AstraZeneca Marketing Company Study Synopsis

Finished product: MERREM™I.V

Active ingredient: Meropenem
Study Code: 3591/9007

Convulsion rates in patients treated with carbapenems in stem cell transplants

Publications: n/a

Status: Completed

Development Phase: 4

First subject recruited: 02/171999

Last subject completed: 07/10/2001

Approval date: n/a

Objectives:

The first month of transplantation is characterized by neutropenia and febrile neutropenic episodes. Carbapenems in this setting can be the first choise owing to the additional Gram positive and anaerob spectrum. The two Carbapenems that can be used for this purpose are Meropenem and Imipenem/Cilastatin. They share the same spectrum of antibacterial activity and have the same potential side effects. There are various studies showing that, Imipenem/Cilastatin differs from Meropenem in lowering the treshhold for convulsions in a dose-dependent manner. SCT patients receive many drugs that may cause convulsions such as cyclosporine and certain cytotoxic drugs. Also, during the course of transplantation, CMV, herpesvirus infections, and other infections causing encephalitis and central nervous system damage results in seizures. Under these circumstances, any drug that may increase the rate of convulsions can carry important risks for the patient.

Methods:

This is an ongoing, open, nonrandomized study comparing the side effects of Meropenem and Imipenem/Cilastatin in patients undergoing STC (autologous and allogeneic) in Ankara University Faculty of Medicine, Department of Hematology between 1999-2000. The primary end-point is the comparison of the side effects, especially convulsion rate. The secondary endpoints are treatment success, microbiological response, morbidity and mortality related to febrile neutropenia. Factors that may increase the rate of convulsions is recorded and compared in both groups. All patients received Meropenem at a dose of 3x1 g/day and Imipenem/Cilastatin 4x0.5 g/day.

Results:

The results showed that there were no convulsions in these groups of patients. This finding can be attributed to the small number of patients in which a seizure rate of 1% was estimated. Also the dose of Imipenem/Cilastatin in our patients was 2 g/day. While at a usual dose of 4 g/day, a 10% convulsion rate is expected, this rate is less than 1% at a dose of 2 g/day. The results indicate that carbapenems are safe in SCT, but the risk of convulsion in cases who need larger doses of Imipenem/Cilastatin still needs to be evaluated.

Table 1 Characteristics of patients

	Meropenem	Imipenem/Cilastatin
No. of Patients	31	15
Sex		
Male/Female	20/11	7/8
Diagnosis		
AML	11	7
ALL	1	2
CML	17	5
Aplastic Anemia	1	1
NHL	1	-
Type of Transplantation		
AlloPBSCT	18	7
AlloBMT	1	8
AutoPBSCT	12	-
Days of neutropenia (mean) in AlloSCT	18.2 (10-34)	16 (7-26)
Days of neutropenia (mean) in AutoSCT	18.9 (10-31)	16.3 (12-22)
Response to treatment without modification	15	8
Response to treatment with modification	16	7
Other toxicity besides convulsion		
Nausea	1	1
Hepatotoxicity	4	3