Evaluation of Bebtelovimab for Treatment of COVID-19 During the SARS-CoV-2 Omicron Variant Era

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Running Head

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ABSTRACT

Background. Monoclonal antibody (mAb) treatment is associated with decreased risk of hospitalization and death in high-risk outpatients with mild to moderate COVID-19 caused by early SARS-CoV-2 variants. Bebtelovimab exhibits *in vitro* activity against the Omicron variant and its sublineages; however, clinical data are lacking.

Methods. A retrospective cohort study was conducted comparing bebtelovimab-treated patients to propensity score-adjusted and matched non-treated control groups. Participants included high-risk outpatients eligible for bebtelovimab treatment under Emergency Use Authorization with a positive SARS-CoV-2 test from March 30 to May 28, 2022. Treated patients received single-dose intravenous treatment with bebtelovimab. The primary outcome was hospitalization or death over 28 days.

Results. Prior to matching/statistical adjustment, mAb-treated patients were, on average, 10 years older than non-treated patients (61.6 vs. 51.3 years) and had higher prevalence of obstructive sleep apnea, hypertension, chronic kidney disease, cancer, organ or cell transplant, and immunocompromised status (standardized mean differences $\geq$0.20). The adjusted odds ratio (OR) of hospitalization or death comparing 1,006 treated to 2,023 non-treated patients was 0.50 (95% confidence interval (CI): 0.31-0.80). Among 930 treated and 930 propensity score matched non-treated patients, the incidence of hospitalization or death was 3.1% vs. 5.5%, respectively (conditional OR=0.53; 95% CI: 0.32-0.86). The lower odds ratio of hospitalization or death associated with bebtelovimab treatment was most evident in older patients, those with immunocompromised status, and fully vaccinated patients.

Conclusions. Monoclonal antibody treatment with bebtelovimab among COVID-19 outpatients is associated with lower odds of hospitalization or death, particularly among immunocompromised and older patients.

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INTRODUCTION

Monoclonal antibody (mAb) treatment has demonstrated decreased risk of hospitalization and death in at-risk outpatients with mild to moderate COVID-19 caused by early SARS-CoV-2 variants, as compared to patients who did not receive treatment [1-4]. As SARS-CoV-2 variants evolve and emerge, the United States (US) Food and Drug Administration (FDA) Emergency Use Authorizations (EUA) for mAb products change. Decisions for EUA modifications are often based on *in vitro* potency of mAbs alone, as randomized controlled trials and real-world clinical data are not available in real time. At the time of this report, bebtelovimab is the only mAb authorized for treatment of COVID-19 and is expected to maintain neutralizing activity against Omicron and its sublineages [5].

There is an absence of clinical data for use of bebtelovimab, and for any mAb product for use in patients infected with the Omicron variant and its sublineages. Due to this lack of clinical data, the NIH positions bebtelovimab as an alternative therapy for non-hospitalized adults with COVID-19 [6]. However, first-line therapies are plagued by drug-drug interactions (nirmaltrevir/ritonavir) and logistical challenges thwarting accessibility (3-day course of intravenous remdesivir); therefore, determining clinical effectiveness of bebtelovimab is important for public health. Additionally, there is a critical need for ongoing evaluation of individual mAb products as new variants emerge to test clinical effectiveness and determine patient populations who optimally benefit from treatment. Therefore, we assessed the real-world effectiveness of bebtelovimab treatment for outpatients with mild to moderate COVID-19 during the Omicron-variant era within a large U.S. healthcare system. We examined the association of bebtelovimab treatment overall with 28-day incidence of hospitalization or death, and stratified results by age, body mass index, immunocompromised status, and COVID-19 vaccination status.

METHODS

This was a retrospective cohort study of outpatients with COVID-19 who had at least one risk factor for progression to severe disease and were eligible for mAb treatment with bebtelovimab per the EUA. Patients treated with bebtelovimab were compared to non-treated control patients. All treated patients verbally consented to treatment with bebtelovimab and reviewed the FDA EUA Fact Sheet prior to treatment. Bebtelovimab treatment assignment occurred via a central management system overseen by a multidisciplinary COVID-19 Therapeutics Committee [7].

Patient Consent Statement

The Quality Improvement Review Committee and Institutional Review Board at the University of Pittsburgh provided ethical review and approval of the study as an exempt protocol that did not require patient written consent, and all data remained deidentified for this analysis.

Data Sources

Health-related data captured in the electronic health record (EHR) and ancillary clinical systems were aggregated and harmonized in a Clinical Data Warehouse (CDW) [1,8]. For treated patients and non-treated control patients, sociodemographic data, medical history, and billing charges were accessed for all outpatient and in-hospital encounters with diagnoses and procedures coded based on the International Classification of Diseases, Ninth and Tenth revisions (ICD-9 and ICD-10, respectively) [9,10]. Race was self-declared and classified as Black versus all others based on overall low minority prevalence. Death identification at 28-day used hospital discharge disposition of "Ceased to Breathe" sourced from the inpatient Medical Record System along with deaths after discharge identified with the Death Master File from the Social Security Administration 2022 National Technical Information Service [11,12]. A

description of definitions for variables used in the analysis, as captured in the EHR, is provided below and in **Appendix A**.

Selection of Patient Cohorts

Treated patients were those 12 years of age or older who received intravenous bebtelovimab (175 mg) during the period March 30 to May 28, 2022 in an outpatient infusion clinic for treatment of COVID-19. Patients were excluded if they were pregnant, received mAb treatment in an emergency department or hospital setting, or received mAb for post-exposure prophylaxis (**Figure 1**). Non-treated patients were identified as any non-pregnant patient 12 years of age or older with a positive SARS-CoV-2 polymerase chain reaction or antigen test within our health system and not treated with any mAb during the same time period. Patients had at least one EUA-eligible risk factor for progression to severe disease identified in the EHR on the day of the positive SARS-CoV-2 test result. Patients were excluded if they were hospitalized or in the emergency department on the day of their positive SARS-CoV-2 test result (**Figure 1**). After identifying patients with at least one health record in the EHR in the past year, both groups had complete covariate data other than for body mass index (509 missing cases, 16.7%).

Outcomes

The primary outcome was the incidence of hospitalization or death at 28 days, with secondary outcomes of 28-day hospitalization, death, emergency department (ED) visit without hospitalization, and the composite outcome ED visit/hospitalization. For treated patients, the 28-day follow-up period started on the day of mAb treatment. For non-treated controls, the 28-day follow-up period started the day after the SARS-CoV-2 test positive date, since the median time from test positive result to mAb treatment was one day (interquartile range 1-3 days).

Covariates

In addition to specific variables used in propensity score adjustment/matching (**Table 1**), key covariates in pre-specified subgroup analyses included: (i) age (years), classified as <65 vs. ≥65; (ii) body mass index (kg/m²), classified as ≤30 vs. >30; (iii) immunocompromised status, classified as no vs. yes; and (iv) COVID-19 vaccination status. Immunocompromised was defined from a range of conditions such as selected cancer diagnoses within the past year (e.g., leukemia), selected autoimmune disorders in the past year (e.g., lupus), and having an encounter in the UPMC health system within the past year and any prior history of transplant (**Appendix B**). Patients were classified as fully vaccinated when there was evidence in the EHR of at least two doses of an approved COVID-19 mRNA technology vaccine (e.g. Pfizer, Moderna) or single dose of an approved virus-based technology vaccine (e.g. Johnson & Johnson). Because many patients may have been vaccinated outside of the system, the subgroup of patients with documented evidence of being fully vaccinated (51.9% of all patients) is reported, and then all other patients with undetermined vaccination status (many of whom were likely vaccinated). Missing body mass index (16.7% of subjects) was imputed using the mean value for subjects with known values.

Statistical Methods

Sociodemographic and clinical characteristics between mAb treated and non-treated subjects (before and after matching) were compared using standardized mean differences (SMD). To calculate a propensity score (for treatment) for each patient [13,14], we fit a logistic regression model with treatment with bebtelovimab as the response variable and inclusion of explanatory variables measured at baseline (**Table 1)**. For each clinical outcome of interest (e.g. hospitalization or death), an indicator variable for treatment (yes/no) was the primary predictor

of interest in an unconditional (non-matched) logistic regression model, with inclusion of the propensity score to adjust for confounding. As a sensitivity analysis. confounding was also adjusted for in the unmatched analyses by use of inverse probability weighting. Results are presented as adjusted odds ratios (ORs). These approaches were used overall, and for the pre-specified subgroups of interests for the primary outcome of hospitalization or death.

In a matched cohort sensitivity analysis, non-treated control subjects were matched to treated subjects by propensity score methodology [13,14]. Specifically, 1:1 propensity score greedy nearest neighbor matching within caliper width of 0.20 was used to construct matched treated and non-treated groups [15]. From the matched groups, the 28-day incidence of patient outcomes were calculated with treated vs. non-treated comparisons of association estimated by use of conditional ORs and 95% confidence intervals [16]. The Kaplan-Meier method was used to plot survival curves for freedom from hospitalization or death by treatment status over follow-up. A third sensitivity analysis was conducted using conditional (matched) logistic regression analysis (described above) among patients with non-missing data on BMI. Analyses were conducted using the SAS System (Cary, NC), version 9.4. Methods and results follow The REporting of studies Conducted using Observational Routinely-Collected Health Data (RECORD) statement (**Appendix C**) [17].

RESULTS

Baseline Characteristics

The unmatched analysis cohort consisted of 1,006 treated patients and 2,023 non-treated controls (**Figure 1**). Of the 1,006 treated patients, 930 were individually matched 1:1 to non-treated control patients. Before 1:1 propensity score matching/adjustment, the mean (SD) age of

treated patients was 61.6 (17.3) years compared to 51.3 (20.6) years in non-treated controls (**Table 1**). Similarly, before matching, the overall risk profile was higher in treated patients compared to non-treated controls, including higher prevalence of obstructive sleep apnea, hypertension, chronic kidney disease, cancer, chemotherapy and being immunocompromised (all SMD $\geq$ 0.20). After 1:1 propensity score matching, treated patients were similar to non-treated patients on all variables (SMD values $\leq$0.07) except for a nominally higher prevalence of history of chemotherapy (8.2% vs. 4.7%, SMD=0.14) and immunocompromised status (25.1% vs. 20.9%, SMD=0.10) (**Table 1**). The mean (SD) propensity score probability (x 100) was 39.4 (16.2) in treated patients compared to 38.4 (15.1) in matched non-treated controls.

Outcomes

The crude overall 28-day incidence of hospitalization or death was 3.3% in treated patients compared to 3.5% in non-treated controls (**Table 2**). This corresponded to an unadjusted OR of 0.95. After statistical adjustment for the propensity score (i.e., higher risk profile of treated patients), the estimated odds of hospitalization or death were 50% lower in treated patients compared to non-treated controls (OR=0.50; 95% CI: 0.31 to 0.80). The corresponding adjusted OR for hospitalization was 0.66 (95% CI: 0.41 to 1.07), and there was only one death (0.1%) in the treated group compared to 13 deaths (0.6%) in the untreated group. Treatment with bebtelovimab was not associated with the adjusted odds of ED admission with or without hospitalization. Results across outcomes were similar with the use of inverse probability weighting.

Sensitivity Analyses. In the matched cohort analysis, the incidence of hospitalization or death was 3.1% in treated patients compared to 5.5% in non-treated controls, with a corresponding conditional OR of 0.53 (95% CI: 0.32 to 0.86) (**Table 3**). The divergence in

freedom from death or hospitalization in the direction favoring the treated group began at about day 4 of follow-up (**Supplement Figure 1**). The conditional OR for hospitalization was 0.68 (95% CI: 0.41 to 1.12) and there was one death (0.1%) in the treated group compared to 11 deaths (1.2%) in the matched untreated group. Thus, results were similar in the unmatched (adjusted) and matched cohort analyses. Results for the OR of hospitalization or death were also similar for the subgroup of patients with non-missing BMI data (COR = 0.52, 95% CI: 0.33 to 0.83).

Subgroup Analyses. There was evidence that the association between treatment with bebtelovimab and odds of hospitalization or death was modified by pre-defined subgroups (**Table 4**). Specifically, among patients less than 65 years of age, there was no association between treatment and odds of hospitalization or death (adjusted OR=1.03, 95% CI: 0.45 to 2.36), whereas there was a strong indication of lower odds in patients ages 65 and older (adjusted OR=0.37, 95% CI: 0.21 to 0.63). There was no indication that the overall lower odds of hospitalization or death in treated patients was modified by obesity status.

Treatment with bebtelovimab was associated with a particularly low odds of hospitalization or death in patients with immunocompromised status (adjusted OR=0.24, 95% CI: 0.11 to 0.50) and those who were fully vaccinated (adjusted OR=0.26, 95% CI: 0.13 to 0.51). Results were similar with the use of inverse probability weighting. In post-hoc subgroup analyses, there was an indication of substantially lower odds of hospitalization or death in immunocompromised patients who were fully vaccinated (adjusted OR=0.19, 95% CI: 0.07 to 0.48), as well as immunocompromised patients with undetermined vaccinations status (adjusted OR=0.39, 95% CI: 0.12 to 1.29).

The absence of treatment association in patients under the age of 65 years and in those with undetermined vaccination status appeared to be driven by very low rates of hospitalization or death in the control group of non-treated patients (1.4% and 2.8%, respectively). In supplemental analyses, patients with undetermined vaccination status were less likely to have received chemotherapy (1.9% vs. 7.5%) or be immunocompromised (11.8% vs. 22.6%) than patients who were fully vaccinated (i.e. lower overall risk).

DISCUSSION

In this analysis, treatment with bebtelovimab was associated with lower odds of hospitalization or death in propensity-score adjusted and matched cohorts during a time period when the Omicron variant and its sublineages predominated. Patients aged 65 years and older, those with immunocompromised status, and those who were fully vaccinated had the lowest odds of hospitalization or death associated with bebtelovimab therapy, whereas OR estimates were not modified by body mass index.

Bebtelovimab was authorized for use in February 2022 as *in vitro* data emerged suggesting previously approved mAbs would be ineffective at neutralizing certain Omicron sublineages, whereas bebtelovimab retained *in vitro* activity against all known variants [18]. This *in vitro* activity has since been confirmed; however, clinical data are lacking [5]. To our knowledge, this study represents the first large observational analysis of bebtelovimab treatment among a heterogeneous group of patients with COVID-19 assumed to be infected with the Omicron variant or an Omicron sublineage [19], and that includes a non-treated matched cohort. A small study of 25 solid organ transplant recipients treated with bebtelovimab suggested a possible treatment benefit with mAb therapy [20], and a larger retrospective cohort study of adult

solid organ transplant recipients treated with either bebtelovimab (n=92) or sotrovimab (n=269) reported similar 30-day rates of hospitalization (~3%) [21]. Our 28-day rate of hospitalization (3.3%) in bebtelovimab treated patients is consistent with the latter study. Throughout the pandemic, some therapies with *in vitro* activity against SARS-CoV-2 have failed to demonstrate clinical benefit; therefore, our data are important for public health by providing reassurance that current *in vitro* assessments of mAbs seemingly track with clinical assessments of effectiveness.

This analysis shows evidence of substantially lower 28-day adjusted OR of hospitalization and death among patients 65 years of age or older and/or immunocompromised patients treated with bebtelovimab compared to no treatment. Patients who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications and/or who may not mount an adequate immune response to COVID-19 vaccination are at high risk of severe SARS-CoV-2 infection and complications. Accordingly, the NIH prioritizes these individuals for mAb treatment during times of scarcity. Our results support continued prioritization of these patients, which occurred intermittently throughout the pandemic at our health system during times of staff or drug shortages (explaining the difference in age and immunocompromised status in the unmatched cohort). Importantly, the lower odds of death or hospitalization among bebtelovimab treated patients was statistically significant despite a nominally higher prevalence of immunocompromised patients in the treated group after matching, and relatively low event rates in the non-treated cohort. These results are consistent with previous data describing an overall lower rate of hospitalization during the Omicron period as compared to the Delta time period [22].

In this study, there was no association between bebtelovimab treatment and 28-day odds of hospitalization or death in patients with unknown vaccination status, which was in contrast to

patients known to be fully vaccinated who had a much lower OR of hospitalization or death with bebtelovimab treatment. Multiple potential explanations exist for this finding. First, the 28-day incidence of hospitalization or death was only 2.8% in non-treated controls with undetermined vaccinated status, and patients with undetermined vaccinated status had a generally lower risk profile than fully vaccinated patients. Thus, the apparent absence of treatment association may simply reflect low overall risk in this subcohort of patients with undetermined vaccination status. Second, "fully vaccinated" was defined as at least two mRNA vaccines or a single dose of an approved virus-based technology vaccine. This definition did not consider or require receipt of a third dose of an mRNA vaccine, which is now considered the primary series for an immunocompromised patient, or receipt of vaccine booster shots (consistent with more recent definitions of "fully" vaccinated). There is evidence that vaccination alone may be insufficient to mount protection against SARS-CoV-2 among immunocompromised and/or patients with advanced age; therefore, fully vaccinated in this population may be less protective against disease than patients without comorbidities [23]. Finally, "fully vaccinated" status may be an indicator of patients more likely to access healthcare with overlap with elderly and immunocompromised patients.

Assessment of existing and new mAb products is paramount, including continuous appraisal of selected patient populations most likely to benefit from treatment. Given the speed of SARS-CoV-2 mutations, the conduct of conventional randomized controlled trials may be impractical, thereby necessitating analyses from large observational cohorts. Nonetheless, our observational study has several limitations.

First, matching of non-treated controls used EUA-eligible risk factors only, and we were unable to determine the time from symptom onset to SARS-CoV-2 test positive result or

symptom severity (whether symptomatic or asymptomatic) of patients. We postulate that many non-treated patients may have been asymptomatic (i.e. due to routine SARS-CoV2 testing or incidental findings) and thereby at low risk of hospitalization, which would tend to bias results against mAb treatment. Second, as previously stated, we were unable to determine vaccination status (including booster status) in all patients and the definition of "fully vaccinated" has changed dramatically with updated dosing schedules and authorization of additional vaccines. Third, receipt of tixagevimab/cilgavimab was not assessed, and we were unable to assess other treatments outside of our health system for control (untreated) patients, although, 3-day remdesivir was not offered by UPMC or any other regional hospital. Fourth, Omicron and its sublineages were the dominant SARS-CoV-2 variant(s) during the study period, yet no patient-specific genotype sampling was conducted. Fifth, our definition of "immunocompromised" is broad with multiple qualifying conditions. Sixth, hospitalizations that may have occurred outside the UPMC system are not captured in the present analyses. Finally, we cannot rule out potential residual confounding of the estimated mAb treatment effects despite our close propensity score matching of treated patients and non-treated "mAb eligible" controls.

CONCLUSIONS

In this cohort study of outpatients with COVID-19 during an Omicron variant period, treatment with bebtelovimab was associated with a significantly lower odds of hospitalization or death. Results indicate that outpatient use of bebtelovimab should be prioritized for older adults and those who are immunocompromised.

Reproducible Research Statement. Study protocol: No separate study protocol was required, *a priori*, as this retrospective analysis was deemed a quality improvement initiative with ethical review and approval granted by the UPMC Quality Improvement Review Committee and Institutional Review Board. Statistical code: Selected statistical code may be requested by contacting by Dr. Kip at: kipke2@upmc.edu. Data set: The data set contains protected health information and will not be available upon request.

ARTICLE INFORMATION

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Author Contributions

Dr. Kip and Dr. Marroquin take full responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Kip, Marroquin, McCreary

Acquisition of data: Collins, Marroquin, McCreary, Kip

Interpretation of data: All authors

Drafting of the manuscript: Kip, Marroquin

Critical revision of the manuscript for important intellectual content: All authors

Study supervision: Kip, Marroquin, McCreary

Potential Conflicts of Interest

No authors report disclosures, conflict of interest or relevant financial interests related to the content of the manuscript.

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FIGURE LEGEND

Figure 1.

CONSORT diagram of selection of treated and non-treated control patients for analysis. mAb: Monoclonal antibodies. EHR: Electronic health record. ED: Emergency department.

APPENDICES

Appendix A. Listing of Variables Used in the Propensity Score Model (Table 1) and Method Defined in the Electronic Health Record (EHR)

Appendix B. Conditions Used to Define Patients as Immunocompromised

Appendix C. RECORD Statement Checklist

6 **Table 1. Comparison of Characteristics in Treated and Nontreated Groups**

7

Characteristic	Unmatched			Matched		
	Treated (N=1006)	Nontreated (N=2023)	SMD	Treated (N=930)	Nontreated (N=930)	SMD
Age, mean (SD)	61.6 (17.3)	51.3 (20.6)	0.53	61.2 (17.5)	62.2 (18.3)	0.05
Female sex, No. (%)	620 (61.6)	1298 (64.2)	0.05	575 (61.8)	571 (61.4)	0.01
Black race, No. (%)	46 (4.6)	161 (8.0)	0.13	42 (4.5)	30 (3.2)	0.07
Area deprivation index >=85, No. (%)	51 (5.1)	156 (7.7)	0.10	47 (5.1)	42 (4.5)	0.03
Body mass index, mean (SD)	31.0 (6.0)	31.3 (7.2)	0.12	31.0 (5.9)	31.6 (6.9)	0.02
History of diabetes, No. (%)	222 (22.1)	304 (15.0)	0.18	198 (21.3)	200 (21.5)	0.01
History of obstructive sleep apnea, No. (%)	232 (23.1)	291 (14.4)	0.22	199 (21.4)	198 (21.3)	0.00
History of hypertension, No. (%)	572 (56.9)	804 (39.7)	0.35	515 (55.4)	499 (53.7)	0.03
History of stroke, No. (%)	88 (8.7)	130 (6.4)	0.09	82 (8.8)	78 (8.4)	0.02
History of valvular heart disease, No. (%)	93 (9.2)	120 (5.9)	0.12	83 (8.9)	86 (9.2)	0.01
History of atrial fibrillation, No. (%)	118 (11.7)	138 (6.8)	0.17	110 (11.8)	104 (11.2)	0.02
History of congestive heart failure, No. (%)	107 (10.6)	121 (6.0)	0.17	90 (9.7)	86 (9.2)	0.01
History of chronic kidney disease, No. (%)	134 (13.3)	146 (7.2)	0.20	108 (11.6)	116 (12.5)	0.03
History of dyspnea, No. (%)	77 (7.7)	129 (6.4)	0.05	71 (7.6)	73 (7.8)	0.01
History of COPD, No. (%)	224 (23.3)	313 (15.5)	0.17	199 (21.4)	187 (20.1)	0.03
History of bronchiectasis, No. (%)	7 (0.7)	5 (0.2)	0.07	6 (0.6)	4 (0.4)	0.03
History of pulmonary hypertension, No. (%)	24 (2.4)	29 (1.4)	0.07	19 (2.0)	15 (1.6)	0.03
History of pulmonary fibrosis, No. (%)	1 (0.1)	6 (0.3)	0.04	1 (0.1)	0 (0.0)	0.05
History of fatty liver disease, No. (%)	46 (4.6)	55 (2.7)	0.10	41 (4.4)	35 (3.8)	0.03
History of cirrhosis, No. (%)	17 (1.7)	14 (0.7)	0.09	13 (1.4)	12 (1.3)	0.01
History of gastrostomy, No. (%)	1 (0.1)	2 (0.1)	0.00	1 (0.1)	1 (0.1)	0.00
History of cancer, No. (%)	207 (20.6)	205 (10.1)	0.29	171 (18.4)	153 (16.5)	0.05
History of chemotherapy, No. (%)	99 (9.8)	47 (2.3)	0.32	76 (8.2)	44 (4.7)	0.14
History of lung cancer, No. (%)	7 (0.7)	11 (0.5)	0.02	6 (0.6)	3 (0.3)	0.05

History of allergic rhinitis, No. (%)	162 (16.1)	301 (14.9)	0.03	151 (16.2)	137 (14.7)	0.04
History of rheumatoid arthritis, No. (%)	62 (6.2)	52 (2.6)	0.18	56 (6.0)	46 (4.9)	0.05
History of sarcoidosis, No. (%)	9 (0.9)	4 (0.2)	0.09	6 (0.6)	4 (0.4)	0.03
History of lupus, No. (%)	24 (2.4)	11 (0.5)	0.15	17 (1.8)	11 (1.2)	0.05
History of viral hepatitis, No. (%)	20 (2.0)	25 (1.2)	0.06	18 (1.9)	18 (1.9)	0.00
History of organ or cell transplant, No. (%)	31 (3.1)	3 (0.1)	0.23	5 (0.5)	3 (0.3)	0.03
History of bone marrow transplant, No. (%)	3 (0.3)	3 (0.1)	0.03	2 (0.2)	1 (0.1)	0.03
History of immunocompromised, No. (%)	301 (29.9)	227 (11.2)	0.48	233 (25.1)	194 (20.9)	0.10
Alpha blocker, No. (%)	21 (2.1)	22 (1.1)	0.08	18 (1.9)	17 (1.8)	0.01
ACE Inhibitors, No. (%)	170 (16.9)	279 (13.8)	0.08	158 (17.0)	165 (17.7)	0.02
Angiotensin II receptor blocker, No. (%)	166 (16.5)	191 (9.4)	0.21	151 (16.2)	151 (16.2)	0.00
Beta blockers, No. (%)	320 (31.8)	446 (22.0)	0.22	285 (30.6)	277 (29.8)	0.02
Corticosteroids as a home medication, No. (%)	427 (42.4)	677 (33.5)	0.18	385 (41.4)	378 (40.6)	0.02
Statins, No. (%)	481 (47.8)	631 (31.2)	0.34	435 (46.8)	448 (48.2)	0.03
Antidepressants, No. (%)	346 (34.4)	628 (31.0)	0.07	318 (34.2)	313 (33.7)	0.01

Abbreviations: SD, standard deviation; SMD: standardized mean difference presented as absolute value. COPD, chronic obstructive pulmonary disease; ACE, angiotensin -converting enzyme. SMD values are presented as absolute values. All variables were used in the propensity score model.

Table 2. 28-Day Outcome Risks and Odds Ratios by Treatment vs. Non-Treatment with Bebtelovimab (Unmatched Cohort)

	Not Treated		Treated			Adjusted Analyses					
Outcome	N	n (%)	N	n (%)	Unadj. OR	PS adj. OR	95% CI	p-value	IPW OR	95% CI	p-value
Hospitalization/Death	2023	70 (3.5)	1006	33 (3.3)	0.95	0.50	0.31 – 0.80	0.004	0.57	0.38 – 0.84	0.005
Hospitalization	2023	58 (2.9)	1006	33 (3.3)	1.15	0.66	0.41 – 1.07	0.09	0.72	0.48 – 1.09	0.12
Death	2023	13 (0.6)	1006	1 (0.1)	0.15	0.05	0.01 – 0.42	0.006	0.08	0.01 – 0.51	0.008
ED admission/No hospitalization	2023	65 (3.2)	1006	46 (4.6)	1.44	1.14	0.75 – 1.74	0.53	1.06	0.74 – 1.53	0.74
ED admission/Hospitalization	2023	118 (5.8)	1006	76 (7.6)	1.32	0.90	0.65 – 1.25	0.52	0.91	0.68 – 1.20	0.49

OR: Odds ratio; CI: Confidence interval; Unadj: Unadjusted; PS: Propensity score adjustment as a continuous variable; IPW: Inverse probability weighting.

Table 3. Risks and Conditional Odds Ratios of 28-Day Outcomes by Treatment vs. Non-Treatment with Bebtelovimab (Matched Cohort)

	Not Treated		Treated			Conditional Matched Analysis*			
Outcome	**N**	**n (%)**	**N**	**n (%)**	**OR**	**pairs in analysis**	**Conditional OR**	**95% CI**	***p*-value**
Hospitalization/Death	930	51 (5.5)	930	29 (3.1)	0.55	74	0.53	0.32 – 0.86	0.01
Hospitalization	930	41 (4.4)	930	29 (3.1)	0.70	66	0.68	0.41 – 1.12	0.13
Death	930	11 (1.2)	930	1 (0.1)	0.09	12	0.09	0.01 – 0.70	0.02
ED admission/No hospitalization	930	35 (3.8)	930	41 (4.4)	1.18	76	1.24	0.77 – 2.01	0.38
ED admission/Hospitalization	930	72 (7.7)	930	67 (7.2)	0.93	127	0.94	0.66 – 1.35	0.75

OR: Odds ratio; CI: Confidence interval; The number of pairs in the analysis represents the number of matched pairs (treated vs. not-treated) with discordant outcomes. *The model includes adjustment for immunocompromised status and history of chemotherapy.

Table 4. Subgroup Analyses of 28-Day Risk and Odds Ratios of Hospitalization or Death by Treatment vs. Non-Treatment with Bebtelovimab (Unmatched Cohort)

	Not Treated		Treated			Adjusted Analyses					
Subgroup	N	n (%)	N	n (%)	Unadj. OR	PS adj. OR	95% CI	p-value	IPW OR	95% CI	p-value
Age											
Less than 65 years	1435	20 (1.4)	470	13 (2.8)	2.01	1.03	0.45 – 2.36	0.95	1.09	0.55 – 2.14	0.81
65 Years and older	588	50 (8.5)	536	20 (3.7)	0.42	0.37	0.21 – 0.63	<0.001	0.38	0.22 – 0.62	<0.001
Body mass index											
30 or less	877	35 (4.0)	378	16 (4.2)	1.06	0.53	0.27 – 1.05	0.07	0.60	0.34 – 1.07	0.08
More than 30	902	32 (3.5)	365	14 (3.8)	1.08	0.56	0.27 – 1.13	0.11	0.69	0.39 – 1.22	0.20
Immunocompromised											
No	1796	43 (2.4)	705	20 (2.8)	1.19	0.85	0.48 – 1.50	0.57	0.92	0.56 – 1.52	0.76
Yes	227	27 (11.9)	301	13 (4.3)	0.33	0.24	0.11 – 0.50	<0.001	0.25	0.12 – 0.51	<0.001
Vaccination status											
Fully vaccinated	957	40 (4.2)	616	15 (2.4)	0.57	0.26	0.13 – 0.51	<0.001	0.29	0.16 – 0.53	<0.001
Not determined	1066	30 (2.8)	390	18 (4.6)	1.67	1.07	0.56 – 2.06	0.84	1.14	0.66 – 1.96	0.63

OR: Odds ratio; CI: Confidence interval; Unadj: Unadjusted; PS: Propensity score adjustment as a continuous variable; IPW: Inverse probability weighting.

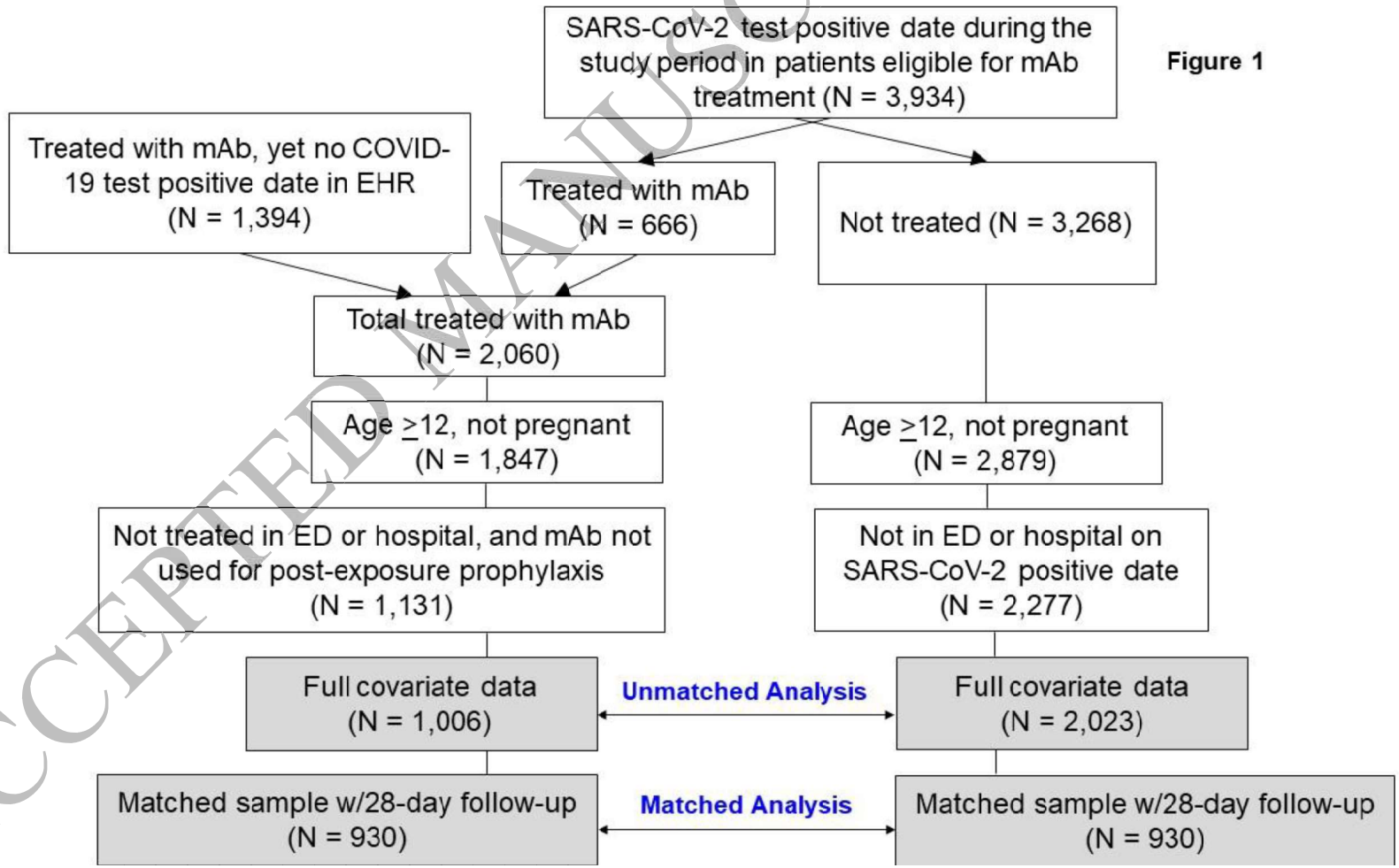

Figure 1

Figure 1
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