

# Pulsed Dye Laser Aids Vascular, Pigmented Lesions

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BOSTON — A modified, high-energy, variable-pulse-duration, pulsed dye laser safely and effectively treated both vascular and pigmentary changes in patients with photoaged skin, a study has shown.

The findings suggest that what has typically been considered a “vascular” laser can be safely used to treat sun damage and associated pigmentary changes as well,

Dr. Nathan Rosen said at the annual meeting of the American Society for Laser Medicine and Surgery.

The pulsed dye laser is considered the laser of choice for most vascular lesions because of its superior clinical efficacy and low risk profile. It has a large spot size, so large lesions can be treated quickly, but the resultant high-energy pulses can cause postoperative bruising and transient pigmentary changes.

The device used in this investigation em-

ploys a modified pulse structure, whereby each pulse comprises six uniform micropulses that evenly distribute the pulse energy, reducing the likelihood of bruising, compared with earlier devices, Dr. Rosen explained.

“The purpura threshold is increased because pigment more selectively absorbs the individual micropulses,” he said.

In addition, the investigational device includes a compression handpiece that, by removing the competing vascular target,

prevents the development of purpura. “The handpiece compresses the blood vessels in the region, allowing all of the energy to be concentrated in the pigmented area,” said Dr. Rosen, who is in private practice in New York.

To evaluate the impact of the new technology on vascular and pigmentary changes associated with photodamage and long-term sun exposure, Dr. Rosen, along with his colleagues Dr. Arielle N.B. Kauvar and Dr. Tatiana Khrom, who are also in private practice in New York, considered the outcomes of its use on 24 patients with photoaged, phototype I-IV skin.

**The new device includes a compression handpiece that, by removing the competing vascular target, prevents the development of purpura.**

photographed, phototype I-IV skin.

Of the 24 subjects who were enrolled in the study, 14 were treated for vascular and pigmented lesions and 10 were treated for pigmented lesions alone.

All of the sub-

jects received a total of one to three treatments at 4-week intervals, and all underwent follow-up evaluations at 3 and 12 weeks.

To treat background erythema, the dermatologists used a 10-ms pulse width and a 12-mm spot at a fluence of 7 J/cm<sup>2</sup>. For telangiectasia, they used a 7-mm spot, a 10-ms pulse width, and fluence of 9-12 J/cm<sup>2</sup>. Pigmented lesions were treated using the compression handpiece with a 7-mm spot, 1.5-ms pulse width, and fluence of 9-15 J/cm<sup>2</sup>.

Only the vascular lesions were treated with cryogen spray cooling (30-ms spray, 30-ms delay) before each laser pulse, and none of the patients received a topical anesthetic prior to laser treatment, Dr. Rosen noted.

“All of the patients tolerated the treatment well, and there was no purpura with the parameters that we used,” Dr. Rosen said.

Three of the patients developed transient hypopigmented macules, and one patient developed a transient atrophic scar as a result of pulse stacking for treating pigmented lesions.

Using blinded comparisons of 35-mm photographs as well as patient self-reports to assess treatment efficacy, the dermatologists observed improvement in the vascular and pigmentary lesions in all of the patients, “and, more importantly, all of the patients were satisfied with their clinical improvement,” he said at the meeting.

The clinical implication of these findings “is that we now are able to use one system, rather than multiple systems, to safely treat both the vascular and pigmentary changes associated with sun damage,” said Dr. Rosen, who reported receiving a research grant for this investigation from Candela Corp., manufacturer of the laser device that was used in the study. ■

Cream for AK or sBCC in patients less than 18 years of age have not been established. **Geriatric Use** Of the 215 patients in the 2X/week clinical studies evaluating the treatment of AK lesions with Aldara Cream, 127 patients (59%) were 65 years and older, while 60 patients (28%) were 75 years and older. Of the 185 patients in the 5X/week treatment groups of clinical studies evaluating the treatment of sBCC with Aldara Cream, 65 patients (35%) were 65 years and older, while 25 patients (14%) were 75 years and older. No overall differences in safety or effectiveness were observed between these patients and younger patients. No other clinical experience has identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. **ADVERSE REACTIONS** Healthcare providers and patients may contact 3M or FDA's Medwatch to report adverse reactions by calling 1-800-814-1795 or 1-800-FDA-1088, or on the internet at <http://www.fda.gov/medwatch>. Dermal safety studies involving induction and challenge phases produced no evidence that Aldara Cream causes photoallergenicity or contact sensitization in healthy skin; however, cumulative irritancy testing revealed the potential for Aldara Cream to cause irritation, and in the clinical studies application site reactions were reported in a significant percentage of study patients. Phototoxicity testing was incomplete as wavelengths in the UVB range were not included and Aldara Cream has peak absorption in the UVB range (320 nm) of the light spectrum. **Actinic Keratosis** The data described below reflect exposure to Aldara Cream or vehicle in 436 patients enrolled in two double-blind, vehicle-controlled, 2X/week studies. Patients applied Aldara Cream or vehicle to a 25 cm<sup>2</sup> contiguous treatment area on the face or scalp 2X/week for 16 weeks. **Summary of All Adverse Events Reported by >1% of Patients in the Combined 2X/ Week Studies** [Body System Imiq 2X/Week Preferred Term (n=215) and Vehicle 2X/Week Preferred Term (n=221)]: **APPLICATION SITE DISORDERS:** APPLICATION SITE REACTION 71 (33.0%) and 32 (14.5%). **BODY AS A WHOLE - GENERAL DISORDERS:** BACK PAIN 3 (1.4%) and 2 (0.9%); FATIGUE 3 (1.4%) and 2 (0.9%); FEVER 3 (1.4%) and 0 (0.0%); HEADACHE 11 (5.1%) and 7 (3.2%); HERNIA NOS 4 (1.9%) and 1 (0.5%); INFLUENZA-LIKE SYMPTOMS 4 (1.9%) and 4 (1.8%); PAIN 3 (1.4%) and 3 (1.4%); RIGORS 3 (1.4%) and 0 (0.0%). **CARDIOVASCULAR DISORDERS, GENERAL:** CHEST PAIN 1 (0.5%) and 4 (1.8%); HYPERTENSION 3 (1.4%) and 5 (2.3%). **CENTR & PERIPH NERVOUS SYSTEM DISORDERS:** DIZZINESS 3 (1.4%) and 1 (0.5%). **GASTRO-INTESTINAL SYSTEM DISORDERS:** DIARRHEA 6 (2.8%) and 2 (0.9%); DYSPEPSIA 6 (2.8%) and 4 (1.8%); GASTROESOPHAGEAL REFLUX 3 (1.4%) and 3 (1.4%); NAUSEA 3 (1.4%) and 3 (1.4%); VOMITING 3 (1.4%) and 1 (0.5%). **HEART RATE AND RHYTHM DISORDERS:** FIBRILLATION ATRIAL 3 (1.4%) and 2 (0.9%). **METABOLIC AND NUTRITIONAL DISORDERS:** HYPERCHOLESTEROLEMIA 4 (1.9%) and 0 (0.0%). **MUSCULO-SKELETAL SYSTEM DISORDERS:** ARTHRALGIA 2 (0.9%) and 4 (1.8%); ARTHRITIS 2 (0.9%) and 3 (1.4%); MYALGIA 3 (1.4%) and 3 (1.4%); SKELETAL PAIN 1 (0.5%) and 3 (1.4%). **NEOPLASMS:** BASAL CELL CARCINOMA 5 (2.3%) and 5 (2.3%); CARCINOMA SQUAMOUS 8 (3.7%) and 5 (2.3%). **RESISTANCE MECHANISM DISORDERS:** 9 (4.2%) and 11 (5.0%); HERPES SIMPLEX 4 (1.9%) and 4 (1.8%); INFECTION VIRAL 3 (1.4%) and 2 (0.9%). **RESPIRATORY SYSTEM DISORDERS:** BRONCHITIS 2 (0.9%) and 3 (1.4%); COUGHING 6 (2.8%) and 10 (4.5%); PHARYNGITIS 4 (1.9%) and 4 (1.8%); PULMONARY CONGESTION 1 (0.5%) and 3 (1.4%); RHINITIS 7 (3.3%) and 8 (3.6%); SINUSITIS 16 (7.4%) and 14 (6.3%); UPPER RESP TRACT INFECTION 33 (15.3%) and 27 (12.2%). **SECONDARY TERMS:** ABRASION NOS 7 (3.3%) and 5 (2.3%); CYST NOS 0 (0.0%) and 4 (1.8%); INFLICTED INJURY 19 (8.8%) and 21 (9.5%); POST-OPERATIVE PAIN 3 (1.4%) and 4 (1.8%). **SKIN AND APPENDAGES DISORDERS:** 47 (21.9%) and 42 (19.0%); ALOPECIA 3 (1.4%) and 0 (0.0%); DERMATITIS 3 (1.4%) and 7 (3.2%); ECZEMA 4 (1.9%) and 3 (1.4%); HYPERKERATOSIS 19 (8.8%) and 12 (5.4%); PHOTOSENSITIVITY REACTION 2 (0.9%) and 4 (1.8%); PRURITUS 2 (0.9%) and 3 (1.4%); RASH 5 (2.3%) and 5 (2.3%); SKIN DISORDER 6 (2.8%) and 7 (3.2%); VERRUCA 1 (0.5%) and 3 (1.4%). **URINARY SYSTEM DISORDERS:** 8 (3.7%) and 10 (4.5%); URINARY TRACT INFECTION 3 (1.4%) and 1 (0.5%). **VISION DISORDERS:** CONJUNCTIVITIS 1 (0.5%) and 3 (1.4%); EYE ABNORMALITY 4 (1.9%) and 1 (0.5%); EYE INFECTION 0 (0.0%) and 3 (1.4%). **Summary of All Application Site Reactions Reported by >1% of Patients in the Combined 2X/ Week Studies** [Imiq 2X/Week Included Term (n=215) and Vehicle 2X/Week Included Term (n=221)]: **BLEEDING AT TARGET SITE** 7 (3.3%) and 1 (0.5%). **BURNING AT REMOTE SITE** 4 (1.9%) and 0 (0.0%). **BURNING AT TARGET SITE** 12 (5.6%) and 4 (1.8%). **INDURATION AT REMOTE SITE** 3 (1.4%) and 0 (0.0%). **INDURATION AT TARGET SITE** 5 (2.3%) and 3 (1.4%). **IRRITATION AT REMOTE SITE** 3 (1.4%) and 0 (0.0%). **ITCHING AT REMOTE SITE** 7 (3.3%) and 3 (1.4%). **ITCHING AT TARGET SITE** 44 (20.5%) and 15 (6.8%). **PAIN AT TARGET SITE** 5 (2.3%) and 2 (0.9%). **STINGING AT TARGET SITE** 6 (2.8%) and 2 (0.9%). **TENDERNESS AT TARGET SITE** 4 (1.9%) and 3 (1.4%). Local skin reactions were collected independently of the adverse event “application site reaction” in an effort to provide a better picture of the specific types of local reactions that might be seen. The most frequently reported local skin reactions were erythema, flaking/scaling/dryness, and scabbing/crusting. The prevalence and severity of local skin reactions that occurred during controlled studies are shown in the following table. **Local Skin Reactions in the Treatment Area as Assessed by the Investigator (Percentage of Patients) 2X/Week Application [Mild/Moderate/Severe Aldara Cream (n=215), Vehicle (n=220) and Severe Aldara Cream (n=215), Vehicle (n=220)]:** Erythema 209 (97%), 206 (93%) and 38 (18%), 5 (2%). Edema 106 (49%), 22 (10%) and 0 (0%), 0 (0%). Weeping/Exudate 45 (22%), 3 (1%) and 0 (0%), 0 (0%). Vesicles 19 (9%), 2 (1%) and 0 (0%), 0 (0%). Erosion/Ulceration 103 (48%), 20 (9%) and 5 (2%), 0 (0%). Flaking/Scaling/Dryness 199 (93%), 199 (91%) and 16 (7%), 7 (3%). Scabbing/Crusting 169 (79%), 92 (42%) and 18 (8%), 4 (2%). The adverse reactions that most frequently resulted in clinical intervention (e.g., rest periods, withdrawal from study) were local skin and application site reactions. Overall, in the clinical studies, 2% (5/215) of patients discontinued for local skin/application site reactions. Of the 215 patients treated, 35 patients (16%) on Aldara Cream and 3 of 220 patients (1%) on vehicle cream had at least one rest period. Of these Aldara Cream patients, 32 (91%) resumed therapy after a rest period. In the AK studies, 22 of 678 imiquimod-treated patients developed treatment site infections that required a rest period of Aldara Cream and were treated with antibiotics (19 with oral and 3 with topical). **Superficial Basal Cell Carcinoma** The data described below reflect exposure to Aldara Cream or vehicle in 364 patients enrolled in two double-blind, vehicle-controlled, 5X/week studies. Patients applied Aldara Cream or vehicle 5X/week for 6 weeks. The incidence of adverse events reported by >1% of subjects during the 6 week treatment period is summarized below. **Summary of All Adverse Events Reported by >1% of Patients in the Combined 5X/ Week Studies** [Body System Imiquimod 5X/Week Preferred Term (n=185) and Vehicle 5X/Week Preferred Term (n=179)]: **APPLICATION SITE DISORDERS:** APPLICATION SITE REACTION 52 (28.1%) and 5 (2.8%). **BODY AS A WHOLE - GENERAL DISORDERS:** ALLERGY AGGRAVATED 2 (1.1%) and 1 (0.6%); BACK PAIN 7 (3.8%) and 1 (0.6%); CHEST PAIN 2 (1.1%) and 0 (0.0%); FATIGUE 4 (2.2%) and 2 (1.1%); FEVER 3 (1.6%) and 0 (0.0%); PAIN 3 (1.6%) and 2 (1.1%). **CARDIOVASCULAR DISORDERS, GENERAL:** HYPERTENSION 5 (2.7%) and 1 (0.6%). **CENTR & PERIPH NERVOUS SYSTEM DISORDERS:** DIZZINESS 2 (1.1%) and 1 (0.6%); HEADACHE 14 (7.6%) and 4 (2.2%). **GASTRO-INTESTINAL SYSTEM DISORDERS:** ABDOMINAL PAIN 1 (0.5%) and 2 (1.1%); DIARRHEA 1 (0.5%) and 2 (1.1%); DYSPEPSIA 3 (1.6%) and 2 (1.1%); GASTRO-INTESTINAL DISORDER NOS 1 (0.5%) and 2 (1.1%); NAUSEA 2 (1.1%) and 2 (1.1%); TOOTH DISORDER 0 (0.0%) and 2 (1.1%). **METABOLIC AND NUTRITIONAL DISORDERS:** GOUT 2 (1.1%) and 0 (0.0%). **MUSCULO-SKELETAL SYSTEM DISORDERS:** SKELETAL PAIN 3 (1.6%) and 2 (1.1%). **PSYCHIATRIC DISORDERS:** ANXIETY 2 (1.1%) and 1 (0.6%). **RESISTANCE MECHANISM DISORDERS:** INFECTION 1 (0.5%) and 3 (1.7%); INFECTION FUNGAL 2 (1.1%) and 2 (1.1%). **RESPIRATORY SYSTEM DISORDERS:** COUGHING 3 (1.6%) and 1 (0.6%); PHARYNGITIS 2 (1.1%) and 1 (0.6%); RHINITIS 5 (2.7%) and 1 (0.6%); SINUSITIS 4 (2.2%) and 1 (0.6%); UPPER RESP TRACT INFECTION 6 (3.2%) and 2 (1.1%). **SECONDARY TERMS:** INFLICTED INJURY 3 (1.6%) and 3 (1.7%); PROCEDURAL SITE REACTION 2 (1.1%) and 3 (1.7%). **SKIN AND APPENDAGES DISORDERS:** HYPERKERATOSIS 3 (1.6%) and 2 (1.1%); RASH 3 (1.6%) and 1 (0.6%); SKIN DISORDER 1 (0.5%) and 3 (1.7%). **WHITE CELL AND RES DISORDERS:** LYMPHADENOPATHY 5 (2.7%) and 1 (0.6%). In controlled clinical studies, the most frequently reported adverse reactions were local skin and application site reactions including erythema, edema, induration, erosion, flaking/scaling, scabbing/crusting, itching and burning at the application site. The incidence of the application site reactions reported by >1% of the subjects during the 6 week treatment period is summarized in the table below. **Summary of All Application Site Reactions Reported by >1% of Patients in the Combined 5X/ Week Studies** [Imiquimod 5X/ Week Included Term (n=185) and Vehicle 5X/ Week Included Term (n=179)]: **ITCHING AT TARGET SITE** 30 (16.2%) and 1 (0.6%). **BURNING AT TARGET SITE** 11 (5.9%) and 2 (1.1%). **PAIN AT TARGET SITE** 6 (3.2%) and 0 (0.0%). **TENDERNESS AT TARGET SITE** 2 (1.1%) and 0 (0.0%). **ERYTHEMA AT REMOTE SITE** 3 (1.6%) and 0 (0.0%). **PAPULE(S) AT TARGET SITE** 3 (1.6%) and 0 (0.0%). **BLEEDING AT TARGET SITE** 4 (2.2%) and 0 (0.0%). **TINGLING AT TARGET SITE** 1 (0.5%) and 2 (1.1%). **INFECTION AT TARGET SITE** 2 (1.1%) and 0 (0.0%). Local skin reactions were collected independently of the adverse event “application site reaction” in an effort to provide a better picture of the specific types of local reactions that might be seen. The prevalence and severity of local skin reactions that occurred during controlled studies are shown in the following table. **Most Intense Local Skin Reactions in the Treatment Area as Assessed by the Investigator (Percentage of Patients) 5X/Week Application [Mild/Moderate Aldara Cream (n=184), Vehicle (n=178) and Severe Aldara Cream (n=184) Vehicle (n=178)]:** Edema 71%, 36% and 7%, 0%. Erosion 54%, 14% and 13%, 0%. Erythema 69%, 95% and 31%, 2%. Flaking/Scaling 87%, 76% and 4%, 0%. Induration 78%, 53% and 6%, 0%. Scabbing/Crusting 64%, 34% and 19%, 0%. Ulceration 34%, 3% and 6%, 0%. Vesicles 29%, 2% and 2%, 0%. The adverse reactions that most frequently resulted in clinical intervention (e.g., rest periods, withdrawal from study) were local skin and application site reactions; 10% (19/185) of patients received rest periods. The average number of doses not received per patient due to rest periods was 7 doses with a range of 2 to 22 doses; 79% of patients (15/19) resumed therapy after a rest period. Overall, in the clinical studies, 2% (4/185) of patients discontinued for local skin/application site reactions. In the sBCC studies, 17 of 1266 (1.3%) imiquimod-treated patients developed treatment site infections that required a rest period of Aldara Cream and were treated with antibiotics. **External Genital Warts** In controlled clinical trials for genital warts, the most frequently reported adverse reactions were local skin and application site reactions. These reactions were usually mild to moderate in intensity; however, severe reactions were reported with 3X/week application. **These reactions were more frequent and more intense with daily application than with 3X/week application.** Some patients also reported systemic reactions. Overall, in the 3X/week application clinical studies, 1.2% (4/327) of the patients discontinued due to local skin/application site reactions. The incidence and severity of local skin reactions during controlled clinical trials are shown in the following table. **Wart Site Reaction as Assessed by Investigator (Percentage of Patients) 3X/Week Application [Mild/Moderate/Severe Females Aldara Cream (n=114), Vehicle (n=99); Males Aldara Cream (n=114), Vehicle (n=99); Males Aldara Cream (n=156), Vehicle (n=157)]:** Erythema 74 (65%), 21 (21%), 90 (58%), 34 (22%) and 4 (4%), 0 (0%), 6 (4%), 0 (0%). Erosion 35 (31%), 8 (8%), 47 (30%), 10 (6%) and 1 (1%), 0 (0%), 2 (1%), 0 (0%). Excoriation/Flaking 21 (18%), 8 (8%), 40 (26%), 12 (8%) and 0 (0%), 0 (0%), 1 (1%), 0 (0%). Edema 20 (18%), 5 (5%), 19 (12%), 1 (1%) and 1 (1%), 0 (0%), 0 (0%), 0 (0%). Induration 6 (5%), 2 (2%), 11 (7%), 3 (2%) and 0 (0%), 0 (0%), 0 (0%), 0 (0%). Ulceration 9 (8%), 1 (1%), 7 (4%), 1 (1%) and 3 (3%), 0 (0%), 0 (0%), 0 (0%). Scabbing 4 (4%), 0 (0%), 20 (13%), 4 (3%) and 0 (0%), 0 (0%), 0 (0%), 0 (0%). Vesicles 3 (3%), 0 (0%), 3 (2%), 0 (0%) and 0 (0%), 0 (0%), 0 (0%), 0 (0%). Remote site skin reactions were also reported in female and male patients treated 3X/week with Aldara Cream. The severe remote site skin reactions reported for females were erythema (3%), ulceration (2%), and edema (1%); and for males, erosion (2%), and erythema, edema, induration, and excoriation/flaking (each 1%). Adverse events judged to be probably or possibly related to Aldara Cream reported by more than 5% of patients are listed below; also included are soreness, influenza-like symptoms and myalgia. **3X/Week Application [Females Aldara Cream (n=117), Vehicle (n=103) and Males Aldara Cream (n=156), Vehicle (n=158)]:** Application Site Disorders: Application Site Reactions Wart Site: Itching 32%, 20% and 22%, 10%. Burning 26%, 12% and 9%, 5%. Pain 8%, 2% and 2%, 1%. Soreness 3%, 0% and 0%, 1%. Fungal Infection\* 11%, 3% and 2%, 1%. Systemic Reactions: Headache 4%, 3% and 5%, 2%. Influenza-like symptoms 3%, 2% and 1%, 0%. Myalgia 1%, 0% and 1%, 1%. \*Incidences reported without regard to causality with Aldara Cream. Adverse events judged to be possibly or probably related to Aldara Cream and reported by more than 1% of patients included: **Application Site Disorders:** Wart Site Reactions (burning, hypopigmentation, irritation, itching, pain, rash, sensitivity, soreness, stinging, tenderness); Remote Site Reactions (bleeding, burning, itching, pain, tenderness, tine cruris); **Body as a Whole:** fatigue, fever, influenza-like symptoms; **Central and Peripheral Nervous System Disorders:** headache; **Gastro-Intestinal System Disorders:** diarrhea; **Musculo-Skeletal System Disorders:** myalgia. **POSTMARKETING ADVERSE EVENTS** The following adverse reactions have been identified during post-approval use of Aldara Cream. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. **Body as a Whole:** angioedema. **Cardiovascular:** capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope. **Endocrine:** thyroiditis. **Hematological:** decreases in red cell, white cell and platelet counts. **Hepatic:** abnormal liver function. **Neuropsychiatric:** agitation, cerebrovascular accident, convulsions, depression, insomnia, multiple sclerosis aggravation, paresis, suicide. **Respiratory:** dyspnea. **Urinary System Disorders:** proteinuria. **Skin and Appendages:** exfoliative dermatitis. **OVERDOSAGE** Persistent topical overdosing of Aldara Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions. The most clinically serious adverse event reported following multiple oral imiquimod doses of >200 mg (equivalent to imiquimod content of >16 packets) was hypotension, which resolved following oral or intravenous fluid administration.

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