

Re: Interleukin-11 Attenuates Ifosfamide-Induced Hemorrhagic Cystitis

Jose M. Mota, Gerly A. Brito, Raphael T. Loiola, Fernando Q. Cunha, Ronaldo de A. Ribeiro

Departments of Physiology and Pharmacology (JMM, RTL, RAR), and Morphology (GAB), School of Medicine, Federal University of Ceara and Department of Pharmacology FQC), School of Medicine, University of Sao Paulo Ribeirao Preto, Sao Paulo, Brazil

Int Braz J Urol, 33: 704-710, 2007

To the Editor:

The study was conducted to investigate the anti-inflammatory effect of rhIL-11 used in prophylaxis of ifosfamide-induced hemorrhagic cystitis in an animal model. There has been no publication on the use of rhIL-11 in prophylaxis of hemorrhagic cystitis in the literature previously.

The study design and methods used in this experiment were chosen and are presented correctly. Although the studied groups (each consisted of 6 mice) were rather small, the statistical methods used in this publication are adequate to the number of animals used.

I do not completely agree with the statement, that there are no adequate methods that prevent hemorrhagic cystitis induced by oxazaphosphorine agents (such as cyclophosphamide or ifosfamide). Several studies indicate the use of hyperhydration (which shortens the exposition time to urotoxins) and mesna (which binds acroleine, responsible for bladder mucosa damage) considerably reduces the incidents of early-onset toxic hemorrhagic cystitis even in patients receiving high-dose chemotherapy (1). Early-onset hemorrhagic cystitis is not a major clinical issue nowadays. Its rate presented in many studies is lower than the 33% quoted by the authors basing on one publication (2-6). However, prevention of late-onset hemorrhagic cystitis related to the reactivation of viruses (mainly human polyoma BK virus), in patients after allogeneic stem-cell transplantation, still remains an unsolved problem (3,7,8-

10). One may speculate that the initial bladder mucosa damage caused by cytostatics used in conditioning regimens may play a role in the occurrence of virus induced hemorrhagic cystitis (10). It has been documented in many publications that not oxazaphosphorine drugs, but rather busulfan is currently the main agent identified as a risk factor for hemorrhagic cystitis (5,6,9,11). No specific prophylactic measures protecting the bladder from busulfan toxicity exist so far. This is the reason why investigation of methods that may prevent from cytostatic-induced urothelium damage remains a challenge.

In this context, the results presented by the authors are encouraging and justify the use of rhIL-11 in clinical trial in human hemorrhagic cystitis.

REFERENCES

1. Bedi A, Miller C, Hanson J, Goodman S, Ambinder R, Charache P, et al.: Assotiation of BK virus with failure of prophylaxis against hemorrhagic cystitis following bone marrow transplantation. *J Clin Oncol.* 1995; 5:1103-9.
2. Cesaro S, Brugiolo A, Faraci M, Uderzo C, Rondelli R, Favre C, et al.: Incidence and treatment of hemorrhagic cystitis in children given hematopoietic stem cell transplantation: a survey from the Italian Association of Pediatric Hematology Oncology- Bone Marrow Transplantation Group. *Bone Marrow Transplant.* 2003; 32, 925-31.

3. Gorczyńska E, Turkiewicz D, Rybka K, Toporski J, Ka³wak K, Dyla A, et al.: Incidence, clinical outcome and management of virus-induced hemorrhagic cystitis in children and adolescents after allogeneic hematopoietic progenitor cell transplantation. *Biol Blood Marrow Transplant.* 2005; 10: 797-804.
4. Hows JM, Mehta A, Ward L, Woods K, Perez R, Gordon MY, et al.: Comparison of mesna with forced diuresis to prevent cyclophosphamide-induced hemorrhagic cystitis in marrow transplantation. *Br J Cancer.* 1984; 50: 753-6.
5. Kirsten D, Hartert A, Willenbacher N, Basara N, Blau A, Fauser A, et al.: Incidence and outcome of BK-Virus-induced hemorrhagic cystitis in patients receiving allogeneic BMT/PBSCT. *Bone Marrow Transplant.* 1999; 23 (suppl. 1): S117.
6. Kondo M, Kojima S, Kato K, Matsuyama T: Late-onset hemorrhagic cystitis after hematopoietic stem cell transplantation in children. *Bone Marrow Transplant.* 1998; 22: 995- 998.
7. Leung AY, Mak R, Lie A, Yuen K, Cheng V, Liang R, et al.: Clinicopathological features and risk factors of clinically overt haemorrhagic cystitis complicating bone marrow transplantation. *Bone Marrow Transpl.* 2002; 29: 509-13.
8. Leung AY, Yuen K, Kwong Y: Polyoma BK virus and haemorrhagic cystitis in haematopoietic stem cell transplantation: a changing paradigm. *Bone Marrow Transpl.* 2005; 36: 929-37.
9. Peinemann F, de Villiers E, Dorries K, Adams O, Vogeli T, Burdach S: Clinical course and treatment of haemorrhagic cystitis associated with BK type of human polyomavirus in nine paediatric recipients of allogeneic bone marrow transplants. *Eur J Pediatr.* 2000; 159: 182-8.
10. Rindgen O, Labopin M, Tura S, Arcese W, Iriondo A, ZittounR, et al.: A comparison of busulfan versus total body irradiation combined with cyclophosphamide as conditioning for autograft or allograft bone marrow transplantation in patients with acute leukaemia. *Br J Hematol.* 1996; 93: 637-45.
11. Seber A, Shu X, Defor T, Sencer S, Ramsay N: Risk factors for severe hemorrhagic cystitis following BMT. *Bone Marrow Transplant.* 1999; 23, 35-50.

Dr. Ewa Gorczynska

Department of Pediatric Hematology

Oncology and Bone Marrow Transplantation

Wroclaw Medical University

Wroclaw, Poland

E-mail: eg@pedhemat.am.wroc.pl