Headline

Dynavax's Heplisav: Hep B vaccine shows favourable safety, immunogenicity in at-risk groups; continued safety needed for wider uptake

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Dynavax's (NASDAQ: DVAX) Heplisav vaccine for hepatitis B (HBV) has demonstrated promising efficacy in adult non-responder patients in several clinical trials, according to physicians. However, the lack of long-term safety data compared to GlaxoSmithKline's (NYSE: GSK) Engerix-B could hamper uptake in the general population, they said.

Heplisav is a Phase III investigational adult HBV vaccine for populations that are less responsive to currently available vaccines, and combines the HBV surface antigen with a proprietary Toll-like Receptor 9 (TLR9) agonist adjuvant to enhance the immune response, according to company statements. Non-responding populations that are being targeted by the company include end stage renal disease, chronic kidney disease, diabetes, HIV, immuno-compromised and adult patients.

Engerix-B is a recombinant DNA vaccine with the HBV surface antigen and an aluminum adjuvant. Engerix-B has been around for some time and is known to have a good safety profile, said Dr Henk Reesink, associate professor, department of gastroenterology and hepatology, Academic Medical Center in Amsterdam, Netherlands.

"We think of the [current] HBV vaccine as being very safe and effective, and we know that based on 20 years of use," said Dr Adrian Di Biscegli, a hepatologist with the St Louis University School of Medicine.

Di Biscegli said that while it may be difficult to convince physicians to use a new vaccine in the general population, an improved risk/benefit ratio in an "at risk" population, such as non-responders or those at risk by lifestyle or disease, could encourage use of the vaccine.

Currently, about 20-30% of at-risk groups do not appropriately respond to HBV vaccination, which is a "high percentage" of non-coverage, said Reesink. Additionally, about 5-10% of the general population does not respond to the HBV vaccination in general, so Heplisav "does have potential to be standard of care," he said.

HBV vaccination is currently a routine childhood immunization administered by primary care doctors, explained Dr Amesh Adalja, an infectious disease physician at the University of Pittsburgh Medical Center. Adults who are vaccinated or re-vaccinated are typically immuno-compromised, for reasons such as kidney disease or HIV infection, explained Dr Paul Gaglio, a hepatologist at Montefiore Medical Center. Given their immuno-compromised status, it is difficult for the patients to mount an appropriate immune response to the vaccine, he added.

Renal units in particular are "hot beds" for HBV; therefore a vaccine for certain renal-compromised patients such as chronic kidney failure patients, or dialysis and renal transplant patients in particular is an unmet need where a better vaccine would be welcome, said Professor Howard Thomas, a hepatologist at Imperial college of London.

The TLR9 adjuvant in Heplisav may enhance the immunogenicity of the vaccine, which is something current vaccines cannot do, Adalja noted.

Still, there are some concerns that autoimmune events could occur with the novel TLR9 adjuvant, as well as a risk of innate immunity stimulation, said Reesink. Thomas agreed, saying there is always a concern that a T-cell receptor agonist could trigger autoimmune diseases or hypersensitivity reactions.

This will be something regulators will be looking at, and the vaccine will need to demonstrate that antibodies for autoimmune diseases are no higher than in placebo patients, Reesink said.

Two additional safety and immunogenicity studies have been requested by the FDA to confirm the safety of the novel adjuvant - one will end in May, the other at the end of 2011, said Dino Dina, Dynaxax's CEO.

Two additional smaller studies are being done "for pure data collection," said Dina, one studying Heplisav as a booster for people immunized by Engerix B to be completed by year end, a second a long-term study collecting data on the longevity of the Heplisav response.

The additional trials should confirm there is "no increase autoimmunity compared to Engerix-B," Dina said.

Heplisav would be given in two shots at zero and one months, whereas current vaccines are given in three shots at zero, one and six months. Minimizing the number of vaccinations with as much, or better efficacy "has a lot of value" as many patients, adults particularly, miss the third dose, said Gaglio.

The convenience of two shots will improve compliance dramatically, said Dina.

In the Heplisav trials completed to date, the vaccine has demonstrated a 98% response rate, Dino noted. He pointed to the 1700 person Phase III HeplisAv Short-regimen Trial (PHAST) study in particular.

There is a specific market for immunization, said Reesink. If there is better coverage from Heplisav, and prices are comparable, "everyone will go for it," he said. The adult formulation prices for Engerix-B are USD 52.50/dose in the private sector and USD 28.00/dose in the public sector. The patent for Engerix-B expires in 2018 in the US, according to a GSK spokesperson.

Dynavax will determine pricing of Heplisav based on an analysis of "an acceptable cost to benefit profile," said a spokesperson for Dynavax.

Dynavax has a market cap of USD 277m.

by Christine Livoti in New York and Surani Fernando in London

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Company:

Dynavax Technologies Corporation

GlaxoSmithKline (GSK)

Company

Dynavax Technologies Corporation

Drug(s)

Heplisav

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Intelligence Type(s)

Product Development

Topic

Product Development

Intelligence Grade

Strong evidence

Sub-sectors

Drug development

Country

USA