AIDS closer to becoming a treatable disease

- Antibody-CD4 chimera in clinical trials
- AZT effective in most cases of HIV infection

Washington

AUGUST has so far been a good month for news of AIDS therapies. Three weeks ago, AZT was shown to delay the progression of AIDS in those with AIDS-related complex, and last week it was shown to postpone the development of symptoms in those whose T-cell counts had dropped below 500. This week, clinical trials are set to begin of another emerging treatment that could be used with AZT to lengthen the lives of those infected with HIV (human immunodeficiency virus). Together with AZT, the hybrid antibody-CD4 molecule termed 'immunoadhesin' offers hope that HIV infection may in future be treated as a chronic disease that can be managed for years before it ultimately become fatal.

Immunoadhesin is a genetically engineered molecule composed of part of the CD4 receptor — the entry point through which HIV infects cells — and the back end of the IgG1 antibody, responsible for activating killer cells in the immune system and initiating a virus-attacking system within the blood named complement. Genentech, the company developing immunoadhesin, has shown that it blocks the infection of CD4-bearing cells in culture, and stays in the blood of rabbits for more than four days (see *Nature* 337, 525; 1989).

Soluble forms of the CD4 receptor alone — being tested by Genentech and Biogen — stay in the bloodstream for only roughly an hour when injected directly into the veins of humans. Partly because it is larger, immunoadhesin is expected to last 20–50 times longer, requiring fewer injections for patients. Unlike plain soluble CD4, immunoadhesin may also kill infected cells and traverse the placental barrier, allowing it to be used to protect the fetuses of HIV-infected pregnant women.

The clinical trial of immunoadhesin will be conducted by Genentech's collaborators at the US National Cancer Institute (NCI), the New England Deaconess Hospital in Boston, Massachusetts, San Francisco General Hospital, the University of Washington and Stanford University. The drug will be tested for safety in a total of 30–40 patients given a range of dosages intravenously. The first patient will be treated this week by Samuel Broder's group at NCI — just six months after the initial publication of immunoadhesin, a speed Broder says is "astounding". If the results are encouraging, efficacy studies could begin within a year.

Genentech is now planning controlled efficacy trials for its first-generation soluble CD4. Since the federal approval of AZT two years ago, all drugs being tested in people with AIDS have been compared to AZT, limiting placebo-controlled trials to those with a less advanced stage of HIV disease. But the announcements that AZT is effective in people with AIDS-related complex and in some asymptomatic HIV-infected individuals will mean that AZT will now be the standard of comparison for nearly all trials of drugs to treat HIV disease.

The manufacturer of AZT, Burroughs-Wellcome, is expected to use data from the new AZT studies to ask the US Food and Drug Administration to broaden the

HIPPARCOS

ESA tries to salvage Hipparcos

Munich

AFTER nearly two weeks of unsuccessful attempts to fire the apogee motor on the European astronomy satellite Hipparcos, project leaders have reluctantly begun to design a salvage operation for the mission. The 1,140-kg satellite is currently in an elliptical orbit between 200 km and 35,000 km from the Earth. Project scientist M.A.C. Perryman says the chances are "very small" that Hipparcos can be brought into a geostationary orbit by the motor, as was originally intended (see *Nature* 340, 491; 1989).

One or two more attempts to fire the motor will be made on 24 or 25 August. If they fail, small thrusters on the satellite will be fired early next week to bring the satellite into a higher orbit at a minimum distance of about 600 km from Earth. The thrusters were originally meant to be used to correct for nutation (wobbling) once the satellite was in geostationary orbit.

Hipparcos was designed to measure the precise positions, parallaxes and proper motions of stars. It was expected over two and a half years to measure the positions of 120,000 stars with a precision of 0.002 arcseconds. A second mission on board, called Tycho, was meant to measure the positions of 400,000 stars with an accuracy of 0.03 arcseconds by 1995.

In the current orbit, Hipparcos could last from six months to two years, depending on how fast the solar cells that power the satellite degrade. In six months, the satellite could achieve only one-third the accuracy initially projected, although this

conditions the company can specify in the drug's labelling. Anticipating that AZT will now be used to treat a much wider spectrum of those with HIV disease, stockholders bid up Wellcome plc's stock price by 32 per cent by the end of last week.

But the drug still costs \$8,000–\$10,000 for a year's treatment at a full dose. Jude Payne of the Health Insurance Association of America says "almost all" US health insurers will begin paying for AZT for those with AIDS-related complex and HIV-infected people with T-cell counts of less than 500, based on the new studies. Senator Ted Kennedy (Democrat, Massachusetts) plans to add an amendment to next year's appropriations bill for the US Department of Health and Human Services which would provide \$30 million for three years to pay for AZT for people with AIDS who have no insurance. When Congress returns from its summer recess, there will be pressure for Kennedy's amendment to be extended to cover all those with HIV infection.

Carol Ezzell

would still improve on ground-based results by a factor of 15.

ESA has not decided to ask its 13 member states for the money to build and launch a second Hipparcos satellite identical to the first. But a preliminary decision is expected "in one month", said Roger Bonnet, director of the ESA scientific programmes, after the extent of the degradation of the solar cells has been determined. The ESA council would have to approach the scientific programme committee to request more money. A replacement satellite would cost an estimated £114 million (\$182 million).

It would be difficult to reapportion the money out of the existing ESA science programme budget, which would require a two-thirds majority vote in the committee. But it would be even more difficult to gain a new appropriation for a second Hipparcos, which would require unanimous support. The length of time in orbit is crucial. In six months, only 8 or 10 observations of each star would be possible instead of the 80 originally planned. If Hipparcos were to survive longer, say for a year or a year and a half, proper motions of stars and parallaxes could begin to be measured. But Perryman said that was not a "realistic" expectation.

In its elliptical orbit, the satellite passes every ten hours through the Van Allen belts, where it is subject to irradiation by protons and electrons in the solar wind 5,000 km above the equator. This radiation degrades the solar panels which power the satellite.

Steven Dickman