AstraZeneca Marketing Company Study Synopsis

Finished product: MERREM™ I.V

Active ingredient: Meropenem
Study Code: 3591/9006

The initial empiric antibiotic treatments in childhood febrile neutropenia: meropenem versus ceftazidime plus amikacin combination

Publications: n/a

Status: Completed

Development Phase: 4

First subject recruited: 02/05/2000

Last subject completed: 11/05/2000

Approval date: n/a

Objectives:

To compared the efficacy of meropenem with ceftazidime plus amikacin in the empirical treatment of febrile neutropenia in pediatric cancer patient.

Methods:

The study was conducted between February and October 2000 during 67 febrile neutropenic episodes developed in 52 children with cancer who are followed at Pediatric Heamatology-Oncology Department, Medicine Faculty, Cukurova University. The age of patients were ranging between 11 months and 15 years (median 7 years). All patients were hospitalized patients with cancer meeting the febrile neutropenia description: absolute neutrophil count < 500 mm^3, a single measurement of oral temperature >38.5^{0}C or on two occasions 38.0^{0}C in 12 hours or 38.0^{0}C on three occasions in 24 hours. Febrile neutropenic episodes were classified as microbiologically documented, clinically documented and unexplained fever and empirical antibiotic treatment was administered.

For 38 episodes (% 56.7) in group I meropenem 20 mg/kg every 8 hours IV and for 29 episodes (% 43.2) in group II 100 mg/kg/day ceftazidime + 15 mg/kg/day amikacin IV combination were administered as empirical antibiotic the therapy. Patients were assessed especially at 72 hours and in patients failing to respond with uncontrolled fever modification was made and a glycopeptide, vancomycin 40 mg/kg/day, was added to therapy. Patients failed to respond at the end of 7 days were considered as “failure” and the antibiotic therapy was changed. Antibiotic therapy was discontinued in patients who are clinically well and are without fever for 5 days. Empirical anti-fungal therapy was given to patients whose fever could not be controlled at the end of 5 days of antibiotic therapy.

Results:

The response rate without modification was 35.3% with meropenem monotherapy and was 26.4% with ceftazidime + amikacin combination therapy. After modification the response rate increased to 84.8% in meropenem group and to 80.2% in the ceftazidime + amikacin group.

1. With respect to total success rates in febrile neutropenia in childhood malignancies, no statistical differences were found between two antibiotic regimens.
2. Meropenem monotherapy was found to be as effective as gold standard ceftazidime + amikacin combination therapy.
3. The success rate of monotherapy without the combination being less than expected could be attributed to the majority of patients being high risk patients with severe neutropenia and our microbiological flora.
4. No major adverse events were observed with two treatment regimens during the study.

TABLE I: Characteristics of patients with febrile neutropenia

	Overall	Meropenem n %	Ceftaz+Amik n %
Number of episodes	67	38 (56,7)	29 (43,2)
Age Mean ± SD	7,1± 3,8	6,9±3,1	7,2±3,1
Girl/Boy	24/28	11/14	13/14
MNS (median)	110	120	110
G-CSF Primary	42	21 (%50)	21 (%50)

TABLE II: Distribution of febrile neutropenia according to underlying malignancy

	Total	Meropenem	Ceftazidime+ Amikacin
ALL	28	15	13
AML	12	6	6
Neuroblastoma	9	5	4
NHL	3	2	1
TOTAL	52	28	24

TABLE III: Isolated microorganisms

	Meropenem	Ceftazidime+Amikacin

MS (coagulase -) Staph	7	2
MR (coagulase -) Staph	1	1
MRSE	5	3
Staph. Aureus	1	1
E. coli	3	2
Pseudomonas	1	_
C. Albicans	_	1
Aerobacter aerogenes	1	_
Strep. Viridans	2	_
Difteroid	1	_
Flavobacterium Ad.	1	_
Acinetobacter	_	_
Enterobacter	_	_

TABLE IV: Modifications in empirical antibiotic therapy

Modification	Meropenem (n=38)	%	Ceftaz+Amik (n=29)	%
Vankomicin	15	39.4	18	62.0
Amphotericin B	17	44.7	14	48.2
Acyclovir	6	15.7	5	17.2
TMP-SMX	1	2.6	1	3.4