

Skin-Directed Tactics Optimal for Early Cutaneous Lymphoma

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GENEVA — For patients with early-stage cutaneous lymphoma, skin-directed treatments, such as topical steroids and phototherapy, can slow or halt progression, but patients are also being treated with systemic therapies, according to the first-of-its kind research on this rare malignancy.

"There's a great heterogeneity of treatments" for this patient population, said investigator Pietro Quaglino, MD, from the University of Turin Medical School in Italy. That is "one of the idiosyncrasies of this disease: few patients but many treatments."

In the early-stage Prospective Cutaneous Lymphoma International Prognostic Index (PROCLIP) trial, Dr Quaglino and his colleagues examined first-line treatment options for early mycosis fungoides. Although mycosis fungoides is considered a rare disease, with a worldwide incidence of approximately 1 in 100,000, it is the most common form of cutaneous lymphoma, accounting for about 70% of all diagnoses.

Typical survival for patients diagnosed with stage IA to IIA mycosis fungoides is 10 to 35 years, but more than one-quarter of patients progress to advanced disease, with a median survival of less than 4 years. Early-stage disease often presents with patchy skin that is localized or diffuse, but with no tumors or involvement beyond the skin. Expected survival drops to less than 12 months when lymph node involvement is extensive.

The investigators hope their data will reveal the factors associated with disease progression and identify which treatments are most effective.

They have skin disease that is visual, often not responding to treatment, and they're fearful.

Because the analysis will continue for another 8 years, the superiority of one treatment over another has not yet been established, said lead investigator Julia Scarisbrick, MD, from University Hospital Birmingham in the United Kingdom.

"Our treatment guidelines give a selection of suitable treatments for each stage of disease, but there's no hierarchy for first treatment choice," she told *Medscape Medical News*. "This depends on patients and the convenience of treatment. For some patients, topical agents will be more attractive than phototherapy, where patients have to visit the hospital 2 or 3 times per week."

Dr Quaglino presented data collected from 42 centers in 14 countries to identify core prognostic factors for treatment, survival, and quality of life here at the 26th European Academy of Dermatology and Venereology Congress.

"Already we have some interesting data on age at diagnosis," Dr Scarisbrick reported. "Patients with early-stage disease tend to be younger, which may be why an increase in age is thought to be a worse prognostic factor. But, in fact, the disease is more common in advanced forms in the elderly."

Two years into the analysis, 472 patients are being tracked. Of these, 80.7% have classic mycosis fungoides and 15.7% have folliculotropic mycosis fungoides. Median age in the cohort is 57 years, but average age creeps up as disease stage advances. Nearly two-thirds of the patients are male.

Early-stage treatments being assessed in this study are topical steroids alone, extracorporeal photopheresis, emollients, watchful waiting, gemcitabine, phototherapy, local radiotherapy, systemic therapies (such as oral bexarotene, acitretin, and interferon), total skin electron-beam therapy, and topical nitrogen mustard.

The most commonly prescribed treatments for early-stage disease, by far, are ultraviolet B (UVB) and psoralen and ultraviolet A (PUVA) phototherapy, and topical steroids, the investigators report.

Table. Response Rates for the Most Frequent First-Line Treatments

Response	Topical Steroids (n = 159), %	Phototherapy (n = 88), %	Systemic Therapy (n = 55), %
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Complete	14.5	35.0	5.5
Partial	8.8	26.0	19.2
Undetermined (treatment ongoing)	65.0	30.7	63.6

Watchful waiting is also a viable approach for early-stage mycosis fungoides. None of the 71 patients in that category experienced disease progression, Dr Quaglino reported. But patients choosing watchful waiting should carefully consider factors such as age and comorbidities.

"It depends clearly on the extent of disease — whether there are limited lesions, the sites of the lesions, and itching — and patients of a younger age are more motivated to receive treatment," he said.

With about 65% of patients still undergoing treatment, response rates are expected to increase over time, Dr Quaglino said. Study participants will continue to accrue until year 5.

"We would like to not only improve treatment choices, but also improve the quality of life of these patients," Dr Scarisbrick said. "We're collecting quality-of-life data to see if any treatment has a more preferential impact on quality of life."

Because cutaneous lymphoma can initially be misdiagnosed as psoriasis or eczema, many patients live with uncertainty, sometimes for years, she pointed out.

"One of the important factors we have identified is a diagnostic delay of 24 to 36 months in both early- and advanced-stage disease, which leads to considerable anxiety and distress for many patients," she explained. "They have skin disease that is visual, often not responding to treatment, and they're fearful."

These findings will help dermatologists and patients with mycosis fungoides make optimal treatment choices, said Seda Purnak, MD, from the Ankara Numune Training and Research Hospital in Turkey.

"To know the response rates will help us choose a first-line treatment," she told *Medscape Medical News*. "It's a rarely curable disease, and we need to follow patients for a long time. If we catch the disease early, the response rates are much better."

Dr Quaglino, Dr Scarisbrick, and Dr Purnak have disclosed no relevant financial relationships.

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