FOREWORD

In recent years, the maintenance or improvement of quality of life has become an increasingly important part of patient management after transplantation. With improvements in pretransplant dialysis and posttransplant immunosuppression, survival rates for transplant recipients are improving. However, numerous factors can reduce quality of life, including co-morbid conditions, kidney function, rejection episodes, hospitalisations, and employment status.[1] Adverse effects of medications can also have a substantial impact on quality of life,[1] with gastrointestinal complaints in particular shown to be associated with impaired functioning in physical, social and psychological domains of quality of life.[2] A recent study using a range of validated patient-reported outcome instruments[3,4] demonstrated that gastrointestinal complaints in renal transplant recipients are associated with a significantly impaired health-related quality of life.[2]

One immunosuppressive agent that is commonly associated with gastrointestinal adverse events is mycophenolate mofetil (MMF). Gastrointestinal symptoms in mycophenolate mofetil (MMF)-treated patients often necessitate reductions or interruptions in the MMF dose, leading to an increased risk of acute rejection and graft loss.[5–8] Enteric-coated mycophenolate sodium (EC-MPS, *myfortic*®) has been developed with the aim of improving mycophenolic acid-related upper gastrointestinal adverse events. In the first paper in this supplement, Professor Bruce Kaplan (University of Illinois at Chicago, USA) reviews the current use of EC-MPS in transplantation. It explains the rationale for the development of EC-MPS and analyses data from the pivotal trials of EC-MPS in *de novo* and maintenance transplant recipients. Patient-reported outcomes after the conversion of patients with gastrointestinal complaints from MMF to EC-MPS are then evaluated. Finally, Professor Kaplan's article provides an overview of the current clinical trial programme, and considers the need for further information to be obtained regarding the use of EC-MPS in different transplant populations and with different immunosuppressive regimens.

For the second part of this supplement, we have invited a number of international experts in the field of transplantation to share their experiences in dealing with kidney recipients and other patients with gastrointestinal adverse events attributed to MMF-based immunosuppression, and the effect of conversion to EC-MPS. The first case study presented in this supplement is from Dr Murat Tuncer (Antalya, Turkey), who describes a patient who experienced nausea and dyspepsia after starting MMF treatment. These gastrointestinal symptoms, which failed to resolve after two consecutive MMF dose reductions, responded to a conversion to EC-MPS, even when the dose reverted to recommended levels. The impact of gastrointestinal symptoms on quality of life is highlighted in a case study presented by Dr Hélène Lord (Montréal, QC, Canada). The patient she describes was prevented from returning to work by severe diarrhoea, and the patient was eventually converted

to EC-MPS. The gastrointestinal symptoms resolved and the patient was able to return to full-time employment. The impact of gastrointestinal symptoms on patients' social functioning is further explored in case studies described by Dr Tariq Shah (Los Angeles, CA, USA). He presents three MMF-treated patients who, as a result of gastrointestinal symptoms felt unable to leave the house, attend social events or maintain full-time employment. In all three patients, conversion to EC-MPS was associated with the resolution of gastrointestinal symptoms and substantial improvements in social functioning.

Conversion from MMF to EC-MPS may also be of value in patients with gastrointestinal symptoms that are exacerbated by co-morbid medical conditions. Anita Boswell and Dr Magdi Shehata (Nottingham, UK) present a patient with ulcerative colitis who experienced diarrhoea leading to weight loss, lethargy and anxiety about leaving the house. They describe their management approach in this patient and in two other cases in which patients developed severe diarrhoea and incontinence. A particularly serious case is presented by Drs Francisco Ortega Suárez and José Baltar Martín (Asturia, Spain), in which a patient experienced abdominal pain and rectal ulcers associated with bleeding that led to severe anaemia and hypotension. After blood transfusion and conversion to EC-MPS, the abdominal pain, rectal ulcers and anaemia resolved.

In addition to the possible reduction of gastrointestinal adverse events, conversion to EC-MPS also often allows full immunosuppressive coverage to be maintained. This is highlighted by a case study in which Dr Thomas Breidenbach and colleagues (Augsburg, Germany) describe a renal transplant recipient who was at high immunological risk of rejection. After experiencing cytomegalovirus-related colitis and increasingly severe episodes of diarrhoea, the patient required a reduction in the MMF dose, which was accompanied by an increase in cyclosporine dosing. Conversion from MMF to an equivalent dose of EC-MPS led to the rapid resolution of the diarrhoea, with the result that the EC-MPS dose could be increased and cyclosporine trough levels could be successfully reduced.

Immunosuppressive agents also have a role to play in patients other than those requiring immunosuppression after renal transplantation. Dr Ibrahim Yakoub-Agha and colleagues (Lille, France) describe a patient with chronic myeloid leukaemia who developed graft-versus-host disease after undergoing allogeneic haematopoietic stem cell transplantation. This was treated with MMF, although the development of diarrhoea resulted in conversion to EC-MPS, after which the patient's condition improved. Dr Pierre-Simon Rohrlich and co-workers (Besançon, France) present a patient with severe idiopathic aplastic anaemia, who received MMF in an attempt to reduce her dose of cyclosporine. As a result of nausea and diarrhoea, however, the patient refused to continue MMF treatment, and was eventually converted to EC-MPS, with good compliance and no gastrointestinal symptoms.

Although the case studies presented in this supplement describe the 'real-world' use of EC-MPS and build on the expanding EC-MPS clinical trial programme, the clinical evidence they provide, although encouraging, is to some extent limited. Additional large-scale, protocol-based studies are required to provide further investigation into the tangible benefits to patients that may be achieved with conversion to EC-MPS in terms of quality of life, anxiety level, and ability to work, with no loss of efficacy.

Roy D. Bloom
Kidney/Pancreas Transplant Program,
University of Pennsylvania Medical Center,
Philadelphia, Pennsylvania 19104-6144, USA

Lionel Rostaing
Nephrology, Hemodialysis, and Multiorgan
Transplant Unit, Hôpital Rangueil, Toulouse
31059, Cedex 9, France

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