In addition to concerns about antibiotic resistance, oral tetracycline-class antibiotic use has been associated with inflammatory bowel disease (IBD),[114] pharyngitis,[179] *Clostridium difficile* infection,[180,181] and *Candida* vulvovaginitis. Outpatient antibiotic stewardship promotes appropriate antibiotic use in which patients receive the *right* dose of the *right* antibiotic at the *right* time for the *right* duration. The Centers for Disease Control and Prevention recommend outpatient antibiotic stewardship programs to include (1) commitment to optimizing antibiotic prescribing and patient safety, (2) implementation action for stewardship policy or practice, (3) tracking prescribing practices through clinician feedback or self-assessment, and (4) access to educational resources and expertise.[182] When treating acne with systemic antibiotics, we recommend concomitant use of BP and other topical therapies as a good practice statement to decrease risk of antibiotic resistance and to limit the duration of systemic antibiotic exposure. Oral antibiotics should not be used as monotherapy for acne treatment. Systemic antibiotic use should also be limited to the shortest duration possible, typically no more than 3-4 months, as recommended by international guidelines.[3,183,184] For patients who have inadequate response or contraindications to nonantibiotic therapies and may require longer courses of systemic antibiotics, consistent follow up and re-evaluation should limit systemic antibiotic use to the shortest duration and should maintain treatment endpoints with concurrent topical therapies during and after systemic antibiotic treatment.[185-189]

Doxycycline

We recommend doxycycline for acne treatment based on moderate certainty evidence from 5 studies (Table III and Supplementary Table XXXVI, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[114-118] Compared to vehicle at 4 months, a greater proportion of patients treated with doxycycline achieved IGA success in 2 RCTs (RR, 1.80 [1.17, 2.77]).[116,117] Treatment withdrawal due to adverse effects was more common with doxycycline compared to placebo in 3 trials (1.3% vs 0.3%; RR, 2.25 [0.38, 13.21]).[115-117] Doxycycline may cause gastrointestinal disturbances (15.7% vs 5.9%; RR, 2.56 [1.05, 6.25]),[115-117] including nausea, vomiting, and diarrhea; esophagitis, phototoxicity; and rarely intracranial hypertension. Taking doxycycline with food and adequate fluids in the upright position may reduce gastrointestinal side effects. Low-dose doxycycline (20 mg twice daily or 40 mg extended release daily) has demonstrated efficacy in patients with moderate inflammatory acne,[115] but there remains insufficient evidence comparing oral doxycycline at different dosages directly.[190]

We conditionally recommend doxycycline over azithromycin for acne treatment based on low certainty evidence from 4 studies (Table III and Supplementary Table XXXVII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[126-129] A greater reduction in total lesion counts was seen in doxycycline versus azithromycin at 12 weeks (MD in the change from baseline, −6.0 [-11.63, −0.37] in 1 RCT.[126] Azithromycin is a broad-spectrum macrolide antibiotic that covers respiratory and other infections; increasing azithromycin use could increase antibiotic resistance.

Minocycline

We conditionally recommend minocycline for acne treatment based on moderate certainty evidence from 5 studies and based on work group discussions related to uncommon potential treatment adverse effects (Table III and Supplementary Table XXXVIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[114,119-122] Compared to vehicle at 12 weeks, a greater proportion of patients treated with minocycline achieved IGA success in 2 RCTs (RR, 1.82 [1.28, 2.57]).[119-121] Adverse effects requiring treatment cessation were higher with minocycline compared to placebo in 2 RCTs (9.1% vs 1.0%; RR, 6.23 [1.20, 32.99]).[120,122] Oral minocycline confers similar common adverse effects as doxycycline. Despite moderate certainty of benefits over risks based on clinical trial evidence, the work group voted on a conditional recommendation due to concerns about rare potential adverse effects of minocycline, which include vertigo, autoimmune hepatitis, skin hyperpigmentation, drug-induced lupus, and hypersensitivity syndrome. As there is insufficient evidence comparing doxycycline and minocycline directly, the potential risks and benefits of each treatment option should be considered (Supplementary Table XXXIX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Moreover, oral minocycline monotherapy is not superior to topical BP 5% or erythromycin 2%/BP 5% in mild to moderate acne in 1 RCT (Supplementary Tables XL-XLII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[191] Available evidence is insufficient to develop a recommendation on the use of long-term minocycline monotherapy or in combination with tazarotene as maintenance therapy beyond 3-4 months over tazarotene gel alone (Supplementary Table XLIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[186]