#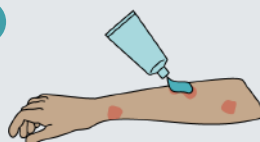 Evaluating the Treatment Patterns of Chlormethine/Mechlorethamine Gel in Patients With Stage I-IIA Mycosis Fungoides: By-time Analysis of a Randomized Controlled Phase 2 Study

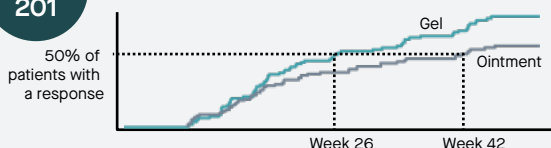Larisa J. Geskin, Ellen J. Kim, James T. Angello, and Youn H. Kim

Background

Chlormethine/mechlorethamine gel is recommended as one of several **first-line therapies** for adults with MF in international guidelines

Its topical application inhibits rapidly proliferating cells, ultimately resulting in cell death

Study 201

The approval of chlormethine/mechlorethamine gel for MF treatment was based upon the findings of the pivotal **Study 201**

50% of patients with a response
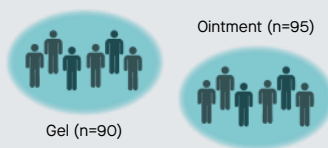

Gel / Ointment / Week 26 / Week 42

Study 201 assessed the overall efficacy of chlormethine/mechlorethamine gel treatment, but it did not evaluate how the response **changes over time**

Can the novel statistical method of **by-time analysis** help clinicians characterize the **patterns** of this response during the course of therapy?

Study methods

In Study 201, patients were randomized to receive **0.02% chlormethine/mechlorethamine gel** or **ointment** as a monotherapy **once-daily** for **12 months**

Ointment (n=95)
Gel (n=90)

· Every month for the first six months

· Every other month for the second 6 months

The efficacy data from Study 201 were re-evaluated with a by-time method

The following "by-time" analyses were performed:

· CAILS data   · mSWAT data   · %BSA

Clinically responsive disease was defined as ≥50% reduction from baseline in CAILS, mSWAT, or %BSA score

Results

All analyses showed increased response over time, with peaks at 10 months for both CAILS and mSWAT

Three response patterns

Percentage change in CAILS from baseline (Visits 1 through 9)
Shaded areas represent response to therapy

Early
Response occurs immediately, sometimes within a month

1	2	3	4	5	6	7	8	9
-52.5	-57.6	-64.4	-72.9	-57.6	-59.3	-57.6	-69.5	-83.1
-44.4	-66.7	-58.3	-83.3	-72.2	-75	-72.2	-63.9	-69.4
-50	-100	-100	-100	-100	-100	-100	-100	-100
-25	-50	-100	-100	-100	-100	-100	-100	-100
-20	-100	-100	-100	-100	-100	-100	-100	-100

Intermittent
Overall improvement from baseline, but response fluctuates over time

1	2	3	4	5	6	7	8	9
-32.4	-51.4	-67.6	-70.3	-56.8	-45.9	-48.6	-62.2	-62.2
-19.4	-29	-22.6	-19.4	-80.6	-35.5	-74.2	-90.3	-90.3
-10.3	-36.8	-36.8	-51.5	-41.2	-60.3	-58.8	-55.9	-70.6
-20	-40	-24	-52	-76	-68	-48	-72	-100
-48	-52	NRBT*	-48	-72	-76	-76	-100	-100

Late
Response takes many months (sometimes > 6) to occur

1	2	3	4	5	6	7	8	9
-28.6	-32.1	-35.7	-28.6	-21.4	-35.7	-75	-71.4	-64.3
-27.8	-38.9	-22.2	-22.2	-27.8	-33.3	-44.4	-55.6	-100
2.9	4.4	-19.1	-23.5	-26.5	-60.3	-58.8	-57.4	-57.4
-20	-16	-34	-32	-32	-36	-60	-60	-100
33.3	57.1	57.1	76.2	57.1	-52.4	-66.7	-76.2	-100

Example of early termination or loss of response

-22	-53.7	-65.9	NRBT	NRBT	NRBT	NRBT	NRBT	NRBT
-12.5	-30	-55	-75	-77.5	-50	NRBT	NRBT	NRBT
-76.9	-100	-41	-66.7	-100	-100	-92.3	NRBT	NRBT
-8.3	-41.7	-50	-50	-33.3	-33.3	0	NRBT	NRBT
-37.5	-75	-75	-50	-50	NRBT	NRBT	NRBT	NRBT

Example of unconfirmed response

-41	-46.2	-46.2	-30.8	-48.7	-100	NRBT	NRBT	NRBT
17.2	-10.3	-55.2	-27.6	-24.1	-20.7	-13.8	6.9	-93.1
-6.3	37.5	25	37.5	18.8	12.5	-6.3	-6.3	-100
33.3	13.3	0	-13.3	13.3	20	0	13.3	NRBT
-29.2	-83.3	NRBT	NRBT	NRBT	NRBT	NRBT	NRBT	NRBT

NRBT, not responder in the by-time analysis due to missing data points

Administering the medication for an extended period of time, generally >6 months, is necessary to identify a patient's response pattern

32.5% of patients experienced a ≥75% improvement over baseline over 2 consecutive visits, indicating that **~1/3 of patients** could expect to have a **very good to complete response** within **1 year**

49 patients discontinued therapy

26 due to dermatitis reactions; 2 due to patient's best interest; 4 due to concurrent illness unrelated to study treatment; 3 withdrew consent; 2 due to noncompliance; 4 lost to follow-up; 4 for other (1 before receipt of study medication, 2 for other treatments that disqualified further participation, 1 for disease progression); and 4 for lack of efficacy

Conclusions

By-time analysis of clinical response data provides information complementary to traditional overall response rate data, including information on **peak response** and **changes over time**

The study findings can help physicians and patients set expectations regarding **response patterns and times** under treatment with **chlormethine/mechlorethamine gel**

%BSA, body surface area score; CAILS, Composite Assessment of Index Lesion Severity; MF, mycosis fungoides; mSWAT, modified severity-weighted assessment tool; NRBT, unhighlighted and missing data points **n**ot counted as **r**esponders using the **by-t**ime analysis approach