TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

LETTER TO THE EDITORS

Everolimus-based immunosuppression in a case of ABO-incompatible liver transplantation with calcineurin inhibitor-related posterior occipital syndrome

doi:10.1111/tri.12304

Dear Sirs,

Owing to its high immunological risk, ABO-incompatible liver transplantation (LT) is usually performed with triple or quadruple calcineurin inhibitor (CNI)-based immunosuppression and association with nondrug immunological treatment modalities, such as plasmapheresis or splenectomy [1,2]. The use of preoperative rituximab has been recently reported in small series of living-related liver transplants too [3]. However, management of CNI-related complications may be challenging for the transplant physician due to the increased risk of graft rejection in case of CNI minimization or withdrawal. We report here an

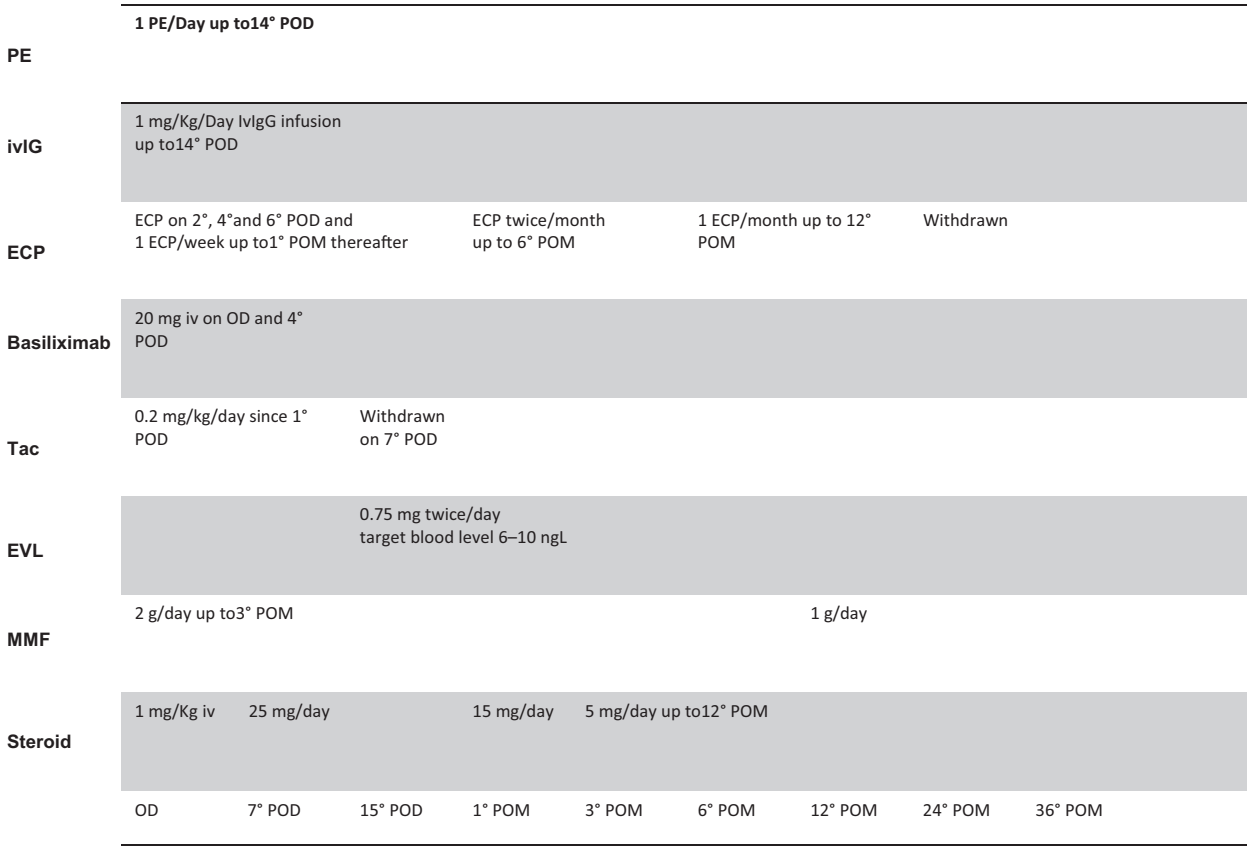

Figure 1 Everolimus-based combined immunosuppressive treatment in a ABO-incompatible cadaveric liver transplant. OP, operative day; POD, postoperative day; POM, postoperative months; Tac, tacrolimus; EVL, everolimus; steroid; MMF, mycophenolate mofetil; PE, plasma exchange; ECP, extracorporeal photoapheresis; ivIgG, intravenous immunoglobulins; basiliximab.

ABO-incompatible LT recipient treated with a combined immunosuppressive therapy everolimus (EVL)-based because of severe tacrolimus (TAC)-related neurotoxicity early after LT.

A 55-year-old, blood group B, male patient with a T2 hepatocellular carcinoma in hepatitis B virus (HBV)-related liver cirrhosis underwent LT from an ABO-incompatible deceased donor (blood group A) due to rapid clinical deterioration as per a model for end-stage liver disease (MELD) score 30 at transplantation. The procedure was conventional way, with native vena cava replacement and veno-venous bypass. Biliary reconstruction was performed with a T-tube.

After transplantation, the patient underwent immunosuppression according to the usual scheme adopted at our centre and described elsewhere [4] and including induction with anti-IL2 receptor antibodies (basiliximab, Simulect, Novartis Pharma, Basel, Switzerland) 20 mg i.v. on days 1 and 5; TAC (Prograf, Astellas, Munich, Germany 0.2 mg/kg/day orally from day 1, steroids (1 mg/kg i.v. intraoperatively tapered to 25 mg/day orally by day 7 post-transplantation), mycophenolate mofetil (MMF) (CellCept, Roche, Basel, Switzerland) 2 g/day orally, in association with daily plasmapheresis from immediate pretransplantation to post-transplant day 14, high-dose IgG infusions (Ig Vena, Kedrion SpA, Lucca, Italy) 1 mg/kg/day for the first 14 days post-transplantation and extracorporeal photopheresis (ECP) on days 2, 4, and 6 and once a week thereafter [4].

On post-transplant day 7, the patient presented neurological impairment with central blindness and confusion consistent with posterior occipital syndrome confirmed on eventual brain CT scan. TAC was withdrawn and replaced with EVL (Certican, Novartis Pharma, Basel, Switzerland) at a starting dosage of 0.75 mg twice a day, aiming at a target trough blood level between 6 and 10 ng/ml. Elimination of TAC was followed by prompt improvement in neurological conditions and confirmed by brain CT scan. The patient was discharged home on day 28 on triple immunosuppression with EVL (3 mg b.i.d.), steroids (25 mg/day) and MMF (2 g/day) in association with bi-weekly ECP up to the third months. After three months post-transplantation, the patient was admitted for the removal of the T-tube. The control cholangiography failed to disclose alterations of the biliary tree and all laboratory tests were within normal range. At a follow-up of 12 months, the patient had been on triple immunosuppressive therapy with EVL (2 mg/day), steroids (5 mg/day) and MMF (1 g/day) in association with monthly ECP, withdrawn at the year (Fig. 1).

The patient is alive with normal liver function and blood test at 36 months after liver transplant; no episode of rejection occurred nor a reswitch to a CNI-based immunosuppressive therapy has been necessary during a long-term follow-up period.

To the best of our knowledge, this is the first report of an ABO-incompatible LT recipient switched to EVL-based immunosuppression for TAC-related neurotoxicity early after transplantation. Several reports have recently confirmed the efficacy and safety of EVL in maintenance [5] and *de novo* LT recipients [6–8]. Our experience shows that EVL might be an option in case of CNI-related toxicity even in the challenging setting of ABO-incompatible LT and its resulting increased immunological risk.

Gabriele Catalano,[1] Paolo De Simone,[1]
Alessandro Mazzoni,[2] Davide Ghinolfi,[1]
Laura Coletti[1] and Franco Filipponi[1]
1 Liver Transplantation Unit, Department of Oncology, Transplantation and New Technologies, Azienda Ospedaliero-Universitaria, Pisa, Italy
2 O.U. of Immunoematology, Azienda Ospedaliero-Universitaria, Pisa, Italy
e-mail: g.catalano@ao-pisa.toscana.it

Conflicts of interest

The authors have declared no conflicts of interest.

Funding

None to be disclosed.

References

1. Hanto DW, Fecteau AH, Alonso MH, Valente JF, Whiting JF. ABO incompatible liver transplantation with no immunological graft loss using total plasma exchange, splenectomy and quadruple immunosuppression: evidence for accommodation. *Liver Transpl* 2003; **9**: 22.
2. Wu J, Ye S, Xu X, Xie H, Zhou L, Zheng S. Recipient outcomes after ABO-incompatible liver transplantation: a systematic review and meta-analysis. *PLoS ONE* 2011; **6**: 1.
3. Song GW, Lu SG, Hwang S, *et al.* Successful experience af ABO incompatible adult living donor transplantation in a single institute: non immunological failure in 10 consecutive cases. *Transplant Proc* 2013; **45**: 272.
4. Urbani L, Mazzoni A, De Simone P, *et al.* Treatment of antibody mediated rejection with high dose immunoglobulin in ABO incompatible liver transplant recipient. *Transpl Int* 2007; **20**: 467.
5. De Simone P, Metselaar HJ, Fischer L, *et al.* Conversion from a calcineurin inhibitor to everolimus therapy in maintenance liver transplant recipients: a prospective, randomized, multicenter trial. *Liver Transpl* 2009; **15**: 1262.

6. Masetti M, Montalti R, Rompianesi G, *et al.* Early withdrawal of calcineurin inhibitors and everolimus monotherapy in de novo liver transplant recipients preserves renal function. *Am J Transplant* 2010; **10**: 2252.
7. Kawahara T, Asthana S, Kneteman NM. m-TOR inhibitors: what role in liver transplantation? *J Hepatol* 2011; **55**: 1441.
8. Gurk-Turner C, Manitpisitkul W, Cooper M. A comprehensive review of everolimus clinical reports: a new mammalian target of rapamycin inhibitor. *Transplantation* 2012; **94**: 659.

