



Posttreatment purpura is noted after PDT + PDL.

Verteporfin, PDL Treat Port-Wine Stains

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San Diego Bureau

CARLSBAD, CALIF. — Combining photodynamic therapy using the photosensitizer verteporfin with pulsed dye laser therapy may be a way to treat port-wine stains, preliminary results from an ongoing study suggest.

The finding is important because early studies of photodynamic therapy (PDT) for port-wine stains resulted in significant scarring and severe photosensitivity for up to 30 days.

“Of course, that was a significant disadvantage,” Dr. Kristen M. Kelly said at a symposium on laser and cosmetic surgery sponsored by SkinCare Physicians.

In the new approach, which was first reported at the annual meeting of the American Society for Laser and Medicine and Surgery, Dr. Kelly and her associates treated four spots, each at 2 cm²: one control spot, one pulsed dye laser (PDL)—only spot before infusion, one PDT-only spot after infusion, and one PDT plus PDL spot.

For PDT, the subjects received IV verteporfin

(Visudyne), a drug marketed by Novartis Ophthalmics Inc. that binds with low-density lipoprotein and is approved for treatment of age-related macular degeneration, pathologic myopia, and presumed ocular histoplasmosis. It causes photosensitivity for 2-5 days. The doses were 6 mg/m² based on the subject's body surface area.

This was followed by treatment with a 576-nm continuous-wave argon-pumped rhodamine dye laser.

The patients were followed at 3 days and at 1, 2, 4, 8, and 12 weeks.

So far, researchers have treated 10 sets of sites on seven patients, with a light dose of 15-75 J/cm² for the PDT spot. “At 45 J/cm² we start to see some interesting results,” said Dr. Kelly of the departments of dermatology and surgery at the University of California, Irvine. “We have seen greater purpuric response, and in some cases improved lightening of the port-wine stain.”

One patient treated at 45 J/cm² had about 50% blanching of the port-wine stain at 8 weeks in the spot treated with PDL and nearly 100% blanching in the PDT plus PDL spot. The patient developed mild hyperpigmentation but that resolved by week 12.

“As we increase the dose [of the laser beam] we'll learn more about the potential of this treatment,” she said.

The researchers received donations of verteporfin from QLT Inc., which developed the drug in conjunction with Novartis Ophthalmics. Dr. Kelly disclosed receiving research grants from 3M, Candela Corp., Reliant Pharmaceuticals LLC, and Thermage Inc. The surgery laser clinic where she works received equipment loans from Candela, Iridex Corp., and Reliant. ■



BRIEF SUMMARY

For Dermatologic Use Only—Not for Ophthalmic, Oral, or Intravaginal Use
Rx only

CONTRAINDICATIONS

FINACEA® Gel, 15%, is contraindicated in individuals with a history of hypersensitivity to propylene glycol or any other component of the formulation.

WARNINGS

FINACEA® Gel, 15%, is for dermatologic use only, and not for ophthalmic, oral, or intravaginal use.

There have been isolated reports of hypopigmentation after use of azelaic acid. Since azelaic acid has not been well studied in patients with dark complexion, these patients should be monitored for early signs of hypopigmentation.

PRECAUTIONS

General: Contact with the eyes should be avoided. If sensitivity or severe irritation develops with the use of FINACEA® Gel, 15%, treatment should be discontinued and appropriate therapy instituted. The safety and efficacy of FINACEA® Gel, 15%, has not been studied beyond 12 weeks.

Information for Patients: Patients using FINACEA® Gel, 15%, should receive the following information and instructions:

- FINACEA® Gel, 15%, is to be used only as directed by the physician.
- FINACEA® Gel, 15%, is for external use only. It is not to be used orally, intravaginally, or for the eyes.
- Cleanse affected area(s) with a very mild soap or a soapless cleansing lotion and pat dry with a soft towel before applying FINACEA® Gel, 15%. Avoid alcoholic cleansers, tinctures, and astringents, abrasives, and peeling agents.
- Avoid contact of FINACEA® Gel, 15%, with the mouth, eyes and other mucous membranes. If it does come in contact with the eyes, wash the eyes with large amounts of water and consult a physician if eye irritation persists.
- The hands should be washed following application of FINACEA® Gel, 15%.
- Cosmetics may be applied after FINACEA® Gel, 15%, has dried.
- Skin irritation (e.g., pruritus, burning, or stinging) may occur during use of FINACEA® Gel, 15%, usually during the first few weeks of treatment. If irritation is excessive or persists, use of FINACEA® Gel, 15%, should be discontinued, and patients should consult their physician (See ADVERSE REACTIONS).
- Avoid any foods and beverages that might provoke erythema, flushing, and blushing (including spicy food, alcoholic beverages, and thermally hot drinks, including hot coffee and tea).
- Patients should report abnormal changes in skin color to their physician.
- Avoid the use of occlusive dressings or wrappings.

Drug Interactions: There have been no formal studies of the interaction of FINACEA® Gel, 15%, with other drugs.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential of FINACEA® Gel, 15%. Azelaic acid was not mutagenic or clastogenic in a battery of *in vitro* (Ames assay, HGPRT in V79 cells [Chinese hamster lung cells], and chromosomal aberration assay in human lymphocytes) and *in vivo* (dominant lethal assay in mice and mouse micronucleus assay) genotoxicity tests.

Oral administration of azelaic acid at dose levels up to 2500 mg/kg/day (162 times the maximum recommended human dose based on body surface area) did not affect fertility or reproductive performance in male or female rats.

Pregnancy: Teratogenic Effects: Pregnancy Category B

There are no adequate and well-controlled studies of topically administered azelaic acid in pregnant women. The experience with FINACEA® Gel, 15%, when used by pregnant women is too limited to permit assessment of the safety of its use during pregnancy.

Dermal embryofetal developmental toxicology studies have not been performed with azelaic acid, 15%, gel. Oral embryofetal developmental studies were conducted with azelaic acid in rats, rabbits, and cynomolgus monkeys. Azelaic acid was administered during the period of organogenesis in all three animal species. Embryotoxicity was observed in rats, rabbits, and monkeys at oral doses of azelaic acid that generated some maternal toxicity. Embryotoxicity was observed in rats given 2500 mg/kg/day (162 times the maximum recommended human dose based on body surface area), rabbits given 150 or 500 mg/kg/day (19 or 65 times the maximum recommended human dose based on body surface area) and cynomolgus monkeys given 500 mg/kg/day (65 times the maximum recommended human dose based on body surface area) azelaic acid. No teratogenic effects were observed in the oral embryofetal developmental studies conducted in rats, rabbits, and cynomolgus monkeys.

An oral peri- and postnatal developmental study was conducted in rats. Azelaic acid was administered from gestational day 15 through day 21 postpartum up to a dose level of 2500 mg/kg/day. Embryotoxicity was observed in rats at an oral dose that generated some maternal toxicity (2500 mg/kg/day; 162 times the maximum recommended human dose based on body surface area). In addition, slight disturbances in the postnatal development of fetuses was noted in rats at oral doses that generated some maternal toxicity (500 and 2500 mg/kg/day; 32 and 162 times the maximum recommended human dose based on body surface area). No effects on sexual maturation of the fetuses were noted in this study. Because animal reproduction studies are not always predictive of human response, this drug should be used only if clearly needed during pregnancy.

Nursing Mothers:

Equilibrium dialysis was used to assess human milk partitioning *in vitro*. At an azelaic acid concentration of 25 µg/mL, the milk/plasma distribution coefficient was 0.7 and the milk/buffer distribution was 1.0, indicating that passage of drug into maternal milk may occur. Since less than 4% of a topically applied dose of azelaic acid cream, 20%, is systemically absorbed, the uptake of azelaic acid into maternal milk is not expected to cause a significant change from baseline azelaic acid levels in the milk. However, caution should be exercised when FINACEA® Gel, 15%, is administered to a nursing mother.

Pediatric Use: Safety and effectiveness of FINACEA® Gel, 15%, in pediatric patients have not been established.

Geriatric: Clinical studies of FINACEA® Gel, 15%, did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

ADVERSE REACTIONS

Overall, treatment related adverse events, including burning, stinging/tingling, dryness/tightness/scaling, itching, and erythema/irritation/redness, were 19.4% (24/124) for FINACEA® Gel, 15%, and 7.1% (9/127) for the active comparator gel at 15 weeks.

In two vehicle controlled, and one active controlled U.S. clinical studies, treatment safety was monitored in 788 patients who used twice daily FINACEA® Gel, 15%, for 12 weeks (N=333) or for 15 weeks (N=124), or the gel vehicle (N=331) for 12 weeks.

Table 3. Cutaneous Adverse Events Occurring in ≥1% of Subjects in the Rosacea Trials by Treatment Group and Maximum Intensity*

| | FINACEA® Gel, 15% N=457 (100%) | | | Vehicle N=331 (100%) | | |
|-----------------------------------|-----------------------------------|---------------------------|------------------------|-------------------------|--------------------------|-----------------------|
| | Mild n=99 (22%) | Moderate n=61 (13%) | Severe n=27 (6%) | Mild n=46 (14%) | Moderate n=30 (9%) | Severe n=5 (2%) |
| Burning/ stinging/ tingling | 71 (16%) | 42 (9%) | 17 (4%) | 8 (2%) | 6 (2%) | 2 (1%) |
| Pruritus | 29 (6%) | 18 (4%) | 5 (1%) | 9 (3%) | 6 (2%) | 0 (0%) |
| Scaling/dry skin/xerosis | 21 (5%) | 10 (2%) | 5 (1%) | 31 (9%) | 14 (4%) | 1 (<1%) |
| Erythema/ irritation | 6 (1%) | 7 (2%) | 2 (<1%) | 8 (2%) | 4 (1%) | 2 (1%) |
| Contact dermatitis | 2 (<1%) | 3 (1%) | 0 (0%) | 1 (<1%) | 0 (0%) | 0 (0%) |
| Edema | 3 (1%) | 2 (<1%) | 0 (0%) | 3 (1%) | 0 (0%) | 0 (0%) |
| Acne | 3 (1%) | 1 (<1%) | 0 (0%) | 1 (<1%) | 0 (0%) | 0 (0%) |

*Subjects may have >1 cutaneous adverse event; thus, the sum of the frequencies of preferred terms may exceed the number of subjects with at least 1 cutaneous adverse event.

FINACEA® Gel, 15%, and its vehicle caused irritant reactions at the application site in human dermal safety studies. FINACEA® Gel, 15%, caused significantly more irritation than its vehicle in a cumulative irritation study. Some improvement in irritation was demonstrated over the course of the clinical studies, but this improvement might be attributed to subject dropouts. No phototoxicity or photoallergenicity were reported in human dermal safety studies.

In patients using azelaic acid formulations, the following additional adverse experiences have been reported rarely: worsening of asthma, vitiligo depigmentation, small depigmented spots, hypertrichosis, reddening (signs of keratosis pilaris), and exacerbation of recurrent herpes labialis.

Post-marketing safety—Skin: facial burning and irritation; Eyes: iridocyclitis on accidental exposure with FINACEA® Gel, 15%, to the eye (see PRECAUTIONS).

OVERDOSAGE

FINACEA® Gel, 15%, is intended for cutaneous use only. If pronounced local irritation occurs, patients should be directed to discontinue use and appropriate therapy should be instituted (See PRECAUTIONS).

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Curettage Plus Imiquimod: Good Results in BCC

MONTEREY, CALIF. — Curettage followed by imiquimod produces better results on basal cell carcinoma than do electrodesiccation and curettage or imiquimod alone. Dr. Abel Torres reported at the annual meeting of the Pacific Dermatologic Association.

Lesions removed with electrodesiccation and curettage commonly have hypertrophic scarring, said Dr. Torres of Loma Linda (Calif.) Medical Center. Imiquimod alone can have relatively good cosmetic results, but there may be some persistent redness and hypopigmentation. Lesions treated with curettage followed by 6 weeks of imiquimod have less persistent redness and hypopigmentation.

The multicenter study enrolled 22 patients at each site, with approximately 60 so far completing the 1-year follow-up.

After treatment with vigorous curettage, and after a 1-week waiting period, patients applied topical 5% imiquimod to the lesion sites 5 days a week for 6 weeks.

Dr. Torres cautioned that this is an off-label use of imiquimod.

—Robert Finn