Summary of Key Points

WHO Position Paper on Vaccines against Hepatitis E Virus (HEV) May 2015

World Health Organization

Background

- **Hepatitis E Virus (HEV):** leading cause of acute viral hepatitis in developing countries.
- **Genotypes 1 and 2:**
  - Primarily infect humans, mainly male young adults
  - WHO estimates 44000 deaths in 2015 (3.3% of mortality from viral hepatitis).*
  - Genotype 1 is:
    - most prevalent;
    - widely found in Asia and Africa;
    - causes high mortality in pregnant women, and poor fetal outcomes
  - Genotype 2 cases in Mexico, Nigeria, Namibia
- **Genotypes 3 and 4:**
  - Primarily infect mammalian animals; occasional transmission to humans
  - Genotype 3 cases almost entirely in developing countries
  - Genotype 4 human cases mainly in mainland China and Taiwan

* Global hepatitis Report, 2017. Geneva: World Health Organization; 2017

Background

- **HEV transmission:**
  - Sporadic disease in endemic countries.
  - Periodic large epidemics due to contamination of water sources.
  - Greatest disease burden in developing areas where clean water is scarce.
- **Treatment**:
  - Treatment is generally supportive.
  - Fulminant cases: no treatment
  - Chronic cases: ribavirin and interferon

Vaccines

- HEV 239 Vaccine:
  - Hecolin®
  - The only experimental vaccine at clinical trial stage in humans that has been developed and manufactured.
  - Currently only licensed in China
  - Licensed for use in people 16-65 years of age who are at high risk for HEV infection based on occupation/lifestyle
    - Those involved in animal husbandry, food handling, students, army personnel, young women, travellers

Immunogenicity and Effectiveness

- Highly immunogenic
  - Almost all recipients seroconverted after 3 doses on a 0,1,6 month schedule.

- Efficacy rate:
  - High efficacy rate in healthy adults between 16-65 years of age in China, primarily against Genotype 4.
  - Limited data on protection against Genotype 1
  - No data on protection against Genotypes 2 and 3
  - However, there is data to show expected protection against all 4 genotypes.

Safety: review by the Global Advisory Committee on Vaccine Safety in 2014

- HEV 239 well tolerated and good safety profile in those aged 16-65 years.
- No safety data in those < 16 years, > 65 years and those organ transplant recipients, other immunosuppressed, or with chronic liver disease.
- Limited reassuring data with respect to maternal and fetal outcomes following use during pregnancy (based on 37 women having received a total of 53 doses).
- Need for post-marketing study.

WHO Position

- Hepatitis E recognized as an important public health problem in developing countries
  - Especially among special populations: pregnant women, displaced individuals living in camps, outbreak situations.

- In the absence of sufficient information, the WHO does not:
  - make a recommendation on the introduction of the vaccine for routine use in national programmes in populations where epidemic and sporadic hepatitis E disease is common. However, national authorities may decide to use the vaccine based on the local epidemiology.
  - Recommend routine use of vaccine in the following groups in endemic areas:
    - Children below age of 16 years
    - Pregnant women
    - Patients with chronic liver disease
    - Patients on organ transplant wait lists
    - Travellers

WHO Position

- In outbreak situations (high risk of Hep E) WHO recommends:
  - Considering use of HEV 239 vaccine to mitigate risk of Hep E outbreaks for high risk groups:
    - Pregnant women
  - Travellers, health-care and humanitarian relief workers deployed or travelling to areas with outbreaks: evaluate risk and benefit of vaccination on an individual basis
- To address information gaps WHO recommends:
  - Pre-emptive design of research protocol to study vaccine safety and immunogenicity in outbreak situations among high risk groups.

Information Gaps

- Incidence and mortality of the Hep E disease in general and in special populations;
- Immunogenicity of HEV 239:
  - outside the 16-65 age range
  - in populations at higher risk for hep E disease
    - E.g. with pre-existing liver disease or immunosuppressive conditions
  - in pregnant women
  - after SC vs. ID administration
  - on an accelerated schedule.

Information Gaps

- Efficacy of HEV 239:
  - against disease caused by genotypes 1, 2 and 3;
  - long term efficacy, duration of protection
  - with fewer than 3 doses or shorter intervals between doses;
  - need and timing of potential booster dose
- Effectiveness of HEV 239
- Cost effectiveness of vaccine programme in outbreak settings

For more information on the WHO HEV position paper, please visit the WHO website:

www.who.int/immunization/documents/positionpapers

World Health Organization