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Gut microbe curbs systemic inflammation in psoriasis

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Reuters Health - 04/11/2020 - It may be possible to effectively treat systemic inflammation in psoriasis with a pill containing a single strain of a commensal gut microbe, according to results of a first-in-human, proof-of-concept study.

The phase 1b study, by Evelo Biosciences, evaluated EDP1815, a non-live, pharmaceutical preparation of the human gut-derived commensal bacterium Prevotella histicola.

"EDP1815 is not absorbed into the body, and it does not colonize the gut. Instead, its pharmacodynamic effect is through interactions with the immune cells within the small intestine - namely dendritic cells and macrophages - leading to coordinated downregulation of multiple inflammatory pathways, mimicking the body's normal physiological processes of inflammation resolution," study investigator Dr. Douglas Maslin, dermatologist and pharmacologist at Addenbrooke's Hospital in Cambridge, U.K., told Reuters Health by email.

"In preclinical studies, EDP1815 is able to resolve inflammation across Th1-, Th2-, and Th17-mediated inflammatory models, such as the imiquimod-induced psoriasis model. It achieves this with an effect size comparable to potent anti-inflammatory treatments such as antibodies and systemic steroids, with a placebo-like safety profile and without any evidence of immunosuppression," Dr. Maslin said.

He presented the phase 1b data October 29 at the European Academy of Dermatology and Venereology (EADV) 2020 Virtual Congress.

EDP1815 was evaluated in two dose cohorts of 12 and 18 patients with mild to moderate psoriasis. Participants were dosed for 28 days (with active or placebo capsules) and followed off treatment through 42 days.

The primary endpoint was safety and tolerability. "EDP1815 was well tolerated, with a side effect profile comparable to placebo and no serious or severe adverse effects," Dr. Maslin told Reuters Health.

"Even though the study was not powered to show efficacy, we did see proof of concept for the efficacy of EDP1815 in mild to moderate psoriasis in both cohorts," he noted.

At day 28, the average reduction in Psoriasis Area Severity Index (PASI) score for both EDP1815 cohorts (low- and high-dose) was 16%, compared to 1% for placebo. There was further improvement to 21% mean PASI reduction in the high-dose cohort at day 42, but not the low-dose cohort (10%) or placebo cohorts (3%).

The mean reduction in Lesion Severity Score (LSS) at 28 days was 15% in the high-dose and 23% in the low-dose EDP1815 cohorts, compared to a 1% increase from baseline in the placebo group. Again, there was further clinical improvement, to a 24% reduction, in the high-dose cohort.

In addition to the beneficial effects of EDP1815 on skin inflammation, a reduction in the production of inflammatory cytokines in treated patients was also observed, Dr. Maslin told Reuters Health.

"These results were the catalyst for progression into the phase 2 study which is now underway in Europe and the U.S., with interim results expected in mid-2021," he said. "This is a 16-week dose-ranging study in approximately 225 patients with mild to moderate psoriasis. This population of patients are the ideal candidates for EDP1815 because of the significant unmet need. Unfortunately, these patients are generally

not classified as having severe enough disease to be treated with drugs such as the biologic therapies; and so are often untreated or have to persist with topical therapies."

EDP1815 is also being studied in a phase 1b trial of atopic dermatitis, and in two trials as a treatment of the excess inflammation seen in hospitalized patients with COVID-19, Dr. Maslin said.

Commenting on the results in an email to Reuters Health, Dr. Marie-Aleth Richard, chair of the EADV communications committee, said, "The use of a bacterium taken orally but acting on the whole body, including the skin, for the treatment of psoriasis is an exciting new theoretical therapeutic approach for skin diseases. Its means that we should be able to change the way we treat patients via the interaction of natural bio-organisms belonging to our body and the immune system, rather than using drugs or chemistry."

Dr. Richard, who was not involved in the study, said, "We can expect systemic anti-inflammatory effects without systemic absorption of a drug, but just via modulating human immune cells mucosa by bacteria in the small intestine. Once in direct contact with the bacteria, these cells modulate inflammation systemically via cytokine signaling and T-cell trafficking. These preliminary data showed moderate psoriasis clearance and response, but with no safety signals. They need to be confirmed but demonstrate the interaction between bacteria and the immune system."

The study was funded by Evelo Biosciences Ltd. Dr. Maslin and his co-authors are employees of the company.

By Megan Brooks

SOURCE: https://eadv.org/ EADV 2020 Virtual Congress, presented October 29, 2020.

