EVIDENCE ASSESSMENT: NVX-CoV2373 COVID-19 vaccine

Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization

16 December 2021

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Key evidence to inform policy recommendations on the use of NVX-CoV2373 COVID-19 vaccine

Population

- Adults (18-64 years)
- Older adults (≥65 years)
- Individuals with comorbidities or health states that increase risk for severe COVID-19

Intervention

- NVX-CoV2373 COVID-19 vaccine (2 doses, day 0 and 21)

Comparison

- Placebo/active control

Outcomes

- Efficacy against (PCR confirmed) COVID-19 or severe COVID-19, any adverse event, serious adverse events, systemic and local adverse events

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Evidence retrieval

- Based on WHO and Cochrane living mapping and living systematic review of Covid-19 trials (www.covid-nma.com/vaccines) and on data submitted to WHO (WHO EUL/PQ evaluation process).

Retrieved evidence

Published data considered for policy recommendations on NVX-CoV2373 COVID-19 vaccine:

Phase I/II

- Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. Keech C, Albert G, Cho I, et al. N Engl J Med 2020; 383:2320-2332
- Different dose regimens of a SARS-CoV-2 recombinant spike protein vaccine (NVX-CoV2373) in younger and older adults: A phase 2 randomized placebo-controlled trial. Formica N, Mallory R, Albert G, et al. PLOS Medicine 18(10): e1003769. https://doi.org/10.1371/journal.pmed.1003769

Phase IIb

- Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant. Shinde V, Bhikha S, Hoosain Z, et al. N Engl J Med 2021; 384:1899-1909.

Phase III

- Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. Heath PT, Galiza EP, Baxter DN, et al. N Engl J Med 2021; 385:1172-1183
- Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico. Dunkle LM, Kotloff KL, Gay CL, et al. N Engl J Med 2021; December 15, 2021. DOI: 10.1056/NEJMoa2116185.
- Safety, immunogenicity, and efficacy of a COVID-19 vaccine (NVX-CoV2373) co-administered with seasonal influenza vaccines: an exploratory substudy of a randomised, observer-blinded, placebo-controlled, phase 3 trial. Toback S, Galiza E, Cosgrove C, et al. Lancet 2021; Published Online November 17, 2021. https://doi.org/10.1016/S2213-2600(21)00409-4.

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Quality assessment*

Type of bias/ Publication	**Keech et al.**	**Formica et al.**	**Shinde et al.**	**Heath et al.**	**Dunkle et al.**
Randomization	Some concerns	Some concerns	Low	Low	Low
Deviations from intervention	Low	Some concerns	Low	Some concerns	Some concerns
Missing outcome data	Low	Low	Some concerns	Some concerns	Low
Measurement of the outcome	Low	Low	Low	Low	Low
Selection of the reported results	Low	Some concerns	Some concerns	Some concerns	Low
Overall risk of bias	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns

*The risk of bias judgement by domain corresponds to the highest risk of bias among outcomes by domain. The overall risk of bias corresponds to the overall highest risk of bias assessed among outcomes.

- See: www.covid-nma.com/vaccines
- Critical outcomes: Incidence of participants with positive test for SARS-CoV-2 infection by RT-PCR OR Nucleic acid amplification testing (NAAT) or other validated test (symptomatic or asymptomatic), Incidence of symptomatic COVID-19 confirmed with positive test for SARS-CoV-2 infection by RT-PCR OR NAAT, Severe or critical disease defined according to the WHO definition or as reported by trialists, All-cause mortality, Incidence of systemic adverse events (D14), Incidence of any adverse events, Incidence of serious adverse events (SAEs).

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World Health Organization

Strategic Advisory Group of Experts (SAGE) on Immunization Evidence to recommendations framework[i]

Question: **Population:** **Intervention:** **Comparison(s):** **Outcome:**							
Background:							
	CRITERIA	**JUDGEMENTS**				**RESEARCH EVIDENCE**	**ADDITIONAL INFORMATION**
PROBLEM	Is the problem a public health priority?	*No* ☐	*Un-certain* ☐	*Yes* ☐	*Varies by setting* ☐		
BENEFITS & HARMS OF THE OPTIONS	Benefits of the intervention Are the desirable anticipated effects large?	*No* ☐	*Un-certain* ☐	*Yes* ☐	*Varies* ☐		

Questions which were considered in SAGE evidence-to-recommendation tables:

1. Should NVX-COV2373 vaccine be administered to adults (18-64 years) to prevent COVID-19?

2. Should NVX-COV2373 vaccine be administered to older adults (≥65 years) to prevent COVID-19?

3. Should NVX-COV2373 vaccine be administered to individuals with comorbidities or health states that increase risk for severe COVID-19 to prevent COVID-19?

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Question: Should NVX-COV2373 vaccine be administered to adults to prevent COVID-19?

CRITERIA	QUESTION	JUDGEMENT	EVIDENCE/ JUSTIFICATION
Problem	Is the problem a public health priority?	YES	Cumulative number of COVID-19 cases and deaths globally (https://covid19.who.int/table)
Benefits of the intervention	Are the desirable anticipated effects large?	YES	Clinical trials (Phase I-III)
Harms of the interventions	Are the undesirable anticipated effects small?	YES	Clinical trials (Phase I-III)
Balance between benefits and harms		**FAVOURS INTERVENTION**	

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Question: Should NVX-COV2373 vaccine be administered to adults to prevent COVID-19?

CRITERIA	QUESTION	JUDGEMENT	EVIDENCE/ JUSTIFICATION
Values and preferences	How certain is the relative importance of the desirable and undesirable outcomes?	Possibly important uncertainty or variability	Different population groups may have different opinions regarding the weights assigned to desirable and undesirable outcomes.
	Are the desirable effects large relative to undesirable effects	Probably Yes	In general, the target population assigns more weight to the desirable effects than to the undesirable effects related to COVID-19 vaccination. This may vary by (sub)population.
Resource use	Are the resources required small?	No	While NVX-COV2373 can be distributed and stored using existing cold chain infrastructure, considerable resources will be needed to ensure the implementation of a COVID-19 vaccination programme.
	Cost–effectiveness	Varies	Formal global cost–effectiveness analyses have not been conducted, but the emerging evidence indicates that the benefits, including the impact on recovery of the global economy, are likely to outweigh the costs of COVID-19 vaccination in general at global level.
Equity	What would be the impact on health inequities?	Reduced	If distributed fairly, COVID-19 vaccines may have considerable impact on reducing health inequities.
Acceptability	Which option is acceptable to key stakeholders (e.g. ministries of health, immunization managers)?	Intervention	As vaccination is an eagerly awaited tool to combat COVID-19, it is assumed that key stakeholders, in particular ministries of health and immunization managers, are strongly in favour of it.
	Which option is acceptable to the target group	Intervention	COVID-19 vaccine acceptability, in general, varies between (sub-) population groups and may be correlated with the perceived risk posed by the vaccine versus the perceived risk posed by the disease.
Feasibilty	Is the intervention feasible to implement?	Intervention	NVX-COV2373 vaccine is assumed to be easily implementable in settings, including low- and middle-income countries, with existing vaccine logistics and delivery infrastructure.
Balance of consequences		**Desirable consequences *clearly outweigh* undesirable consequences in most settings**	

GRADEing of Evidence	Statement on quality of evidence	SAGE Working Group Judgement
Efficacy against PCR confirmed COVID-19 (Adults)	**High level of confidence**	We are very confident that 2 doses of NVX-COV2373 vaccine are efficacious in preventing PCR-confirmed COVID-19 in adults (18–64 years).
Safety-serious adverse events (Adults)	**Moderate level of confidence**	We are moderately confident that the risk of serious adverse events following 1 or 2 doses of NVX-COV2373 vaccine in adults (18–64 years) is low.
Efficacy PCR confirmed COVID-19 (Older adults)	**Moderate level of confidence**	We are moderately confident that 2 doses of NVX-COV2373 vaccine are efficacious in preventing PCR-confirmed COVID-19 in older adults (≥65 years).
Safety-serious adverse events (Older adults)	**Moderate level of confidence**	We are moderately confident that the risk of serious adverse events following 1 or 2 doses of NVX-COV2373 vaccine in older adults (≥65 years) is low.
Efficacy PCR confirmed COVID-19 (*Individuals with comorbidities or health states that increase risk for severe COVID-19*)	**Moderate level of confidence**	We are moderately confident that 2 doses of NVX-COV2373 vaccine are efficacious in preventing PCR-confirmed COVID-19 in individuals with comorbidities or health states that increase risk for severe COVID-19 as included in the clinical trial. No data were obtained on vaccination of pregnant or breastfeeding women, or persons who were immunocompromised.
Safety-serious adverse events (*Individuals with comorbidities or health states that increase risk for severe COVID-19*)	**Low level of confidence**	We have low confidence in the quality of evidence that the overall risk of serious adverse events in individuals with comorbidities or health states that increase risk for severe COVID-19 following 1 or 2 doses of NVX-COV2373 vaccine is low.

Heterologous primary series – Com-COV2

Overview

Study	Stuart et al; Lancet
Country	UK
Study type	Single-blind RCT
Population	Adults ≥50y

Groups (ranked by increasing post-D2 GMC)

Dose 1	Dose 2	N	Day 28 NAb GMC (95% CI), NT_{50}
AZ	AZ	171	109 (70–168)
AZ	NVX	167	432 (301–618)
BNT	NVX	172	1109 (805–1529)
BNT	BNT	167	1501 (1188–1896)
AZ	MOD	167	1684 (1313–2162)
BNT	MOD	164	1883 (1546–2294)

+9.5w

Conclusions

- Antibody response: AZ-NVX > AZ-AZ but BNT-NVX < BNT-BNT
- Across all groups, cellular response was strongest for AZ-NVX but weakest for BNT-NVX
- NVX as second dose had equivalent or lower reactogenicity compared with homologous doses

Heterologous boosters – COV-BOOST

Overview

Study	Munro et al; Lancet
Country	UK
Study type	Blinded RCT
Population	Adults ≥30y

Groups (ranked by increasing post-boost GMC)

Primary	Boost	N	Day 28 NAb GMC (95% CI), pseudo-NT_{50}
2 x AZ	AZ	98	193 (161–231)
2 x AZ	JNJ	95	563 (454–698)
2 x AZ	NVX	87	727 (598–883)
2 x BNT	NVX	94	766 (624–939)
2 x BNT	AZ	98	950 (802–1126)
2 x BNT	JNJ	75	1441 (1188–1749)
2 x AZ	BNT	93	1621 (1314–1998)
2 x BNT	BNT	95	1789 (1520–2107)
2 x BNT	MOD	91	2019 (1621–2513)
2 x AZ	MOD	97	2368 (2054–2730)

>10w

Conclusions

- All WHO EUL vaccines boosted antibodies in relative to MenACWY control
- Antibody response: AZ-AZ-NVX > AZ-AZ-AZ but BNT-BNT-NVX < BNT-BNT-BNT
- After AZ-AZ, NVX boosted cellular response more than AZ
- After BNT-BNT, NVX boosted cellular response less than BNT
- NVX had equivalent or lower reactogenicity compared with homologous booster doses


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