



Hospital Length of Stay for Patients with Severe COVID-19: Implications for Remdesivir's Value

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1 Introduction

In June 2020, the Gilead Sciences chief executive officer announced that US hospitals would be charged \$US3120 for a course of remdesivir for the treatment of coronavirus 2019 (COVID-19), a price roughly 33% higher than that the company plans to charge other high-income countries [1]. The sole justification offered was that remdesivir would save hospitals \$US12,000 per patient by shortening hospital length of stay (LOS) by 4 days. This presumed benefit was extrapolated from the ACTT-1 trial, which found median time to recovery (an approximation of median time to hospital discharge) of 11 days in patients receiving remdesivir versus 15 days in those receiving placebo [2].

However, to be used as justification for such a high price, it is critical that the ACTT-1 finding is robust. It may not be, either because patients who were expected to be discharged within 72 h were excluded from the trial or because the outcomes of the study population are not generalizable. A subsequent open-label, adaptive, randomized trial failed to demonstrate a significant reduction in hospital LOS with remdesivir treatment [3]. Remdesivir is a 5-day treatment and can only be administered during an inpatient stay. Hospital stays that would otherwise be 5–8 days could be shortened with remdesivir therapy, but by fewer than 4 days. Patients who would otherwise be discharged in fewer than 5 days could not experience any reduction in LOS and might

instead have their hospital stay prolonged to complete their treatment course. An open-label randomized trial of remdesivir demonstrated a peak in discharge rates upon completion of therapy, suggesting that physicians actually delayed discharge to complete treatment [4]. Remdesivir's US FDA approval does not limit its use based on LOS and specifies that intravenous remdesivir be given in an in-patient setting [5, 6]. We assessed what percentage of patients with severe COVID-19 belonged to each of these LOS groups in a real-world cohort prior to the FDA's emergency use authorization of remdesivir.

2 Methods

Our study cohort consisted of adults aged ≥ 18 years with severe COVID-19 consecutively hospitalized from the emergency department (ED) at New York-Presbyterian Columbia University Irving Medical Center and the Allen community hospital between March 9 and April 23, 2020, with follow-up through June 10, 2020. Data abstraction methods have been published previously [7, 8]. We defined severe COVID-19 based on remdesivir trial and FDA criteria: an initial oxygen saturation $\leq 94\%$ on room air or the use of any supplemental oxygen within 24 h of ED presentation [2, 9]. LOS was measured from presentation to death or hospital discharge.

3 Results

In total, 1643 adults were admitted with severe COVID-19, after excluding 21 (1%) who were discharged in < 9 days to another hospital. The median age was 67 years (interquartile range 56–78), a majority were Hispanic or Black and had one or more comorbidity, 12% required mechanical ventilation within 24 h, median LOS was 7 (3–14) days, and in-hospital 28-day mortality was 26%. In total, 586 patients

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Table 1 Baseline characteristics by hospital length of stay

Characteristics	Length of stay			p value
	1–4 days (n=586)	5–8 days (n=384)	≥9 days (n=673)	
Age, years	68 (55–80)	68 (57–79)	67 (56–75)	0.03
Sex, male	325 (55)	212 (55)	424 (63)	0.008
Race/ethnicity				0.67
White non-hispanic	44 (8)	33 (9)	63 (9)	
Black non-hispanic	60 (10)	41 (11)	78 (12)	
Hispanic	318 (54)	198 (52)	329 (49)	
Other	83 (14)	65 (17)	104 (15)	
Declined	81 (14)	47 (12)	99 (15)	
Comorbidities				
Asthma/COPD	84 (14)	70 (18)	125 (19)	0.10
Hypertension	297 (51)	194 (51)	339 (50)	0.99
Chronic kidney disease	79 (13)	79 (21)	123 (18)	0.009
Cancer	53 (9)	42 (11)	102 (15)	0.003
Smoking	42 (7)	52 (14)	83 (12)	0.002
Diabetes	209 (36)	153 (42)	280 (42)	0.045
Pulmonary heart disease	33 (6)	24 (6)	45 (7)	0.74
Comorbidities	1 (0–2)	1 (0–3)	1 (0–3)	0.005
Participation in remdesivir trial ^a	7 (1)	3 (1)	35 (5)	<0.001
Discharge disposition				<0.001
Home	356 (61)	238 (62)	219 (33)	
Rehabilitation center	35 (6)	47 (12)	190 (28)	
Death	168 (29)	81 (21)	173 (26)	
Hospice	27 (5)	18 (5)	30 (4)	
Transferred to other hospital	0 (0)	0 (0)	8 (1)	
Hospitalized at study completion	0 (0)	0 (0)	53 (8)	

Values are presented as n (%) or median (interquartile range). P values were calculated using the Kruskal–Wallis or Chi-squared tests

COPD chronic obstructive pulmonary disease

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(36%) had a LOS of 1–4 days, 384 (23%) had a LOS of 5–8 days, and 673 (41%) were hospitalized for ≥9 days (Table 1). The distribution was similar when patients who died during their hospital stay were excluded (Table 1). The majority of those with a LOS of 1–4 or 5–8 days were aged ≥60 years (67% and 70%, respectively; Fig. 1).

4 Discussion

In our cohort, the median LOS was markedly shorter than the equivalent endpoint in the ACTT-1 trial (7 vs. 15 days). This difference raises immediate questions as to whether remdesivir could reduce LOS by the 4 days used to justify the treatment's price. We found that only 41% of patients could both receive a 5-day course of remdesivir and have

LOS shortened by 4 days or more, whereas 36% could have their LOS potentially prolonged to complete therapy.

Our evaluation is relevant to the extent that our older-adult multimorbidity-predominant cohort is representative of those with severe COVID-19; LOS may be even shorter in younger and healthier populations. Our data are from patients hospitalized before dexamethasone became standard of care. Some patients may be prescribed 10 rather than 5 days of remdesivir, which could further prolong LOS (both durations are authorized by the FDA). Whether physicians will keep patients who otherwise could be discharged to complete treatment could not be determined, but evidence suggests this will occur [4].

Re-evaluating remdesivir's pricing, studying shorter remdesivir treatment courses, developing intranasal remdesivir [10], and implementing programs to facilitate outpatient intravenous remdesivir administration should be considered.

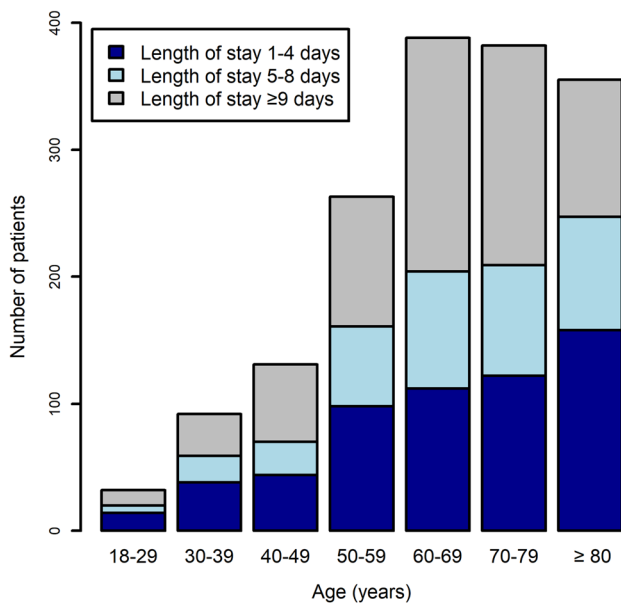


Fig. 1 Frequency histogram by age groups for hospital length of stay among patients with severe coronavirus 2019 with hospital length of stay of 1–4 days ($n=586$ [36%]), 5–8 days ($n=384$ [23%]), and ≥ 9 days ($n=673$ [41%])

Declarations

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Data availability Data sharing would be considered with appropriate institutional review board approval.

Ethics approval Columbia University IRB#AAAS9982.

Consent Not applicable.

Code availability Code is available upon reasonable request.

Author contributions MRA and MRB had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design, drafting of the manuscript, and critical revision of the manuscript for important intellectual content: MRA, PBB, MRB. Acquisition, analysis, and interpretation of data and statistical analysis: MRA, MRB.

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