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Editorial

GS-5245, A New Oral Nucleoside Prodrug is Efficacious Against SARS-CoV-2 and Other Coronaviruses and Post-COVID-19 Conditions After COVID-19 Vaccination

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A recent retrospective study in the United States by using electronic health records (EHR) among positive-SARS-CoV-2 patients during March 2021 to February 2022. Both unvaccinated (161,531) and vaccinated (161,531) COVID-19 patients were matched on age, sex, acute infection severity, test date, and location. The analyzed data revealed that, except mental health disorders, vaccinated patients had lower risk of all post-COVID-19 conditions (PCC) categories (relative risk (RR): 1.06, 95% confidential interval (CI): 1.02-1.10) [1]. COVID-19 vaccination was related to lower risk of cardiovascular (RR: 0.88, 95% : 0.83-0.94), blood and hematologic (RR: 0.79, 95% CI: 0.71-0.89), more than 10% of lower risk of sensory (RR: 0.90, 95% CI: 0.86-0.95), skin and subcutaneous (RR: 0.69, 95% CI: 0.66-.72) (Figure 1) [1]. Recently, Martinez et al conducted a study on the efficacy on obeldesivir (or GS-5245), an orally available small molecule targeting the RdRp of SARS-CoV-2 in mice infected with one of several coronaviruses, including SARS-CoV-2 (COVID-19), SARS-CoV, and MERS-CoV [2]. They demonstrated that GS-5245 could decrease disease severity and improvement of outcome with GS-5245 and nirmatrelvir combination in infected mice (Figure 2) [2].

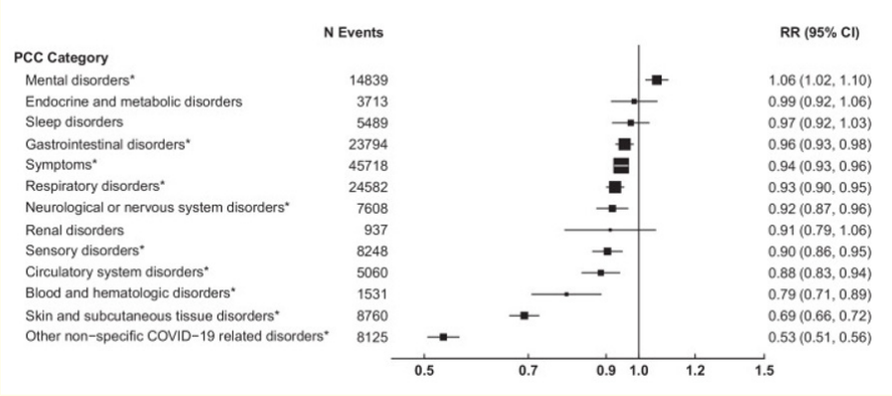

Figure 1: Demonstrating the relation of prior COVID-19 vaccination and risk of PCC categories 6 months following SARS-CoV-2 infection [1].

Relation of prior vaccination status with Post-COVID Conditions (PCC) was studied among 161,531 vaccinated patients matched with 161,531 unvaccinated patients on Vaccine Safety Datalink site, age (exact year), sex, date of SARS-CoV-2 positive test (± 7 days), COVID-19-infection severity (hospital admission with COVID-19 diagnosis within 7 days of SARS-CoV-2 positive test). Relative risks (RR) and 95% confidence intervals (CI) were calculated by Poisson regression adjusted for matched variables and prior SARS-CoV-2 infection, race and ethnicity, Charlson comorbidity score, Medicaid status, influenza vaccination, and healthcare utilization in the year prior. Box sizes are inverse-variance weighted. PCC category of symptoms included weight loss, fever/fatigue/malaise, headache, vertigo, body ache/myalgia, or lymphadenopathy. Significant Bonferroni correction was applied to main analysis of 13 PCC categories, with 2-sided p-values at a level of significance of 0.004 to limit the impact of multiple testing [1].

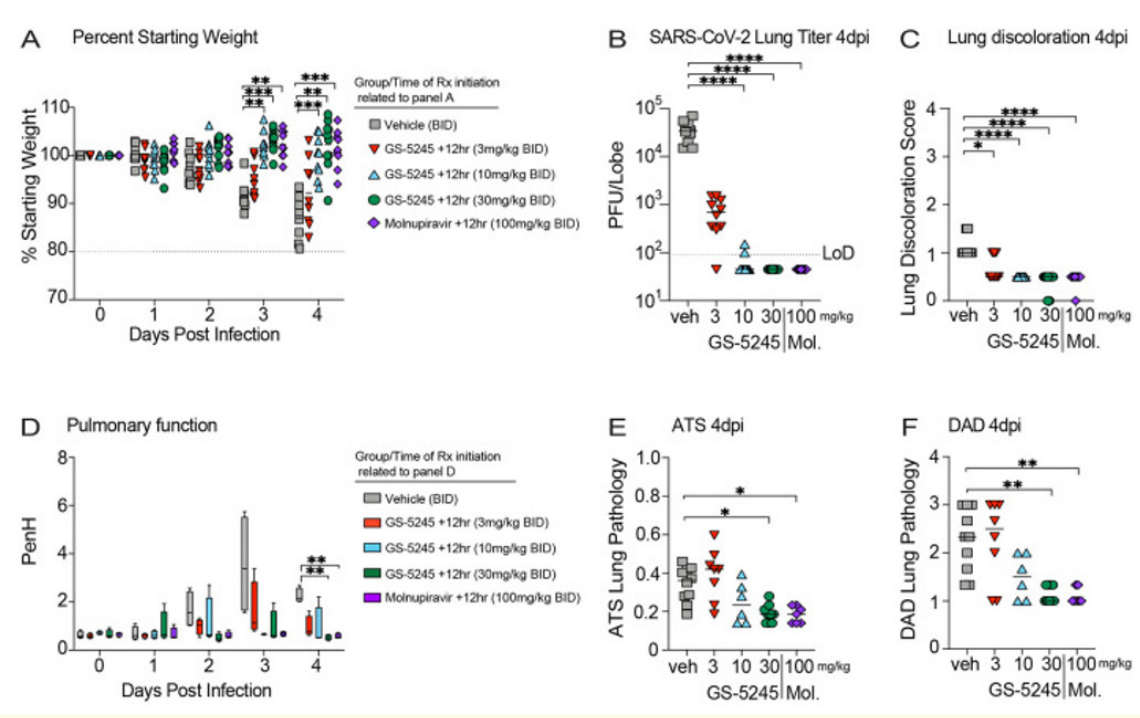

Figure 2: Demonstrating the dose-dependent therapeutic efficacy of GS-5245 against SARS-CoV-2 MA10 in BALB/c mice [2].

(A) Percent starting weight through 4 dpi in 10-week-old female BALB/c mice infected with SARS-CoV-2 MA10 at 1 x 104 PFU. Mice were treated BID with vehicle (veh: gray squares), 3 mg/kg GS-5245 (upside-down red triangles), 10 mg/kg GS-5245 (right-side-up blue triangles), 30 mg/kg GS-5245 (green circles), and 100 mg/kg molnupiravir (purple diamonds) starting at 12 hpi. N=10 mice per group. Rx = drug. Asterisks denote p values from a two-way ANOVA after a Dunnett's multiple comparisons test [2].

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$.

(B) SARS-CoV-2 MA10 lung infectious viral titers 4 dpi in mice treated with vehicle or GS-5245 at increasing concentrations and 100 mg/kg molnupiravir (Mol.). Asterisks denote p values from a Kruskal-Wallis test after a Dunnett's multiple comparisons test [2].

(C) Macroscopic lung discoloration at 4 dpi in therapeutically treated mice compared to vehicle. Asterisks denote p values from a Kruskal-Wallis test after a Dunnett's multiple comparisons test [2].

(D) Pulmonary function (PenH) monitored by whole-body plethysmography from day zero through 4 dpi in SARS-CoV-2-infected treated mice. Asterisks denote p values from a two-way ANOVA after a Dunnett's multiple comparisons test [2].

(E) Microscopic ATS acute lung injury pathology scoring at day 4 post infection in vehicle vs. GS-5245 or molnupiravir-treated mice. Asterisks denote p values from a Kruskal-Wallis test after a Dunnett's multiple comparisons test [2].

(F) Microscopic DAD acute lung injury pathology scoring at 4 dpi in vehicle, GS-5245, or molnupiravir-treated mice. Asterisks denote p values from a Kruskal-Wallis test after a Dunnett's multiple comparisons test [2].

In conclusion, at younger ages, the relations to post-COVID-19 conditions were strong, but mostly persisted with the receipt of 3 or more doses of COVID-19 vaccination, compared to 1-2 doses, or time since vaccination. regardless of SARS-CoV-2 variant period. PPC outcomes and the COVID-19-long-term consequences or long-COVID-19 conditions could be reduced with pre-infection-COVID-19 vaccination and the new promising prodrug, such as obeldesivir (GS-5245).

Bibliography

1. Michener Charles D. "The Bees of the World (2nd edition)". Johns Hopkins University Press (2007).
2. Sedivy C., *et al*. "Host range evolution in a selected group of osmiine bees (Hymenoptera: Megachilidae): the Boraginaceae-Fabaceae paradox". *Biological Journal of the Linnean Society* 108.1 (2013): 35-54.
3. Fabre JH. "The Mason-Bees". trans. Alexander Teixeira De Mattos, New York: Dodd, Mead and Company (1914).
4. Gullan PJ and Cranston PS. "The insects: an outline of entomology". John Wiley and Sons (2014).
5. Holland Jennifer S. "Flower Beds". *National Geographic* 218.6 (2010).
6. Sedivy C., *et al*. "Molecular phylogeny of the bee genus *Hoplitis* (Megachilidae: Osmiini)-how does nesting biology affect biogeography?" *Zoological Journal of the Linnean Society* 167.1 (2013): 28-42.
7. Zurbuchen A., *et al*. "Long foraging distances impose high costs on offspring production in solitary bees". *Journal of Animal Ecology* 79.3 (2010): 674-681.
8. Rozen JG., *et al*. "Nests, petal usage, floral preferences, and immatures of *Osmia (OzbekOsmia) avosetta* (Megachilidae: Megachilinae: Osmiini), including biological comparisons with other osmiine bees". *American Museum Novitates* 3680 (2010): 1-22.
9. Rozen JG., *et al*. "Biology of the bee *Hoplitis (Hoplitis) monstrabilis* Tkalců and descriptions of its egg and larva (Megachilidae: Megachilinae: Osmiini)". *American Museum Novitates* 3645 (2009): 1-12.
10. Mader E., *et al*. "Managing alternative pollinators". *NRAES, Ithaca, NY* (2010).
11. McKinney MI., *et al*. "Nesting Activity and Behavior of *Osmia cornifrons* (Hymenoptera: Megachilidae) Elucidated Using Videography. *Psyche: A Journal of Entomology* (2012): 1-7.
12. LeCroy KA., *et al*. "Decline of six native mason bee species following the arrival of an exotic congener". *Scientific Reports* 10.1 (2020): 1-9.