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Exploring Early COVID-19 Therapies, Variants, and Viral Clearance Dynamics: Insights from a High-Risk Outpatients Study

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Introduction

Numerous approved drugs, including antiviral therapies and monoclonal antibodies (mAb), have demonstrated efficacy in preventing COVID-19 progression by targeting early stages of the disease in high-risk outpatients[1,2]. However, evidence supporting earlier swab negativization with early therapy remains limited, particularly concerning specific variants of concern (VoCs) and especially in the prevalent Omicron VoC context[3]. Our study aims to explore whether a particular early therapy targeting a specific sublineage of Omicron VoC is associated with an expedited time to achieve negative swab results for SARS-CoV-2.

Methods

This retrospective, observational study was conducted at Luigi Sacco Hospital in Milan from December 2021 to March 2023. The study focused on outpatients with confirmed COVID-19 diagnosis by positive SARS-CoV-2 RT-PCR on nasal swab, with data extracted from medical records. Demographic, virological, and clinical data were collected, including information on early treatments following guidelines provided by the Italian Medicines Agency. Whole genome sequencing was performed to identify Omicron sublineages, and cycle thresholds (Ct) were utilized to assess viral load dynamics. Statistical analyses were conducted to assess associations between treatment, sublineage, and swab negativization.

Results

Of 104 patients, most received antivirals (n=99, 95.2%), predominantly Paxlovid (51.9%). No patients required hospitalization or experienced mortality during the one-month follow-up period. Omicron sublineages BA.1 (22.1%), BA.2 (51%), and BA.4/BA.5 (26.9%) were detected among the patient cohort. However, no significant difference in swab negativization was observed across sublineages or treatment modalities. Trends suggested potential faster clearance in patients infected with non-BA.1 sublineages, but statistical significance was not reached.

Predictors	Estimates	95%CI†	p-value
(Intercept)	0.90	0.04; 1.76	0.041
Days	-0.06	-0.20; 0.07	0.371
Treatments-VoC			
Antiviral BA.1	Reference		
mAb†† BA.1	0.16	-1.65; 1.98	0.861
Antiviral BA.2 BN, XBB, OM4	-0.05	-1.07; 0.97	0.917
mAb BA.2 BN, XBB, OM4	0.08	-2.83; 3.00	0.955
Antiviral BA3,4,5, BE, BQ, BF	-0.11	-1.23; 1.00	0.841
Interaction terms			
Days*Antiviral BA.1	Reference		
Days*Antiviral BA.2 BN, XBB, OM4	0.03	-0.13; 0.19	0.739
Days*Antiviral BA3,4,5, BE, BQ, BF	0.03	-0.14; 0.21	0.717
Days*mAb¶ BA.1	0.00	-0.25; 0.26	0.975
Days*mAb BA.2 BN, XBB, OM4	0.01	-0.49; 0.51	0.974
Regression model analysis of deviance table. Terms added sequentially			
	Df†††	Deviance	F value	p-value
Null model	103	89.534		
Days	1	0.166	18.204	0.181
Groups	4	0.223	0.614	0.654
Days*Groups	4	0.016	0.045	0.996
Number of observations: 104				

Table 1. Interaction (symbol: *) between early treatments-VoC (Variant of Concern) and days between SARS-CoV-2 swabs. The Ct value is the dependent variable of the regression model.

† CI: confidence interval
†† mAb: monoclonal antibody
†††: degrees of freedom

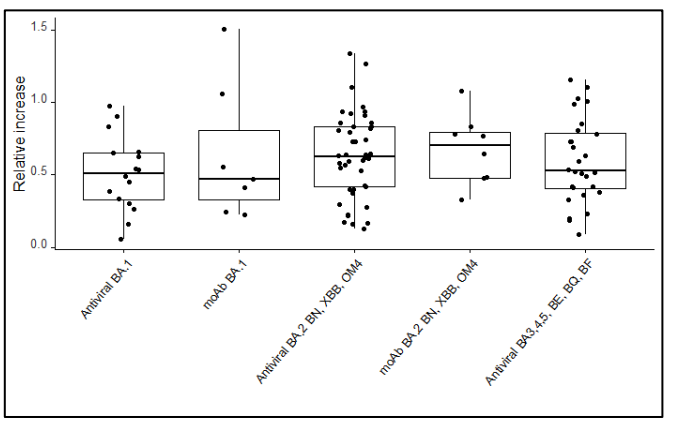

Figure 1. Boxplot of relative Ct value increase between the two times.

moAb: monoclonal Antibodies

Conclusion

In conclusion, while a subtle trend suggested potentially faster Ct growth in certain groups, the evidence is weak due to small sample size and lack of a definitive trend curve. Importantly, the study did not establish a significant association between specific therapies and swab conversion time, highlighting the intricate dynamics of viral clearance and the need for further research in larger cohorts to refine treatment protocols for high-risk COVID-19 patients.

References

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