1148: Relationship Between the Duration of Symptoms Before and COVID-19 Disease Outcome After Monoclonal Antibody Therapy

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INTRODUCTION

- In fall 2020, The U.S. Food and Drug Administration (FDA) granted an Emergency Use Authorization (EUA) for 3 different monoclonal antibodies (MAB) for treatment of mild-to-moderate COVID-19 infection based on the results from 3 different clinical trials that confirmed that MAB reduce COVID-19 disease progression and all cause mortality if given within 7 days of symptom onset.
- Despite the initial trials evaluating patients' outcomes within 7 days of symptom onset, the EUA allowed for MAB administration within 10 days of symptom onset.
- Efficiency of MAB in patients treated between days 8 and 10 from the symptom onset has not been studied.

OBJECTIVES

- To compare outcomes between individuals who were treated within 1-7 days of COVID-19 symptom onset and those who were treated between days 8-10 of symptom onset.

METHODS

- Retrospective chart review of patients treated with MAB at a single quaternary care center in West Michigan between March 1, 2021, and November 30, 2021.
- Groups:
  - Typical: duration of symptoms 0-7 days prior to infusion
  - Late: duration of symptoms 8-10 days prior to infusion
- Outcomes:
  - Number of Emergency Department (ED) visits within 14 days,
  - Number of hospitalizations within 14 days,
  - Progression to severe disease defined as intensive care unit (ICU) admission within 14 days or death within 30 days.
- All COVID positive patients with complete documentation who were at least 18 years old at the time of treatment and who met EUA criteria for MAB treatment were included in the study
- Collected data included basic demographics, comorbidities, timing and location of MAB administration, vaccination status, number of ED visits, hospitalizations and ICU admissions within 14 days, and number of deaths within 30 days from MAB infusion
- Statistical analysis: Data collected from typical and late treatment group were used to create models of adjusted relative risk for ED visits and hospitalizations 14 days after MAB therapy. Outcomes by adjusted relative risk were assessed with a confidence interval of 95% and a statistical significance at $p < 0.05$.

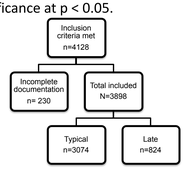

Figure 1 (left): The Subject Flow Diagram (n= number of patients; Typical= patients treated within 7 days from the symptom onset; Late = patients treated 8-10 days from the symptom onset)

RESULTS

Demographics n=3898		
Vaccination Status (none or partial = unvaccinated)	Typical group n (%)	Late Group n (%)
Unvaccinated	1540 (50.1)	469 (56.9)
Vaccinated	1534 (49.9)	355 (43.1)
Insurance Status		
Medicaid	242 (7.9)	59 (7.2)
Medicare	896 (29.1)	219 (26.6)
Commercial	1720 (56.0)	489 (59.3)
Self-pay/Other/ Unknown	216 (7.0)	57 (6.9)
Infusion Location		
Infusion Clinic	2230 (72.5)	646 (78.4)
Emergency Department	624 (20.3)	117 (14.2)
Mobile Unit/ In home	220 (7.2)	61 (7.4)
Patient Sex		
Female	1741 (56.6)	465 (56.4)
Male	1333 (43.4)	359 (43.6)
Patient Race		
Non-Hispanic White	2786 (90.6)	739 (89.7)
Black or African American	88 (2.9)	23 (2.8)
Hispanic/Latin	75 (2.4)	24 (2.9)
Other	54 (1.8)	20 (2.4)
Unknown/Missing	71 (2.3)	18 (2.2)
Patient Ethnicity		
Non-Hispanic/Latin	2880 (93.7)	763 (92.6)
Hispanic/Latin	99 (3.2)	33 (4.0)
Unknown	95 (3.1)	28 (3.4)
Patient Age		
Mean age by group and standard deviation	54.8 ± 15.9	55.2 ± 16.5
Four or more	458 (14.9)	103 (12.5)

Table 1: Demographics by Typical vs. Late group. Non-Hispanic Caucasians made up the most in both groups. Patients in the late group were more likely to be unvaccinated (56.9 vs 50.1%), and to be treated in the infusion clinic (78.4 vs 72.5%), compared with typical group who were treated more frequently in the ED (20.3 vs 14.2%).

Comorbidities n=3898		
	Typical group, n (%)	Late group, n (%)
Conditions Present		
BMI	2257 (73.4)	630 (76.5)
Hypertension	1022 (33.2)	280 (34.0)
Smoker	871 (28.3)	226 (27.4)
Lung Disease	596 (19.4)	142 (17.2)
Cardiovascular Disease	488 (15.9)	135 (16.4)
Diabetes	435 (14.2)	111 (13.5)
Cancer	251 (8.2)	67 (8.1)
Immunosuppression	227 (7.4)	34 (4.1)
Chronic Kidney Disease	149 (4.8)	40 (4.9)
Neurological condition	123 (4.0)	23 (2.8)
Pregnancy	38 (1.2)	6 (0.7)
Transplant Patient	32 (1.0)	4 (0.5)
Liver Disease	29 (0.9)	3 (0.4)
Neurodevelopmental Disorder	24 (0.8)	2 (0.2)
Technologically Dependent	12 (0.4)	5 (0.6)
Sickle Cell or Thalassemia	2 (0.1)	2 (0.2)
Count of Comorbidities		
Zero or one	1179 (38.4)	321 (39.0)
Two	892 (29.0)	243 (29.5)
Three	545 (17.7)	157 (19.1)
Four or more	458 (14.9)	103 (12.5)

Table 2: Comorbidities by Typical vs. Late group. Distribution was similar except obesity was more frequent in the late group (76.5 vs 73.4%) and immunosuppression was more common in the typical group (7.4 vs 4.1%).

RESULTS (continued)

Outcomes	Number of events n (%)
Deaths	12 (0.31%)
Severe Disease (ICU admission and deaths)	25 (0.64%)
Hospital Admissions	154 (3.95%)
ED Visits	296 (7.59%)

Table 3: Outcomes Following MAB Therapy. Overall Morbidity and mortality were low in MAB Recipients

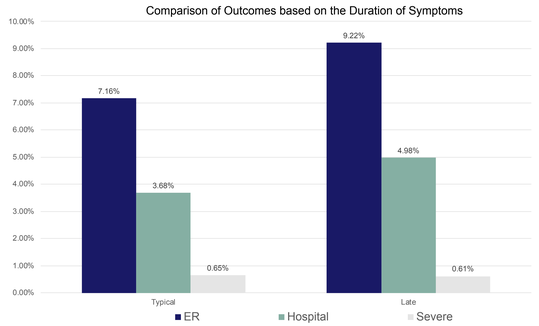

Figure 2: MAB therapy outcomes by Typical vs. Late group. Patients from the late group had more ER visits, hospitalizations and ICU admissions/ deaths comparing with vaccinated.

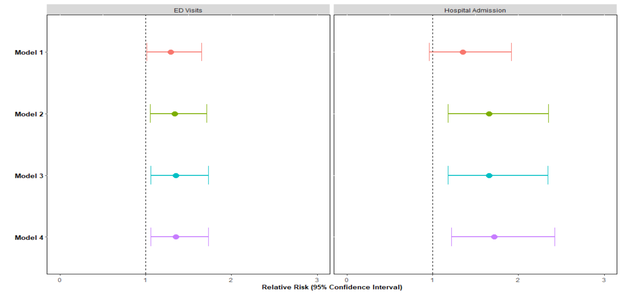

Figure 3: Outcomes by Adjusted Relative Risk, 95% CI. Adjusted relative risk is higher in all models for ED visits and hospital admissions in individuals who received MAB after the day 7 of the symptom onset.

Figure 3/ Table 3 Legend: Relative risk
- Model 1 – Unadjusted
- Model 2 – Adjusted for demographics, infusion location and vaccination status (table 1)
- Model 3 – Table 1 Variables + Comorbidity Count (table 2)
- Model 4 – Table 1 Variables + Comorbidities (table 2)

RESULTS (continued)

	ED visits RR (CI)	Hospitalization RR (CI)
Model 1	1.29 (1.01;1.65)	1.35 (0.96;1.92)
Model 2	1.34 (1.05;1.71)	1.66 (1.18; 2.35)
Model 3	1.35 (1.06; 1.73)	1.66 (1.18; 2.34)
Model 4	1.35 (1.06;1.73)	1.72 (1.22;2.42)

Table 4: Outcomes by Adjusted Relative Risk, 95% CI. Adjusted relative risk is higher in all models for ED visits and hospital admissions in individuals who received MAB after the day 7 of the symptom onset.

Table 4 Legend: Relative risk
- Model 1 – Unadjusted
- Model 2 – Adjusted for demographics, infusion location and vaccination status (table 1)
- Model 3 – Table 1 Variables + Comorbidity Count (table 2)
- Model 4 – Table 1 Variables + Comorbidities (table 2)

DISCUSSION

- Overall morbidity and mortality in both groups were low and consistent with clinical trials data.
- There was significant difference in the frequency of ED visits (absolute risk reduction 2.1%, p = 0.04) and marginally significant difference in the frequency of hospitalizations (absolute risk reduction 1.3%, p=0.08) both in favor of patients treated within 7 days of the symptom onset.
- The absolute risk of progression to the severe outcome was low in both groups, and there was no significant difference between the groups.
- Our adjusted models demonstrated the increased risk for ED visits and hospitalizations in patients treated later in the course of illness, particularly in those with multiple comorbidities .
- Typical group was more likely to be treated in the ER, suggesting that these patients might had been sicker at the time of treatment and thus at higher risk for poor outcome, but also, they were more likely to be vaccinated, which might had provided additional protection and affected MAB treatment outcomes.
- Study limitations include retrospective nature, data collection from a single site, limited comorbidity data to conditions determined by the EUA guidelines, limited data to the certain strains of COVID-19 (prior to the omicron occurrence) and lack of data on clinical presentation.

CONCLUSION

- Patients who received monoclonal antibody therapy within 7 days of symptom onset utilized fewer hospital and emergency department resources than those who received monoclonal antibody therapy between 8-10 days after the onset of symptoms.
- Our findings are of particular importance when resources are scarce. Patients within the 7-day window can be prioritized when access to MAB is limited as they will receive a greater benefit.

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