World Health Organization

What evidence do we have that omicron is evading immunity and what are the implications?
Meeting objectives

Phil Krause, M.D.
Chair, WHO COVID Vaccines Research Expert Group
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R&DBlueprint
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to prevent epidemics

Now that the omicron variant has been detected in many countries:

Assessment of the threat will depend on its:

- Transmissibility
- Virulence
- Capacity for evading immunity in those previously vaccinated or infected

Key decisions will need to be made:

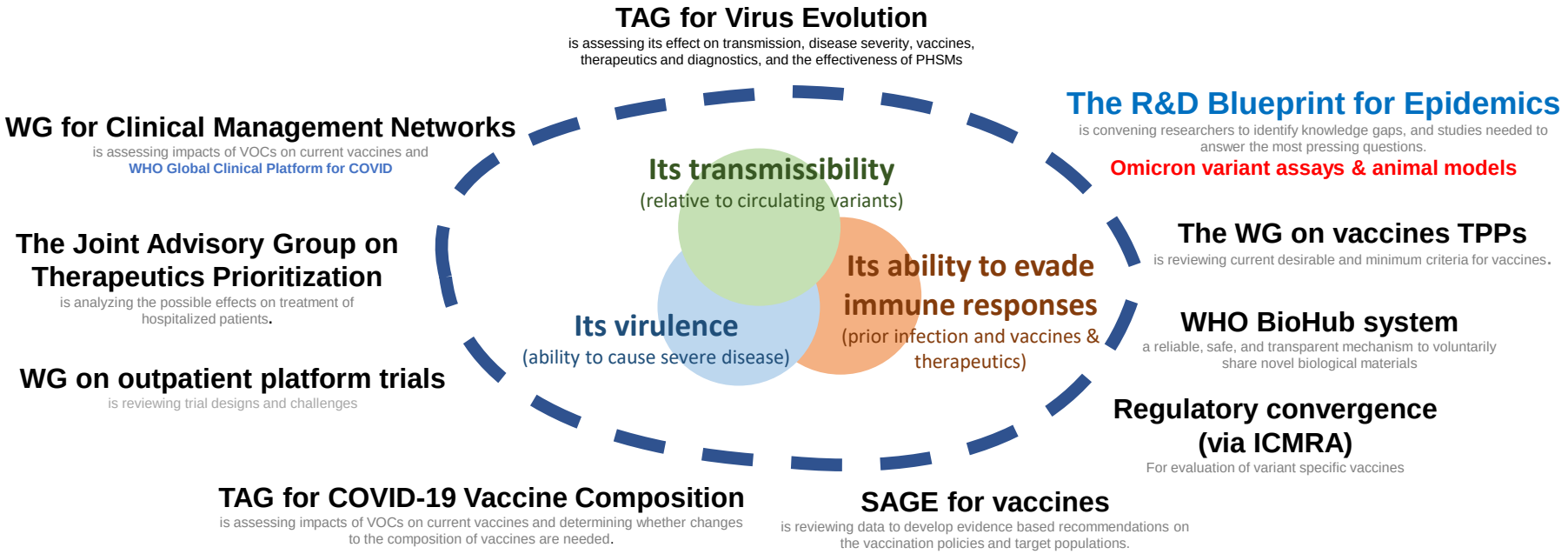
- What are the implications for vaccine development, vaccine evaluation, and vaccine deployment?

Assessment of the threat and decision-making will depend on results of research

- What needs to be done to facilitate the global response?

Under an IMST, WHO is assessing the threat of VOCs (including omicron)

3 key properties of a variant are likely to influence the overall threat from it.



Hundreds of researchers around the world are contributing their data and expertise to the deliberations

Key knowledge gaps (from December 6 meeting)

Specific information about omicron variant- transmissibility, virulence, adaptive immune avoidance for various vaccines

Omicron exposed gaps in global seroepidemiology

Still need more information on best vaccine regimens

New vaccines might be needed, and manufacturers are getting started. This is easier for mRNA and vectored vaccines. This will also require at least some new assays.

Standardization of assays is critical

Other research needs: original antigenic sin, role of T cells in severe disease, more broadly protective vaccines, improved effectiveness studies (e.g., operational research during deployment), vaccine effectiveness against severe disease

In all decisions, consider likely consequences among the unvaccinated, the previously infected, and the vaccinated. Global access to vaccines is critical.

Data on omicron variant continue to emerge

Epidemiology

Clinical course

Immunology

Vaccine induced immunity

- neutralizing antibody responses
- protection

Even if disease is milder, rapid spread of omicron has the potential to overcome other responses and to saturate health care systems

These data are rapidly emerging and are critically important but have not yet been peer reviewed

Goals of the meeting

Present and review the available evidence

Critically appraise the data

Outline research and other priorities for omicron variant response

What I heard…

Need to be careful about conclusions when assays are new (e.g., unstandardized) and sample numbers are small. Different omicron sequences may also be relevant. Nonetheless, some consistent findings emerged.

Variants have greatest impact on neutralizing antibody responses. Fc dependent antibody mechanisms, CD8, CD4, memory B cells are less susceptible but also important for protection against SARS-CoV-2

CD4 and CD8 T cell responses to vaccines and previous infection remain largely intact against variants including omicron

Reduced omicron neutralization vs ancestral virus & previous variants. Some differences in results may be due to differences in standardization, comparators, or cohort differences, which should be further explored. This reduction observed in CP and with several vaccines.

Booster or additional exposure of vaccinees via infection increases neutralization, may also increase breadth of neutralizing response. But response also may wane quickly (within 3 months).

Reduced ADCC activity vs. omicron compared with other variants

Loss of neutralization in naturally infected people may be lower. Vaccination of these people increases neutralizing capacity of their serum.

Loss in neutralization by many monoclonals (possible exceptions Vir7831 and DXP-604)

Many point mutations in omicron permit escape from neutralizing antibodies

The virus, and even the omicron variant, is continuing to evolve

Omicron virus requires ACE-2 and doesn't grow as well as previous variants in Vero cells especially with additional passage

Reduced RBD-ACE binding in omicron vs. WT or beta or delta, and reduced serum RBD binding

Milder disease possibly also in Israel- with no omicron hospitalization so far.

Other data not presented

Pfizer effectiveness vs omicron in UK vs. symptomatic illness <40% increased to ~75% with boost. AZ vaccine had negative effectiveness point estimate vs. symptomatic illness increased to ~75% with boost (Nick Andrews, UKHSA)

Pfizer vaccine effectiveness vs. hospital admission with omicron in South Africa was (~70%-- higher in younger people). Hospital admission rate for omicron was ~30% less than that with first wave (Mia Malan)

Modeling indicates importance of PHSM in addition to vaccination (John Edmunds)

Greater omicron replication in (ex vivo) bronchus vs. lung (Muge Cevik)

Breakthrough infections in boosted individuals (Wolfgang Preiser)

What does this mean?

Reduced neutralizing titers to omicron suggests that vaccine effectiveness will be reduced against symptomatic disease– this is being borne out. This also suggests that vaccine will be less effective against transmission, and has implications for PHSM.

Protection against severe disease which is mediated more by other mechanisms is more likely to be preserved– this also appears to be the case with some possible reduction based on early data from South Africa

Emerging data suggests the possibility that disease could be less severe, with lower numbers hospitalized, shorter duration of hospitalization

What does this mean (2)?

Even if disease is milder, rapid onslaught of the virus could overwhelm health care systems (doubling time of 2.5 days means 50X increase in 2 weeks)

Projected transmission rates, if borne out, do not give us much time for interventions.

PHSM can be rapidly implemented by everyone– and along with redoubled vaccination efforts (especially for the unvaccinated) will be critical for spreading out the projected impact of omicron

Boosters may provide a short term benefit but possible short duration of effect, continuing virus evolution suggest they may not have a major effect on course of the pandemic

We should consider further accelerating the development of new vaccines to cover omicron, even if we are not sure we will need them

Key research needs:

Increase standardization of assays and readouts

More information about mechanisms of protection especially vs. severe disease

Larger studies

Animal studies

Sharing of reagents, e.g. convalescent omicron serum

Omicron-specific responses to more vaccines including other variant-specific vaccines

What is the source of VOC? Need to prepare for future variants…

Connection of lab results to clinical outcomes

More epidemiological data

- vaccine effectiveness vs omicron (especially for more vaccines & in different groups)
- severity of omicron disease in different groups
- spread and transmissibility of omicron