A Closer Look at Skyrizi

The newest IL-23 blocker for psoriasis may prove to be a blockbuster, according to analysts.

BY JERRY BAGEL, MD, FAAD

>> In a previous psoriasis Clinical Focus column (February 2019, available online at PracticalDermatology.com/issues/2019-feb), I urged readers to become more familiar with Interleukin-23 (IL-23) monoclonal antibodies. Now we will take a closer look at a newcomer to this growing class.

Risankizumab (Skyrizi, AbbVie) is a humanized IgG1 monoclonal antibody that binds the p19 subunit of IL-23, inhibiting Th17 differentiation, proliferation, and cytokines involved in the pathogenesis of psoriasis. The agent received FDA approval last month.

RISANKIZUMAB DATA

The approval of risankizumab was based on two replicate phases 3 trials—UltIMMa-1 (506 subjects) and UltIMMa-2 (491 subjects)—that compared the efficacy and safety of risankizumab against that of ustekinumab (Stelara, Janssen). Study patients were stratified by weight and previous exposure to tumor necrosis factor (TNF) inhibitors and randomly assigned (3:1:1) to receive 150mg risankizumab at weeks 0 and 4 and then every 12 weeks, 45mg or 90mg ustekinumab (weight-based per label), or placebo. The demographics of the three cohorts were similar. Patients had an average age of 47, and one quarter had a body weight above 220 lbs. Thirty percent of patients had psoriatic arthritis (PsA) and 38 percent had been on a biologic therapy in the past. The average Psoriasis Area Severity Index (PASI) was 20 when the studies began. Co-primary endpoints were proportions of patients achieving a 90 percent improvement in the PASI (PASI 90) and a static Physician's Global Assessment (PGA) score of 0 or 1 at week 16.

At week 16, 75 percent of risankizumab-treated patients achieved a PASI 90, and 82 percent hit this mark at week 52. By contrast, 42 percent of patients in the ustekinumab group achieved PASI 90 at week 16, and 44 percent did so at week 52. For PASI 100, the numbers were 42 percent at 16 weeks and 57 percent at 52 weeks for the risankizumab-treated patients and 18 percent at 16 weeks and 25 percent at 52 weeks in the ustekinumab arm. The scores on the Dermatology Life Quality index and PGA were significantly higher for risankizumab-treated patients compared with their counterparts who recieved ustekinumab.

> **"The duration of response was also impressive. Fifty percent of subjects who obtained a PASI 90 at week 28 with the last dose given at week 16 were able to maintain PASI 90 out until week 52—nine months after their final dose."**

Risankizumab also begins to work faster than ustekinumab. Forty-four percent of risankizumab patients achieved a PASI 90 at week four, compared with 19 percent in the ustekinumab group. There were fewer adverse events seen with risankizumab than with ustekinumab. Moreover, there were no reports of malignancy, death,

Psoriasis By The Numbers

21.11 Billion Estimated value in dollars of the global psoriasis drugs market by 2022.

9.4% Compound Annual Growth Rate (CAGR) for the global psoriasis market through 2022.

21% Predicted (CAGR) for interleukin-inhibitors during the forecast period.

—Grand View Research

> As with all new therapies, more data will be accrued to determine both long-term safety and durability, but from the look of phase 3 data, risankizumab will clearly up the number of psoriatic patients that we can help."

tuberculosis, inflammatory bowel disease, suicide, or demyelination attributed to risankizumab. The serious infection rate was equal to what was seen with ustekinumab.

Risankizumab, given at the same frequency of administration to ustekinumab, has higher efficacy and similar safety profiles. There is no variation in PASI 90 response at week 52 in risankizumab-treated groups based on age, baseline PASI, PsA diagnosis, or biologic status. There was a slight loss of response seen in patients with BMI >30.

The duration of response was also impressive. Fifty percent of subjects who obtained a PASI 90 at week 28 with the last dose given at week 16 were able to maintain PASI 90 out until week 52—nine months after their final dose. If a patient is 90 percent improved and has to stop treatment, there is 50 percent rate of maintaining response for nine months with risankizumab.

Utilizing the same dosing pattern in PsA, American College of Rheumatology (ACR) 20, 50, and 70 responses for risankizumab-treated patients were 48 percent, 33 percent, and 15 percent, respectively at week 24. Total sharp scores improved by 60 percent.

THE BIG PICTURE

The IL-23 monoclonal antibodies are the most recent generation of psoriasis therapies. The first, guselkumab (Tremfya, Janssen) is administered at weeks 0, 4, and then every eight weeks. Tildrakizumab (Ilumya, Sun Dermatology) is administered in the same manner as risankizumab (week 0, 4 and every 12 weeks). All three have good efficacy, but risankizumab has a faster onset of action.

In addition, I have considered ustekinumab to be one of the safest biologic agents; when risankizumab went head-to-head with this drug, the adverse event profile was similar. Hence, risankizumab was twice as effective and the safety was equal.

As with all new therapies, more data will be accrued to determine both long-term safety and durability, but from the look of phase 3 data, risankizumab will clearly up the number of psoriatic patients that we can help. ■

Jerry Bagel, MD, MS, FAAD is Director of the Psoriasis Treatment Center of Central New Jersey. He recently received the Excellence in Leadership Award from the National Psoriasis Foundation (NPF).

EU Approval for Risankizumab

Also last month, the European Commission (EC) approved Skyrizi (risankizumab) for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy. Approval allows for the marketing of Skyrizi in all member states of the European Union, as well as Iceland, Liechtenstein and Norway.

"In clinical studies, patients saw significantly higher rates of skin clearance with Skyrizi compared to current standards of care," says Hervé Bachelez, professor at the University Paris Diderot and the Department of Dermatology of the Saint-Louis Hospital-Assistance Publique Hôpitaux de Paris, France and a principal investigator of the ultIMMa-2 study. "As many as 80 percent of patients who achieved clear skin at 16 weeks maintained completely clear skin through one year. We look forward to seeing more of the two-year data from the IMMhance study at the World Congress of Dermatology in June."

AbbVie received approval for Skyrizi from the Japanese Ministry of Health, Labour and Welfare for the treatment of plaque psoriasis, generalized pustular psoriasis, erythrodermic psoriasis and psoriatic arthritis in March 2019, as well as approval for the treatment of adults with moderate to severe plaque psoriasis from Health Canada.

For further reading:
Papp KA, et al. "Risankizumab versus Ustekinumab for Moderate-to-Severe Plaque Psoriasis." N Engl J Med. 2017; 376:1551-1560
Gordon KB, et al. "Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials." Lancet 2018: 392:650-661
Papp KA, et al. "Safety and Efficacy Results from the Open Label Extension of a Phase 2 Trial of Risankizumab, a Selective IL-23p19 Inhibitor in Patients with Active Psoriatic Arthritis." Papp et al. Eposter. 2019 American Academy of Dermatology (AAD) meeting.
Langley RG, et al. "Efficacy and Safety of Continuous Q12W Risankizumab Versus Treatment Withdrawal: Results from the Phase 3 IMMhance Trial. Oral Presentation." 2019 AAD meeting.