

## THROMBOCYTONIA AND LEUKOPENIA

- → Self- limited in most patients, shown to decrease significantly by week 7 without any dose modification. (1)
- → If persistent, dose reduction may be considered and amelioration of toxic effects is generally evident by 24 hours, though some patients may require up to 57 days for full recovery. The toxicity of sirolimus is most marked at trough concentrations >15 ng/ml.<sup>(1)</sup>
- → If grade 3 or higher neutropenia (ANC <1000/mm3)<sup>(2)</sup>, temporary interruption of therapy may be required.<sup>(3)</sup>
- → When administered with MMF, limiting dose of MMF to 1 g/day may be considered. (4)(5)(6)

<sup>(1)</sup> Hong, Johnny C.; Kahan, Barry D.3 SIROLIMUS-INDUCED THROMBOCYTOPENIA AND LEUKOPENIA IN RENAL TRANSPLANT RECIPIENTS: RISK FACTORS, INCIDENCE, PROGRESSION, AND MANAGEMENT12, Transplantation: May 27, 2000 - Volume 69 - Issue 10 - p 2085-2090

<sup>(2)</sup> Common Terminology Criteria for Adverse Events (CTCAE) Version 5. Published: November 27. US Department of Health and Human Services, Nat Institutes of Health, National Cancer Institute.

<sup>(3)</sup> Alasker, A., Meskawi, M., Sun, M., Ismail, S., Hanna, N., Hansen, J., ... Karakiewicz, P. I. (2013). A contemporary update on rates and managemer toxicities of targeted therapies for metastatic renal cell carcinoma. Cancer Treatment Reviews, 39(4), 388–401.

<sup>(4)</sup> Buchler M, Lebranchu Y, Beneton M, Le Meur Y, Heng AE, Westeel PF y cols.: Higher exposure to mycophenolic acid with sirolimus than with cyclosporine cotreatment. Clinical Pharmacology & Therapeutics 78 (1): 34-42, 2005.

<sup>(5)</sup> El Haggan W, Ficheux M, Debruyne D, Rognant N, Lobbedez T, Allard C y cols.: Pharmacokinetics of Mycophenolic Acid in Kidney Transplant Patient Receiving Sirolimus Versus Cyclosporine. Transplantation Proceedings 37 (2): 864-866, 2005.

<sup>(6)</sup> Oppenheimer F, Alonso A, Arias M, Campistol JM, González Molina M, González Posada JM, Grinyo JM, Morales JM, Sánchez Fructuoso A, Sánchez Plumed J, Ruiz JC. Handling sirolimus in clinical practice. Spanish Nephrology Society. Nefrologia. 2006;26 Suppl 2:64-93. English, Spanish. PMID: 17937635.