COST EFFECTIVENESS OF NIRMATRELVIR/RITONAVIR FOR MILD-MODERATE COVID-19 IN SPAIN

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BACKGROUND

A need exists for safe, affordable, and effective antiviral treatments for less severe COVID-19 outpatients that can prevent infection progression, hospitalization, and death; shorten the time to clinical recovery; and reduce transmission. In our study we aim to evaluate cost-effectiveness of oral nirmatrelvir plus ritonavir in COVID-19 mild to moderate outpatients with at least one risk factor for disease progression in Spain.

METHODS

A simulation model was constructed in R (figure 1), to assess the clinical consequences and costs associated with COVID-19 in a hypothetical cohort of non-hospitalized patients older than 65 years with mild-to-moderate COVID and at least one risk factor for progression in Spain. The intervention assessed was nirmatrelvir plus ritonavir 300 mg plus 100mg every 12 hours for 5 days. The comparator was symptomatic treatment with no antiviral drugs against SARS-CoV-2. The study was contextualized in the Spanish National Health System and the perspective of the service provider was adopted. Quality of life adjusted life years (QALYs) was used as a measure of effectiveness. Drug effectiveness was obtained from a literature review. As a threshold willing to pay, the Spanish Gross National Product per capita was used. A discount of 3% per year was applied on future health effects. Parameters for the development of the model were obtained from direct measures, scientific literature, and when no other source was found, by consultation with experts (table). We used a decisional tree model (figure 1). A univariate sensitivity analysis and probabilistic sensitivity analysis was performed.

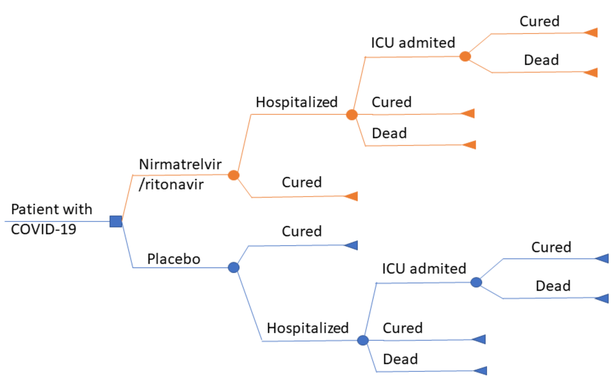

Figure 1. Representation of the tree model used.

CONCLUSIONS

Nirmatrelvir/ritonavir **is not cost-effective** in the Spanish National Health System for outpatients older than 65 years with at least one risk factor for COVID progression.

A drug price of 70€ per treatment would meet the willingness to pay threshold.

RESULTS

Nirmatrelvir/ritonavir yielded an extra 620.89 QALYs compared to a baseline scenario without it, at an increase in cost of 89,630,442 € with an Incremental cost-effectiveness ratio of 144,356.4 €/QALY gained. One way sensitivity analysis and probabilistic sensitivity analysis using Monte-Carlo simulations were undertaken and showed that the probability of not being cost-effective was 1 at the current price and willingness to pay threshold. To meet our willingness to pay threshold, nirmatrelvir plus ritonavir 5-days treatment price should be lowered down to 70 €.

Parameter	Value and range	Source
Hospitalization probability of patients receiving Nirmatrelvir/ritonavir	0.0041 (0.0028-0.034)	Arbel et al. Wong et al. Hammond et al.
ICU hospitalization probability of patients receiving Nirmatrelvir/ritonavir	0.0014 (0.0026-0.00168)	Wong et al.
Probability of death in patients admitted to ICU that received Nirmatrelvir/ritonavir	0.3 (0.25-0.35)	Semi-COVID registry Direct query.
Probability of death of patients receiving Nirmatrelvir/ritonavir not admitted to ICU	0.0011 (0.0011-0.0008)	Wong et al.
Hospitalization probability of patients not receiving Nirmatrelvir/ritonavir	0.016 (0.016-0.062)	Arbel et al. Hammond et al.
ICU hospitalization probability of patients not receiving Nirmatrelvir/ritonavir	0.09 (0.083-0.1)	Semi-COVID registry Direct query.
Probability of death in patients admitted to ICU that did not receive Nirmatrelvir/ritonavir	0.3 (0.25-0.35)	Semi COVID registry Direct query.
Probability of death of patients not receiving Nirmatrelvir/ritonavir not admitted to ICU	0.0039 (0.0030-0.01)	Arbel et al. Hammond et al.
Mortality of general population	Life tables	Spanish National Institute of Statistics
Cost of Nirmatrelvir/ritonavir treatment	520 €	Lee et al.
Cost of COVID hospitalization	5000€	Catalonian Decree.
Cost of ICU hospitalization	43400€	Catalonian Decree.

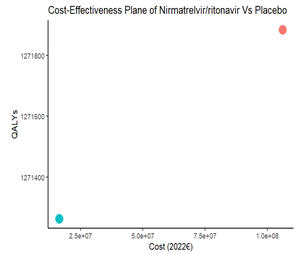

Figure 2. Cost effectiveness plane of nirmatrelvir/ritonavir versus placebo for outpatients with mild-moderate COVID-19 and one risk factor for progression to severe COVID-19.

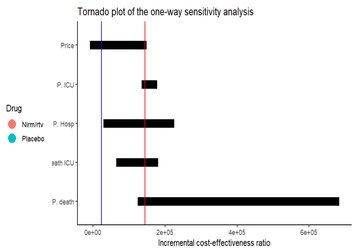

Figure 3. Tornado plots of one-way sensitivity analyses. Blue line represents the willingness to pay threshold and the red line the Incremental cost-effectiveness ration determined in the cost-effectiveness analysis.

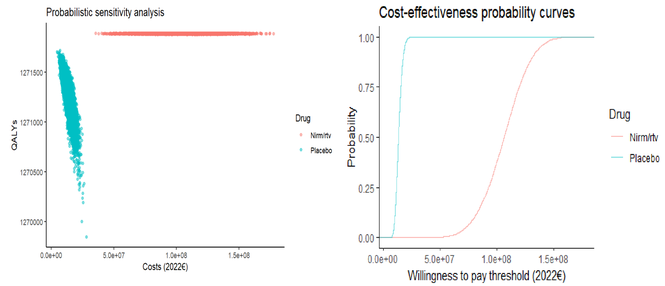

Figure 4. Scatter plot of the probabilistic sensitivity analysis and cost-effectiveness probability curves.

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Decreto-ley 12/2020, de 10 de abril, por el que se adoptan medidas presupuestarias, en relación con el Sistema sanitario integral de utilización pública de Cataluña, en el ámbito tributario y en la estructura de la Administración de la Generalidad, para p. *Bol Of del Estado* 2020. https://www.boe.es/buscar/doc.php?id=BOE-A-2020-5649.

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