

Supplementary information

Extended version of Table 1, Studies examining isotretinoin, depression and suicide.

Study	Study type	Subject numbers	Results / comments
Jick 2000 (1)	Retrospective cohort studies of acne patients using Canadian and UK health databases	7195 users of isotretinoin 13700 users of antibiotics (Canada) 340 users of isotretinoin 676 users of antibiotics (UK)	Prevalence rates of neurotic & psychotic disorders, suicide and attempted suicide were compared between isotretinoin and antibiotic users and within isotretinoin users (pre- & post-treatment). Relative risk estimations, comparing isotretinoin use and oral antibiotic use with non-exposure to either drug for newly diagnosed depression were approximately 1.0 for both data sources. Relative risks were also ~ 1.0 comparing before with after isotretinoin use. No increased risk of suicide or suicidal ideation, but event numbers were small and confidence intervals were wide. Has been criticised for potential underascertainment of psychiatric disease and suicide, but it isn't apparent that this would have been differential ascertainment.
Hersom 2003 (2)	Retrospective prescription sequence symmetry analysis of isotretinoin and antidepressant prescriptions	2821 users of isotretinoin in a United States pharmacy database	Adjusted ratios (of numbers of patients filling isotretinoin prescriptions first versus numbers filling antidepressant prescriptions first) was not significantly greater than 1.0 – indicating no association between use of isotretinoin and the onset of depression.
Szarfman cited in Wyskowski 2001 (3)	Statistical data-mining analysis	Of all adverse effects and drug combinations in the Food and Drug Administration Adverse Event Reporting System database	Six suicides could be expected in patients taking isotretinoin compared to the 36 suicides observed.
Hull 2000 (4)	Prospective, uncontrolled study	189 patients commenced on isotretinoin and treated for 4 months	4% reported depression – by self-report in response to questionnaire item at clinical reviews. No objective ascertainment of depression. Depression “tended to persist throughout the treatment” and did not prevent completion of the course of isotretinoin.
Bruno 1984 (5)	Prospective, uncontrolled study	92 patients commenced on isotretinoin and treated for 16 weeks.	11% reported depression – by self-report at clinical review. No objective ascertainment of depression.
Layton 1993 (6)	Prospective, uncontrolled study	88 patients treated with isotretinoin, followed annually for 10 years	“Patients were questioned about, and examined for, recognised cutaneous and systemic adverse effects of isotretinoin” at the end of therapy and annually for 10 years. “No long term clinical side-effects were identified in any of the patients”. It is not reported whether evidence of depression or other psychiatric symptoms were specifically sought.

Goulden 1994 (7)	Prospective, uncontrolled study	720 patients treated with one or more courses of tretinoin.	Patients followed up for from 2 to ten years. Asked at each follow-up visit (4-6 monthly) re symptoms since last visit, then specifically asked about skin, eye or joint symptoms (i.e. not specifically asked about psychiatric symptoms). Three subjects reported persistent depression – and all three of these were reported to be dysmorpnhobic.
McElwee 1991 (8)	Prospective, uncontrolled study	466 patients treated with, and compliant with, isotretinoin, observed through a 4 to 5 month course.	No depression or other psychiatric effects recorded – but depression and psychiatric morbidity seemingly not specifically sought (though multiple cutaneous and musculoskeletal effects and biochemical abnormalities recorded).
McLane (1) 2001 (9)	Prospective, uncontrolled study	67 patients receiving isotretinoin for 16 to 20 weeks	No psychiatric side effects in any subjects. Study incompletely reported.
McLane (2) 2001 (9)	Prospective, uncontrolled study	300 patients receiving isotretinoin for 20 weeks	0.3% of subjects reported psychiatric adverse events (nature not specified). Study incompletely reported.

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