Poster EE572

# Cost-Effectiveness of AZD7442 (Tixagevimab and Cilgavimab) for Pre-exposure Prophylaxis Against COVID-19 in the Immunocompromised Population

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## Introduction

- People who are immunocompromised (IC) are 4 times more likely to die of COVID-19, have prolonged symptoms that can last 10 times longer and are twice as likely to require hospitalisation than the general population.[1,2]
- AZD7442 (tixagevimab/cilgavimab) received conditional marketing authorisation in the UK for pre-exposure prophylaxis (PrEP) against SARS-CoV-2 (the virus that causes COVID-19) in adults currently uninfected with it, and without known recent exposure to an individual infected with it, and:
  - who are unlikely to mount an adequate immune response to COVID-19 vaccination, or
  - for whom COVID-19 vaccination is not recommended.

## Objective

- To determine whether PrEP using AZD7442 improves health outcomes and is cost-effective versus standard of care (SoC) among patients who are IC in the UK.

## Plain Language Summary

Compared with the general population, people with weakened immune systems are more likely to have longer-lasting symptoms of COVID-19, require hospitalisation due to the virus, and die. AZD7442 received approval in the UK for adults who were not infected with COVID-19, and without any known recent exposure to anyone infected with COVID-19. AZD7442 could be given to people whose immune system would be too weak for a COVID-19 vaccination or for whom COVID-19 vaccination is not recommended.

We used a model to investigate if AZD7442 improves health outcomes and is cost-effective compared with standard care among UK patients with weakened immune systems. We looked at the effect of AZD7442 on health and cost compared with standard care in the UK. Clinical and cost data were used from clinical trials and clinical practice.

The model showed that prevention with AZD7442 was cost-effective, and that AZD7442 prevented 213,210 symptomatic cases and 54,582 hospitalisations. In summary, AZD7442 significantly reduced COVID-19 risk and was cost-effective in patients with weakened immune systems.

## Results and Interpretation

### Model Scenarios

- A range of model scenarios were analysed (**Table 1**, **Figure 1**, **Figure 2**), based on:
  - Use of alternative efficacy data (PROVENT study[3] and real-world evidence).
  - Inclusion of AZD7442 prophylaxis utility benefit over 1 year.
  - Alternative long-COVID probabilities and inclusion of re-infection parameters.

### Model Healthcare Burden and Quality of Life

- Each million IC individuals who received AZD7442 versus SoC:
  - Gained an additional 75,743 to 84,486 life years (LYs) and 118,830 to 206,214 quality-adjusted life years (QALYs) (**Table 1** and **Figure 2**).
  - Avoided 149,052 to 186,992 COVID-19 cases and 4,717 to 5,262 acute deaths (**Figure 1**).
  - Avoided 33,657 to 37,541 COVID-19–related hospitalisations and 379,983 to 423,841 bed days (**Figure 1**).
  - Avoided 53,489 to 83,840 long-COVID cases.

### Model Risk Reduction

- Variation of the symptomatic infection risk between 8% and 36% and hospitalisation risk among symptomatic patients between 12% and 46% resulted in a reduction of:
  - 8,352 to 144,072 hospitalisations per million IC patients when using efficacy estimates derived from the 2022 study of Young-Xu et al.[4]
  - 9,316 to 160,706 hospitalisations per million IC patients when using efficacy estimates derived from the PROVENT study.[3]

### Model Costs

- AZD7442 carried a >50% probability of cost-effectiveness versus SoC at a £20,000 per QALY willingness-to-pay threshold, with the majority of scenarios generating a >90% probability of cost-effectiveness.
- AZD7442 carried a >90% probability of cost-effectiveness versus SoC at a £30,000 per QALY willingness-to-pay threshold.

**Figure 1. Scenario Modelling Demonstrated Reductions in Healthcare Burden and Deaths**

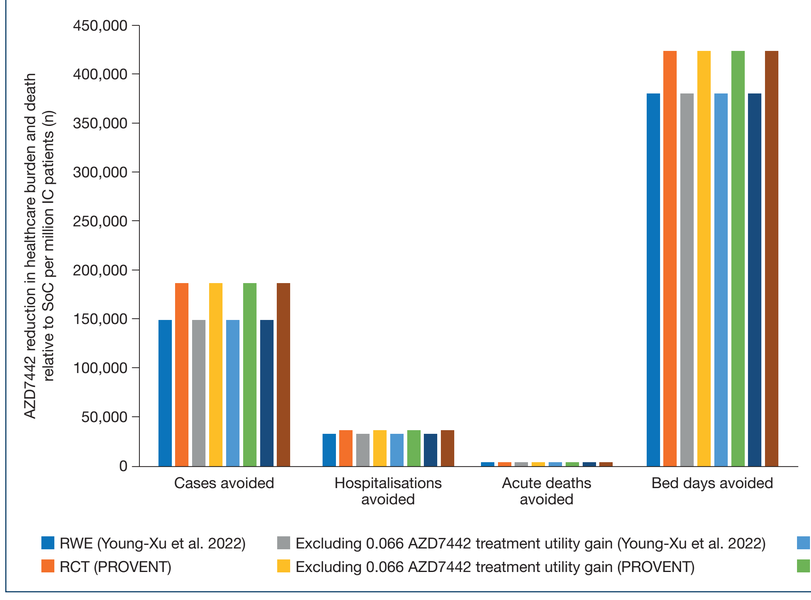
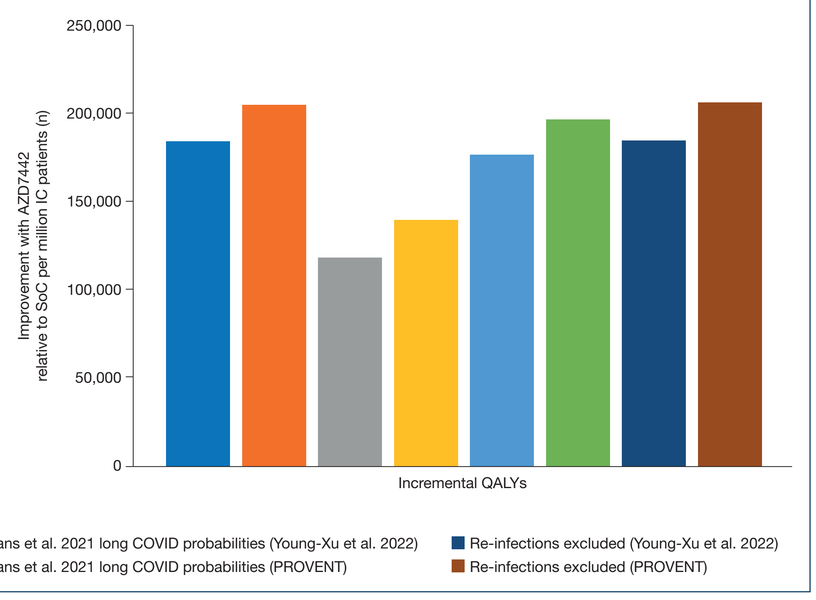



**Figure 2. Improved Quality of Life Using Scenario-Based Modelling**




AZD7442, tixagevimab/cilgavimab; IC, immunocompromised; QALY, quality-adjusted life year; RCT, randomised control trial; RWE, real-world evidence; SoC, standard of care.

**Table 1. Improvements in LYs and PSA Simulations**

| Model outcome vs SoC – per million IC patients | Model Scenario | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | RWE | RCT | Excluding 0.066 AZD7442 treatment utility gain[5] | | Evans et al. 2021[6] long-COVID probabilities | | Re-infections excluded | |
| | Young-Xu et al. 2022[4] | PROVENT[3] | Young-Xu et al. 2022[4] | PROVENT[3] | Young-Xu et al. 2022[4] | PROVENT[3] | Young-Xu et al. 2022[4] | PROVENT[3] |
| Incremental LYs, n | 75,743 | 84,486 | 75,743 | 84,486 | 75,743 | 84,486 | 75,743 | 84,486 |
| % of PSA simulations where AZD7442 was cost-effective at £20,000 per QALY, n | 97.8% | 99.6% | 58.1% | 80.7% | 94.6% | 99.2% | 99.6% | 100.0% |
| % of PSA simulations where AZD7442 was cost-effective at £30,000 per QALY, n | 100.0% | 100.0% | 92.6% | 97.9% | 100.0% | 100.0% | 100.0% | 100.0% |

AZD7442, tixagevimab/cilgavimab; IC, immunocompromised; LY, sum-of-life years; PSA, probabilistic sensitivity; QALY, quality-adjusted life year; RCT, randomised control trial; RWE, real-world evidence; SoC, standard of care.

## Conclusions

- The current study shows the economic value of AZD7442 as PrEP for COVID-19 versus placebo or SoC.
- AZD7442 improves health outcomes and is cost-effective versus SoC among patients who are IC in the UK.
  - The study was in accordance with clinical and treatment pathways for patients with COVID-19 and based on a thorough review of published economic modelling approaches for COVID-19 with extensive flexibility in how to estimate the clinical benefits of AZD7442.
  - The results were generally robust across different scenarios analysed, with probabilistic sensitivity analysis results, indicating a high probability of cost-effectiveness at both £20,000 and £30,000 per QALY willingness-to-pay thresholds.
  - Bivariate sensitivity analysis indicated that the model was sensitive to variations in symptomatic infection risk and hospitalisation risk among symptomatic patients.

## Methods

### AZD7442 Versus SoC Model Overview

- We evaluated the impact on health and economic outcomes of AZD7442 PrEP versus SoC from a UK National Health Service and Personal Social Services payer perspective over a lifetime horizon (**Figure 3**).
- Costs and health outcomes were discounted at 3.5% per annum.[7]
- Outcomes were expressed mostly in terms of incremental health outcomes and probability of cost-effectiveness for AZD7442 versus SoC at both £20,000 and £30,000 per QALY willingness-to-pay thresholds at both £20,000 and £30,000 per QALY willingness-to-pay thresholds.

### Model Inputs

- Model inputs were derived from a targeted literature review for epidemiological, clinical and cost data, as well as the PROVENT study[3] and real-world evidence data.[4]

### Model Case Distribution

#### Model Acute Phase

- Symptomatic COVID-19 infection risk of 22.6% was derived from the UK general population case notification data.[8]
- Symptomatic infected patients were further categorised based on hospitalisation status, with 17.1% of infected patients hospitalized.[9]

#### Model Distribution at the End of the Acute Phase

- For ambulatory/non-hospitalised patients, 34.5% were assigned to the long-COVID state at the end of the acute phase based on criteria provided.[10]
- Long-COVID risk assumptions for hospitalised patients were informed by cited data.[11]
- Alternative long-COVID probabilities were also explored.[6]

#### Model Post-Acute Phase

- Following entry into the long-term Markov model, patients could be transitioned from recovery to death, long COVID to recovery or from long COVID to death.

### Model Assessment of AZD7442 Versus SoC: Efficacy

- Efficacy data were explored both from the PROVENT trial[3] as well as real-world evidence from a US veterans' study.[4]

### Model Assessment of AZD7442 Versus SoC: Costs

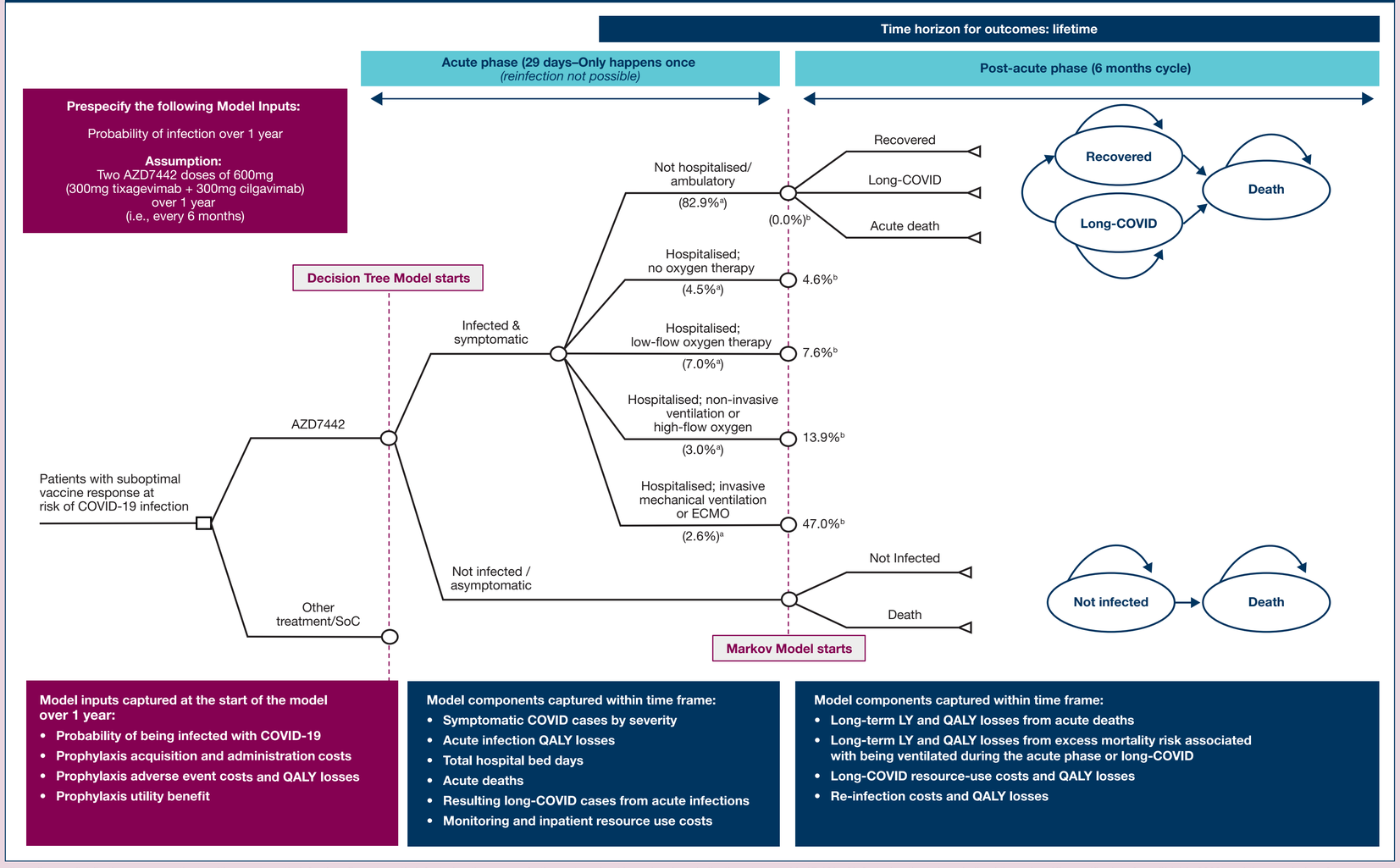
#### The analysis included the following costs:

- Acquisition and administration costs for prophylaxis treatment.[12]
- Treatment-emergent serious adverse events.[3]
- Daily aggregated medical resource utilisation costs.[13,14]
- Monitoring costs and long-COVID costs.[11,14-17]
- Cost of re-infections based on the overall acute infection cost from the acute phase.
- Exclusion of re-infections was also explored.

#### Model Assessment of AZD7442 Versus SoC: Quality of Life

- To account for decreasing quality of life for patients with increasing age, the model incorporated general population utility estimates from a published regression model.[18]

**Figure 3. A Decision-Tree Approach Enabled Capture of Trial and Real-World Efficacy Data During the Acute Infection Period**




[a]Overall case distribution among patients with symptomatic infection. Symptomatic infected patients were further categorised based on hospitalisation status, with 17.1% of infected patients hospitalised (based on IC-specific data from Shields 2022) and the remainder of symptomatic patients not hospitalised or ambulatory. [b]Acute disease phase mortality risk with COVID-19 by level of health state. Percentages reflect case distribution as per SoC.
AZD7442, tixagevimab/cilgavimab; ECMO, extracorporeal membrane oxygenation; LY, sum-of-life years; QALY, quality-adjusted life year; SoC, standard of care.

## Acknowledgements

- Medical writing support for this manuscript was provided by Christopher Spencer, PhD, Martin Griffiths, PhD, and Ian Phillips, PhD, of Parexel International and was funded by AstraZeneca.

## Disclosures

- SA and NB are employees of AstraZeneca and hold or may hold stock in AstraZeneca. KS, PM, MM, CB, TH, KB and GB were subcontracted by AstraZeneca to complete this study. JQ reports grants from MRC, HDR UK, GSK, Bayer, BI, asthma+lung, Chiesi and AstraZeneca and personal fees for advisory board participation or speaking fees from SK, BI, AstraZeneca, Chiesi, Teva, Insmed and Bayer. HM was an unpaid chair of COVID critical care committee; reports consultancy fees, speaker fees and travel support from AstraZeneca; and attended AstraZeneca advisory boards.

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Presented at ISPOR EU | 6–9 November 2022 | Vienna, Austria and Virtual
This research was funded by AstraZeneca