RobotReviewer report

Once-Daily Plazomicin for Complicated Urinary Tract Infections

Risk of bias table

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Wagenlehner FM, 2019	RCT	27	+	+	?	?

Characteristics of studies

Wagenlehner FM, 2019

Population	1. Eligible patients were 18 years of age or older and had a creatinine clearance of more than 30 ml per minute, pyuria, and clinical symptoms of a complicated UTI or acute pyelonephritis that would require at least 4 days of intravenous therapy with an antibiotic agent. 2. m e dicine all population, composite cure at the test-of-cure visit was assessed in prespecified subgroups de- fined according to geographic region (region 1 or 2), baseline diagnosis (complicated UTI or acute pyelonephritis), presence of bacteremia, treatment received (intravenous only or intravenous plus oral), presence of indwelling catheter (yes or no), and previous antibiotic use (yes or no) and in post hoc subgroups defined according to age (<65 or ,â•65 years), renal function (creatinine clearance ,â§60 ml per minute or >60 ml per min- ute), and sex.
Intervention	1. Patients were assigned to receive plazomicin (15 mg per kilogram of body weight once daily) or meropenem (1 g every 8 hours), administered intravenously, with the option for oral step-down therapy after a minimum of 4 days of intrave- nous therapy, for a total of 7 to 10 days of therapy. 2. Randomization and Treatment Patients were randomly assigned in a 1:1 ratio to receive plazomicin or meropenem. 3. The mean duration of intravenous therapy was 5.5 days in each group; the mean duration of intrave- nous plus oral therapy was 9.2 days in the plazo- micin group and 8.9 days in the meropenem group.
Outcomes	1. Clinical cure was defined as a reduction in severity (at day 5 and at the end of intravenous therapy) or complete resolution (at the test-of-cure visit) of all core symptoms with no new symptoms or as a return to the patient's status before development of the UTI, with no use of nontrial antibiotics for the current complicated UTI. 2. Additional end points assessed in the micro- biologic modified intention-to-treat

population were clinical cure and microbiologic eradication at day 5, at the end of intravenous therapy (within 24 hours after the last dose of intrave- nous trial drug and before oral therapy), at the test-of-cure visit, and during late follow-up (days 24 to 32); and microbiologic response at the test- of-cure visit according to baseline pathogen.

3. Clinical cure was defined as a reduction in severity (at day 5 and at the end of intravenous therapy) or complete resolution (at the test-of-cure visit) of all core symptoms with no new symptoms or as a return to the patient's status before development of the urinary tract infec- tion (UTI).

Bias	Judgement	Support for judgement
Random sequence generation	low	1. Randomization and Treatment Patients were randomly assigned in a 1:1 ratio to receive plazomicin or meropenem. 2. The microbiologic modified intention-to-treat population included all patients who underwent randomization, received at least one dose of the assigned trial drug, and had at least one qualifying baseline pathogen that was susceptible to meropenem and that had a minimum inhibitory concentration (MIC) for plazomicin of 4 Œºg per milliliter or less. 3. Randomiza- tion was performed by the site pharmacist or designated staff member according to a prespeci- fied randomization schedule.
Allocation concealment	low	1. The sponsor, investigators, trial staff participating in patient care or clinical evaluations, and patients were unaware of the group assignments. 2. Randomization and Treatment Patients were randomly assigned in a 1:1 ratio to receive plazomicin or meropenem. 3. Randomiza- tion was performed by the site pharmacist or designated staff member according to a prespeci- fied randomization schedule.
Blinding of participants and personnel	high/unclear	1. The sponsor, investigators, trial staff participating in patient care or clinical evaluations, and patients were unaware of the group assignments. 2. Randomiza- tion was performed by the site pharmacist or designated staff member according to a prespeci- fied randomization schedule. 3. Desig- nated staff members who prepared the trial drugs had knowledge of the group assignments.
Blinding of outcome assessment	high/unclear	1. The sponsor, investigators, trial staff participating in patient care or clinical evaluations, and patients were unaware of the group assignments. 2. This category includes hypoacusis and tinnitus; the events were identified in a blinded review and were classified ac- cording to the preferred terms in MedDRA. ¬ß 3. Data were collected by Achaogen and analyzed in collaboration with three of the academic authors.

References

1. Wagenlehner FM et al. Once-Daily Plazomicin for Complicated Urinary Tract Infections J Microbiol Immunol Infect 2019. 8(2); 729-740 PMID: 11561574