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New data point to benefits of Bristol's novel psoriasis pill, but safety issues will be scrutinized

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By Adam Feuerstein[2] [3] April 23, 2021

Courtesy Bristol Myers Squibb

Last November and then again in February, Bristol Myers Squibb said its oral drug designed to treat psoriasis differently from currently approved medicines had achieved the goals of large Phase 3 clinical trials.

On Friday, the actual data from those two studies were presented publicly for the first time at the annual meeting of the American Academy of Dermatology. The Bristol drug, called deucravacitinib, proved more effective at clearing the chronic skin disease — numerically and statistically — compared to a placebo and a competing drug from Amgen.

The safety data from the two clinical trials also suggest deucravacitinib, taken as a

once-daily pill, is better tolerated and less toxic than a related class of autoimmune pills called JAK inhibitors, all of which carry the highest level of FDA-mandated safety warnings for serious infections, blood clots, and cancer.

Deucravacitinib is a particularly important drug for Bristol because of its potential to treat a wide range of autoimmune diseases with the efficacy approaching currently approved injected medicines but with the convenience of a pill.

Otezla, the Amgen drug that deucravacitinib beat in the two psoriasis clinical trials, generated sales totaling $2.2 billion last year. If Bristol manages to secure deucravacitinib's approval in psoriasis and several other autoimmune diseases, the drug's peak annual sales could reach $4 billion, according to J.P. Morgan pharma analyst Chris Schott.

Bristol chemists developed deucravacitinib in its own labs to work differently than other autoimmune disease drugs by blocking a cell-signaling enzyme called TYK2 involved in inflammation and immune response. While TYK2 and JAK belong to the same family of cell-signaling enzymes that play a role in certain autoimmune diseases, deucravacitinib is designed to leave JAK enzymes untouched, thereby avoiding the serious side effects associated with those drugs.

"What we know about JAK inhibitors from a side-effect perspective is there are laboratory abnormalities such as liver dysfunction and decreased lipids. There are thrombotic [blood clotting] episodes associated with those molecules. We do not see that with deucravacitinib. We don't have lab abnormalities. We don't have a thrombotic signal," said Samit Hirawat, Bristol's chief medical officer.

In the first Phase 3 study, 59% of patients on deucravacitinib — compared to 13% of patients on a placebo — achieved a so-called PASI 75 response, which measures improvement in the severity and spread of skin lesions. The assessment was done after four months.

Just over 35% of the patients in the study assigned to treatment with Amgen's Otezla achieved a PASI 75 response at four months..

Deucravacitinib also beat the comparators by scoring a "clear or almost clear" skin assessment from treating physicians — 54% for the Bristol drug compared to 7% and 32% for placebo and Otezla, respectively. The psoriasis-clearing benefit

of deucravacitinib was sustained in follow-up visits at six months and one year.

The Phase 3 study enrolled 666 patients with moderate to severe psoriasis, of which 32% were female, 80% were white, and 18% were Asian. People identified as “other” race made up the remaining 2% of participants.

Bristol’s second Phase 3 study was larger, enrolling just over 1,000 patients, with equally positive results confirming the superiority of deucravacitinib compared to placebo and Otezla.

While not studied directly in either of the Phase 3 trials, deucravacitinib remains less effective than currently approved injectable medicines used to treat psoriasis, based on cross-study comparisons. Abbvie’s Humira gets about 60% of patients to a PASI 75 skin-clearance rate, when adjusted for placebo; newer injectable medicines, including Novartis’ Cosentyx and Skyrizi, also from Abbvie, achieve placebo-adjusted PASI 75 scores in the 70%-80% range.

April Armstrong, a dermatologist and associate dean at University of Southern California, said patients with psoriasis who do well with an injectable medicine would probably stick with it. However, “patients have always also wanted better oral therapies. Deucravacitinib fills that important need for having something that is both efficacious and safe.” Armstrong was involved in the Bristol studies and presented the deucravacitinib data on Friday.

The safety profile of deucravacitinib will be closely scrutinized and debated for any evidence of JAK-like side effects that may compel regulators to apply significant safety warnings to its label, if approved.

During the 16 weeks of the combined Phase 3 studies, the most common side effects reported by patients on deucravacitinib were colds (9%) and upper respiratory tract infections (5.5%) — both at levels similar to placebo and Otezla.

Just over 2% of deucravacitinib patients discontinued from the studies due to side effects, lower than the comparable discontinuation rates for placebo and Otezla.

Bristol also conducted safety analyses of the two studies using data collected over one year. Here, serious side effects occurred at a rate of 5.7 events per 100 patient-years for both deucravacitinib and placebo. The rate for Otezla was slightly lower at 4 events per 100 patient-years.

Serious infections attributed to deucravacitinib occurred at a rate of 1.75 events per 100 patient-years across the two Phase 3 studies

For comparison, Xeljanz, an approved JAK inhibitor from Pfizer, causes serious infections at a rate of 2.7 events per 100 patient-years, according to its FDA-approved label for rheumatoid arthritis. For Olumiant, another JAK inhibitor from Eli Lilly, the comparable serious infection rate is 4.2 events per 100 patient-years.

Jak inhibitors are not approved to treat psoriasis, but Bristol has ongoing clinical trials investigating deucravacitinib as a treatment for other autoimmune diseases where JAK inhibitors are used, including psoriatic arthritis and inflammatory bowel disease.

Across both Phase 3 trials, the rates of malignancy and major heart-related events were low for deucravacitinib and similar to placebo and Otezla comparators. A single patient on deucravacitinib experienced a venous blood clot but that occurred after heart surgery and a prior blood clot. More cases of herpes zoster were reported among deucravacitinib-treated patients but none of the cases were considered serious.

“My hope is that deucravacitinib would get a cleaner safety label” compared to JAK inhibitors, said Armstrong.

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