Dalbavancin Reduces Hospital Stay and Improves Productivity for Patients with Acute Bacterial Skin and Skin Structure Infections-- the ENHANCE Trial

Supplementary Materials

Supplementary Text: Inclusion/Exclusion criteria

Adults (≥18 years) admitted into the hospital, and those who met the clinical definition for ABSSSI (eg, diagnosis of cellulitis/erysipelas, wound infection, or major cutaneous abscess [1-3] were eligible for enrollment in either the pre- or post-period. Patients with known or suspected infection caused by susceptible isolates of Gram-positive microorganisms (eg, *Staphylococcus aureus* [including methicillin-susceptible and methicillin-resistant strains], *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus* group [including *S. anginosus, S. intermedius, S. constellatus]* and *Enterococcus faecalis* [vancomycin susceptible strains]) were included in the study. Patients were required to follow all study procedures (eg, were required to return to the hospital or designated clinical for scheduled visits, and were in contact with the study coordinator, through telephone communication). All patients provided written informed consent prior to study enrollment.

Patients that had a history of allergy to glycopeptide antibiotics, or had known or suspected Gram-negative infections including bacteremia, anaerobic infections, or fungemia, even in the presence of Gram-positive infection were excluded from the study. Patients were also excluded if they had severe or life-threatening infections (eg, gangrene, known or suspected necrotizing fasciitis, known or suspected osteomyelitis, septic arthritis or endocarditis, diabetic foot infection or decubitus or ischemic ulcer), or infections that likely required therapy with multiple antibiotics or more intensive care or observation (eg, infection due to abdominal surgery, post-operative wound infection, with the exception of skin and soft tissue laceration repair, perirectal or perineal infections, infections that required drainage or debridement in the operating room, hand and facial infections, or animal bites). In addition, patients with an unstable comorbidity at ED presentation (eg, severe sepsis, hemodynamic

instability, active immunocompromised/profound immunosuppression), injection drug users with a fever, those patients that had a positive pregnancy test result, or were currently breastfeeding, had severe neurological disorder leading to severe immobility or confinement to a wheelchair or bed, or had bilateral lower extremity involvement of the suspected infection were excluded from the study.

Supplementary Text: Study Definitions

The presence of systemic inflammatory response syndrome (SIRS) was compared at baseline and at Day 10. SIRS criteria were defined as having two or more of the following clinical characteristics: (1) Temperature of > 38.0°C or < 36.0°C; (2) heart rate > 90 beats/minute; (3) respiratory rate of > 20 breaths/minute or $PaCO_2$ < 32mmHg; (4) white blood cell count >12,000/microliter, or <4,000/microliter, or >10% immature cells (bands) [4]. Response to treatment was assessed at the day 10-14 visit and categorized as "Complete Response" (no pain, tenderness, nor fever, and the primary lesion area was less than 75 cm^2), "Partial Response" (no pain, tenderness, nor fever, and the primary lesion area was greater than or equal to 75 cm^2), or "Failure" (all other outcomes). The final model was adjusted for age and immunocompromised status, which was defined as any of the following conditions at baseline: connective tissue disease, diabetes mellitus, leukemia, or malignant lymphoma.

Supplementary References

1. US Department of Health and Human Services, US Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Guidance for industry. Acute bacterial skin and skin structure infections: developing drugs for treatment. Available at: https://www.fda.gov/files/Acute-Bacterial-Skin-and-Skin-Structure-Infections---Developing-Drugs-for-Treatment.pdf. Accessed May 15, 2019.

2. Pollack CV, Jr., Amin A, Ford WT, Jr., et al. Acute bacterial skin and skin structure infections (ABSSSI): practice guidelines for management and care transitions in the emergency department and hospital. J Emerg Med. 2015;48:508-19.
3. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59:e10-52.
4. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39:165-228.

Table S1. Schedule of Assessments at Baseline and Follow-up Visits

Assessment	Baseline Visit	Follow-up Visit Hour 48-72 (Telephone)	Follow-up Visit Day 10-14 (In-person or telephone at physician/patient discretion)	Final Visit Day 44 (Telephone)
Informed Consent	X			
Complete Examination (Medical history, Infection characteristics, Vital signs)	X			
Limited Examination (Limited physical exam of infection site and vital signs, safety monitoring)			X	
Patient Interview (Demographic data, Safety monitoring, Healthcare utilization)	X		X	X
Limited Patient Interview (Safety monitoring)		X		
Medical Chart Review (Safety monitoring, healthcare utilization)	X		X	X
SF-12	X		X	
WPAI:SPH			X	
Patient Satisfaction Survey			X	

Table S2. All variables considered for the multivariable model

Age
Gender (Male, Female)
Race (White/Caucasian, Black or African American, Other)
Employment status (Full-Time, Part-Time, None)
Insurance plan type (Private commercial plan, Government funded, Uninsured, Other)
Charlson Comorbidity Index
Lesion surface area (<75cm cm2, =>75 cm2 - 150 cm2, >150 cm2)
Infection type (Wound infection, Cellulitis/erysipelas, Abscess)
Prior health resource utilization (Yes, No, Unknown)
Prior antibiotic treatment failure (Yes, No, Unknown)
Presence of SIRS criteria (<2 or >=2)
Presence of recurrent infection in prior 6 months (Yes, No, Unknown)
Any health resource utilization in prior 3 months (Yes, No, Unknown)
Immunocompromised (Yes, No, Unknown)[a]

[a]Patients were defined as immunocompromised if they had evidence of any of the following at baseline: connective tissue disease, diabetes mellitus, leukemia, or malignant lymphoma.

Supplementary Text: Patient Satisfaction Survey

Antibiotics are commonly used to work against the germs that cause infection. Antibiotics can be given either by mouth (oral antibiotic therapy) or injected into the vein (intravenous (IV) antibiotic therapy).

1. In general, how would you rate your overall health?
Please select one response.

□ Excellent
□ Very good
□ Good
□ Fair
□ Poor

2. Where 0 is the worst experience possible and 10 is the best experience possible, what number would you use to rate your **satisfaction with how long you waited in the emergency department when you first received care** for your skin infection?
Please select one response.

□ 0 (Worst)
□ 1
□ 2
□ 3
□ 4
□ 5
□ 6
□ 7
□ 8
□ 9
□ 10 (Best)

3. Did you stay overnight in a hospital to treat your skin infection for one or more nights?
Please select one response.

□ Yes (If you marked "yes", please proceed to questions **4 and 5**)
□ No (If you marked "no", please proceed to question **6**)

4. Where 0 is the worst experience possible and 10 is the best experience possible, what number would you use to rate your **satisfaction with your hospital stay** for your skin infection**?**
Please select one response.

□ 0 (Worst)
□ 1
□ 2
□ 3
□ 4
□ 5
□ 6

□ 7
□ 8
□ 9
□ 10 (Best)

5. What factors contributed to your **dissatisfaction with your hospital stay** for your skin infection? Please select all that apply.

□ Hospital stay interfered with work/school
□ Hospital stay got in the way of performing my normal activities of daily living (caring for myself, housework, preparing meals, etc.)
□ Hospital stay got in the way of providing care to others (family members, dependents, etc.)
□ Hospital stay was expensive
□ Hospital stay did not provide adequate monitoring by healthcare providers
□ Hospital stay did not provide well trained healthcare providers
□ Hospital stay made me feel worse
□ Hospital stay made me feel concerned
□ Hospital stay was uncomfortable
□ Hospital stay disrupted my sleep
□ Other
□ I was not dissatisfied with my hospital stay

Intravenous (IV) antibiotic therapy can be used in the hospital, at an infusion center (either within the hospital or at a clinic), at a physician's office, or at home. In order to give IV antibiotic therapy, a small narrow tube (catheter) is used. The catheter is put into a vein using a needle, then the needle is removed and the catheter is secured to the body or arm. This helps to more easily administer IV antibiotics each day. Different types of catheters include peripherally inserted central catheters (PICC lines) and central catheters (central lines).

6. Did you receive IV antibiotic therapy to treat your skin infection? Please select one response.

□ Yes (If you marked "yes", please proceed to question **7** and continue the survey)
□ No (If you marked "no", please proceed to question 14)

7. Where 0 is the worst experience possible and 10 is the best experience possible, what number would you use to rate your **satisfaction with receiving IV antibiotic therapy**? Please select one response.

□ 0 (Worst)
□ 1
□ 2
□ 3
□ 4
□ 5
□ 6
□ 7
□ 8
□ 9

□ 10 (Best)

8. What factors contributed to your **satisfaction with receiving IV antibiotic therapy**? Please select all that apply.

□ IV antibiotic therapy allowed me to return to work/school
□ IV antibiotic therapy allowed me to return to performing my normal activities of daily living (caring for myself, housework, preparing meals, etc)
□ IV antibiotic therapy allowed me to return to providing care to others (family members, dependents, etc)
□ IV antibiotic therapy was affordable
□ IV antibiotic therapy was administered at appointments that I could schedule
□ IV antibiotic therapy was administered quickly once I arrived at my scheduled appointment
□ IV antibiotic therapy was administered at a healthcare setting that had convenient hours of operation
□ IV antibiotic therapy ensured regular monitoring by healthcare providers
□ IV antibiotic therapy was administered by skilled healthcare providers
□ IV antibiotic therapy made me feel better
□ IV antibiotic therapy allowed me to receive care for my skin infection at home
□ IV antibiotic therapy was convenient to administer to myself or from a caregiver at home
□ Other
□ I was not satisfied with receiving IV antibiotic therapy

9. What factors contributed to your **dissatisfaction with receiving IV antibiotic therapy**? Please select all that apply.

□ IV antibiotic therapy got in the way of work/school
□ IV antibiotic therapy got in the way of performing my normal activities of daily living (caring for myself, housework, preparing meals, etc.)
□ IV antibiotic therapy got in the way of providing care to others (family members, dependents, etc.)
□ IV antibiotic therapy was expensive
□ IV antibiotic therapy required me to make appointments
□ IV antibiotic therapy was administered at a healthcare setting that had limited hours of operation
□ IV antibiotic therapy required traveling to and from appointments
□ IV antibiotic therapy required me to spend time waiting to be seen by healthcare providers
□ IV antibiotic therapy took too long to administer
□ IV antibiotic therapy was administered too frequently (once a day, twice a day, etc.)
□ IV antibiotic therapy required having a peripherally inserted or central catheter IV line (PICC line or central line) inserted
□ IV antibiotic therapy caused an IV site infection (PICC line or central line infection)
□ IV antibiotic therapy made me feel worse (discomfort, diarrhea, nausea, rash, or other adverse effects)
□ IV antibiotic therapy was not adequately monitored by healthcare providers
□ IV antibiotic therapy was not administered by skilled healthcare providers
□ IV antibiotic therapy made me feel concerned
□ IV antibiotic therapy required a nurse/healthcare worker coming to my home
□ IV antibiotic therapy required administration to myself or from caregiver at home

□ Other
□ I was not dissatisfied with receiving IV antibiotic therapy

10. How often did receiving IV antibiotic therapy get in the way of performing your normal activities of daily living (caring for yourself, housework, preparing meals, etc.)? Please select one response.

□ None of the time
□ A little of the time
□ Some of the time
□ Most of the time
□ All of the time

11. How often were you concerned about receiving your IV antibiotic therapy? Please select one response.

□ None of the time
□ A little of the time
□ Some of the time
□ Most of the time
□ All of the time

Many different IV antibiotics can be used to treat skin infections, and may require more than one daily dose-also called 'infusions' or 'bags'.

12. Where 0 is the worst experience possible and 10 is the best experience possible, what number would you use to rate your **satisfaction with the number of IV antibiotic therapy infusions you received per day**? Please select one response.

□ 0 (Worst)
□ 1
□ 2
□ 3
□ 4
□ 5
□ 6
□ 7
□ 8
□ 9
□ 10 (Best)

13. Where 0 is the worst experience possible and 10 is the best experience possible, what number would you use to rate your **satisfaction with the average length of time that it took to administer each IV antibiotic therapy infusion**? Please select one response.

□ 0 (Worst)
□ 1
□ 2
□ 3
□ 4

□ 5
□ 6
□ 7
□ 8
□ 9
□ 10 (Best)

14. If you were treated again for a similar skin infection with IV antibiotic therapy, which of the following regimens would you prefer?
Please select one response.

□ One single IV antibiotic dose to complete your course of treatment
□ One or two daily IV antibiotic doses every day for 7-14 days to complete your course of treatment
□ One or two daily IV antibiotic doses for a few days, then oral antibiotics three or four times per day for the remaining 7-14 day course of treatment

15. If you were treated again for a similar skin infection with IV antibiotic therapy how long would you want to spend receiving each IV antibiotic therapy dose?
Please select one response.

□ About 30 minutes or less
□ About 1 hour
□ About 1.5 to 2 hours
□ About 3 hours or longer

16. If you were treated again for a similar skin infection, would you find value in a physician who recommended that you receive an IV antibiotic therapy that may shorten your hospital length of stay? Please select one response.

□ Definitely not
□ Probably not
□ Probably so
□ Definitely so