Cost-effectiveness of casirivimab/imdevimab in patients with COVID-19 in the ambulatory setting

Nick Jovanoski, PhD; Andreas Kuznik, PhD; Ursula Becker, MSc; Mohamed Hussein, PhD; Andrew Briggs, DPhil

Plain language summary

Patients who have mild symptoms of COVID-19 at home may develop more serious illness that might lead to hospitalization and possibly death. A new treatment, casirivimab/imdevimab, has been shown to prevent the illness becoming worse and can reduce the need to go to the hospital. This study shows that for most patients with COVID-19, the money spent on casirivimab/imdevimab is a good use of the health care budget.

Implications for managed care pharmacy

Casirivimab/imdevimab is a new treatment that has been shown, in a large clinical trial, to reduce the risk of hospitalization in ambulatory patients with mild to moderate COVID-19. The treatment has been shown to be cost-effective by reducing the risk of developing more severe illness that may require hospitalization. Accordingly, managed care pharmacy organizations may want to not only limit access barriers for this medication but also consider initiating strategies or programs to proactively increase its use.

Author affiliations

F Hoffman-La Roche Ltd, Basel, Switzerland (Jovanoski); Regeneron Pharmaceuticals, Inc., Tarrytown, NY (Kuznik); F Hoffman-La Roche Ltd, Basel, Switzerland (Becker); Regeneron Pharmaceuticals, Inc., Tarrytown, NY (Hussein); London School of Hygiene & Tropical Medicine, London, UK (Briggs).

AUTHOR CORRESPONDENCE:
Nick Jovanoski, +41.79.909.4704;
nick.jovanoski@roche.com

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ABSTRACT

BACKGROUND: Most patients infected with SARS-CoV-2, resulting in COVID-19, have only mild symptoms that can be managed in an ambulatory setting. However, a significant number of patients develop a more severe form of the disease and require hospital care, with the risk of long-term sequelae or death. Casirivimab/imdevimab is a combination of 2 recombinant human monoclonal antibodies that has been shown to significantly reduce the risk of hospitalization or death in patients with mild to moderate COVID-19 in the ambulatory setting.

OBJECTIVE: To establish the cost-effectiveness of casirivimab/imdevimab in ambulatory individuals with COVID-19.

METHODS: A cost-effectiveness model was constructed to simulate the natural history of COVID-19 in ambulatory patients and to

identify those patients for whom casirivimab/imdevimab may be a cost-effective treatment from a US payer perspective. Patients enter the model in the ambulatory health state and can receive either active treatment with casirivimab/imdevimab or usual care. Patients can either recover from the infection or be hospitalized, from where they can recover from infection or die. Following this acute phase, patients enter a Markov model to estimate lifetime quality-adjusted life years. The model uses the risk of hospitalization in both the active treatment and usual care cohorts, and age- and sex-specific risk of mortality. Other model inputs include hospitalization costs and health-related utilities in the ambulatory acute treatment phase, the hospitalized setting, and the post-acute phase. Accounting for the heterogeneity of risk by age and comorbidities, results are presented separately for various combinations of baseline age and usual care risk in a 7×9

matrix. Outcomes related to “long COVID” are assessed in scenario analyses.

RESULTS: In the base case, at a willingness-to-pay threshold of \$100,000, treatment with casirivimab/imdevimab was found to be cost-effective in most patients, including those older than 40 years of age with a baseline hospitalization risk greater than or equal to 2% and patients aged 20 years with a baseline risk of hospitalization greater than or equal to 4%, whereas for hospitalization risk greater than or equal to 10%, casirivimab/imdevimab is dominant. Casirivimab/imdevimab was not cost-effective in patients aged 20 years with a 3% or lower risk of hospitalization or in patients aged 30 years with a 2% risk.

CONCLUSIONS: This economic analysis found that casirivimab/imdevimab is a cost-effective treatment for most ambulatory patients with COVID-19.

The COVID-19 pandemic, due to infection with SARS-CoV-2, has had devastating effects worldwide. By January 2022, the COVID-19 pandemic had resulted in more than 330 million confirmed cases and 5.5 million deaths globally, with approximately 65 million confirmed cases and more than 850,000 deaths in the United States alone.¹

The natural history of COVID-19 is heterogeneous. After becoming infected with SARS-CoV-2, most patients either are asymptomatic or have only mild symptoms that can be managed in an ambulatory setting. However, some patients develop a more severe form of the disease and require hospital care.^{2,3} In a subset of these patients, more severe disease and hypoxemia develops, necessitating oxygen therapy or ventilatory assistance, which creates a high demand for long-term hospital care in comparison with the general population.^{4,5}

Current evidence suggests that risk factors for severe COVID-19 include older age, male sex, and comorbidities such as cardiovascular disease, lung disease, hypertension, diabetes, or obesity,^{6,7} and race or ethnicity and socioeconomic status have a substantial effect on burden of disease, morbidity, and mortality.⁸

Emerging reports suggest that for some individuals the symptoms of COVID-19 also persist beyond the acute phase.^{9,10} These delayed or long-term complications of COVID-19 are increasingly being recognized and are associated with considerable morbidity. The term *post-acute COVID-19 syndrome*, which we denote here as “long COVID,” characterized by the persistence of clinical symptoms and/or long-term organ damage beyond 4 weeks from the onset of acute symptoms of COVID-19, has been described in a substantial proportion of patients who have recovered from the acute infection.^{9,11-14} The prevalence of residual symptoms has been reported to be approximately 35% in patients treated for COVID-19 on an outpatient basis but around 87% among cohorts of hospitalized patients.¹⁵

Several therapeutic options, such as antiviral agents, immunomodulators, glucocorticoids, and convalescent plasma, have been investigated for patients hospitalized with COVID-19, yet there have been few large randomized controlled trials of targeted treatments that are able to attenuate disease progression in patients with early acute disease.^{16,17} However, blockade of host cell entry through the use of neutralizing monoclonal antibodies against the spike protein receptor-binding domain of SARS-CoV-2 has been shown to provide an effective mechanistic strategy to reduce viral replication.^{18,19}

The combination of 2 recombinant human immunoglobulin G1 monoclonal antibodies, casirivimab and imdevimab, was developed to target the receptor-binding domain of the spike protein of SARS-CoV-2. A pivotal, double-blind, phase

3 trial investigating the efficacy and safety of casirivimab/imdevimab in ambulatory patients with mild to moderate COVID-19 showed that the combination significantly reduced the risk of hospitalization or death by more than 70% compared with placebo.²⁰ Casirivimab/imdevimab received US Food and Drug Administration emergency use authorization in November 2020 for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct viral testing who are at high risk for progressing to severe COVID-19, including hospitalization or death.^{19,21}

The COVID-19 pandemic has resulted in a global socioeconomic burden and has had a significant impact on health-related quality of life, functional decline, and long-term morbidity and mortality.²²⁻²⁴ Although a recent study reported a cost-effectiveness evaluation of treatments for patients hospitalized with COVID-19 from both a US health payer and societal perspective,²⁵ we are not aware of any studies that investigate the economic effects of early treatment of patients with mild to moderate COVID-19 in the ambulatory setting.

The objectives of this study were to assess the cost-effectiveness of casirivimab/imdevimab relative to usual care in ambulatory patients with mild to moderate COVID-19 from the US payer perspective and to provide an illustration of the population of patients for whom treatment with casirivimab/imdevimab is cost-effective.

Methods

MODEL DESIGN

A decision-analytic model was constructed in Microsoft Excel (version 2016) to simulate the natural history of COVID-19 in patients who initiate treatment in an ambulatory setting. The model uses a short-term decision tree and long-term Markov model, similar to the model previously published by the Institute for Clinical and Economic Review (ICER), but uses a modified structure, as the original ICER model estimated the cost-effectiveness of remdesivir in hospitalized patients with moderate to severe COVID-19,²⁶ rather than in patients with mild to moderate disease in an ambulatory setting.

Our model comprises 2 parts—a decision tree consisting of 2 treatment settings (ambulatory and hospitalized) and 2 outcomes, recovered or dead, and a Markov model consisting of 3 health states that reflect the outcomes in the decision tree (Figure 1). To ensure that the results of this analysis are most relevant to decision makers, the model includes an additional matrix of incremental

FIGURE 1 Cost-Effectiveness Model Structure

In the base case, the proportion of patients with no health issues is set to 100% in all Markov simulations. In scenario analyses, the proportion of patients with moderate and severe health issues is set at 10% and 10%, respectively, but only in the Markov simulation after hospitalization.

cost-effectiveness ratios as a function of hospital admission risk and age.

DECISION TREE: ACUTE PHASE

The **acute phase** of COVID-19 is modeled through the decision tree in which casirivimab/imdevimab is assessed against placebo, in addition to a background of usual care (which was also allowed in the treatment arm). Patients enter the model in the ambulatory health state and can receive either active treatment with casirivimab/imdevimab or usual care. Patients can either recover from the infection without new health issues or be hospitalized. These new health issues can be caused either directly by the infection or indirectly by the treatment, which was necessary (eg, invasive ventilation).

In the model base case, hospitalized patients can either recover without new health issues or die. The model stratifies hospitalized patients by oxygen support to account for differences in the risk of death and treatment costs that they may confront, using an estimate of the proportion of patients who receive no oxygen support, supplemental oxygen, noninvasive ventilation or high-flow oxygen, and mechanical ventilation or extracorporeal membrane oxygenation on hospitalization from the Adaptive COVID-19 Treatment Trial (ACTT-1; Table 1).²⁷

DAYS WITH SYMPTOMS/LENGTH OF HOSPITALIZATION

The model uses the number of days with and without symptoms to calculate the quality of life of patients who do not become hospitalized in the acute phase. In addition, the model uses data on the length of hospitalization by levels of oxygen support from ACTT-127 to calculate a weighted average length of hospitalization and estimate the quality of life of hospital patients (Table 1).

MARKOV MODEL: POST-ACUTE PHASE

In the **post-acute phase**, all patients with a full resolution of symptoms enter a long-term Markov model in which they face age- and sex-matched quality of life as well as mortality risk, consistent with that of the general US population.^{28,29} In scenario analyses, this assumption was relaxed to allow a proportion of patients to face moderate (temporary, assumed to last for 1 year) or severe (assumed to last for the patient's lifetime) new health issues after discharge (Table 2), which could impact quality of life and mortality risk. Death is an absorbing health state in which patients remain until the end of the model's time horizon.

The model uses 2 separate standard mortality ratios (SMRs) to adjust background mortality for patients who enter the Markov model without newly acquired health issues (reflecting general population SMRs) or newly acquired health issues (due to SARS-CoV-2 infection). An

TABLE 1 Model Parameters and Assumptions

Model parameter	Value	Source
Model settings		
Discount rate (efficacy), %	3.0	²⁶
Discount rate (costs), %	3.0	²⁶
WTP, \$/QALY	100,000	²⁶
Time horizon, years	Lifetime	Assumed
Males, %	48.7	²⁰
Average age, year deciles	20-80	Assumed
Efficacy inputs		
Ambulatory setting		
Duration of acute phase, d	30	Assumed
Cost of casirivimab/imdevimab, US \$	2,100	³³
Outcomes (casirivimab/imdevimab)		
Treatment effect (relative risk reduction, %) casirivimab/imdevimab	70.73	⁴²
Recover, no new health issues, %	98.8	⁴²
Recover, moderate new health issues, %	0	Assumed
Recover, severe new health issues, %	0	Assumed
Hospitalization, %	1.2	⁴²
Days with symptoms	10	⁴²
Outcomes (placebo)		
Recover, no health issues, %	95.9	⁴²
Recover, moderate health issues, %	0	Assumed
Recover, severe health issues, %	0	Assumed
Hospitalization, %	4.1	⁴²
Days with symptoms	14	⁴²
Hospital setting		
No oxygen support, %	13.1 ^b	²⁷
Supplemental oxygen, %	41.4 ^b	²⁷
NV or HFO, %	18.4 ^b	²⁷
MV or ECMO, %	27.1 ^b	²⁷
Recover, no health issues	Varies ^a	³¹
Recover, moderate health issues	0	Assumed
Recover, severe health issues	0	Assumed
Dead	Varies ^a	³¹
Days to death	15	Assumed
Length of hospital stay, days		
No oxygen support	5.7	²⁷
Supplemental oxygen	8.6	²⁷
NV or HFO	19.0	²⁷
MV or ECMO	26.6	²⁷
Recovered patients (weighted average)	15	Calculated from ²⁷

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SMR of 1 represents no health issues, whereas moderate or severe health issues are represented by SMRs between 1.25 and 2 (Table 2). As previously described, moderate newly acquired health issues are assumed to last for just 1 year, whereas severe health issues are assumed to last for the remainder of a patient's lifetime.

The model also adjusts the age- and sex-matched general population quality of life to account for the potential impact of moderate and severe health issues (a decrease in utility value of 5%-20%) and adjusts the health care costs of patients with no health issues, moderate health issues, and severe health issues in comparison with those costs incurred in the general population (an increase in value of 25%-100%; Table 2).

The assumption of all hospitalized patients recovering without health issues was relaxed within scenario analyses, in which the impact of long-term conditions after hospital discharge, including long COVID, was assessed. Post-infection health issues were considered to be long COVID for the purposes of the model, given the paucity of evidence on the long-term effects that are related to COVID-19.

SCOPE AND TIME HORIZON

The model evaluates the cost-effectiveness of casirivimab/imdevimab with a lifetime horizon that enables the inclusion of the quality of life of survivors as well as future health care costs. The Markov model uses a cycle length of 1 year and applies the standard half-cycle correction. Given the lack of evidence on long-term outcomes, data are not available to estimate the transition probabilities from moderate or severe health issues to the recovered setting, such that a more granular cycle length may not be necessary. Costs are assessed from a third-party US payer perspective; both costs and outcomes are discounted at 3%.

EVENT AND TRANSITION PROBABILITIES

Probability of Hospital Admission in the Decision Tree. In view of the heterogeneity of patients with COVID-19, the model includes a hypothetical cohort of patients receiving usual care with varying levels of risk of hospitalization. In addition, given that expected lifetime quality-adjusted life years (QALYs) in the model are highly influenced by baseline age, it was decided to also vary the baseline age of the population of interest, thereby creating a matrix of size 7×9 (7 baseline age categories ranging from 20 years to 80 years, in 10-year increments, and 9 hospital admission risk categories, ranging from 2% to 10%, based on Wei et al³⁰).

In the treatment arm of the model, the relative reduction in the risk of hospital admission of 71% recorded in the phase 3 trial population²⁰ is applied to each cell of the matrix with the assumption that the reduction in risk is

TABLE 1 Model Parameters and Assumptions (continued)

Model parameter	Value	Source
Utility inputs		
General population age-adjusted utility	Varies ^a	28
Ambulatory setting		
Disutility COVID-19 symptoms	0.19	Calculated from ³⁶
Hospital setting		
Disutility of COVID-19, weighted average	0.61	Calculated from ⁴³
Hospitalization costs, US \$		
With or without supplemental oxygen	12,692	34
NV or HFO	34,223	34
MV or ECMO	61,169	34
Weighted average	29,791	Calculated from ³⁴
Age-adjusted general health care costs	Varies ^a	35

^aVaries with age (refer to Table 2).

^bThe ICER model divides the number of patients requiring oxygen support by 1,051 rather than the sample size of overall patients of 1,062 to calculate the proportions of patients requiring hospitalization (11 patients were excluded from the ICER calculation as they were not hospitalized, not hospitalized with limitations of activities and/or requiring home oxygen requirement, or hospitalized but not requiring ongoing medical care, at baseline).

d = days ECMO = extracorporeal membrane oxygenation; HFO = high-flow oxygen; MV = mechanical ventilation; NV = noninvasive ventilation; QALY = quality-adjusted life year; WTP = willingness to pay.

constant across all age and risk categories. Safety outcomes were not included in the model because there was no difference in the frequency of adverse events between treatment and placebo arms of the phase 3 trial.

Probability of Mortality Among Hospitalized Patients. The age-specific risk of mortality was obtained from a retrospective observational cohort study of more than 66,000 patients who were hospitalized with a primary diagnosis of COVID-19 during the second quarter of 2020 across more than 600 geographically diverse hospitals in the United States.³¹ The risk of in-hospital death was shown to increase with every decade of life (Table 3).

The model uses US lifetables for the general population to inform the annual probability of death for patients in the Markov model.²⁹ Because patients who become infected with SARS-CoV-2 may be a subpopulation of those who face a higher probability of death (eg, greater number of comorbidities), the model allows the probabilities of death from the lifetable to be adjusted for SMRs using the following formula³²:

$$\text{Adjusted probability of death}_{\text{age,health state}} = 1 - e^{\left(\ln\left[1 - \text{probability of death}_{\text{age}}\right] \times \text{SMR}_{\text{health state}}\right)}$$

At the time of writing, there are no published studies that compare the SMRs for patients with and without long-term conditions (eg, long COVID) after infection with SARS-CoV-2.

COSTS

Acute Phase. The model uses the current price of casirivimab/imdevimab in the United States of \$2,100 per treatment course.³³ Because casirivimab/imdevimab is available as a subcutaneous injection, no further costs of administration are assumed in the model. Patients who become hospitalized incur hospital costs, which is a weighted treatment cost depending on the need for oxygen support and the associated costs.³⁴ Patients incur costs in the model as a fixed amount, irrespective of the length of hospital stay (Table 1).

Post-Acute Phase. The model does not consider long-term health care costs in the base case, as the evidence around the long-term effects of COVID-19 on quality of life and costs is still maturing, but does allow for it in the scenario analyses (age-adjusted general health care costs³⁵).

UTILITIES

Acute Phase. The model uses data on age-adjusted general population utility values from Sullivan and Ghushchyan²⁸ and smooths the utility values using a linear function as applied in the ICER model²⁶:

$$\text{Utility} = 0.9442 - 0.0027 \times \text{age}$$

The model applies a disutility of 0.19 due to COVID-19 for nonhospitalized patients³⁶ for the number of days patients have symptoms (casirivimab/imdevimab: 10 days; no treatment: 14 days) and a weighted average disutility for hospital patients based on the proportion of patients stratified by type of oxygen support of 0.61 for the weighted average length of hospital stay (15 days).²⁷

Post-Acute Phase. Similar to the acute phase, in the post-acute phase, the model uses data on age-adjusted general population utility values from Sullivan and Ghushchyan²⁸ and allows this utility to differ by health state by adjusting the utilities using utility value multipliers described above.

SCENARIO ANALYSIS

Current evidence suggests that the risk of hospital admission in patients diagnosed with COVID-19 depends on underlying risk factors, with age being the most important factor.¹²

TABLE 2 Inputs for Scenario Analysis

Variable	Base case	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Hospitalized patients who recover with moderate new health issues, %	0	10	10	10	10
Hospitalized patients who recover with severe new health issues, %	0	10	10	10	10
SMR for patients who recover with new health issues (irrespective of severity)	n/a	1.25	1.5	1.75	2
Increase in health care costs (health issues versus none, irrespective of severity), %	n/a	25	50	75	100
Decrease in utility (health issues vs. none, irrespective of severity), %	n/a	5	10	15	20
Duration of effects (SMR, cost, utility) for patients with moderate health issues, years	n/a	1	1	1	1
Duration of effects (SMR, cost, utility) for patients with severe health issues in years	n/a	Lifetime	Lifetime	Lifetime	Lifetime

n/a = not applicable - base case includes only patients with no health issues; SMR = standard mortality ratio.

The analysis alters the inputs shown in Table 2, while varying the risk of hospitalization (from 2% to 10% for patients in the usual care arm³⁰), maintaining the treatment effect constant (71% reduction in hospitalization in the treatment arm^{20,30}), and varying the age of patients across both arms. In all 4 scenarios, it is assumed that 10% of patients have moderate health issues and 10% of patients have severe health issues after hospitalization.

Results

The model provides an array of incremental cost-effectiveness ratios, expressed as cost per QALY obtained (Table 4). This shows the age range and risk of hospitalization in the cohort of ambulatory patients with mild to moderate COVID-19 and highlights those patients for whom casirivimab/imdevimab may be considered cost-effective at willingness-to-pay thresholds of \$100,000–\$150,000.

In the base case, the cost-effectiveness of treatment with casirivimab/imdevimab is positively associated with increasing risk of hospitalization and increasing age. For example, at a willingness-to-pay threshold of \$100,000, casirivimab/imdevimab is cost-effective in patients older than 40 years of age and with a baseline risk of greater than or equal to 2%, whereas in relatively younger patients aged 20 years, casirivimab/imdevimab is cost-effective at baseline risks of hospitalization of greater than or equal to 4% (Table 4). Conversely, casirivimab/imdevimab is not cost-effective in patients aged 20 years with a 3% or lower risk of hospitalization or in patients aged 30 years with a 2% risk.

Similarly, casirivimab/imdevimab appears to be dominant in scenario analyses among patients across all age groups who are at higher risk of hospitalization, and with higher health care costs and poorer quality of life (increased disutility), as a result of more serious long-term health issues from the infection. Depending on the degree by which health care costs are assumed to increase over the long run, treatment with casirivimab/imdevimab is found to be cost saving at hospitalization risks ranging from 5% to 8%, and this finding is largely consistent across age categories.

In additional sensitivity analyses, the treatment effect was set to the limits of the 95% CI for efficacy (relative risk reduction on the probability of becoming hospitalized from the 1.2 g cohort with casirivimab/imdevimab) as reported from the Weinreich et al trial²⁰ (ie, results were recalculated using risk reductions rates of 31.6% and 87.1%; [Supplementary Table 1](#), available in online article). In the optimistic scenario with a relative risk of hospitalization of 0.129, casirivimab/imdevimab was cost-effective in all combinations except in patients aged 20 years with a 3% or lower risk of hospitalization and in patients aged 30 years with a 2% risk.

In the more conservative scenario that assumes a relative risk of hospitalization of 0.684, casirivimab/imdevimab was not cost-effective if the risk of hospitalization in the following age groups was as follows (risk of hospitalization in parentheses): 20 years (8% and lower), 30 years (6% and lower), 40 years (4% and lower), 50 years (3% and lower), and 60 and older (2%).

TABLE 3 Probability of 30-Day Death by Age in Hospitalized Patients

	Age group (years)						
	20-29	30-39	40-49	50-59	60-69	70-79	80+
Probability of death, %	1.6	3.0	5.8	10.6	18.0	26.5	34.4

Discussion

The results of our analysis of a cohort of ambulatory patients with mild to moderate COVID-19 at high risk of developing severe disease indicate that at a cost of \$2,100, casirivimab/imdevimab is cost-effective in most patients, depending on age and risk of hospitalization. This includes patients who are 65 years of age or older or who have certain chronic medical conditions and are therefore already at higher risk of hospitalization.³⁰

The ICER value framework has recently been used to produce an estimate of an operational cost-effectiveness threshold of approximately \$100,000 per QALY, although \$150,000 has been suggested as a more flexible and upper boundary, with a broader range from \$50,000 to \$200,000 per QALY around this value.³⁷ The benchmarks of \$100,000 and \$150,000 were used to estimate the cost-effectiveness of remdesivir plus usual care compared with usual care alone in patients hospitalized with COVID-19, stratified into mild or moderate to severe hospitalized populations.²⁶

Our study uses a similar model structure and many of the same parameters as in the ICER value framework to estimate the long-term health outcomes of surviving patients, with notable exceptions. First, in contrast to the ICER remdesivir model, our model includes outpatients for whom hospital admission is treated as an outcome and not an inclusion criterion. Second, we followed recommendations by the UK National Institute for Health and Care Excellence, which suggest that costs that are considered to be unrelated to the condition of interest should be excluded.³⁸ Finally, because favorable health outcomes and QALYs do not become less valuable in a pandemic scenario, we continued to use the traditional \$100,000 to \$150,000 willingness-to-pay threshold range³⁷ rather than the \$50,000 threshold used in the ICER remdesivir assessment.

As data on long COVID emerge, the model results are subject to change. With increasing disease burden resulting from long COVID and the corresponding increasing cost of managing this disease burden, the value of treatment with casirivimab/imdevimab could potentially increase substantially and might, in the long term, even

be cost saving to health systems. Through prevention of hospitalization, casirivimab/imdevimab could not only reduce the economic burden of COVID-19 but, importantly, also increase the capacity for secondary care of patients without COVID-19.

Although severe illness due to COVID-19 can occur across all age groups, accumulating data suggest there are several factors that can place patients at risk of more serious illness and potentially lead to hospitalization, emergency department visits, or other medically attended visits.¹⁶ Thus, there is currently an urgent need for therapies capable of reducing viral load and preventing COVID-19 disease progression. When administered to ambulatory patients (ie, outpatients) with mild to moderate COVID-19, casirivimab/imdevimab has the potential to significantly reduce COVID-19-related medically attended visits (including hospitalizations and potential deaths), particularly among those with one or more baseline risk factors.

There is also a role for the treatment of acute, mild to moderate COVID-19 with casirivimab/imdevimab, in a post-pandemic world in which vaccines are largely effective but where treatment will be important in communities with a higher proportion of individuals who are not protected by vaccination. An early intervention that could prevent hospitalization and intensive care unit (ICU) stay could offset treatment-related costs, and a therapy that costs the same or less than the ICU cost per day, and reduces ICU stay by even 1 day, has been shown to achieve cost neutrality in countries with limited intensive care resources.³⁹

LIMITATIONS

These results are limited to the specific indication of ambulatory patients and, although casirivimab/imdevimab has similarly been approved for prophylactic use, and is being evaluated for inpatient administration, the cost-effectiveness results of the present analysis cannot be generalized to other indications.

At the time of writing, no comparator treatments were available, so the model compared casirivimab/imdevimab with usual care. The most critical assumption in the model is that by reducing the rate of hospital admission, the rate of mortality is expected to fall proportionately. This assumption is not supported by data from the phase 3 trial of casirivimab/imdevimab, which was not powered to show changes in mortality. Also, we applied the 71% reduction in the risk of hospitalization equally to all modeled subgroups; however, it is possible that there could be some variation in the treatment effect across the subgroups of interest.

Long COVID has been reported in a growing number of patients as a constellation of symptoms that are persistent and debilitating but have yet to be fully explained by known

TABLE 4 Incremental Cost-Effectiveness Ratios by Varying Risk of Hospitalization and Age

Relative risk of hospitalization - base: 0.293								
Base case								
Age, y								
Probability of hospitalization (placebo arm)		20	30	40	50	60	70	80
	2%	222,671	150,191	96,676	66,061	50,219	47,359	57,819
	3%	142,966	93,351	58,705	39,593	29,897	28,160	34,532
	4%	96,733	62,014	38,509	25,794	19,409	18,270	22,456
	5%	66,546	42,161	25,975	17,324	13,008	12,240	15,066
	6%	45,287	28,457	17,437	11,596	8,695	8,180	10,077
	7%	29,505	18,428	11,247	7,464	5,591	5,259	6,483
	8%	17,325	10,771	6,554	4,343	3,250	3,057	3,770
	9%	7,641	4,733	2,873	1,901	1,422	1,337	1,650
	10%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
a) Scenario 1								
Age, y								
Probability of hospitalization (placebo arm)		20	30	40	50	60	70	80
	2%	157,084	113,733	77,575	55,226	43,479	42,299	53,110
	3%	91,692	64,432	42,952	30,289	23,936	23,645	30,391
	4%	55,082	37,688	24,658	17,326	13,865	14,046	18,622
	5%	31,680	20,902	13,345	9,382	7,723	8,196	11,424
	6%	15,430	9,386	5,657	4,015	3,586	4,257	6,566
	7%	3,488	994	93	145	610	1,425	3,068
	8%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	428
	9%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	10%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
b) Scenario 2								
Age, y								
Probability of hospitalization (placebo arm)		20	30	40	50	60	70	80
	2%	117,601	88,955	63,309	46,727	38,088	38,284	49,480
	3%	62,008	45,174	31,299	23,026	19,180	20,066	27,203
	4%	31,528	21,683	14,468	10,733	9,447	10,699	15,672
	5%	12,280	7,031	4,088	3,208	3,514	4,992	8,623
	6%	Dom.	Dom.	Dom.	Dom.	Dom.	1,152	3,867
	7%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	443
	8%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	9%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	10%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.

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or measurable mechanisms.⁴⁰ It is feasible that, when more long-term data are available, future analysis could also examine the impact of long COVID. Although it is not yet known who is at greatest risk of developing long COVID, it is acknowledged that there is a relationship between the severity of the acute illness and the likelihood of developing the condition.⁴¹ It is because of this limited knowledge of the longer-term outcomes of COVID-19 that the model base case does not incorporate long COVID, health states other than death after discharge from hospital, or any cross-state transitions.

The treatment of ambulatory patients with casirivimab/imdevimab is also expected to reduce viral load and therefore render them less infectious. However, this dynamic benefit on the course of the COVID-19 epidemic is beyond the scope of the present model, such that the results are likely to be conservative.

Conclusions

This analysis showed that in the ambulatory setting, casirivimab/imdevimab is a cost-effective treatment option for most patient populations studied. For example, at a willingness-to-pay threshold of \$100,000, casirivimab/imdevimab is cost-effective in patients aged 40 years and older and with a baseline risk greater than or equal to 2%, whereas in relatively younger patients aged 20 years, casirivimab/imdevimab is cost-effective at baseline risks of hospitalization greater than 3%.

These findings are driven by the clinically meaningful and statistically significant reduction in the risk of hospitalization that is modeled to subsequently reduce mortality rates in ambulatory patients with COVID-19. Our findings further suggest that casirivimab/imdevimab has the potential to be cost saving to

TABLE 4 Incremental Cost-Effectiveness Ratios by Varying Risk of Hospitalization and Age (continued)

c) Scenario 3								
Probability of hospitalization (placebo arm)	Age, y							
		20	30	40	50	60	70	80
	2%	91,152	70,924	52,162	39,815	33,627	34,976	46,551
	3%	42,628	31,370	22,264	17,143	15,252	17,120	24,633
	4%	16,390	10,316	6,603	5,404	5,802	7,945	13,295
	5%	Dom.	Dom.	Dom.	Dom.	45	2,358	6,366
	6%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	1,693
	7%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	8%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	9%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	10%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
d) Scenario 4								
Probability of hospitalization (placebo arm)	Age, y							
		20	30	40	50	60	70	80
	2%	72,168	57,167	43,164	34,046	29,846	32,176	44,111
	3%	28,976	20,965	15,019	12,249	11,927	14,630	22,493
	4%	5,852	1,811	322	981	2,720	5,618	11,316
	5%	Dom.	Dom.	Dom.	Dom.	Dom.	132	4,488
	6%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	7%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	8%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	9%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.
	10%	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.	Dom.

Incremental cost-effectiveness ratios at a willingness-to-pay threshold of \$100,000 or less are displayed in green, between \$100,000 and \$150,000 are displayed in yellow, and above the \$150,000 threshold are displayed in red. Dom (dominant) means that treatment with casirivimab/imdevimab results in better outcomes than usual care at a lower cost.

y=years

managed care payers, while providing a safe, clinically effective, and valuable prescription drug benefit.

DISCLOSURES

N. Jovanoski and U. Becker are employees of F Hoffman-La Roche Ltd.; A. Kuznik and M. Hussein are employees of Regeneron Pharmaceuticals Inc. and hold stock and stock options; A. Briggs has provided consultancy to F Hoffman-La Roche Ltd. and has received consultancy fees from Merck and Co., Inc., GlaxoSmithKline plc., and Novartis. This study was funded by Regeneron Pharmaceuticals, Inc.

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