Rate of Infusion Reactions Among Patients Receiving Casirivimab/Imdevimab in the Home Setting

Michelle Simpson, PharmD, BCSCP, Clinical Program Manager
National Home Infusion Association

Danell Haines, PhD, *D.J. Haines Research Consulting*

BACKGROUND

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 7.1% (59/827) 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%).[1] In a retrospective cohort, 696 patients who received casirivimab/imdevimab were compared to a propensity-matched control of 696 untreated 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 (1.3% in the treatment group vs 3.3% in control).[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 patients studied showed a consistently low rate of hospitalization (See 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.

References

1. Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H, Bhore R, et al. REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19. New England Journal of Medicine. 2021;385(23):e81. doi: 10.1056/nejmoa2108163.
2. Razonable RR, Pawlowski C, O'Horo JC, Arndt LL, Arndt R, Bierle DM, et al. Casirivimab-Imdevimab treatment is associated with reduced rates of hospitalization among high-risk patients with mild to moderate coronavirus disease-19. EClinicalMedicine. 2021;40:101102. doi: 10.1016/j.eclinm.2021.101102.

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

	Randomized Controlled Trial[1]	Retrospective Cohort[2]	NHIF Home Infusion Study
	N=696	N=827	N=396
Hospitalization Rate *f* (%)	9 (1.3%)	15 (1.8%)	5 (1.3%)

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=<.001). (See Table 2: Infusion Time and Rate of ADRs).

TABLE 2 : Infusion Time and Rate of ADR

Infusion Time (minutes)	Number of Infusions (%)	Adverse Event by Infusion Time *f* (%)
20	236 (62.59%)	1 (0.42%)
30	140 (37.14%)	15 (10.71%)
TOTAL	376 (100%)	16 (4.26%)

A significant difference was found between ADR and infusion time (p=<.001).

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=.012) (see Table 3). Using the demographic information collected, patients were compared by age and gender (Table 4).

TABLE 3: ADR by Gender (n=464)

			Female	Male	Total
ADR (Yes/No)	No	Count	239	203	442
		%	97.55	92.69	95.26
	Yes	Count	6	16	22
		%	2.45	7.31	4.74
TOTAL		Count	245	219	464
		%	100	100	100

TABLE 4: Patient Age (Mean) by Gender (n=459)

Gender	Mean	N	SD
Female	64.56	243	16.83
Male	63.81	216	15.04
TOTAL	64.21	459	15.99

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 (7.1%). (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=.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 7.11 days for the patients with an ADR versus 5.98 days for those without an ADR. No significant difference (p=.064) was found between adverse events and vaccination status. Post-infusion patient (n=396) follow-up data results showed 1 patient expired (0.3%) and 5 patients were hospitalized (1.3%).

FIGURE 1: Rate Reported for "Any" ADR Related to Infusion of Casirivimab/Imdevimab Comparison Between Clinical Trial ADR[2] and Home Infusion ADR

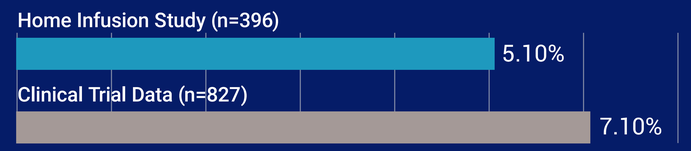

TABLE 5: ADR and Time from Onset of COVID-19 Symptoms to Medication Administration (n=392)

			0-5 Days	6-8 Days	9-13 Days	Total
ADR (Yes/No)	No	Count	167	128	77	372
		%	96.53	94.81	91.67	94.90
	Yes	Count	6	7	7	20
		%	3.47	5.19	8.33	5.10
TOTAL		Count	173	135	84	392
		%	100	100	100	100

No significant difference (p=.251) was found between ADR and the "Time from Onset of COVID-19 symptoms and the first dose of Monoclonal Antibody treatment group.

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, BSPharm, 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