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The
Transplantation
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A Review on the Roles of mTOR Inhibitors in Pediatric Liver Transplant Recipients

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Background

- Immunosuppressive medications play a crucial role in determining both organ and patient survival following liver transplantation (LT).
- Inhibitors of mammalian target of rapamycin (mTOR) have demonstrated beneficial outcomes in adult LT recipients; However, their application in pediatric liver transplant recipients is a matter of debate due to uncertain efficacy and potential adverse effects.

Objectives:

- This review evaluates the potential roles of mTOR inhibitors in the context of pediatric LT patients.

Methods:

- This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol. Databases were searched until August 31, 2023. All clinical studies focusing on mTOR inhibitors in pediatric LT were included.

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Results

- ❖ Of 888 identified articles, 30 studies involving 386 children met the inclusion criteria.
- ❖ Beneficial impacts of switching from CNI to mTOR inhibitor or adding mTOR inhibitor to CNI-reduced immunosuppression in LT pediatrics with impaired kidney function is controversial.
- ❖ It appears that enhancing the immunosuppression through the addition of an mTOR inhibitor to CNI is helpful for pediatric LT recipients who are experiencing refractory acute rejection or chronic rejection.
- ❖ mTOR inhibitor-containing regimens failed to reduce post-transplant lymphoproliferative disorders (PTLD) happening among LT children. This finding may be due to concomitant high CNI concentration among studied patients.

Results

- ❖ The effectiveness of mTOR inhibitors in treating PTLD remains uncertain, however, in patients with PTLD who are at high risk of rejection, mTOR inhibitors may be administered.
- ❖ Conversion to or adding mTOR inhibitors to maintenance immunosuppression seems to be suitable for pediatrics who are transplanted due to hepatic malignancies such as hepatoblastoma or hepatocellular carcinoma or for those with post-transplant primary or recurrent malignancies.
- ❖ Switching to mTOR inhibitor may improve some CNI-related adverse effects such as gingival hyperplasia, neurotoxicity, nephropathy, hypertrophic cardiomyopathy, or thrombotic microangiopathy.

Conclusion

Two algorithms are presented to guide converting from CNIs to mTOR inhibitors (Fig 1) or adding mTOR inhibitor to a CNI-minimization immunosuppressive regimen (Fig 2) for pediatrics that may benefit this class of drugs.

Figure 1.

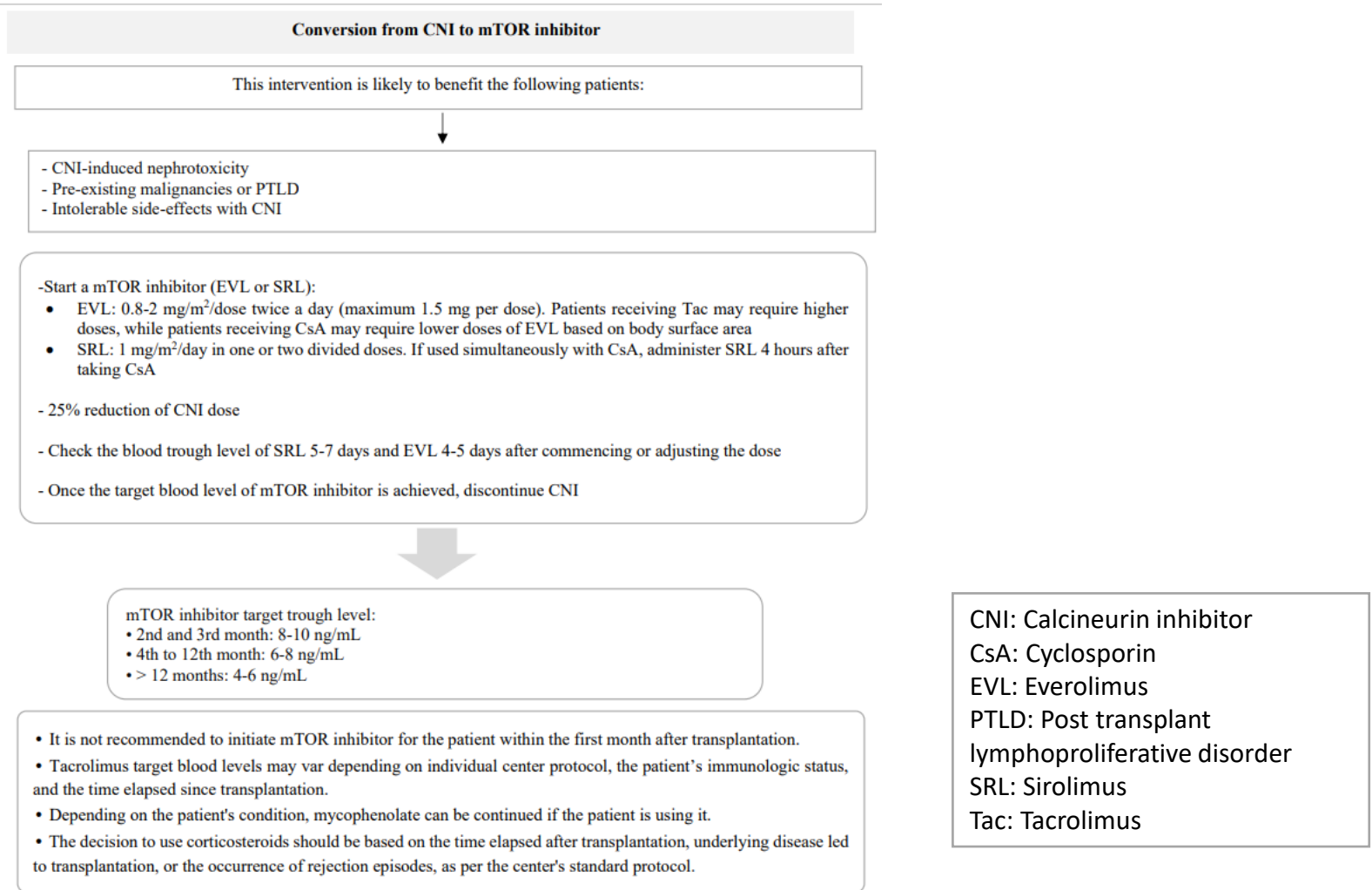
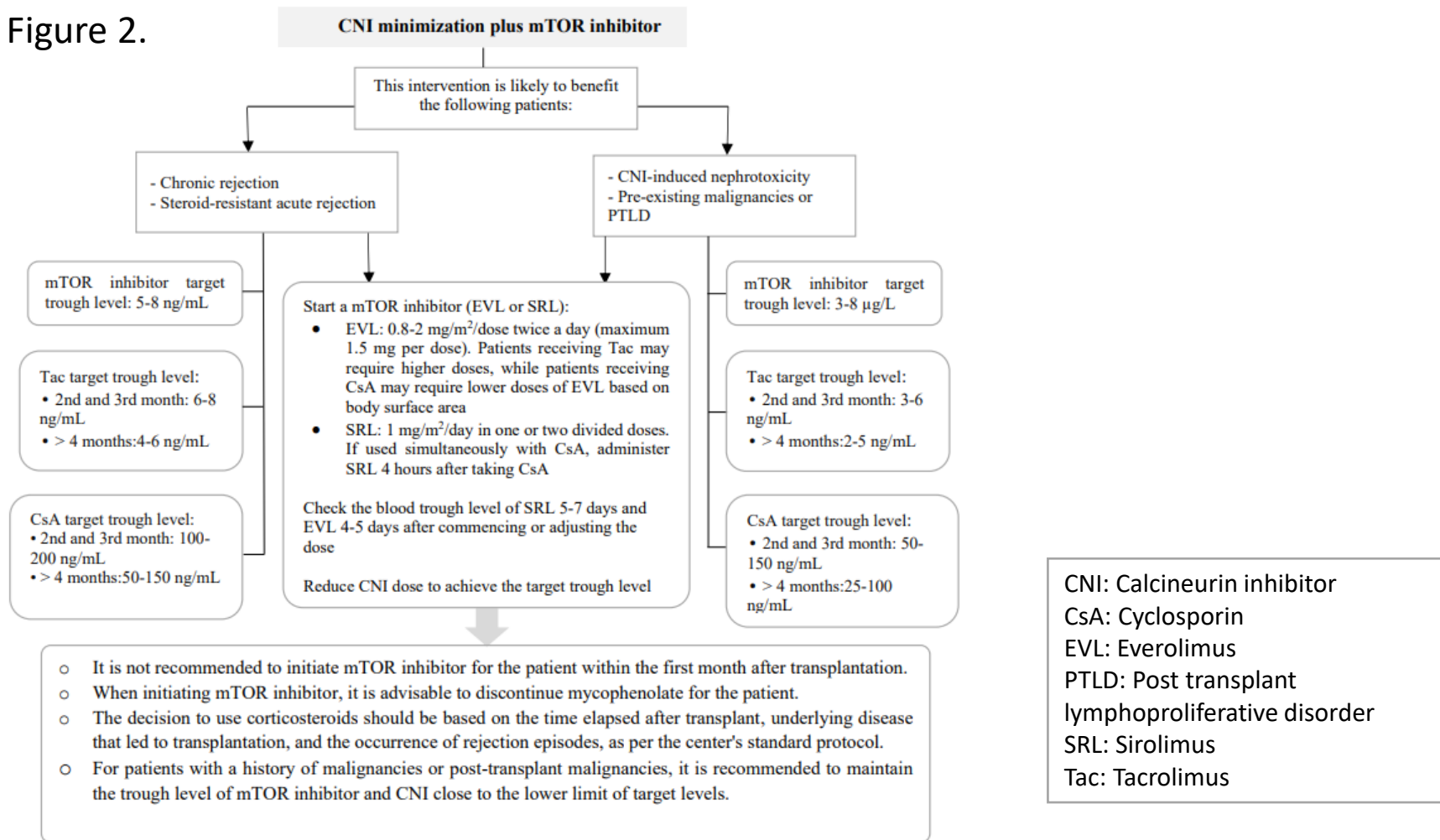


Figure 2.



Limitations

- This review mainly consisted of retrospective studies with inadequate sample sizes and lack of control group.

Future Research

- Clinical trials with suitable sample sizes are necessary to determine the exact effects of mTOR inhibitors in pediatric LT recipients.

Publication:

- This research has been accepted for publication in: *Pediatric Drugs*; 2024.
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