Therapeutic Equivalence of Generic Imipenem/Cilastatin for Therapy of Infections at Siriraj Hospital

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Background: *Several generic imipenem/cilastatin formulations have been approved by Thai FDA and a generic imipenem/cilastatin (Yungjin^{R}) has been available in Siriraj Hospital since 2007. Since imipenem/cilastatin is usually given to the patients with serious hospital-acquired infections, the generic imipenem/cilastatin must be therapeutically equivalent to the original imipenem/cilastatin. The objective of the study was to compare effectiveness and safety of generic imipenem/cilastatin with original imipenem/cilastatin for therapy of infections in hospitalized patients at Siriraj Hospital.*

Material and Method: *Medical records of adult hospitalized patients at Siriraj Hospital who received imipenem/cilastatin at least 48 hours during June 2007 to September 2008 were reviewed. The effectiveness data of 300 patients who received original imipenem/cilastatin were compared with those of 300 patients who received generic imipenem/cilastatin in order to determine if a difference in composite favorable outcome of both formulations was within 10%.*

Results: *The demographics, clinical features of infections, site of infections, type of causative organisms and concomitant antibiotics of the patients in both groups were not significantly different. The overall favorable outcomes in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 65% and 58.7% respectively (absolute difference 6.3%, 95% CI -1.4% to 14%). Cure rates of infections in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 35% and 28.7% respectively (absolute difference 6.3%, 95% CI -1.1% to 13.7%). Super-infection rates in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 4.7% and 9% respectively (absolute difference -4.3%, 95% CI -8.5% to 0.3%). Mortality due to infections in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 18.3% and 21.3% respectively (absolute difference -3%, 95% CI -9.4% to 3.4%). Overall mortality in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 35.3% and 43% respectively (absolute difference -7.7%, 95% CI -15.3% to 0.1%). The occurrence of adverse events in the patients in both groups was not significantly different.*

Conclusion: *Although the point estimate of composite favorable outcome of the patients who received generic imipenem/cilastatin (Yungjin^{R}) was < 10% of those who received original imipenem/cilastatin (Tienam^{R}), generic imipenem/cilastatin showed a trend for therapeutic non-equivalence to original imipenem/cilastatin because the upper limits of 95% confidence interval of differences of several important clinical outcomes were more than 10%.*

Keywords: *Therapeutic Equivalence, Generic Drug, Imipenem/Cilastatin*

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Imipenem is an antibiotic in the carbapenem group. Imipenem is an amidine derivative of thienamycin. Imipenem is much more stable than the mother compound. A substitution of a methyl moiety in place of sulphur was introduced to increase bactericidal activity and beta-lactamase stability of imipenem. Imipenem is rapidly degraded by kidney dehydropeptidase-1. Therefore, imipenem is combined with cilastatin, an inhibitor of this enzyme, in order to prevent the degradation of imipenem. Cilastatin also protects the kidneys against potential toxic effects exerted by higher doses of imipenem. Imipenem and cilastatin are combined in 1:1 ratio. Cilastatin has no antibacterial activity, thus only the amount of imipenem is given for dosing purposes. Imipenem/cilastatin is active against a variety of pathogens including resistant gram negative bacteria acquired in hospitals. Imipenem/cilastatin is indicated for the treatment of serious gram negative and mixed aerobic/anaerobic infections, as well as initial empirical treatment of hospital- and

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healthcare-acquired pneumonia, intra-abdominal infections and febrile neutropenia[1,2]. Imipenem/cilastatin dosing in adults is usually 2 grams per day. Imipenem/cilastatin dosing should be decreased in the patients with impaired renal function and geriatric patients[3]. Patients with creatinine clearance of < 70 mL/min/ 1.73 sq m and/or body weight < 70 kg require dosage reductions. Imipenem/cilastatin efficacy depends on the dosing interval duration during which free drug concentration exceeds the MIC. Imipenem/cilastatin plasma concentration time above MIC is the best pharmacodynamic predictor of imipenem/cilastatin efficacy, with optimum bacterial kill achieved when 40% of the dosing interval has drug concentrations higher than the MIC[3].

An ideal generic drug product is one that is chemically equivalent, bioequivalent and therapeutically equivalent to an innovator or first version of the drug product approved by the FDA. If a generic drug is clearly shown to be chemically equivalent, bioequivalent and therapeutically equivalent to an original drug, it can be substituted for the original product with much lower cost. Unfortunately, many generic drugs do not meet the required chemical parameters[4]. Some generic piperacillin/ tazobactam products had reduced in vitro activity varying from -5% to -35% when compared with that of the original product[5]. Evaluations of generic broad-spectrum β-lactams documented violations of European and US Pharmacopoeia quality standards related to sterility, potency and product impurities[6-8]. Bioequivalence study of generic intravenous drug is not required for drug registration. Therefore, a microbiological assay to determine pharmaceutical equivalence of generic intravenous antibiotics was proposed[9]. Randomized controlled trials comparing the generic drugs with the original drugs to determine a therapeutic equivalence are rarely conducted. The experimental studies in animals using some generic anti-infective agents revealed poor clinical responses[10-13]. Randomized controlled trials on therapeutic equivalence of generic drugs and original drugs revealed that effectiveness of some generic drugs were significantly inferior to that of the original products[14,15]. A higher incidence of postoperative infections in adult patients undergoing coronary artery bypass graft surgery receiving generic cefuroxime was noted when compared with original cefuroxime due to the ineffective production of a stable molecule[14]. Clinical equivalence was noted in 71% of randomized controlled trials comparing the generic calcium channel blockers with the original calcium channel blockers[15]. Generic substitution for original antiepileptic drugs in the treatment of epilepsy led to breakthrough seizures[16]. Therefore, chemical equivalence and bioequivalence of generic drugs may not be sufficient to assure therapeutic equivalence especially for the life-saving drugs and the drugs with a narrow therapeutic index.

The original product of imipenem/cilastatin from an innovator pharmaceutical company has been used in Siriraj Hospital for longer than 15 years. The cost of this original product of imipenem/cilastatin in Thailand is still high. In 2007, a generic product of imipenem/ cilastatin (Yungin^{R}) became available in Siriraj Hospital. All formulations of generic imipenem/cilastatin that are currently used in Thailand are imported from other countries since formulation of imipenem/cilastatin requires a sophisticated technology that is unavailable in Thailand. Therefore, there is concern among patients and physicians that generic imipenem/cilastatin may be clinically inferior to original imipenem/cilastatin.

The objective of the study was to compare effectiveness and safety of generic imipenem/cilastatin with original imipenem/cilastatin for therapy of infections in hospitalized patients at Siriraj Hospital.

Material and Method

The identifications of hospitalized patients aged 18 years or older who received imipenem/cilastatin for at least 48 hours from June 2007 to September 2008 were retrieved from pharmacy database of Siriraj Hospital. The medical records of the chosen patients were provided by Department of Medical Records of Siriraj Hospital. The eligible patients were selected by systematic random sampling and the predetermined patients' information was extracted from the medical records to the case report forms. The predetermined information included demographic data, location of the patients, underlying conditions, prior use of antibiotics, type of infections, site of infections, type of causative agents, indication of imipenem/cilastatin prescriptions, dosage of imipenem/cilastatin, duration of treatment with imipenem/cilastatin, concomitant antibiotics, clinical outcomes, microbiological outcomes and adverse events due to imipenem/cilastatin.

This study is intended to be a non-inferiority study. It was expected that a favourable response rate (cure and improvement) of the patients who received original imipenem/cilastatin would be 70%. If the generic imipenem/cilastatin had therapeutic equivalence to that of original imipenem/cilastatin, the favorable response rate of the patients who received generic

imipenem/cilastatin would be ≥ 60%. A sample size of 300 patients per group would be needed in order to claim non-inferiority of generic imipenem/cilastatin when the type I and type II errors were 5% and 20%, respectively.

The data were analyzed by descriptive statistics, Chi-square statistics, Fisher exact test, and student t test where appropriate. A p-value of ≤ 0.05 was considered statistically significant.

Results

The general characteristics of the patients in the original imipenem/cilastatin group and the generic imipenem/ cilastatin group are shown in Table 1. Fifty percent of the patients were males. The mean age of the patients was 66 years. Most of the patients were hospitalized at the Department of Medicine. Many patients had chronic underlying conditions such as diabetes mellitus, heart diseases, cancer, chronic renal diseases, receiving immunosuppressive agents, pulmonary diseases, chronic liver diseases. Eighty-seven percent of the patients received antibiotics prior to receiving imipenem/cilastatin. The general characteristics of the patients in both groups were not significantly different.

The infections of the patients in the original imipenem/cilastatin group and the generic imipenem/ cilastatin group are shown in Table 2. Hospital-acquired infections were observed in 81% to 84% of the patients. Nearly all patients had clinical features of infections. The common sites of infections were respiratory tract, urinary tract, skin and skin structures, and blood stream. Unknown site of infection was found in 9% to 10% of the patients. Microbiological documented infections were observed in 68% to 73% of the patients. The common causative agents of infections were *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. All isolates of extended-spectrum-beta-lactamase producing *E. coli* and *K. pneumoniae* were susceptible to imipenem/ cilastatin. *P. aeruginosa* isolates were susceptible to imipenem in 84.8% and 82.9% of the patients in the original imipenem/cilastatin group and the generic imipenem/cilastatin group, respectively. *Acinetobacter baumannii* isolates were susceptible to imipenem in 65.5% and 60% of the patients in the original imipenem/ cilastatin group and the generic imipenem/cilastatin group, respectively. The characteristics of infections

Table 1. General characteristics of the patients

	Original Imipenem/ cilastatin (n = 300)	Generic Imipenem/ cilastatin (n = 300)	p-value
Gender			
Male	150 (50%)	154 (51.3%)	0.81
Female	150 (50%)	146 (48.7%)	
Age (yr.)			
Mean (SD)	66.10 (17.8)	66.58 (18)	0.93
Median	70	70	
Department			
Medicine	235 (78.3%)	221 (73.7%)	0.21
Surgery	58 (19.3%)	65 (21.7%)	
Others	7 (2.3%)	14 (4.7%)	
Underlying Diseases			
Diabetes Mellitus	111 (37.0%)	119 (39.7%)	0.56
Heart Diseases	111 (37.0%)	108 (36.0%)	0.87
Cancer	99 (33%)	110 (36.7%)	0.39
Chronic Renal Diseases	67 (22.3%)	54 (18.0%)	0.22
Immunosuppressive	32 (10.7%)	36 (12.0%)	0.7
Pulmonary Diseases	28 (9.3%)	30 (10.0%)	0.89
Chronic Liver Diseases	26 (8.7%)	20 (6.7%)	0.44
HIV Infections	5 (1.7%)	4 (1.3%)	1.00
Previous Use of antibiotics			
No	38 (12.7%)	37 (12.3%)	1.00
Yes	262 (87.3%)	263 (87.7%)	

Table 2. Infections in the patients who received imipenem/ cilastatin

	Original Imipenem/ cilastatin (n = 300)	Generic Imipenem/ cilastatin (n = 300)	p-value
Type of Infection			
Community-acquired	47 (15.7%)	54 (19.7%)	0.39
Hospital-acquired	253 (84.3%)	244 (81.3%)	
Clinically Documented Infections			
No	5 (1.7%)	3 (1.0%)	0.73
Yes	295 (98.3%)	297 (99.0%)	
Site of Infection			
Respiratory Tract	120 (40.0%)	139 (46.3%)	0.14
Genitourinary Tract	97 (32.3%)	96 (32.0%)	1.00
Skin & Soft tissue	21 (7.0%)	21 (7.0%)	1.00
Intra-abdominal Infections	24 (8.0%)	26 (8.7%)	0.88
Bacteremia	27 (9%)	24 (8%)	0.77
Others	2 (0.7%)	6 (2%)	0.29
Unknown	31 (10.3%)	26 (8.7%)	0.58
Microbiologically Documented Infections			
No	97 (32.3%)	81 (27.0%)	0.18
Yes	203 (67.7%)	219 (73.0%)	
Causative Organism			
E.coli (ESBL-ve)	14 (4.7%)	21 (7.0%)	0.3
E.coli (ESBL+ve)	64 (21.3%)	62 (20.7%)	0.92
K.pneumoniae (ESBL-ve)	14 (4.7%)	22 (7.3%)	0.23
K.pneumoniae (ESBL+ve)	37 (12.3%)	43 (14.3%)	0.55
Pseudomonas aeruginosa	33 (11.0%)	35 (11.7%)	0.9
Acinetobacter baumannii	26 (8.7%)	30 (10.0%)	0.67
MSSA	3 (1.0%)	8 (2.7%)	0.22
MRSA	12 (4.0%)	7 (2.3%)	0.35
Enterococcus spp	-	1 (0.3%)	1.00

and causative agents of infections of the patients in both groups were not significantly different.

Eighty-six to 88% of the patients received imipenem/cilastatin according to the following indications: 1) confirmed or suspected infection due to *P. aeruginosa*, 2) infection due to pathogen resistant to cephalosporins, aminoglycosides, fluoroquinolones, beta-lactam plus beta-lactamase inhibitor, 3) severe infection due to ESBL-producing pathogens, 4) empiric therapy for febrile neutropenia. The indications of imipenem/cilastatin of the patients in both groups were not significantly different as shown in Table 3.

The dosage and duration of imipenem/ cilastatin therapy are shown in Table 4. The average dose of imipenem/cilastatin was 1.2 grams and the mean duration of treatment was 8 days. The dosage and duration of imipenem/cilastatin therapy of the patients in both groups were not significantly different.

The concomitant antibiotics are shown in Table 5. The concomitant antibiotics were given to 25% to 32% of the patients. The common concomitant antibiotics were glycopeptide, colistin and aminoglycoside. The rates of concomitant antibiotics given to the patients in both groups were not significantly different.

The outcomes of imipenem/cilastatin therapy are shown in Table 6 and Table 7. The overall favorable outcomes in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 65% and 58.7% respectively (absolute difference 6.3%, 95% CI -1.4% to 14%). Cure rates of infections in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 35% and 28.7% respectively (absolute difference 6.3%, 95% CI -1.1% to 13.7%). Super-infection rates in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 4.7% and 9% respectively (absolute difference -4.3%, 95% CI -8.5% to 0.3%). Mortality due to infections in the original imipenem/cilastatin and the generic imipenem/cilastatin

Table 3. Indications of imipenem/cilastatin

	Original Imipenem/ cilastatin (n = 300)	Generic Imipenem/ cilastatin (n = 300)	p-value
Indication of imipenem/cilastatin			
No	35 (11.7%)	43 (14.3%)	0.40
Yes	265 (88.3)	257 (85.7%)	
- Confirmed or suspected infection due to *P.aeruginosa*	44 (14.7%)	56 (18.7%)	0.31
- Infection due to pathogen resistant to cephalosporins, aminoglycosides, fluoroquinolones, beta-lactam + beta-lactamase inhibitor	97 (32.7%)	80 (26.7%)	0.15
- Severe infection due to ESBL-producing pathogens	97 (32.3%)	97 (32.3%)	1.00
- Empiric therapy for febrile neutropeni	27 (9.0%)	24 (8.0%)	0.77

Table 4. Dosage and duration of imipenem/cilastatin therapy

	Original Imipenem/ cilastatin (n = 300)	Generic Imipenem/ cilastatin (n = 300)	p-value
Dosage of Imipenem/cilastatin (g per day) Mean $\pm$ SD	1.23 $\pm$ 0.53	1.24 $\pm$ 0.63	0.73
Duration of Imipenem/cilastatin (day) Mean (SD)	8.04 (6.2)	8.09 (6.6)	0.95

Table 5. Concomitant antibiotics

	Original Imipenem/ cilastatin (n = 300)	Generic Imipenem/ cilastatin (n = 300)	p-value
Concomitant Antibiotic			
No	205 (68.3%)	223 (74.3%)	0.13
Yes	95 (31.7%)	77 (25.7%)	
Glycopeptides	47 (15.7%)	40 (13.3%)	0.49
Colistin	12 (4%)	12 (4%)	1.00
Aminoglycosides	12 (4%)	10 (3.3%)	0.83
Beta-lactams	9 (3%)	8 (2.7%)	1.00
Fluoroquinolones	9 (3%)	10 (3.3%)	1.00
Others	16 (5.3%)	12 (4%)	0.56

groups were 18.3% and 21.3% respectively (absolute difference -3%, 95% CI -9.4% to 3.4%). Overall mortality in the original imipenem/cilastatin and the generic imipenem/cilastatin groups were 35.3% and 43% respectively (absolute difference -7.7%, 95% CI -15.3% to 0.1%). The occurrence of adverse events in the patients in both groups was not significantly different.

Discussion

Imipenem/cilastatin is administered intravenously and bioequivalence study of the generic imipenem/cilastatin is not required for drug registration in Thailand. Imipenem/cilastatin is indicated in serious life-threatening infections and therapeutic equivalence of generic imipenem/cilastatin should be

Table 6. Outcomes of imipenem/cilastatin therapy

	Original Imipenem/ cilastatin (n = 300)	Generic Imipenem/ cilastatin (n = 300)	p-value
Clinical Outcome			
Cure of infection	105 (35.0%)	86 (28.7%)	0.09
Improvement of Infection	90 (30.0%)	90 (30.0%)	1.00
Worsening or persistence of Infection	50 (16.7%)	60 (20.0%)	0.34
Death due to infection	55 (18.3%)	64 (21.3%)	0.41
Microbiological outcome			
eradication	147 (49.0%)	133 (44.3%)	0.29
Persistence	63 (21.0%)	60 (20%)	0.84
Super-infections	14 (4.7%)	27 (9%)	0.05
Undetermined	76 (25.3%)	80 (26.7%)	0.60
Length of Hospital Stay, d.			
Mean (SD)	28.7 (30.3)	28.9 (28.5)	0.93
Median	20	20.5	
Status at Hospital Discharge			
Alive	191 (63.7%)	168 (56.0%)	0.06
Against advice	3 (1.0%)	3 (1.0%)	1.00
Death	106 (35.3%)	129 (43.0%)	0.06
Adverse Effect			
Antibiotic Allergy	1 (0.3%)	5 (1.7%)	0.12
Antibiotic-Associated Colitis	3 (1%)	2 (0.7%)	0.61
Seizure	1 (0.3%)	-	1.00

Table 7. Summary of effectiveness of therapy with imipenem/cilastatin

	Original Imipenem/ cilastatin	Generic Imipenem/ cilastatin	Absolute Difference (95% CI)	Relative Difference
Overall Favorable Response	65%	58.7%	6.3% (-1.4% to 14%)	9.6%
Cure	35%	28.7%	6.3% (-1.1% to 13.7%)	18%
Super-infections	4.7%	9%	-4.3% (-8.5% to 0.3%)	47.7%
Mortality due to infections	18.3%	21.3%	-3% (-9.4% to 3.4%)	14.1%
Overall Mortality	35.3%	43%	-7.7% (-15.3% to 0.1%)	21.8%

demonstrated before it could be substituted for original imipenem/cilastatin. Although the randomized controlled trial of generic imipenem/cilastatin is ideal for assessing a therapeutic equivalence, it is not feasible because the study needs a large number of patients, has a very high cost and requires a long duration of study. Moreover, the data on therapeutic equivalence of generic drugs from randomized controlled trials are not required for drug registration with Thai FDA. Therefore, drug utilization data on effectiveness and safety of generic imipenem/cilastatin at Siriraj Hospital were collected and compared with the original drugs to replace a prospective randomized controlled study. We collected the data from 300 patients who received generic imipenem/ cilastatin and 300 patients who received original imipenem/cilastatin because it was estimated

that a favourable response rate of the patients who received original imipenem/cilastatin was 70%[17-24] and the generic imipenem/cilastatin should have favorable response rate of $\geq$ 60% to declare a non-inferiority.

There were more patients who received original imipenem/cilastatin during June to December 2007 and more patients who received generic imipenem/cilastatin during January to September 2008 because the policy of the government healthcare insurance schemes stating the hospitalized patients should receive generic drugs if such drugs were available, if the patients wanted to have their healthcare cost covered by the government healthcare insurance. This observation might be a confounder for the study results. Nonetheless, the characteristics of the patients in terms of patients' demographics, type of infections, type of causative agents, resistance profiles of the organisms, dose and duration of imipenem/cilastatin, prior antibiotics, concomitant antibiotics were comparable between both groups. However, we found that the overall favorable outcome in the original imipenem/cilastatin group was only 65%. The first explanation was the mean dose of imipenem/cilastatin used in the patients in both groups of 1.2 grams per day was low when compared with a recommended dose of 2 grams per day. The dose of imipenem/cilastatin was low because most of the patients were aged 60 years or older and 20% of them had renal impairment. Therefore, imipenem/cilastatin dosing had to be reduced and thus the plasma concentrations of imipenem might be inadequate to treat infections since it was recently shown that 2-hour infusions of 1 gram of imipenem/cilastatin every 6 hours were needed to provide plasma concentrations above the MIC of 4 mg/L for 60% of a 6-hour interval in patients with ventilator-associated pneumonia[25]. The second explanation was approximately 10% of the patients were infected with documented imipenem-resistant bacteria *i.e.* imipenem-resistant *A. baumannii* and MRSA. Although the point estimate of a difference in overall favourable response rates between the original imipenem/cilastatin group and the generic imipenem/cilastatin group was less than 10%, the upper limit of 95% confidence interval of the difference in overall response rate was up to 14%. A smaller absolute difference in overall favourable response rate than 6.3% should be observed and many more patients are needed to be enrolled to the study in order to demonstrate a 95% confidence interval limit of a difference of a clinical outcome within $\pm$ 10%. Similar observations were also noted in the cure rates of infections and overall mortality in the generic imipenem/cilastatin group which showed that the upper limit of 95% confidence interval of the differences was greater than 10%. The reason for observing a trend toward therapeutic non-equivalence of generic imipenem/cilastatin should be explored. It should be kept in mind that the results of this study were from the treatment of the patients with a specified generic imipenem/cilastatin (Yungjin^{R}) and the results of this study can not be generalized to other generic imipenem/cilastatin products.

In conclusion, generic imipenem/cilastatin (Yungjin^{R}) showed a trend for therapeutic non-equivalence to original imipenem/ cilastatin because the upper limits of 95% confidence interval of differences of several important clinical outcomes were more than 10%.

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ความเท่าเทียมของประสิทธิผลของยาสามัญ Imipenem/Cilastatin ในการรักษาผู้ป่วยที่มีการติดเชื้อที่โรงพยาบาลศิริราช

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***บทนำ**: ยาสามัญ imipenem/cilastatin หลายขนานมีใช้ในประเทศไทยตั้งแต่ พ.ศ. 2550 โดยโรงพยาบาลศิริราชได้นำยาสามัญ imipenem/cilastatin (ชื่อการค้า Yungin) มาใช้ในโรงพยาบาลศิริราชตั้งแต่ พ.ศ. 2550 ยา imipenem/cilastatin มีข้อบ่งใช้ที่สำคัญคือการรักษาการติดเชื้อรุนแรงในโรงพยาบาล ดังนั้นยาสามัญ imipenem/cilastatin ต้องมีประสิทธิผลไม่แตกต่างจากยาต้นแบบ imipenem/cilastatin การศึกษานี้มีวัตถุประสงค์เพื่อทราบประสิทธิผลของยาสามัญ imipenem/cilastatin ในการรักษาผู้ป่วยที่มีการติดเชื้อในโรงพยาบาลศิริราช*

***วัสดุและวิธีการ**: วิเคราะห์เวชระเบียนผู้ป่วยที่รับไว้รักษาในโรงพยาบาลศิริราช ที่ได้รับการรักษาด้วยยาต้นแบบ imipenem/cilastatin หรือยาสามัญ imipenem/cilastatin อย่างน้อย 48 ชั่วโมงกลุ่มละ 300 ราย ตั้งแต่มิถุนายน พ.ศ. 2550 ถึง กันยายน พ.ศ. 2551 โดยมีสมมติฐานว่าการรักษาด้วยยาสามัญ imipenem/cilastatin มีประสิทธิผลแตกต่างจากยาต้นแบบ imipenem/cilastatin ไม่เกิน 10%*

***ผลการศึกษา**: ลักษณะทั่วไป ลักษณะของการติดเชื้อ ชนิดของเชื้อก่อโรค และยาต้านจุลชีพที่ผู้ป่วยได้รับมาก่อนไม่แตกต่างกันระหว่างผู้ป่วยทั้งสองกลุ่ม ประสิทธิผลของการรักษาโดยรวมของผู้ป่วยที่ได้รับยาต้นแบบ imipenem/cilastatin และยาสามัญ imipenem/cilastatin คือ 65% และ 58.7% ตามลำดับ (ความแตกต่าง 6.3%, 95% CI -1.4% ถึง 14%) อัตราหายจากการติดเชื้อของผู้ป่วยที่ได้รับยาต้นแบบ imipenem/cilastatin และยาสามัญ imipenem/cilastatin คือ 35% และ 28.7% ตามลำดับ (ความแตกต่าง 6.3%, 95% CI -1.1% ถึง 13.7%) อัตราการติดเชื้อซ้ำเติมของผู้ป่วยที่ได้รับยาต้นแบบ imipenem/cilastatin และยาสามัญ imipenem/cilastatin คือ 4.7% และ 9% ตามลำดับ (ความแตกต่าง -4.3%, 95% CI -8.5% ถึง 0.3%) อัตราตายจากการติดเชื้อของผู้ป่วยที่ได้รับยาต้นแบบ imipenem/cilastatin และยาสามัญ imipenem/cilastatin คือ 18.3% และ 21.3% ตามลำดับ (ความแตกต่าง -3%, 95% CI -9.4% ถึง 3.4%) อัตราตายรวมของผู้ป่วยที่ได้รับยาต้นแบบ imipenem/cilastatin และยาสามัญ imipenem/cilastatin คือ 35.3% และ 43% ตามลำดับ (ความแตกต่าง -7.7%, 95% CI -15.3% ถึง 0.1%) อัตราการเกิดผลข้างเคียงในผู้ป่วยทั้งสองกลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญ*

***สรุป**: ประสิทธิผลโดยรวมของยาสามัญ imipenem/cilastatin (Yungjin) ในการรักษาผู้ป่วยที่มีการติดเชื้อในโรงพยาบาลศิริราชแตกต่างจากยาต้นแบบ imipenem/cilastatin (Tienam) น้อยกว่า 10% แต่ประสิทธิผลของยาสามัญ imipenem/cilastatin มีแนวโน้มว่าไม่เท่าเทียมกับยาต้นแบบ imipenem/cilastatin เนื่องจากค่าด้านสูงของความเชื่อมั่นร้อยละ 95 ของความแตกต่างของผลลัพธ์หลายชนิดของการรักษาของผู้ป่วยที่ได้รับยาสามัญ imipenem/cilastatin แตกต่างจากผู้ป่วยที่ได้รับยาต้นแบบ imipenem/cilastatin มากกว่า 10%*