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Dalbavancin

A Viewpoint by Lawrence Eron

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The treatment of skin and soft tissue infections (SSTIs) is complicated by the increase in serious community-acquired meticillin-resistant *Staphylococcus aureus* (MRSA) infections. Vancomycin has been the gold standard for treatment, but newer antibacterials, such as daptomycin, tigecycline and linezolid, provide the clinician with additional choices. Because it is seldom necessary to hospitalize patients with SSTIs (unless they have sepsis syndrome, a limb-threatening infection or need surgery), outpatient parenteral antibacterial therapy (OPAT) of SSTIs may be an option. With the exception of linezolid, which is bioavailable when taken orally, the other antibacterials require an indwelling intravenous device as they must be administered parenterally. This can lead to phlebitis and occasionally sepsis.

Dalbavancin, a new glycopeptide antibacterial, has several features that suggest it will be very useful in the treatment of serious SSTIs caused by MRSA. It is highly bactericidal for MRSA as well as streptococcal infections. No dosage adjustment is necessary for severe hepatic impairment or mild renal impairment. It is well tolerated with few serious adverse effects. Finally, it has a prolonged half-life (8.5 days) which allows it to be administered once weekly.

There are several advantages to an antibacterial with such a long half-life. Its infrequent administration obviates the need for an indwelling intravenous device, which should shorten the length of hospitalization and would be especially useful for OPAT. OPAT patients receiving dalbavancin would not be required to learn daily self-administration of the antibacterial, as they could return to an infusion clinic once a week for administration.

The prolonged half-life of dalbavancin carries theoretical risks. Allergic reactions could be prolonged, as traces of the drug may remain in the body for months following its administration; however, during phase II and III trials such adverse effects were not encountered. Additionally, with a very slow decay in serum level, it is possible that selection of mutant clones resistant to dalbavancin may occur more easily as the serum level approaches the minimum inhibitory concentration of the organism. While no single-step mutations to high-level resistance to dalbavancin have been observed in early trials, multi-step mutations selected by this slow decay in serum level could lead to dalbavancin resistance. While its prolonged half-life will provide dalbavancin with a niche in the treatment of serious MRSA SSTIs, it will be necessary to conduct extensive phase IV trials to look for possible adverse effects. ▲