The study findings accord with European guidelines,[11] with a balanced recommendation for putting patients with ESBL-producing non-*E coli* infections or patients from an epidemic outbreak in single-bed rooms while also enforcing contact precautions. On the other hand, in an endemic situation, with most cases being ESBL-producing *E coli* infections, standard precautions might be enough, with no need for a single-bed room.[11]

The study by Kluytmans-van den Bergh and colleagues did not address the question of the role of standard precautions compared with contact precautions for controlling the spread of ESBL-producing Enterobacteriacae and whether the combination of contact precautions and placement in a single-bed room could be synergistic. Findings of a cluster-randomised study[3] showed that contact precautions were not superior to standard precautions for control of the spread of ESBL-producing Enterobacteriacae, confirming results of several observational, cohort, and before-and-after studies.[12] The fact that only 5% of ESBL-colonised wardmates later had a positive clinical culture in the study by Kluytmans-van den Bergh and colleagues further supports a horizontal approach, with high adherence to hand hygiene required for all patients, irrespective of ESBL-producing Enterobacteriacae status.

Among multidrug-resistant organisms, including meticillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus* spp, and emerging Gram-negative bacilli resistant to carbapenems, ESBL-producing Enterobacteriacae have not received enough attention. This study comes at the perfect time in view of the massive and widespread burden of these microorganisms.

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Enriching the antibiotic armamentarium for acute bacterial skin and skin structure infections

Omadacycline is a newly developed, once-daily, oral and intravenous aminomethylcycline with a broad spectrum of activity.[1] In 2018, the US Food & Drug Administration (FDA) approved omadacycline for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia on the basis of the results of two phase 3 randomised controlled trials (RCTs).[2,3]

To date, omadacycline has been shown to be non-inferior to linezolid in one RCT investigating an

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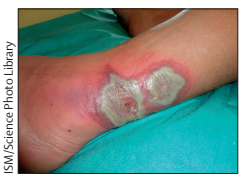
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intravenous-to-oral regimen in patients with ABSSSI (OASIS-1 study).[2,4] The Article by William O'Riordan and colleagues[5] in *The Lancet Infectious Diseases* provides interesting data about an omadacycline oral-only regimen in ABSSSI (OASIS-2 study). OASIS-2 had a similar design to the OASIS-1 non-inferiority trial (10% margin, 90% power), with the same primary efficacy endpoint of early clinical response based on objective reduction in lesion size at 48–72 h after the first dose, following US FDA guidance for industry.[6] The primary endpoint of investigator-assessed clinical response 7–14 days after the last dose was assessed in patients in the modified intention-to-treat population (ie, patients without solely Gram-negative pathogens at baseline) and clinically evaluable population (ie, modified intention-to-treat patients who had a qualifying infection as per study-entry criteria, received study drug, did not receive a confounding antibiotic, and had an assessment of outcome during the protocol-defined window).[7]

OASIS-2 was an oral-treatment-only trial in which patients were randomly assigned to receive omadacycline (two 450 mg once-daily doses over 48 h , then 300 mg once daily) or linezolid (600 mg twice daily) in the outpatient setting for 7–14 days. OASIS-2 corroborated the results of OASIS-1, with an integrated analysis of both trials showing that omadacycline was non-inferior to linezolid for all primary endpoints.[4] OASIS-1 showed that patients receiving either linezolid (600 mg twice daily) or omadacycline (100 mg twice daily for two doses, then 100 mg once daily) could be effectively switched from intravenous administration in the inpatient setting to oral outpatient treatment after at least 3 days of treatment.[2]

The strength of the OASIS trials was their ability to show omadacycline's consistent efficacy in the treatment of severe skin infections with large lesions (approximately four times larger than the minimum inclusion criteria of 75 cm^2) and in a population with high proportions of identified bacterial pathogens, including meticillin-resistant *Staphylococcus aureus* (MRSA). Furthermore, both studies followed US FDA guidance and reduced potential for confounding by minimising the use of other antibiotics within 72 h before the first trial dose.[6] OASIS-2 supports the use of omadacycline as an oral-only regimen, analysing early clinical response and post-therapy success, consistent with guidance and previous studies.[6–8]

OASIS-2 has some limitations. Compared with OASIS-1, OASIS-2 included only sites in the USA. Furthermore, the majority of patients were intravenous drug users. Although inclusion of intravenous drug users is common in RCTs assessing ABSSSI, patients included in OASIS-2 might not be representative of the general population with ABSSSI or of other countries. Intravenous drug use is a known risk factor for ABSSSI, particularly for abscess and MRSA. The over-representation of this population might explain a high proportion of infections caused by *S aureus*. Additionally, OASIS-2 was underpowered to conclude non-inferiority of omadacycline in clinically relevant subgroups (eg, type of skin infection or lesion size). Patients with various comorbidities and commonly encountered skin infections, such as chronic wound infections, were excluded, limiting the assessment of omadacycline in common real-world scenarios. Finally, the mandatory 7–10 days of therapy did not inform on the potential usefulness of omadacycline in short therapies, such as 6-day regimens that have been previously tested.[9]

Safety of oral omadacycline will require attention in real-world studies. Nausea and vomiting were more frequently associated with omadacycline than with linezolid during the first 2 days of treatment in the OASIS-2 study, when the patients received an increased dose, but were not associated with maintenance oral treatment or with intravenous therapy.[4,5] Moderate nausea was associated with omadacycline discontinuation in only one patient. If the good safety profile of omadacycline is confirmed in post-marketing studies, omadacycline might also be a valid alternative to linezolid in regimens where linezolid is contraindicated because of potential drug–drug interactions.

The OASIS population limits any speculation about the effects of omadacycline against Gram-negative bacteria. No oral options are currently available against multidrug-resistant Gram-negative bacteria, and the optimisation of their treatment is a global unmet clinical need. Omadacycline has a promising resistance profile, showing activity against extended-spectrum β-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*, as well as *Acinetobacter baumannii*.[10] New tetracyclines, mainly represented by omadacycline and eravacycline, on the basis of microbiological and pharmacological characteristics, could be potential treatment options

for treatment of Gram-negative antibiotic-resistant infections, not only in the setting of ABSSSI.

In conclusion, oral omadacycline adds to the armamentarium against ABSSSI pathogens, including MRSA, and might allow early discharge, with treatment management in outpatient settings, contributing to reducing the costs associated with hospitalisation.[11] The potential use of omadacycline in sequential therapy against difficult-to-treat pathogens, including tetracycline-resistant Gram-negative bacteria, extended-spectrum β-lactamase-producing Enterobacteriaceae, and *A baumannii* deserves further study in clinical trials.

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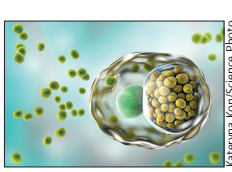
First genital chlamydia vaccine enters in-human clinical trial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Genital *Chlamydia trachomatis* infection and associated diseases remain a major global health burden, with an estimated 131 million new cases occurring annually.[1] In women, the risk of developing pelvic inflammatory disease increases when chlamydia ascends from the infected cervix to the uterus and fallopian tubes. Serious sequelae of pelvic inflammatory disease include tubal factor infertility, ectopic pregnancy, and chronic pelvic pain. Prospective studies have estimated that 10–15% of untreated chlamydia infections lead to symptomatic pelvic inflammatory disease, and 10–15% of women with symptomatic pelvic inflammatory disease, as well as many with subclinical pelvic inflammatory disease, will develop tubal factor infertility.[2,3] Despite the high prevalence of *C trachomatis* infection and associated pelvic inflammatory disease, the infection can provide a detectable level of natural immunity, as evidenced by decreased infection concordance between older sex partners and lower bacterial loads in individuals with a history of previous infection.[4] A recent study showed that young women in whom the infection was spontaneously cleared were able to resist reinfection, providing further evidence that protective adaptive immunity can be achieved.[5] However, chronic and repeated infections are common, illustrating the need for an efficacious vaccine.

In *The Lancet Infectious Diseases*, Sonya Abraham and colleagues[6] report the safety and immunogenicity results from the first phase 1 study of a genital *C trachomatis* vaccine candidate, CTH522, containing engineered heterologous immunorepeats from segments of the chlamydial major outer membrane protein (MOMP). Participants received CTH522 adjuvanted with either liposomal CAF01 or aluminium hydroxide three times via intramuscular injection, followed by two unadjuvanted intranasal inoculations. Both vaccines were well tolerated