La Renon®

FOCUS FOR
SUCCESS

RAPAREN®

Sirolimus 1 mg

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Sirolimus 1 mg

Safety and immunologic benefits of conversion to sirolimus in kidney transplant recipients with long-term exposure to calcineurin inhibitors.[1]

BACKGROUND:

- Sirolimus (SRL) is a promising immunosuppressant replacing calcineurin inhibitors (CNIs).
- The study was performed to evaluate the safety and immunologic benefits of conversion to SRL in stable kidney transplant (KT) recipients exposed to CNIs for long periods.

METHOD:

- 14 CNI-treated KT recipients with stable renal function for more than 10 years were included.
- Either 2 or 3 mg per day of SRL was administered while CNIs were reduced by half starting on day 1, and then stopped 2 weeks after SRL introduction.
- The safety of SRL conversion was assessed considering the graft function, acute rejection, and graft loss.
- Immunologic alterations were measured via serial changes of T cell and B cell subsets after SRL conversion. Adverse effects of SRL conversion were also evaluated.

RESULTS:

- Conversion to SRL was successful in 9 patients (64.2%).
- Conversion to SRL preserved graft function as compared to the baseline value.
- No acute rejection or allograft loss was observed during the follow-up period.
- Immune monitoring of T and B cells revealed a regulatory T cells increase after SRL conversion.
- Most adverse events developed within 6 weeks after SRL conversion, and oral mucositis was the main cause of SRL withdrawal.

CONCLUSIONS:

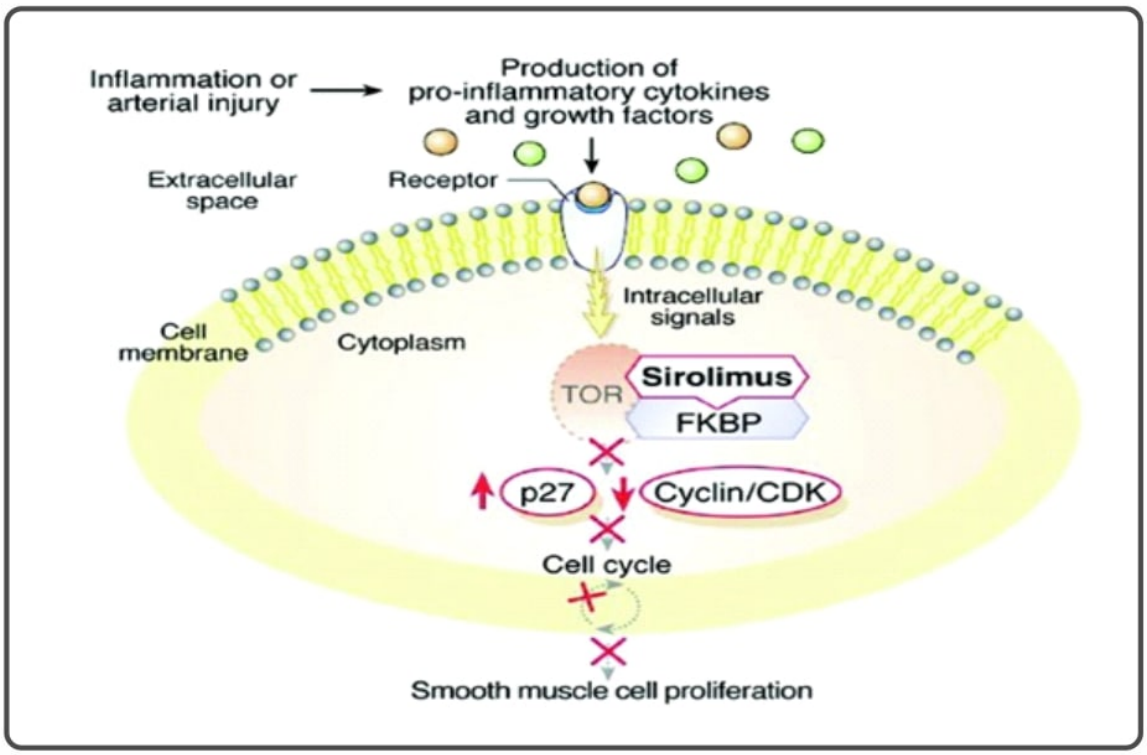
- Conversion to SRL can be safe and has immunologic benefits in KT recipients with long-term CNI exposure.
- Close monitoring of mucocutaneous adverse events is, however, required in the early period after SRL conversion.

KEY FEATURES:

- An initial maintenance regimen based on Sirolimus provides a long-term improvement in renal function for kidney transplant patients, especially for those maintained on sirolimus[2].
- Sirolimus maintains the proportion of Tregs in kidney transplant recipients[3].
- Conversion to SRL in patients with prolonged delayed graft function (DGF) helps salvage renal graft function and achieve long-term graft survival in some cases where conventional treatment has failed[4].

MECHANISM OF ACTION OF SIROLIMUS:

- Sirolimus is produced by a strain of Streptomyces hygroscopicus, isolated from a soil sample collected from Rapa Nui commonly known as Easter Island.
- Although sirolimus was isolated as an antifungal agent with potent anticandida activity, subsequent studies revealed impressive antitumor and immunosuppressive activities.
- Sirolimus is the alternative name for rapamycin, a rarely used antibiotic.
- Sirolimus is highly lipophilic and has two mechanisms of action, i.e., antiproliferation of the intima and reduction of inflammatory cell activity.
- The selectivity for proliferating cells and preferential targeting of smooth muscle cells occurs via target of rapamycin (TOR).
- It also has a cytostatic mode of action whereby it acts before the critical checkpoint in the G1 phase of the cell cycle.
- Sirolimus also has the ability to stop the proliferation of smooth muscle cells effectively. The mechanism of action is shown in Figure:



References:

1. Korean J Intern Med; 31(3): 2016: 552-559
2. Transpl Int; 29(1): 2016: 41-50
3. Cell Immunol; 297(2): 2015: 87-93
4. Transplant Proc; 47(6): 2015: 1610-1615

RAPAREN®

Sirolimus 1 mg

DESCRIPTION:

Sirolimus also known as rapamycin, is a macrolide (one of a group of drugs containing a macrolide ring) produced by the bacterium Streptomyces hygroscopicus. It has immunosuppressant functions in humans and is used to prevent rejection in organ transplantation; it is especially useful in kidney transplants. It prevents activation of T cells and B cells by inhibiting the production of interleukin-2 (IL-2).

COMPOSITION:

Each Tablet of **RAPAREN®** contains 1mg of Sirolimus.

INDICATION:

RAPAREN® is indicated for the Prophylaxis of organ rejection in kidney allograft recipients.

MECHANISM OF ACTION:

Sirolimus is a potent non-calcineurin inhibiting immunosuppressant used for renal transplantation. It inhibits T-lymphocyte activation and proliferation by inhibiting their response to interleukin-2 (IL-2). It also inhibits antibody production. It has been shown to possess antifungal and antineoplastic properties.

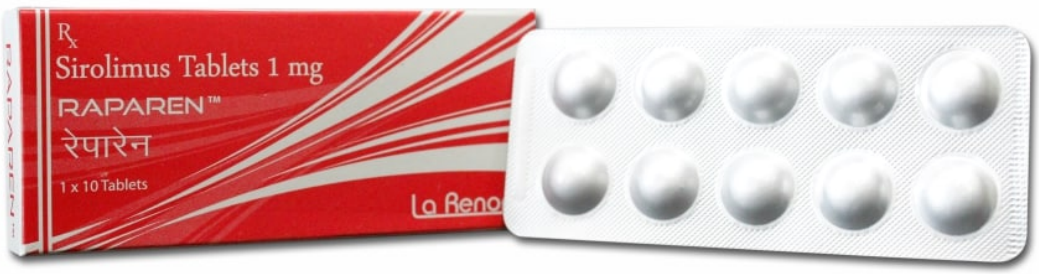
DOSAGE:

ADULT: For low-moderate risk patients: Loading dose: 6 mg on day 1, followed by a maintenance dose of 2 mg once daily, given 4 hr after ciclosporin. Adjust dose to obtain whole blood trough concentrations of 4-12 ng/ml, and reduce doses of ciclosporin and corticosteroids gradually. After 2-3 months, ciclosporin should be gradually discontinued over 4-8 wk while dose of Sirolimus is adjusted to obtain trough concentrations of 12-20 ng/ml.

CHILD: Used with ciclosporin and corticosteroids: >13 yr and weighing <40 kg: Loading dose of 3 mg/m² BSA, followed by initial maintenance of 1 mg/m²/day. Adjust dose to obtain whole blood trough concentrations of 4-12 ng/ml, and reduce doses of ciclosporin and corticosteroids gradually. After 2-3 month, ciclosporin should be gradually discontinued over 4-8 wk while dose of sirolimus adjusted to obtain trough concentrations of 12-20 ng/ml. If ciclosporin withdrawal is unsuccessful, usage of sirolimus should not exceed 3 month after transplantation. Max: 40 mg/day.

PRESENTATION:

RAPAREN® is available as a strip of 10 tablets in Alu-Alu blister Packing.



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