SUMMARY TABLE. Trials included in the article review.

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#1**<br>**Adams, 1991**<br>Wellington, New Zealand<br>Parallel | Doxycycline<br>Fusidin cream<br>2, 4, 6, 10 | n=110 **Mild/mod**<br>female 31<br>male 79<br>Age 18.0 y | Overall change/investigator<br>Overall change/patient<br>Side effects<br>Total lesions (count) | ↑<br>Randomized. Specific population.<br>↓<br>Patient not blinded. | Topical fusidin was as effective as oral doxycycline. |
| **#2**<br>**Adams, 1970**<br>Palo Alto, USA<br>Parallel<br>split face | Vehicle<br>Delta-0.2%-chlormadione<br>Delta-5%-chlormadione<br>7 | n=20 **Can't say**<br>female 9<br>male 11 | Overall change/patient<br>Overall change/physician | ↑<br>No losses to followup.<br>↓<br>Not randomized. | Neither 0.2% delta chlormadinone acetate nor 5% delta chlormadinone acetate cream had any treatment effect on acne. |
| **#3**<br>**Agrawal, 1985**<br>Varanasi, India<br>Parallel | Placebo<br>Zinc sulfate<br>12 | n=42 **Can't say**<br>female 11<br>male 31 | Overall change/physician<br>Severity (Agrawal) | ↓<br>Arms not comparable. | Oral zinc sulphate was no more effective than placebo in mild acne but improvement was seen in patients with pustules, nodules and cysts. |
| **#4**<br>**Akamatsu, 1996**<br>Osaka, Japan<br>Parallel | Roxithromycin (300)<br>Roxithromycin (150)<br>8 | n=30 **Can't say**<br>female 28<br>male 2<br>Age 14.0-26 y | Severity change (Akamatsu) | ↑<br>No losses to followup. General population.<br>↓<br>Not randomized. Patient not blinded. Enroller not blinded. Outcome assessor not blinded. Arms not comparable. Execution not as designed. | A daily dose of 300 mg of roxithromycin was more effective than a lower dose of 150mg in treating severe acne. |

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|---|---|---|---|---|---|
| **#5**<br>**Al Mishari, 1986**<br>Kuwait<br>Parallel | Isotretinoin (0.5)<br>Isotretinoin (0.3)<br>Isotretinoin (0.1)<br>16 | n=30 **Sev**<br>female 16<br>male 14<br>Age 23.1 y | Overall change/physician<br>Side effects | ↑<br>No losses to followup. Referral population.<br>↓<br>Not randomized. Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Best clinical response with lowest range of side effects was achieved with a dosage of 0.3 mg/kg. |
| **#6**<br>**Al Mishari, 1987**<br>Kuwait<br>Parallel | Erythromycin<br>Tetracycline<br>16 | n=40 **Can't say**<br>female 22<br>male 18<br>Age 12.5-26 y | Severity change<br>Side effects | ↑<br>No losses to followup.<br>↓<br>Not randomized. Patient not blinded. Enroller not blinded. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. | Tetracycline and erythromycin, at low doses, were safe and effective in treating acne vulgaris. |
| **#10**<br>**Anderson, 1976**<br>Cincinnati, USA<br>Parallel | Vehicle (topical) + placebo (oral)<br>Tetracycline (topical) + placebo (oral)<br>Tetracycline (oral) + vehicle (topical)<br>1, 2, 3, 4, 5, 6, 7, 8 | n=60 **Mod**<br>female 0<br>male 60 | Severity (Anderson)<br>Severity change | ↓<br>Arms not comparable. Execution not as designed. | Oral and topical tetracycline were each as better than placebo in reducing acne severity. |
| **#12**<br>**Anonymous, 1963**<br>Scotland<br>Parallel<br>multicenter | Placebo<br>Vitamin A<br>12 | n=80 **Can't say**<br>female 34<br>male 46 | Overall change/dermatologist<br>Overall change/generalist | ↑<br>Data shows outcome assessor blinded. Local population.<br>↓<br>Arms not comparable. | No evidence that Vitamin A improved acne. |

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|---|---|---|---|---|---|---|
| **#13**<br>**Anonymous, 1974**<br>UK<br>Parallel<br>split face<br>multicenter | Tretinoin<br>Methyl prednisolone + neomycin<br>2, 4, 8 | n=68<br>female 76<br>male 60 | **Mild/mod/sev** | Change (GPRG)<br>Comedone-free<br>Comedones (count)<br>Inter-treatment preference/patient<br>Side effects | ↓<br>Major losses to followup. Inconsistent ascertainment across arms. | No significant difference was found between tretinoin lotion and methylprednisolone lotion. |
| **#15**<br>**Ashorn, 1985**<br>Tampere, Finland<br>Parallel | Saline<br>Fractionated tfd<br>Unfractionated tfd<br>12 | n=39<br>female 21<br>male 18<br>Age 21.5 y | **Sev** | Overall change | ↑<br>No losses to followup.<br>↓<br>Arms not comparable. | Human dialyzable transfer factor produced the same clinical improvement in acne as placebo. |
| **#16**<br>**Ashurst, 1964**<br>Manchester, UK<br>Cross-over<br>matched | Hydroxyquinoline + benzoyl peroxide<br>Hydroxyquinoline + benzoyl peroxide + hydrocortisone<br>8 | n=54 | **Mild/mod** | Cysts change [cystic]<br>Papules change [papules]<br>Pustules change [pustular]<br>Severity change | ↑<br>Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded. Referral population. | Quinoderm-hydrocortisone was superior to quinoderm alone. |
| **#17**<br>**Balambal, 1985**<br>Madras, India<br>Parallel | Ocimum basilicum<br>Tetracycline<br>8 | n=51<br>female 18<br>male 33<br>Age 11.0-30 y | **Can't say** | Severity change (grade) | ↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. | Responses to tetracycline and osmium basilicum leaves were similar; Leaves were much less expensive. |
| **#18**<br>**Bassett, 1990**<br>Sydney, Australia<br>Parallel | Benzoyl peroxide<br>Tea tree oil<br>4, 8, 12 | n=124<br>female 60<br>male 64<br>Age 19.7 y | **Mod** | Inflammatory (count)<br>Non-inflammatory (count)<br>Unwanted effects | ↑<br>Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded. | Tea tree oil may be a useful alternative treatment for mild to moderate acne. |

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| **#19**<br>**Becker, 1965**<br>Duluth, USA<br>Parallel<br>multicenter | Placebo<br>16-epiestriol-3-allyl ether<br>12 | n=134 **Can't say**<br>female 87<br>male 47 | Oiliness<br>Severity change | ↓<br>Not randomized. Major losses to followup. Arms not comparable. | No significant difference in acne or in reduction of oiliness with respect to placebo. |
| **#20**<br>**Becker, 1981**<br>San Diego, USA<br>Parallel<br>multicenter | Vehicle<br>Clindamycin hydrochloride<br>Clindamycin phosphate<br>2, 4, 6, 8 | n=358 **Mod**<br>female 224<br>male 133<br>Age 21.5 y | Diarrhea<br>Overall change/patient<br>Papules (count)<br>Papules change (count)<br>Pustules (count)<br>Pustules change (count) | | Topical clindamycin hydrochloride and topical clindamycin phosphate were both effective and similar to one another. |
| **#21**<br>**Bettley, 1976**<br>Middlesex, UK<br>Cross-over | Phisohex<br>Triclosan<br>6, 12 | n=34 **Mild/mod/sev** | Overall change/patient<br>Overall change/physician<br>Side effects | ↓<br>Enroller not blinded. Outcome assessor not blinded. | The mixture of triclosan and a detergent was as effective as Phisohex®. |
| **#22**<br>**Bladon, 1986**<br>Leeds, UK<br>Parallel | Tetracycline + placebo<br>Azelaic acid + placebo<br>4, 8, 16, 24 | n=45 **Mod/sev**<br>female 0<br>male 45<br>Age 18.5 y | Abdominal pain<br>Face severity (Leeds)<br>Inflammatory (count)<br>Non-inflammatory (count)<br>Non-inflammatory (count/median)<br>Total inflammatory (count)<br>Total lesions (count)<br>Total lesions (count/median)<br>Total severity (Leeds) | ↓<br>Not randomized. Major losses to followup. | Topical azelaic acid was as effective as systemic tetracycline. |
| **#23**<br>**Blaney, 1976**<br>Cincinnati, USA<br>Parallel | Placebo (topical) + tetracycline hydrochloride (oral)<br>Placebo (topical) + placebo (oral)<br>Tetracycline hydrochloride (topical) + placebo (oral)<br>2, 4, 6, 8, 10, 13 | n=75 **Mod**<br>female 12<br>male 63<br>Age 16.3±2.3 y | Severity change (Cook)<br>Severity change (Cook)) | ↑<br>Randomized. Data shows outcome assessor blinded. | Tetracycline reduced acne severity more than placebo. |

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| **#24**<br>**Bleeker, 1983**<br>lidkoping, Sweden<br>Parallel | Erythromycin (stearate)<br>Erythromycin (base)<br>2 | n=40 **Mod**<br>Age 20.2 y | Papules (count)<br>Side effects | ↑<br>Randomized. | Oral erythromycin was effective in the treatment of acne vulgaris. |
| **#25**<br>**Bleeker, 1981**<br>Lidkoping, Sweden<br>Parallel<br>multicountry | Erythromycin stearate + placebo<br>Doxycycline + placebo<br>2, 6 | n=56 **Mod**<br>female 29<br>male 27<br>Age 20.3 y | Inflammatory change (%)<br>Severity (Kligman) | ↑<br>Randomized. Data show patient blinded. Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded.<br>↓<br>Arms not comparable. | Both erythromycin and doxycycline produced improvement after 2 weeks and neither had side effects. |
| **#28**<br>**Bojar, 1994**<br>Leeds, UK<br>Parallel | Erythromycin + zinc acetate<br>Erythromycin<br>4, 8, 12 | n=45 **Mild/mod**<br>female 15<br>male 30<br>Age 14.1 y | Inflammatory (count)<br>Non-inflammatory (count)<br>Severity (Leeds) | ↑<br>Randomized.<br>↓<br>Arms not comparable. | |
| **#29**<br>**Borglund, 1984**<br>Stockholm, Sweden<br>Parallel | Tetracycline + vehicle<br>Clindamycin phosphate + placebo<br>4, 8 | n=20 **Mod**<br>female 13<br>male 7<br>Age 18.0 y | Nodules (count)<br>Papules (count)<br>Pustules (count) | ↑<br>No losses to followup.<br>↓<br>Arms not comparable. | No clinical difference was found between topical clindamycin and oral tetracycline. |
| **#30**<br>**Borglund, 1991**<br>Stockholm, Sweden<br>Parallel<br>multicountry | Meclocycline + benzoyl peroxide<br>Meclocycline<br>Benzoyl peroxide<br>6, 10 | n=102 **Mod**<br>female 54<br>male 48<br>Age 19.0 y | Adverse effects<br>Comedones (count)<br>Papules (count)<br>Pustules (count)<br>Skin discoloration | ↑<br>No losses to followup.<br>↓<br>Outcome assessor not blinded. Arms not comparable. | For acne patients susceptible to skin irritation from benzoyl peroxide, combined treatment with benzoyl peroxide and a topical antibiotic was advantageous. |

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| **#31**<br>**Bottomley, 1993**<br>Leeds, UK<br>Parallel<br>split face | Fulguration<br>Tretinoin<br>2, 4 | n=11 **Mild**<br>female 10<br>male 1<br>Age 22.0-36 y | Closed comedone change (%)<br>Overall change/patient | Data shows outcome assessor blinded. Referral population.<br>↓<br>Patient not blinded. | Fulguration can offer a simple but effective treatment for eliminating white heads. |
| **#32**<br>**Bottomley, 1993**<br>Leeds, UK<br>Parallel<br>split face | Electrocautery<br>Fulguration<br>4 | n=12 **Mild**<br>female 8<br>male 4<br>Age 23.0 y | Large comedone change (%)<br>Small comedones change (%) | Data shows outcome assessor blinded. Referral population.<br>↓<br>Patient not blinded. | Use electrocautery on large closed comedones. |
| **#33**<br>**Braathen, 1984**<br>Oslo, Norway<br>Parallel | Vehicle (oral) + vehicle (topical)<br>Tetracycline + vehicle<br>Clindamycin + vehicle<br>8 | n=87 **Mild**<br>female 44<br>male 43<br>Age 20.3 y | Diarrhea<br>Inflammatory (count)<br>Overall change/patient<br>Overall change/physician | | Both oral tetracycline and topical clindamycin reduced the number of acne lesions. |
| **#34**<br>**Bradford, 1974**<br>Birmingham, USA<br>Parallel | Vitamin A<br>Vehicle<br>12 | n=75 **Mild/mod**<br>Age 13.0-30 y | Response<br>Side effects | ↑<br>No losses to followup. Referral population.<br>↓<br>Not randomized. Enroller not blinded. Outcome assessor not blinded. Arms not comparable. | Topical vitamin A was more effective than placebo. |

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| **#35**<br>**Bradford, 1974**<br>Birmingham, USA<br>Parallel<br>matched | Vehicle<br>Vitamin A<br>12 | n=72 **Mild/mod**<br>female 23<br>male 49<br>Age 15.6±2.7 y | Comedones (group count)<br>Comedones [female] (count)<br>Comedones [male] (count)<br>Overall change<br>Overall change [female]<br>Overall change [male]<br>Papules (group count)<br>Papules [female] (group count)<br>Papules [male] (group count)<br>Pustules (total count)<br>Pustules [female] (total count)<br>Pustules [male] (total count) | ↑<br>Randomized. No losses to followup.<br>↓<br>Outcome assessor not blinded. Arms not comparable. | Topical vitamin A was more effective than placebo. |
| **#36**<br>**Brandt, 1994**<br>Helsinki, Finland<br>Parallel<br>multicenter | Tetracycline<br>Erythromycin acistrate<br>12, 24 | n=60 **Mod/sev**<br>female 19<br>male 41<br>Age 21.0±4.4 y | Back severity (Harcup/median)<br>Chest severity (Harcup/median)<br>Face/neck severity (Harcup/median)<br>Side effects | ↑<br>Local population. | Erythromycin acistrate was a safe, well tolerated alternative to tetracycline for systemic treatment of acne. |
| **#37**<br>**Brookes, 1978**<br>Lancaster, UK<br>Parallel<br>multicenter | Chloramphenicol + hydrocortisone<br>Tretinoin<br>2, 4, 6, 8, 10, 12 | n=56 **Mod**<br>Age 18.0-22 y | Comedones change (count)<br>Cysts change (count)<br>Overall change/patient<br>Overall change/patient (vas)<br>Papules change (count)<br>Pustules change (count) | ↑<br>Randomized.<br>↓<br>Patient not blinded. Major losses to followup. Outcome assessor not blinded. | Chloramphenicol/hydrocortisone and tretinoin showed similar activity over 12 weeks. |
| **#38**<br>**Bucknall, 1977**<br>St. Georges, UK<br>Parallel | Benzoyl peroxide<br>Tretinoin<br>12 | n=97 **Mod**<br>female 39<br>male 58<br>Age 12.0-36 y | Comedones (count)<br>Overall change/patient<br>Overall change/physician<br>Papules (count)<br>Pustules (count)<br>Side effects | ↓<br>Patient not blinded. Inconsistent ascertainment across arms. Arms not comparable. | Tretinion produced greater improvement than benzoyl peroxide. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#39**<br>**Burke, 1983**<br>Leeds, UK<br>Parallel<br>matched | Placebo<br>Erythromycin (topical)<br>Benzoyl peroxide<br>4, 8 | n=94 **Mild/mod/sev**<br>female 19<br>male 70<br>Age 18.8±18.9 y | Inflammatory (count)<br>Inflammatory (counts)<br>Non-inflammatory (count)<br>Severity (Leeds)<br>Total Lesions (count)<br>Withdrawal due to side effects | ↓<br>Not randomized. Inconsistent ascertainment across arms. | Benzoyl peroxide and topical erythromycin are equally effective in reducing the number of superficial inflamed lesions. |
| **#40**<br>**Burton, 1990**<br>Bristol, UK<br>Parallel<br>multicenter | Tetracycline (topical) + tetracycline (oral)<br>Placebo + tetracycline (oral)<br>4, 8, 12, 16 | n=85 **Can't say**<br>female 44<br>male 38<br>Age 20.4±4.9 y | Adverse reactions<br>Adverse-gastrointestinal<br>Adverse-skin<br>Overall change/patient, investigator<br>Severity (Cook) | ↑<br>No losses to followup.<br>↓<br>Not randomized. | Topical tetracycline, in combination with 8 weeks of oral tetracycline was well accepted by patients and reduced acne severity at 16 weeks. |
| **#41**<br>**Cahn, 1959**<br>Phildelphia, USA<br>Cross-over | Placebo<br>Sulfadimethoxine<br>5, 10 | n=134 **Sev**<br>female 107<br>male 27<br>Age 15.0-41 y | Inter-treatment preference/physician | ↑<br>No losses to followup. | Sulfadlimethoxine was a "useful and safe" agent in the treatment of acne vulgaris. |
| **#42**<br>**Cambazard, 1998**<br>France<br>Parallel<br>multicenter | Tretinoin<br>Tretinoin + clindamycin<br>2, 4, 8, 12 | n=40 **Mod/sev**<br>Age 14.0-26 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity (Cook) | No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Combination more effective in inflamed acne. |
| **#43**<br>**Cambazard, 1998**<br>France<br>Parallel<br>multicenter | Tretinoin<br>Tretinoin + clindamycin<br>2, 4, 8, 12 | n=161 **Mod/sev**<br>Age 14.0-26 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity (Cook) | No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Combination more effective than tretinoin alone. |

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| **#44**<br>**Cambazard, 1998**<br>France<br>Parallel<br>multicenter | Tretinoin<br>Tretinoin + clindamycin<br><br>2, 4, 8, 12 | n=157 **Mod/sev**<br><br>Age 14.0-26 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity (Cook) | No losses to followup.<br>🡻<br>Inconsistent ascertainment across arms. Arms not comparable. | Combination not demonstrated superior to tretinoin in Velac gel®. |
| **#45**<br>**Cambazard, 1998**<br>France<br>Parallel<br>multicenter | Clindamycin<br>Tretinoin + clindamycin<br><br>2, 4, 8, 12 | n=209 **Mod/sev**<br><br>Age 14.0-26 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity (Cook) | No losses to followup.<br>🡻<br>Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. | Combination superior for inflammatory acne. |
| **#46**<br>**Cambazard, 1998**<br>France<br>Parallel<br>multicenter | Clindamycin<br>Tretinoin + clindamycin<br><br>2, 4, 8, 12 | n=40 **Mod/sev**<br><br>Age 14.0-26 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity (Cook) | No losses to followup.<br>🡻<br>Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. | Combination not superior to clindamycin. |
| **#47**<br>**Cambazard, 1998**<br>France<br>Parallel<br>multicenter | Clindamycin<br>Tretinoin + clindamycin<br><br>2, 4, 8, 12 | n=162 **Mod/sev**<br><br>Age 14.0-26 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity (Cook) | No losses to followup.<br>🡻<br>Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. | Combination superior to clindamycin for non-inflammatory acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#48**<br>**Carlborg, 1986**<br>Halmstad, Sweden<br>Parallel<br>multicenter | Levonorgestrel + ethinyl estradiol (0.030)<br>Cyproterone + ethinyl estradiol (0.035)<br>Cyproterone + ethinyl estradiol (0.05)<br><br>16, 24 | n=133 **Can't say**<br>female 133<br>male 0<br>Age 15.0- y | Discontinuation due to side effects<br>Total lesions change<br>Total lesions change (%) | ↑<br>Data shows enroller blinded. | Lower frequency of side effects in the 35 mcg group. |
| **#49**<br>**Caron, 1997**<br>Sophia Antipoli, France<br>Parallel<br>split face | Tretinoin<br>Adapalene<br>2 | n=15 **Mild/mod**<br>female 26<br>male 4<br>Age 28.4±6.3 y | Burning severity (patient)<br>Desquamation severity (investigator)<br>Edema severity (investigator)<br>Erythema severity (investigator)<br>Papules severity (investigator)<br>Pruritis severity (patient)<br>Tightness severity (patient)<br>Vesicle severity (investigator) | ↑<br>No losses to followup. Data shows outcome assessor blinded.<br>↓<br>Not randomized. Patient not blinded. | Adapalene was better tolerated than tretinoin. |
| **#52**<br>**Cavicchini, 1989**<br>Milan, Italy<br>Parallel<br>multicenter | Benzoyl peroxide<br>Azelaic acid<br>2, 4, 6, 12, 16, 20, 24 | n=309 **Mild** | Good/excellent response (%)<br>Inflammatory (count)<br>Inflammatory (count/median)<br>Local side effects<br>Overall change/physician (%) | ↓<br>Enroller not blinded. Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. Execution not as designed. | Treatments showed equal benefit. Benzoyl peroxide produced a more rapid effect on cutaneous lesions; azelaic acid applications were better tolerated. |
| **#53**<br>**Chalker, 1983**<br>NY, USA<br>Parallel | Erythromycin + benzoyl peroxide<br>Benzoyl peroxide<br>Vehicle<br>Erythromycin<br><br>2, 4, 6, 8, 10 | n=177 **Mod/sev**<br>female 81<br>male 115<br>Age 15.0-30 y | Comedones change (%)<br>Inflammatory change (%)<br>Papules change (%)<br>Pustules change (%) | ↓<br>Inconsistent ascertainment across arms. | The combination is more effective than vehicle. |

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| **#54**<br>**Chalker, 1987**<br>Augusta, USA<br>Parallel<br>multicenter | Vehicle<br>Isotretinoin<br>2, 5, 8, 11, 14 | n=313 **Can't say**<br>female 112<br>male 156<br>Age 19.5 y | Erythema score<br>Inflammatory change (%)<br>Non-inflammatory change (%)<br>Peeling score<br>Severity change (Cook %) | ↑<br>Specific population.<br>↓<br>Inconsistent ascertainment across arms. | Isotretinoin 0.05% gel is useful for mild to moderately severe acne. |
| **#55**<br>**Charoenvisal, 19**<br>Songkhla, Thailand<br>Parallel | Desogestrel + ethinyl estradiol<br>Cyproterone + ethinyl estradiol (.05)<br>4, 12, 24 | n=66 **Can't say**<br>female 66<br>male 0<br>Age 16.0-30 y | Overall change/patient [center a]<br>Overall change/patient [center b]<br>Severity [center a] (Charoenvisal)<br>Severity [center b] (Charoenvisal)<br>Side effects | ↓<br>Patient not blinded. Enroller not blinded. Inconsistent ascertainment across arms. Outcome assessor not blinded. | Decreased mean acne score occured with both ethinyl estradiol-desogestrel and ethinyl estradiol-cyproterone. No difference between groups was reported. |
| **#56**<br>**Christian, 1975**<br>Salt Lake City, USA<br>Parallel | Vehicle<br>Clindamycin<br>1, 2, 4, 6, 10, 13 | n=98 **Mod/sev**<br>female 32<br>male 49<br>Age 21.0 y | Comedones change (%)<br>Pustules change (%)<br>Side effects | | Clindamycin is effective in treating moderate-severe acne. |
| **#57**<br>**Christiansen, 197**<br>Copenhagen, Denmark<br>Parallel<br>multicenter | Vitamin A + placebo<br>Vehicle + oxytetracycline<br>Vitamin A + oxytetracycline<br>2, 4, 8 | n=238 **Can't say**<br>female 135<br>male 103<br>Age 11.0-44 y | Comedones change<br>Papules change<br>Pustules change<br>Side effects | ↑<br>Data shows enroller blinded.<br>↓<br>Major losses to followup. | Vitamin A was better than oxytetracycline for comedones and, less effective for pustules, and equally good for papules. Vitamin A produced more local side effects. |
| **#58**<br>**Christiansen, 197**<br>Copenhagen, Denmark<br>Parallel<br>multicenter | Vehicle<br>Tretinoin (0.05%)<br>Tretinoin (0.02%)<br>4, 8 | n=256 **Sev** | Comedones (Christiansen)<br>Comedones severity (Christiansen)<br>Nodes+cysts (score)<br>Papules severity (Christiansen)<br>Pustules (score)<br>Side effects | ↓<br>Major losses to followup. | 0.05% tretinoin was more effective than 0.02% tretinoin and placebo for papules and comedones but not pustules. Side effects of 0.05% and 0.02% were similar. |

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|---|---|---|---|---|---|
| **#59**<br>**Christiansen, 197**<br>Arhus, Denmark<br>Parallel | Motretinide<br>Tretinoin<br>2, 4, 6, 8 | n=37 **Mild**<br>female 20<br>male 11<br>Age 21.0 y | Burning<br>Erythema desquamation<br>Total lesions<br>Total lesions change (count/median) | ↑<br>Referral population.<br>↓<br>Major losses to followup. | Motretinide and tretinoin 0.05% were equivalent but authors acknowledge study was too small to detect differences. |
| **#60**<br>**Christiansen, 197**<br>Copenhagen, Denmark<br>Parallel<br>multicenter | Vehicle<br>Tretinoin<br>Motretinide<br>2, 4, 8 | n=257 **Mild/mod** | Overall change/physician<br>Reduction in application due to side effects<br>Side effects<br>Total lesions change | ↓<br>Arms not comparable. | Retinoic acid the most potent, but motretinide better tolerated. |
| **#61**<br>**Christiansen, 197**<br>Aarhus, Denmark<br>Parallel<br>multicenter | Motretinide<br>Vehicle<br>2, 4, 6, 8 | n=19 **Can't say**<br>female 22<br>male 7<br>Age 18.5 y | Comedones change (count)<br>Local reactions<br>Total lesions change (count) | ↓<br>Major losses to followup. Arms not comparable. Execution not as designed. | Motretinide was superior to placebo. |
| **#62**<br>**Chu, 1997**<br>London, UK<br>Parallel | Zinc + erythromycin<br>Benzoyl peroxide + erythromycin<br>2, 4, 6, 8, 10 | n=72 **Mod**<br>Age 24.0 y | Adverse effects<br>Clinical assessment/physician (score)<br>Comedones change (median %)<br>Improved by 50% or more<br>Inflammatory change (count/median) | ↓<br>Patient not blinded. | Benzoyl peroxide 5% + erythromycin 3% was superior to erythromycin + zinc 1.2%. |
| **#63**<br>**Clucas, 1997**<br>Sophia Antipolis, France<br>Parallel<br>multicountry | Tretinoin<br>Adapalene<br>2, 4, 8, 12 | n=591 **Mod/sev**<br>female 276<br>male 317<br>Age 12.0-30 y | Adverse reaction<br>Discontinuation due to side effects | ↑<br>Randomized. Specific population.<br>↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. Arms not comparable. | Adapalene 1% was better tolerated than tretinoin .025%. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#64**<br>**Cochran, 1985**<br>Houston, USA<br>Parallel | Vehicle<br>Zinc<br>3, 6, 9, 12 | n=30 **Mild/mod**<br>Age 16.0-30 y | Irritation (score)<br>Severity (Michaelsson) | ↓<br>Not randomized. Major losses to followup. Arms not comparable. | Topical zinc therapy alone produced no significant benefit. |
| **#66**<br>**Colver, 1988**<br>Oxford, UK<br>Parallel | Cyproterone + ethinyl estradiol (0.05)<br>Cyproterone + ethinyl estradiol (0.035)<br>8, 12, 24, 36 | n=96 **Can't say**<br>female 78<br>male 0<br>Age 16.0-35 y | Back severity<br>Chest severity<br>Face severity<br>Severity change/patient (vas)<br>Side effects | ↓<br>Not randomized. | Cyproterone-ethinyl estradiol-35 and cyproterone-ethinyl estradiol-50 were equally effective. |
| **#69**<br>**Cornbleet, 1961**<br>Chicago, USA<br>Parallel | Topical treatment<br>Tetracycline<br>48-78 (unspecified) | n=68 **Can't say**<br>female 27<br>male 41<br>Age 19.0 y | Improvement<br>Side effects | ↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. | Systemic tetracycline was better than topical treatment. |
| **#70**<br>**Cornbleet, 1964**<br>Chicago, USA<br>Parallel | Tetracycline<br>Demethylchortetracycline<br>4-22 (unspecified) | n=100 **Can't say**<br>female 59<br>male 41<br>Age 21.3 y | Overall change/physician<br>Relapse<br>Side effects | ↑<br>Randomized. Data show patient blinded. Data shows enroller blinded. No losses to followup.<br>↓<br>Outcome assessor not blinded. | Demethylchlorotetracycline was superior to tetracycline. |
| **#71**<br>**Crounse, 1965**<br>Miami, USA<br>Cross-over matched | Tetracycline hydrochloride<br>Demethylchlortetracycline<br>Vehicle<br>4, 8, 12 | n=150 **Can't say**<br>female 99<br>male 51 | Severity change<br>Side effects | | Antibiotics were not superior to vehicle. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#72**<br>**Cullen, 1976**<br>Gainesville, USA<br>Parallel | Tetracycline<br>Minocycline<br>19 | n=100 **Mod/sev**<br>female 73<br>male 27<br>Age 20.0 y | Comedones (count)<br>Cysts (count)<br>Papules (count)<br>Pustules (count)<br>Side effects | ↑<br>Data shows enroller blinded. Data shows outcome assessor blinded. | Minocycline was as effective as tetracycline. |
| **#74**<br>**Cunliffe, 1979**<br>Leeds, UK<br>Parallel | Zinc sulfate/citrate complex<br>Tetracycline<br>4, 8, 12 | n=48 **Mod** | Nodules (count)<br>Non-inflammatory (count)<br>Overall change/patient (vas)<br>Papules (count)<br>Pustules (count)<br>Severity (Burton) | ↓<br>Patient not blinded. Enroller not blinded. Arms not comparable. Execution not as designed. | Tetracycline was superior to zinc complex in mild/severe acne. |
| **#75**<br>**Cunliffe, 1980**<br>Leeds, UK<br>Parallel<br>matched | Benzoyl peroxide<br>Chloramphenicol + hydrocortisone + sulfur<br>4, 8, 12 | n=48 **Mod**<br>female 24<br>male 24<br>Age 15.0-17 y | Erythema<br>Inflammatory (count)<br>Non-inflammatory (count)<br>Overall assessment/patient (vas)<br>Scaling<br>Severity (Leeds) | ↑<br>No losses to followup.<br>↓<br>Not randomized. | Chloramphenicol and benzoyl peroxide 5% were equally effective. |
| **#76**<br>**Cunliffe, 1981**<br>Leeds, UK<br>Parallel<br>matched | Benzoyl peroxide (lotion)<br>Benzoyl peroxide (gel)<br>4, 8 | n=48 **Mod**<br>female 28<br>male 20 | Erythema<br>Inflammatory (count)<br>Non-inflammatory (count)<br>Overall change/patient (% improvement)<br>Scaling<br>Severity (Pillsbury) | ↓<br>Major losses to followup. | Benzoyl peroxide gel and lotion were equally effective. |
| **#77**<br>**Cunliffe, 1989**<br>Leeds, UK<br>Parallel<br>matched | Azelaic acid<br>Placebo<br>8, 12 | n=40 **Can't say**<br>female 14<br>male 26 | Inflammatory change (%)<br>Local side effects<br>Non-inflammatory change (%) | ↑<br>Randomized.<br>↓<br>Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. | 20% azelaic acid can be used as monotherapy for papulo-pustular acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#78**<br>**Cunliffe, 1997**<br>Montpellier, France<br>Parallel<br>multicountry | Tretinoin<br>Adapalene (0.03%)<br>Adapalene (0.1%)<br>0, 1, 2, 4, 8, 12 | n=89<br>Age 12.0-30 y | **Mild/mod/sev** | Inflammatory (count)<br>Non-inflammatory (count)<br>Severity (Leeds)<br>Total lesions change (%) | ↑<br>Randomized. Data shows enroller blinded. Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. Arms not comparable. | Adapalene 0.1% and tretinoin were equally effective; adapalene had fewer side effects. |
| **#80**<br>**Cunliffe, 1997**<br>Leeds, UK<br>Parallel<br>multicountry | Tretinoin<br>Adapalene<br>2, 4, 8, 12 | n=268<br>female 125<br>male 143<br>Age 19.5 y | **Can't say** | Burning<br>Dryness<br>Inflammatory change (%)<br>Non-inflammatory change (%)<br>Scaling | ↑<br>Randomized. Data shows enroller blinded. Data shows outcome assessor blinded. | Adapalene was as effective as tretinoin and had superior skin safety results. |
| **#82**<br>**Danto, 1966**<br>Vancover, Canada<br>Parallel<br>multicenter | Benzoyl peroxide + sulfur<br>Sulfur<br>2 | n=113<br>female 59<br>male 54<br>Age 12.0-40 y | **Mild/mod/sev** | Overall change/physician<br>Skin irritation | ↑<br>Data show patient blinded. Data shows enroller blinded.<br>↓<br>Arms not comparable. | Benzoyl peroxide plus sulphur was better than sulphur alone. |
| **#84**<br>**De Bersaques, 19**<br>Ghent, Belgium<br>Parallel | Salicylic acid + resorcinol + sulfur<br>Tretinoin (.05%)<br>Tretinoin (.02%)<br>2, 7 | n=60 | **Can't say** | Irritation<br>Overall change/physician | ↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. Execution not as designed. | Vitamin A acid (tretinoin) is no cure-all. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#85**<br>**Degreef, 1982**<br>Louvain, Belgium<br>Parallel | Benzoyl peroxide<br>Miconazole + benzoyl peroxide<br>4, 8, 12 | n=105 **Mod**<br>female 49<br>male 56<br>Age 12.0-24 y | Comedones (count)<br>Overall change/patient<br>Overall change/physician<br>Severity change (score shift)<br>Side effects | ↑<br>Randomized. No losses to followup. | Combination of miconazole + benzoyl peroxide was more effective therapy benzoyl peroxide alone. |
| **#86**<br>**Delaney, 1959**<br>Detriot, USA<br>Parallel | Polythionate + quaternary ammonia complex of polythionate<br>Polythionate<br>Unspecified | n=72 **Can't say**<br>female 46<br>male 26<br>Age 11.5-35 y | Post-therapy overall change<br>Side effects | ↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. Arms not comparable. | Two preparations of polythionate produced benefits in patients with mild to severe acne. |
| **#87**<br>**Dieben, 1994**<br>Oss, The Netherlands<br>Parallel<br>multicountry | Cyproterone + ethinyl estradiol (0.035)<br>Desogestrel + ethinyl estradiol<br>16 | n=183 **Mild**<br>female 183<br>male 0<br>Age 18.0-35 y | Comedones change (count/median)<br>Papules change (count/median)<br>Pustules change (count/median)<br>Severity (Leeds)<br>Severity change (Dieben/median) | ↓<br>Major losses to followup. | Cyproterone + ethinyl estradiol had a similar effect on mild to moderate acne. |
| **#89**<br>**Dobson, 1980**<br>Buffalo, USA<br>Parallel<br>multicenter | Erythromycin<br>Vehicle<br>2, 4, 8, 10, 12 | n=253 **Mod/sev**<br>female 161<br>male 93 | Closed comedones change (%)<br>Open comedones change (%)<br>Overall change/physician<br>Papules change (%)<br>Pustules change (%)<br>Skin reaction<br>Total lesions change (%)<br>Withdrawals | ↓<br>Major losses to followup. | Erythromycin base 1.5% liquid is effective. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#90**<br>**Dominguez, 1998**<br>Mexico City, Mexico<br>Parallel | Tretinoin<br>Isotretinoin<br>2, 4, 8, 12 | n=30 **Mod**<br>female 18<br>male 12<br>Age 13.0-30 y | Comedones (count)<br>Inflammatory (count)<br>Irritation<br>Stinging, erythema, desquamation | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. Enroller not blinded. | Isotretinoin and tretinoin had a similar effect. |
| **#91**<br>**Dreno, 1989**<br>France<br>Parallel<br>multicenter | Zinc<br>Placebo<br>4, 8 | n=66 **Mod**<br>female 27<br>male 39<br>Age 22.0±7.0 y | Abdominal pain<br>Inflammatory severity (Dreno)<br>Nausea<br>Severity/patient<br>Severity/photo | ↑<br>No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Oral zinc gluconate at a low dose showed significantly better results than placebo in the treatment of inflammatory acne. |
| **#92**<br>**Dunlap, 1998**<br>Tucson, USA<br>Parallel<br>split face | Adapalene-immediate<br>Adapalene-delayed<br>2 | n=25 **Mild/mod**<br>female 36<br>male 14<br>Age 19.4±6.9 y | Dryness (score)<br>Erythema (score) | ↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Adapalene 0.1% was well tolerated, even when applied immediately after washing. |
| **#93**<br>**Dunlap, 1998**<br>USA<br>Parallel<br>split face<br>multicenter | Adapalene<br>Tretinoin<br>1, 2, 3, 4 | n=100 **Mild/mod**<br>female 96<br>male 104<br>Age 18.5 y | Desquamation<br>Dryness (score)<br>Erythema (score)<br>Inter-treatment preference<br>Intolerance<br>Local reactions/Dryness (score)<br>Stinging/burning<br>Total adverse skin symptom (score)<br>Total adverse skin symptoms (score) | ↑<br>Randomized. No losses to followup.<br>↓<br>Patient not blinded. | Majority of patients prefer 0.1% adapalene gel over tretinoin 0.025% cream. Adapalene causes less skin irritation. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#94**<br>**Dunlop, 1995**<br>Camperdown, Australia<br>Parallel | Benzoyl peroxide<br>Isolutrol<br>2, 4, 8, 12 | n=70 **Mild/mod**<br>female 26<br>male 44<br>Age 18.6 y | Burning<br>Dryness<br>Erythema<br>Inflammatory (count)<br>Non-inflammatory (count)<br>Pruritis<br>Scaling | ↓<br>Major losses to followup. | Benzoyl peroxide and isolutrol were both effective at reducing inflamed lesions. Isolutrol was not effective for non-inflamed lesions. Isolutrol produced fewer side effects. |
| **#95**<br>**Eady, 1996**<br>Leeds, UK<br>Parallel | Vehicle<br>Salicylic acid<br>4, 8, 12 | n=114 **Mild/mod**<br>female 28<br>male 86<br>Age 16.0-25 y | Inflammatory (count)<br>Non-inflammatory (count)<br>Overall change/patient (scale)<br>Severity (Leeds)<br>Total lesions (count) | | 2% salicylic acid has a significant effect on non-inflammatory lesions at 8 to 12 weeks and on inflammatory lesions at 12 weeks, with few side effects. |
| **#97**<br>**Ede, 1973**<br>Cincinnati, USA<br>Parallel | Benzoyl peroxide + chlorhydroxyquinoline<br>Benzoyl peroxide + chlorhydroxyquinoline + hydrocortisone<br>Vehicle<br>Benzoyl peroxide<br>2, 4 | n=196 **Mild/mod**<br>Age 14.0-24 y | Overall change/investigator<br>Total lesions change (%) | ↑<br>Randomized. No losses to followup. | Benzoyl peroxide alone, in combination with chlorhydoxyquinoline alone or with hydrocortisone were all clinically superior to placebo. Loroxide HC® demonstrated the most rapid benefit. |
| **#98**<br>**Elbaum, 1988**<br>Stanford, USA<br>Parallel | Isotretinoin<br>Tretinoin<br>2, 4, 8, 12 | n=18 **Can't say** | Comedones change<br>Comedones change (%)<br>Inflammatory change (%)<br>Total lesions change (%) | ↓<br>Arms not comparable. | Tretinoin and isotretinoin had similar efficacy. |
| **#99**<br>**Ellis, 1988**<br>Ann Arbor, USA<br>Parallel | Clindamycin phosphate (lotion)<br>Clindamycin phosphate (gel)<br>Placebo<br>3, 6, 9, 12 | n=135 **Mod**<br>Age 13.0-35 y | Papules (count)<br>Pustules (count) | ↓<br>Patient not blinded.<br>Enroller not blinded. | Clindamycin solution and gel were effective. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#100**<br>**Ellis, 1998**<br>USA<br>Parallel<br>multicenter | Tretinoin<br>Adapalene<br><br>2, 4, 8, 12 | n=297 **Mod**<br>female 145<br>male 152 | Comedones change (count)<br>Dose regime altered<br>Inflammatory (count)<br>Inflammatory change (%)<br>Non-inflammatory (count)<br>Non-inflammatory change (%)<br>Severity (Leeds)<br>Side effects<br>Total lesions change (%) | ↑<br>Specific population.<br>↓<br>Patient not blinded. Major losses to followup. | Both adapalene and tretinoin were effective. Adapalene was more useful than tretinoin for treating open comedones.Side effects were similar. |
| **#101**<br>**Elstein, 1981**<br>Los Angeles, USA<br>Parallel | Vehicle<br>Sulfurated lime<br><br>2, 4, 7, 10 | n=59 **Mod**<br><br>Age 13.0-30 y | Comedones (count)<br>Erythema<br>Papules (count)<br>Peeling<br>Pustules (count)<br>Severity change | | Sulphurated lime produced faster and greater improvement with significant reduction in papule counts compared to vehicle. Clay mask system eliminates odor and staining associated with Vleminckx's solution®. |
| **#102**<br>**Ereaux, 1965**<br>Montreal, Canada<br>Parallel | Methyl prednisolone + neomycin + sulfur<br>Vehicle<br><br>Unspecified | n=134 **Can't say** | Overall change | ↑<br>Randomized. Data show patient blinded. Data shows enroller blinded.<br>↓<br>Major losses to followup. Arms not comparable. | Methylprednisolone/neomycin/sulphur was effective for early and late stages of acne vulgaris. |
| **#103**<br>**Erkkola, 1990**<br>Turku, Finland<br>Parallel<br>multicenter | Cyproterone + ethinyl estradiol (0.035)<br>Desogestrel + ethinyl estradiol<br><br>12, 32 | n=162 **Can't say**<br>female 162<br>male 0<br>Age 20.0-40 y | Back improvement<br>Chest improvement<br>Complete healing<br>Face improvement<br>Side effects | ↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. | Cyproterone produced greater improvement for facial acne than desogestrel. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#106**<br>**Farrell, 1980**<br>Iwoa city, USA<br>Parallel | Isotretinoin (1.0)<br>Isotretinoin (0.1)<br>Isotretinoin (0.5)<br><br>1, 2, 3, 4, 5, 6, 7, 8, 10, 12; post-therapy:2, 4, 6, 8 | n=16 **Sev**<br>female 0<br>male 16<br>Age 16.0-31 y | Cheilitis duration (%)<br>Cystic change (%)<br>Cystic change post-treatment (%)<br>Cystic diameter change (%)<br>Cystic diameter change post-treatment<br>Desquamation duration (week)<br>Pruritus duration (weeks) | Randomized. Data show patient blinded. Data shows enroller blinded.<br>🡻<br>Arms not comparable. | No significant difference is efficacy were noted between the groups. |
| **#108**<br>**Feucht, 1980**<br>Augusta, USA<br>Parallel | Erythromycin + zinc (gel) + Placebo (oral)<br>Erythromycin + zinc (liquid) + placebo (oral)<br>Tetracycline (oral) + placebo (topical)<br>Placebo (topical) + placebo (oral)<br><br>2, 4, 6, 8, 10 | n=149 **Mild/mod/sev**<br>female 0<br>male 149<br>Age 18.0-26 y | Medication used (mg/kg)<br>Papules change (%)<br>Severity change (Cook %)<br>Severity change (Cook) | Randomized. Data show patient blinded. Data shows outcome assessor blinded. Local population. | Erythromycin/zinc gel or liquid are as effective as oral tetracycline. |
| **#109**<br>**Flanders, 1985**<br>Athens, USA<br>Parallel | Benzoyl peroxide (contingent contract)<br>Benzoyl peroxide (non-contingent contract)<br>Benzoyl peroxide (self monitoring)<br>Untreated<br><br>12 | n=42 **Mod**<br>female 34<br>male 8 | Severity (Cook)<br>Total lesions (count) | 🡻<br>Patient not blinded. Enroller not blinded. Major losses to followup. Arms not comparable. | Methods that monitor compliance improve acne outcomes. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#110**<br>**Flinn, 1961**<br>Madison, USA<br>Parallel | Vehicle<br>Tolbutamide<br>2, 4, 6, 8, 10, 12 | n=30 **Mod/sev** | Overall change/patient<br>Overall change/physician<br>Severity/photo | ↑<br>Data shows outcome assessor blinded.<br>↓<br>Not randomized. Major losses to followup. Arms not comparable. | Tolbutanide was no better than placebo. |
| **#111**<br>**Fluckiger, 1988**<br>Basel, Switzerland<br>Parallel | Benzoyl peroxide + miconazole<br>Benzoyl peroxide<br>4, 8, 12 | n=52 **Mod/sev**<br>female 26<br>male 26<br>Age 18.0 y | Comedones (count)<br>Irritation<br>Irritation [female]<br>Irritation [females]<br>Irritation [male]<br>Papules (count)<br>Pustules (count)<br>Total lesions (count)<br>Total lesions change (%)<br>Total lesions change [female] (%)<br>Total lesions change [male] (%) | ↓<br>Patient not blinded. Major losses to followup. | Benzoyl peroxide and benzoyl peroxide + miconazole were equally effective. Benzoyl peroxide + miconazole was more effective in women and was better tolerated. |
| **#114**<br>**Franz, 1978**<br>Hamburg, Germany<br>Parallel | Triclosan + propylene phenoxetol<br>Triclosan<br>Vehicle<br>-4, 0, 4, 8 | n=72 **Mild/mod**<br>female 0<br>male 72<br>Age 18.0-22 y | Inflammatory (adjusted count)<br>Inflammatory (count)<br>Inflammatory (score)<br>Non-inflammatory (count)<br>Overall change/patient (vas) | ↓<br>Major losses to followup. | Topical triclosan combined with topical acne creams was more effective than acne creams alone. |
| **#115**<br>**Fraser, 1980**<br>Aberdeen, UK<br>Parallel<br>multicenter | Hydrocortisone + sulfur<br>Chloramphenicol + hydrocortisone + sulfur<br>4, 8, 12 | n=37 **Can't say**<br>female 25<br>male 12 | Local reactions<br>Overall change/patient<br>Overall change/physician<br>Severity change (Fraser %) | ↑<br>Randomized. | Both preparations produced comparable decreases in number of lesions. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#117**<br>**Fugere, 1990**<br>Montreal, Canada<br>Parallel<br>multicenter | Cyproterone + ethinyl estradiol (0.035)<br>Cyproterone + ethinyl estradiol (0.05)<br>24, 48 | n=73 **Mod/sev**<br>female 73<br>male 0<br>Age 23.0±3.3 y | Comedones severity (Cook)<br>Macules score (Cook)<br>Papules score (Cook)<br>Papules time (Cook)<br>Severity (Cook) | ↓<br>Major losses to followup. | Both cyproterone-ethinyl estradiol-35 and cyproterone-ethinyl estradiol-50 produced improvement;the lower estrogen dose was as effective as the higher dose. |
| **#118**<br>**Fyrand, 1986**<br>Norway<br>Parallel<br>split face | Benzoyl peroxide (alcohol)<br>Benzoyl peroxide (water)<br>4, 8 | n=49 **Can't say**<br>female 64<br>male 34<br>Age 14.0-44 y | Burning<br>Closed comedones change (%)<br>Cysts change (%)<br>Erythema (patient)<br>Erythema (physician)<br>Open comedones change (%)<br>Papules change (%)<br>Pustules change (%)<br>Scaling (patient)<br>Scaling (physician)<br>Stinging | | Water-based benzoyl peroxide produced less irritation than alcohol based benzoyl peroxide. |
| **#119**<br>**Galvin, 1998**<br>USA<br>Parallel<br>split face | Petrolatum<br>Tretinoin (0.025% cream)<br>Tretinoin (0.01% gel)<br>Tretinoin (0.025% gel)<br>Tretinoin (0.05% cream)<br>Tretinoin (0.1% cream)<br>Adapalene<br><br>1-21days (unspecified) | n=28 **Can't say**<br>female 25<br>male 3<br>Age 22.0-72 y | Discontinuation due to side effects<br>Irritation (score) | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. | Adapalene was better tolerated than tretinoin. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#120**<br>**Galvin, 1998**<br>USA<br>Parallel<br>split face | Petrolatum<br>Tretinoin (0.025% cream)<br>Tretinoin (0.1% gel)<br>Tretinoin (0.05% cream)<br>Tretinoin (0 .1% cream)<br>Adapalene<br><br>1-21 days (unspecified) | n=27 **Can't say**<br>female 20<br>male 7<br>Age 22.0-72 y | Discontinuation due to side effects<br>Irritation (score)<br>Local reactions/Irritation (Cumulative score) | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. | Adapalene produced less irritation than any concentration of tretinoin. |
| **#121**<br>**Gamborg-Nielsen,**<br>Varberg, Sweden<br>Parallel | Benzoyl peroxide + metronidazole<br>Vehicle<br><br>6 | n=43 **Mod/sev**<br>female 24<br>male 19<br>Age 19.0 y | Overall change/patient<br>Severity change/photo | ↑<br>No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Benzoyl peroxide + metronidazole was superior to placebo. |
| **#122**<br>**Gamborg-Nielsen,**<br>Varberg, Sweden<br>Parallel | Benzoyl peroxide<br>Benzoyl peroxide + metronidazole<br><br>6 | n=60 **Mod/sev**<br>female 33<br>male 27<br>Age 24.0 y | Overall change/patient<br>Overall change/physician<br>Severity change/photo | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. Inconsistent ascertainment across arms. Arms not comparable. | Benzoyl peroxide + metronidazole was superior to benzoyl peroxide alone. |
| **#123**<br>**Gamborg-Nielsen,**<br>Varberg, Sweden<br>Parallel | Oxytetracycline + vehicle<br>Benzoyl peroxide + metronidazole + placebo<br><br>6 | n=52 **Mod/sev**<br>female 30<br>male 22<br>Age 26.0 y | Overall change/patient<br>Overall change/physician<br>Severity change/photo | ↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Benzoyl peroxide + metronidazole was comparable to oxytetracycline. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#125**<br>**Gammon, 1986**<br>Chapel Hill, USA<br>Parallel<br>multicenter | Tetracycline + placebo<br>Erythromycin + placebo<br>2, 4, 8, 12 | n=178 **Mild/mod**<br>female 87<br>male 91 | Closed comedones change (%)<br>Open comedones change (%)<br>Overall change/patient<br>Papules change (%)<br>Pustules change (%)<br>Side effects | ↑<br>Randomized. | Tetracycline and erthromycin both reduced acne severity, but the reduction was faster in the tetracycline group for closed comedones. |
| **#126**<br>**Gandola, 1976**<br>Como, Italy<br>Parallel<br>multicenter | Placebo + cotrimoxazole<br>Sulfur-resorcinol + cotrimoxazole<br>Tretinoin + cotrimoxazole<br>2, 3, 4, 5, 6, 7, 8 | n=211 **Can't say**<br>female 146<br>male 65<br>Age 19.3 y | Comedones change (count)<br>Desquamation<br>Erythema<br>Papules change (count)<br>Pustules change (count)<br>Severity change (severity) | ↑<br>General population.<br>↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. | With each in combination with cotrimoxazole, retinoic acid was more effective than sulphur-resorcinol and placebo; sulphur-resorcinol was more effective than placebo. |
| **#127**<br>**Geiger, 1996**<br>Geneva, Switzerland<br>Parallel<br>matched<br>multicountry | Alitretinoin<br>Isotretinoin<br>2, 4 | n=26 **Can't say**<br>female 0<br>male 26<br>Age 17.0-40 y | Abdominal pain/diarrhea<br>Dry eyes/conjunctivitis<br>Dry mouth<br>Dry nose<br>Dry skin<br>Dryness/cheilitis<br>Headache<br>Increased appetite<br>Pruritis<br>Red/scaling face<br>Skin fragility | ↑<br>No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Outcome assessor not blinded. | All subjects had muco-cutaneous reactions; other side effects were reported to a greater extent with alitretinoin. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#128**<br>**Gibson, 1982**<br>London, UK<br>Parallel | Oxytetracycline<br>Trimethoprim<br>4, 8 | n=45 | **Mild** | Active papules (sqrt count)<br>Active pustules (sqrt count)<br>Back severity (log Leeds)<br>Chest severity (log Leeds)<br>Face severity (log Leeds)<br>Less active papules (sqrt count)<br>Less active pustules (sqrt count)<br>Overall change/patient<br>Side effects | ↑<br>Randomized. Data shows enroller blinded. Data shows outcome assessor blinded.<br>↓<br>Patient not blinded. Execution not as designed. | Oxytetracycline and trimethoprim were both effective. |
| **#130**<br>**Goldstein, 1982**<br>Boston, USA<br>Parallel<br>multicenter | Isotretinoin<br>Etretinate<br>2, 4, 6, 8;4, 8 post-therapy | n=56<br>female 0<br>male 56<br>Age 23.4 y | **Sev** | Mucous membrane side effects<br>Nodulocystic change (%)<br>Nodulocystic change post-therapy (%)<br>Nodulocystic change post-treatment/face (%)<br>Nodulocystic change/face (%)<br>Skin side effects<br>Systemic side effects | Data show patient blinded. Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Isotretinoin was significantly more effective than etretinate in reducing severe acne. |
| **#131**<br>**Goltz, 1985**<br>Minneapolis, USA<br>Parallel | Clindamycin (lotion)<br>Clindamycin (solution)<br>6, 12 | n=70<br>Age 22.0 y | **Mod/sev** | Burning<br>Closed comedones (count)<br>Diarrhea<br>Dryness<br>Erythema<br>Itching<br>Open comedones (count)<br>Overall change/patient<br>Overall change/physician<br>Papules (count)<br>Peeling<br>Pustules (count)<br>Severity (Goltz) | ↑<br>Randomized. Data shows enroller blinded.<br>↓<br>Patient not blinded. | Clindamycin lotion was less drying than solution and was equally effective. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#132**<br>**Goodfellow, 1984**<br>London, UK<br>Parallel | Placebo<br>Spironolactone (200)<br>Spironolactone (150)<br>Spironolactone (100)<br>Spironolactone (50)<br><br>12 | n=36 **Sev**<br>female 19<br>male 17<br>Age 24.0 y | Overall change<br>Overall change/patient<br>Overall change/photo | ↑<br>Randomized. Data shows enroller blinded. Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. Arms not comparable. | The clinical response to spironolactone was dose dependent and was best at a dose of 1250-200mg. |
| **#133**<br>**Goransson, 1978**<br>Umea, Sweden<br>Parallel | Placebo<br>Zinc sulfur<br>3, 6 | n=59 **Mod**<br>female 22<br>male 27<br>Age 20.3 y | Comedones change (count)<br>Overall change/patient<br>Papules change (count)<br>Pustules change (count)<br>Severity change (% Michaelsson)<br>Severity change (Michaelsson) | ↑<br>Randomized. Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded. | Zinc and placebo showed comparable effectiveness. |
| **#136**<br>**Gratton, 1982**<br>Montreal, Canada<br>Parallel | Placebo<br>Tetracycline + placebo<br>Clindamycin + placebo<br><br>2, 4, 6, 8 | n=305 **Mod/sev**<br><br>Age 18.0-35 y | Overall change/patient<br>Overall change/physician<br>Papules (count)<br>Pustules (count)<br>Side effects | Specific population. | Both topical clindamycin phosphate and oral tetracycline hydrochloride were effective in moderate to severe acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#137**<br>**Greenwood, 1985**<br>Leeds, UK<br>Parallel | Tetracycline + placebo<br>Cyproterone + ethinyl estradiol + placebo<br>Cyproterone + ethinyl estradiol + tetracycline<br><br>8, 16, 24, 32 (= 4 post-therapy) | n=92 **Can't say**<br>female 92<br>male 0<br>Age 16.0-30 y | Face severity change (Leeds %)<br>Inflammatory change (%)<br>Non-inflammatory change (%)<br>Post-therapy facial severity change (Leeds %)<br>Post-therapy inflammatory change (%)<br>Post-therapy non-inflammatory change (%)<br>Post-therapy total severity change (Leeds %)<br>Systemic reactions<br>Total severity change (Leeds %) | ↑<br>Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. Arms not comparable. | Cyproterone + ethinyl estradiol was as effective as tetracycline<br>in treating women. |
| **#138**<br>**Groot, 1963**<br>Amsterdam, The Netherlands<br>Parallel<br>split face | Sham rays<br>Grenz rays<br>7, 7-11, 12-14, 14-18 (unspecified) | n=40 **Can't say**<br>female 42<br>male 38<br>Age 15.0-25 y | Post-therapy overall state/observer | ↑<br>Randomized.<br>↓<br>Arms not comparable. | Treatment with Grenz rays is not recommended. |
| **#139**<br>**Groot, 1963**<br>Amsterdam, The Netherlands<br>Parallel<br>split face | Grenz rays<br>Sham rays<br>7, 7-11, 12-14, 14-18 (unspecified) | n=33 **Can't say** | Post-therapy overall state/observer | ↑<br>Randomized.<br>↓<br>Major losses to followup. Arms not comparable. | Treatment with Grenz rays is not recommended. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#140**<br>**Grosshans, 1998**<br>Strasburg, France<br>Parallel<br>multicountry | Adapalene<br>Tretinoin<br>1, 4, 12 | n=105 **Mild/mod**<br>female 39<br>male 66<br>Age 20.5 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity [intention to treat] (Leeds)<br>Severity [per protocol] (Leeds)<br>Severity change [intention to treat] (Leeds %)<br>Severity change [per protocol] (Leeds %)<br>Side effects<br>Withdrawal due to side effects | ↑<br>Randomized.<br>↓<br>Patient not blinded. | Adapalene 0.1% gel reduced inflammatory and total lesions more rapidly than tretinoin 0.025% gel and was better tolerated. |
| **#141**<br>**Gruber, 1998**<br>Vienna, Austria<br>Parallel | Vehicle<br>Cyproterone (topical)<br>Cyproterone + ethinyl estradiol (0.035)<br>4, 8, 12 | n=45 **Mild/mod**<br>female 45<br>male 0<br>Age 30.3 y | Face severity (Leeds)<br>Face severity change (Leeds)<br>Total lesions (count)<br>Total lesions change (count) | ↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Topical cyproterone acetate and oral cyproterone + ethinyl estradiol were equally effective. |
| **#142**<br>**Guerrier, 1980**<br>Northampton, UK<br>Parallel | Chloramphenicol + sulfur<br>Chloramphenicol + hydrocortisone + sulfur<br>2, 4, 8, 12 | n=50 **Mild/mod**<br>female 29<br>male 15 | Overall change/patient<br>Overall change/physician<br>Severity (score)<br>Total lesions change (%) | ↓<br>Arms not comparable. | Chloramphenicol/sulphur with or without hydrocortisone was effective for mild to moderate acne. |
| **#143**<br>**Guin, 1979**<br>USA<br>Parallel<br>split face | Clindamycin hydrochloride<br>Clindamycin phosphate<br>2+ (unspecified) | n=42 **Sev** | Nodules (count)<br>Papules (count)<br>Pustules (count) | ↑<br>Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. Arms not comparable. | Clindamycin hydrochloride was slightly better than clindamycin phosphate. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#144**<br>**Guin, 1981**<br>Indianapolis, USA<br>Parallel<br>split face | Vehicle<br>Clindamycin | n=31 | **Mod/sev** | Overall change/physician<br>Side effects | No losses to followup.<br>↓<br>Not randomized. | The study was too small to demonstrate a difference. |
| **#145**<br>**Gunning, 1994**<br>Ames, USA<br>Parallel | Retinyl beta-glucuronide<br>Vehicle<br>2, 4, 8, 12 | n=29<br>female 0<br>male 29<br>Age 20.4 y | **Mild/mod** | Adverse reaction<br>Efficacy to initial (Spearman)<br>Inflammatory (count/median)<br>Inflammatory change (ratio to initial)<br>Non-inflammatory (count/median)<br>Non-inflammatory change (ratio to initial)<br>Non-responders<br>Overall change/physician (score)<br>Total lesions (count/median)<br>Total lesions (ratio to initial)<br>Total lesions change (ratio to initial) | ↑<br>No losses to followup. | RBG reduced both inflammatory and non-inflammatory lesions. |
| **#146**<br>**Gunning, 1994**<br>Ames, USA<br>Parallel | Retinyl beta-glucuronide<br>Tretinoin<br>2, 4, 6, 8, 14, 19, 28 | n=15<br>Age 22.5 y | **Mild/mod** | Adverse reaction<br>Inflammatory (count/median)<br>Inflammatory lesion (ration to initial)<br>Non-inflammatory (count/median)<br>Non-inflammatory change (ratio to initial)<br>Non-responders<br>Overall change/physician (score)<br>Total lesions (count/median)<br>Total lesions change (ratio to initial) | ↑<br>No losses to followup.<br>↓<br>Outcome assessor not blinded. | RBG and tretinoin were equally effective for mild to moderate acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#147**<br>**Habbema, 1989**<br>Rotterdam, The Netherlands<br>Parallel<br>multicountry | Erythromycin<br>Erythromycin + zinc<br>2, 4, 8, 12 | n=122 | **Mod** | Comedones change (%)<br>Comedones change (count)<br>Inflammatory change (%)<br>Local side effects<br>Macules (count)<br>Nodules (count)<br>Severity (Cook) | ↑<br>Data shows enroller blinded. | Erythromycin/zinc lotion was more effective than 2% erythromycin in reducing number of acne lesions and severity grade of acne. |
| **#149**<br>**Handojo, 1979**<br>Surabaya, Indonesia<br>Parallel | Benzoyl peroxide (10%)<br>Benzoyl peroxide (5%)<br>Tretinoin<br>Tretinoin + benzoyl peroxide (10%)<br>Tretinoin + benzoyl peroxide (5%)<br>10 | n=250<br>female 202<br>male 48<br>Age 11.0-39 y | **Mild/mod/sev** | Inflammatory changes (Witkowski discretized %)<br>Non-inflammatory change (Witkowski discretized %)<br>Overall change (Witkowski discretized % )<br>Overall change (Witkowski discretized %)<br>Side effects/Withdrawal<br>Time to favorable status (Mean weeks) | No losses to followup.<br>↓<br>Patient not blinded. Enroller not blinded. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. | Tretinoin + benzoyl peroxide is the treatment of choice. |
| **#151**<br>**Hansted, 1985**<br>Copenhagen, Denmark<br>Parallel | Vehicle<br>Fusidin<br>2, 4, 6 | n=79<br>female 16<br>male 54<br>Age 19.0 y | **Mild/mod** | Comedones (count)<br>Inflammatory (count)<br>Side effects | ↓<br>Inconsistent ascertainment across arms. | Fusidin cream was superior to placebo cream in mild to moderate acne. |
| **#152**<br>**Harcup, 1980**<br>Malvera, UK<br>Parallel<br>matched | Oxytetracycline<br>Co-trimoxazole<br>4, 8, 12 | n=16<br>female 10<br>male 6<br>Age 15.5 y | **Mild/mod/sev** | Inter-treatment severity comparison<br>Overall change/matched (vas)<br>Severity (Leeds)<br>Severity change/photo<br>Side effects | ↑<br>No losses to followup. Local population. | Trimethoprim + sulphamethoxazole was more effective than oxytetracycline. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#155**<br>**Harrison, 1988**<br>Lancaster, UK<br>Parallel | Minocycline<br>Doxycycline<br>12 | n=43<br>female 21<br>male 22<br>Age 20.0 y | **Mild/mod/sev** | Cysts change (%)<br>Nodules change (%)<br>Papules changes (%)<br>Pustules change (%)<br>Severity change (% Wright)<br>Side effects<br>Total lesions (%) | ↓<br>Patient not blinded. Major losses to followup. | Doxycycline is just as effective as minocycline. |
| **#156**<br>**Hatwal, 1988**<br>Varanari, India<br>Parallel | Spironolactone [women]<br>Spironolactone [men]<br>Cimetidine [men]<br>Cimetidine [women]<br>12 | n=50<br>female 31<br>male 19<br>Age 14.0-25 y | **Mod/sev** | Severity (Michaelsson) | ↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. Arms not comparable. | Acne severity decreased with spironolactone and cimetidone, but more so with spironolactone. |
| **#157**<br>**Hellgren, 1980**<br>Irondheim, Norway<br>Parallel<br>matched<br>split face | Vehicle<br>Erythromycin<br>Unspecified | n=29<br>female 16<br>male 12<br>Age 15.0-34 y | **Mod/sev** | Overall comparison<br>Severity change (Plewig) | Data show patient blinded. No losses to followup. Data shows outcome assessor blinded. | |
| **#158**<br>**Henderson, 1995**<br>Raritan, USA<br>Parallel | Erythromycin<br>Clindamycin phosphate<br>2, 4, 8 | n=120<br>female 56<br>male 49<br>Age 21.3±1.0 y | **Mod** | Adverse reactions<br>Comedones (count)<br>Comedones change (%)<br>Cysts change (%)<br>Inflammatory (count)<br>Inflammatory change (%)<br>Overall change/investigator<br>Total lesions change (%)<br>Total lesions change (count) | ↑<br>Data shows outcome assessor blinded.<br>↓<br>Patient not blinded. Enroller not blinded. | Topical erythromycin was more effective than topical clindamycin phosphate for inflammatory acne. Erythromycin pledgets were more convenient, sanitary, and easier to use than clindamycin lotion. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#160**<br>**Hersle, 1972**<br>Gothenburg, Sweden<br>Cross-over<br>matched | Co-trimoxazole<br>Vehicle<br>5, 10 | n=42 **Can't say**<br>female 14<br>male 70<br>Age 13.0-30 y | Severity change [phase i] (Witkowski %)<br>Severity change [phase ii] (Witkowski %) | ↑<br>No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Trimethoprim + sulphamethoxazole was superior to vehicle. |
| **#161**<br>**Hersle, 1976**<br>Gothenburg, Sweden<br>Cross-over | Placebo<br>Minocycline<br>5 | n=43 **Can't say**<br>female 14<br>male 29<br>Age 14.0-34 y | Severity (Witkowski)<br>Severity change [phase ii] (group %)<br>Side effects | ↑<br>Data shows outcome assessor blinded. | Minocycline was superior to placebo. |
| **#162**<br>**Hicks, 1962**<br>Miami, USA<br>Parallel | Placebo<br>Demethylchlortetracycline<br>2-18 (unspecified) | n=37 **Mod/sev** | Adverse effects<br>Severity change | ↑<br>No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Demethylchlortetracycline was effective. Photosensitivity was the most common side effect. |
| **#163**<br>**Hillstrom, 1977**<br>Gavle, Sweden<br>Parallel<br>multicenter | Placebo<br>Zinc sulfate<br>4, 8, 12 | n=112 **Mod/sev**<br>Age 18.4 y | Overall change/patient<br>Overall change/physician<br>Side effects<br>Withdrawal due to side effects | | Zinc treatment was better than placebo. |
| **#164**<br>**Hjorth, 1984**<br>Rodovre, Denmark<br>Parallel | Meclocycline sulfosalicylate + placebo<br>Tetracycline + vehicle<br>4, 8 | n=60 **Mild/mod**<br>female 34<br>male 26<br>Age 20.0 y | Closed comedones change (%)<br>Cysts change (%)<br>Open comedones change (%)<br>Papules change (%)<br>Pustules change (%)<br>Total lesions change (%) | ↑<br>Randomized. No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Topical meclocycline sulfosalicylate was an effective and safe alternative to systemic tetracycline. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#165**<br>**Hjorth, 1985**<br>Rodovre, Denmark<br>Parallel<br>split face | Vehicle<br>Aluminum chloride<br>2, 4, 8 | n=25 **Mild/mod**<br>female 36<br>male 14<br>Age 23.0 y | Overall change | ↑<br>Data show patient blinded. | Topical 6.25% aluminum in anhydrous alcohol had a good clinical effect. |
| **#166**<br>**Hjorth, 1989**<br>Copenhagen, Denmark<br>Parallel<br>multicenter | Azelaic acid + placebo<br>Tetracycline hydrochloride<br>12, 20 | n=333 **Mild/mod**<br>female 155<br>male 178 | Overall change/physician<br>Total lesions (count/median) | ↑<br>Randomized.<br>↓<br>Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. Execution not as designed. | 20% azelaic acid cream was an effective topical treatment for inflammatory acne. |
| **#167**<br>**Hjorth, 1989**<br>Coppenhagen, Denmark<br>Parallel<br>multicenter | Tetracycline hydrochloride + placebo<br>Azelaic acid + placebo<br>4, 8, 12, 16, 20, 24 | n=261 **Mod/sev**<br>female 68<br>male 193 | Inflammatory (count/median)<br>Nodes+cysts (count/median)<br>Overall change/patient | ↑<br>Randomized.<br>↓<br>Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. Execution not as designed. | 20% azelaic acid cream was an effective topical treatment for inflammatory acne. |
| **#171**<br>**Hubbell, 1982**<br>Lackland, USA<br>Cross-over | Minocycline<br>Tetracycline<br>3, 6, 9, 12, 15, 18, 21, 24 | n=104 **Mod/sev**<br>female 27<br>male 22<br>Age 17.4 y | Mild/mod local side effects<br>Mild/mod systemic side effects<br>Persistent severity reduction<br>Severe side effects<br>Severity change<br>Severity reduction (cumulative %)<br>Time to severity reduction (days) | ↓<br>Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. | No statistically significant difference between the two treatments. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#172**<br>**Hughes, 1983**<br>Coral Gables, USA<br>Parallel<br>matched | Relaxation training + benzoyl peroxide + erythromycin<br>Group therapy<br>Benzoyl peroxide + erythromycin<br>4, 8 | n=30 **Mild/mod**<br>female 24<br>male 6<br>Age 27.1±6.6 y | Post-therapy severity (Cook)<br>Severity (Cook)<br>Severity difference/staff, patient<br>Severity/patient (Cook) | ↑<br>Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded. | Biofeedback relaxation combined with cognitive imagery reduced acne severity. |
| **#173**<br>**Hughes, 1992**<br>Leeds, UK<br>Parallel | Vehicle<br>Benzoyl peroxide<br>Isotretinoin<br>4, 8, 12 | n=77 **Mild/mod**<br>female 31<br>male 46<br>Age 18.7 y | Inflammatory (count)<br>Local reactions I<br>Local reactions II<br>Non-inflammatory (count)<br>Severity (Leeds) | ↑<br>Referral population.<br>↓<br>Arms not comparable. | Both topical benzoyl peroxide (5%) and topical isotretinoin (5%) were effective treatments for mild/moderate acne. Isotretinoin had a slower response rate for resolution of inflamed lesions. |
| **#175**<br>**Hull, 1989**<br>Leeds, UK<br>Parallel<br>split face | Vehicle<br>Clobetasol<br>3 | n=11 **Mod**<br>female 14<br>male 8<br>Age 15.0-25 y | Inflammatory (count)<br>Severity change | ↑<br>No losses to followup.<br>↓<br>Not randomized. Patient not blinded. Enroller not blinded. Inconsistent ascertainment across arms. Outcome assessor not blinded. Execution not as designed. | Clobetasol propionate did not significantly reduce the number of inflamed acne lesions. |
| **#176**<br>**Hunt, 1992**<br>Sydney, Australia<br>Parallel | Vehicle<br>Gluconolactone<br>Benzoyl peroxide<br>2, 4, 8, 12 | n=150 **Mod/sev**<br>female 65<br>male 70<br>Age 20.1 y | Inflammatory change (%)<br>Local effects<br>Non-inflammatory change (%)<br>Total lesions change (%) | ↓<br>Arms not comparable. | Topical gluconolactone as effective as benzoyl peroxide for inflamed and total lesions, and was better tolerated. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#177**<br>**Jaffe, 1989**<br>UK<br>Parallel<br>multicenter | Vehicle<br>Hydroxyquinoline + benzoyl peroxide + hydrocortisone<br>Hydroxyquinoline + benzoyl peroxide<br>Benzoyl peroxide<br><br>12 | n=107 | **Can't say** | Clinical assessed facial lesions<br>Clinical assessment back lesions<br>Clinical assessment chest lesions<br>Face severity (Jaffe)<br>Greasiness | ↑<br>Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded. | The combination cream better was superior. |
| **#178**<br>**Jelinek, 1972**<br>New York City, USA<br>Cross-over | Hydrochlorthiazide<br>Vehicle<br>4, 8 | n=42<br>female 42<br>male 0 | **Can't say** | Adverse reactions/No withdrawals<br>Adverse reactions/Withdrawals<br>Premenstrual change/patient [phase ii]<br>Premenstrual overall change/patient [phase ii]<br>Premenstrual overall change/physician [phase i]<br>Premenstrual overall change/physician [phase ii] | ↓<br>Major losses to followup. | Hydrochlorothiazide was ineffective in premenstrual acne. |
| **#179**<br>**Jelliffe, 1969**<br>London, UK<br>Parallel<br>matched<br>split face | Sham rays<br>Grenz rays<br><br>16, 24 | n=40 | **Can't say** | Improvement | ↑<br>No losses to followup.<br>↓<br>Not randomized. Enroller not blinded. | Grenz rays had no effect. |
| **#180**<br>**Jelliffe, 1969**<br>London, UK<br>Parallel<br>matched<br>split face | Sham rays<br>Grenz rays<br><br>4, 7 | n=42 | **Can't say** | Severity change (group %) | ↑<br>No losses to followup.<br>↓<br>Not randomized. Enroller not blinded. | Grenz rays at 50 kV may be beneficial. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#184**<br>**Jones, 1981**<br>Indianapolis, USA<br>Parallel | Vehicle<br>Erythromycin<br>3, 6, 9, 12 | n=175 **Mod**<br>female 88<br>male 68<br>Age 22.6±5.6 y | Burning-irritation<br>Dryness<br>Exudate<br>Eye irritation<br>Herpes simplex<br>Inflammatory (group count)<br>Oiliness<br>Overall change/physician<br>Pruritis<br>Redness<br>Scaling<br>Side effects | ↑<br>Data shows outcome assessor blinded. Specific population. | 2% topical erythromycin improved moderate to severe acne, but some side effects were seen. |
| **#185**<br>**Jones, 1983**<br>Leeds, UK<br>Parallel | Isotretinoin (1.0)<br>Isotretinoin (0.5)<br>Isotretinoin (0.1)<br>4, 8, 12, 16, 20, 24, 28, 32 | n=76 **Mod**<br>female 45<br>male 31<br>Age 24.3±6.2 y | Local reactions/Cheilitis severity<br>Local reactions/Conjunctivitis<br>Local reactions/Dermatitis severity<br>Local reactions/Desquamation severity<br>Non-inflammatory change (%)<br>Post-therapy non-inflammatory change (%)<br>Systemic reactions/Arthralgia<br>Systemic reactions/Epistaxis severity<br>Systemic reactions/Malaise | ↑<br>No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Execution not as designed. | Isotretinoin at 0.5 mg/kg was recommended over 0.1 or 1.0 mg/kg for initial treatment, balancing relapse rate and side effects. |
| **#186**<br>**Katsambas, 1987**<br>Athens, Greece<br>Parallel | Tetracycline hydrochloride + placebo<br>Clindamycin + placebo<br>3, 6, 9, 12 | n=44 **Mod**<br>female 42<br>male 2<br>Age 13.0-30 y | Closed comedones (count)<br>Nodules (count)<br>Open comedones (count)<br>Papules (count)<br>Pustules (count)<br>Side effects | ↓<br>Major losses to followup. | Topical clindamycin was effective to treat moderate acne vulgaris. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#187**<br>**Katsambas, 1989**<br>Athens, Greece<br>Parallel | Vehicle<br>Azelaic acid<br>4, 8, 12 | n=92 **Mod**<br>female 65<br>male 27<br>Age 19.0 y | Burning<br>Comedones change (%)<br>Erythema<br>Inflammatory (count/median)<br>Itching<br>Overall change/physician<br>Scaling | ↑<br>Randomized.<br>↓<br>Inconsistent ascertainment across arms. | Azelaic acid was a therapeutically active drug. |
| **#188**<br>**Katsambas, 1989**<br>Athens, Greece<br>Parallel | Tretinoin<br>Azelaic acid<br>20 | n=289 **Can't say**<br>female 152<br>male 137<br>Age 17.5 y | Comedones (count)<br>Comedones (count/median)<br>Erythema<br>Overall change/physician<br>Scaling | ↑<br>Randomized.<br>↓<br>Major losses to followup. Inconsistent ascertainment across arms. | 20% azelaic acid cream showed the same therapeutic benefit in comedonal acne as 0.05% tretinoin cream but caused side effects. |
| **#189**<br>**Kern, 1962**<br>Providence, USA<br>Parallel | Placebo<br>Gamma-globulin<br>6-48 (unspecified) | n=40 **Mod/sev**<br>female 21<br>male 19<br>Age 15.0-30 y | Overall change/physician<br>Side effects | ↓<br>Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. | Gamma-globulin every two weeks was not useful in the management of moderate acne. |
| **#190**<br>**King, 1982**<br>Leeds, UK<br>Parallel | Isotretinoin (0.1)<br>Isotretinoin (1.0)<br>Isotretinoin (0.5)<br>4, 8, 12, 16 | n=48 **Mild/mod/sev**<br>female 24<br>male 24<br>Age 25.0 y | Severity/face (king) | ↓<br>Major losses to followup. Arms not comparable. | No evidence of dose response. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#191**<br>**Kirton, 1967**<br>UK<br>Parallel<br>split face | Proprietary formula (sulfur + salicylic acid + resorcinol)<br>Placebo<br>Komed® (sulfur + salicylic acid + resorcinol)<br><br>16, end of study (up to 36) | n=51<br>female 38<br>male 13<br>Age 13.0-28 y | **Mild/mod/sev** | Overall change/physician | ↑<br>No losses to followup.<br>Referral population.<br>↓<br>Arms not comparable. | Komed was an effective treatment. |
| **#192**<br>**Knox, 1965**<br>Houston, USA<br>Parallel | Demethylchlortetracycline<br>Placebo<br>3 | n=74 | **Can't say** | Overall change/physician | ↑<br>No losses to followup.<br>↓<br>Arms not comparable. | Systemic demethylchlortetracycline was effective in treating acne vulgaris. |
| **#193**<br>**Knox, 1965**<br>Houston, USA<br>Cross-over | Placebo<br>Demethylchlortetracycline<br>3, 7 | n=74 | **Can't say** | Overall change/physician, patient | ↑<br>No losses to followup. | Demethylchlortetracycline was better than placebo. |
| **#194**<br>**Knutson, 1981**<br>Sioux Falls, USA<br>Parallel<br>multicenter | Vehicle<br>Meclocycline<br><br>2, 4, 8, 11 | n=134 | **Mod/sev** | Comedones (count)<br>Inflammatory change<br>Inflammatory change (median %)<br>Side effects | No losses to followup.<br>Referral population.<br>↓<br>Not randomized.<br>Inconsistent ascertainment across arms. | Meclocycline is effective and safe. Twice daily is as effective as once-daily, but perhaps achieves effect quicker. |
| **#195**<br>**Knutson, 1981**<br>Sioux Falls, USA<br>Parallel<br>multicenter | Vehicle<br>Meclocycline<br><br>2, 5 | n=217 | **Mod/sev** | Adverse effects<br>Inflammatory change (median %) | No losses to followup.<br>Referral population.<br>↓<br>Not randomized.<br>Inconsistent ascertainment across arms. | Meclocycline is safe and effective. Once daily administration is as effective, but longer time to reach maximal effect. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#197**<br>**Korting, 1995**<br>Munich, Germany<br>Parallel | Acidic syndet bar<br>Soap<br>12 | n=114 **Mild**<br>female 47<br>male 67<br>Age 20.0±3.3 y | Inflammatory (count)<br>Itching<br>Non-inflammatory (count)<br>Redness<br>Scaling | ↑<br>Randomized. Data shows enroller blinded.<br>↓<br>Patient not blinded. Outcome assessor not blinded. | Acidic syndet lowerd the number of inflammatory acne lesions in acne-prone patients more than regular use of soap. |
| **#198**<br>**Krishnan, 1976**<br>Liecester, UK<br>Parallel | Vehicle<br>Tretinoin (0.025%)<br>Tretinoin (0.05%)<br>12 | n=60 **Can't say**<br>Age 18.0-21 y | Clinical assessment<br>Comedones (count)<br>Papules (count)<br>Pustules (count)<br>Severity/patient (vas)<br>Side effects | ↑<br>Data shows enroller blinded. No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. Arms not comparable. | Topical tretinoin 0.05% and 0.025% were both better than placebo and about equally effective. There were fewer side effects with 0.025% tretinoin. |
| **#199**<br>**Kuhlman, 1986**<br>Louisville, USA<br>Parallel | Vehicle<br>Clindamycin phosphate<br>3, 6, 12 | n=45 **Mild/mod**<br>Age 12.0-30 y | Closed comedones (count)<br>Dryness, peeling, erythema, burning and itching<br>Nodes+cysts (count)<br>Open comedones (count)<br>Overall change/physician<br>Papules (count)<br>Pustules (count)<br>Severe side effects | ↑<br>No losses to followup.<br>↓<br>Inconsistent ascertainment across arms. | Topical clindamycin was effective for moderate to severe acne and was well tolerated. [By the Combined Acne Severity Classification, these patients' acne is classified as "mild to moderate."] |
| **#201**<br>**Lane, 1969**<br>Leeds, UK<br>Parallel | Tetracycline<br>Placebo<br>6, 12 | n=51 **Can't say**<br>female 25<br>male 26<br>Age 18.0 y | Clinical change (grouped)<br>Clinical change/photo (grouped)<br>Clinical improvement/photo (grouped)<br>Severity change (Pillsbury modified)<br>Side effects | ↑<br>Randomized. Data shows enroller blinded. Data shows outcome assessor blinded. Referral population.<br>↓<br>Arms not comparable. | Tetracycline was better than placebo for moderate acne. (Note that baseline data was not provided to document acne severity.) |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#202**<br>**Langner, 1994**<br>Warsaw, Poland<br>Parallel | Vehicle<br>Isotretinoin (0.05%)<br>Isotretinoin (0.1%)<br><br>4, 8, 12 | n=82 **Mild/mod** | Closed comedones (count)<br>Papules (count)<br>Side effects | | .01% and 0.05% istretinoin reduced acne grade, particulary closed comedones, more than placebo. 0.1% isotretinoin was better tolerated. |
| **#204**<br>**Lassus, 1996**<br>Helsinki, Finland<br>Parallel | Silicic acid<br>Vehicle<br>6 | n=30 **Mod**<br>female 19<br>male 11<br>Age 19.0 y | Comedones (count)<br>Cysts (count)<br>Papules (count)<br>Pustules (count) | ↑<br>No losses to followup.<br>↓<br>Enroller not blinded. | Silicic acid was more effective than placebo. |
| **#205**<br>**Lesher, 1985**<br>Augusta, USA<br>Parallel<br>multicenter | Vehicle<br>Erythromycin<br>2, 4, 8, 10, 12 | n=225 **Mild/mod**<br>female 76<br>male 132<br>Age 18.6 y | Erythema<br>Inflammatory (count )<br>Inflammatory (count)<br>Peeling<br>Severity (Cook )<br>Severity change (Cook %) | ↑<br>Randomized. | 2% erythromycin was better than vehicle. |
| **#206**<br>**Lester, 1985**<br>Toronto, Canada<br>Parallel | Tetracycline hydrochloride<br>Isotretinoin<br>2, 4, 8, 12, 16, 20, 24, 35 | n=30 **Sev**<br>female 1<br>male 29<br>Age 25.4±6.5 y | Comedones+pustules (count)<br>Cysts (count)<br>Cysts diameters (mm)<br>Integumentary side effects I<br>Integumentary side effects II<br>Integumentary side effects III<br>Post-therapy back total lesions change<br>Post-therapy chest total lesion change<br>Post-therapy comedones+pustules (count)<br>Post-therapy cyst diameters (mm)<br>Post-therapy long term cyst (count)<br>Systemic reactions<br>Systemic reactions/Special senses | ↓<br>Enroller not blinded. Major losses to followup. | After 16 weeks treatment both isotretinoin and tetracycline produced similar improvement in patients with severe recalcitrant nodulocystic acne. 8 weeks after treatment, patients treated with isotretinoin continued to improve more than those treated with tetracycline. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#208**<br>**Leyden, 1987**<br>Brooklyn, USA<br>Parallel<br>multicenter | Erythromycin<br>Clindamycin phosphate<br>4, 8, 12 | n=109<br>female 50<br>male 52<br>Age 17.8 y | **Mild/mod** | Closed comedones change (count)<br>Inflammatory change (count)<br>Local tolerability<br>Non-inflammatory change (count)<br>Open comedones change (count)<br>Overall change/patient<br>Papules change (count)<br>Pustules change (count)<br>Severity change (% response) | ↓<br>Patient not blinded. | Topical erythromycin 2% gel was as effective as topical clindamycin phosphate 1% solution in reducing number of lesions and in improving overall acne condition. |
| **#211**<br>**Liden, 1980**<br>Umea, Sweden<br>Parallel | Placebo<br>Zinc sulfate<br>3, 6 | n=59<br>female 22<br>male 32<br>Age 20.3 y | **Mild/mod/sev** | Severity change (Pillsbury %) | | Zinc had a weak but statistically significant effect. |
| **#212**<br>**Lim, 1974**<br>London, UK<br>Parallel | Tetracycline hydrochloride<br>Tetracycline (sustained release)<br>4, 8, 12 | n=55<br>female 23<br>male 16<br>Age 20.0 y | **Can't say** | Overall change/physician<br>Side effects | ↑<br>Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. Arms not comparable. | Sustained-release tetracycline (at half the standard dose of tetracycline) was as effective as treracycline hydrochloride. |
| **#213**<br>**Lookingbill, 1992**<br>Hershey, USA<br>Parallel<br>multicenter | Vehicle<br>Inocoterone acetate<br>4, 8, 16 | n=153<br>female 0<br>male 153 | **Mod** | Comedones (count)<br>Inflammatory (count)<br>Local adverse reactions | ↑<br>Randomized. | Topical inocoterone acetate produced a modest clinical effect. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#214**<br>**Lookingbill, 1997**<br>Hershey, USA<br>Parallel<br>multicenter | Vehicle<br>Benzoyl peroxide<br>Clindamycin<br>Clindamycin + benzoyl peroxide<br><br>2, 5, 8, 11 | n=393 **Mod**<br>female 202<br>male 191<br>Age 18.5 y | Inflammatory change (%)<br>Local side effects<br>Non-inflammatory change (%)<br>Overall change/physician | ↑<br>Randomized. Data shows enroller blinded. Data shows outcome assessor blinded. General population.<br>↓<br>Major losses to followup. Arms not comparable. | A combination was better than either component alone. |
| **#215**<br>**Lowney, 1964**<br>Philadelphia, USA<br>Parallel<br>matched<br>split face | Comedone extraction (cheeks/forehead)<br>Comedone extraction (forehead)<br><br>12 | n=20 **Can't say**<br>female 4<br>male 16<br>Age 15.0-22 y | Inflammatory change | ↑<br>No losses to followup.<br>↓<br>Not randomized. Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Comedones extraction was effective in superficial, but not cystic, acne. It was more effective on the forehead than the cheeks. |
| **#216**<br>**Lowney, 1964**<br>Philadelphia, USA<br>Parallel<br>matched<br>split face | Comedone extraction (cheeks/forehead)<br>Untreated<br><br>Unspecified | n=12 **Can't say**<br>female 3<br>male 9<br>Age 14.0-18 y | Inflammatory change | ↑<br>No losses to followup.<br>↓<br>Not randomized. Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Comedones extraction was effective in superficial, but not cystic, acne. It was more effective on the forehead than the cheeks. |
| **#217**<br>**Lucchina, 1996**<br>Boston, USA<br>Parallel | Clindamycin<br>Vehicle<br>2, 4, 8, 12 | n=42 **Mod**<br>female 19<br>male 13<br>Age 13.0-31 y | Closed comedones (count)<br>Open comedones (count)<br>Papules (count)<br>Pustules (count)<br>Severity (Leeds)<br>Severity/flash photo (Leeds)<br>Severity/fluorescent photo-face+nose (Leeds)<br>Severity/fluorescent photo-nose (Leeds)<br>Severity/fluorescent photography | ↑<br>Data shows outcome assessor blinded.<br>↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. | Clindamycin was more effective than placebo in a study using fluorescence photography. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#218**<br>**Lucky, 1997**<br>Cinncinnati, USA<br>Parallel<br>multicenter | Norgestimate + ethinyl estradiol + inactive drug<br>Placebo<br>4, 8, 12, 16, 20, 24, 25, 26 | n=257 **Mod**<br>female 231<br>Age 27.0 y | Closed comedones change (count)<br>Comedones change (count)<br>Inflammatory (count)<br>Nodules change (count)<br>Open comedones change (count)<br>Overall change/investigator<br>Overall change/patient<br>Total lesions change (%)<br>Total lesions change (count) | ↑<br>Randomized. Data shows outcome assessor blinded. Specific population.<br>↓<br>Major losses to followup. | Norgestimate-ethinyl estradiol use led to greater decreases in acne lesion counts and better global ratings than placebo in women with moderate acne |
| **#219**<br>**Lucky, 1998**<br>Cincinnati, USA<br>Parallel<br>multicenter | Polyoprepolymer-2<br>Tretinoin<br>Tretinoin + polyoprepolymer-2<br>2, 4, 8, 12 | n=344 **Mild/mod**<br>female 135<br>male 136<br>Age 20.0±5.8 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Overall change/physician<br>Side effects<br>Total lesions change (%) | ↑<br>Data show patient blinded. Data shows enroller blinded. Referral population. | Tretinoin and tretinoin with polymer were equally efficacious and safe for mild-moderate acne. |
| **#220**<br>**Lucky, 1998**<br>Cincinnati, USA<br>Parallel<br>multicenter | Vehicle<br>Tretinoin (ethanol)<br>Tretinoin (polyoprepolymer-2)<br>2, 4, 8, 12 | n=215 **Mild/mod**<br>female 118<br>male 97 | Adverse effect<br>Adverse effects<br>Any adverse outcome<br>Dry skin<br>Eruption<br>Inflammatory change (%)<br>Non-inflammatory change (%)<br>Other skin symptoms<br>Systemic adverse effects<br>Total lesions change (%) | ↓<br>Arms not comparable. | Ethanol and polyprepolymer-2 gels containing 0.025% tretinoin had similar efficacy but polyoprepolymer-2 caused less peeling and drying. |
| **#221**<br>**Lyons, 1978**<br>San Antonio, USA<br>Parallel<br>multicenter | Benzoyl peroxide (alcohol)<br>Benzoyl peroxide (acetone)<br>Tretinoin<br>2, 4, 6, 8 | n=147 **Mod**<br>female 107<br>male 40<br>Age 18.7 y | Adverse reaction<br>Comedones (count)<br>Comedones change (%)<br>Papules (count)<br>Papules change (%)<br>Pustules (count)<br>Pustules change (%)<br>Severity change | ↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Benzoyl peroxide and tretinoin were equally effective. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#222**<br>**Macdonald, 1951**<br>UK<br>Parallel | Vehicle<br>Staphylococcal toxoid<br>10, 24 | n=66<br>female 0<br>male 66 | **Mild/mod/sev** | Adverse reaction<br>Overall change/patient<br>Overall change/physician [mild]<br>Overall change/physician [moderate]<br>Overall change/physician [severe] | ↑<br>No losses to followup. Specific population. | Staphylococcal toxoid injection was efficacious in management of recalcitrant pustular acne. |
| **#223**<br>**Macdonald, 1972**<br>Glasgow, UK<br>Cross-over matched | Placebo<br>Co-trimoxazole<br>4 | n=40<br>Age 18.5 y | **Can't say** | Comedones change [phase i+ii] (count)<br>Dizziness and headaches<br>Pustules change [phase i+ii] (count)<br>Red macular rash | ↑<br>Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded. | Trimethoprim-sulphamethoxazole was as effective as placebo. |
| **#224**<br>**Macdonald, 1976**<br>Manchester, UK<br>Cross-over | Hydrocortisone + buttoxethyl nicotinate + chloramphenicol<br>Vehicle<br>4, 10 | n=120<br>female 78<br>male 42 | **Mild/mod/sev** | Comedones reduction percentage change (%)<br>Inter-group difference papule % change (%)<br>Inter-group difference pustule % change (%)<br>Side effects | ↑<br>Data show patient blinded.<br>↓<br>Enroller not blinded. Major losses to followup. Outcome assessor not blinded. | Topical mixture of sulphur chloramphenicol hydrocortisone and buttoxyl ethyl nicotinate was better than vehicle. |
| **#225**<br>**Mango, 1996**<br>Rome, Italy<br>Parallel | Gestodene + ethinyl estradiol<br>Desogestrel + ethinyl estradiol<br>12, 24, 36 | n=24<br>female 24<br>Age 24.0±3.7 y | **Mild/mod** | Severity (Pillsbury)<br>Severity change (Pillsbury)<br>Severity/arm (Pillsbury)<br>Systemic adverse effects | ↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. | Ethinyl estradiol desogestrel and ethinyl estradiol-gestodene were effective in reducing acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#228**<br>**Mcguiness, 1965**<br>Sussex, UK<br>Parallel<br>multicenter | Neomycin + methyl prednisolone<br>Vehicle<br>Aluminum chlorhydroxide + sulfur<br><br>4-6 (unspecified) | n=776 | **Can't say** | Overall change/physician | ↓<br>Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. Execution not as designed. | Neomycin + methylprednisolone was effective. |
| **#229**<br>**McKenzie, 1981**<br>Gainesville, USA<br>Parallel<br>split face | Ionax®<br>E-solve®<br>Clindamycin hydrochloride (Ionax®)<br>Clindamycin hydrochloride (E-solve®)<br>Clindamycin phosphate (Ionax®)<br>Clindamycin phosphate (E-solve®)<br><br>4, 8, 12 | n=88<br>female 64<br>male 20<br>Age 20.3 y | **Mod/sev** | Inflammatory change (%) | ↑<br>Randomized. Local population. | The effectiveness of clindamycin compared with the hydroalcoholic products was not significantly greater. |
| **#231**<br>**Mesquita Guimar**<br>Porto, Portugal<br>Parallel | Benzoyl peroxide<br>Benzoyl peroxide + miconazole<br>2, 4, 8 | n=20<br><br>Age 17.0±2.4 y | **Mild/mod/sev** | Comedones change (geometric mean)<br>Exfoliation<br>Inflammatory change (geometric mean)<br>Overall assessment/patient<br>Overall assessment/physician<br>Pustular lesions<br>Side effects | ↑<br>Randomized. No losses to followup. | Benzoyl peroxide + miconazole was better than benzoyl peroxide alone, particularly for inflammatory acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#232**<br>**Michaelsson, 197**<br>Uppsala, Sweden<br>Parallel | Oxytetracycline<br>Zinc sulfate<br>2, 4, 8, 12 | n=40 **Mod/sev**<br>female 16<br>male 24<br>Age 15.0-29 y | Comedones change (count)<br>Comedones severity change (Michaelsson difference)<br>Overall change/patient<br>Overall change/physician<br>Papules change (count)<br>Papules severity change (Michaelsson difference)<br>Pustules change (count)<br>Pustules severity change (Michaelsson difference)<br>Total severity change/photo (Michaelsson) | ↑<br>No losses to followup. | The effects of oral zinc and chlortetracycline were comparable in patients with moderate to severe acne. |
| **#233**<br>**Michaelsson, 197**<br>Uppsala, Sweden<br>Parallel | Zinc sulfate + Vitamin A palmitate<br>Zinc sulfate<br>Vitamin A palmitate<br>Vehicle<br>2, 4, 6, 8, 12 | n=64 **Mod/sev**<br>female 26<br>male 38<br>Age 13.0-25 y | Severity change (Michaelsson %)<br>Side effects | ↑<br>No losses to followup.<br>↓<br>Arms not comparable. | Zinc decreased the number of papules, pustules and infiltrates. There was no significant effect for Vitamin A. |
| **#235**<br>**Milikan, 1976**<br>Columbia, USA<br>Parallel | Vehicle<br>Povidone-iodine<br>12-16 (unspecified); 14 average | n=30 **Mild** | Itching<br>Overall change/physician | ↓<br>Major losses to followup. Outcome assessor not blinded. | Betadine was an effective treatment for mild acne. |
| **#236**<br>**Milikan, 1976**<br>Columbia, USA<br>Parallel | Tetracycline + vehicle<br>Povidone-iodine + tetracycline<br>12-16 (unspecified) | n=30 **Mod/sev** | Itching<br>Overall change/physician | ↓<br>Major losses to followup. Outcome assessor not blinded. | Povidone-iodine skin cleanser may not penetrate deeply enough to produce significant improvement in moderate acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#237**<br>**Miller, 1986**<br>London, UK<br>Parallel | Cyproterone (2 mg) + ethinyl estradiol<br>Cyproterone (.05 mg) + ethinyl estradiol<br>Norethisterone + placebo + ethinyl estradiol<br>8, 16, 26 | n=90 **Mod/sev**<br>female 90<br>male 0<br>Age 23.7 y | Face severity (Leeds)<br>Face severity/photo<br>Macules (count)<br>Nodules (count)<br>Papules (count)<br>Systemic reactions I > once<br>Systemic reactions I once only<br>Systemic reactions II > once<br>Systemic reactions II once only<br>Total severity (Leeds) | | Cyproterone and norethisterone were both effective.Cyproterone achieved effects faster. Side effects rates were comparable. |
| **#238**<br>**Mills, 1978**<br>Philadelphia, USA<br>Parallel | Vehicle<br>Tretinoin<br>Erythromycin<br>Erythromycin + tretinoin<br>2, 4, 6, 8 | n=80 **Mod/sev**<br>female 35<br>male 45<br>Age 16.5 y | Overall change/physician | ↓<br>Not randomized. Patient not blinded. Enroller not blinded. Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. | Erythromycin + tretinoin was more effective than either alone. |
| **#239**<br>**Mills, 1979**<br>Philadelphia, USA<br>Parallel | Polystyrene<br>Polyethylene<br>Polyester<br>Aluminum oxide<br>Pumice<br>8 | n=50 **Mod/sev** | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Total lesion change (%) | ↓<br>Not randomized. Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. Arms not comparable. | The beneficial effects of these abradants were slight. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#241**<br>**Mills, 1986**<br>Philadelphia, USA<br>Parallel | Vehicle<br>Benzoyl peroxide<br>2, 4, 6, 8 | n=50 | **Mild/mod** | Total lesions change (%) | ↑<br>No losses to followup.<br>↓<br>Not randomized. Inconsistent ascertainment across arms. Arms not comparable. | 2.5% benzoyl peroxide was more effective than vehicle and caused more side effects. |
| **#242**<br>**Mills, 1986**<br>Philadelphia, USA<br>Parallel | Benzoyl peroxide (5%)<br>Benzoyl peroxide (2.5%)<br>2, 4, 6, 8 | n=52 | **Mild/mod** | Total lesions change (%) | ↑<br>No losses to followup.<br>↓<br>Not randomized. Inconsistent ascertainment across arms. Arms not comparable. | There was no difference in efficacy or side effects between the 2.5% and 5.0% benzoyl peroxide. |
| **#243**<br>**Mills, 1986**<br>Philadelphia, USA<br>Parallel | Benzoyl peroxide (10%)<br>Benzoyl peroxide (2.5%)<br>2, 4, 6, 8 | n=50 | **Mild/mod** | Burning<br>Erythema<br>Peeling<br>Total lesions change (%) | ↑<br>No losses to followup.<br>↓<br>Not randomized. Inconsistent ascertainment across arms. Arms not comparable. | 2.5% and 10% benzoyl peroxide showed equal efficacy.The 10% formulation caused more frequent and severe burning, erythema, and peeling. |
| **#244**<br>**Mills, 1992**<br>East Brunswick, USA<br>Parallel | Erythromycin<br>Clindamycin<br>2, 4, 8 | n=120<br>Age 18.0-30 y | **Mild/mod** | Comedones change (%)<br>Dryness change (score)<br>Erythema change (score)<br>Inflammatory change (%)<br>Papules change (%)<br>Pustules change (%)<br>Total lesions change (%) | ↑<br>No losses to followup.<br>↓<br>Enroller not blinded. Arms not comparable. | Erythromycin produced a greater reduction in pustules, papules, total inflamed lesions and total lesions, and was preferred by patients in terms of convenience, ease of application, and portability. Clindamycin was more effective for comedones. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
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| **#245**<br>**Monk, 1987**<br>London, UK<br>Parallel<br>multicenter | Cyproterone + ethinyl estradiol<br>Minocycline hydrochloride<br>8, 16, 24 | n=98 **Mild/mod**<br>female 98<br>male 0<br>Age 23.4±5.1 y | Comedones (count/max range)<br>Comedones (count/median)<br>GI+other side effects<br>Gyn side effects<br>Overall change/patient<br>Papules (count/max)<br>Papules (count/median)<br>Papules range (count/max)<br>Pustules (count/max)<br>Pustules (count/median)<br>Skin side effects | ↓<br>Patient not blinded. Enroller not blinded. Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. | Cyproterone-ethinyl estradiol and minocin were found to be equally effective in reduced the lesion count for comedones, papules and pustules and in pts subjective assessment of their skin. |
| **#246**<br>**Morganti, 1997**<br>Italy<br>Parallel<br>split face | Soybean liposome<br>Glycolic acid + soybean liposome<br>4, 8, 12 | n=40 **Mild/mod**<br>female 20<br>male 20<br>Age 16.0±3.0 y | Closed comedones (count)<br>Closed comedones change (%)<br>Open comedones (count)<br>Open comedones change (%)<br>Papules (count)<br>Papules change (%)<br>Pustules (count)<br>Pustules change (%)<br>Withdrawals due to side effects | ↑<br>No losses to followup. | Glycolic acid and soybean liposome was more effective and acted more quickly than soybean liposome alone. |
| **#247**<br>**Morginson, 1960**<br>Salt Lake City, USA<br>Parallel | Oleandomycin<br>Triacetyl-oleandomycin<br>4-8 (unspecified) | n=142 **Can't say** | Overall change/physician | ↓<br>Not randomized. Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. Execution not as designed. | Triacetyl-oleandomycin is effective. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#248**<br>**Moroni, 1976**<br>Reggio Emilia, Italy<br>Parallel | Quinestradol<br>Placebo<br>8 | n=60 **Mild/mod**<br>female 60<br>male 0 | Comedones (count)<br>Total lesions (count) | ↓<br>Not randomized. Major losses to followup. | Quinestradol is effective, especially for comedones. |
| **#249**<br>**Muhlemann, 198**<br>London, UK<br>Cross-over | Placebo<br>Spironolactone<br>12 | n=58 **Mild/mod**<br>female 58<br>male 0 | Change (count)<br>Overall change/patient<br>Positive side effects<br>Severity/photo<br>Side effects<br>Total lesions [phase i+phase ii] (count) | ↑<br>Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. | Spironolactone significantly improved acne. |
| **#250**<br>**Murphy, 1962**<br>Unknown<br>Cross-over | Placebo<br>Oxytetracycline<br>Unspecified | n=76 **Mod/sev**<br>female 50<br>male 26<br>Age 11.0-33 y | Severity change [phase i]<br>Severity change [phase ii]<br>Side effects | ↓<br>Not randomized. Inconsistent ascertainment across arms. Arms not comparable. | Oxytetracycline in low dosage over a prolonged period of time was safe and effective. |
| **#253**<br>**Nordin, 1981**<br>Vasteras, Sweden<br>Parallel | Tretinoin<br>Motretinide (bid)<br>Motretinide (qd)<br>8 | n=60 **Mod/sev**<br>female 39<br>male 21<br>Age 15.0 y | Overall change/physician<br>Papules (count)<br>Pustules (count) | ↑<br>No losses to followup. | Motretinide was an effective alternative to tretinoin. |
| **#255**<br>**Norris, 1991**<br>Leeds, UK<br>Parallel | Oxytetracycline (oral) + vehicle<br>Benzoyl peroxide + placebo (oral)<br>Tetracycline (topical) + placebo (oral)<br>8, 12 | n=69 **Mod**<br>female 45<br>male 24<br>Age 12.0-33 y | Back severity (Leeds)<br>Chest severity (Leeds)<br>Face severity (Leeds)<br>Inflammatory (count)<br>Non-inflammatory (count)<br>Side effects | ↓<br>Inconsistent ascertainment across arms. | Topical tetracycline was as effective as either 5% benzoyl peroxide gel or oral tetracycline. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#257**<br>**Olafsson, 1989**<br>Reykjavik, Iceland<br>Parallel | Doxycycline + placebo<br>Minocycline + placebo<br>4, 8, 12 | n=79 **Mod/sev**<br>female 44<br>male 35<br>Age 20.5 y | Closed comedones (count)<br>Open comedones (count)<br>Papules (count)<br>Pustules (count)<br>Total lesions (count)<br>Withdrawal due to side effects | | Doxycyline and minocycline were equally effective. |
| **#259**<br>**Orris, 1978**<br>New York City, USA<br>Parallel<br>multicenter | Vehicle<br>Zinc sulfate<br>4, 6, 8, 10, 12 | n=30 **Mild/mod**<br>female 0<br>male 22<br>Age 19.1 y | Closed comedones (count)<br>Open comedones (count)<br>Papules (count)<br>Pustules (count) | ↓<br>Major losses to followup. | Oral zinc produced no benefit in males with moderate acne. |
| **#260**<br>**Packman, 1996**<br>Collegeville, USA<br>Parallel<br>multicenter | Erythromycin + benzoyl peroxide<br>Clindamycin phosphate<br>2, 4, 7, 10 | n=205 **Mild/mod**<br>female 205<br>male 0<br>Age 23.0-50 y | Comedones (count)<br>Inflammatory (count)<br>Overall change (score)<br>Side effects | ↑<br>Data show patient blinded. Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded. | Topical erythromycin with benzoyl peroxide was more effective than clindamycin. |
| **#261**<br>**Padilla, 1981**<br>Albuquerque, USA<br>Parallel | Tetracycline hydrochloride<br>Clindamycin<br>2, 4, 6, 8 | n=52 **Mild/mod**<br>female 26<br>male 23<br>Age 22.3 y | Erythema<br>Itching/burn<br>Overall improvement (discretized %)<br>Peeling<br>Side effects<br>Total lesions (count) | ↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Topical clindamycin was superior to topical tetracycline for treatment of mild-moderate acne. Both produced minimal side effects. |
| **#263**<br>**Palatsi, 1984**<br>Oulu, Finland<br>Parallel<br>multicenter | Levonorgestrel + ethinyl estradiol<br>Desogestrel + ethinyl estradiol<br>24 | n=54 **Can't say**<br>Age 24.0 y | Severity change<br>Side effects | ↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. Arms not comparable. | Desogestrel + ethinyl estadiol was superior to levonorgestrel + ethinyl estadiol. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#264**<br>**Palatsi, 1986**<br>Oulu, Finland<br>Parallel | Levonorgestrel + ethinyl estradiol<br>Desogestrel + ethinyl estradiol<br>24 | n=33 **Mild/mod**<br>Age 24.0 y | Severity (Allen-Smith) | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Desogestrel and ethinyl estadiol produced more improvement than levonorgestrel + ethinyl estadiol. |
| **#265**<br>**Panzer, 1977**<br>New Orleans, USA<br>Parallel | Tetracycline<br>Clindamycin<br>1, 2, 4, 8 | n=48 **Mod**<br>female 30<br>male 18<br>Age 17.5 y | Comedones (count)<br>Esophagitis<br>Mild diarrhea and cramping<br>Overall change/physician<br>Overall change/physician (rating)<br>Pustules (count)<br>Severity (Panzer) | ↑<br>Randomized. Referral population.<br>↓<br>Major losses to followup. Arms not comparable. | Clindamycin 1% and tetracycline showed similar efficacy. |
| **#266**<br>**Paranjpe, 1995**<br>Pune, India<br>Parallel | Sunder vati<br>Shankhabhasma vah<br>Placebo<br>Thiostanin<br>Sookshama triphala<br>2, 4, 6 | n=82 **Mod**<br>female 40<br>male 42<br>Age 21.1 y | Inflammatory (count)<br>Non-inflammatory (count) | ↑<br>Data shows outcome assessor blinded. | Sunder vati taken orally was effective in the treatment of acne vulgaris. |
| **#267**<br>**Parker, 1987**<br>Portland, USA<br>Parallel | Clindamycin (solution)<br>Clindamycin (gel)<br>3, 6, 9, 12 | n=60 **Mild** | Open comedones (count)<br>Overall change/investigator<br>Overall change/patient<br>Pustules (count)<br>Side effects | ↓<br>Patient not blinded. Inconsistent ascertainment across arms. Arms not comparable. | Topical clindamycin phosphate gel and topical 1% clindamycin phosphate solution showed equal efficacy for treatment of moderately severe acne. [By the Combined Acne Severity Classification, these patients' acne is classified as "mild."] Gel was less drying than solution. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#268**<br>**Peacock, 1990**<br>Manchester, UK<br>Parallel<br>multicenter | Minocycline<br>Clindamycin<br>2, 4, 8, 12 | n=80<br>female 28<br>male 52<br>Age 21.0 y | **Mod/sev** | Inflammatory (count)<br>Non-inflammatory (count)<br>Overall assessment (vas)<br>Overall change/patient<br>Side effects | ↑<br>Data shows enroller blinded. No losses to followup. Specific population.<br>↓<br>Patient not blinded. | Minocycline was twice as expensive as clindamycin. Both treatments were effective and there were no major differences in efficacy or side effects. |
| **#269**<br>**Peck, 1982**<br>Bethesda, USA<br>Parallel | Isotretinoin<br>Placebo<br>4, 8 | n=33 | **Sev** | Cysts change (%)<br>Reduction in application due to side effects | ↑<br>Randomized. No losses to followup. | Isotretinoin was more efficacious than placebo for patients with treatment-resistant cystic acne. |
| **#270**<br>**Pedace, 1971**<br>San Diego, USA<br>Parallel | Tretinoin<br>Vehicle<br>4-12 (unspecified) | n=61<br>Age 17.0-21 y | **Can't say** | Comedones severity<br>Improvement in papules<br>Improvement on pustules<br>Overall change<br>Side effects | ↓<br>Enroller not blinded. Arms not comparable. | Tretinoin was superior to placebo. |
| **#271**<br>**Pettit, 1959**<br>Liverpool, UK<br>Parallel | Serum gonadotrophin<br>Placebo<br>12 | n=40<br>female 17<br>male 23 | **Mild/mod/sev** | Overall change/patient with physician | ↑<br>Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. | Treatment with serum gonadotrophin treatment did not improve acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
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| **#272**<br>**Plewig, 1969**<br>Philadelphia, USA<br>Parallel | Vitamin A<br>Sulfur + resorcinol<br>Benzoyl peroxide<br><br>14 | n=189 **Can't say** | Total lesions change (%) | ↓<br>Not randomized. Patient not blinded. Enroller not blinded. Major losses to followup. Inconsistent ascertainment across arms. Outcome assessor not blinded. Arms not comparable. Execution not as designed. | Vitamin A was superior to both benzoyl peroxide and sulphur + resorcinol. |
| **#273**<br>**Plewig, 1970**<br>Philadelphia, USA<br>Cross-over | Doxycycline<br>Placebo<br>4, 8 | n=62 **Mild**<br>female 36<br>male 88<br>Age 19.0 y | Comedones (discretized %)<br>Cysts<br>Inflammatory (discretized %)<br>Papules change<br>Pustules<br>Side effects<br>Total inflammatory [phase i] (count)<br>Total inflammatory [phase ii] (count) | ↓<br>Major losses to followup. | Doxycycline was an effective treatment for inflammatory acne but not for non-inflammatory acne. |
| **#274**<br>**Pochi, 1988**<br>Boston, USA<br>Parallel<br>multicenter | Vehicle<br>Erythromycin<br>4, 8 | n=187 **Mild/mod**<br>female 98<br>male 89<br>Age 20.8±6.4 y | Closed comedones (count)<br>Open comedones (count)<br>Papules (count)<br>Pustules (count) | ↑<br>Randomized. Specific population.<br>↓<br>Inconsistent ascertainment across arms. | Erythromycin 2% gel produced greater improvement than vehicle in facial acne. |
| **#275**<br>**Poulos, 1976**<br>St. Louis, USA<br>Parallel | Tetracycline hydrochloride<br>Clindamycin hydrochloride<br><br>8 | n=47 **Sev**<br>female 19<br>male 28<br>Age 13.0-34 y | Diarrhea<br>Lesions change<br>Overall change/patient (vas) | ↓<br>Not randomized. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. Arms not comparable. | Clindamycin and tetracycline were equivalent. |

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| **#276**<br>**Prendiville, 1988**<br>Middlesex, UK<br>Parallel<br>multicenter | Isotretinoin<br>Dapsone<br>4, 8, 16, 20, 28, 36 | n=40 **Sev**<br>female 0<br>male 40<br>Age 16.0-31 y | Chest/back total lesions (count)<br>Face/neck total lesions (count)<br>Overall change/patient vas (p value)<br>Overall change/patient vas (p-value)<br>Post-therapy chest/back total lesions (count)<br>Post-therapy face/neck total lesions (count)<br>Post-therapy overall change/patient vas (p value)<br>Post-therapy total severity/photo (Leeds)<br>Side effects<br>Total severity/photo (Leeds) | ↓<br>Patient not blinded.<br>Enroller not blinded.<br>Outcome assessor not blinded. | Isotretinoin was better than dapsone. |
| **#277**<br>**Prince, 1981**<br>Iowa City, USA<br>Parallel<br>matched<br>split face | Erythromycin<br>Vehicle<br>2, 4, 6, 8 | n=73 **Mild/mod**<br>female 68<br>male 70<br>Age 20.3±2.2 y | Inter-treatment lesion change<br>Inter-treatment lesion change [female]<br>Inter-treatment lesion change difference (count)<br>Inter-treatment lesions change [male]<br>Lesions change<br>Lesions change [female]<br>Lesions change [male] | ↓<br>Enroller not blinded. | Topical erythromycin solution showed greater reduction in lesion counts than placebo solution, but differences were not clinically significant. |
| **#278**<br>**Prince, 1982**<br>Iowa city, USA<br>Parallel<br>split face | Benzoyl peroxide + urea<br>Benzoyl peroxide<br>2, 4, 6, 8 | n=39 **Mod**<br>female 64<br>male 14<br>Age 23.0±3.6 y | Inflammatory (count)<br>Inflammatory change<br>Total lesions (count) | | There was no added benefit associated with addition of urea to benzoyl peroxide in treating moderate acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#279**<br>**Rapaport, 1982**<br>Los Angeles, USA<br>Parallel | Tetracycline hydrochloride + placebo (topical)<br>Erythromycin + placebo (oral)<br>2, 4, 8, 12 | n=54 **Mod/sev**<br>female 32<br>male 22<br>Age 22.9±5.7 y | Closed comedone change (count)<br>Closed comedones change (count)<br>Closed comedones severity change (vas)<br>Comedones change (count)<br>Inflammatory change (count)<br>Open comedone change (count)<br>Open comedones severity change (vas)<br>Overall change/physician, patient<br>Papules change (count)<br>Papules severity change (vas)<br>Pustules change (count)<br>Pustules severity change (vas)<br>Withdrawals due to side effects | ↑<br>Data show patient blinded. Data shows outcome assessor blinded. | Topical erythromycin was more effective and produced fewer side effects than oral tetracyline. |
| **#280**<br>**Redmond, 1997**<br>USA<br>Parallel<br>multicenter | Norgestimate + ethinyl estradiol<br>Placebo<br>4, 8, 12, 16, 20, 24, 26 | n=250 **Mod**<br>female 231<br>male 0<br>Age 28.4 y | Adverse events<br>Comedones change (count)<br>Inflammatory change (count)<br>Overall change/investigator<br>Overall change/patient<br>Total lesions change (count) | ↑<br>Randomized. Data show patient blinded. | Norgestimate + ethinyl estradiol was effective. |
| **#283**<br>**Rietschel, 1983**<br>Atlanta, USA<br>Parallel | Tretinoin + clindamycin<br>Tretinoin<br>Clindamycin<br>2, 4, 6, 8 | n=64 **Mild/mod/sev**<br>Age 19.6 y | Comedones change (%)<br>Dryness (severity)<br>Erythema (severity)<br>Overall change<br>Papules change (%)<br>Pustules change (%)<br>Severity (Cook) | No losses to followup.<br>↓<br>Arms not comparable. | All were similar in efficacy and well tolerated. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#284**<br>**Riley, 1961**<br>Charleston, USA<br>Parallel | Placebo<br>Hydrochlorthiazide<br>8 | n=50 **Can't say**<br>female 28<br>male 22<br>Age 8.0-29 y | Overall change | ↓<br>Not randomized. Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. Arms not comparable. | Hydrochlorothiazide was no more effective than placebo. |
| **#285**<br>**Rivkin, 1980**<br>Los Angeles, USA<br>Parallel | Erythromycin<br>Vehicle<br>2, 4, 8, 10, 12 | n=26 **Mod/sev**<br>female 20<br>male 6<br>Age 24.9 y | Overall change/physician<br>Papules change (%)<br>Pustules change (%) | Data show patient blinded. Data shows enroller blinded. No losses to followup.<br>↓<br>Outcome assessor not blinded. Arms not comparable. | Topical erythromycin is efficacious for moderately severe acne. |
| **#287**<br>**Robinson, 1961**<br>Baltimore, USA<br>Parallel | Neomycin<br>Vehicle<br>Hydrocortisone<br>Sulfur<br>Resorcinol + neomycin + hydrocortisone F + sulfur<br>Resorcinol<br>8-24 (unspecified) | n=79 **Can't say**<br>Age 11.0-30 y | Overall change/physician<br>Side effects | ↓<br>Not randomized. Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. Execution not as designed. | Resorcinol, neomycin, and sulphur, did not differ from base (vehicle) in effectiveness. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#288**<br>**Robinson, 1961**<br>Baltimore, USA<br>Parallel | Vehicle<br>Hydrocortisone + sulfur<br>Neomycin + sulfur<br>Neomycin + resorcinol + hydrocortisone + sulfur<br>Resorcinol<br>Hydrocortisone<br>Neomycin<br>Sulfur<br><br>Unspecified | n=188 | **Can't say** | Overall change/physician<br>Side effects | ↓<br>Not randomized. Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. Execution not as designed. | Sulphur, neomycin, and hydrocortisone did not differ in effectiveness. |
| **#291**<br>**Robledo, 1988**<br>Madrid, Spain<br>Parallel<br>multicenter | Tetracycline<br>Clindamycin<br>2, 4, 6, 8 | n=92<br><br>Age 15.0-30 y | **Mild** | Open comedones change (count)<br>Papules change (count)<br>Pustules change (count )<br>Pustules change (count)<br>Severity assessment<br>Side effects | ↑<br>No losses to followup. Referral population.<br>↓<br>Inconsistent ascertainment across arms. | Topical clindamycin was better at reducing pustules than topical tetracycline. There was no significant difference in reduction of comedones or papules. |
| **#293**<br>**Ross, 1961**<br>Pretoria, South Africa<br>Parallel | Placebo<br>Dapsone<br>Unspecified | n=46<br><br>female 25<br>male 19 | **Mild/mod/sev** | Severity change<br>Severity change [female]<br>Severity change [male]<br>Side effects<br>Side effects [female]<br>Side effects [male] | ↑<br>No losses to followup.<br>↓<br>Not randomized. | A statistically significant number of cases responded favorably to dapsone. |
| **#294**<br>**Roth, 1964**<br>Daly City, USA<br>Parallel<br>matched | Salicylic acid<br>Placebo<br><br>1, 2, 3, 4, 5, 9-10 | n=30<br>female 11<br>male 19<br>Age 13.0-32 y | **Mild/mod** | Acne change<br>Acne change (% face)<br>Face oiliness change (% face)<br>Local reactions<br>Oiliness change | ↓<br>Not randomized. Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. Execution not as designed. | Salicylic acid reduced oiliness and improved acne. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#295**<br>**Rushton, 1962**<br>Sheffield, UK<br>Parallel<br>split face | Vehicle<br>Epiestriol<br>12 | n=50 | **Can't say** | Inter-treatment severity change<br>Overall change/physician | ↑<br>Referral population. | Epiestriol did not produce any significant effect. |
| **#297**<br>**Saihan, 1981**<br>Bristol, UK<br>Parallel | Vehicle<br>Chloramphenicol + hydrocortisone<br>4, 8 | n=32<br>female 22<br>male 10 | **Mild/mod** | Overall change/patient<br>Overall change/physician<br>Severity (Burton)<br>Withdrawals due to side effects | ↓<br>Arms not comparable. | Chloranpheniol + hydrocortisone was more effective. |
| **#298**<br>**Samuelson, 1985**<br>East Stroudsburg, USA<br>Parallel | Minocycline<br>Tetracycline<br>6, 12 | n=62<br>female 40<br>male 22<br>Age 19.0 y | **Mod/sev** | GI symptoms<br>Severity/investigator (Samuelson)<br>Severity/patient (Samuelson)<br>Vaginal infection | ↑<br>Data shows enroller blinded. Data shows outcome assessor blinded. | Minocycline was better than tetracycline using photographic assessment. |
| **#299**<br>**Savin, 1966**<br>New Haven, USA<br>Parallel | Placebo<br>Tetracycline + sodium novobiocin<br>4 | n=42<br>female 24<br>male 18<br>Age 15.0-25 y | **Mod/sev** | Overall change/physician<br>Side effects | ↑<br>Data show patient blinded. Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded.<br>↓<br>Arms not comparable. | Tetracycline + sodium novobiocin was more effective than placebo. |
| **#300**<br>**Schachner, 1990**<br>Miami, USA<br>Parallel | Clindamycin phosphate<br>Erythromycin + zinc<br>3, 6, 9, 12 | n=103<br>female 40<br>male 52<br>Age 19.1 y | **Mod** | Comedones change (%)<br>Cutaneous<br>Severity change (Cook %)<br>Total inflammatory change (%) | ↓<br>Patient not blinded. Enroller not blinded. | Erythromycin plus zinc provided better therapeutic benefits, in a shorter time, than topical clindamycin. Both medications were equally tolerated. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#301**<br>**Schachner, 1990**<br>Miami, USA<br>Parallel | Vehicle<br>Erythromycin + zinc<br>2, 6, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 | n=73 **Mod**<br>female 73<br>male 0<br>Age 13.0-36 y | Comedones (count)<br>Inflammatory (count)<br>Severity (Cook)<br>Severity change (Cook)<br>Side effects | ↓<br>Major losses to followup. Arms not comparable. | Erythromycin + zinc was more effective than vehicle after 6 weeks treatment. |
| **#302**<br>**Schafer Korting,**<br>Berlin, Germany<br>Parallel<br>split face<br>multicenter | Tretinoin combined<br>Tretinoin (0.01%)<br>Tretinoin (0.05%)<br>Tretinoin (0.025%)<br>2, 4, 6, 12 | n=20 **Mild**<br>female 14<br>male 6<br>Age 24.0 y | Acne flare-up<br>Burning<br>Comedones (count)<br>Comedones (improvement)<br>Erythema<br>Inflammatory (count)<br>Inflammatory (improvement)<br>Scaling | ↓<br>Execution not as designed. | Liposomal tretinoin (combined) provided comparable efficacy to tretinoin 0.025% and tretinoin 0.05%, and performed slightly better for comedones. It was also better tolerated. |
| **#303**<br>**Shalita, 1984**<br>Brooklyn, USA<br>Parallel<br>multicenter | Clindamycin<br>Erythromycin<br>2, 4, 8, 12 | n=178 **Mod**<br>female 116<br>male 50<br>Age 22.6 y | Inflammatory (count)<br>Inter-treatment preference/patient<br>Non-inflammatory (count)<br>Side effects | | Erythromycin and clidamycin showed comparable effectiveness but erythromycin produced somewhat more side effects. |
| **#304**<br>**Shalita, 1989**<br>Brooklyn, USA<br>Cross-over | Salicylic acid<br>Benzoyl peroxide<br>2, 4 | n=30 **Mild**<br>female 15<br>male 15<br>Age 13.0-31 y | Comedones change [phase i] (%)<br>Comedones change [phase ii] (%) | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Salicylic acid was effective in treatment of comedonal acne; benzoyl peroxide was not. |
| **#305**<br>**Shalita, 1995**<br>Brooklyn, USA<br>Parallel<br>multicenter | Nicotinamide<br>Clindamycin<br>4, 8 | n=76 **Mod**<br>female 53<br>male 23<br>Age 21.3 y | Inflammatory change (%)<br>Local side effects<br>Overall change/physician<br>Severity (Allen-Smith)<br>Severity change (Allen-Smith %) | ↓<br>Major losses to followup. Outcome assessor not blinded. Arms not comparable. | 4% nicotinamide and 1% clindamycin gel were equivalent in efficacy. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#306**<br>**Shalita, 1996**<br>Brooklyn, USA<br>Parallel<br>multicenter | Adapalene<br>Tretinoin<br>2, 4, 8, 12 | n=288 **Mod**<br>Age 12.0-30 y | % Burning grade I<br>% Dryness grade I<br>% Erythema grade I<br>% Scaling grade<br>Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity change<br>Total lesions change (%) | ↑<br>Randomized. General population.<br>↓<br>Outcome assessor not blinded. Arms not comparable. | Adapalene 0.1% gel bid was more effective than tretinoin 0.025% gel. |
| **#307**<br>**Sheehan-Dare, 19**<br>Leeds, UK<br>Parallel<br>matched | Clindamycin phosphate + placebo<br>Minocycline + placebo<br>4, 8, 12 | n=64 **Mod/sev**<br>female 24<br>male 42<br>Age 14.0-35 y | Diarrhea<br>Facial erythema<br>Facial stinging<br>Inflammatory (count)<br>Non-inflammatory (count)<br>Severity (Leeds) | ↑<br>No losses to followup. Referral population. | Both topical clindamycin and oral minocycline were effective in the treatment of moderate-severe acne. |
| **#310**<br>**Sklar, 1996**<br>Dallas, USA<br>Parallel | Placebo<br>Benzoyl peroxide + glycolic acid + zinc sulfur<br>Benzoyl peroxide + erythromycin<br>1, 2, 4, 8, 12 | n=92 **Mild/mod**<br>Age 16.0-30 y | Comedones (count)<br>Inflammatory (count)<br>Side effects<br>Total lesions (count) | ↑<br>Data show patient blinded. Data shows enroller blinded. No losses to followup. | Triaz 10% as a special gel seems to optimize therapeutic power of benzoyl peroxide as a combo drug rather than by itself. |
| **#311**<br>**Smit, 1978**<br>Wageningen, The Netherlands<br>Parallel | Minocycline<br>Doxycycline<br>12 | n=18 **Mild/mod** | Severity change (Smit)<br>Side effects | ↓<br>Arms not comparable. | Doxycycline and minocycline were equally effective for severe acne. [By the Combined Acne Severity Classification, these patients' acne is classified as "mild."] |
| **#312**<br>**Smith, 1962**<br>London, UK<br>Parallel | Placebo<br>Demethylchlortetracycline<br>Phenethicillin<br>4 | n=66 **Mild/mod/sev**<br>female 22<br>male 38 | Overall change/patient (score)<br>Overall change/physician<br>Severity change/photo (score) | ↑<br>Referral population.<br>↓<br>Patient not blinded. | There were no significant differences, between the treatments, including placebo. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#313**<br>**Smith, 1976**<br>Augusta, USA<br>Parallel | Tetracycline hydrochloride (oral) + placebo<br>Tetracycline hydrochloride (topical) + placebo<br>Placebo + placebo<br>2, 4, 7, 10, 12 | n=149 **Mild/mod**<br>female 80<br>male 55<br>Age 19.9 y | Severity (Cook) | ↑<br>Local population. | Topical tetracycline plus oral tetracycline and oral tetracycline were both more effective than placebo. |
| **#314**<br>**Smith, 1980**<br>Albequerque, USA<br>Parallel | Vehicle<br>Benzoyl peroxide (20%)<br>8 | n=59 **Mod**<br>female 35<br>male 16<br>Age 23.0 y | Allergic dermatitis<br>Redness/peeling<br>Total lesion (count)<br>Total lesions change (descretized %) | Local population. | Benzoyl peroxide 20% was significantly more effective in reducing inflammatory acne. |
| **#315**<br>**Sommer, 1997**<br>Leeds, UK<br>Parallel | Placebo<br>Fusidin<br>1, 4, 9, 12 | n=56 **Can't say**<br>female 15<br>male 41<br>Age 18.8±1.1 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Severity change (Leeds) | | Fusidin was no better than placebo. |
| **#316**<br>**Spellman, 1998**<br>San Diego, USA<br>Parallel<br>multicenter | Azelaic acid + glycolic acid<br>Tretinoin + vehicle<br>4, 8, 12 | n=70 **Mild**<br>female 53<br>male 17<br>Age 24.5 y | Dryness (severity)<br>Erythema (severity)<br>Inflammatory change (%)<br>Non-inflammatory change (%)<br>Papules change (%)<br>Scaling (severity)<br>Side effects (patient assessment) | | Azelaic acid + glycolic acid led to a greater reduction in papules and inflammatory lesions,and caused less dryness, scaling and erythema than tretinoin. |
| **#317**<br>**Stankler, 1976**<br>Aberdeen, UK<br>Parallel | Tetracycline<br>Tetracycline + proteolytic enzymes<br>12 | n=51 **Sev**<br>female 19<br>male 32 | Severity change | ↑<br>Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded.<br>↓<br>Arms not comparable. | The combination of tetracycline and enzyme was better than tetracycline alone, but not at a statistically significant level. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#318**<br>**Stoughton, 1980**<br>San Diego, USA<br>Parallel | Clindamycin (lotion) + Placebo (oral)<br>Tetracycline (oral) + Placebo (lotion)<br>2, 3, 4, 6, 8 | n=50 **Mod**<br>Age 18.0-30 y | Overall change/patient (Stoughton)<br>Papules (count)<br>Side effects | No losses to followup. Referral population.<br>🡻<br>Not randomized. Outcome assessor not blinded. | Clindamycin phosphate 1% is at least equal to tetracycline 500mg/d. |
| **#320**<br>**Strauss, 1984**<br>Iowa City, USA<br>Parallel<br>multicenter | Isotretinoin (1.0)<br>Isotretinoin (0.1)<br>Isotretinoin (0.5)<br>4, 8, 12, 16, 20; 4, 8, 12 post-therapy; 60-90 post-therapy or 4, 8, 12, 16, 20;24, 28, 32, 80-110. | n=150 **Sev**<br>female 14<br>male 109<br>Age 22.9 y | Inflammatory change post therapy/face (%)<br>Inflammatory change/face (%)<br>Inflammatory change/trunk (%)<br>Inflammatory change/trunk post-therapy (%)<br>Local side effects<br>Overall assessment/patient 1 yr. later<br>Skin side effects<br>Systemic side effects | Randomized. Data shows outcome assessor blinded. Specific population. | The maintenance of the clinical improvement was much greater when higher dosages were used. There was no sufficiently consistent pattern of side effects differences. |
| **#321**<br>**Strauss, 1984**<br>Iowa City, USA<br>Parallel | Zinc + erythromycin<br>Vehicle<br>4, 8, 10 | n=22 **Mild/mod**<br>Age 13.0-35 y | Inflammatory change (%) | Randomized. No losses to followup.<br>🡻<br>Inconsistent ascertainment across arms. Arms not comparable. | Topical erythromycin 4% with zinc decreases inflammatory lesion counts. |
| **#323**<br>**Swinyer, 1980**<br>Salt Lake City, USA<br>Parallel | Tretinoin + benzoyl peroxide + water avoidance<br>Tretinoin + emollient + tetracycline<br>Tetracycline + sulfur/salicylic acid + polyethylene<br>4, 8, 12, 16 | n=122 **Mild/mod/sev**<br>female 78<br>male 44<br>Age 18.2±2.3 y | Comedones change (%)<br>Dryness<br>Erythema<br>Inflammatory change (%)<br>Oiliness<br>Papules+pustules change (%)<br>Peeling<br>Total lesions change (%) | 🡹<br>Randomized. Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded. Referral population.<br>🡻<br>Patient not blinded. | A topical program of tretinoin, benzoyl peroxide, and water avoidance was as effective as tetracycline and tretinoin and better than tetracycline with abrasive cleansers. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#324**<br>**Swinyer, 1988**<br>Salt Lake City, USA<br>Parallel | Clindamycin phosphate<br>Benzoyl peroxide<br>2, 4, 8, 12 | n=60 **Mod**<br>female 34<br>male 26<br>Age 19.8 y | Inflammatory change (%)<br>Local reactions/Dryness<br>Local reactions/Erythema<br>Local reactions/Oiliness<br>Local reactions/Peeling<br>Non-inflammatory change (%)<br>Total lesions change (%) | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. | Benzoyl peroxide gel was superior to clindamycin phosphate. |
| **#325**<br>**Thappa, 1994**<br>Bajaj Nagar, India<br>Parallel | Gugulipid<br>Tetracycline<br>12 | n=20 **Sev**<br>female 5<br>male 15<br>Age 16.0-25 y | Inflammatory change (%)<br>Non-inflammatory change (%)<br>Post-therapy relapse<br>Severity change (Michaelsson) | ↑<br>No losses to followup.<br>↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. Arms not comparable. | There was no statistical difference between tetracycline and gugulipid. Patients with oily skin responded better to gugulipid suggesting use of gugulipid in nodulocystic acne. |
| **#326**<br>**Thomas, 1982**<br>Gavelson, USA<br>Parallel<br>multicenter | Erythromycin<br>Clindamycin<br>2, 4, 8, 12 | n=72 **Mod/sev**<br>Age 12.0-55 y | Closed comedones (count)<br>Nodes+cysts (count)<br>Non-inflammatory (count)<br>Open comedones (count)<br>Overall change/patient<br>Total inflammatory (count)<br>Total lesions (count) | | Patients responded equally to erythromycin and clindamycin. |
| **#327**<br>**Thomsen, 1980**<br>Iowa City, USA<br>Parallel | Clindamycin hydrochloride<br>Vehicle<br>2, 4, 6, 8 | n=18 **Mild/mod**<br>female 11<br>male 3<br>Age 22.3 y | Diarrhea<br>Erythema<br>Itching<br>Nodules (count)<br>Papules (count)<br>Peeling<br>Pustules (count)<br>Severity/patient | ↓<br>Not randomized. | 3 of 9 clindamycin patients showed clinical improvement. |

| Trial information | Treatments<br>Time points (wks) | Participants | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|
| **#328**<br>**Tong, 1994**<br>New South Wales/Canperdown, Australia<br>Parallel | Metronidazole<br>Placebo<br>4, 8, 12 | n=96 **Mild/mod**<br>female 47<br>male 49<br>Age 20.7±4.6 y | Inflammatory (count)<br>Local irritation<br>Non-inflammatory (count)<br>Side effects | ↑<br>No losses to followup. Data shows outcome assessor blinded. | There was no significant benefit to using 0.75% metronidazole gel over placebo in reducing counts of inflamed and non-inflamed lesions. |
| **#329**<br>**Tucker, 1984**<br>Houston, USA<br>Parallel | Clindamycin<br>Benzoyl peroxide<br>Clindamycin + benzoyl peroxide<br>2, 4, 6, 8, 10 | n=79 **Mod**<br>female 45<br>male 34<br>Age 12.0-30 y | Comedones (count)<br>Cysts (count)<br>Irritancy (score)<br>Papules (count)<br>Pustules (count)<br>Severity change (Michaelsson %) | ↓<br>Not randomized. Patient not blinded. Enroller not blinded. Major losses to followup. Outcome assessor not blinded. Arms not comparable. | Combination therapy consistently demonstrated the best overall efficacy as regards severity. |
| **#332**<br>**van der Meeren,**<br>Amsterdam, The Netherlands<br>Parallel<br>multicenter | Isotretinoin (1.0)<br>Isotretinoin (0.5)<br>4, 8, 12 | n=58 **Mild/mod/sev**<br>female 0<br>male 58<br>Age 22.0±6.0 y | Comedones (median)<br>Infiltrates (median)<br>Local reaction<br>Papules (median)<br>Pustules (median)<br>Side effects (number)<br>Withdrawals | Referral population.<br>↓<br>Patient not blinded. Enroller not blinded. Outcome assessor not blinded. | Isotretinoin 0.5 mg/kg is preferred to 1.0 mg/kg for conglobate acne. |
| **#335**<br>**Van Neste, 1986**<br>Brussels, Belgium<br>Parallel<br>matched<br>split face | Benzoyl peroxide + isoconazole nitrate<br>Benzoyl peroxide + miconazole nitrate<br>2, 4, 8 | n=20 **Mild/mod**<br>female 26<br>male 6<br>Age 13.0-28 y | Closed comedones change (count)<br>Erythema<br>Mild itching<br>Open comedones change (count)<br>Open comedones change(count)<br>Papules change (count)<br>Pustules change (count)<br>Transient scaling | ↑<br>Randomized. Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded. | There was no difference between benzoyl peroxide + isoconazole nitrate and benzoyl peroxide + miconazole nitrate. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#336**<br>**Verma, 1980**<br>Rohtah, India<br>Parallel | Zinc sulfate<br>Vehicle<br><br>6 | n=56<br>female 21<br>male 35 | **Mod** | Cysts (count)<br>Infiltrates (count)<br>Oiliness<br>Papules (count)<br>Pustules (count)<br>Severity change<br>Side effects | ↑<br>No losses to followup. Data shows outcome assessor blinded.<br>↓<br>Not randomized. Inconsistent ascertainment across arms. | Zinc was better than placebo. |
| **#338**<br>**Verschoore, 1991**<br>Warsaw, Poland<br>Parallel | Adapalene (0.1%)<br>Tretinoin<br>Adapalene (0.03%)<br><br>8, 12 | n=72 | **Mild/mod/sev** | Inflammatory change (%)<br>Non-inflammatory (count)<br>Severe erythema<br>Severity (Leeds) | ↑<br>Data shows enroller blinded. No losses to followup.<br>↓<br>Outcome assessor not blinded. Arms not comparable. | 0.1% adapalene may be an effective and safe treatment for mild to moderate acne. |
| **#340**<br>**Wansker, 1961**<br>Charlotte, USA<br>Parallel | Placebo<br>Tetracycline-novobiocin<br>Triacetyl-oleandomycin<br>Tetracycline-citric acid<br>Tetracycline phosphate<br>Erythromycin proprionate<br>Erythromycin stearate<br><br>24-72 (unspecified) | n=91<br><br>Age 12.0-36 y | **Mod/sev** | Inter-treatment severity comparison | ↑<br>Data show patient blinded. Data shows enroller blinded. Data shows outcome assessor blinded.<br>↓<br>Major losses to followup. Inconsistent ascertainment across arms. Arms not comparable. | All of the antibiotics were more effective than placebo. |
| **#341**<br>**Weimar, 1978**<br>Iowa city, USA<br>Parallel | Placebo<br>Zinc sulfate<br>2, 4, 6, 8, 12 | n=52<br>female 28<br>male 24<br>Age 19.7 y | **Mild/mod** | Comedones (count)<br>Cysts (count)<br>GI distress<br>Papules (count)<br>Pustules (count)<br>Severity (Michaelsson) | ↑<br>Randomized. Local population.<br>↓<br>Major losses to followup. Arms not comparable. | Zinc had a beneficial effect on pustules, but significant side effects were observed. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#342**<br>**Weismann, 1977**<br>Copenhagen, Denmark<br>Parallel | Vehicle<br>Zinc sulfate<br>4, 8, 12 | n=39<br>female 9<br>male 30<br>Age 17.0-37 y | **Mod** | Infiltrates (count)<br>Papules (count)<br>Pustules (count)<br>Side effects | ↑<br>Randomized.<br>↓<br>Major losses to followup. | Oral zinc sulphate did not affect acne. |
| **#344**<br>**Wethered, 1964**<br>UK<br>Parallel<br>multicenter | Fusidin (oral)<br>Fusidin (topical)<br>2 | n=70<br>female 29<br>male 41 | **Mild/mod/sev** | Overall change/physician<br>Severity change/photo<br>Side effects | ↑<br>Data shows outcome assessor blinded.<br>↓<br>Not randomized. Patient not blinded. Enroller not blinded. Major losses to followup. Arms not comparable. | Fusidin orally or in ointment was not effective. |
| **#346**<br>**Wexler, 1968**<br>New York, USA<br>Parallel | Vehicle<br>Neomycin + methylprednisolone + sulfur + aluminum<br>4 | n=48 | **Mild/mod/sev** | Overall change/physician<br>Patient satisfaction | Randomized. Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded. Referral population.<br>↓<br>Arms not comparable. | A polyvalent approach produces the best results. |
| **#347**<br>**Wexler, 1968**<br>New York, USA<br>Parallel | Sulfur + aluminum chlorhydroxide<br>Neomycin + methylprednisolone + sulfur + aluminum c<br>4 | n=48 | **Mild/mod/sev** | Overall change/physician<br>Patient satisfaction | Randomized. Data shows enroller blinded. No losses to followup. Data shows outcome assessor blinded. Referral population.<br>↓<br>Arms not comparable. | A polyvalent approach produces the best results. |

| Trial information | Treatments<br>Time points (wks) | Participants | | Outcomes | Methodological Qualifications | Authors' Bottom Line |
|---|---|---|---|---|---|---|
| **#349**<br>**Wong, 1984**<br>Ann Arbor, USA<br>Parallel | Ibuprofen + placebo<br>Ibuprofen + tetracycline<br>Tetracycline + placebo<br>Placebo<br>4, 8 | n=68<br>female 12<br>male 48<br>Age 20.5 y | **Mild/mod** | Improvement<br>Side effects overall<br>Side effects specific<br>Total change (%)<br>Total lesion (count) | Randomized. Data show patient blinded.<br>↓<br>Outcome assessor not blinded. | The combination of ibuprofen tetracyline is effective when administered for 2 months. |
| **#350**<br>**Wright, 1964**<br>San Francisco, USA<br>Parallel<br>matched<br>split face | Sham rays + hexachlorophene<br>Grenz rays<br>Grenz ray + hexachlorophene<br>Untreated<br>24 | n=95 | **Sev** | Overall change/patient [acne conglobata]<br>Overall change/patient [acne vulgaris]<br>Pigmentation<br>Severity change/patient-treated side [acne vulgaris] | ↑<br>No losses to followup.<br>↓<br>Enroller not blinded.<br>Outcome assessor not blinded. | Grenz rays were not effective in treatment of acne. |
| **#351**<br>**Yong, 1979**<br>Singapore<br>Parallel | Benzoyl peroxide (5%)<br>Benzoyl peroxide(2.5%)<br>4-18 (end of therapy) | n=200<br>female 140<br>male 60 | **Mild/mod/sev** | Desquamation<br>Eczematous reaction<br>Erythema<br>Hair discoloration<br>Itching or burning<br>Overall change/physician<br>Pigmentation<br>Pustular<br>Side Effects | No losses to followup.<br>Local population.<br>↓<br>Patient not blinded.<br>Enroller not blinded.<br>Outcome assessor not blinded. Arms not comparable. | No significant difference was found either in efficacy or severity of side effects. |