Tolerance and clinical outcomes of COVID-19 antiviral therapy in long-term care residents

INTRODUCTION

Oral antivirals, Paxlovid® (nirmatrelvir tablets; ritonavir tablets, Pfizer) and molnupiravir (Merck), were authorized recently to treat individuals with confirmed mild to moderate COVID-19 within 5 days of symptom onset and at risk for progression to severe disease.1,2 Median ages in these medication trials were 46 and 43 years, respectively. Limited real-world data exist on tolerance and clinical outcomes on these antivirals, particularly in older individuals, such as long-term care facility (LTCF) residents.

In early 2022, Indiana Department of Health (IDOH) established a call center (8 AM to 5 PM Monday to Friday and 10 AM to 2 PM on Saturday) to assist LTCFs to locate and secure antiviral medications for eligible residents (Figure 1). The establishment of the IDOH call center provided a unique opportunity to prospectively track the outcomes of these agents.

METHODS

We performed a prospective observational study by tracking LTCF residents who received antiviral therapy through call center assistance. We evaluated adherence, tolerance, and outcomes. LTCFs were educated on the availability of antiviral therapy, eligibility criteria, drug–drug interactions (DDI) and assistance via the call center. When an eligible LTCF resident was identified, LTCF staff contacted the call center. The call center identified a pharmacy with antiviral therapy in stock, placed a hold on the course, informed the LTCF staff, and the LTCF provider sent the prescription to the pharmacy holding the medication for that resident (Figure 1).

Per protocol, call center staff contacted LTCFs 7–10 days later to inquire about the residents’ adherence, tolerance of the medication, and clinical outcomes, such as improvement or worsening of symptoms based on assessment by the LTCF resident and staff, hospitalization (COVID and non-COVID related), and death. In one instance, a second phone call was made to get additional follow up on an adverse event.

RESULTS

Between January 5 and February 18, 2022, the call center secured antivirals for a total of 125 residents living at 26 LTCFs. Residents’ ages ranged from 46 to 99 years (median = 81 years), 85% were aged 65 years or older, 66% were female, 95% were white. Regarding vaccinations, 54% were up to date (received a booster when eligible) and 26% were fully vaccinated. Outcomes of 17 residents were not available as the LTCF personnel could not be reached despite multiple attempts. Of the 108 residents who were successfully tracked, 91 (84%) completed the treatment as prescribed, and 17 did not complete the treatment.

Of 59 residents completing molnupiravir therapy, two developed self-limiting diarrhea. Of 32 residents completing Paxlovid® therapy, five developed mental status changes, described as delusions, hallucinations, and paranoia, while on Paxlovid®. Four of them had another factor that could cause or contribute to the change in mental status (two started Decadron at the same time for severe COVID-19, one suffered an acute stroke, and one had a urinary tract infection). The changes in four of them were resolved by the second follow up.

Of the 91 residents who completed treatment, 82 (90%) noticed improvement in COVID-19 symptoms. Of the nine residents who did not report symptom improvement, one was hospitalized due to stroke and died, one had a hospitalization not related to COVID-19, two had worsened symptoms, and five had no change in their condition (Figure 2). A total of six residents were hospitalized (5.6%) including two who completed treatment (2.2%).

Of the 17 (16%) residents who did not complete the therapy, 11 were related to refusal by the resident or their power of attorney. Only one resident’s treatment was not initiated because of possible DDI.

DISCUSSION

In this study, we observed a hospitalization rate of 2.2% in LTCF residents, higher than the rate reported in the
Paxlovid trial (0.8%) but lower than the rate reported in the molnupiravir trial (7.3%). Nevertheless, the hospitalization rate of 2.2% is lower than the previously reported hospitalization rate of 4% in LTCF residents during the omicron period and 10.8% during the pre-omicron period. This hospitalization rate is also lower than the 3%–7% incidence of hospitalization or death with placebo in clinical trials evaluating monoclonal antibody treatments.

Limitations of the study include having no control arm, subjective assessment of clinical improvement and not tracking comorbidities. Subgroup complete analysis of outcomes was not performed due to small number of study subjects.

We report an adverse event of mental status changes in five residents while receiving Paxlovid, however four had competing etiologies. This serves as important reminder to observe for mental status changes in all residents with COVID, regardless of intervention, for acute changes in mental status.

AUTHOR CONTRIBUTIONS
Contributed to conception or design: Shireesha Vuppalanchi, Pam Pontones. Contributed to acquisition, analysis, or interpretation: Shireesha Vuppalanchi, Lindsay Weaver, Pam Pontones. Drafted the manuscript: Shireesha Vuppalanchi. Critically revised the manuscript: Shireesha Vuppalanchi, Lindsay Weaver, Kristina Box, Pam Pontones. Gave final approval: Kristina Box, Pam Pontones. Agrees to be accountable for all aspects of work ensuring integrity and accuracy: Shireesha Vuppalanchi, Pam Pontones.

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CONFLICT OF INTEREST
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