

Appendix 2 (as supplied by the authors): Updated search for the period March 2013 to July 14, 2015, for studies pertaining to treatments recommended by these guidelines

| Year | Author and study title | Acne severity | Drug | Comparator | Randomization | Blinding (single, double) | ITT | Differences between groups | Trial size | N in each arm | Overall drop outs | Drop outs due to SEs | Drop outs due to inefficiveness | Week of evaluation | Δ in TL | Δ in IL | Δ in NIL | Comments | Consensus grade |
|------|--|-----------------|--|--|-------------------------|---------------------------|-----------|----------------------------|--------------------------|---------------|-------------------------|----------------------|---------------------------------|--------------------|---------|---------|---------------|---|------------------------|
| 2014 | Tan et al. A treatment for severe nodular acne: a randomized investigator-blinded, controlled, noninferiority trial comparing fixed-dose adapalene/benzoyl peroxide plus doxycycline vs. oral isotretinoin | severe, nodular | fixed-dose adapalene/BPO and doxy200, once daily | isotretinoin oral 0.5mg/kg for 4 weeks then 1mg/kg for 16 weeks, cumulative dose of 126mg/kg | RANU NI from SAS, 1:1 | single (investigator) | Yes, LOCF | No | 226 (217 in PP analysis) | 133 | 28 (doxy A/BPO) 17(iso) | 6(A/bPO) 4(A/bPO) | 1 (A/BPO) 0(iso) | 20 | N/A | N/A | N/A | was composite success (>=75% reduction of nodules, absence of safety issues) of 63.9% (A/BPO) vs 54.9%); single blind | A |
| 2014 | Jacobs et al. Systematic review on the rapidity of the onset of action of topical treatments in the therapy of mild-to-moderate acne vulgaris | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | [BPO] and [ada] make no difference, BPO> tretinoin, clinda/BPO > adap, Adap> tretinoin, clin/BPO =ada/BPO | A |
| 2014 | El-Latif. Intense pulsed light versus benzoyl peroxide 5% gel in treatment of acne | mild to severe | IPL | BPO5% | No, "randomly selected" | No | | | | | | | | | | | not conducted | not RCT, too short; many unclear details | NC (C, do not include) |
| 2013 | Mohd Nor et al. A systematic review of benzoyl peroxide for acne vulgaris | N/A | BPO | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | well designed; interesting conclusion: BPO may work but evidence are not firm | A |

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|------|--|------------------------------|------------------------|--------------------------------------|---------------------|--------------------------|-----|------------|-----|------------------------|-----|-----------------------|---|---|-------------------------------------|---|------------|------------|--|---|
| 2013 | Kar et al. Comparative study of oral isotretinoin versus oral isotretinoin + 20% salicylic acid peel in the treatment of active acne study of oral isotretinoin versus oral isotretinoin + 20% salicylic | mod to severe | oral 20mg isotretinoin | oral isotretinoin +20% sal acid peel | random number table | single (assessor) | ? | No | 60 | 30 | ? | ? | ? | ? | 16 | MASI score | MASI score | MASI score | hard to assess due to MASI score; 20 mg for 16 weeks is not a the routine regimen | B |
| 2014 | Webster et al. Results of a Phase III, double-blind, randomized, parallel-group, non-inferiority study evaluating the safety and efficacy of isotretinoin-Lidose in patients with severe recalcitrant nodular acne | | isotretinoin-lidose | generic isotretinoin | block | double | yes | no | 925 | 464 liose, 461 generic | 130 | 19 lidose, 15 generic | ? | ? | 16 | 76.9 % reduction in nodules in lidose, 81% with generic | | | noninferioirty | A |
| 2013 | Bettoli et al. Maintenance therapy for acne vulgaris: efficacy of a 12-month treatment with adapalene-benzoyl peroxide after oral isotretinoin and a review of the literature. | severe, recalcitrant nodular | adapalene BPO | oral isotretinoin | None | open label, not compared | no | not stated | 69 | | 1 | none | ? | ? | q12 weeks, 12 mos total, q 12 weeks | n/a | n/a | n/a | relapse in 3%, a few others did not meet criteria for relapse and treated with addition of clindamycin. prob should not have been graded | C |

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| 2014 | Rademaker et al. Isotretinoin 5 mg daily for low-grade adult acne vulgaris--a placebo-controlled, randomized double-blind | low grade | 5mg isotretinoin | placebo | yes | RCT 16 weeks then open label 16 weeks | yes, LOCF | no | 60 | 29 | 15 | 3 | ? | weekly visit to 36 weeks, then final visit at 42 weeks: at 16 weeks evaluation | 3.2 at 16 weeks vs 8.6 in placebo | not stated | not stated | Adds to evidence concerning low dose isotretinoin | A |
| 2014 | Koo et al. Meta-analysis comparing efficacy of antibiotics versus oral contraceptives in acne vulgaris | any? | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | not a systematic review; only searched pubmed; did not evaluate bias, not sure why they excluded crossover, unless stats issue | B |
| 2014 | Faghihi et al. The efficacy of 5% dapsone gel plus oral isotretinoin versus oral isotretinoin alone in acne vulgaris: A randomized double-blind study. | mod to severe | oral isotretinoin | oral isotretinoin + 5% dapsone gel | yes but not sure how | double blind | yes | No | 58 | 29 | 0 | 0 | 0 | 12 | not stated | change is significant, but not stated | change is significant, but not stated | cannot add anything because we don't know if it was a 10% reduction | B |
| 2014 | Application of intense pulsed light in the treatment of dermatologic disease: a systematic review | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | IPL alone: studies at 8weeks eval, graded 2b; IPL-PDT graded 1b | A |

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| 2014 | Murray et al. The phototoxic and photoallergy potential of clindamycin phosphate 1.2%/tretinoin 0.025% gel for facial acne: results of two single-center, evaluator-blinded, randomized, vehicle-controlled phase 1 studies in healthy volunteers | N/A | CTG: 1.2% 0.025 % | vehicle | all patients had vehicle, CTG and blank patch | single (assessor) | No | N/A | 37 phototoxic, 58 photoallergic | N/A | 1 phototoxic, 8 photoallergic study | 0 phototoxic; 2 photoallergic | N/A | N/A | N/A | N/A | N/A | low rate of Aes | B |
| 2015 | Moore et al. Efficacy and Safety of Subantimicrobial Dose, Modified-Release Doxycycline 40 mg Versus Doxycycline 100 mg Versus Placebo for the treatment of Inflammatory Lesions in Moderate and Severe Acne: A Randomized, Double-Blinded, Controlled Study | mod to severe | doxy 40 daily | placebo and doxy 100 daily | 1:1:1, unsure how | stated double blind | Yes, LOCF | yes; more severe acne in placebo group; more NIL in doxy 40 group, although median same | 662 | 216 doxy 40, 224 doxy 100, 222 placebo | 175 | states in text 2 in doxy 40, 5 in doxy 100 | unknown | 16 | not stated | mean change in inflammatory lesion count: doxy 40 16.1 vs 12.6 placebo, 12.9 doxy 100; percent change median num | not stated | this provides better evidence than previous for 40=100. Interesting that doxy 100 is the same as placebo for change in inflammatory lesions. Note that all authors are conflicted. Antimicrobial resistance issue still not addressed | B |

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| | | | | | | | | | | | | | | | | | | ber: 51.6 % doxy 40, 44.3 % plac ebo, 47.6 % doxy 100 | | | |
| 2014 | Ullah et al. Comparison of oral azithromycin with oral doxycycline in the treatment of acne vulgaris. | moderate | azithromycin 500 4 days once a month x 3 months | doxy 100 daily | yes, "lottery method" | unsure | yes, no drop outs | age difference, rest unknown | 386 | 193 | 0 | 0 | 0 | 3 mos | not stated | not stated | not stated | doxy is better but is due to dosing schedule? Daily vs 4 days a month. Also concern re promoting resistance this way | C | | |
| 2015 | Cao et al. Complementary therapies for acne vulgaris (cochrane review) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | does not change our conclusion for diet; maybe we should include teatree oil and bee venom somewhere in text | A | | |

BPO: benzoyl peroxide; CTG: clindamycin-tretinoin gel; doxy: doxycycline; IL: inflammatory lesions; IPL: intense pulsed light; ITT: intent to treat; TL: total lesions; N/A: information not available; NC: no consensus; NIL: non-inflammatory lesions; SE: side-effects