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POSTER perspectives

Research Developments in Psoriasis Treatment

A CME Activity

Overview

Mark Lebwohl, MD, Waldman Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York, provides his perspectives on key posters presented at the American Academy of Dermatology annual meeting on the management of patients with moderate-to-severe psoriasis.

Content Areas:

Plaque psoriasis • Psoriasis • Psoriatic arthritis

Faculty

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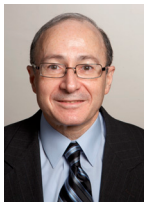

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CE/CME Information

Target Audience
This activity was developed for dermatologists, advanced nurse practitioners, physician assistants, and other health care professionals who have an interest in patients with moderate-to-severe psoriasis.

Learning Objectives
At the conclusion of this activity, participants should be better able to:

- Summarize the latest research developments in the treatment of moderate-to-severe psoriasis
- Incorporate evidence-based research into clinical practice

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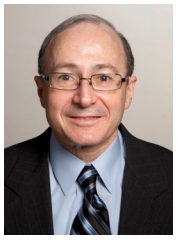
Secukinumab Retreatment Shows Rapid Recapture of Treatment Response in Analysis of a Phase 3 Extension Trial in Psoriasis



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Waldman Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Secukinumab Retreatment Shows Rapid Recapture of Treatment Response in Analysis of a Phase 3 Extension Trial in Psoriasis, presented by Dr. Blauvelt and colleagues at the American Academy of Dermatology annual meeting that took place in Orlando from March 3–7, 2017.

To summarize this poster, secukinumab re-treatment restored efficacy within 16 weeks in patients with psoriasis after being withdrawn from therapy. The safety profile of secukinumab was consistent with previous reports. The reason this study is important is that treatment interruption is a common occurrence in patients with psoriasis and has been shown to often lead to reduced efficacy upon re-treatment. The results of this study showing the recapture of treatment response with secukinumab re-treatment indicates secukinumab is a good option in this challenging population.

Summary & Importance

- Secukinumab retreatment restored efficacy within 16 weeks
- The safety profile of secukinumab was consistent with previous reports
- Treatment interruption is common in patients with psoriasis and may lead to diminished efficacy upon retreatment
- The results suggest secukinumab may be a good option in this challenging population

Here's how the study was designed. This analysis reports from the extension phase of the ERASURE and FIXTURE phase 3 studies. In the ERASURE and FIXTURE studies, patients were randomized equally to secukinumab 150 or 300 mg or placebo. There was a fourth arm in the FIXTURE study in which patients received etanercept 50 mg per week. Treatment was administered at baseline and at weeks 1, 2, 3 and 4, and then every 4 weeks. At week 12, placebo patients who did not achieve a PASI-75 response were randomized to secukinumab 150 mg or 300 mg.

Study Design and Methods

- This analysis reports results from the extension phase of the ERASURE and FIXTURE phase 3 studies
- In the ERASURE and FIXTURE studies, patients were randomized equally to secukinumab 150 mg or 300 mg or placebo
  - There was a fourth arm in the FIXTURE study in which patients received etanercept 50 mg
  - Treatment was administered at baseline, weeks 1, 2, 3, and 4, then every 4 weeks.
- At week 12, placebo patients who did not achieve a PASI-75 response were randomized to secukinumab 150 mg or 300 mg.

Patients who had PASI-75 responses at week 52 were randomized in the extension study 2:1 to continue on the same dose of secukinumab or to receive placebo every 4 weeks. Patients who relapsed in the placebo arms of the 2 studies were re-treated with secukinumab at weeks 0, 1, 2, 3 and 4, and then every 4 weeks. Relapse was defined as a loss of 50% of the maximum PASI gain compared with baseline in the ERASURE and FIXTURE studies.

Study Design and Methods (cont)

- Patients who had PASI-75 responses at week 52 were randomized in the extension study 2:1 to continue on the same dose of secukinumab or to receive placebo every 4 weeks
  - Patients who relapsed in the placebo arms of the 2 studies were retreated with secukinumab at weeks 0, 1, 2, 3, 4, and then every 4 weeks
  - Relapse was defined as a loss of >50% of the maximum PASI gain compared with baseline in the ERASE and FIXTURE studies

This poster is an analysis of patients who had a good response to secukinumab, and by that we mean that they were required to have a PASI-75 response

and then were switched to placebo to create active treatment withdrawal, and were then re-started on secukinumab once they had relapsed.

Study Design and Methods (cont)

- This analysis is limited to patients who had a good response to secukinumab (they were required to have a PASI-75 response), were then switched to placebo to create active treatment withdrawal, and were then restarted on secukinumab once they had relapsed

Key findings were as follows. One hundred eighty-one patients were included in this treatment response, then treatment withdrawal, then treatment re-start group. One hundred thirty-six of the 181 patients, or 75.1%, relapsed upon treatment withdrawal at a median of 28 weeks, and were subsequently re-treated with secukinumab. Recall that these patients had a PASI-75 score at 52 weeks, so all of them with PASI-75. In these 136 patients, 93.8% achieved a PASI-75 response at 16 weeks, following initiation of re-treatment with secukinumab, which is an excellent recapture rate.

Results Summary

- 181 patients were included in this treatment response, then treatment withdrawal, then treatment restart group
  - 136 of the 181 patients (75.1%) relapsed upon treatment withdrawal at a median of 28 weeks and were subsequently retreated with secukinumab
  - These patients had a PASI-75 score at 52 weeks
- In these 136 patients, 93.8% achieved a PASI-75 response at 16 weeks following initiation of retreatment with secukinumab

In the patients who had a PASI-90 at 52 weeks, 95.8% had a PASI-75 at 16 weeks following initiation of re-treatment, and 78.8% had a PASI-90. 67.3% had a PASI-100 at 16 weeks following initiation of re-treatment. In the retreated patients, the mean exposure to secukinumab per patient was 202.2 days. Adverse events were consistent with previous studies and presented no unexpected safety findings.

Results Summary (cont)

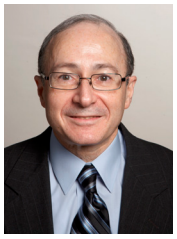
- In the patients who had a PASI-90 at 52 weeks, 95.8% had a PASI-75 at 16 weeks following initiation of retreatment and 78.8% had a PASI-90
- In the patients who had a PASI-100 at 52 weeks, 67.3% had a PASI-100 at 16 weeks following initiation of retreatment
- In the retreated patients, the mean exposure to secukinumab per patient was 202.2 days
- Adverse events were consistent with previous studies and presented no unexpected safety findings

Now I will say that one of the striking results of this trial was that 25% of patients actually never relapsed. They continued in the trial long term and did not relapse. Long remissions in 25% of patients. Literally the nature of the disease appeared to have been modified by treatment with secukinumab. The median time to relapse following the withdrawal of secukinumab was 28 weeks in those who did relapse.

Faculty Commentary

- It is striking that 25% of the patients never relapsed suggesting that the nature of the disease was modified by treatment with secukinumab
- In those who did relapse following withdrawal of secukinumab, the median time to relapse was 28 weeks

Safety and Efficacy of Apremilast Through 104 Weeks in Patients With Moderate to Severe Psoriasis Who Continued on Apremilast or Switched From Etanercept Treatment in the LIBERATE Study



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Waldman Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Safety and Efficacy of Apremilast Through 104 Weeks in Patients With Moderate to Severe Psoriasis Who Continued on Apremilast or Switched From Etanercept Treatment in the LIBERATE Study. This was presented by Dr. Kristian Reich and colleagues at the American Academy of Dermatology annual meeting in Orlando, which took place from March 3–7, 2017.

In summary, compared to placebo, apremilast demonstrated significant efficacy at week 16 that was maintained through week 104 in biologic-naïve patients with moderate-to-severe plaque psoriasis. Significant improvements in scalp and nail psoriasis were also observed at week 16 with apremilast and were sustained through week 104. Patients switched from etanercept to apremilast maintained efficacy. The safety profile of apremilast was as expected and did not increase over time.

Summary

- In biologic-naïve patients with moderate-to-severe psoriasis, apremilast demonstrated significant efficacy compared to placebo from week 16 through week 104
- Efficacy was maintained in patients switched from etanercept to apremilast
- Safety profile of apremilast was as expected

The importance of this study is that many of the medications used to treat moderate-to-severe plaque psoriasis are limited by adverse events, safety, and tolerability issues, as well as the route of administration. The results of this study indicated that the orally administered apremilast may be an important treatment alternative in this patient population.

Importance

- Many medications for moderate-to-severe plaque psoriasis are limited by adverse events, safety, tolerability, or route of administration
- Orally administered apremilast may be an important alternative

Now let's talk about this study design. The LIBERATE Study is a randomized, placebo-controlled, multicenter phase 3b study. It involved biologic-naïve patients with chronic moderate-to-severe plaque psoriasis as demonstrated by PASI scores greater than or equal to 12, a static Physician's Global Assessment equal to 3 or moderate disease, and a body surface area involvement greater than or equal to 10%. Patients who had an inadequate response, intolerance, or contraindication to at least one conventional systemic agent were included.

Study Design and Methods

- The LIBERATE study is a randomized, placebo-controlled, multicenter phase 3b study
- LIBERATE involved biologic-naïve patients with chronic moderate-to-severe plaque psoriasis as demonstrated by:
  - Psoriasis Area and Severity Index score ≥12
  - Static Physician's Global Assessment score ≥3
  - Body surface area involvement ≥10%
- Patients were those who had an inadequate response, intolerance, or contraindication to at least 1 conventional systemic agent

Patients were randomized 1:1:1 to receive either etanercept 50 mg once weekly, apremilast 30 mg twice daily, or placebo. At 16 weeks, the apremilast patients continued treatment, while the etanercept and placebo patients were switched to apremilast 30 mg twice daily. Treatment was continued through week 104. Starting at week 32, all non-responders, and that was defined by those who were less than PASI-50, had the option of adding topical therapies and/or UVB phototherapy.

Study Design and Methods (cont)

- Patients were randomized 1:1:1 to
  - Etanercept 50 mg once weekly
  - Apremilast 30 mg twice daily or
  - Placebo
- At 16 weeks
  - Apremilast patients continued treatment
  - Etanercept and placebo patients switched to apremilast 30 mg twice daily
  - Treatment was continued through week 104
- Starting at week 32, all nonresponders (<PASI-50) had the option of adding topical therapies and/or UV-B phototherapy

Three hundred fifty patients with a mean PASI score of 19 to 20 at baseline were randomized. The mean duration of psoriasis ranged from 16.6 to 19.7 years. A PASI-75 score at week 16 was achieved in 39.8% of apremilast patients, 48% of the etanercept patients, and 11.9% of placebo patients. The differences were statistically significant compared with the placebo. A PASI-75 score at week 104 was achieved in 45.9% to 51.9% of patients with no statistically significant differences between the 3 groups.

Results Summary

- 250 patients with a mean PASI score of 19-20 at baseline were randomized
  - Mean duration of psoriasis ranged from 16.6 to 19.7 years
- A PASI-75 score at week 16 was achieved in
  - 39.8% of apremilast patients (*P*<0.0001 vs placebo)
  - 48.2% of etanercept patients (*P*<0.0001 vs placebo)
  - 11.9% of placebo patients
- A PASI-75 score at week 104 was achieved in 45.9% to 51.9% of patients

At week 16, significantly more patients treated with apremilast or etanercept than placebo achieved a minimally clinically important difference in the DLQI, which is a quality of life tool. Responses in the apremilast and etanercept switched to apremilast groups were maintained through week 104.

Results Summary (cont)

- At week 16, a minimally clinically important difference in the Dermatology Life Quality Index was achieved in
  - 65.1% of apremilast patients (*P*=0.0032 vs placebo)
  - 65.1% of etanercept patients (*P*=0.0032 vs placebo)
  - 41.7% of placebo patients
- Responses in the apremilast and etanercept/apremilast groups were maintained through week 104

Among patients with at least moderate scalp involvement at baseline, significantly more patients treated with apremilast or etanercept, than placebo, achieved a response of clear or almost clear at week 16. The response was maintained or improved through week 104. Similar findings were observed with respect to improvement in nail psoriasis. The incidences of adverse events were similar among the 3 groups from week 16 through 104 occurring in approximately 2/3 of patients. Diarrhea was the most frequent adverse event in each group.

Results Summary (cont)

- Among patients with at least moderate scalp involvement at baseline, significantly more patients treated with apremilast or etanercept than placebo achieved a response of clear or almost clear at week 16
  - The response was maintained or improved through week 104
- Similar findings were observed with respect to improvement in nail psoriasis
- The incidences of adverse events were similar among the 3 groups from weeks 16 through 104, occurring in approximately two-thirds of patients
  - Diarrhea was the most frequent adverse event in each group

There were a number of important take home messages from this poster. It is noteworthy that at week 16, 48% of etanercept patients and 40% of apremilast patients, achieved PASI-75, both reasonably good levels of improvement. It is also noteworthy that results in scalp psoriasis were a little bit better than in body psoriasis, a finding that has occurred in other studies as well. It is not surprising that the improvement in nail psoriasis lags behind the improvement in body psoriasis and scalp psoriasis. Nonetheless, given enough time, the nails do start to catch up. The bottom line message is that switching at week 16 to apremilast, 30 mg twice a day, did result in continued improvement in all of the arms, or maintenance of improvement in the etanercept arm.

Faculty Commentary

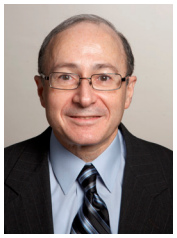
- At week 16, 48% of etanercept patients and 40% of apremilast patients achieved PASI 75
- Scalp psoriasis improved slightly more than body psoriasis
- Improvement in nail psoriasis is slower
- Switching to apremilast result in continued improvement, except in the etanercept group, which maintained response

Finally, it is noteworthy that between week 16 and 104, the patients who had started on apremilast, and continued on apremilast, had only a 5.4% frequency of diarrhea, which was lower than the other 2 groups, suggesting that perhaps patients who developed diarrhea during the first 16 weeks, and were at most risk for it, may have dropped out during that period, or suggesting that patients acclimatized to the diarrhea and ended up having the diarrhea go away, as a symptom, after a short period of time. Regardless of what the reason was, the rate of it from week 16 to 104 was quite low in the group that continued on apremilast.

Faculty Commentary (cont)

- Patients treated with apremilast for the 104 weeks of the study experienced a lower rate of diarrhea
  - The reason(s) for this is unclear

Efficacy of Guselkumab Within Specific Body Regions in Patients With Moderate-to-Severe Plaque Psoriasis: Results From the Phase 3 VOYAGE 1 Study



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Chairman of Dermatology at the Icahn School of Medicine of Mount Sinai in New York. I will be discussing, Efficacy of Guselkumab Within Specific Body Regions in Patients With Moderate-to-Severe Plaque Psoriasis: Results From the Phase 3 VOYAGE 1 Study, presented by Dr. Blauvelt and colleagues at the American Academy of Dermatology annual meeting that took place in Orlando from March 3–7, 2017.

To summarize this poster, treatment with guselkumab for 1 year is efficacious in treating regional disease of the scalp, nails, hands, and/or feet, in patients with moderate-to-severe psoriasis. Treatment response to guselkumab was significantly better than with adalimumab. This study is important because psoriasis involves the scalp, nails, hands, and/or feet commonly. It is troubling to patients and particularly difficult to treat. Guselkumab may be a safe and effective option for these patients.

Summary & Importance

- One-year treatment with guselkumab is significantly better than adalimumab in treating regional disease of the scalp, nails, hands, and/or feet in patients with moderate-to-severe psoriasis
- Psoriasis typically involves the scalp, nails, hands, and/or feet
  - Troubling to patients
  - Particularly difficult to treat

Here's how this study was designed. VOYAGE 1 was a phase 3 randomized, double blind, placebo-controlled, multicenter, active comparator study in patients with moderate-to-severe plaque psoriasis. Patients were randomized 1:2:2 to receive either placebo at weeks 0, 4, and 12, followed by crossover to guselkumab 100 mg at weeks 16 and 20, and then every 8 weeks through week 44. The second arm patients received guselkumab 100 mg at weeks 0 and 4, and then every 8 weeks through week 44. In the third arm, patients were treated with adalimumab 80 mg at week 0, 40 mg at week 1, and then 40 mg every 2 weeks through week 47.

Study Design and Methods

- VOYAGE 1 was a phase 3, randomized, double-blind, placebo-controlled, multicenter, active comparator study in patients with moderate-to-severe plaque psoriasis
- Patients were randomized 1:2:2 to:
  - Placebo at weeks 0, 4, and 12 followed by crossover to guselkumab 100 mg at weeks 16 and 20, then every 8 weeks through week 44
  - Guselkumab 100 mg at weeks 0 and 4, then every 8 weeks through week 44
  - Adalimumab 80 mg at week 0, 40 mg at week 1, then 40 mg every 2 weeks through week 47

The key findings were as follows. Eight hundred thirty-seven patients, with a mean duration of psoriasis of 17.5 years, were randomized. Twenty point nine percent had been treated with a biologic previously. Seventy-eight point one percent had moderate-to-severe scalp disease. Fifty-five point eight percent had moderate-to-severe fingernail

Results Summary

- 837 patients with a mean duration of psoriasis of 17.5 years were randomized
  - 20.9% had been treated with a biologic
  - 78.1% had moderate-to-severe scalp disease
  - 55.8% had moderate-to-severe fingernail disease
  - 58.0% had moderate-to-severe hands and/or feet disease

disease. Fifty-eight percent had moderate-to-severe hand and/or foot disease.

The proportion of patients who achieved a score of absence of disease or very mild disease, and more than a two-grade improvement in the scalp-specific Investigator's Global Assessment score from baseline at week 16 was 83.4% for guselkumab, 70.3% for adalimumab, and 14.5% for placebo. Significantly more patients treated with guselkumab than adalimumab achieved the same endpoint at weeks 24 and 48.

Results Summary

- The proportion of patients who achieved a score of absence of disease or very mild disease and ≥2 grade improvement in the scalp-specific Investigator's Global Assessment score from baseline at week 16 was
  - 83.4% for guselkumab
  - 70.3% for adalimumab
  - 14.5% for placebo
  - Significantly more patients treated with guselkumab than adalimumab achieved this same endpoint at weeks 24 and 48

At week 48, for example, 78.3% of patients treated with guselkumab and 60.5% of patients treated with adalimumab achieved a score of absence of disease or very mild disease, and more than a two-grade improvement in the scalp specific Investigator's Global Assessment score.

The proportion of patients who achieved a fingernail Physician's Global Assessment score of clear or minimal from baseline at week 16 was 39.1% for guselkumab, 50.9% for adalimumab, and 15.9% for placebo. A similar proportion of patients treated with guselkumab as adalimumab achieved this endpoint at week 24.

Results Summary (cont)

- The proportion of patients who achieved a fingernail Physicians Global Assessment score of clear or minimal from baseline at week 16 was
  - 39.1% for guselkumab
  - 50.9% for adalimumab
  - 15.9% for placebo
  - At week 24, a similar proportion of patients treated with guselkumab as adalimumab achieved this endpoint

However, at week 48 significantly more patients treated with guselkumab than adalimumab achieved a fingernail PGA score of clear or minimal, 74.7% with guselkumab vs 61.8% with adalimumab. The mean percent improvement from baseline in the Nail Psoriasis Severity Index at week 16 was significantly greater with guselkumab and adalimumab than with placebo. There was no difference between guselkumab and adalimumab at weeks 24 or 48.

Results Summary (cont)

- At week 48, a fingernail Physicians Global Assessment score of clear or minimal was achieved by
  - 74.7% of patients treated with guselkumab (*P*=0.038)
  - 61.8% of patients treated with adalimumab
- The mean percent improvement from baseline in the Nail Psoriasis Severity Index at week 16 was significantly greater with guselkumab and adalimumab than placebo
  - There was no difference between guselkumab and adalimumab at weeks 24 or 48

The proportion of patients who achieved a score of clear or almost clear, and more than a 2-grade improvement in the hands and/or feet PGA from baseline at week 16 was 73.3% for guselkumab, 55.8% for adalimumab and 14.0% for placebo. At week 24 and 48, significantly more patients treated with guselkumab than adalimumab achieved this same endpoint.

Results Summary (cont)

- The proportion of patients who achieved a score of clear or almost clear and ≥2 grade improvement in the hands and/or feet Physician's Global Assessment score from baseline at week 16 was
  - 73.3% for guselkumab
  - 55.8% for adalimumab
  - 14.0% for placebo
  - At weeks 24 and 48, significantly more patients treated with guselkumab than adalimumab achieved this same endpoint

At week 48, 73.9% of guselkumab patients and 74.5% of adalimumab patients experienced an adverse event. Nasopharyngitis was the most common, occurring in 25.2% of guselkumab and 22.2% of adalimumab patients. 4.9% of guselkumab patients and 4.5% of adalimumab patients

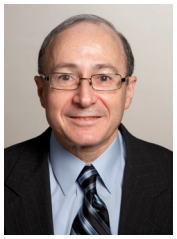
experienced serious adverse events. An infection requiring antibiotic treatment occurred in 16.4% of guselkumab and 18.0% of adalimumab patients.

Results Summary (cont)

- At week 48:

	Guselkumab	Adalimumab
Adverse event	73.9%	74.5%
Serious adverse event	4.9%	4.5%
Nasopharyngitis	25.2%	22.2%
Infection requiring antibiotic treatment	16.4%	18.0%

Secukinumab Provides Faster and More Sustained 52-Week Complete Relief From Psoriasis-Related Pain, Itching, and Scaling Than Ustekinumab in Subjects With Moderate-to-Severe Plaque Psoriasis



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Chairman of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Secukinumab Provides Faster and More Sustained 52-Week Complete Relief From Psoriasis-Related Pain, Itching, and Scaling Than Ustekinumab in Subjects With Moderate-to-Severe Plaque Psoriasis. This was presented by Dr. Bruce Strober and colleagues at the American Academy of Dermatology annual meeting in Orlando from March 3–7, 2017.

To summarize, this analysis reports the patient-reported outcomes of patients with psoriasis treated over 52 weeks in the CLEAR study. In this analysis, significantly greater proportions of patients treated with secukinumab than ustekinumab achieved and sustained complete relief of pain, itching, and scaling. This study is important because these patient-reported outcomes are consistent with the superior and sustained efficacy results observed in the CLEAR study.

Safety & Importance

- In the CLEAR study, significantly more patients with moderate-to-severe treated with secukinumab than ustekinumab achieved and sustained complete relief of patient-reported outcomes of pain, itching, and scaling
- The results of these patient-reported outcomes are consistent with the efficacy results reported in the CLEAR study

This study was conducted as follows. CLEAR was a phase 3 study comparing the efficacy and safety of secukinumab 300 mg with ustekinumab, per label, for moderate-to-severe plaque psoriasis. This analysis compared the effect of secukinumab vs ustekinumab over 52 weeks on patient-reported outcomes of psoriasis related pain, itching, and scaling. Assessments were carried out at weeks 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 48, and 52, using the Numeric Rating Scale of 0 to 10.

Study Design and Methods

- CLEAR was a phase IIIb study comparing the efficacy and safety of secukinumab 300 mg with ustekinumab per label in adults with moderate-to-severe plaque psoriasis
- This analysis compared the effect of secukinumab versus ustekinumab over 52 weeks on patient-reported outcomes of psoriasis-related
  - Pain
  - Itching
  - Scaling
- Assessments were carried out at weeks 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 48, 52 using the numeric rating scale (0-10)

Key findings were as follows. There were 336 patients in the secukinumab group and 339 in the ustekinumab group. On a scale from 0 to 10, mean scores at baseline for secukinumab vs ustekinumab were similar. For pain, 4.0 in secukinumab vs 3.8 for ustekinumab. Itching was 6.3 for both, and scaling was 6.5 for both.

Results Summary

- There were 336 patients in the secukinumab group and 339 in the ustekinumab group
- On a scale from 0 to 10, mean scores at baseline (secukinumab vs ustekinumab) were
  - Pain: 4.0 vs 3.8
  - Itching: 6.3 vs 6.3
  - Scaling: 6.5 vs 6.5

Patients treated with secukinumab achieved significantly greater mean reductions in psoriasis-

related pain, itching, and scaling, beginning as early as week 2. At week 52, mean reductions for secukinumab, compared to ustekinumab, were for pain 3.02 for secukinumab vs 2.56 for ustekinumab. For itching, 4.88 for secukinumab vs 4.27 for ustekinumab, and for scaling, 5.41 for secukinumab vs 4.68 for ustekinumab.

Results Summary (cont)

- Patients treated with secukinumab achieved significantly greater mean reductions in psoriasis-related pain, itching, and scaling beginning as early as week 2
  - At week 52, mean reductions for secukinumab vs ustekinumab were
    - Pain: -3.02 vs -2.56 ($P<0.05$)
    - Itching: -4.88 vs -4.27 ($P<0.05$)
    - Scaling: -5.41 vs -4.68 ($P<0.05$)

At weeks 16 and 52, a significantly greater proportion of patients treated with secukinumab reported complete relief from psoriasis-related pain, itching, and scaling, than those treated with ustekinumab.

Results Summary (cont)

- At weeks 16 and 52, a significantly proportion of patients treated with secukinumab reported complete relief from psoriasis-related pain, itching, and scaling than those treated with ustekinumab

At week 52, the proportions of patients achieving complete relief with secukinumab compared to ustekinumab were for pain 65.6% with secukinumab vs 55.9% for ustekinumab. For itching 46.3% for secukinumab vs 38.4% for ustekinumab, and scaling 52.7% for secukinumab vs 37.4% for ustekinumab.

Results Summary (cont)

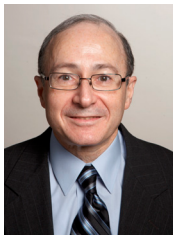
- At week 52, the proportions of patients achieving complete relief with secukinumab vs ustekinumab were
  - Pain: 65.6% vs 55.9% ($P<0.05$)
  - Itching: 46.3% vs 38.4% ($P<0.05$)
  - Scaling: 52.7% vs 37.4% ($P<0.01$)

Just as we saw marked improvement in erythema, scaling, and plaque thickness, in patients treated with secukinumab, we saw corresponding improvements in pain and itching. Also scaling, which is also a patient-reported outcome.

Faculty Commentary

- Consistent with improvement in erythema, scaling, and plaque thickness previously reported in the CLEAR study, this analysis showed corresponding improvement in patient-reported outcomes of pain, itching, and scaling

Efficacy and Safety of Ixekizumab for the Treatment of Moderate-to-Severe Plaque Psoriasis: Results Through 108 Weeks of a Randomized, Phase III Clinical Trial (UNCOVER-3)



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Waldman Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Efficacy and Safety of Ixekizumab for the Treatment of Moderate-to-Severe Plaque Psoriasis: Results Through 108 Weeks of a Randomized, Phase III Clinical Trial called UNCOVER-3, presented by Dr. Andy Blauvelt and colleagues at the American Academy of Dermatology annual meeting in Orlando that took place from March 3–7, 2017.

To summarize the poster, the efficacy of ixekizumab was maintained over 2 years of treatment, showing high rates of skin clearance in patients with moderate-to-severe plaque psoriasis. The safety profile of ixekizumab was comparable to shorter treatment periods.

Summary

- Efficacy of ixekizumab was maintained over 2 years of treatment
- Ixekizumab resulted in high rates of skin clearance in patients with moderate-to-severe plaque psoriasis
- Safety profile of ixekizumab was comparable to shorter treatment periods.

This study is important because long-term treatment is usually required to maintain adequate disease control for moderate-to-severe plaque psoriasis, the long-term efficacy and safety demonstrated in this study are reassuring.

Importance

- Since long-term treatment is usually required to maintain adequate disease control in moderate-to-severe plaque psoriasis, the long-term efficacy and safety with ixekizumab demonstrated in this study is reassuring.

Now let's discuss study design. UNCOVER-3 was a randomized, double-blind, multicenter phase 3 clinical trial of ixekizumab. Patients were randomized 2:2:2:1 to receive either ixekizumab 80 mg every 2 or 4 weeks, etanercept 50 mg twice weekly, or placebo for 12 weeks. The ixekizumab patients received a loading dose of 160 mg.

Study Design and Methods

- UNCOVER-3 was a randomized, double-blind, multicenter, phase 3 clinical trial of ixekizumab
- Patients were randomized 2:2:2:1 to 12 weeks of treatment with
  - Ixekizumab 160 mg loading dose, then 80 mg every 2 weeks
  - Ixekizumab 160 mg loading dose, then 80 mg every 4 weeks
  - Etanercept 50 mg twice weekly or
  - Placebo

At week 12, patients entered an open-label extension phase. Patients continued on—or were switched to—ixekizumab 80 mg every 4 weeks to complete a total of 108 weeks of treatment. Etanercept patients had a 4-week washout period from weeks 12 to 16. At weeks 60, patients could increase their dose of ixekizumab to 80 mg every 2 weeks at the investigator's discretion.

Study Design and Methods (cont)

- At week 12, patients entered an open-label extension phase
  - Patients continued on or were switched to ixekizumab 80 mg every 4 weeks to complete a total of 108 weeks of treatment
  - Etanercept patients had a 4-week washout period from weeks 12 to 16
- At week 60, patients could increase their dose of ixekizumab to 80 mg every 2 weeks at the investigator's discretion

Here are the key findings. One thousand three hundred forty-six patients were randomized. At baseline, the mean psoriasis duration was 18.1 years. PASI score was 20.9, and the percentage of body surface area involved was 28.3%. At week 12, a PASI-75 score was achieved in approximately 90% of ixekizumab patients compared with 55% of etanercept patients, and less than 10% of placebo patients. By week 36, more than 90% of patients in each of the 4 groups achieved PASI-75. The rate remained stable through week 108.

Results Summary

- 1346 patients were randomized
- At baseline
  - Mean psoriasis duration was 18.1 years
  - Psoriasis Area and Severity Index (PASI) score 20.9
  - Percentage of body surface area involved 28.3%
- At week 12, a PASI-75 score was achieved in
  - ~90% of ixekizumab patients
  - 55% of etanercept patients
  - <10% of placebo patients
- By week 36, >90% of patients in each of the 4 groups achieved PASI-75
  - The rate remained stable through week 108

In patients originally randomized to ixekizumab every 2 weeks, then switched to every 4weeks, 80% achieved a PASI-90 score at week 108, and 56% achieved a PASI-100, not a dot of psoriasis left. Following week 60, 3.8% of all patients increased the ixekizumab dose to 80 mg every 2 weeks, although the majority had a PASI-75 score. Increasing the dose had little effect on the overall efficacy analysis.

Results Summary (cont)

- In patients originally randomized to ixekizumab every 2 weeks then switched to every 4 weeks
  - 80% achieved a PASI-90 score at week 108
  - 56% achieved a PASI-100 score at week 108
- Following week 60, 3.8% of all patients increased the ixekizumab dose to 80 mg every 2 weeks, although the majority had a PASI-75 score
  - Increasing the dose had little effect on the overall efficacy analysis

Eighty-four to eighty-five percent of patients experienced 1 or more treatment emergent adverse events. Most were mild or moderate in severity. Nasopharyngitis was the most frequent adverse event, occurring in 23.5% of all patients combined. Upper respiratory tract infection or injection site reaction each occurred in 7.5%.

Results Summary (cont)

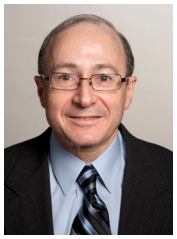
- 84% to 85% of patients experienced one or more treatment-emergent adverse events; most were mild or moderate in severity
  - Nasopharyngitis was the most frequent adverse event (23.5%)
  - Upper respiratory tract infection or injection site reaction each occurred in 7.5%

The conclusion of the study was that over 2 years, ixekizumab showed maintenance of efficacy at every endpoint that was looked at, and there was a very high rate of skin clearance. Only 3.8% of all patients increased the ixekizumab dose to every 2 weeks after week 60. Even those that chose to increase to that every 2-week dosage, the majority had PASI scores above 75 at the time that they increased that dosage. The safety profile over the 108 weeks was comparable to the shorter-term treatment safety profile. Overall, excellent maintenance of efficacy and very good safety for the 108 weeks.

Faculty Commentary

- Efficacy at 2 years was maintained
- There was a high rate of skin clearance
- Few patients increased their dose of ixekizumab
  - Majority had a PASI 75 score or greater
- Safety was comparable to shorter-term treatment
- Overall, excellent maintenance of efficacy and safety with ixekizumab over 108 weeks

Psychiatric Adverse Events in Brodalumab Psoriasis Studies



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Waldman Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Psychiatric Adverse Events in Brodalumab Psoriasis Studies. I was the principal investigator and presented the results at the American Academy of Dermatology annual meeting in Orlando from March 3–7, 2017.

To summarize the results of the study, in patients with moderate-to-severe plaque psoriasis, anxiety and depression scores were reduced from baseline in patients treated with oral brodalumab. Patient satisfaction and quality of life were higher with brodalumab compared with placebo. Suicidal ideation and behavior were similar over 52 weeks in patients treated with brodalumab compared with ustekinumab. The rate did not increase with long-term brodalumab treatment. This study is important because it provides reassurance that brodalumab does not lead to a higher rate of psychiatric outcomes, including depression and suicidal ideation and behavior.

Summary & Importance

- In patients with moderate-to-severe psoriasis, anxiety and depression scores were reduced in patients treated with brodalumab
- Compared with placebo, patient satisfaction and quality of life were greater with brodalumab
- Compared with ustekinumab, suicidal ideation and behavior were similar with brodalumab
- Provides reassurance regarding psychiatric outcomes with brodalumab

This study was designed as follows. It actually is a report that was a retrospective analysis of 1 phase 2 and 3 phase 3 clinical trials involving brodalumab in patients with moderate-to-severe plaque psoriasis.

There were no specific exclusion criteria for psychiatric or substance abuse disorders. Brodalumab was given as 140 mg or 210 mg every 2 weeks. The majority of patients were treated with the 210 mg dose by the end of the 52 week controlled period in the phase 3 studies.

Study Design and Methods

- Retrospective analysis of one phase 2 and three phase 3 trials involving brodalumab in patients with moderate-to-severe plaque psoriasis
  - No specific exclusion criteria for psychiatric or substance abuse disorders
- Brodalumab was given as 140 mg or 210 mg every 2 weeks
  - Majority were treated with the 210 mg dose by the end of the 52-week controlled period in the phase 3 studies

The HADS, or Hospital Anxiety and Depression Scale, was utilized in 1 of the phase 3 studies. All 3 phase 3studies utilized the DLQI, the Dermatology Life Quality Index, to assess the socio-psychological impact of this skin disease on patients' lives. Data on psychiatric events were pooled for all trials and were summarized as follow-up, time-adjusted event rates.

Study Design and Methods (cont)

- The Hospital Anxiety and Depression Scale (HADS) was utilized in one of the phase 3 studies
- All three phase 3 studies utilized the Dermatology Life Quality Index to assess the socio-psychological impact of the skin disease on patients' lives
- Data on psychiatric events were pooled for all trials and were summarized as follow-up time-adjusted event rates

The key findings of this study were as follows. In the 4 studies 3,066 patients receiving brodalumab, 613 receiving ustekinumab, and 879 receiving placebo were reported.

Results Summary

- In the 4 studies
  - 3066 patients received brodalumab
  - 613 received ustekinumab
  - 879 received placebo

In the AMAGINE-1 phase 3 study, approximately 75% of patients with either dose of brodalumab experienced improvement in depression compared with approximately 45% of placebo patients. Improvement of depressive symptoms to normal was observed in approximately 40% with either dose of brodalumab. Symptoms worsened in 5% of brodalumab patients and 10% of placebo patients. Approximately 65% of patients in both brodalumab groups experienced improvement of depressive symptoms with improvement to normal in 30-35%

Results Summary (cont)

- In AMAGINE-1 phase 3 study
  - Depression improved in
    - ~75% of patients with either dose of brodalumab
    - 45% of placebo patients
  - Depressive symptoms improved to normal in ~40% with either dose of brodalumab
  - Depressive symptoms worsened in
    - 5% of brodalumab patients
    - 10% of placebo patients
  - Approximately 65% of patients in both brodalumab groups experienced improvement of depressive symptoms, with improvement to normal in 30% to 35%

In the phase 3 studies, patient satisfaction with treatment was significantly better with both doses of brodalumab compared with placebo. Patient satisfaction was similar for brodalumab 140 mg and ustekinumab.

Results Summary (cont)

- In the 3 phase III studies
  - Patient satisfaction with treatment was significantly better with both doses of brodalumab compared with placebo
  - Patient satisfaction was similar for brodalumab 140 mg and ustekinumab

In the 4 studies, insomnia and depression both occurred in less than 1% of patients treated with brodalumab, ustekinumab, or placebo. The integrated analysis of follow-up, time-adjusted patient incidence ratios of suicidal ideation and behavior were 0.20 for brodalumab and 0.40 for ustekinumab in the 52-week pooled data, 0.37 for brodalumab for the long-term data, that included an uncontrolled, open-label extension phase. The rates were greater in patients with a history of depression or a history of suicidality compared to those without those histories. Two suicide attempts in 1 patient treated with brodalumab were reported during the 12-week induction phase.

Results Summary (cont)

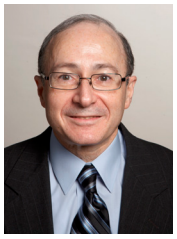
- In the 4 studies
  - Insomnia and depression both occurred in <1% of patients treated with brodalumab, ustekinumab, or placebo
  - The integrated analysis of follow-up time-adjusted patient incidence rates of suicidal ideation and behavior were
    - 0.20 for brodalumab and 0.40 for ustekinumab in the 52-week pooled data
    - 0.37 for brodalumab for the long-term data that included an uncontrolled open-label extension phase
    - The rates were greater in patients with a history of depression or history of suicidality compared with those without
  - Two suicide attempts in one patient treated with brodalumab were reported during the 12-week induction phase

Brodalumab, in its approved label, received a black box warning for suicides that occurred through the course of the phase 3 trials. In this study, the authors looked at the hospital anxiety and depression scale and report a reduction in the HAD scale and an improvement in the dermatology life quality index. The suicidal ideation and behavior reported in the trial was similar in brodalumab-treated patients compared to ustekinumab-treated patients. Based on the results in the study there was no causal role suggested for brodalumab and depression or suicide.

Faculty Commentary

- The product labeling for brodalumab includes a black box warning for suicides
- This report indicates brodalumab
  - reduces anxiety and depression
  - improves dermatology-related quality of life
  - is associated with a similar rate of suicidal ideation and behavior as ustekinumab
  - has no causal role for depression or suicide

Tildrakizumab, a Selective Anti-IL-23 Monoclonal Antibody, Is Effective in Subjects With Chronic Plaque Psoriasis Who Do Not Adequately Respond to Etanercept



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Chairman of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Tildrakizumab, a Selective Anti-IL-23 Monoclonal Antibody, Is Effective in Subjects With Chronic Plaque Psoriasis Who Do Not Adequately Respond to Etanercept, the poster that was presented by Dr. Kristian Reich and colleagues at the American Academy of Dermatology annual meeting in Orlando, which took place from March 3–7, 2017.

To summarize the results of this poster, patients with moderate-to-severe plaque psoriasis who did not achieve PASI-75 response with etanercept by week 28 were able to achieve clinically meaningful improvement in chronic plaque psoriasis upon switching to tildrakizumab.

Tildrakizumab is a high-affinity, humanized monoclonal antibody targeting IL-23p19, with demonstrated efficacy in the treatment of patients with moderate-to-severe plaque psoriasis. This study is important because etanercept is an important treatment option for patients with plaque psoriasis, but not all patients achieve adequate improvement and symptom relief. For these patients, tildrakizumab may be a good treatment option.

Summary & Importance

- Patients with moderate-to-severe psoriasis who did not achieve PASI 75 with etanercept by week 28 achieved clinically meaningful improvement when switched to tildrakizumab
- Tildrakizumab is a monoclonal antibody with demonstrated efficacy in patients with moderate-to-severe psoriasis
- Although etanercept is an important treatment for plaque psoriasis, not all patients achieve adequate symptom relief.
  - For these patients, tildrakizumab may be a good option

Here's how that study was designed. The poster presents the results of patients in the reSURFACE 2 study who had achieved partial, meaning PASI-50 to PASI-75, or no response, meaning less than a PASI-50, when treated with etanercept 50 mg at week 28. At week 28 of reSURFACE, 120 of 313 patients treated with etanercept were partial responders or non-responders, and were switched to tildrakizumab 200 mg. Tildrakizumab was continued until week 52.

Study Design and Methods

- This report presents the results of patients in the reSURFACE 2 study who achieved partial (PASI ≥50 to <75) or no response (PASI <50) to etanercept 50 mg at week 28
- At week 28, 120 of 313 patients treated with etanercept were partial or nonresponders and were switched to tildrakizumab 200 mg
  - Tildrakizumab was continued until week 52

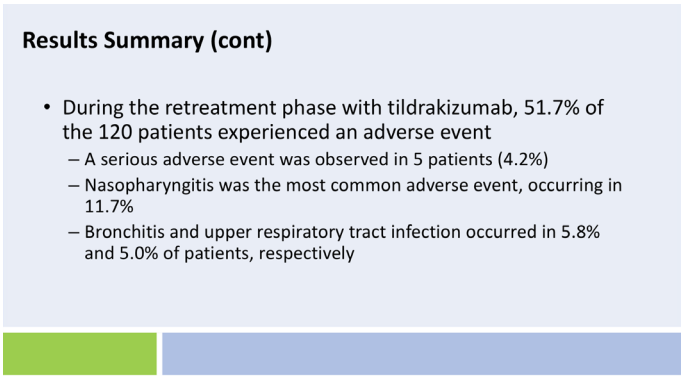
The main findings were as follows. At week 52, which meant they were 20 weeks on tildrakizumab, PASI-75 was achieved in 81.4%, PASI-90 in 41.6%, and PASI-100 in 15.9%. Physician's Global Assessments of clear or minimal disease, meaning a score of zero or one, occurred in 68.5%.

Results Summary

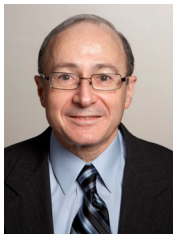
- At week 52 (20 weeks on tildrakizumab)
  - PASI-75 was achieved in 81.4%
  - PASI-90 in 41.6%
  - PASI-100 in 15.9%
  - Physicians Global Assessment of 0 or 1 (clear or minimal) in 68.5%

During the re-treatment phase with tildrakizumab 51.7% of 120 patients experienced an adverse event. A serious adverse event was observed in 5 patients, or 4.2%. Nasopharyngitis was the most common adverse event, occurring in 11.7%. Bronchitis and upper respiratory tract infection occurred in 5.8% and 5.0% of patients, respectively.

The main take-home message here is that even in etanercept failures, switching to tildrakizumab, an IL-23 blocker, resulted in dramatically beneficial responses.



Rapid Onset of Efficacy in Patients With Psoriasis Treated With Brodalumab Versus Ustekinumab: A Pooled Analysis of Data From Two Phase III Randomized Clinical Trials



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Waldman Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Rapid Onset of Efficacy in Patients With Psoriasis Treated With Brodalumab Versus Ustekinumab: A Pooled Analysis of Data From Two Phase III Randomized Clinical Trials. AMAGINE-2 and AMAGINE-3 were the names of the trials reported by Dr. Papp and colleagues at the American Academy of Dermatology annual meeting that took place in Orlando from March 3–7.

To summarize the findings of this poster, in patients with moderate-to-severe plaque psoriasis, brodalumab demonstrated a rapid onset of action with significantly more patients achieving efficacy endpoints compared to ustekinumab as early as week 1. The 2 groups persisted through week 12. The study is important because psoriasis has profound psychosocial implications, making it important that treatment rapidly and reliably resolves symptoms such as pruritus. Such treatment benefit was observed with brodalumab in the AMAGINE-2 and -3 studies.

Summary & Importance

- In patients with moderate-to-severe psoriasis, brodalumab demonstrated a more rapid onset of action than ustekinumab beginning as early as week one
- The psychosocial consequences of psoriasis necessitate rapid and reliable resolution of symptoms as demonstrated by brodalumab

Here's how the study was designed. AMAGINE-2 and -3 were 2 randomized, double blind, multicenter studies in patients with moderate-to-severe psoriasis. Patients were randomized 2:2:1:1 to brodalumab 140 mg or 210 mg every 2 weeks, ustekinumab, or placebo for 12 weeks. Speed of response was evaluated by measuring the time to achieve static Physician Global Assessment success of 0 or 1, that means clear or almost clear, or 75% improvement in PASI score.

Study Design and Methods

- AMAGINE-2 and -3 were two randomized, double-blind, multicenter studies in patients with mild-to-moderate psoriasis
- Patients were randomized 2:2:1:1 to 12 weeks of treatment with
  - Brodalumab 140 mg every 2 weeks
  - Brodalumab 210 mg every 2 weeks
  - Ustekinumab or
  - Placebo
- Speed of response was evaluated by measuring the time to achieve
  - Static Physician's Global Assessment (sPGA) success (0/1)
  - Psoriasis Area and Severity Index-75 (PASI-75)

The key findings were as follows. A total of 3,712 patients were randomized in the 2 studies. At week 12, the static Physician Global Assessment success, meaning clear or almost clear, was observed in 79.1% of patients treated with brodalumab, 59.1% of patients treated with ustekinumab. PASI-75 score was observed in 85.7% and 69.7% of brodalumab and ustekinumab patients, respectively.

Results Summary

- A total of 3712 patients were randomized in the two studies
- At week 12,
  - sPGA success was observed in
    - 79.1% of patients treated with brodalumab
    - 59.1% of patients treated with ustekinumab
  - A PASI-75 score was observed in
    - 85.7% of patients treated with brodalumab
    - 69.7% of patients treated with ustekinumab

weeks with ustekinumab. The PASI-75 score was achieved in 25% of patients at 2.1 weeks with brodalumab and 4.8 weeks for ustekinumab.

Results Summary (cont)

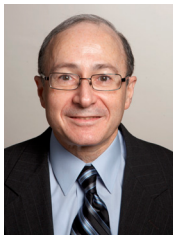
- Statistically significant differences favoring brodalumab in sPGA and PASI-75 were seen beginning at week 1 and continuing through week 12
- Time to achieve sPGA in 25% of patients was
  - 2.5 weeks with brodalumab
  - 5.6 weeks for ustekinumab
- A PASI-75 score was achieved in 25% of patients at
  - 2.1 weeks with brodalumab
  - 4.8 weeks for ustekinumab

Now here are the comments from Dr. Papp, the principal investigator of this study. The 3 key findings of this study are: 1) treatment with brodalumab provides faster clinical response than ustekinumab; 2) all signs and symptoms of psoriasis show rapid improvement in patients treated with brodalumab; and 3) the level of response in brodalumab-treated patients is greater than ustekinumab. It is likely that treatment with brodalumab will result in more rapid and superior response than treatment with ustekinumab. Moreover, maintenance of the high level of response is comparable between the 2 treatments.

Principal Investigator Commentary

- The three key findings of this study are
  - Treatment with brodalumab provides faster clinical response than ustekinumab
  - All signs and symptoms of psoriasis show rapid improvement in patients treated with brodalumab
  - The level of response in brodalumab-treated patients is greater than ustekinumab
- It is likely that treatment with brodalumab will result in more rapid and superior response than treatment with ustekinumab. Moreover, maintenance of the high level of response is comparable between brodalumab and ustekinumab.

Seven Year Interim Results From the ESPRIT 10-Year Post-Marketing Surveillance Registry of Adalimumab for Moderate-to-Severe Psoriasis



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the Waldman Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing, Seven Year Interim Results From the ESPRIT 10-Year Post-Marketing Surveillance Registry of Adalimumab for Moderate-to-Severe Psoriasis, which was presented by Dr. Francisco Kerdel and colleagues at the American Academy of Dermatology annual meeting in Orlando from March 3–7, 2017.

In summary, this report provides interim results from the ESPRIT registry showing that the safety of adalimumab over 7 years is consistent with its known safety profile. Treatment emergent death in the registry was below the expected rate for a comparable general population. The analysis also showed that the effectiveness of adalimumab—including improvement from baseline and patient reported outcomes—was maintained throughout the 7 years. This study is important because the interim analysis provides reassurance that long-term use of adalimumab in patients with moderate-to-severe psoriasis is safe, and that efficacy is maintained.

Summary & Importance

- Interim analysis of ESPRIT registry indicates that the safety of adalimumab over 7 years is consistent with its known safety profile
- Treatment-emergent death rate was below expected rate for a comparable general population
- Effectiveness of adalimumab was maintained throughout the 7 years

- These interim results provide reassurance that long-term use of adalimumab in patients with moderate-to-severe psoriasis is safe and efficacy is maintained

The methods of the study were as follows. The study included adult patients from 13 countries in Europe and North America in the registry from 2008 through 2012. Patients were treated with adalimumab for chronic plaque psoriasis as recommended in the local product label. Otherwise, adalimumab could have been previously initiated, but if so, patients could not have been off adalimumab for more than 70 consecutive days. For patients previously initiated on adalimumab, treatment history was provided by the prescribing physician.

Study Design and Methods

- Adult patients from 13 countries in Europe and North America were enrolled in the ESPRIT registry from 2008 through 2012
- Patients were treated with adalimumab for chronic plaque psoriasis as recommended in the local product label
- Adalimumab could have been newly initiated within 4 weeks of entry into the registry
- Otherwise, adalimumab could have been previously initiated, but if so, patients could not have been off adalimumab for more than 70 consecutive days
  - Treatment history was provided by the prescribing physician

Key findings were as follows. There were 6,051 patients with chronic plaque psoriasis included in the analysis. Forty-two point three percent were newly initiated on adalimumab and 57.7% had previously initiated treatment with adalimumab. Forty-nine point three percent of all patients had moderate, severe, or very severe plaque psoriasis according to the Physician Global Assessment. The percentage was much higher, 80.2%, in patients newly initiated on adalimumab. Forty-nine point three percent of all registry patients discontinued adalimumab, with lack of efficacy the most common reason, 18.2% of all of those patients.

Results Summary

- 6051 patients with chronic plaque psoriasis were included in the analysis
  - 42.3% were newly initiated on adalimumab and 57.7% had previously initiated treatment
  - 49.3% of all patients had moderate, severe, or very severe plaque psoriasis according to the Physician's Global Assessment
    - The percentage was much higher (80.2%) in patients newly initiated on adalimumab
- 49.3% of all registry patients discontinued adalimumab
  - Lack of efficacy was the most common reason (18.2% of all patients)
  - 2.8% of all registry patients discontinued adalimumab due to an adverse event

Two point eight percent of all registry patients discontinued adalimumab due to an adverse event.

The median duration of overall exposure to adalimumab was 1,398 days in all registry patients, and approximately half that in the patients newly treated with adalimumab. Twelve point five percent of all patients had a duration of exposure to adalimumab greater than 7 years. The incidence of treatment- emergent adverse events was approximately 51% for patients who received adalimumab for less than a year. It declined to 13% to 22% for patients treated for more than 1 year, up to 7 years, and increased to 37% for those treated with adalimumab for more than 7 years.

Results Summary (cont)

- Median duration of overall exposure to adalimumab was 1398 days in all registry patients and approximately half that in patients newly treated with adalimumab
- 12.5% of all patients had a duration of exposure to adalimumab >7 years
- Incidence of treatment-emergent adverse events
  - 51% for patients who received adalimumab ≤1 year
  - 13% to 22% for patients treated for more than 1 year up to 7 years
  - 37% for those treated with adalimumab for >7 years
    - The higher incidence in patients treated with adalimumab >7 years probably reflects the fact that the majority of these patients began adalimumab as part of a clinical trial

The higher incidence in patients treated with adalimumab for more than 7 years probably reflects the fact that the majority of these patients began adalimumab as part of a clinical trial.

A serious adverse event occurred in 4.4% of all patients. The incidence of serious infection and malignancy was 1% of all patients, whereas oral candidiasis, active tuberculosis, congestive heart failure, and lupus each occurred in less than 0.1% of patients. The standardized mortality ratio was 0.27, indicating that the observed number of deaths was below expected, based on age, sex, and country.

Results Summary (cont)

- Serious adverse event occurred in 4.4% of all patients
- Incidences of serious infection and malignancy were 1% of all patients
  - Oral candidiasis, active tuberculosis, congestive heart failure, and lupus each occurred in <0.1% of patients
- The standardized mortality ratio was 0.27
  - Indicating that the observed number of deaths was below expected based on age, sex, and country

Fifty-six point nine percent to 81.8% of all patients treated with adalimumab achieved Physician Global Assessment of clear or minimal during 1 to 7 years of registry participation. Patient-reported improvements related to quality of life and work productivity were maintained throughout the first 7 years of registry participation.

Results Summary (cont)

- 56.9% to 81.8% of all patients treated with adalimumab achieved PGA clear or minimal during 1 to 7 years of registry participation
- Patient-reported improvements related to life quality and work productivity were maintained throughout the first 7 years of registry participation

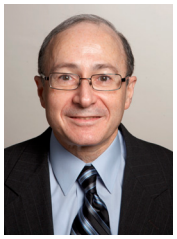
The first and most important take-home message from this study is that the safety of adalimumab was maintained throughout the 7 years of treatment. In fact, the mortality in patients on adalimumab did not exceed the expected mortality, in fact was reduced. Side effects did not emerge during the 7 years of follow-up; that was a surprise, based on the initial studies of adalimumab.

The second most important message was that the dropout rate in patients started on adalimumab was substantial during the course of the 7 years. However, the rate of dropout was greatest during the first year of treatment. After that, the rate of dropout leveled off. Lastly, there were significant numbers of patients who maintained clear or almost clear disease throughout the 7 years of treatment. Those, of course, are the ones most likely to stay in the study, and they did report maintenance of improvements in quality of life and work productivity.

Faculty Commentary

- Safety of adalimumab was maintained throughout 7 years of treatment
- Moreover, the mortality rate was lower in patients treated with adalimumab
- There was a high drop-out rate, particularly during the first year
- Many patients maintained clear or almost clear disease throughout the 7 years
  - Associated with improved patient-reported outcomes

The Efficacy of Certolizumab Pegol Over Four Years in Psoriatic Arthritis Patients With and Without Concomitant Use of DMARD



Dr. Mark Lebwohl, MD

Hello. This is Dr. Mark Lebwohl. I am the chairman of dermatology at the Icahn School of Medicine at Mount Sinai in New York. I will be discussing a poster entitled The Efficacy of Certolizumab Pegol Over Four Years in Psoriatic Arthritis Patients With and Without Concomitant Use of DMARD, presented by Dr. Walsh and colleagues at the American Academy of Dermatology annual meeting in Orlando which took place from March 3–7, 2017.

To summarize this poster, RAPID-PsA was a phase 3 study that showed rapid improvement in both joint and skin manifestations of psoriatic arthritis which were maintained over 4 years of treatment. This analysis reports sustained improvements in the joint, skin, and extra-articular manifestation of psoriatic arthritis with certolizumab pegol as monotherapy, or with concomitant, non-biologic DMARD therapy. This study is important because patients with psoriatic arthritis may be treated with either monotherapy or with combination therapy, depending on the extent and severity of their signs and symptoms.

Safety & Importance

- Treatment with certolizumab pegol as monotherapy or in combination with non-biologic DMARD therapy resulted in rapid and sustained improvement in both joint, skin, and extraarticular manifestations of psoriatic arthritis
- Patients with psoriatic arthritis may be treated with monotherapy or combination therapy depending on the extent and severity of their signs and symptoms

Sustained improvement in symptoms was observed with certolizumab pegol as monotherapy, or in combination with non-biologic DMARD therapy.

The methods of this study were as follows. Rapid-PsA was a randomized, double blind, multicenter, placebo-controlled, parallel group, phase 3 study that investigated the efficacy of certolizumab pegol in adults with psoriatic arthritis. Adults who had failed previous DMARD therapy were included if they had active psoriatic arthritis with greater than or equal to 3 tender joints, greater than or equal to 3 swollen joints, and either an erythrocyte sedimentation rate greater than or equal to 28 mm, or a C-reactive protein greater than or equal to 7.9.

Study Design and Methods

- RAPID-PsA was a randomized, double-blind, multicenter, placebo-controlled, parallel-group phase III study that investigated the efficacy of certolizumab pegol in adults with psoriatic arthritis
- Adults who had failed previous DMARD therapy were included if they had active psoriatic arthritis with
  - ≥3 tender joints
  - ≥3 swollen joints and
  - Either an erythrocyte sedimentation rate ≥28 mm/h or C-reactive protein >7.9 mg/L

Patients were randomized 1:1:1 to certolizumab 200 mg or 400 mg once a week, or placebo. Patients randomized to certolizumab pegol 200 mg received a 400 mg loading dose on weeks 0, 2, and 4.

Study Design and Methods (cont)

- Patients were randomized 1:1:1 to
  - Certolizumab pegol 200 mg once-weekly
    - 400 mg loading dose on weeks 0, 2, and 4
  - Certolizumab pegol 400 mg once-weekly
  - Placebo

After 24 weeks, placebo patients were re-randomized to double-blind treatment with certolizumab pegol 200 mg or 400 mg. Patients treated with certolizumab

200 mg or 400 mg continued double-blind treatment through week 48, then open-label treatment through week 216.

Study Design and Methods (cont)

- After 24 weeks
  - Placebo patients were rerandomized to double-blind treatment with certolizumab pegol 200 mg or 400 mg through week 48, then open-label treatment through week 216
  - Patients treated with certolizumab 200 mg or 400 mg continued double-blind treatment through week 48, then open-label treatment through week 216

This post hoc study examined the efficacy and safety of certolizumab pegol in patients with or without concomitant DMARD therapy. I will refer to these patients as DMARD+ and DMARD-.

Study Design and Methods (cont)

- This post hoc study examined the efficacy and safety of certolizumab pegol in patients with (DMARD+) or without (DMARD–) concomitant DMARD therapy

Key findings were as follows. Two hundred seventy-three patients were treated with certolizumab from week 0, 199 patients in the DMARD+ group and 74 in the DMARD- group. 58 DMARD+ patients were discontinued treatment, 5 due to lack of efficacy and 22 due to an adverse event. Thirty-two DMARD- patients discontinued treatment, 4 due to lack of efficacy and 14 due to an adverse event.

Results Summary

- 273 patients were treated with certolizumab from week 0
  - 199 patients in the DMARD+ group and 74 in the DMARD– group
- 58 DMARD+ patients discontinued treatment; 5 due to lack of efficacy and 22 due to an adverse event
- 32 DMARD– patients discontinued treatment; 4 due to lack of efficacy and 14 due to an adverse event

In the DMARD+ group, 75% had no change in DMARD therapy over the 4 years, while the majority of the remainder reduced or discontinued DMARD use. In the DMARD- group, 8% initiated DMARD therapy.

Results Summary (cont)

- In the DMARD+ group, 75% had no change in DMARD therapy over the 4 years, while the majority of the remainder reduced or discontinued DMARD use
- In the DMARD– group, 8% initiated DMARD therapy

The results after 4 years showed the following. The American College of Rheumatology scored 20, that means ACR 20 was achieved in 79.7% of DMARD+ patients and 83.3% of DMARD- patients. PASI-75 scores were achieved in 78.1% of DMARD- patients and 79.2% of DMARD+ patients. Improvements in the dactylitis and enthesitis symptom scores were similar between groups, although improvement in enthesitis was more stable in the DMARD+ group.

Results Summary (cont)

- The results after 4 years showed the following
  - ACR20 was achieved in 79.7% of DMARD+ patients and 83.3% of DMARD– patients
  - PASI-75 was achieved in 79.2% of DMARD+ patients and 78.1% of DMARD- patients
  - Improvements in the dactylitis and enthesitis symptom scores were similar between groups, although improvement in enthesitis was more stable in the DMARD+ group

Fifty point six percent of patients treated with certolizumab experienced an adverse event judged to be related to study drug. The serious adverse event rate was 11.9 per 100 patient-years. Six deaths occurred in RAPID-PsA judged to be related or possibly related to certolizumab. An infection or infestation occurred in 5.9%.

Results Summary (cont)

- 50.6% of patients treated with certolizumab experienced an adverse event judged to be related to study drug
- The serious adverse event rate was 11.9 per 100 patient-years
- 6 deaths occurred in RAPID-PsA, 2 of which were judged to be related or possibly related to certolizumab
- An infection or infestation occurred in 5.9%

There are a couple of messages from this poster. First of all, it's a response, whether patients were on DMARDs or not.

Looking at the ACR20 responses, these responses were a nice, almost flat line, with the ACR response rates staying in the 80% range. A little bit lower in the low-dose treatment group, but very close to the high-dose treatment group. Whether it was with concomitant DMARDs or without concomitant DMARDs, the proportion of patients who maintained the ACR20 response remained very high in both groups for 216 weeks. It's an excellent maintenance in response in psoriatic arthritis.

Similarly, the PASI responses were maintained in those groups as well. The improvement in PASI score was dramatically improved and stayed flat from weeks 24 to 216. The PASI-75 rate, again, remained relatively flat and there's actually a very respectable PASI-100 rate in the patients who were treated with both doses of certolizumab pegol. Similarly, there was marked improvement that was maintained throughout the 216 weeks in both dactylitis and enthesitis. All of those results were similar, whether patients were maintained on DMARDs or not maintained on DMARDs.

Faculty Commentary

- Responses were similar irrespective of whether patients received DMARD therapy or not
- The ACR20 response rate with certolizumab pegol was in the 80% range, remaining relatively stable over the study, with little difference between the low-dose and high-dose group
- The PASI 75 response rate was high and remained relatively stable from weeks 24 to 216
- There was marked improvement in dactylitis and enthesitis with certolizumab pegol

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