VA GLAHS ED-ASP Dalbavancin for Acute Bacterial Skin and Skin Structure Infections

Introduction

Dalbavancin is a second-generation lipoglycopeptide antibiotic that is approved for acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive microorganisms, including *Streptococcus spp., Enterococcus spp.* (excluding vancomycin-resistant VanA phenotype), and both methicillin-susceptible and -resistant *Staphylococcus aureus* (MSSA and MRSA). It exerts potent bactericidal activity by interfering with the final stages of peptidoglycan synthesis, thereby inhibiting cell wall formation. Due to its improved tissue penetration and extended half-life, convenient once-weekly dalbavancin dosing for ABSSSI treatment is an attractive option for selected patients.

Efficacy

In two pivotal phase 3 clinical trials (DISCOVER 1 and DISCOVER 2) that informed dalbavancin's approval, dalbavancin was shown to be as effective (e.g., non-inferior) as daily conventional therapy (e.g., IV vancomycin with optional switch to oral linezolid) for treatment of ABSSSI caused by Gram-positive bacteria.[a] The primary efficacy endpoint was early clinical response at 48-72 hours (e.g., cessation of spread of lesion and the absence of fever at 48 to 72 hours). Subsequent analysis of other randomized clinical trials (RCTs) has also demonstrated comparable efficacy between dalbavancin and standard of care therapies for ABSSSI with likely improved cost-effectiveness when dalbavancin is used.

[a]The single-dose strategy is equally efficacious and safe as the two-dose regimen (FDA approved as an acceptable alternative dosing strategy for ABSSSI treatment)

Safety

DISCOVER 1 and 2 demonstrated that dalbavancin was generally well tolerated and most common adverse reactions (incidence >2%) included nausea, headache, diarrhea, vomiting, rash, and pruritis. Of note, more patients treated with dalbavancin had ALT elevations greater than 3x upper limit of normal than patients treated with comparator therapy in the trials; rapid IV infusion can cause a reaction that resembles Red-Man Syndrome, including flushing of the upper body, urticaria, and pruritis.

Therapeutic Advantages

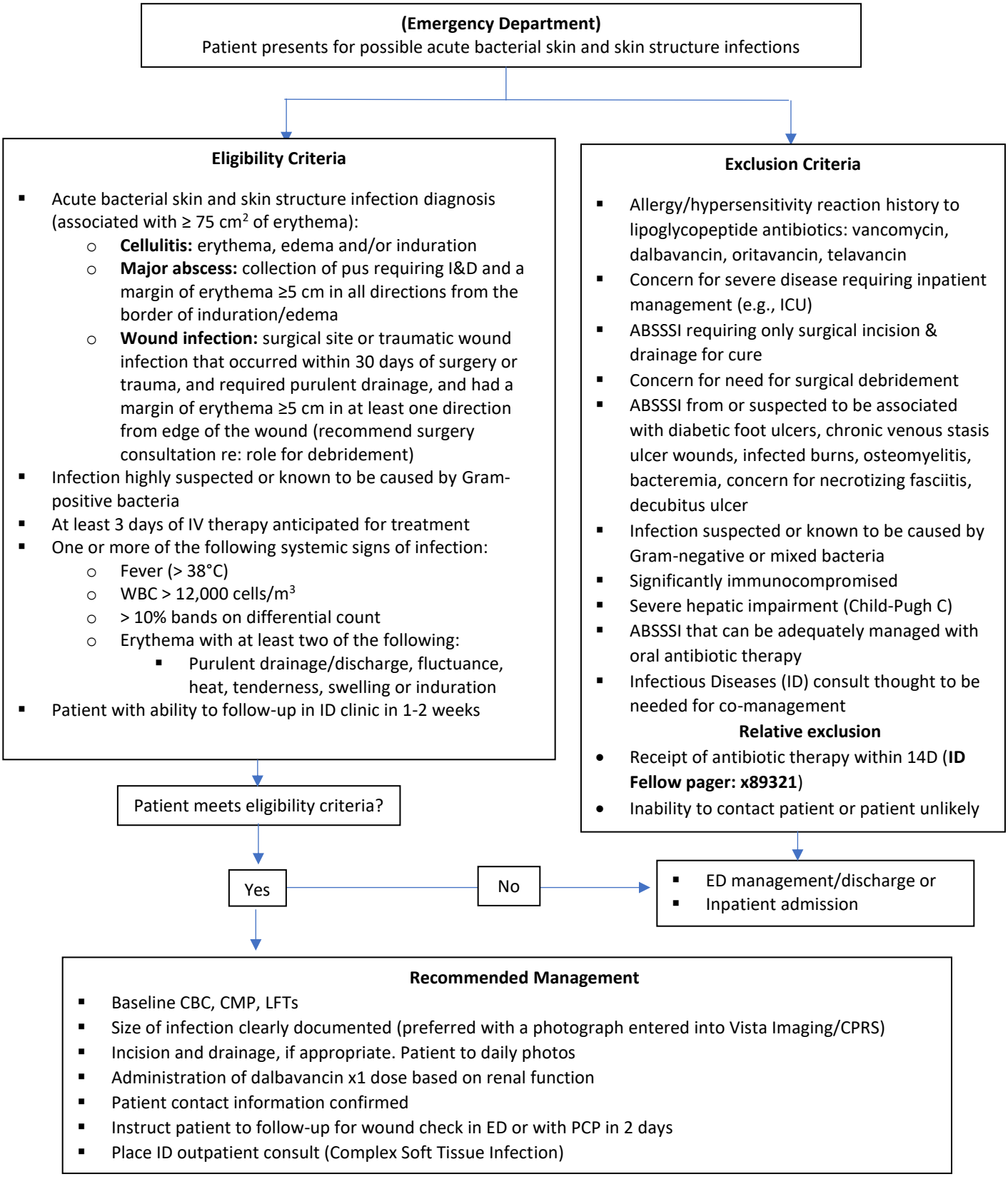
- Favorable safety profile
- Improved tissue penetration into skin, bone, peritoneal space, etc. (e.g., large volume of distribution, V_d: 7.85 to 15.7 L)
- Convenient weekly dosing (e.g., elimination/effective half-life of ~8.5 days)
- Short infusion time (e.g., 30 minutes)
- Therapeutic drug monitoring not routinely indicated
- Minimal risk for drug-drug interactions (e.g., dalbavancin is not a substrate, inhibitor, or inducer of CYP450 enzymes)
- Potential cost-savings for ABSSSI treatment (e.g., hospital re/admission avoidance, decreased LOS)

Dosing/Administration

Creatinine Clearance (CrCl)	Single-dose regimen[a]
$\geq$ 30 mL/min or receiving regular hemodialysis (HD)	1500mg
< 30 mL/min and not on HD	1125mg

[a]Administered by intravenous infusion over 30 minutes

Figure 1. Dalbavancin for Acute Bacterial Skin and Skin Structure Infections Workflow



References

1. Dalbavancin [package insert]. DALVANCE label (fda.gov). Irvine, CA: Allergan USA, Inc.; 2018. Accessed September 2022.
2. Dalbavancin. In: Micromedex Online. IBM Micromedex. Drug Result Page - Quick Answers - Dosing/Administration - Adult Dosing (micromedexsolutions.com). Updated 11/6/21; last accessed 9/9/22.
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(2): 147-159.
4. Boucher HW, Wilcox M, Talbot GH, et al. Once-weekly dalbavancin versus daily conventional therapy for skin infection. *N Engl J Med.* 2014;370(23): 2169-2179.
5. Dunne MW, Puttagunta S, Giordano P, et al. A randomized clinical trial of single-dose versus weekly dalbavancin for treatment of acute bacterial skin and skin structure infection. *Clin Infect Dis.* 2016;62(5):545-551.
6. Agarwal R, Bartsch SM, Kelly BJ, et al. Newer glycopeptide antibiotics for treatment of complicated skin and soft tissue infections: systematic review, network meta-analysis and cost analysis. *Clin Microbiol and Infect*. 2018;24(4):361-368.
7. Dunne MW, Talbot GH, Boucher HW, et al. Safety of dalbavancin in the treatment of skin and skin structure infections: a pooled analysis of randomized, comparative studies. *Drug Saf.* 2016;39(2):147-157.
8. Simonetti O, Rizzetto G, Molinelli E, et al. Review: a safety profile of dalbavancin for on- and off-label utilization. TCRM. 2021;Volume 17:223-232.