

Scars: The Battle Over Isotretinoin

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One of the premier issues in dermatologic therapy during the past year has been the future status of isotretinoin (Accutane®). The core of the controversy arises from 2 issues: the most effective program for pregnancy prevention and the potential link between the drug and depression and suicide. Practitioners have observed several changes in the manner in which they prescribe isotretinoin, including a new informed consent and medication guide, additional pregnancy tests, and the discussion of potential patient and physician registries. The public has been faced with media propagation of the possible link with suicide, particularly in light of the unfortunate suicide of Michigan Congressman Bart Stupak's son BJ, who was on isotretinoin therapy for cystic acne.

While these events have unfolded, many physicians and patients have become increasingly confused and uncertain. Both are faced with similar questions. What is fact and what is fiction? How are the risks and benefits best weighed in light of this information? Some patients, or their parents, have been frightened by something they saw on the news or heard from a friend. Often, they do not want to take isotretinoin, even if they are appropriate candidates. Some physicians have become tentative as well.

Several studies have been presented recently which refute this association. Jick et al¹ analyzed data from 7195 isotretinoin users and 13,700 oral antibiotic users with acne from the Canadian Health Database and from 340 isotretinoin users and 676 oral antibiotic users with acne from the United Kingdom General Practice Research Database. The relative risk estimates, comparing isotretinoin use and oral antibiotic use with nonexposure to either drug for newly diagnosed depression or psychosis, were approximately 1.0, regardless of the data source. The relative risk for suicide and attempted suicide was 0.9% when comparing current isotretinoin exposure with nonexposure. The authors concluded that the study provided no evidence that use of the drug is associated with an increased risk for depression, suicide, or other psychiatric disorders. A recent study from Wake Forest also found no direct correlation between isotretinoin and depression, in a retrospective analysis of patients with acne and depression (Fleischer AB Jr, unpublished data).

In March 2001, the FDA addressed new measures

to manage risks associated with Accutane²: "The medication guide—to be dispensed with each filled prescription—summarizes important information from the professional labeling. It emphasizes the possible association of Accutane with psychiatric problems and suicide—at least 66 Accutane users have committed suicide—and the well-established risk of Accutane-induced birth defects. ... Additional measures to strengthen the existing program to prevent patients from becoming pregnant while taking Accutane are in development."

The debate continues.

At this juncture, we have to evaluate what we do know for certain:

1. Isotretinoin is extremely effective for the vast majority of patients with cystic acne.
2. We have no conclusive evidence that there is a correlation between isotretinoin and depression and suicide; we will require further investigation into this question.
3. Isotretinoin is a definite teratogen.
4. We need this drug for our patients with severe cystic acne, whose disease has both negative physical and psychological implications.

Therefore, we should not be afraid or tentative. Clinicians should use the drug as always, with appropriate caution in appropriate patients. We should carefully keep abreast of all new precautions introduced to protect our patients and most effectively prevent pregnancy during therapy. We should try to identify patients who may be prone to depression and consider psychiatric screening prior to therapy, and potential comanagement with a mental health professional during the course of treatment. Prospective data gathered from this time forward hopefully will serve to clarify many of these issues. Until that time, we will be doing our acne patients a disservice if we limit ourselves in the treatment of their disease.

REFERENCES

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2. Schwetz BA. From the Food and Drug Administration: new measures to manage risks associated with Accutane. *JAMA*. 2001;285:1146.