**Dalbavancin: a new IV antibiotic for skin infections**

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**Dalbavancin (Xydalba) is a new intravenous antibiotic for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults. This article discusses its properties, efficacy and adverse effects.**

**KEY POINTS**

- Dalbavancin is a lipoglycopeptide antibiotic active against Gram-positive organisms
- It is licensed for the treatment of acute bacterial skin and skin structure infections in adults but is likely to be reserved for severe infections
- It is administered by a single intravenous infusion of 1500mg or an infusion of 1000mg followed one week later by 500mg
- In clinical trials, dalbavancin was noninferior to vancomycin/linezolid in patients with severe infections and was associated with similar frequency and nature of adverse events
- The most frequent adverse effects of dalbavancin are headache, nausea and diarrhoea
- A course of dalbavancin costs £1676

**Indications and dosage**

Dalbavancin is licensed for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults. It is administered by intravenous infusion. It has a long elimination half-life (about 15 days), allowing a recommended dose regimen of a single 30-minute infusion of 1500mg or an infusion of 1000mg followed one week later by 500mg. Therapeutic drug monitoring is unnecessary.

No dose adjustment is recommended for older people, those with mild or moderate renal impairment, or those who are undergoing haemodialysis. The dose should be reduced to 1000mg (or 750mg plus 375mg a week later) in patients with chronic renal impairment and creatinine clearance <30ml/min who are not undergoing haemodialysis. No clinically significant drug interactions are known. No dose adjustment is recommended for patients with mild hepatic impairment but there is no clinical experience in moderate or severe hepatic impairment. There is no experience with dalbavancin in severely immunocompromised patients.

Dalbavancin has not been appraised by NICE. The Scottish Medicines
Efficacy

Intravenous dalbavancin (1000mg followed by 500mg one week later) has been compared with intravenous vancomycin (1000mg or 15mg/kg 12-hourly for three days, switching to oral linezolid 600mg 12-hourly if required to complete 10–14 days of treatment) in the phase 3 double-blind, placebo-controlled DISCOVER 1 and 2 trials, with supporting evidence from smaller studies.

The identical DISCOVER trials have been reported as a pooled analysis. Eligible outpatients and inpatients met criteria for severe skin and soft tissue infection (cellulitis, major abscess or wound infection), each associated with $\geq 75\text{cm}^2$ of erythema, for which at least three days of intravenous therapy was indicated, plus at least one systemic sign of infection, eg fever, raised white cell count, and at least two local signs such as purulent discharge, fluctuance, swelling or induration.

The primary endpoint was non-inferiority of dalbavancin (within 10% in each study) for early clinical response (after 48–72 hours) indicating treatment success, defined as both cessation of spread of the erythema associated with the infection and a temperature of $\leq 37.6^\circ\text{C}$ at three consecutive readouts, six hours apart. About 8% of patients in each treatment arm did not complete the scheduled treatment; 25% of participants were treated entirely as outpatients.

Early clinical response was achieved in 83% of patients treated with dalbavancin and 82% with vancomycin/linezolid in DISCOVER 1 and in 77% and 78% respectively in DISCOVER 2 (see Table 1). Dalbavancin was therefore noninferior to vancomycin/linezolid. In the pooled analysis, the outcome was the same in both treatment groups (80% early clinical response rate) and this was supported by investigators’ assessments. The most frequent reason for failure was missing temperature data.

Outcomes were also similar between the treatment groups for analysis by pathogen, co-morbidity (diabetes) and infection severity (as indicated by the systemic inflammatory response syndrome). In the pooled analysis, a successful clinical outcome occurred in 91% of patients treated with dalbavancin and 94% with vancomycin/linezolid for single S. aureus infections, 89% and 96% respectively for MRSA, and 95% and 85% for Streptococcus pyogenes.

Adverse effects

In the DISCOVER trials, there were no significant differences between dalbavancin and vancomycin/linezolid in the proportion of patients reporting any (12% vs 14%) or serious (0.3% vs 0.6%) treatment-related adverse events. In phase 2/3 clinical trials, the most frequent adverse events associated with dalbavancin were mild to moderate nausea (5.5%), headache (4.7%) and diarrhoea (4.4%) lasting one to two days; the corresponding figures for comparator treatments were 6.4%, 4.8% and 5.9%. In particular, no differences were apparent in blood and lymphatic disorders or renal adverse events. About 3% of patients in each treatment arm discontinued therapy due to adverse events.

Table 1. Proportion of patients reaching the primary endpoint of success rate at 48 to 72 hours after the initiation of therapy (ie early clinical response) in the DISCOVER 1 and DISCOVER 2 trials

<table>
<thead>
<tr>
<th></th>
<th>Dalbavancin n/N (%)</th>
<th>Vancomycin/linezolid n/N (%)</th>
<th>Absolute difference (95% CI) in percentage points</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISCOVER 1</td>
<td>240/288 (83.3)</td>
<td>233/285 (81.8)</td>
<td>1.5 (-4.6 to 7.9)</td>
</tr>
<tr>
<td>DISCOVER 2</td>
<td>285/371 (76.8)</td>
<td>288/368 (78.3)</td>
<td>-1.5 (-7.4 to 4.6)</td>
</tr>
<tr>
<td>Both trials</td>
<td>525/659 (79.7)</td>
<td>521/653 (79.8)</td>
<td>-0.1 (-4.5 to 4.2)</td>
</tr>
</tbody>
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References


Declaration of interests

None to declare.

Steve Chaplin is a medical writer specialising in therapeutics