

RESPONSE TO REVIEWERS

Reviewer's code: 03294115

The proposed review is an expression of long lasting aspirations and expectations of transplant community about the possibility of achieving transplant tolerance to solid organ allograft. The article discusses a wide variety of aspects of the immune response and immune tolerance to liver transplant. It seems to be a very interesting element in the discussion about the phenomenon called "operative tolerance".

Answer: We thank the reviewer for the comments.

I would propose to mention the danger associated with end stage liver graft failure that may be the consequence of attempts of reduction or discontinuation of immunosuppression. There is no long-term therapeutic alternative for this condition, unlike in the course of stage renal disease.

Answer: We have added the next text in the last paragraph of page 26 : " The potential impact of IS minimization or withdrawal protocols on long-term subclinical histological graft damage (e.g., idiopathic chronic hepatitis and/or progressive fibrosis) also remains to be properly investigated. This is relevant considering that most protocol biopsy studies have revealed substantial histological abnormalities in long-term surviving liver recipients with unremarkable liver function tests."

The article contains also a very large number of references cited.

Answer: We agree with you in the great number of references cited, but it is so complicated to remove some reference due to the length and complexity of the manuscript.

There are some punctuation errors requiring corrections.

Answer: We have newly edited the complete text by native English Editors.

Reviewer's code: 01191924

Quite nice review of the mechanisms and clinical interest of tolerance induction in liver transplantation. I recommend to require the assistance of a native English speaker to improve the quality of the manuscript.

Answer: We thank the reviewer for the comments. We have newly edited the complete text by native English Editors.