Phase III Results Promising for Oral Psoriasis Agent

Results from two pivotal Phase III trials from the Oral treatment Psoriasis Trials (OPT) Program indicate that the investigational oral Janus Kinase (JAK) inhibitor tofacitinib (Pfizer) is both safe and effective for patients with moderate to severe psoriasis. The OPT Pivotal #1 and OPT Pivotal #2 studies showed that tofacitinib, as a 5mg or a 10mg dose taken as a pill twice-daily, met the primary efficacy endpoints of statistically significant superiority over placebo at Week 16 in the proportion of subjects achieving a Physician’s Global Assessment response of “clear” or “almost clear,” and the proportion of subjects achieving at least a 75 percent reduction in Psoriasis Area and Severity Index, two commonly used measures of efficacy in psoriasis. In addition, no new safety signals for tofacitinib were observed in the OPT Pivotal #1 or OPT Pivotal #2 studies. Detailed analyses of these studies, including additional efficacy and safety data, will be submitted for presentation at a future scientific meeting. Pfizer intends to submit a supplemental New Drug Application (sNDA) to the FDA for the approval of tofacitinib 5mg and 10mg twice daily for the treatment of adults with moderate to severe chronic plaque psoriasis by early 2015.

Anti-Interleukin-23 Monoclonal Antibody Guselkumab Shows Significant Efficacy in Treatment of Moderate to Severe Plaque Psoriasis

New findings presented at the 2014 Annual Meeting of the American Academy of Dermatology (AAD) showed up to 86 percent of patients with moderate to severe plaque psoriasis receiving guselkumab (CNTO 1959) achieved a Physician’s Global Assessment (PGA) score of cleared or minimal at week 16, the study’s primary endpoint. The Phase IIb Janssen Research & Development, LLC (Janssen)-sponsored X-PLORE study demonstrated significantly higher levels of efficacy at all doses of guselkumab studied at week 16 when compared with the placebo group. Similar proportions of patients achieving a PGA score of cleared or minimal were observed at week 40 of the study. The trial also included an adalimumab arm. Guselkumab is an investigational human monoclonal antibody with a novel mechanism of action that targets the protein interleukin (IL)-23, and is being developed as a subcutaneously administered therapy for the treatment of moderate to severe plaque psoriasis. Beyond week 16, the proportions of patients achieving a PGA score of 0 or 1, a PASI 75 response and a PASI 90 response remained consistent or showed additional improvement over time for guselkumab through the final dosing visit at week 40.

Through week 16, the placebo-controlled period, adverse events (AEs) were reported in 50 percent of patients receiving guselkumab (combined groups), 56 percent of patients receiving adalimumab and 52 percent of patients receiving placebo; 1 percent, 2 percent and 2 percent of patients reported at least one serious AE in these respective groups. Serious infections occurred in two patients treated with guselkumab (appendicitis, lung abscess). No malignancies or major adverse cardiovascular events (MACE) were observed in any group. Through week 52, AEs were reported in 66 percent of patients receiving guselkumab (combined groups) and 72 percent of patients receiving adalimumab; three percent and five percent reported at least one serious AE in these respective groups. No additional serious infections occurred in guselkumab-treated patients; one serious infection occurred in a patient treated with adalimumab (pneumonia). There were no cases of tuberculosis or opportunistic infections. One guselkumab-treated patient reported a malignancy (cervical intraepithelial neoplasia III, including carcinoma in situ). Three MACE were reported in guselkumab-treated patients (one fatal myocardial infarction [MI], one nonfatal MI, one cerebrovascular accident), all of whom had multiple pre-existing cardiovascular risk factors.

Study Analyzes Cost of Temporary Dose Escalation vs. Cost to Switch to Another Biologic After Failure of Maintenance Therapy

In the event of failure of maintenance therapy with biologic agents for moderate to severe plaque psoriasis, physicians may choose to switch patients to a different biologic or escalate the dose of the current agent (generally by increased dosing frequency). Researchers recently conducted an analysis to determine when the annualized additional cost of escalation exceeds a specified cost overrun. Based on the purchase cost (average wholesale price) of approved biologics for the treatment of moderate to severe psoriasis, researchers found the number of weeks of escalation of the initial biologic until the
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Percentage of psoriasis and psoriatic arthritis patients surveyed who thought that better psoriasis therapies are needed, according to a May 2014 Journal of the American Academy of Dermatology article. Although oral medications and biologics are available to treat the diseases, almost 60 percent of patients reported they were not currently receiving treatment. Of those surveyed, 57 percent of patients who had taken an oral medication discontinued treatment. For those who had taken a biologic, 45 percent discontinued treatment.

The annualized cost of dose escalation ran €1000 over the cost of switching to another biologic was calculated for a typical patient weighing 80kg.

According to this model, the analysis determined, switching to another biologic is cost effective, with adalimumab followed by ustekinumab the best choices in this respect. Ustekinumab allows for a longer trial escalation period (two to four injections) before the cost overrun threshold is reached, whereas the threshold is reached in a single infusion if a patient is on infliximab.

The authors noted that this study does not take into account the differential efficacy of the various biologic therapies as rescue treatment for failure of maintenance therapy given the lack of scientific evidence, but the results show substantial differences in the period during which treatment can be intensified before reaching the preset cost overrun.

—Actas Dermosifiliogr. 2014 Apr 9. [Epub ahead of print]

Patient Satisfaction High with Biologics

Although effectiveness of biologics for psoriasis has been measured extensively with objective outcome measures, there have not been many studies based on subjective, patient-reported outcome measures.

A recent study was designed to investigate satisfaction with medication as measured by the Treatment Satisfaction Questionnaire for Medication (TSQM) for biologics in daily practice psoriasis care in the first six months of treatment and to identify possible differences in satisfaction with medication between biologics-experienced versus biologics-inexperienced patients.

For this study, 106 patients were eligible for analysis. Patients were treated with etanercept (n=34), adalimumab (n=49), or ustekinumab (n=23). Of these patients, 54 percent were biologics-inexperienced. On all domains of TSQM (effectiveness, side-effects, convenience and global satisfaction), a statistical significant improvement was seen comparing month three or six with baseline (all p-values ≤0.02). After six months, biologics-inexperienced patients scored better on the domain ‘global satisfaction’ than biologics-experienced patients (p<0.01).

This study found high satisfaction rates were achieved in this group. The two domains that showed the most room for improvement as reported by the patient were effectiveness and convenience.

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Growing Emerging Psoriasis Therapies Market

The market for moderate to severe plaque psoriasis therapeutics is becoming increasingly competitive with three promising new drug classes: interleukin-17 (IL-17) inhibitors, a janus kinase (JAK) inhibitor, and a phosphodiesterase-4 (PDE-4) inhibitor, the last two being oral therapies.

Recent analysis from Frost & Sullivan’s Product and Pipeline Analysis of the Global Psoriasis Therapeutics Market finds the development pipeline for moderate to severe psoriasis therapeutics has at least 37 investigational biologic and small molecule drugs in various stages of development. The particularly competitive classes include IL-17 with three candidates in the late stages development and anti-interleukin-23 (IL-23), with five candidates in various stages of development.

“The discovery of the role of tumor necrosis factor alpha (TNFα) in inflammatory diseases led to the commercial launch of several popular TNF blockers,” said a Frost & Sullivan Life Sciences analyst. “These highly effective therapies for severe cases of plaque psoriasis are being upstaged by several new drug classes with improved efficacy, safety and tolerability.”

While next-generation biopharmaceuticals and novel oral therapies offer superior efficacy and safety, roadblocks, in the form of inadequate clinical differentiation and endorsement of pharmacoeconomic benefits, exist. Hence, pharmaceuticals are lining up numerous head-to-head trials to demonstrate the superiority of their therapies over marketed drugs. Regulator and payer scrutiny of these new therapies for chronic plaque psoriasis is increasing, and the bar for approval and reimbursement is significantly higher than it was a decade ago. The availability of several effective and approved TNF blockers places additional pressure on the developers of novel therapies to demonstrate superior profiles in terms of efficacy, safety, tolerability, and patient acceptance.

“If the cost and safety profiles are comparable, therapies that offer better patient convenience will be preferred to improve adherence to therapy and prevent relapse,” noted the analyst. “Advanced devices and improvements in formulations to reduce the inconvenience of frequent injections could set otherwise similar products apart in the eyes of patients.”