



## Letters to the editor

**The role of basiliximab in renal function after liver transplantation**

I read with interest the recent experience from Hashim et al. [1] regarding the use of basiliximab as initial immunosuppression in liver transplantation (LT). The authors conclude that the combination of basiliximab with delayed tacrolimus is safe and reduces mid-term renal dysfunction with similar survival rates compared with an immunosuppression protocol based on tacrolimus and steroids.

The beneficial effect of induction therapy with basiliximab in combination with reduced-delayed tacrolimus in the mid-term renal function after liver transplantation has been reported not only with the use of standard tacrolimus but also with the extended-released tacrolimus (ER-Tac) [2–4]. Reduction of tacrolimus exposure immediately after LT with the use of interleukin-2 receptor (IL-2R) antagonists significantly reduced the glomerular filtration rate change from baseline to 1 year after LT in the RESPECT study [2]. In addition, a combination of ER-Tac plus basiliximab and mycophenolate mophetil (MMF) was associated with a significant reduction in renal function impairment during the first 24 weeks in the DIAMOND study [4]. In this sense, immunosuppression with induction therapy and reduced-delayed tacrolimus has been recommended in patients with pre-transplant renal dysfunction [5]. Together with a tacrolimus minimization policy, this combination has also been beneficial for the maintenance of renal function in the long term after LT [6].

The benefit on renal function of the immunosuppression protocols based on induction therapy with IL-2R antagonists and tacrolimus minimization is probably related to reducing tacrolimus exposure during the early period after LT. The direct effect of cumulative exposure of tacrolimus on renal function has been recently demonstrated [7]. In this study, high tacrolimus exposure defined as trough concentration >10 ng/mL within the first month and > 8 ng/mL thereafter resulted in a more pronounced decline of the glomerular filtration rate within the first 3 months after LT when compared with tacrolimus minimization defined as 4–6 ng/mL within the first month and around 4 ng/mL thereafter: 23.3 mL/min versus 9.5 mL/min, respectively ( $P < 0.001$ ).

From my point of view, the main limitation of the study by Hashim et al. [1] is the definition of the study groups. In the first regimen, which can be considered as the control group, immunosuppression was achieved with tacrolimus plus steroids with tacrolimus trough levels of 10–12 ng/mL during the first month. This protocol used to be recommended during the first decade of the present century but not currently. At present, the most frequently used immunosuppression regimen is the combination of tacrolimus, MMF and steroids [8] with tacrolimus trough levels of 7–10 ng/mL during the

first month. Unfortunately, this combination was not considered in the present study. On the other hand, the study group included basiliximab and MMF, which makes it difficult to determine whether the benefit observed in the renal function is derived from the use of basiliximab or the combination of tacrolimus and MMF with the subsequent reduction of the initial tacrolimus trough levels. A study group based on the aforementioned triple therapy without induction would have been desirable for this purpose.

**Conflicts of interest and Source of Funding**

MG has participated in advisory boards and has received honoraria from Astellas, Novartis and Chiesi.

**References**

- 1 Hashim M, Alsebaey A, Ragab A, Soliman HE, Weked I. Efficacy and safety of basiliximab as initial immunosuppression in liver transplantation: a single center study. *Ann Hepatol* 2020;19:541–5.
- 2 Neuberger JM, et al. Delayed introduction of reduced-dose tacrolimus, and renal function in liver transplantation: the 'ReSpECT' study. *Am J Transplant* 2009;9:327–36.
- 3 Llado L, Gonzalez-Castillo A, Fabregat J, Baliellas C, Ramos E, Gonzalez-Vilatarsana, et al. Efficacy and safety of delayed prolonged-release tacrolimus initiation in de novo hepatitis C virus-negative orthotopic liver transplant recipients: a single-center, single arm, prospective study. *Ann Transplant* 2019;24:36–44.
- 4 Trunečka P, Klempnauer J, Bechstein WO, Pirenne J, Friman S, Zhao A, et al. Renal function in *De novo* liver transplant recipients receiving different prolonged-release tacrolimus regimens—the DIAMOND study. *Am J Transplant* 2015;15:1843–54.
- 5 Duvoux C, Pageaux GP. Immunosuppression in liver transplant recipients with renal impairment. *J Hepatol* 2011;54:1041–54.
- 6 Gastaca M, Prieto M, Palomares I, Bustamante J, Fernandez JR, Ruiz P, et al. Long-term outcomes of liver transplantation in patients with pretransplant renal dysfunction treated with induction therapy and delayed reduced de novo once-daily tacrolimus. *Transplant Proc* 2020;52:1489–92.
- 7 Rodríguez-Perálvarez M, Guerrero M, De Luca L, Gros B, Thorburn D, Patch D, et al. Area under trough concentrations of tacrolimus as a predictor of progressive renal impairment after liver transplantation. *Transplantation* 2019;103:2539–48.
- 8 OPTN/SRTR. 2019 Annual data report: liver. *Am J Transplant* 2021;21(Suppl 2):208–315.

Mikel Gastaca, MD\*

*Hepatobiliary Surgery and Liver Transplantation Unit, Biocruces Bizkaia Health Research Institute, Hospital Universitario Cruces, University of the Basque Country, Bilbao, Spain;*

\*Correspondence to: Mikel Gastaca, MD, Unidad de Cirugía Hepatobiliar y Trasplante Hepático, Hospital Universitario Cruces-Bilbao, Plaza de Cruces 12. 48903. Barakaldo, Spain.  
E-mail addresses: [mikalgastaca@gmail.com](mailto:mikalgastaca@gmail.com), [mikel.gastacamateo@osakidetza.eus](mailto:mikel.gastacamateo@osakidetza.eus)