Monoclonal antibodies used in the treatment and prevention of COVID-19 infection are an emerging area of infectious disease. In November of 2020, Casirivimab/imdevimab received emergency use authorization (EUA) for the prophylaxis and treatment of COVID-19.

In a phase 3 double-blind, randomized controlled trial of casirivimab/imdevimab in non-hospitalized patients with mild to moderate COVID-19, outcome data revealed a rate of any reported adverse drug reaction (ADR) of 7.3% (99/1342) to 7.7% (142/1849) in the 1200 mg and 2400 mg groups respectively. For the 1200 mg dose, a combined rate of COVID-19-related hospitalization or death from any cause was reported at a rate of 1.3% (placebo 4.6%). In a retrospective cohort, 696 patients who received casirivimab/imdevimab were compared to a propensity-matched control of 696 uninfected patients with mild to moderate COVID-19. Data revealed that patients who received casirivimab/imdevimab had significantly lower all-cause hospitalization rates at day 14 (1.1% in the treatment group vs 3.3% in control). 1,2

During the casirivimab/imdevimab EUA, the National Home Infusion Foundation (NHIF) collected data to study ADR rates, hospitalization, and death in patients administered casirivimab/imdevimab in the home. An initial comparison of hospitalization rates between the two published studies and the home infusion patients showed a consistently low rate of hospitalization (Table 1: Comparison of COVID-19 Related Hospitalization after Administration of Casirivimab/Imdevimab). 1,2

Biologic medications are labeled with a warning for ADRs that can be assessed and treated. Home infusion providers follow standard protocols for managing ADRs. Patients are provided premedications to treat or prevent an infusion reaction, and nurses can adjust the infusion rate to slow or stop the infusion.

Methods

Home infusion companies nationwide were invited to participate in this study by completing a short survey to determine eligibility. Medication administration data was collected between June 2021 and December 2021. The data variables collected were the ADR rate, hospitalization, and death. Additional variables analyzed were time from exposure to medication administration and infusion time. Demographic data collected included age, gender, and vaccination status. Patients were contacted 7 days after infusion to assess for changes and collect outcome information. The data was collected using an Excel® spreadsheet and deidentified before submission. A follow-up survey with infusion providers verified the relationship between the length of infusion and ADR incidence. The data was imported to IBM SPSS® (Statistical Package for Social Sciences®) for additional analysis. This study was exempt from IRB review since the data was deidentified prior to submission to NHIF.

Results

Infusion time reported for the administration of casirivimab/imdevimab was either 20, 30, or 50 minutes with most (62.60%) being 20 minutes. The 50-minute infusion rate was for a single patient, and the data point was removed before analysis. A significant difference was found between ADR and infusion time (p=0.001) (See Table 2: Infusion Time and Rate of ADR). Of the 464 patient cases, 95.26% (n=442) had no reported ADR. Of the 22 cases with a reported ADR, all were classified as mild in severity. When compared by gender, a significant difference was found between the incidence of ADR by gender, with a higher rate in males (p=0.031) (See Table 3: ADR by Gender). Using the demographic information collected, patients were compared by age and gender (Table 4).

References


TABLE 1: Comparison of COVID-19 Related Hospitalization after Administration of Casirivimab/Imdevimab

<table>
<thead>
<tr>
<th></th>
<th>Randomized Controlled Cohort</th>
<th>Retrospective Cohort</th>
<th>NHIF Home Infusion Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>696</td>
<td>827</td>
<td>396</td>
</tr>
<tr>
<td>Hospitalization Rate (%)</td>
<td>1.3%</td>
<td>1.8%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

A significant difference was found between ADR and infusion time (p=0.001).

Results

Rates of "Any" ADR reported during home infusion of casirivimab/imdevimab were compared to rates reported in clinical trials. A lower rate of ADR was reported in the home infusion patients (5.1%) than in the clinical trial data (7.7%) (see Figure 1).

With this patient sample, the time from onset of symptoms to medication administration was a mean of 6.2 days. No significant difference (p=0.251) was found between ADR and the "Time from Onset of COVID-19 symptoms and the first dose of Monoclonal Antibody" treatment group. (See Table 5) An interesting finding was that the mean number of days was 711 days for the patients with an ADR versus 5.98 days for those without an ADR. No significant difference (p=0.046) was found between adverse events and vaccination status. Few infusion patient (n=396) follow-up data results showed 1 patient expired (0.3%) and 5 patients were hospitalized (1.3%).

Discussion

In this study, patients who received infusions of casirivimab/imdevimab in the home setting had a lower rate of ADR than reported during clinical trials. At 7 days post-infusion, patient follow-up showed a low rate of hospitalization and death. Gender differences in the ADR rates showed a significant difference between males and females, with females having a lower rate of ADR. When infusion rates were compared, shorter infusion times were associated with fewer ADRs.

Conclusions

In this study, COVID-19 monoclonal antibodies (casirivimab/imdevimab) administered in the home setting were not associated with higher rates of ADRs compared to clinical trials, and patients treated at home had similar outcomes to patients in clinical trials.

Acknowledgments

The authors gratefully acknowledge Ryan Garst, PharmD, MBA, IgCP, BCSCP, Connie Sullivan, BPharm, and Jennifer Charron, RN, MSN, VA-BC for their contributions to study design, data collection, and poster content communication.

Author Contact: michelle.simpson@NHIA.org

Michelle Simpson, PharmD, BCSCP, Clinical Program Manager
National Home Infusion Association
Danell Haines, PhD, D.J. Haines Research Consulting

TABLE 2: Infusion Time and Rate of ADR

<table>
<thead>
<tr>
<th>Infusion Time (minutes)</th>
<th>Number of Infusions (%)</th>
<th>Adverse Event by Infusion Time (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>236 (62.59%)</td>
<td>1 (0.42%)</td>
</tr>
<tr>
<td>30</td>
<td>140 (37.14%)</td>
<td>15 (10.71%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>376 (100%)</td>
<td>16 (4.26%)</td>
</tr>
</tbody>
</table>

No significant difference (p=0.001) was found between ADR and infusion time.

TABLE 3: ADR by Gender (n=454)

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR (Yes/No)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>239</td>
<td>203</td>
<td>442</td>
</tr>
<tr>
<td>%</td>
<td>97.55</td>
<td>92.69</td>
<td>95.26</td>
</tr>
<tr>
<td>Yes</td>
<td>6</td>
<td>16</td>
<td>22</td>
</tr>
<tr>
<td>%</td>
<td>2.45</td>
<td>7.31</td>
<td>4.74</td>
</tr>
<tr>
<td>TOTAL</td>
<td>245</td>
<td>219</td>
<td>464</td>
</tr>
<tr>
<td>%</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

No significant difference (p=0.031) was found between ADR and gender.

TABLE 4: Patient Age (Mean) by Gender (n=450)

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Mean</td>
<td>N</td>
<td>SD</td>
</tr>
<tr>
<td>Female</td>
<td>64.56</td>
<td>243</td>
<td>16.83</td>
</tr>
<tr>
<td>Male</td>
<td>63.81</td>
<td>216</td>
<td>15.04</td>
</tr>
<tr>
<td>TOTAL</td>
<td>64.21</td>
<td>459</td>
<td>15.99</td>
</tr>
</tbody>
</table>

No significant difference (p=0.251) was found between ADR and the "Time from Onset of COVID-19 symptoms and the first dose of Monoclonal Antibody" treatment group.