SANOFI PASTEUR

Sanofi Pasteur communication on SAGE recommendation about Dengvaxia® dengue vaccine

19th April 2018 – Today, the Strategic Advisory Group of Experts (SAGE) on Immunization communicated an updated recommendation on Dengvaxia® dengue vaccine to the World Health Organization (WHO).

- The new SAGE recommendation confirms the public health value of Dengvaxia and its potential to reduce the overall burden of dengue in high endemic populations.
- For dengue-endemic countries that would like to use Dengvaxia as part of their integrated dengue control and prevention strategy, SAGE recommends as a preferred option pre-vaccination screening in which only previously dengue infected individuals are vaccinated. As will be made clear in forthcoming published documents from SAGE, current available sero-tests or Rapid Diagnostic Tests (RDT) could be considered in high transmission settings until better tests are available. We maintain our efforts to develop a dengue RDT that can reliably assess prior dengue infection as an aid to vaccination.
- SAGE also acknowledges the public health value of vaccinating without pre-vaccination screening in very high endemic settings (80% seroprevalence at 9 years of age).

This guidance from the SAGE will help to inform an updated World Health Organization position on the vaccine expected to be published in the coming months. The WHO's mandate is to promote global public health, and their positions on new vaccines provide guidance to countries to make decision on public program implementation, based on their specific disease burden and epidemiology.

The SAGE updated their recommendation on the vaccine taking into account the results of a supplementary analysis of clinical data on the vaccine, for which findings were communicated publically last year by Sanofi.

These new data[1], which were finalized and shared by Sanofi at the end of November 2017 and submitted to a peer-reviewed medical journal, contribute to the scientific understanding of how this vaccine can be used optimally in dengue prevention efforts at individual and population levels. They show that for people 9 years of age or older who had a dengue infection prior to vaccination, which includes most of the people living in high transmission areas[2], the vaccine provides sustained protective benefit up to 5 years after the first injection which highlights the public health value of the vaccine in high endemic settings. These findings also represent the first clinical evidence that the vaccine's long-term safety profile in individuals 9 years and older differs according to prior dengue infection exposure. Sanofi has proposed a label update for the vaccine that takes these new findings into account. The label update is currently under review or has been accepted already by some of the regulatory agencies in the countries where the vaccine is either approved today or under regulatory consideration.

We are confident in Dengvaxia's safety and its proven potential to reduce dengue disease burden in endemic countries. As we previously communicated in November, in our new analysis, the risk and severity of cases in vaccinated individuals not previously infected with dengue was similar to those observed in unvaccinated individuals previously infected. Over five years, in vaccinated individuals not previously infected this increased risk was of 0.2% for vaccinated vs unvaccinated individuals. The severe dengue symptoms observed were a temperature over 38°C for 2 days or more coupled with symptoms such as bruising and abnormal laboratory findings. All fully recovered after symptomatic treatment.

At Sanofi, we have worked to provide an innovative vaccine against dengue in spite of the challenges posed by this complex infection. Dengue can be caused by 4 distinct dengue viruses capable of making a person sick up to four times in a lifetime. Most dengue infections are 'silent' which means people have dengue but do not feel ill. However, in rare cases, dengue can be severe, leading to a range of clinical symptoms that require hospital treatment and can deteriorate into a life-threatening form of the disease called dengue hemorrhagic fever. Severe dengue can occur at any of the four infections yet, for reasons not fully understood by the scientific community, secondary dengue infections lead more often to severe dengue than a first infection with the virus[3]. Therefore, prevention of subsequent dengue infections has the potential to significantly reduce the human suffering, as well as the economic impact caused by dengue every year[4].

Dengue continues to represent a significant public health challenge for countries where almost half the world's population lives today. An estimated 390 million dengue infections are reported annually; about 100 million of which cause overt illness[2]. Dengue is spread by mosquitoes that bite during the daytime which contributes to rapid spread of the disease during the rainy season and can often result in overburdened community healthcare services and societal disruption and anxiety.

The global strategy for dengue prevention and control was adopted by the WHO member states in 2012 aiming to reduce the mortality associated with dengue by 50% and the morbidity or illness caused by dengue by 25% by the Year 2020. To achieve this goal, the WHO recommends that countries adopt an integrated approach to dengue infection prevention and disease management[5].

Sanofi shares the same goal as the WHO and endemic countries to significantly reduce global dengue burden. The WHO recognizes the important role of vaccination together with vector control, robust disease surveillance and proper medical management in addressing dengue burden. Appropriate introduction of Dengvaxia as part of such an integrated approach has the potential to significantly reduce overall dengue burden, particularly leading to lower impact of severe dengue on human lives and healthcare expenditures in highly endemic countries. Sanofi continues our long-term commitment to global dengue burden reduction. We developed the first approved vaccine to fight this complex infection and we will continue to work with the international public health community and endemic countries, to ensure the best usage of the vaccine to increase protection for populations at risk of subsequent dengue infections, potentially more debilitating.

[1] http://www.who.int/immunization/diseases/dengue/q_and_a_dengue_vaccine_dengvaxia_use/en/
[2] World Health Organization. Dengue and severe dengue. Fact sheet No 117. www.who.int/mediacentre/factsheets.fs117 updated April 2017. Last accessed May 2017
[3] Mizumoto, K., Ejima, K., Yamamoto, T. & Nishiura, H. On the risk of severe dengue during secondary infection: a systematic review coupled with mathematical modeling. J. Vector Borne Dis. 51, 153–164 (2014)
[4] http://www.who.int/immunization/sage/meetings/2016/april/1_Background_Paper_Dengue_Vaccines_2016_03_17.pdf
[5] World Health Organization. Dengue guidelines for diagnosis, treatment, prevention and control. WHO/HTM/NTD/DEN/2009.1.http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf