Immunosuppressive therapy after solid organ transplantation in Italy: a pilot study of the CESIT* project

Authors: Rosa Alessandro Cesare[1], Marino Maria Lucia[1], Finocchietti Marco[1], Poggi Francesca Romana[1], Massari Marco[2], Spila Alegiani Stefania[2], Masiero Lucia[3], Ricci Andrea[3], Cardillo Massimo[3], Kirchmayer Ursula[1], Marino Claudia[1], Enrico Calandrini[1], Agabiti Nera[1], Marina Davoli[1], Addis Antonio[1], Belleudi Valeria[1] on behalf of CESIT group

(1) Department of Epidemiology, Lazio Regional Health Service, ASL RM1, Rome, Italy (2) Pharmacoepidemiology Unit, National Centre for Drug Research and Evaluation, National Institute of Health, (3) National Transplant Centre - National Institute of Health

Background

Post-transplant immunosuppressive therapy represents the most effective strategy to ensure graft survival and prevent rejection. These interventions are commonly associated with multidrug approach involving medications with different mechanisms of action. A pilot study was performed to explore immunosuppressant prescription patterns and trends in the last decade across different transplant settings in Lazio region. This analysis will be replicated in three other Italian regions (Veneto, Lombardy and Sardinia) involved in a multi-database network for post-marketing surveillance of immunosuppressive drugs in transplant patients (CESIT project).

Objectives

To describe immunosuppressive maintenance therapy for kidney, liver, and heart transplantation.

Methods

The present pilot study is a cornerstone to develop a multicentre retrospective observational study. The Lazio transplant cohort was based on the national Transplant Information System (SIT) and regional healthcare claims data. In particular, regional analytical dataset was created using an open-source tool for distributed analysis, "The ShinISS", that was customized for the purpose of the study. To link SIT data to transplant cohort, a semi-deterministic record linkage procedure was performed within the tool.

Patients underwent to kidney, liver and hearth transplant for the first time in the years 2009-2019 were identified. On the basis of immunosuppressive treatment regimen prescribed in the first month after discharge, patients were defined in calcineurin inhibitor mono or multi-therapy: ciclosporin (CIC) or tacrolimus (TAC) based. In particular, the combination with an antimetabolite: [mycophenolate mofetil/mycophenolic acid (MMF) or azathioprine (AZA)] or an mTOR inhibitor [i.e. sirolimus, SIR or everolimus, EVE] as well as the use of steroids were investigated. Maintenance therapy was presented using sunburst chart [Figure 1].

Results

Overall, 2,017 transplant patients were identified: 61.7% in kidney (K), 32.7% liver (L), 5.6% hearth (H); the percentage of male were 61.6%, 76.8%, 64.6% respectively. Median age was 55 years for K-cases, 54 years for L-cases and 36 years for H-cases; in this last setting the low median age was due to the contribution of paediatric heart transplants.

In the first two settings, the most patients received TAC-based therapy (K: 75.6%; L: 92.6%) while patients with H-transplant received mainly CIC-based therapy (78.,8%). The percentage of K and L patients treated with TAC-based therapy increased over time (K: 2009: 52.7% 2019: 94.4%; L: 2009: 84.9% 2019: 97.3%). The percentage of H-transplant patients treated with CIC remained stable (2009: 81.0% 2019: 83.3%).

The most frequent drug combination was calcineurin inhibitor plus MMF, observed in 65.9% of K-cases, 60.7% of L-cases, 63.7% of H-cases.

Among K-transplant patients, triple therapy including TAC, MMF and steroids was prescribed for 55.5 % of cases versus 51.0% in L-setting; while in H-setting triple therapy CIC-based was 49.6%.

Figure 1. Sunburst Chart. The inner circle (the CIC/TAC based therapy) is surrounded by rings of deeper hierarchy levels (multi-therapy: MMF, AZA, EVE, SIR, steroids).
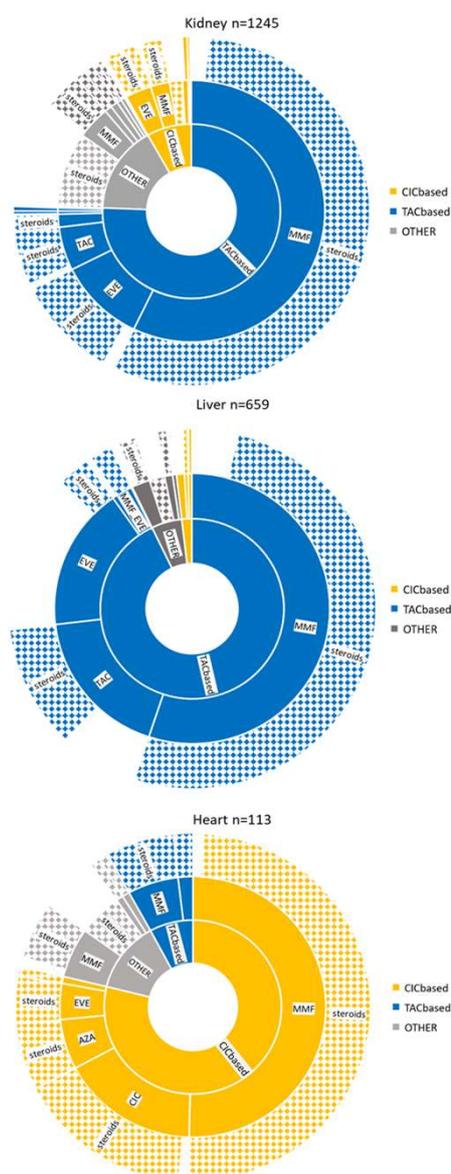
Conclusions

In the study period, an increase of TAC-based therapy in K and L setting was observed; on the contrary, the most widely prescribed therapy for H transplants was based on CIC. For all settings, the most frequent drug combination was calcineurin inhibitor plus MMF, mostly associated with steroids. Further studies are necessary to explore maintenance therapy and its determinants in a larger multicentre sample.

Correspondence: Alessandro Cesare Rosa – arosa@deplazio.it - Via C. Colombo, 112 - 00147 Rome tel. +39 06 99722159 - www.deplazio.net