Update with the development of Ebola vaccines and implications to inform policy recommendations

Conclusions and recommendations

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Considerations (1)

13 candidate Ebola vaccines underwent or are actively undergoing clinical development at different trial phases.

A prime/boost candidate vaccine based on rVSV- and Ad5-vectored components (GamEvac-Combi) is licensed in Russia and a monovalent Ad5-EBOV is licensed in China, both for emergency use.

Considerations (2)

- ✓ The rVSVΔG-ZEBOV-GP is currently being deployed under Expanded Access/Compassionate Use in outbreak response in Nord-Kivu, DRC as per SAGE recommendations
- ✓ The rVSVΔG-ZEBOV-GP candidate and a prime/boost Ad26.ZEBOV/MVA-BN-Filo candidate vaccine have submitted EUAL documentation to the WHO Secretariat.
- ✓ There are plans for additional evaluation of the Ad26.ZEBOV/MVA-BN-Filo in at risk countries.

1. Are there **remaining challenges that may prevent access** to Ebola vaccines in future outbreaks?

If yes, can SAGE make recommendations on how these might be addressed?

Conclusions

- Recognition of momentous progress made in the development and evaluation of several vaccine platforms against Ebola and other filoviruses

- Intensification of efforts in reaching a consensus and clarity on specific aspects of regulatory pathways that would allow the development and registration of candidate Ebola vaccines.
- Ongoing facilitation by Secretariat regulatory convergence through development of WHO Guidelines for Ebola vaccines evaluation

Conclusions

- Encouragement to developers to engage relevant NRAs, in particular, national and regional regulatory agencies/structure of African countries.
- Submission of additional data on the GamEvac-Combi and monovalent Ad5-EBOV to apply for WHO evaluation
- Encouragement for clinical evaluation of other candidate vaccines in the pipeline

The duration of the immune responses elicited by the Ebola vaccines under development is currently being evaluated.

The information on the duration of protection for various candidate Ebola vaccines is up to 360 days post vaccination for the rVSVΔG-ZEBOV-GP, Ad26.ZEBOV/MVA-BN-Filo, and ChAd3-EBOZ vaccines.

Although the understanding of the immune response to both natural infection and vaccination remains incomplete, it is expected that prime/boost vaccines offer better prospects of long-term protection to an Ebola virus infection than a single dose schedule.

However, vaccines that elicit an earlier immune response after a single/first dose are likely to be more useful during outbreaks.

Another uncertainty is whether vaccines protecting against Zaire Ebola virus species afford cross-protection against other species of Ebola virus and other filoviruses.

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There is no data on cross-protection against Marburg virus for any candidate vaccine.

2. Is the current **evidence sufficient for SAGE to adjust current recommendations** regarding the use of Ebola vaccines in case of another Ebola outbreak?

- If yes, which recommendations can be proposed?
- If not, what key data are missing?

Overall, modelling suggests that pre-emptive vaccination of HCW combined with a reactive ring vaccination strategy is the most effective strategy to contain future Ebola outbreaks.

Replacing ring vaccination by mass vaccination is less efficient as it reduces the chances of preventing large outbreaks (e.g. from 80% to 50% for R0 = 1.8)

Interim recommendations (1)

"Should an Ebola disease outbreak occur before the candidate vaccine is licensed, SAGE recommended that the rVSVΔG-ZEBOV-GP vaccine be promptly deployed under the Expanded Access framework, with informed consent and in compliance with Good Clinical Practice.

If the outbreak is caused by an Ebola virus species other than Zaire, consideration should be given to the use of other candidate vaccines that target the putative viral species.

Interim recommendations (2)

Ring vaccination, as used in the Phase 3 study in Guinea, is the recommended delivery strategy.

This should be adapted to the social and geographic conditions of the outbreak areas and include people at risk including but not limited to:

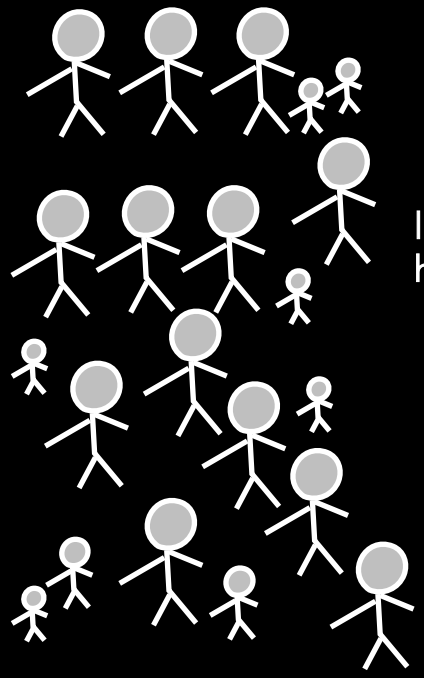
(i) contacts and contacts of contacts;

(ii) local and international health-care and front-line workers in the affected areas and

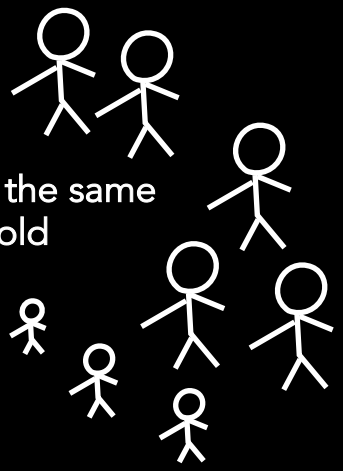
(iii) health-care and front-line workers in areas at risk of expansion of the outbreak."

Who is offered Ebola vaccine in a ring vaccination?

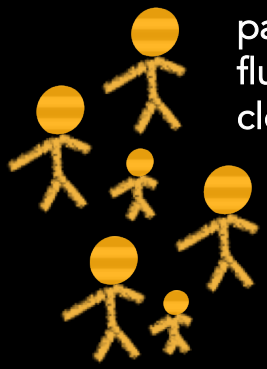
Contacts and contacts of contacts



extended family



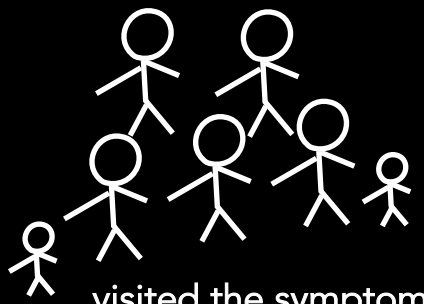
lived in the same household



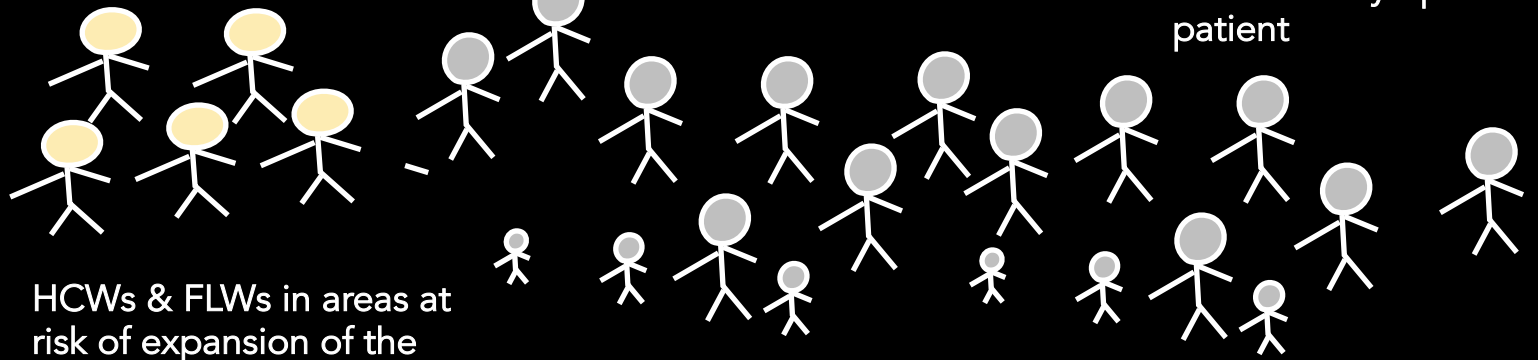
High risk contact: close contact with patient body or body fluids, linen, or clothes

household members of high risk contacts

Lab confirmed EVD case

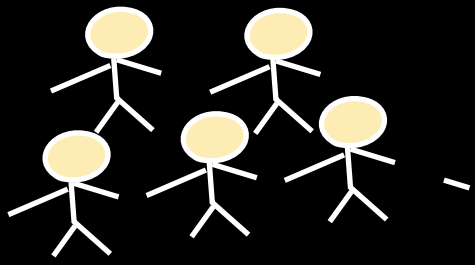


visited the symptomatic patient



neighbors

HCWs & FLWs in areas at risk of expansion of the outbreak



local & international HCWs & FLWs in the affected areas

Interim recommendations (3)

A geographically targeted vaccination strategy can be considered in settings where it is not possible to identify the individuals making up the ring vaccination cohorts because of serious security, social or epidemiological issues.

In this case, the geographic area immediately around an Ebola case, such as a village or a neighborhood, is most likely to include those individuals who were the contacts or contacts-of-contacts of the index case.

Interim recommendations (4)

An expanded strategy to vaccinate all individuals in this defined geographic area will require a larger number of vaccinations than would be used in a ring vaccination intervention in the same area.

Even in this setting, informed consent and compliance with Good Clinical Practice will be required, but the intensity of follow up of vaccinated individuals will be determined by the context of the intervention.

In this geographically targeted approach, the intent remains to immunize those people most at risk of secondary spread from an identified Ebola case."

3. What are the **conclusions from the benefits and risk analysis of vaccination of pregnant women** with rVSV-ZEBOV as part of Expanded Access/ Compassionate Use during Ebola outbreaks?

Thank you