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## Randomized Trial in Primary Liver Transplantation Under Immunosuppression With FK 506 or Cyclosporine

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**T**HE USE of cyclosporine (CyA) has greatly impacted the success of liver transplantation. FK 506 is a newly described immunosuppressive agent, with mechanisms of action similar to those of CyA, but more potent on a weight-to-weight basis. Pilot studies of FK 506 in primary liver transplantation have shown encouraging results.<sup>1</sup> A randomized trial using FK 506 with low-dose steroids (LDS) was compared to two different CyA regimens, one with LDS and the other with standard steroid therapy (SST). The primary end point was to examine the incidence of rejection following liver transplantation, and to compare graft and patient survival rates after FK 506 with LDS, CyA with LDS, and CyA with SST.

### METHODS

One hundred fifty-four patients were enrolled in a single center between February 17, 1990, and December 30, 1991. The details of randomization, the exclusion criteria, the dosing of FK 506 and CyA, and the definition of rejection have been described elsewhere.<sup>2</sup> LDS therapy consisted of 1 g of methylprednisolone (MP), while SST consisted of 1 g of MP followed by a 6-day steroid taper, for both induction and treatment of rejection.

### RESULTS

The patient demographics and results are shown in Table 1.

A total of 53 (70%) of the patients on CyA were converted to FK 506 with LDS immunosuppression, 43 patients because of recurrent or refractory rejection after steroid treatment for rejection, 5 patients for preservation injury, 3 patients following retransplantation, 1 patient for Rh incompatibility, and 1 patient drop-out. Only one patient on FK 506 was converted to CyA. Of the patients who were converted to FK 506, 22 (42%) of patients are on FK 506 only (no steroids), as compared to 41% of patients who were randomized to the FK 506 limb initially.

### CONCLUSIONS

FK 506 with LDS in primary liver transplantation is associated with a statistically significant decrease in the incidence of rejection. In addition, patient and graft survival rates are at least the same as, if not better than, after CyA-based immunosuppression. CyA with SST appears to

Table 1. Patient Demographics and Results

| Parameter                | FK 506 | Total | CyA      |          |
|--------------------------|--------|-------|----------|----------|
|                          |        |       | With LDS | With SST |
| Number                   | 78     | 76    | 40       | 36       |
| Age (y)                  | 43     | 42    |          |          |
| Diagnosis                |        |       |          |          |
| Biliary cirrhosis        | 13     | 16    |          |          |
| Hepatocellular carcinoma | 65     | 60    |          |          |
| Median follow-up (days)  | 611    | 594   | 700      | 402      |
| Deaths                   | 7      | 9     | 7        | 2        |
| Retransplants            | 7      | 11    | 8        | 3        |
| Rejection free           |        |       |          |          |
| Actual (current)         | 34     | 7     | 2        | 5        |
| 1 Month after            | 39     | 16    | 7        | 9        |
| Switch                   | 1      | 53    | 32       | 21       |
| Steroid free             | 32     | 1     |          |          |

have the same rate of development of rejection as compared to CyA with LDS, both of which are lower than FK 506 with LDS. The side effects, including nephrotoxicity, appear to be similar in all three groups. Early reports from other centers enrolled in a multicenter randomized trial with FK 506 and cyclosporine for liver transplantation have noted the efficacy of FK 506, although there exists a learning curve for the use of this drug to prevent excessive side effects.

### REFERENCES

1. Todo S, Fung JJ, Demetris AJ, et al: *Transplant Proc* 22:13, 1990
2. Fung J, Abu-Elmagd K, Jain A, et al: *Transplant Proc* 23:2977, 1991

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