Tixagevimab/Cilgavimab (EVUSHELD™)

A Review of Pertinent Drug Information for SARS-CoV-2

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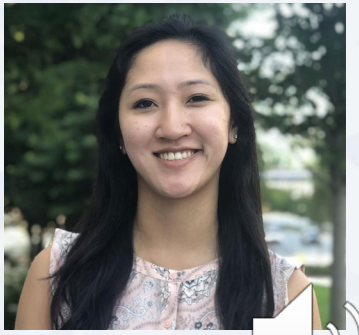

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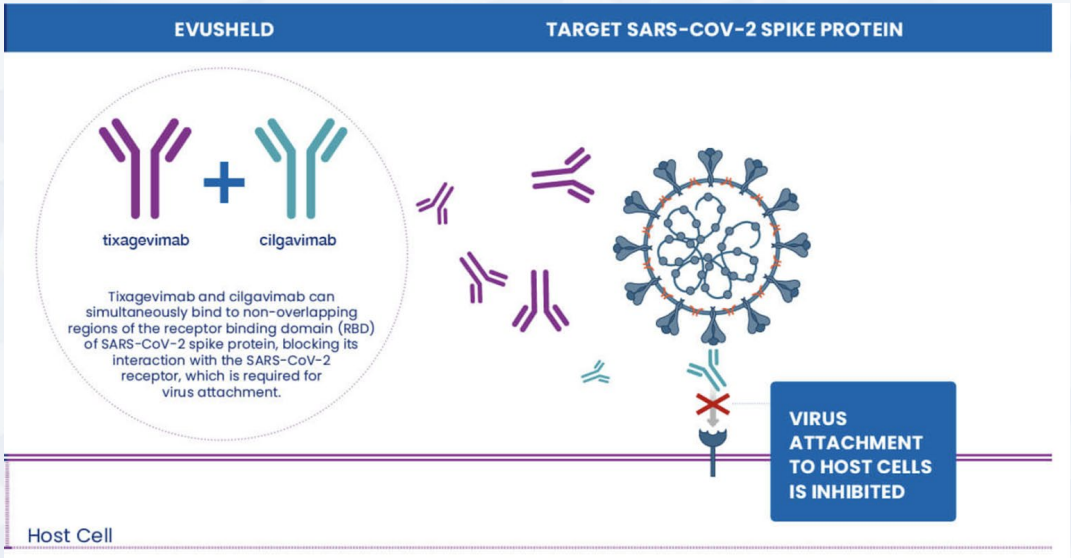
Data as of April 10, 2022

Tixagevimab/Cilgavimab

- Drug class: combination of two monoclonal antibodies
- Mechanism of action: SARS-CoV-2 spike protein-directed attachment inhibitors
- Status: investigational, ongoing COVID-19 phase 3 studies



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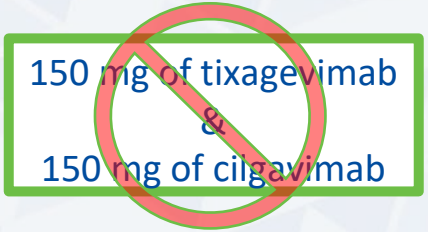
FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Dosing

- Dosage: 300 mg of tixagevimab and 300 mg of cilgavimab



- Dosage forms: each available as 150 mg/1.5 mL single-dose vials
  - Tixagevimab 300 mg = 2 vials = 3 mL
  - Cilgavimab 300 mg = 2 vials = 3 mL
- Administration: two separate consecutive IM injections, preferably one in each gluteal muscle
  - Monitor for at least 1 hour after injection

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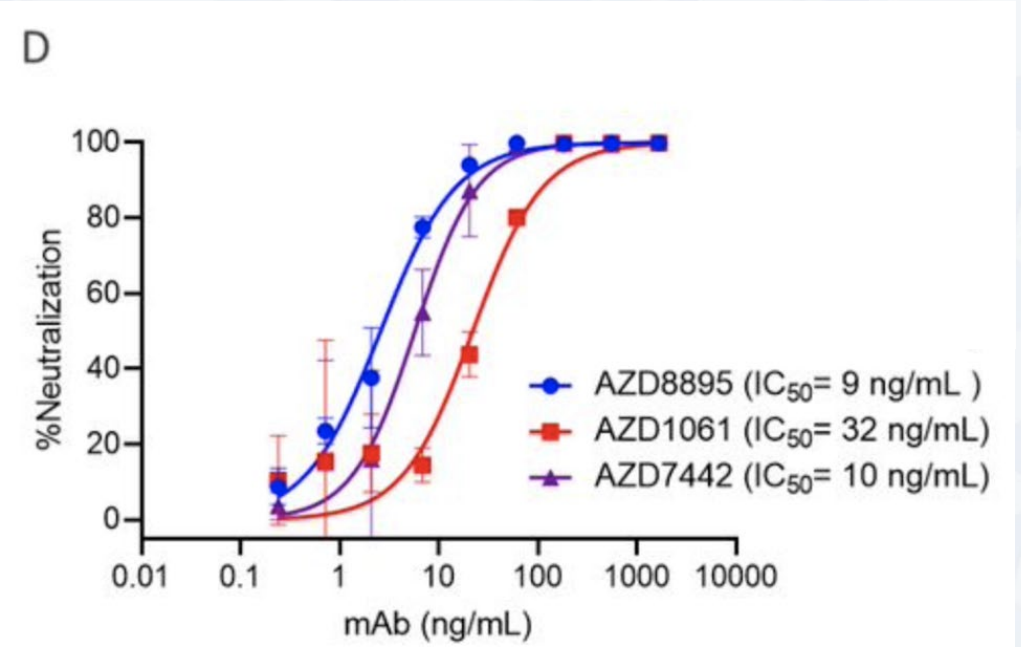
IM: intramuscular

FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

In vitro Activity

Tixagevimab (AZD8895) Cilgavimab (AZD1061) EVUSHELD (AZD7442)

Neutralizing activity of tixagevimab, cilgavimab, and EVUSHELD against USA-WA1/2020 reference strain



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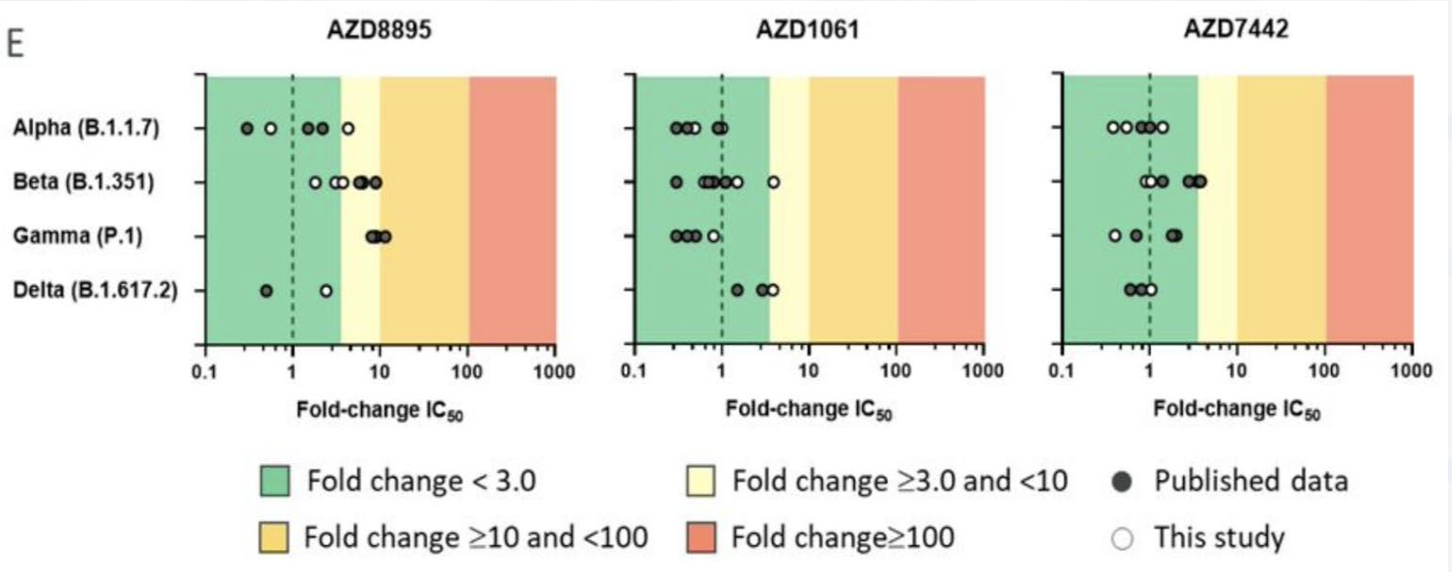
Loo Y-M, et al. AZD7442 demonstrates prophylactic and therapeutic efficacy in non-human pr[illegible]tes and extended half-life in humans. medRxiv. 2021. doi:https://doi.org/10.1101/2021.08.30.21262666.

In vitro Activity

Tixagevimab (AZD8895) Cilgavimab (AZD1061) EVUSHELD (AZD7442)

Fold-change in neutralization potencies against VOCs compared to reference strain



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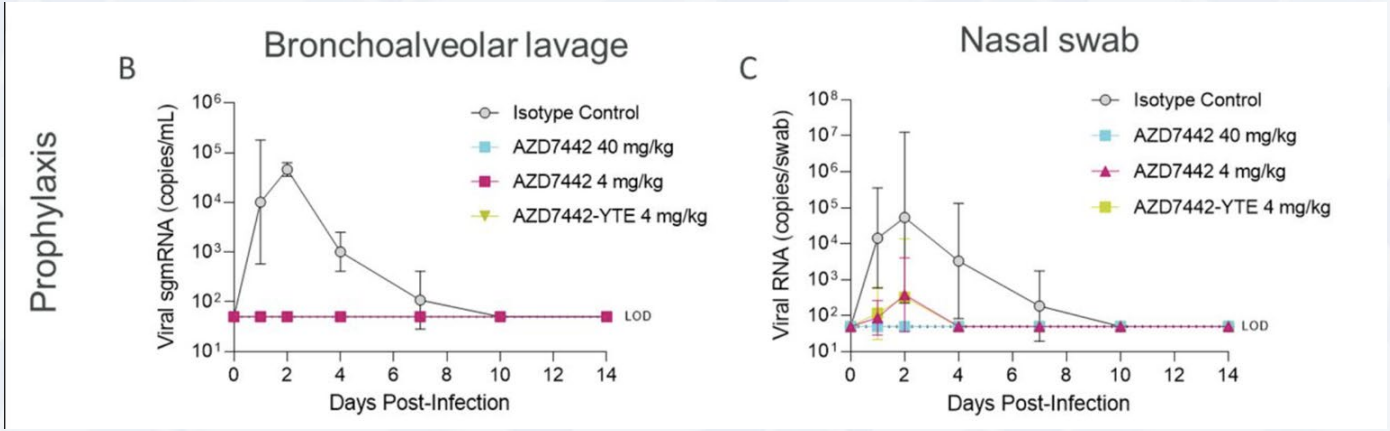
VOCs: variants of concern

Loo Y-M, et al. AZD7442 demonstrates prophylactic and therapeutic efficacy in non-human primates and extended half-life in humans. medRxiv. 2021. doi:https://doi.org/10.1101/2021.08.30.21262666.

In vivo Animal Data

Rhesus macaque

- Received AZD7442 3 days prior to infection
- 4 mg/kg comparable to human 300 mg dose



Key finding

Viral sgmRNA undetectable in BAL and low levels detected in nasal swab with prophylactic treatment

Conclusion

Prophylactic administration of AZD7442 can protect against SARS-CoV-2 lower respiratory tract infection in rhesus macaques

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Loo Y-M, et al. AZD7442 demonstrates prophylactic and therapeutic efficacy in non-human [illegible]tes and extended half-life in humans. medRxiv. 2021. doi:https://doi.org/10.1101/2021.08.30.[illegible]26266[illegible].

In vivo Animal Data

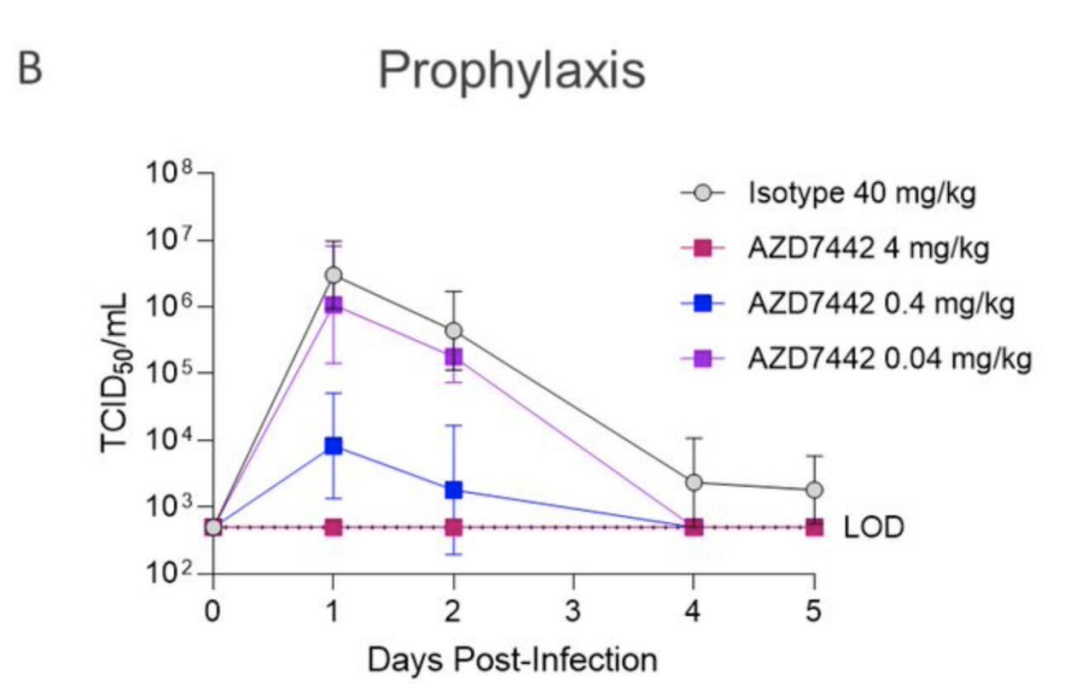
Cynomolgus macaque

Key finding

Prophylactic AZD7442 administration showed dose-dependent reduction of infectious virus titers in BAL

Conclusion

4 mg/kg dose fully protective against SARS-CoV-2



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Loo Y-M, et al. AZD7442 demonstrates prophylactic and therapeutic efficacy in non-human [illegible]tes and extended half-life in humans. medRxiv. 2021. doi:https://doi.org/10.1101/2021.08.30.[illegible]26266f.

Pharmacokinetics

	Tixagevimab	Cilgavimab
Cmax (µg/mL)	21.9	20.3
Tmax (days)	14.9	15.0
Half-life* (days)	87.9	82.9
Metabolism	Catabolic pathways	

*based on 150 mg tixagevimab and 150 mg cilgavimab dose

- Renal impairment: not eliminated intact in the urine
- Hepatic impairment: not studied

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FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Pharmacokinetics

- Extended duration of action – amino acid substitution (YTE)
  - Triples durability of action compared to conventional antibodies
  - Provide months of protection following a single administration

- Reduced Fc receptor binding – amino acid substitution (TM)
  - Minimize risk of antibody-dependent enhancement of disease

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1. FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.
2. Case JB, et al. Resilience of S309 and AZD7442 monoclonal antibody treatments against infection by SARS-CoV-2 Omicron lineage strains. bioRxiv. 2022. doi: https://doi.org/10.1101/2022.03.17.484787.

Adverse Drug Reactions

- PROVENT*

	EVUSHELD (n=3461)	Placebo (n=1736)
Headache	6%	5%
Fatigue	4%	3%
Cardiac SAEs	22 (0.6%)	3 (0.2%)

- STORM CHASER*
  - AEs: 22% EVUSHELD vs 30% placebo
  - Cardiac SAEs: none reported
- TACKLE
  - AEs: 29% EVUSHELD vs 36% placebo
  - Cardiac SAEs: 3 EVUSHELD vs 1 placebo

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*150 mg tixagevimab and 150 mg cilgavimab dose

AEs: adverse events
SAEs: serious adverse events

FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Cardiovascular Events

- PROVENT*
  - All patients with cardiac SAEs had cardiac risk factors and/or history of cardiovascular disease

	EVUSHELD (n=3461)
Myocardial infarction	8 (0.2%)
Cardiac failure	6 (0.2%)
Arrhythmia	4 (0.1%)

- STORM CHASER*
  - No cardiac SAEs reported
  - Younger subjects (median 48 vs 57 years) and less patients with cardiac risk factors compared to PROVENT
- TACKLE
  - All patients with cardiac SAEs had cardiac risk factors and/or history of cardiovascular disease

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*150 mg tixagevimab and 150 mg cilgavimab dose

SAEs: serious adverse events

FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Warnings/Precautions

- Cardiovascular events
  - Consider risks and benefits prior to initiating EVUSHELD in individuals at high risk for cardiovascular events
- Hypersensitivity including anaphylaxis
- Clinically significant bleeding disorders

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FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Use in Specific Populations

	• Insufficient data to evaluate risk of major birth defects, miscarriage, or adverse maternal/fetal outcomes • IgG1 antibodies are known to cross the placental barrier • EVUSHELD should only be used if the potential benefit outweighs the potential risk for the mother and the fetus
	• No available data on the presence of tixagevimab or cilgavimab in human milk or animal milk, the effects on the breastfed infant, or the effects of the drug on milk production
	• EVUSHELD is not authorized for use in individuals under 12 years of age or weighing ≤ 40 kg • Safety and effectiveness of EVUSHELD have not been established

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FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. ... ble from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Drug-Drug Interactions

- Tixagevimab and cilgavimab are not metabolized by cytochrome P450 (CYP) enzymes
  - Interactions with concomitant medications that are substrates, inducers, or inhibitors of CYP enzymes are unlikely

- COVID-19 vaccine – EVUSHELD may reduce immune response to the vaccine
  - EVUSHELD should be administered two weeks after vaccination

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1. FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.
2. FDA. Frequently Asked Questions on the Emergency Use Authorization for Evusheld (ti mab co packaged with cilgavimab) for Pre-exposure Prophylaxis (PrEP) of COVID-19. Available f https://www.fda.gov/media/154703/download. Accessed 9 April 22.

PROVENT

Study Characteristic	PROVENT
Design	Phase III, randomized (2:1), double-blind, placebo-controlled
Status	Ongoing
Recruitment dates	11/21/2020 – 5/1/2021
Sponsor	AstraZeneca
Sites, countries	87 sites, 5 countries
Intervention	Single IM dose of EVUSHELD (150 mg of tixagevimab and 150 mg of cilgavimab) vs placebo
Primary analysis	Efficacy of a single IM dose of EVUSHELD compared to placebo for prevention of COVID-19

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ClinicalTrials.gov [Internet]. Identifier NCT04625725. Available from: https://clinicaltrials.gov/ct2/show/NCT04625725.

PROVENT

Inclusion	Exclusion

• ≥ 18 years of age
• Meet ≥ 1 of the following:
  • Immunocompromised and/or at increased risk for inadequate COVID-19 vaccine response
  • Increased risk for SARS-CoV-2 infection as determined by the investigator
	• History of SARS-CoV-2 infection
	• Positive for SARS-CoV-2 antibody
	• Received COVID-19 vaccine*
	• Pregnant or breastfeeding

*Once COVID-19 vaccines were locally available, subjects were permitted to make an informed decision on vaccine timing and to receive COVID-19 vaccination

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1. ClinicalTrials.gov [Internet]. Identifier NCT04625725. Available from: https://clinicaltrials.gov/ct2/show/NCT04625725
2. FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

PROVENT

Combined data across EVUSHELD and placebo arms (n=5192)

Baseline Characteristics	
Median age	57 years
Female gender	46%
White	73%
Black/African American	17%
Hispanic/Latino	15%
Asian	3%
Baseline co-morbidities	78%

Co-morbidities	
Obesity	42%
Diabetes	14%
Cardiovascular disease	8%
History of cancer	7%
COPD	5%
CKD	5%
Chronic liver disease	5%
Immunosuppressive medications	3%
Immunosuppressive disease	1%

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COPD: chronic obstructive pulmonary disease
CKD: chronic kidney disease

1. ClinicalTrials.gov [Internet]. Identifier NCT04625725. Available from: https://clinicaltrials.gov/ct2/show/[illegible]6257[illegible]25
2. FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

PROVENT

Efficacy data

Incidence of Symptomatic COVID-19 in Adults				
	Treatment arm	**n**	**Number of events, n (%)**	**Relative risk reduction, % (95% CI)**
Primary analysis • Only included events occurring prior to unblinding or vaccine receipt • Median follow-up 83 days	EVUSHELD	3441	8 (0.2)	77 (46, 90)
	Placebo	1731	17 (1.0)	

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FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

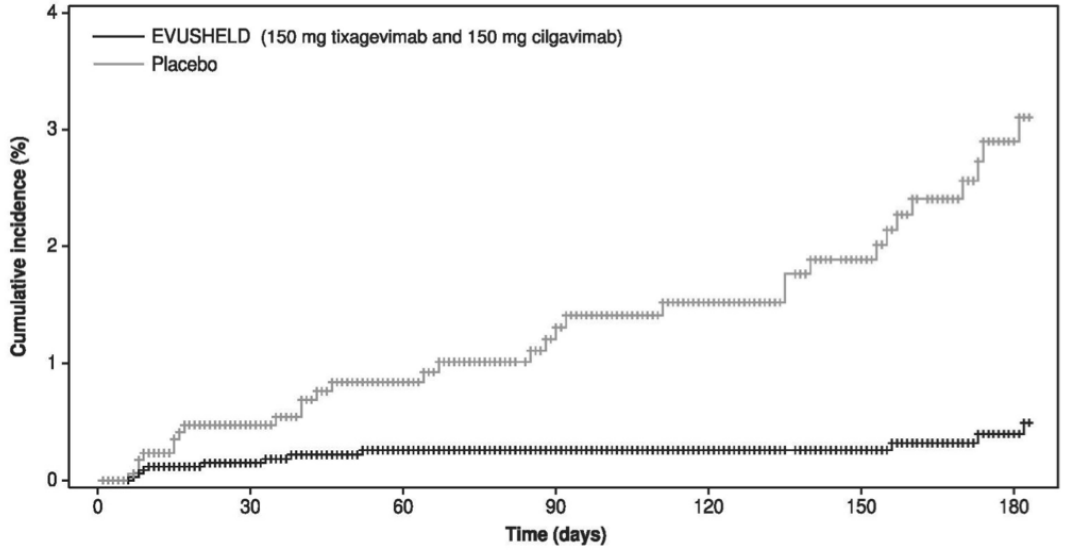
PROVENT

Efficacy data

Takeaway

One dose of EVUSHELD may be effective for six months for pre-exposure prevention in certain individuals

Figure 1 Kaplan Meier: Cumulative Incidence of Symptomatic COVID-19* (PROVENT)



Number of participants at risk

EVUSHELD	3441	2957	2393	2054	1815	1667	1044
Placebo	1731	1483	1177	991	856	774	472

* Subjects who do not experience a primary endpoint event (and had not discontinued) are censored at Day 183. Subjects who were unblinded/vaccinated prior to an event are also censored at the earlier time of unblinding/vaccination.

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FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. A[illegible]e from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Emergency Use Authorization

- Announced December 8, 2021

- FDA granted EUA for EVUSHELD for pre-exposure prophylaxis (PrEP) of COVID-19 in adults and adolescents (≥ 12 years and ≥ 40 kg):
  - Not currently infected with nor had recent exposure to a person with SARS-CoV-2 **and**
  - Moderate to severe immune compromise due to a medical condition or immunosuppressive medications **and** may not mount an adequate immune response to COVID-19 vaccination **or**
  - Unable to receive any COVID-19 vaccines due to history of severe adverse reaction to a COVID-19 vaccine

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FDA: Food and Drug Administration

FDA. FDA News Release: Coronavirus (COVID-19) Update: FDA Authorizes New Long-Acting Monoclonal Antibodies for Pre-exposure Prevention of COVID-19 in Certain Individuals. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-new-long-acting-monoclonal-antibodies-pre-exposure. Accessed 27 March 22.

Emergency Use Authorization

- Dose: 150 mg of tixagevimab and 150 mg of cilgavimab

- EVUSHELD is not authorized for:
  - Treatment of COVID-19
  - Post-exposure prophylaxis of COVID-19

- PrEP with EVUSHELD is not a substitute for COVID-19 vaccination
  - EVUSHELD should be administered two weeks after vaccination

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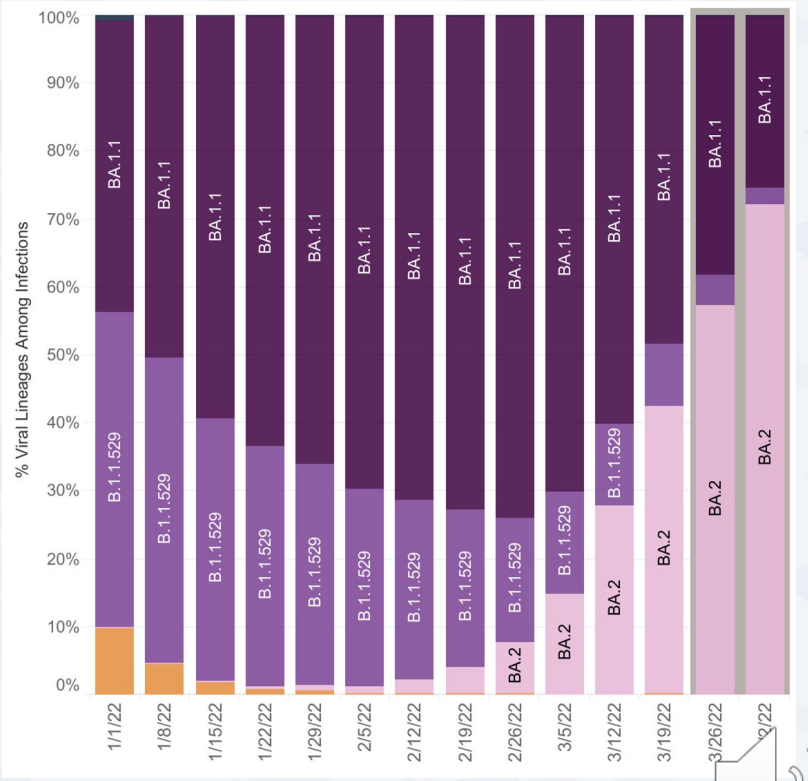
FDA: Food and Drug Administration
PrEP: pre-exposure prophylaxis

FDA. FDA News Release: Coronavirus (COVID-19) Update: FDA Authorizes New Long-Acting Monoclonal Antibodies for Pre-exposure Prevention of COVID-19 in Certain Individuals. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-new-long-acting-monoclonal-antibodies-pre-exposure. Accessed 27 March 22.

Omicron Variants

- PROVENT data were available before prevalence of Omicron

- As of 4/2/2022 – cases in US by variant
  - BA.2 – 72.2%
  - BA.1.1 – 25.3%



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CDC. COVID Data Tracker: Variant Proportions. Available from https://covid.cdc.gov/covid-data-tracker/#variant-proportions. Accessed 9 April 22.

Emergency Use Authorization

- Announced February 24, 2022

- FDA revised EVUSHELD dosing for PrEP of COVID-19

150 mg of tixagevimab and 150 mg of cilgavimab	→	300 mg of tixagevimab and 300 mg of cilgavimab

- Due to concerns that the originally authorized dose may not
  - Be able to prevent infection by the Omicron subvariants
  - Provide the duration of protection shown in the initial clinical trial

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FDA. FDA News Release: Coronavirus (COVID-19) Update: FDA authorizes revisions to Evushe[illegible]sing. Available from https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-revisions-evushe[illegible]d-dosing. Accessed 27 March 22.

Neutralizing Activity

FDA data

WHO Nomenclature	Tixagevimab	Cilgavimab
	Fold Reductions in Susceptibility (VLPs)	
Omicron BA.1	>600 to >1000-fold	460-fold
Omicron BA.1.1	>700 to >1000-fold	>500-fold
Omicron BA.2	>1000-fold	1.9-fold

WHO Nomenclature	EVUSHELD	
	Fold Reductions in Susceptibility (VLPs)	Fold Reductions in Susceptibility (authentic)
Omicron BA.1	132 to 183-fold	12 to 30-fold
Omicron BA.1.1	424-fold	176-fold
Omicron BA.2	No change	5.4-fold

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VLPs: virus-like particles

FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Neutralizing Activity

Touret et al

- *In vitro* data
- Neutralizing activity of tixagevimab, cilgavimab, and EVUSHELD against reference strain, Delta, BA.1 and BA.2

Antibody		Strains			
		BavPat B.1	**Delta**	**BA.1**	**BA.2**
Cilgavimab	EC_{50}	32.8	40.3	1617.0	49.8
	Fold-change	-	1.2	49.2	1.5
Tixagevimab	EC_{50}	18.3	17.2	Non-neutralizing	Non-neutralizing
	Fold-change	-	0.9	Non-neutralizing	Non-neutralizing
EVUSHELD	EC_{50}	27.0	24.7	712.2	73.3
	Fold-change	-	0.9	26.3	2.7

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Touret F, et al. In vitro activity of therapeutic antibodies against SARS-CoV-2 Omicron BA.1 and [illegible] Research Square. 2022. doi: https://doi.org/10.21203/rs.3.rs-1415749/v1.

Neutralizing Activity

Touret et al

Conclusions

- Cilgavimab exhibits greater activity against BA.2 compared to BA.1
- EVUSHELD retains potency against BA.1 and BA.2
- *In vivo* experiments needed to determine whether the combination of cilgavimab and tixagevimab is still relevant compared to cilgavimab alone

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Touret F, et al. In vitro activity of therapeutic antibodies against SARS-CoV-2 Omicron BA.1 and [illegible] Research Square. 2022. doi: https://doi.org/10.21203/rs.3.rs-1415749/v1.

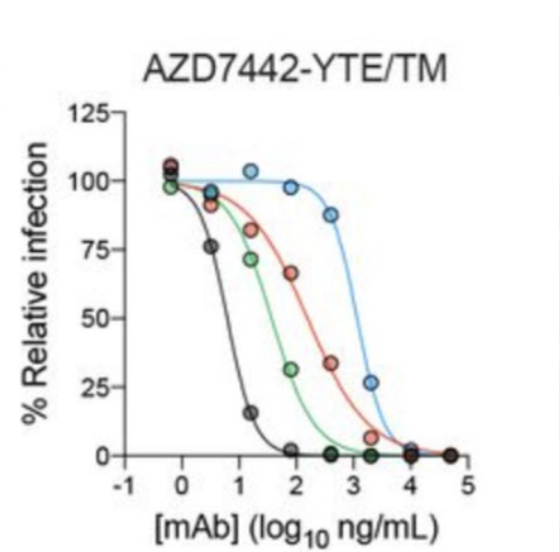
Neutralizing Activity

Case et al

In vitro data from Washington University School of Medicine

EVUSHELD neutralizing activity against Omicron subvariants and reference strain

AZD7442 = EVUSHELD



	Fold-change in EC_{50} value relative to D614G			
mAb	D614G	BA.1	BA.1.1	BA.2
S309	-	2.4	3.9	31.8
AZD8895	-	117.6	127.1	67.5
AZD1061	-	206.1	> 1,694	1.1
AZD7442	-	25.5	175.9	5.4

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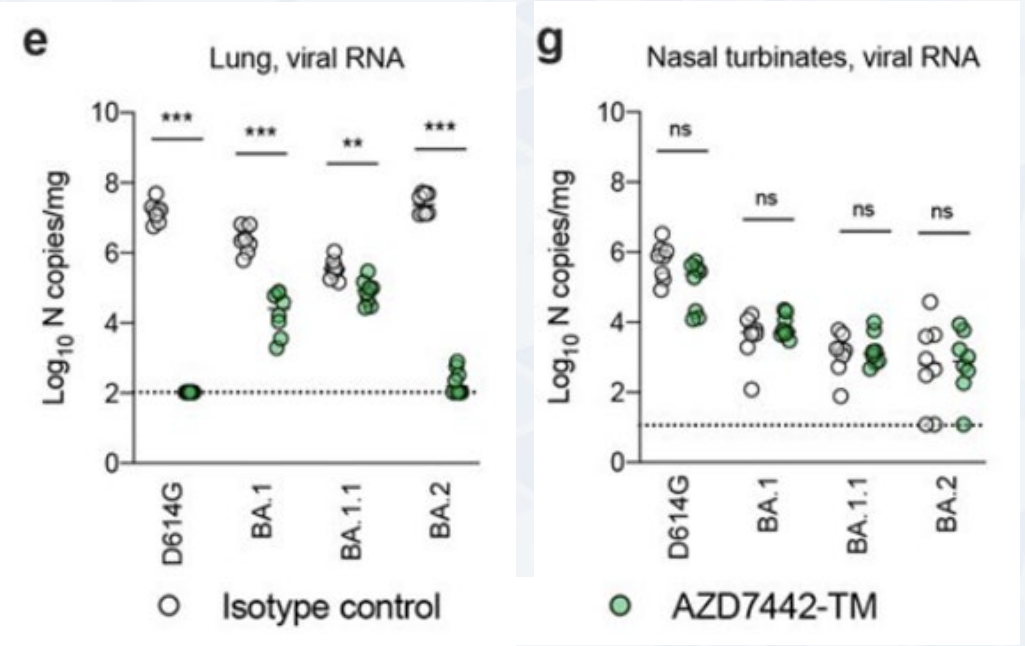
Case JB, et al. Resilience of S309 and AZD7442 monoclonal antibody treatments against infection by SARS-CoV-2 Omicron lineage strains. bioRxiv. 2022. doi: https://doi.org/10.1101/2022.03.17.484787.

Neutralizing Activity

Case et al

- First *in vivo* data evaluating EVUSHELD's efficacy against the Omicron variants
- 10 mg/kg dose administered to mice 1 day prior to infection
- Viral RNA in lungs and nasal turbinates of mice against Omicron variants and reference strain



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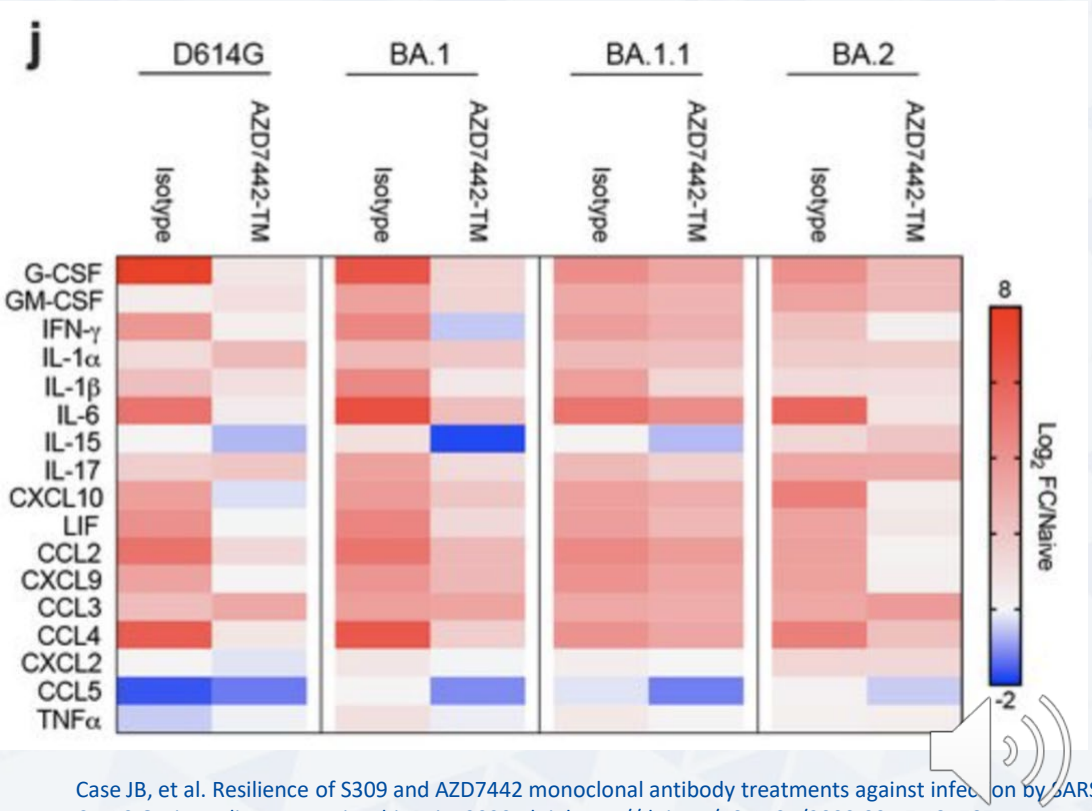
Neutralizing Activity

Case et al

- Heat map of cytokine and chemokine protein expression levels in lungs of mice
- Expression levels compared against isotype control mAbs and EVUSHELD for different Omicron variants and reference strains
- AZD7442 = EVUSHELD



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Neutralizing Activity

Case et al

Conclusions

- Neutralizing potency of EVUSHELD is reduced against BA.1.1 compared to BA.1 and BA.2 strains
- Despite losses in neutralization potency against BA.1, BA.1.1, and BA.2 strains *in vitro*, EVUSHELD reduced viral burden and pro-inflammatory cytokine levels in the lungs of mice

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Case JB, et al. Resilience of S309 and AZD7442 monoclonal antibody treatments against infection by SARS-CoV-2 Omicron lineage strains. bioRxiv. 2022. doi: https://doi.org/10.1101/2022.03.17.484787.

Emergency Use Authorization

- Clinical significance of reduced neutralizing activity *in vitro* against the Omicron variants remains to be determined
- FDA revised EVUSHELD dosing for PrEP of COVID-19

150 mg of tixagevimab and 150 mg of cilgavimab	→	**300 mg of tixagevimab and 300 mg of cilgavimab**

- If received initial dose ≤ 3 months ago, should receive a dose of 150mg of tixagevimab and 150 mg of cilgavimab
- If received initial dose > 3 months ago, should receive a dose of 300 mg of tixagevimab and 300 mg of cilgavimab

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1. FDA. FDA News Release: Coronavirus (COVID-19) Update: FDA authorizes revisions to Evusheld dosing. Available from https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-revisions-evusheld-dosing. Accessed 27 March 22.
2. FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. Available from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

NIH COVID-19 Treatment Guidelines

- Recommend EVUSHELD as PrEP for individuals approved under the EUA
  - EVUSHELD is not a substitute for COVID-19 vaccination
  - Should not be used in unvaccinated individuals for whom COVID-19 vaccination is recommended and who are anticipated to have an adequate response
  - *Updated 2/1/22*

Moderate to severe immunocompromising conditions (not comprehensive)	
Receiving active treatment for solid tumors and hematologic malignancies	Have a moderate or severe primary immunodeficiency
Received a solid-organ transplant and are taking immunosuppressive therapy	Have advanced or untreated HIV infection
Received chimeric antigen receptor T cell therapy or hematopoietic stem cell transplant	Receiving active treatment with high-dose corticosteroids

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NIH. COVID-19 Treatment Guidelines. Prevention of SARS-CoV-2 Infection. Available from https://www.covid19treatmentguidelines.nih.gov/overview/prevention-of-sars-cov-2/. Accessed 9 April 22.

Other Clinical Trials

STORM CHASER	
Design	Phase III, randomized (2:1), double-blind, placebo-controlled
Status	Ongoing
Intervention	Single IM dose of EVUSHELD (150 mg of tixagevimab and 150 mg of cilgavimab) vs placebo
Primary analysis	Efficacy of EVUSHELD for post-exposure prophylaxis of COVID-19 in adults

Primary efficacy analysis	• EVUSHELD (N= 749), placebo (N= 372)
	• Positive COVID-19 infections:
	  • 3.1% (EVUSHELD) vs 4.6% (placebo)
	  • Relative risk reduction of 33%, 95% CI: -26, 65
	• EVUSHELD did not demonstrate benefit in preventing symptomatic COVID-19 as post-exposure prophylaxis

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FDA. Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD. [illegible] from https://www.fda.gov/media/154701/download. Accessed 9 April 22.

Other Clinical Trials

TACKLE	
Design	Phase III, randomized (1:1), double-blind, placebo-controlled
Status	Ongoing
Intervention	Single IM dose of EVUSHELD (300 mg of tixagevimab and 300 mg of cilgavimab) vs placebo
Primary analysis	Efficacy of EVUSHELD for outpatient treatment of COVID-19
Inclusion	Adults ≥ 18 years of age, not hospitalized with mild-moderate COVID-19 and symptomatic for ≤ 7 days
Primary efficacy analysis	• EVUSHELD (N= 452), placebo (N= 451) • 90% of participants had high risk of progression to severe COVID-19 • EVUSHELD reduced the risk of developing severe COVID-19 or death by 50% compared to placebo • If administered within 5 days of symptom onset, EVUSHELD reduced risk by 67%

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AstraZeneca. AZD7442 reduced risk of developing severe COVID-19 or death in TACKLE Phase [illegible] outpatient treatment trial. Available from https://www.astrazeneca.com/media-centre/press-releases/2021/azd7442-phiii-trial-positive-in-covid-outpatients.html. Accessed 27 March 22.

NIH Supply Constraints Recommendations

Table 1: Limited supply; prioritize PrEP in individuals at highest risk for severe COVID-19 (not comprehensive)

- Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Chimeric antigen receptor T cell recipients
- Post-hematopoietic cell transplant recipients who have cGVHD or who are taking immunosuppressive medications for another indication
- Patients with hematologic malignancies who are on active therapy
- Lung transplant recipients
- Patients who are within 1 year of receiving a solid-organ transplant (other than lung transplant)
- Solid-organ transplant recipients with recent treatment for acute rejection with T or B cell depleting agents
- Patients with severe combined immunodeficiencies
- Patients with untreated HIV who have a CD4 T lymphocyte cell count <50 cells/mm^3

Table 2: Extremely limited supply; prioritize PrEP in individuals who meet criteria from Table 1 and have additional risk factors for severe disease

- Age ≥ 50
- Cardiovascular disease
- Chronic kidney disease
- Chronic lung disease
- Diabetes
- Obesity (body mass index ≥30)
- Sickle cell disease
- Full list : https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

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cGVHD: chronic graft versus host disease

NIH. COVID-19 Treatment Guidelines. The COVID-19 Treatment Guidelines Panel's Interim Statement on Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies When There Are Critical Supply Constraints. Available from https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies/. Accessed 28 March 22.

Summary

- EVUSHELD is indicated for PrEP for individuals who are immunocompromised and may have an inadequate immune response to COVID-19 vaccination
- In the primary analysis of PROVENT, EVUSHELD recipients saw 77% reduced risk of developing COVID-19 compared to placebo, but the study was conducted prior to emergence of Omicron
- FDA updated EVUSHELD EUA dose to 600 mg due to decreased neutralization activity against Omicron subvariants
- More data to determine clinical significance of reduced neutralizing activity *in vitro* against the Omicron subvariants

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Tixagevimab/Cilgavimab (EVUSHELD™)

A Review of Pertinent Drug Information for SARS-CoV-2

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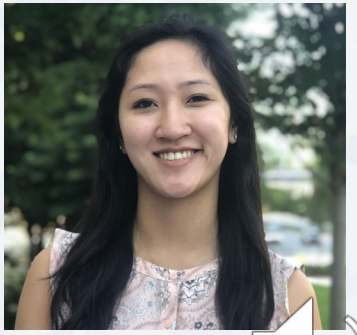

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Data as of April 10, 2022