

DENGUE TREATMENT versus VACCINE

A **TREATMENT** is defined as, "Administration or application of remedies to a patient or for a disease or an injury; medicinal or surgical management; therapy."* Further, a treatment indicates, the care and management of a patient to combat, ameliorate, or prevent a disease, disorder or injury."** A treatment or cure is applied after a medical problem has already begun. Treatment, in the medical field, is synonymous with the word Therapy, which literally means "curing, healing" and is the attempted remediation of a health problem, usually following a diagnosis.

DENGUE Treatment Today:



ActRx TriAct® is a new treatment for Dengue, based on decades of study, years of research and advanced medical innovation.



This "first-of-its-kind" combination treatment for Dengue has recently proven to be safe and effective in Clinical Trials.

A **VACCINE** is defined as, "A suspension of attenuated or killed microorganisms (viruses, bacteria, or rickettsiae), or of antigenic proteins derived from them, administered for prevention, amelioration, or treatment of infectious diseases."*** Further, a vaccine is, "A preparation of a weakened or killed pathogen, such as a bacterium or virus, or a portion of the pathogen's structure that upon administration stimulates antibody production against the pathogen but is incapable of causing severe infection."* A vaccine is viewed as a preventative measure to avoid the complications of a more serious disease or infection.

DENGUE Vaccines Today:

Today's most recent development toward a potential Dengue vaccine only offers modest results. In 2012, efficacy was shown at 33%, with a failure to protect against one of the four known types of Dengue, which is still the case. The three-dose injectable vaccine (1 shot taken every 6 months over an 18 months period) has an increased **efficacy of 56%** as of this time, but note that most common vaccines, like those for measles and polio are more than 95% effective. In the recent studies, the vaccine provided only 35% protection against Dengue serotype 2.

People infected with one type of Dengue develop antibodies that may protect them from further infections of that type. However, if they are infected by another Dengue type, those same antibodies appear to make them far more susceptible to more severe forms

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of Dengue that could include hemorrhaging. Scientists worry that the antibodies from a Dengue vaccine might have the same effect and say that vaccinated children should be monitored for several years.



"We don't understand the antibody response in dengue well enough to know if this (problem) would also occur with a vaccine," said Martin Hibberd, a professor of emerging infectious diseases at the London School of Hygiene and Tropical Medicine, who wasn't part of the study. The vaccine injection appears to work by boosting pre-existing antibodies in people previously infected with Dengue, since younger children didn't appear to get much protection from the shot. "It's a bit scary that it looks like the vaccine only works in people who have already had Dengue, which would make the vaccine useless for Western tourists traveling to dengue-endemic countries", he said.

The results suggest that the new vaccine acts best as an immune booster for patients with some previous exposure, and therefore may be most useful in tropical regions where Dengue is common, rather than as a vaccination for travellers.

The vaccine offers poor to no protection to young children – who are most at risk from Dengue. Most patients survive dengue but it kills more than tens of thousands of people each year. Most of the deaths are children, which this latest vaccine does not appear to work very well on.

Dengue causes one hospitalization every minute around the globe. Nearly half the world's population is at risk of contracting Dengue - also known as "*breakbone fever*" because of the severe pain it can cause. The disease infects some 100 million people each year, according to the World Health Organization (WHO), and some experts aggregate the actual number infected at over \$392 million worldwide.



Questions remain as to what the threshold of Dengue incidence might be for countries to decide that it is worth launching costly vaccination programs. Whether the vaccine's efficacy is enough for countries to invest in is a question for economists. Nonetheless, the logistics for such national programs are highly complex.

For the moment, this latest vaccine "is the best we have," Annelies Wilder-Smith, a professor of infectious diseases at Nanyang Technological University in Singapore, wrote in a commentary accompanying the study. "However, with a 56% efficacy, this vaccine will never be a single solution." The vaccine was more effective in people who had been exposed to dengue previously than those who had never been exposed, suggesting it may be "of limited use in countries with low Dengue endemicity, or in international travelers from non- dengue-endemic countries," Wilder-Smith said.

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"It's still not an optimal vaccine, "said Scott Halstead, a senior adviser to the Dengue Vaccine Initiative, a group of four organizations that encourages the development of vaccines. "We're all accustomed to efficacy rates of 95 percent, which is what you get when you have the measles, mumps and rubella vaccine."

Potential Dengue vaccines are being developed by a number of international pharmaceutical companies, as well as the U.S. National Institutes of Health. To date, no vaccine has stood out as a viable total solution to the growing Dengue epidemic or as a proven preventative for Dengue. (07-2014)

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It is important to understand the difference between a “vaccine” and a “treatment”, as ActRx supports the advancement of a treatment for dengue fever.

A vaccine is a preventative for those who do not have dengue fever, or have not previously contracted the disease, supporting patients in developing immunity and potentially preventing the future contraction of dengue fever.

A treatment is for patients who do have dengue fever, where proper medical care, medications and supplements supports the recovery process, heals the patient from dengue fever, and prevents death. ActRx TriAct® is a TREATMENT for dengue fever which has successfully completed its Clinical Trials in the Philippines

POINTS OF DISCUSSION for SANOFI VACCINE:

- Most advanced vaccine for dengue only offers modest results
- In 2012 found the vaccine's efficacy was 33 percent and that it **failed to protect against one type of dengue, which is still the case, as it proved notably inefficient in tackling one of the viral disease's four strains.**
- The shot's efficacy improved to 56 percent. Most common vaccines like those for **measles and polio are more than 95 percent effective.**
- Whether this vaccine's efficacy is enough for countries to invest in is a question for economists.
- People infected with one type of dengue develop antibodies that protect them from further infections of that type. **But if they catch another kind of dengue, their antibodies make them susceptible to more serious disease that could include hemorrhaging.** Scientists worry the antibodies from a dengue vaccine might have the same effect and say vaccinated children should be monitored for several years. “We don't understand the antibody response in dengue well enough to know if this (problem) would also occur with a vaccine,” said Martin Hibberd, a professor of emerging infectious diseases at the London School of Hygiene and Tropical Medicine, who wasn't part of the study.
- The shot seemed to work by boosting pre-existing antibodies in people previously infected with dengue, **since younger children didn't get much protection from the shot. "It's a bit scary that it looks like the vaccine only works in people who have already had dengue,"** which would make the vaccine useless for Western tourists traveling to dengue-endemic countries, he said.
- **The vaccine offers poor to no protection to young children - who are most at risk from dengue.**

- The results suggest the new vaccine acts best as an immune booster for patients with some previous exposure, and therefore may be most useful in tropical regions where dengue is common, rather than as a vaccination for travellers.
- Since there is no vaccine now, it could still in a minimal way make it a weapon in the fight against dengue.
- **The study was led by Maria Rosario Capeding from the Research Institute for Tropical Medicine in the Philippines, and funded by Sanofi.**
- Nearly half the world's population is at risk of contracting dengue fever - also known as "breakbone fever" because of the severe pain it can cause. The disease infects some 100 million people each year, according to the World Health Organization, and **some experts put the number at triple that level.**
- Most patients survive dengue but it kills more than 50,000 people each year, most of them children, which this vaccine does not appear to work on. It causes one hospitalization every minute around the globe.
- **Some analysts believe the three-dose vaccine could sell 1 billion euros a year, significantly boosting Sanofi's vaccine business, which generated sales of 3.7 billion euros in 2013.**
- But there are many uncertainties - including whether Governments or patients will return and be willing to pay each six months for the additional two shots of what is likely to be a pricey vaccine.
- Coming up with a vaccine that can protect against the disease has puzzled scientists for over 70 years, since the movement of troops during World War II helped dengue spread across the Pacific and become a worldwide pandemic.
- **In the Asian study, the vaccine provided only 35 percent protection against serotype 2.**
- **Questions remain as to what the threshold of dengue incidence might be for countries to decide that it is worth launching a costly vaccination programs.**
- The most advanced experimental vaccine against dengue **protected some children against the disease in a study**, though a more effective weapon is still needed to curb the most widespread mosquito-borne infection, **or at least a successful treatment.**
- **The inoculation was less effective among the youngest children who are most in danger of contracting dengue, and failed to protect against one of four viruses that cause it.**
- For the moment, Sanofi's vaccine "is the best we have," Annelies Wilder-Smith, a professor of infectious diseases at Nanyang Technological University in Singapore, wrote in a commentary accompanying the study. **"However, with a 56 percent efficacy, this vaccine will never be a single solution."**
- Sanofi shares rose 0.4 percent to 76.03 euros as of 10:19 a.m. in Paris.
- Dengue is caused by four related viruses spread by mosquitoes. About half the world's population lives in countries threatened by dengue, the World Health Organization estimates. There are **about 390 million infections a year**, with about 96 million people getting sick to some degree, according to research published last year.
- **"It's still not an optimal vaccine,"** said Scott Halstead, a senior adviser to the Dengue Vaccine Initiative, a group of four organizations that encourages the development of vaccines. "We're all accustomed to efficacy rates of 95 percent, which is what you get when you have the measles, mumps and rubella vaccine."

- The vaccine was **more effective in people who had been exposed to dengue previously** than those who had never been exposed, suggesting it may be “of limited use in countries with low dengue endemicity, or in international travelers from non- dengue-endemic countries,” Wilder-Smith said.
- The frequency of dengue infections has **increased more than 30-fold** in the past 50 years as urbanization gives the city- dwelling mosquitoes that spread the disease more places to breed.
- Other dengue vaccines are being developed by Inviragen, a subsidiary of Osaka, Japan-based Takeda Pharmaceutical Co., and by Merck & Co. and the U.S. National Institutes of Health.
- Sanofi will build a factory to make the vaccine in Neuville-sur-Saone, near Lyon in France, that will be capable of churning out about 100 million doses a year, The vaccine requires three doses, each six months apart.
- The company said that it may sell the three-dose course for about \$30 at a minimum in developing nations and about \$150 for travelers from rich countries.