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Resolution of COVID-19 induced anosmia following treatment with ST266

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ABSTRACT

Background: Persistent anosmia following COVID-19 disease affects a significant subset of patients. Symptoms of this olfactory dysfunction negatively impact patient quality of life, and effective treatments are lacking; therefore, novel therapies that restore the ability to smell have tremendous clinical potential.
Case report: A 46-year-old female enrolled in a phase I clinical trial to assess the safety of targeted intranasal administration of a novel acellular secretome therapy (ST266) in patients diagnosed as glaucoma suspects. The patient reported greater than one year history of loss of smell that started following a presumed positive case of COVID-19. Following a 28-day treatment course of bilateral intranasal administration of ST266, the patient had resolution of her long-standing anosmia.
Conclusion: This case demonstrates resolution of COVID-19-induced persistent anosmia after intranasal treatment with a novel acellular secretome therapy. Further studies are warranted to determine the potential of ST266 and its components to treat anosmia.

1. Introduction

The World Health Organization declared the novel SARS-CoV-2 coronavirus-induced COVID-19 disease an international Public Health Emergency on January 30, 2020 [1]. As of May 2, 2022, there were more than 510 million COVID-19 cases and nearly 6 million deaths worldwide (https://covid19.who.int/). Typical COVID-19 symptoms include fever, cough, shortness of breath, and fatigue, and in severe cases patients may die from pneumonia and/or multiple organ failure [1]. In addition, many patients experience neurologic complications from COVID-19 [1].

One common symptom in COVID-19 patients is loss or change of smell (olfactory dysfunction including anosmia or hyposmia), which has aided in disease diagnosis. Anosmia is often transient; however, a substantial proportion of patients (21.1%) self-report persistent anosmia/hyposmia, including 8.6% who report unchanged or increased severity one year after onset [2]. It is estimated that as many as 1.6 million people in the United States have developed chronic olfactory dysfunction due to COVID-19 [3], which the authors point out is associated with multiple morbidities including decreased quality of life; potential harm due to inability to smell gas, smoke, rancid foods, or other warning signs of danger; and social issues related to anxiety about personal hygiene potentially contributing to depression. Thus, the prevalence and effects of COVID-19-induced anosmia suggest a need for effective treatments.

ST266, a novel biologic containing secreted anti-inflammatory cytokines and growth factors, is created from Amnion-derived Multipotent Progenitor cells [4,5]. Intranasal ST266 administration provides neuroprotective effects with the potential to suppress inflammation in preclinical models of autoimmune [4] and traumatic optic neuropathies [5].

2. Case presentation

Preliminary Phase I Clinical Trial (NCT03901781) results investigating safety of intranasal ST266 targeted to the cribriform plate in glaucoma suspects showed no severe adverse events. Patients were treated in three cohorts: 200μL daily in alternating single nostrils for 14 days, 200μL daily to each nostril for 14 days, or 200μL daily to each nostril for 28 days using a targeted intranasal delivery device (SipNose, Ltd, Yokneam, Israel). Patients were monitored for ocular, nasopharyngeal, central nervous system, and systemic safety for one-year post-treatment.

Subject 9, a 46-year-old Caucasian woman followed as a glaucoma suspect due to moderate optic nerve cupping and family history, enrolled in study arm three, receiving 200μL of ST266 to each nostril for

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28 days. Prior to enrolling, she experienced persistent anosmia for one year. Approximately one-week post final treatment, the patient reported to the study investigator she had a return of her sense of smell. Specifically, in early March 2020 (13 months prior to entering the study), the patient experienced fevers, fatigue, dry cough, shortness of breath, and new onset anosmia. Her anosmia included an inability to detect the odor of cat urine, spoiled milk, burning items on the stove, and perfume, as well as an ability to cut onions without epiphora and to tolerate spicy foods which she could not do previously. On March 9, 2020, she underwent extensive respiratory testing, including PCR for adenovirus, RSV, influenza A and B, parainfluenza, parvovirus, human metapneumovirus, human rhino/enterovirus, and mycoplasma pneumonia. Due to lack of available testing at that time, a COVID-19 infection could not be confirmed, but she was presumed positive with COVID-19 induced anosmia, and her anosmia persisted unchanged for more than one year.

The patient enrolled in the ST266 intranasal trial after meeting study criteria including normal nasopharynx exam; normal ocular exam, ocular imaging, and visual field testing; normal MRI of the head; and a normal physical exam. One week after her final ST266 treatment, the patient reported she detected odors again—first describing she could smell cinnamon and coffee. Over the next several months she noticed a return of epiphora when cutting onions, and regained her ability to smell cat urine, smoke, perfume, and fragrant spices. More than six months post-treatment she felt her sense of smell returned to baseline.

3. Discussion

This case suggests that intranasal ST266's anti-inflammatory cytokines and growth factors likely reversed persistent COVID-19 induced anosmia following targeted administration to the cribriform plate impacting the olfactory nerves. The persistence of this patient's anosmia for more than one year following her presumptive positive COVID-19 disease suggests that her loss of smell was permanent and not expected to resolve spontaneously. The marked improvement beginning within one week of completing a course of intranasal ST266 treatment suggests ST266 likely played a key role in stimulating restoration of her ability to smell.

While prior studies demonstrated that components of ST266 accumulate in optic nerves [4] and provide neuroprotective effects in preclinical models of optic neuropathies [4,5] following intranasal administration, the exact mechanism underlying this nose-to-optic nerve pathway is not known. Of note, the rapidity (within 30 minutes) and selectivity of protein accumulation [4] suggests a likely localized entry into the central nervous system through the cribriform plate with direct exposure to olfactory nerve fibers. Thus, results in the current case suggest that exposure of olfactory nerves to the combination of growth factors, cytokines, and other components in ST266 may promote a return of function capable of reversing COVID-19-induced anosmia.

4. Conclusion

Given the extent of the COVID-19 pandemic across the world, and the high percentage of affected patients that develop persistent anosmia [2,3] with associated decreased quality of life and increased risks of harm, identifying novel therapies to restore a sense of smell is a critical need. This case demonstrates resolution of COVID-19-induced persistent anosmia after intranasal treatment with a novel acellular secretome therapy. Further studies are warranted to determine the potential of ST266 and its components to treat anosmia.

Ethical statement

Appropriate consent and permission were obtained from the patient regarding the writing of this case report.

Declaration of competing interest

The ST266 safety trial the patient was enrolled in is sponsored by Noveome Biotherapeutics, Inc. (Pittsburgh, PA). Noveome provided the ST266 and funding to AGR and KSS for the clinical trial. Observed effects on anosmia were not part of the study protocol. KSS has also served on Scientific Advisory Boards and as a paid consultant for Noveome, providing expertise related to treating optic neuropathies. The authors declare no other relevant conflicts of interest.

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