

New Laser System Offers Another Skin Tx Option

BY SHARON WORCESTER
Southeast Bureau

ATLANTA — Fractional photothermolysis for skin rejuvenation provides results similar to those achieved with ablative laser resurfacing, but without the downtime, Dr. Tina Alster said at the joint annual meeting of the American Society for Dermatologic Surgery and the American College of Mohs Micrographic Surgery and Cutaneous Oncology.

The new fiber laser technology is particularly good for treating dyspigmentation and rhytides, and can be used on areas other than the face, such as the arms, neck, chest, and hands, said Dr. Alster, director of the Washington Institute of Dermatologic Laser Surgery.

Of about 20 lasers that she uses in her practice, the Fraxel laser (Reliant Technologies Inc., Palo Alto, Calif.) is one of those she uses most often.

According to information from Reliant,

the Fraxel laser system—which is approved for the treatment of melasma but also has been used for surgical and acne scars, striae, and actinic keratoses—treats the skin fractionally, with patterns of microscopic laser spots that are 70-100 μm in diameter. Each laser spot is called a microthermal zone, or MTZ, and the laser can deliver 2,000 MTZs per cm^2 in a typical treatment session. About 200-300 μm of untreated space is left between each MTZ. However, the treating physician has

the ability to vary spot pitch and fluence.

The use of the MTZs with adjacent untreated tissue allows fractional wound healing with rapid reepithelialization of the epidermis and collagen remodeling to depths of 400-700 μm . This is compared with the 200- μm depth achieved with traditional ablative laser treatments.

Histology following treatment shows that the stratum corneum remains intact and epidermal tissue is coagulated. Collagen remodeling is also demonstrated, explained Dr. Alster, who reported no financial interest in the device.

“You see reepithelialization of the whole site within 24 hours,” she said.

Her treatment protocol involves skin cleansing and application of a blue tint, which is required for the laser to work. About 30-60 minutes prior to the procedure, she also applies a topical anesthetic containing 30% lidocaine.

Dr. Alster said she usually uses 8-10 MJ per cm^2 , energy density of 250 MTZs per cm^2 , and four to eight passes. An air cooler is used to increase patient comfort.

Patients usually require two to four treatments at 2- to 4-week intervals. Most come back monthly to complete the series of treatments, she said. The skin is erythematous immediately after each treatment and remains so for approximately 2 days. On day 2 or 3, a variable amount of peeling occurs, resulting in rough-feeling skin.

Results are incremental, with additional improvement seen after each treatment. Most patients will achieve 50% improvement when being treated for dyspigmentation and/or rhytides. Although the laser is not marketed as a skin tightening device, it does provide some skin tightening, Dr. Alster noted.

The results are better than what she has experienced with trichloroacetic acid peels, particularly for fine lines, she said, and the recovery time is much quicker than with ablative resurfacing.

Dr. David Goldberg of Skin Laser and Surgery Specialists of New York and New Jersey agreed that fractional photothermolysis has several applications and a relatively good safety profile, but he cautions that adverse events are still possible. Scarring, for example, can occur when the device is held in one place for too long.

Dr. Goldberg also noted that many of the effects of this laser can be achieved with other modalities.

“It clearly works,” he said, but it’s not the “end all and be all.”

For example, acne scarring responds well to the Fraxel laser, but it can also be treated effectively with the CoolTouch or Smoothbeam lasers. Crow’s-feet can be treated effectively with botulinum toxin, and lentigines can be treated effectively with the Q-switched laser and intense pulsed light, Dr. Goldberg said.

“This is not a system that you buy simply to treat lentigines; this is not a system you buy simply to treat crow’s-feet ... but I think that you can’t argue the fact that when you put the whole picture together, it’s got tremendous diversity, and that diversity has led to its popularity,” he said.

Dr. Goldberg has received a research grant from Reliant Technologies Inc. ■

DIFFERIN® (adapalene) Cream, 0.1%

Rx Only BRIEF SUMMARY

For topical use only. Not for ophthalmic, oral, or intravaginal use.

INDICATIONS AND USAGE: DIFFERIN® Cream is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS: DIFFERIN® Cream should not be administered to individuals who are hypersensitive to adapalene or any of the components in the cream vehicle.

PRECAUTIONS: General: If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued. Exposure to sunlight, including sunlamps, should be minimized during use of adapalene. Patients who normally experience high levels of sun exposure, and those with inherent sensitivity to sun, should be warned to exercise caution. Use of sunscreen products and protective clothing over treated areas is recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with adapalene.

Avoid contact with the eyes, lips, angles of the nose, and mucous membranes. The product should not be applied to cuts, abrasions, eczematous or sunburned skin. As with other retinoids, use of “waxing” as a depilatory method should be avoided on skin treated with adapalene.

Information for Patients: Patients using DIFFERIN® Cream should receive the following information and instructions:

1. This medication is to be used only as directed by the physician.
2. It is for external use only.
3. Avoid contact with the eyes, lips, angles of the nose, and mucous membranes.
4. Cleanse area with a mild or soapless cleanser before applying this medication.
5. Moisturizers may be used if necessary; however, products containing alpha hydroxy or glycolic acids should be avoided.
6. Exposure of the eye to this medication may result in reactions such as swelling, conjunctivitis, and eye irritation.
7. This medication should not be applied to cuts, abrasions, eczematous or sunburned skin.
8. Wax epilation should not be performed on treated skin due to the potential for skin erosions.
9. During the early weeks of therapy, an apparent exacerbation of acne may occur. This is due to the action of this medication on previously unseen lesions and should not be considered a reason to discontinue therapy. Overall clinical benefit may be noticed after two weeks of therapy, but at least eight weeks are required to obtain consistent beneficial effects.

Drug Interactions: As DIFFERIN® Cream has the potential to produce local irritation in some patients, concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices or lime rind) should be approached with caution. Particular caution should be exercised in using preparations containing sulfur, resorcinol, or salicylic acid in combination with DIFFERIN® Cream. If these preparations have been used, it is advisable not to start therapy with DIFFERIN® Cream until the effects of such preparations in the skin have subsided.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity studies with adapalene have been conducted in mice at topical doses of 0.4, 1.3, and 4.0 mg/kg/day, and in rats at oral doses of 0.15, 0.5, and 1.5 mg/kg/day. These doses are up to 8 times (mice) and 6 times (rats) in terms of mg/m²/day the maximum potential exposure at the recommended topical human dose (MRHD), assumed to be 2.5 grams DIFFERIN® Cream, which is approximately 1.5 mg/m² adapalene. In the oral study, increased incidence of benign and malignant pheochromocytomas in the adrenal medullas of male rats was observed. No photocarcinogenicity studies were conducted. Animal studies have shown an increased risk of skin neoplasms with the use of pharmacologically similar drugs (e.g., retinoids) when exposed to UV irradiation in the laboratory or to sunlight. Although the significance of these studies to human use is not clear, patients should be advised to avoid or minimize exposure to either sunlight or artificial UV irradiation sources.

Adapalene did not exhibit mutagenic or genotoxic effects *in vivo* (mouse micronucleus test) and *in vitro* (Ames test, Chinese hamster ovary cell assay, mouse lymphoma TK assay) studies.

Reproductive function and fertility studies were conducted in rats administered oral doses of adapalene in amounts up to 20 mg/kg/day (up to 80 times the MRHD based on mg/m² comparisons). No effects of adapalene were found on the reproductive performance or fertility of the F₂ males or females. There were also no detectable effects on the growth, development and subsequent reproductive function of the F₂ generation.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DIFFERIN® Cream is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS: In controlled clinical trials, local cutaneous irritation was monitored in 285 acne patients who used DIFFERIN® Cream once daily for 12 weeks. The frequency and severity of erythema, scaling, dryness, pruritus and burning were assessed during these studies. The incidence of local cutaneous irritation with DIFFERIN® Cream from the controlled clinical studies is provided in the following table:

| | Incidence of Local Cutaneous Irritation with DIFFERIN® Cream from Controlled Clinical Studies (N=285) | | | |
|-------------------------------|---|-----------|----------|---------|
| | None | Mild | Moderate | Severe |
| Erythema | 52% (148) | 38% (108) | 10% (28) | <1% (1) |
| Scaling | 58% (166) | 35% (100) | 6% (18) | <1% (1) |
| Dryness | 48% (136) | 42% (121) | 9% (26) | <1% (2) |
| Pruritus (persistent) | 74% (211) | 21% (61) | 4% (12) | <1% (1) |
| Burning/Stinging (persistent) | 71% (202) | 24% (69) | 4% (12) | <1% (2) |

Other reported local cutaneous adverse events in patients who used DIFFERIN® Cream once daily included: sunburn (2%), skin discomfort-burning and stinging (1%) and skin irritation (1%). Events occurring in less than 1% of patients treated with DIFFERIN® Cream included: acne flare, dermatitis and contact dermatitis, eyelid edema, conjunctivitis, erythema, pruritus, skin discoloration, rash, and eczema.

OVERDOSAGE: DIFFERIN® Cream is intended for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and marked redness, scaling, or skin discomfort may occur. The acute oral toxicity of DIFFERIN® Cream in mice and rats is greater than 10 mL/kg. Chronic ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

Marketed by: GALDERMA LABORATORIES, L.P. Fort Worth, Texas 76177 USA
Manufactured by: DPT Laboratories, Ltd. San Antonio, Texas 78215 USA GALDERMA is a registered trademark. www.differin.com 325069-0805 Revised: August 2005

DIFFERIN® (adapalene gel) Gel, 0.1%

Rx Only BRIEF SUMMARY

INDICATIONS AND USAGE: DIFFERIN® Gel is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS: DIFFERIN® Gel should not be administered to individuals who are hypersensitive to adapalene or any of the components in the vehicle gel.

WARNINGS: Use of DIFFERIN® Gel should be discontinued if hypersensitivity to any of the ingredients is noted. Patients with sunburn should be advised not to use the product until fully recovered.

PRECAUTIONS: General: If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued. Exposure to sunlight, including sunlamps, should be minimized during the use of adapalene. Patients who normally experience high levels of sun exposure, and those with inherent sensitivity to sun, should be warned to exercise caution. Use of sunscreen products and protective clothing over treated areas is recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with adapalene.

Avoid contact with the eyes, lips, angles of the nose, and mucous membranes. The product should not be applied to cuts, abrasions, eczematous skin, or sunburned skin.

Certain cutaneous signs and symptoms such as erythema, dryness, scaling, burning, or pruritus may be experienced during treatment. These are most likely to occur during the first two to four weeks and will usually lessen with continued use of the medication. Depending upon the severity of adverse events, patients should be instructed to reduce the frequency of application or discontinue use.

Drug Interactions: As DIFFERIN® Gel has the potential to produce local irritation in some patients, concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices, or lime) should be approached with caution. Particular caution should be exercised in using preparations containing sulfur, resorcinol, or salicylic acid in combination with DIFFERIN® Gel. If these preparations have been used, it is advisable not to start therapy with DIFFERIN® Gel until the effects of such preparations in the skin have subsided.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity studies with adapalene have been conducted in mice at topical doses of 0.3, 0.9, and 2.6 mg/kg/day and in rats at oral doses of 0.15, 0.5, and 1.5 mg/kg/day, approximately 4-75 times the maximal daily human topical dose. In the oral study, positive linear trends were observed in the incidence of follicular cell adenomas and carcinomas in the thyroid glands of female rats, and in the incidence of benign and malignant pheochromocytomas in the adrenal medullas of male rats.

No photocarcinogenicity studies were conducted. Animal studies have shown an increased tumorigenic risk with the use of pharmacologically similar drugs (e.g., retinoids) when exposed to UV irradiation in the laboratory or to sunlight. Although the significance of these studies to human use is not clear, patients should be advised to avoid or minimize exposure to either sunlight or artificial UV irradiation sources.

In a series of *in vivo* and *in vitro* studies, adapalene did not exhibit mutagenic or genotoxic activities.

Pregnancy: Teratogenic effects. Pregnancy Category C. No teratogenic effects were seen in rats at oral doses of adapalene 0.15 to 5.0 mg/kg/day, up to 120 times the maximal daily human topical dose. Cutaneous route teratology studies conducted in rats and rabbits at doses of 0.6, 2.0, and 6.0 mg/kg/day, up to 150 times the maximal daily human topical dose exhibited no fetotoxicity and only minimal increases in supernumerary ribs in rats. There are no adequate and well-controlled studies in pregnant women. Adapalene should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DIFFERIN® Gel is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS: Some adverse effects such as erythema, scaling, dryness, pruritus, and burning will occur in 10-40% of patients. Pruritus or burning immediately after application also occurs in approximately 20% of patients. The following additional adverse experiences were reported in approximately 1% or less of patients: skin irritation, burning/stinging, erythema, sunburn, and acne flares. These are most commonly seen during the first month of therapy and decrease in frequency and severity thereafter. All adverse effects with use of DIFFERIN® Gel during clinical trials were reversible upon discontinuation of therapy.

OVERDOSAGE: DIFFERIN® Gel is intended for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and marked redness, peeling, or discomfort may occur. The acute oral toxicity of DIFFERIN® Gel in mice and rats is greater than 10 mL/kg. Chronic ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

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