

RESEARCH/CLINICAL UPDATE

June 22, 2001

**Keyword: Comparative studies
(Avonex vs. Rebif)**

**SECTION: TREATMENT,
INVESTIGATIONAL**

ADDITIONAL ROUTING

- _____ Research Advocate Staff Liaison
- _____ Chapter President
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REBIF VERSUS AVONEX IN RELAPSING-REMITTING MS: FINAL TRIAL RESULTS PRESENTED AT SCIENTIFIC MEETING

Summary: Results from Serono, Inc.'s (Geneva, Switzerland) head-to-head clinical trial pitting its product, Rebif[®] (interferon beta-1a), against Avonex[®] (Biogen, Cambridge, MA), in relapsing-remitting MS were presented today at the World Congress of Neurology in London.

- This trial, called the EVIDENCE study, is the largest prospective comparative study of two disease-modifying treatments in MS to date.
- The results indicate that, during 6 months of study, Rebif showed a statistically significant benefit over Avonex for all primary and secondary outcomes, including the proportion of patients remaining relapse-free, and accumulation of MRI-detected lesions.
- The meaning of these results for long-term clinical use is not known. These data will be used by Serono in discussions with the U.S. Food and Drug Administration (FDA) in the company's efforts to obtain U.S. marketing approval for Rebif.

Details: Final data from Serono Inc.'s international, 56-center clinical trial comparing two forms of interferon beta-1a, Rebif[®] (Serono, Inc.) and Avonex[®] (Biogen, Inc), were presented at the World Congress of Neurology in London on June 22. This trial, called the EVIDENCE study (**E**vidence for **i**nterferon **d**ose effect: **E**uropean-**N**orth American **c**omparative **e**fficacy), is the largest prospective comparative study of two disease-modifying treatments in MS to date. Dr. Patricia Coyle (State University of New York, Stony Brook), one of the study's lead investigators, presented results comparing clinical relapses, changes in lesions detected by magnetic resonance imaging and other outcomes after six months of treatment. The data, which were statistically significant in favor of Rebif on all primary and secondary outcomes of the trial, confirmed and amplified information provided in a Serono, Inc. corporate press release of May 11, 2001.

The National MS Society... One thing people with MS can count on.

The Study: In the short six-month study, 677 people with relapsing-remitting MS were treated. Half were randomly assigned to receive Rebif (at the standard subcutaneous injection dose of 44 mcg, 3 times per week) and half to receive Avonex (at the standard intramuscular injection dose of 30 mcg, 1 time per week).

Results: Of those treated with Rebif, 25.1% had MS relapses during six months, compared with 36.7% of those treated with Avonex. This means that those on Rebif had a 90% greater chance of remaining relapse-free during the treatment period compared to those on Avonex. Not all participants were relapse-free with either treatment, but those treated with Rebif had 27% fewer relapses relative to those treated with Avonex, based on a determination of the average number of relapses during the short study. Also, the relative risk of having a relapse during the trial was 37% lower for those treated with Rebif than those treated with Avonex. Steroid use – a standard of therapy for MS relapses – was 46% less in the Rebif group.

There were also differences in accumulation of lesions in the brain detected by magnetic resonance imaging. Those on Avonex showed 50% more “combined unique lesions” in the brain than those on Rebif during the treatment period, based on the average number of new lesions detected per scan in both groups. There was also a statistically significant reduction in the proportion of MRI scans showing lesion activity for those on Rebif, and a statistically significant reduction in individuals showing no new lesion activity with Rebif during the study.

Both agents were relatively well tolerated, with expected flu-like reactions in both, and slightly higher injection site reactions and liver function abnormalities with Rebif. Ninety-seven percent of all enrolled patients completed the trial, with very few drop-outs.

Rebif is available for relapsing-remitting MS in 67 countries around the world, but cannot currently be marketed in the U.S. because of the orphan drug status of Avonex. FDA regulations provide a 7-year market protection for new drugs found to be effective for rare or “orphan” disorders to help stimulate investment by pharmaceutical companies in such disorders, unless clinical superiority from a competitive product can be demonstrated. Lacking such, Rebif cannot be marketed in the US until mid-2003. The Serono study was designed in part in an attempt to demonstrate such clinical superiority. Serono, Inc. will submit to the FDA all of the data from this trial as a part of its ongoing discussions in this regard.

Conclusions: Results reported from this relatively short EVIDENCE trial indicate that Rebif performed better than Avonex in several measures of clinical relapses and MRI-detected lesion activity over a 24-week treatment period. The meaning of these results for long-term clinical use is not known. These data will be submitted by Serono to the U.S. FDA in the company’s effort to obtain Rebif marketing approval in the U.S. prior to 2003. If this research leads to more treatment options, it will be good news for people who have MS.