MELTDOSE® TECHNOLOGY PROLONGED RELEASE TACROLIMUS IN DE NOVO LIVER TRANSPLANT RECIPIENTS: MID-TERM EVALUATION OF THE SAFETY AND EFFICACY

FABIO MELANDRO[1], PAOLA CARRAI[1], STEFANIA PETRUCCELLI[1], DAVIDE GHINOLFI[1], LUCIA BINDI[1], GABRIELE CATALANO[1], EMANUELE BALZANO[1], GIOVANNI TINCANI[1], GIANDOMENICO BIANCOFIORE[2], PAOLO DE SIMONE[2]

[1]AZIENDA OSPEDALIERA UNIVERSITARIA PISANA, PISA, Italy,
[2]PISA UNIVERSITY, PISA, Italy

INTRODUCTION

Liver transplantation (LT) is a life-saving procedure that can restore patients with end-stage liver disease or acute liver failure to good health and normal activity.

Tacrolimus is a calcineurin inhibitor (CNI) that is the cornerstone of immunosuppression in solid organ transplantation.

Tacrolimus was originally marketed as a twice-daily, immediate-release formulation, but in 2007, a once-daily, pro- longed-release formulation was marketed in many countries worldwide for use in stable liver transplant recipients or for administration to de novo patients .

AIM

MeltDose® TAC (LCP- TAC) is a novel formulation resulting in increased dissolution and better absorption. However, scanty evidence is available on safety of LCP-TAC in de novo LT with regard to neurologic toxicity. This study aimed to evaluate the safety of LCP-TAC compared to twice-daily (TD- TAC).

METHOD

This observational study was performed on patients who had undergone first cadaveric LT at Pisa Liver Transplant Center (Italy), from January 1, 2018 thru December 31, 2019: Both groups received delayed-TAC in the setting of triple/quadruple IS with basiliximab (BAX), steroids (S), and mycophenolate mofetil (MMF). TAC was given at a dose of 0.1 mg/kg twice daily with a target trough concentration of 8–10 ng/mL during the first month, 6–8 ng/mL from months 2 to 3, and 3–5 ng/mL thereafter.
Data were analysed over a 12-month follow-up and censored at death, graft loss or latest follow-up.

RESULTS

A total of 271 patients were included in this study: 166 in LCP-TAC group and 105 in TD- TAC group. An overview of recipients, donors and LT is shown in Table 1.

At 1-y posttransplant, overall graft survival was 94,3% in LCP-TAC group and 96,4% in TD- TAC group (log rank P=0,402; fig.1). Graft survival was 93,3% in both groups (log rank P=0,973; fig.2).

The postoperative courses of the two sets are displayed in Table 2.

The treated biopsy proven acute rejection (t/BPAR) rate was 3.6% vs 3.8% (P=ns). Renal failure (moderate and severe renal impairment, eGFR under 60 mL/min) was 10,5% in LCP-TAC group and 9.6% in TD- TAC group (P=ns). The incidence of new onset diabetes mellitus was 14.5% for LCP-TAC versus 7.6 for TD-TAC group (P=0.089). Patients in TD-TAC had lower neurological complications although the difference was not significant (6% for LCP-TAC and 9.5% for TD-TAC (p=0.283).

Post-transplant infections was significantly higher in TD-TAC (21,9% vs 12,7%, p=0,044).

Table 1. Baseline demographics and clinical characteristics

Parameter	LCP-TAC (N=166)	TD-TAC (N=105)	p value
Recipient Age, y, mean (SD)	57 (9,2)	55,3 (9,05)	0,056
Recipient Male sex, n (%)	120 (72,3)	88 (83,8)	0,029
Recipient Body mass index, kg/m2, mean (SD)	25,5 (3,5)	25,8 (3,6)	0,625
Recipient MELD mean (SD)	12,7 (6,4)	13,3 (6,5)	0,412
Acute liver failure n (%)	3 (1,8)	5 (4,8)	0,162
Recipient HCV positive, n (%)	72 (43,4)	45 (42,9)	0,933
Recipient HCC, n (%)	99 (61,5)	57 (54,3).	0,254
Donor age, y, mean (SD)	70,9 (16,8)	68,7 (15,4).	0,092
Donor Male sex, n (%)	77 (46,4)	58 (55,2)	0,156
Donor Body mass index, kg/m2, mean (SD)	25,7 (4,5)	26,1 (4,1).	0,357
CIT, min, mean (SD)	432,4 (70,2)	423,5 (87,9)	0,131

Table 2. Posttransplant Complications

Parameter	LCP-TAC (N=166)	TD-TAC (N=105)	p value
Neurotological, n (%)	10 (6)	10 (9,5)	0,283
NO diabetes mellitus n (%)	24 (14,5)	8 (7,6)	0,089
Acute rejection, n (%)	6 (3,6)	4 (3,8)	0,934
Renal failure, n (%)	16(9,6)	11 (10,5)	0,823
Infection, n (%)	21 (12,7)	23 (21,9)	0,044

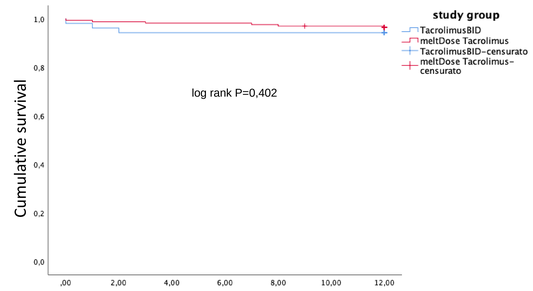

Fig 1. 12-months Patients Survival

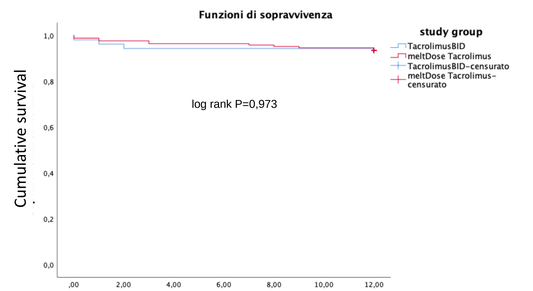

Fig 2. 12-months Graft Survival

CONCLUSIONS

To the best of our knowledge, this is the largest series of de novo use of LCP-TAC in LT. LCP-TAC is safe and effective with a numerical reduction of neurological adverse events and post-operative infections versus TD-TAC.

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CONTACT INFORMATION

Fabio.melandro@ao-pisa.Toscana.it

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