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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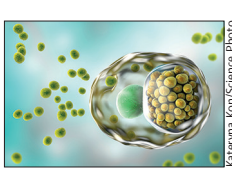
First genital chlamydia vaccine enters in-human clinical trial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Genital *Chlamydia trachomatis* infection and associated diseases remain a major global health burden, with an estimated 131 million new cases occurring annually.[1] In women, the risk of 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

and immunogenic, but CTH522:CAF01 induced more consistent cell-mediated interferon-γ responses, and higher serum antibody titres than CTH522 adjuvanted with aluminium hydroxide. The promising results obtained with the CTH522:CAF01 vaccine candidate should provide the impetus for phase 2 trials.

Interferon-γ-secreting CD4 T cells are key players in the protective immune response to chlamydia, an obligate intracellular bacterium that replicates within a protective vacuole inside epithelial cells, and vaccine-elicited CD4 T-cell immunity can be enhanced in the presence of chlamydia-specific IgG.[7,8] Although a robust systemic T-cell response was induced by CTH522:CAF01, we think efficacy will depend on effective trafficking of these protective cells to the cervix—the initial site of infection. This is a key point that was not examined in this phase 1 trial. Only the CAF01-adjuvanted vaccine induced mucosal IgA responses, and these responses required intranasal boosting. Studies in mice suggest that a robust CD4 T-cell response should protect from disease, but that antigen-specific IgA is dispensable for protection.[9] However, vaccine efficacy might require intranasal boosting for induction of memory T cells residing in the genital tract.[10] An intramuscular regimen that complements currently available human papillomavirus vaccines would be ideal for vaccine uptake, but future studies will dictate the need for intranasal booster doses.

Future clinical testing will require careful consideration of appropriate endpoints to ascertain efficacy. The use of chlamydia genital infection as a primary outcome would involve interval testing in placebo-treated versus vaccinated women. Although conceptually straightforward, women at highest risk for infection will need to be enrolled, and many will possibly have some pre-existing immunity from previous infections, given the high prevalence of chlamydia among sexually active adolescent girls and young women. Thus, careful evaluations of baseline immune response will be needed to ensure treatment groups are comparable. Data from mouse models indicate that partial immunity resulting from vaccination or from repeated infections alleviated by antibiotic treatment can prevent development of upper genital tract disease.[10,11] Upon challenge, mice exhibit a shorter duration of infection with lower bacterial burdens and reduced ascension. Thus, inclusion of disease endpoints could be valuable if sterilising immunity is not achieved in vaccinated women. However, many infected women with uterine and fallopian tube infection and inflammation are asymptomatic. In our view, non-invasive biomarkers of chlamydia upper genital tract infection and inflammation could be useful as additional endpoints for vaccine efficacy in the future.[12]

A vaccine for prevention of *C trachomatis* infection would have enormous public health and economic impact. Findings from this phase 1 trial might also help guide the development of vaccines for other mucosal pathogens. Although clinical vaccine testing for chlamydia is in its infancy, this trial suggests optimism for the future.

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