SAGE Working Group on Varicella and Herpes Zoster Vaccines

Conclusions and Recommendations

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Varicella Disease Burden- General Population Conclusions

- Information on burden of varicella is available primarily from industrialized countries
- It is likely that the burden in low and middle income countries is higher than in industrialized countries.
- In countries where burden is well described, the severe disease burden is much lower than for measles, rotavirus or pneumococcal disease.
- In temperate climates varicella exhibits a strong seasonality. Most cases occur before 10 years and the great majority of adults are seropositive when tested.
- In tropical areas, varicella may show a seasonal distribution, but a larger proportion of adults, especially in low population density areas, are seronegative.
- Varicella causes higher morbidity and mortality in immunocompromised populations.

Varicella Vaccine- General Population
Conclusions

- Varicella vaccine is effective and safe and results in substantial declines in morbidity and mortality in countries that have introduced vaccination
- **Coverage levels of <80% in children could result in an increase in morbidity and mortality due to an overall shift of varicella burden to a higher age group.**
- Private market use of vaccine, might reach coverage levels high enough (20%-80%) to have a detrimental effect of increasing the median age of varicella and the burden of varicella, but not sufficiently high to ensure protection at a country level.
- Cost-effectiveness results are subject to the uncertainty of the boosting effect of circulating varicella on the incidence of herpes zoster later in adulthood although studies to date have not confirmed that increases in herpes zoster incidence seen globally are attributable to varicella vaccine.

Varicella Vaccine- General Population Recommendations

- **Countries where varicella is an important public heath and socio-economic burden should assess whether adequate resources can be allocated to implement varicella vaccination in a routine childhood immunization schedule to achieve and maintain high coverage levels (>80%).**

- **Countries in which coverage levels from use of varicella vaccine in the private sector reach between 20%-80% should give a higher priority to considering implementing a routine vaccination program to reach the coverage ≥80% due to the likelihood that the incidence of disease that occurs in adults would otherwise increase.**

Varicella Vaccine- General Population Recommendations

- Dosage is dependent on the goal of the program:
  - one dose schedule: country focus is to reduce mortality and severe morbidity from varicella.
  - two doses schedule: country focus, in addition to decreasing mortality and severe morbidity, is to further reduce the number of cases and outbreaks which might continue to occur with a one dose schedule.

- Countries with a high average age (≥15 years) of infection could take into consideration alternate vaccination strategies such as vaccination of susceptible adolescents and adults.

Varicella Vaccine
Immunocompromised Patients
Recommendations

- Varicella vaccine is usually contraindicated in persons with congenital or acquired immune deficiencies. However, it has been used in selected immunocompromised populations because of the risk of severe vaccine-related complications.

- Use of the vaccine in these specific populations should only be considered in health care settings where specific antiviral therapy is readily available and physicians have expertise with the vaccine in these populations.

Varicella Vaccine- Immunocompromised Patients with HIV Recommendations

- The use of the vaccine (2 doses administered 3 months apart) should be considered in clinically stable HIV-infected children including those receiving highly active antiretroviral therapy (HAART) with CD4 determinations ≥15%.

- The vaccine has not been studied in individuals with CD4 <15% or in those who are not clinically and immunologically stable and should not be used in these situations.

Varicella Vaccine
Immunocompromised Patients with Malignancies
Recommendations

- In general children who have successfully completed chemotherapy and remain in remission can receive the vaccine approximately 3-6 months after all chemotherapy is completed.

- Protocols defining timing of vaccination in terms of time in remission on maintenance chemotherapy, when to interrupt that chemotherapy (including corticosteroids) before and after vaccination, and minimal acceptable lymphocyte and platelet counts at the time of vaccination should be followed.

Varicella Vaccine
Immunocompromised Patients with other Types of Immunodeficiencies
Recommendations

- Varicella vaccine can be safely given to subjects with isolated defects in antibody production (i.e. hypo- or agammaglobulinemia).

- It should not be given to those with conditions where defects in antibody production are part of an immunodeficiency condition that includes defects in cellular immunity (i.e. severe combined immunodeficiency, etc.) or on any condition characterized by defects in cellular immunodeficiency, except as described previously for HIV, ALL and certain solid tumors.

Varicella Vaccine- Immunocompromised Patients
Household Contacts
Recommendations

- Varicella vaccine can be safely used in household contacts of immunocompromised patients given the risk of transmission from a vaccinated person to the patient or their household contacts is very low.

- Household contacts of immunocompromised patients should be considered for vaccination.

- Two doses are recommended for household contacts of immunocompromised persons for higher effectiveness even if the country has a routine one dose childhood program.

Varicella Vaccine- Pregnant Women Recommendations

- Varicella vaccine is contraindicated during pregnancy and pregnancy should be delayed for 4 weeks after vaccination.

- Routine laboratory documentation of pregnancy status prior to vaccination is not recommended.

- Termination of pregnancy is not recommended for pregnant woman who are inadvertently vaccinated.

- Given implementation of varicella vaccination in the routine program, efforts should be made to counsel and vaccinate susceptible women post-partum in order to prevent infections during subsequent pregnancies.

Varicella Vaccine- Health Care Workers (HCWs) Recommendations

- In view of a higher risk of exposure and consequently transmission of the varicella-zoster virus to patients at high risk for serious complications, countries should consider vaccination of susceptible HCWs with two doses of varicella vaccine even in absence of varicella vaccination in the routine immunization schedule.

- Where financial constraints prohibit vaccination of all susceptible HCWs, priority should be given to vaccination of HCWs in close contact with persons at high risk of serious varicella complications such as immunocompromised individuals, neonates and pregnant women.

Herpes Zoster (HZ) Disease and Vaccine Conclusions

- Burden of HZ disease data are missing from most middle and low income countries including the effect of life expectancy, HIV prevalence, availability of treatment, and other factors.

- The impact of large-scale varicella vaccination programs on the incidence of HZ disease warrants continued surveillance. Although an increase in HZ incidence has been observed in countries with universal VZV vaccination programs the increase precedes the commencement of the varicella vaccination programs. Additionally, an increase has been observed in countries without childhood varicella vaccination programs.

Herpes Zoster (HZ) Disease and Vaccine Conclusions

- The vaccine is safe and effective against herpes zoster and post-herpetic neuralgia. However no data are available on long term protection induced by the HZ vaccine. Available data shows short term protection and waning of immunity.

- Assuming long-term protection (10-15 years), which appears now to be an unlikely scenario, modeling demonstrated the vaccine to be cost-effective in high-income countries. No data on cost-effectiveness is available from low- and middle-income countries.

Herpes Zoster Vaccine
Recommendations

- **Due to very limited data and the unknown burden of HZ disease in most countries, initial evidence of waning of protection over time and uncertainty of the optimal age for vaccination and the potential role of a booster dose, the working group cannot make any recommendation about routine HZ vaccination at this time.**
- Some countries may decide to introduce vaccination if they have an important burden of disease and consider the program beneficial.
- For those countries deciding to proceed with a HZ vaccination program, the optimal age and dosing schedule of herpes zoster vaccination should take into consideration vaccine effectiveness, efficacy of booster doses, age-dependent burden of disease, cost-effectiveness and duration of vaccine protection.

Varicella
High Priority Research Areas

- Burden of varicella in low and middle income countries
- Better data on varicella age-specific morbidity and mortality, especially in low and middle income countries
- More data to understand the effect of varicella vaccination on herpes zoster, both through observational studies and modeling
- More evidence to help determine how different varicella vaccine coverage levels would change varicella epidemiology

Herpes Zoster
High Priority Research Areas

- Disease burden studies in low- and middle-income countries.
- Duration of vaccine protection against HZ and severe complications (PHN, other).
- Safety and efficacy of investigational vaccines in immunocompromised patients such as those with HIV.
- Cost-effectiveness of herpes zoster vaccine in immunocompetent and immunocompromised populations, especially in low and middle income countries.