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The OVIVA Trial: Oral versus intravenous antibiotics in the management of bone and joint infection - a multicentre open label randomised non-inferiority study.

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Background: Management of bone and joint infection commonly includes a prolonged course of intravenous antibiotics, but without clear evidence of an advantage over oral therapy. We set out to establish whether clinical outcomes are non-inferior in patients managed primarily with oral antibiotics as compared to intravenous antibiotics (ISRCTN91566927).

Material/methods: Adults presenting with bone, joint or orthopaedic metalware-associated infection, who had received ≤7 days of intravenous antibiotics following definitive surgery (or the start of planned curative therapy if managed conservatively), were randomised to either oral or IV antibiotics to complete the initial 6 weeks of therapy. The choice of agent was determined by an infection specialist. Adjunctive oral rifampicin and follow-on therapy beyond six weeks were permitted in either arm. The primary endpoint was definitive treatment failure within one year of randomisation, as assessed by a blinded endpoint committee. Secondary endpoints included SAEs, line complications, *C.difficile* diarrhoea, resource allocation and quality of life (EQ-5D). Emerging data are presented here; final results by randomisation arm will be available for presentation at ECCMID.

Results: Between June 2010-October 2015, 1054 participants, including 228 from a pilot study, were randomized across 26 UK sites; median age (IQR) was 60 (49,70) and 64% were male. The most common baseline surgical procedures were debridement of osteomyelitis in 322 (31%) participants, removal of orthopaedic device/joint implant in 302 (29%), DAIR in 247 (23%) and single-stage revision in 90 (9%). The lower limb was involved in 855 (81%) cases (hip 214, knee 248, foot 175, other 218), the upper limb in 102 (10%) and the spine in 72 (7%). Common co-morbidities included diabetes (19%) and smoking (13%). Histological confirmation of infection was available in 543 (52%) cases; in 409 (39%), no samples were submitted for histology. Microbiologically, 157 (15%) cases were culture-negative, and in 41 (4%) no samples were submitted for culture. *S.aureus,* coagulase-negative staphylococci and streptococci were identified in 381/1004 (38%), 273/1004 (27%) and 146/1004 (15%) respectively, and Gram-negative organisms in 220/1004 (22%). For those randomised to IV therapy, glycopeptides and cephalosporins were used in 214/521 (41%) and 173/521 (33%) respectively; for oral therapy, quinolones and penicillins were used in 191/523 (37%) and 83/523 (16%) respectively. The median (IQR) duration of hospitalisation was 13 (9,22) days, and 785/1049 (74%) patients continued antibiotic therapy beyond 6 weeks. 444 serious adverse events were reported in 284/1054 (27%) patients; 103/444 (23%) were graded as severe. Thirty-nine participants were withdrawn or lost to follow-up without having met a primary endpoint; complete case analysis will therefore include 1015 patients (96%).

Conclusions: If oral therapy proves non-inferior to IV therapy in bone and joint infection, potential gains are possible for length of hospital stay, complication rate, antimicrobial stewardship, patient convenience and treatment costs.