIDS Clinical Trials Group has reported results from a clinical trial of vicriviroc, an experimental entry inhibitorbeing developed by Schering-Plough. Results from the study werereported today at the International AIDS Conference (IAC) in Toronto.

Theprimary goal of the study (A5211) was to see how well vicriviroc workedover 14 days in HIV-positive people who had tried other HIV treatmentsin the past and who were failing their current HIV regimen. Other goalswere to study the safety of vicriviroc and to study the effects ofvicriviroc on viral load and CD4 cell counts (T cell counts) – whenused in combination with other HIV medications – over 24 weeks.

After HIV binds to the CD4 protein on T-cells,the virus must then latch onto another receptor on the cell's surface –either CCR5 or CXCR4. Vicriviroc, like another entry inhibitor maraviroc, blocks CCR5 and, in turn, prevents HIV from entering CD4 cells that carry this receptor.

Studyparticipants were randomized to add one of three doses of vicriviroc(5mg, 10mg, or 15mg once a day) or a placebo to their current HIV drugregimen. After two weeks, participants continued vicriviroc, orplacebo, and changed their other HIV drugs to an optimized backgroundtreatment (OBT) consisting of approved HIV medications that their virusmay be sensitive to.

An independent study monitoringboard reviewed the clinical trial for safety from time to time. Attheir review on October 6, 2005, the committee recommended stopping the5mg vicriviroc dose because it wasn't working as well as the otherdoses. At their review on February 15, 2006, they noted five cancers inparticipants taking vicriviroc and recommended that all participants betold whether they were taking vicriviroc or not.

Theresults, reflecting data collected up until February 15, were reportedat IAC by Roy Gulick, MD, MPH, of Weill Cornell Medical College in NewYork. Dr. Gulick said that 118 patients were enrolled in the study. Theaverage viral load at study entry was 36,380 and the average CD4 countwas 146. Unlike the patients in the maraviroc study also reviewed atthe conference today (see this AIDSmeds report), all patients in A5211 had HIV that targeted CCR5 on CD4 cells.

Aftertwo weeks, participants taking either 10mg or 15mg vicriviroc decreasedtheir viral loads by approximately 1.15 and 0.92 log, respectively.Participants taking placebo experienced a slight

increase in theirviral loads.

Over 24 weeks, participants taking placeboor 5mg vicriviroc plus OBT were more likely to see their viral loadsrebound compared to patients taking either 10mg or 15mg vicriviroc plusOBT. In the 10mg vicriviroc group, viral loads decreased, on average,by 1.86 log after 24 weeks; in the 15mg vicriviroc group, the averageviral load drop was 1.68 log. These results were significant comparedto the viral load change seen in the placebo group after 24 weeks –only a 0.29 log drop.

The percentage of subjects withviral loads below 400 at week 24 was 11% in the placebo group, 53% inthe 10mg vicriviroc group, and 47% in the 15mg vicriviroc group. Thepercentage of subjects with viral loads below 50 at week 24 was 7% inthe placebo group, 40% in the 10mg vicriviroc group, and 27% in the15mg vicriviroc group.

Dr. Gulick also reportedchanges in CD4 counts after six months of treatment. In the placebogroup, CD4 counts decreased by 6 cells, compared to a 142-cell increasein both vicriviroc groups.

A central concern withentry inhibitor treatment targeting CCR5 is that it will result in theemergence of HIV using CXCR4, a form of the virus that is believed tobe associated with more rapid disease progression. In A5211, CXCR4virus emerged in 13 patients, including one patient in the placebogroup, three patients in the 10mg vicriviroc group, and two patients inthe 15mg vicriviroc group (the rest were in the 5mg vicriviroc group).At this point in time, however, it is not clear if this CCR5-to-CXCR4“switch” is really associated with more rapid disease progression or ifthe switch is permanent once the CCR5-blocking medication isdiscontinued.

As for side effects, there were nodifferences between the placebo and vicriviroc groups. However, thefive cancers reported – all in patients taking vicriviroc – areconcerning and still being investigated.

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