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ABSTRACT

The goal of post-transplant immunosuppressive drug therapy is to prevent organ rejection while minimizing drug toxicities. In clinical practice, a multidrug approach is commonly used and involves drugs with different mechanisms of action, including calcineurin inhibitors (CNI) (tacrolimus or cyclosporine), antimetabolite (antimet) (mycophenolate or azathioprine), inhibitors of mechanistic target of rapamycin (mTOR) (sirolimus or everolimus), and/or steroids. Although evidence based on several randomized clinical trials is available, the optimal immunosuppressive therapy has not been established and may vary among organ transplant settings. To improve the knowledge on this topic, a multiregional research network to Compare the Effectiveness and Safety of Immunosuppressive drugs in Transplant patients (CESIT) has been created with the financial support of the Italian Medicines Agency. In this article, we describe the development of this network, the framework that was designed to perform observational studies, and we also give an overview of the preliminary results that we have obtained. A multi-database transplant cohort was enrolled using a common data model based on healthcare claims data of four Italian regions (Lombardy, Veneto, Lazio, and Sardinia). Analytical datasets were created using an open-source tool for distributed analysis. To link the National Transplant Information System to the regional transplant cohorts, a semi-deterministic record linkage procedure was performed. Overall, 6,914 transplant patients from 2009-19 were identified: 4,029 (58.3%) for kidney, 2,219 (32.1%) for liver, 434 (6.3%) for heart, and 215 (3.1%) for lung. As expected, demographic and clinical characteristics showed considerable variability among organ settings. Although the triple therapy in terms of CNI + antimet/mTOR + steroids was widely dispensed for all settings (63.7% for kidney, 33.5% for liver, 53.3% for heart, and 63.7% for lung), differences in the active agents involved were detected. The CESIT network represents a great opportunity to study several aspects related to the use, safety, and effectiveness of post-transplant maintenance immunosuppressive therapy in real practice.

Keywords: distributed analysis; immunosuppressive treatment; multidisciplinary approach; pharmaco-utilization; pharmacoepidemiology; research network; transplant.

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