Topical gel proves safe, effective treatment for patients with skin T cell lymphoma

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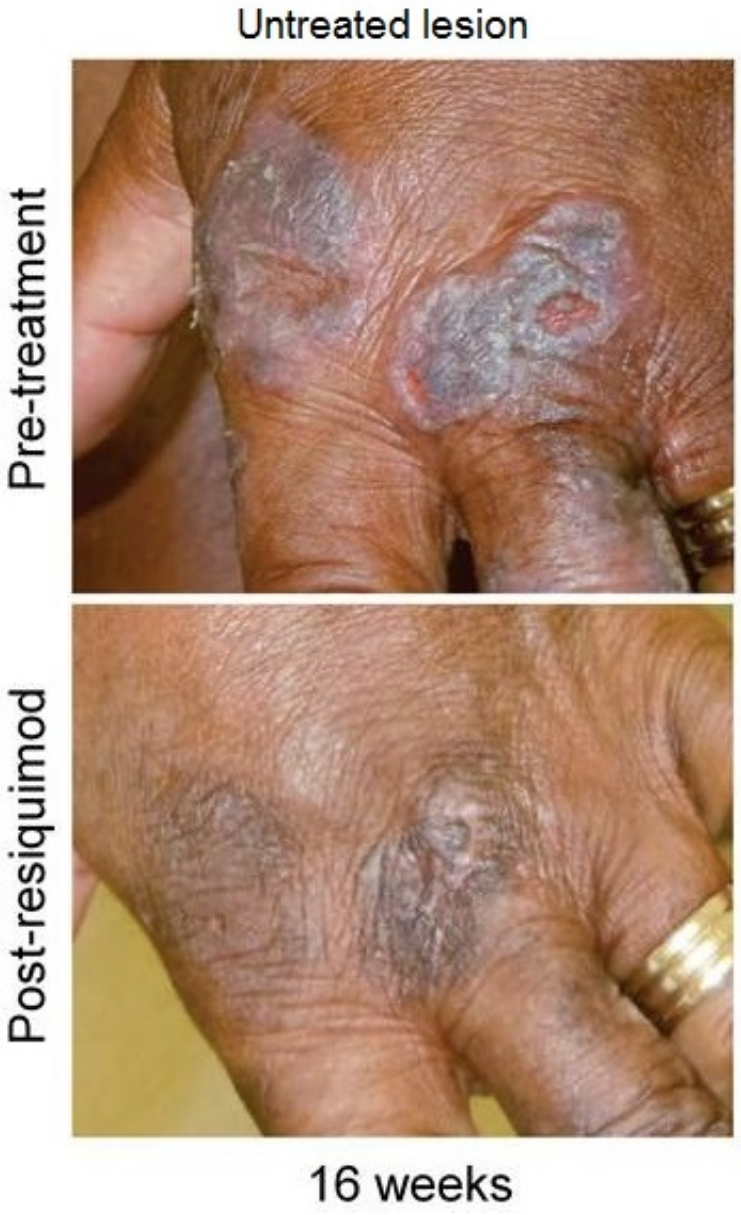

Using resiquimod on some CTCL legions has a systemic effect, which can be seen in significantly diminished legions that did not directly receive treatment. Credit: Penn Medicine

Results of a phase one trial show that an investigational topical drug, resiquimod gel, causes regression of both treated and untreated tumor lesions and may completely remove cancerous cells from both sites in patients with early stage cutaneous T cell lymphoma (CTCL) - a rare type of non-Hodgkin lymphoma that affects the skin. Currently, there is no cure for CTCL aside from a bone marrow transplant. However, the new study from researchers at the Perelman School of Medicine at the University of Pennsylvania, shows that the topical gel can eliminate malignant T cells, leading to diminished lesions. Results, which build upon previous research, are giving hope to patients who have not responded to other modalities, including certain types of topical chemotherapy, phototherapy and even systemic treatment with interferon alpha and oral bexarotene.

The study is published online this month in the journal Blood.

In the trial, co-led by Rachael Clark, MD, PhD, associate professor of Dermatology at Harvard Medical School, Alain Rook, MD, professor of Dermatology and director of the Cutaneous Lymphoma Program at Penn Medicine, and Joel M. Gelfand, MD, MSCE, associate professor of Dermatology and medical director of the Clinical Studies Unit at Penn Medicine, twelve patients who had previously undergone an average of six treatments for early stage CTCL were treated with topical resiquimod gel at varying doses and intervals. Patients applied specified doses (0.03 percent of 0.06 percent) to select skin lesions for 16 weeks. However, some patients using the 0.06 percent dose showed a full clearing of all malignant cells after only eight weeks.

By the final evaluation, treated lesions were significantly improved in 75 percent of patients, and 30 percent saw full resolution in all treated lesions. Unlike other treatments, resiquimod also improved untreated lesions, resulting in more than 50 percent improvement for more than 90 percent of patients. Two participants, one of whom had been living with CTCL for more than 15 years without response to treatment, saw full eradication of the disease.

"The results of the trial suggest that resiquimod is safely and effectively absorbed into the skin, and beyond diminishing treated lesions, also enhances the immune response, leading to healing of even untreated lesions," first author and principal investigator Rook, said.. "To our knowledge, this is the first topical therapy that can clear untreated lesions and lead to complete remission in some patients."

Using a method known as high throughput sequencing (HTS), the team was able to determine how many distinct malignant cells were present within a sample of healthy cells. The technique showed it could identify a single malignant cell amongst 100,000 healthy cells. DNA from biopsies of the same treated lesion were analyzed before treatment and eight weeks after treatment began to identify the number of malignant T cells. The percentage of malignant T cells was reduced significantly in nine of ten tested participants, three of whom had complete eradication of the malignant population, and one of whom had a 99.6 percent reduction.

"Overall, lesions responded far better to topical resiquimod than they have with other topical therapies, including some potent topical steroids and topical chemotherapy, and was extremely well tolerated by patients," Rook said. "Building upon previous research, our study suggests resiquimod might be useful in combination with other therapies in the treatment of more advanced CTCL. Further research with larger participant populations is needed to determine the best approach and

application for these patients."

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