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MEDIA RELEASE · COMMUNIQUE AUX MEDIAS · MEDIENMITTEILUNG

Results of LIS2T study indicate that Neoral® is associated with less diabetes and diarrhoea than tacrolimus in liver transplantation

New study data found that liver transplant patients receiving Neoral (cyclosporin for microemulsion) and managed by C_2 monitoring experience significantly less diabetes and diarrhoea compared to those given tacrolimus.

Basel, 23 June 2003 - Neoral® is as effective as tacrolimus in preventing acute rejection in liver transplant patients whilst also being better tolerated according to the 6 month analysis of the LIS2T study presented today at the annual International Liver Transplant Society (ILTS) meeting in Barcelona.[1] The study is the first ever multi-centre head-to-head comparison of the efficacy and tolerability of Neoral versus tacrolimus, where Neoral was monitored by C_2 blood levels. Previous studies have compared Neoral and tacrolimus based on trough monitoring (C_0), however the benefits of Neoral C_2 monitoring have since been recognised.[2]

The analysis of the randomised, multi-centre study assessed 499 patients up until six months following their transplant and compared the efficacy and tolerability of Neoral using C_2 monitoring versus tacrolimus, in combination with steroids or steroids and azathioprine.

The results showed that the rates of acute liver rejection for Neoral and tacrolimus were similar, as were the incidences of graft loss and death. However, the study found that significantly more patients treated with tacrolimus suffered from diabetes and diarrhoea following their transplant. Specifically, the results showed that:

- Significantly more patients treated with tacrolimus suffered from new-onset diabetes following transplantation compared to patients treated with Neoral (14% versus 7% respectively, $p<0.05$)
- Significantly more patients treated with tacrolimus suffered from diarrhoea compared to patients treated with Neoral (28% versus 14% respectively, $p<0.001$)
- There were no significant differences in rates of acute graft rejection (29% in the Neoral group versus 25% in the tacrolimus group).
- There were no significant differences in the incidence of graft loss or death (11% in patients receiving Neoral versus 12% in patients receiving tacrolimus).

Professor Federico Villamil, Medical Director of the Liver Unit at Favaloro Foundation and Professor of Medicine at Favaloro University (Buenos Aires, Argentina) who presented the results today commented: "The important result to note is that Neoral and tacrolimus have comparable efficacy and that there is a difference in tolerability – patients receiving Neoral experienced significantly less diabetes and diarrhoea compared to those receiving tacrolimus. Diabetes increases the patient's risk of organ failure, the long term risk of cardiovascular disease and finally the risk of death. Minimising the risk of diabetes in transplant patients is a key challenge facing physicians today."

A total of 499 patients were recruited into the study from 17 countries. Patients will be followed up until one year after transplantation. These results follow an independent

analysis presented earlier this month at the American Transplant Congress in Washington which showed that the long-term chances of survival of a transplant kidney from a living donor are significantly greater with immunosuppressive therapy based on Neoral than with therapy based on tacrolimus.[3]

Neoral is a cornerstone of immunosuppressive therapy for the majority of transplant patients, with one of the longest records of proven clinical experience. Neoral C_2 monitoring involves making Neoral dose adjustments based on the measurement of the concentration of cyclosporine in a patient's blood two hours (C_2) after the dose. This allows for more precise dosing of Neoral in individual patients. Patient management by Neoral C_2 has been demonstrated to improve the outcome of transplantation with Neoral when compared to the traditional C_0 monitoring, including reducing significantly the incidence of moderate and severe rejection episodes in liver transplantation.[2]

This release contains certain "forward-looking statements," relating to the Company's business, which can be identified by the use of forward-looking terminology such as "long-term", "will be", or similar expressions, or by express or implied discussions regarding potential future sales of Neoral. Such statements reflect the current views of the Company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. There can be no guarantees that Neoral will reach any particular sales levels. Any results expressed or implied by such forward-looking statements can be affected by, among other things, uncertainties relating to product development and clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection, competition in general, increased government pricing pressures, as well as factors discussed in the Company's Form 20-F filed with the Securities and Exchange Commission. Should one or more of these risks or uncertainties materialise, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

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