Pharmacy Times

Nasal Foralumab Shows Promise in Regulating Inflammatory Response of COVID-19

Mar 15, 2023

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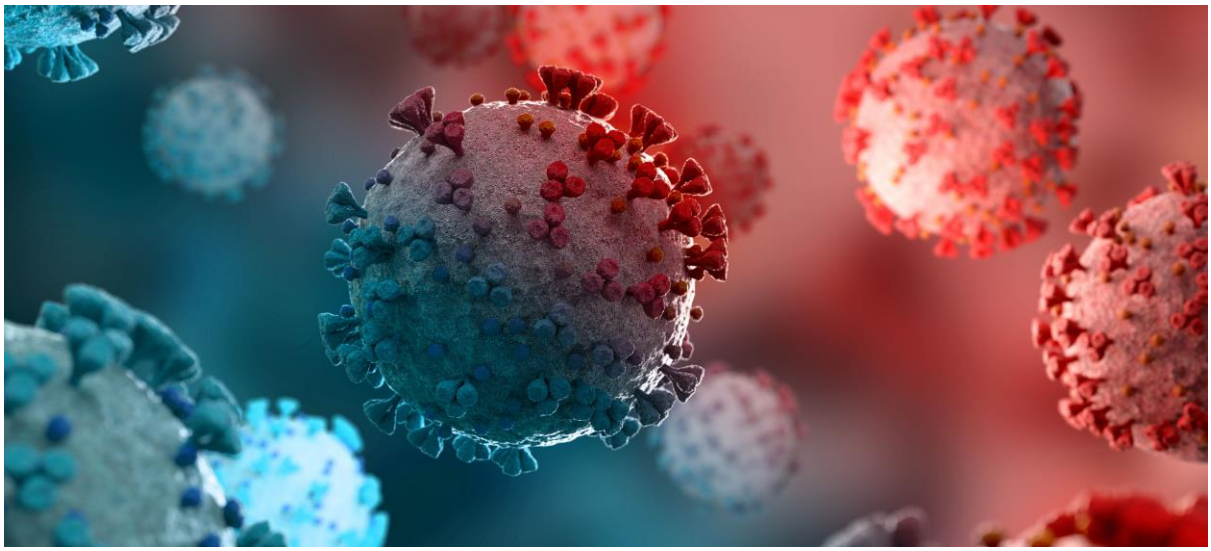
Study includes healthy individuals and those who had progressive multiple sclerosis with the nasally administered treatment.



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Nasal administration of foralumab helps regulate the inflammatory response of COVID-19, providing an alternative way to treat the virus, according to the results of a study published in *Proceedings of the National Academy of Sciences.*

In the study, investigators used RNA sequencing and serum proteomics to analyze the immune changes for individuals treated with nasal foralumab.

Outpatients with mild-to-moderate COVID-19 received a nasal administration for foralumab in the 100 µg/d dosage for 10 consecutive days. They were compared with individuals who did not receive the drug.

Individuals were treated at the Santa Casa de Misericordia de Santos in São Paulo State, Brazil. Investigators collected blood for immunologic analysis at baseline and day 10 of the study.

There were 28 total individuals included in the study: 12 were treated with foralumab, and 16 were untreated. Investigators chose 8 individuals from each group for the immunologic analysis. For RNA sequencing, 8 individuals treated with foralumab, 8 untreated participants, and 7 healthy controls were included.

Investigators found that naïve-like T cells increased in individuals who were treated with foralumab. They also noted that NGK7+ effector T cells were reduced.

Furthermore, they observed that *CCL4, CCL5, CST7, GZMA, GZMB, GZMH IL32,* and *PRF1* expressions were downregulated in T cells.

CASP1 was downregulated in B cells, monocytes, and T cells in individuals who were treated with foralumab.

Additionally, investigators found that there was increased expression of *GIMAP7*, a glutamate-pyruvate transaminase 1 (GPT)-binding gene, for those who were treated.

They observed that Rho/ROCK1, a GTPases signaling pathway, was also downregulated.

Further, *GIMAP7, NKG7, and TGDB1* transcriptomic changes were similar in those who were treated, as well as those who were healthy volunteers and mice that were treated with nasal anti-CD3.

In previous studies, investigators tested the administration of nasal and oral anti-CD3 monoclonal antibodies in animal models of autoimmunity an inflammation. They included arthritis, diabetes, inflammatory bowel diseases, lupus, and multiple sclerosis (MS).

In addition to the treatment of individuals with COVID-19, investigators also treated healthy patients and those who had progressive MS with nasally administered foralumab.

Investigators also performed single-cell RNA sequencing analysis on these patients to determine the CD3+ subsets. They found that *GIMAP7* and *TGFB1* gene expression were upregulated, but *NKG7* gene expression was downregulated in all 3 cohorts.

Investigators also saw the same changes in CD3+ cells from the cervical lymph nodes of C57BL/6J mice that were treated with the nasally administered anti-CD3.

They noted that the cohort was limited in size, therefore it could not be generalizable. Additionally, the cohort was not equipped to present a biomarker association with clinical outcomes in COVID-19.

The usage of foralumab in humans could help advance the use of the drug as an adjunct therapy for COVID-19 and also guide the long-term use for autoimmune conditions, according to investigators.

Reference

G Moreira T, Gauthier CD, Murphy L, Lanser TB, et al. Nasal administration of anti-CD3 mAb (Foralumab) downregulates NKG7 and increases TGFB1 and GIMAP7 expression in T cells in subjects with COVID-19. *Proc Natl Acad Sci U S A*. 2023;120(11):e2220272120. doi:10.1073/pnas.2220272120