Zoetis introduces

VANGUARD® crLyme

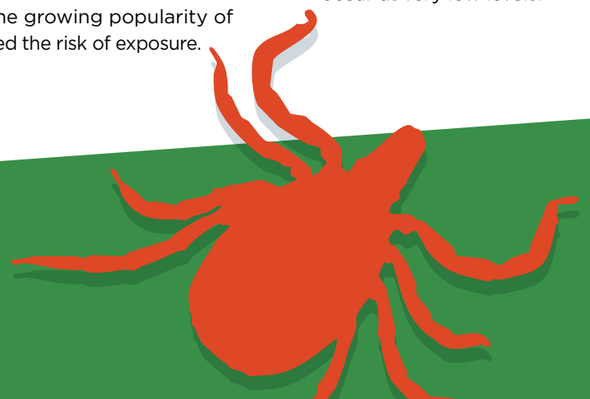
BROAD COVERAGE IS BETTER COVERAGE

VANGUARD® crLyme is the first and only canine Lyme disease vaccine that helps prevent Lyme disease in dogs with two recombinant proteins: an outer surface protein A (OspA) and a chimeric protein containing antigenic material from seven common types of outer surface protein C (OspC) that have been detected in dogs infected with Lyme disease.[1] Its selective design helps provide relevant antigenic coverage, while the use of recombinant technology helps minimize extraneous proteins, resulting in a safe and low-reactive vaccine.

Prevalence of Lyme disease is increasing

Lyme disease is caused by the bacterium *Borrelia burgdorferi* and is transmitted by *Ixodes spp*. (black-legged ticks). It is the most common vector-borne disease in North America, with the prevalence continuing to increase.[2] The Centers for Disease Control and Prevention (CDC) estimates that over 300,000 cases of Lyme disease in humans occur annually,[3] and the Companion Animal Parasite Council (CAPC) reports one in 16 dogs tested positive for Lyme disease in 2015.[4]

The CDC published a study in January 2016 noting *Ixodes spp*. are present in almost half of the counties in the U.S.[5] The geographic spread of Lyme disease may be aided by expanding favorable tick habitats, longer transmission seasons and larger rodent host population.[6] Moreover, the lines between urban and suburban boundaries continue to blur, and the growing popularity of pet-friendly travel has increased the risk of exposure.



Vaccination is a critical aspect of a complete tick control plan

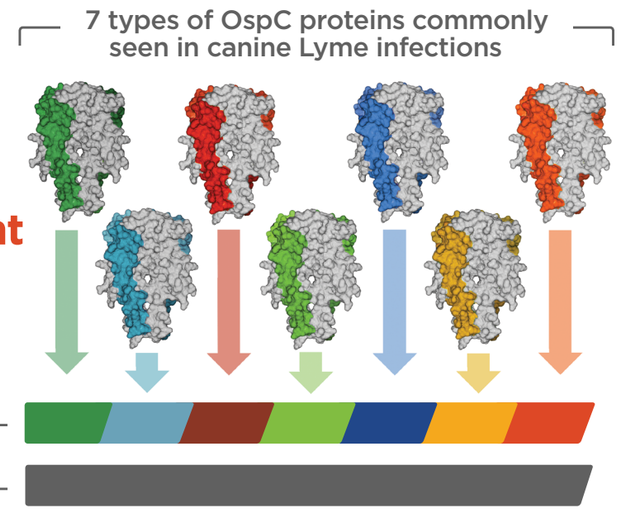
The CAPC advises that vaccination helps provide comprehensive protection against Lyme disease.[4] Helping prevent canine Lyme disease with a vaccine helps reduce the possible complications associated with diagnosis and treatment since 90 percent of seropositive dogs may not show clinical signs of infection.[7] Therefore, relying solely on parasiticides may not always lead to sufficient protection.[8]

Pathogenesis and proteins

B. burgdorferi adapt to and invade a host by expressing different outer surface proteins (Osp). Two key outer surface proteins needed for infecting the host and evading the host's immune system are outer surface proteins A and C (OspA and OspC). When Lyme disease vaccination is considered, the two relevant proteins are OspA and OspC. OspA is predominantly expressed in the tick and helps the bacteria maintain residence in the tick by facilitating adherence to the epithelial cells of the midgut. As the tick feeds, the associated rise in temperature and change in pH causes the downregulation of OspA expression and the upregulation of another protein, OspC, which is required in order for the bacteria to infect a mammalian host.

When a dog has been adequately vaccinated with a Lyme disease vaccine that contains OspA antigens, the intent is that it will have sufficient circulating OspA antibodies in its blood to help kill the *B. burgdorferi* bacteria while they are still in the tick. These OspA antibodies will also help prevent transmission from the tick to the dog. Antibodies to relevant types of OspC are also critical vaccination targets as this outer surface protein is expressed early in mammalian infection. As OspC proteins are consistently expressed in the dog, they are an attractive vaccination target not only because they can help kill *B. burgdorferi* in the dog, but exposure to the bacteria also has the possibility of generating an effective memory immune response. Such a response may not be possible or as effective with OspA because its maximal expression occurs in the tick—and if expressed in the dog, it will occur at very low levels.[9]

VANGUARD crLyme Chimeric Recombinant Technology



Discovering OspC variability

It has been known for several years that unlike OspA, which is consistently seen as a single type throughout North America, OspC has a great deal of variability. More than 30 types have been recognized in various species worldwide.[1] A 2013 publication evaluated the types of OspC present in canine tissue after infestation with wild-caught ticks. The results of this study indicated that there were 11 OspC types present in canine tissue post-infection.[1] The OspC types seen in this and other studies were carefully considered during the development of VANGUARD crLyme in order to produce a broadly protective vaccine containing OspC types relevant in canine infection.

VANGUARD crLyme and chimeric recombinant technology

Zoetis introduces VANGUARD crLyme in response to the need for a canine Lyme disease vaccine that addresses OspC variability. This next-generation vaccine includes a recombinant OspA protein and a recombinant OspC chimeric protein. VANGUARD crLyme is the first Lyme disease vaccine of its kind in the animal health industry.

Until now, it was not immunologically feasible to address OspC variability via vaccination.[1] At most, commercially available vaccines only contained one type of OspC.

Chimeric recombinant technology allows for relevant antigenic material from multiple OspC types to be combined into a single protein.

VANGUARD crLyme: The first and only chimeric recombinant Lyme disease vaccine

- Helps provide coverage to outer surface protein A (OspA), found in the tick, and multiple types of OspC commonly found in the tick and in the dog.
- Chimeric recombinant technology can help provide broad OspC coverage.
- Two recombinant proteins can help provide a safe, low-reactive vaccine.

Indication: For vaccination of healthy dogs 8 weeks of age or older as an aid in the prevention of clinical disease and subclinical arthritis associated with *B. burgdorferi*.

Administration: 1 mL subcutaneously; dogs should be administered 2 doses, 3 weeks apart; annual revaccination recommended.

1 Rhodes DV, Earnhart CG, Mather TN, Meeus PF, Marconi RT. Identification of Borrelia burgdorferi OspC genotypes in canine tissue following tick infestation: implications for Lyme disease vaccine and diagnostic assay design. *Vet J*. 2013;198(2):412–418.
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3 How many people get Lyme disease? Centers for Disease Control and Prevention National Center for Emerging and Zoonotic Infectious Diseases Division of Vector-Borne Diseases. http://www.cdc.gov/lyme/stats/humancases.html. Accessed February 27, 2016.
4 Current advice on parasite control: vector-borne diseases – Lyme disease. Companion Animal Parasite Council. http://www.capcvet.org/apc-recommendations/lyme-disease/. Accessed February 27, 2016.
5 Eisen RJ, Eisen L, Beard CB. County-scale distribution of Ixodes scapularis and Ixodes pacificus (Acari: Ixodidae) in the continental United States. *J Med Entomol*. 2016;Jan 18:1-38.
6 Ogden NH, Bouchard C, Kurtenbach K, et al. Active and passive surveillance and phylogenetic analysis of Borrelia burgdorferi elucidate the process of Lyme disease risk emergence in Canada. *Environ Health Perspect*. 2010;118(7):909–914.
7 Littman MP, Goldstein RE, Labato MA, Lappin MR, Moore GE. ACVIM small animal consensus statement on Lyme disease in dogs: diagnosis, treatment, and prevention. *J Vet Intern Med*. 2006;20(2):422–434.
8 Stevenson B, Schwan TG, Rosa PA. Temperature-related differential expression of antigens in the Lyme disease spirochete, Borrelia burgdorferi. *Infect Immun*. 1995;63(11):4535–4539.
9 Wagner B, Freer H, Rollins A, et al. Antibodies to Borrelia burgdorferi OspA, OspC, OspF and C6 antigens as markers for early and late infections in dogs. *Clin Vaccine Immunol*. 2012;19(4):527–535.

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