Introduction

T.E. Starzl

1063

IT has been little more than 3 years since Ochiai et al[1] presented a preliminary report of FK 506 at the meeting of the International Transplantation Society in Helsinki. FK 506 had been developed by Kino, Sawada, Goto, and other workers at the Fujisawa Company, but the first reports of this work did not appear in the literature until 1987.[2,3] A few weeks after the Helsinki meeting, Dr Satoru Todo and I flew to Japan, where arrangements were made with company officials for a small supply of FK 506 to be tested in Pittsburgh, PA. In vitro systems of evaluation were used at first and, subsequently, experiments were carried out in rats, dogs, and subhuman primates.

Progress with this drug came fast and, in June 1987, at the European Society of Organ Transplantation meeting in Gothenberg, a satellite symposium on FK 506 was held.[3] The proceedings, which were published as a monograph, had the appropriate title "FK 506: A Potential Breakthrough in Immunosuppression." The promise was there, but the toxicity profiles that were presented from the University of Pittsburgh investigators were not reconcilable with those developed in Cambridge.[3] The drug appeared to the English investigators to be intolerably toxic. However, it had been impossible at that juncture to do kinetic or good dose control studies of the drug, since there was not a satisfactory assay system. This deficit was remedied by the announcement at the Gothenberg meeting by Tamura et al[4] of a sensitive assay method which made subsequent research far more discriminating.

Today, we return to the European Society of Organ Transplantation, where much new information will be given about FK 506, with particular emphasis on the clinical trials in Pittsburgh, PA, which began in February 1989. The most extensive experience has been with liver transplant recipients, and this experience can be divided into two components. The first was from the "rescue" treatment of patients whose liver grafts were failing because of rejection despite state-of-the-art treatment with conventional immunosuppression. The second, and later, component was in patients who were treated from the outset with FK 506. In our original plans, it was hoped to use FK 506 with CyA because these two agents had been shown to be synergistic in animals. However, the FK 506 was found to greatly aggravate CyA toxicity and, consequently, FK 506 was used alone.[5]

What has been learned about FK 506 is now extremely extensive. You may judge for yourself the extent to which, in the time ahead, the clinical use of this drug will permit or contribute to the next plane of achievement in transplantation.

REFERENCES

1. Ochiai T, Nakajima K, Nagata M, et al: Transplant Proc 19:1284, 1987

2. Goto T, Kino T, Hatanaka H, et al: Transplant Proc 19:4, 1987 (suppl 6)

3. Starzl TE, Makowka L, Todo S: Transplant Proc 19:3, 1987 (suppl 6)

4. Tamura K, Kobayashi M, Hasimoto K, et al: Transplant Proc 19:23, 1987 (suppl 6)

5. Starzl TE, Todo S, Fung J, et al: Lancet 2:1000, 1989

Address reprint requests to Dr T.E. Starzl, Department of Surgery, Division of Transplant Surgery, University of Pittsburgh, 3601 Fifth Avenue, Pittsburgh, PA 15213.

0041-1345/90/$3.00/+0