



Could Treating Deer with a Pill that Kills Ticks on Dogs Eliminate Lyme Disease from Humans?

Lyme disease is the most common tick-borne infection in the United States, with over 470,000 cases estimated to be diagnosed annually.¹ The tick species responsible for the majority of cases of Lyme disease in the United States is *Ixodes scapularis*. Besides *Borrelia burgdorferi*, bites from this tick species can potentially also transmit multiple other pathogens, including *Anaplasma phagocytophilum* and *Babesia microti*.² No vaccine for humans to prevent Lyme disease has been available since 2002,³ although clinical trials are currently in progress for a new vaccine to prevent Lyme disease. Of course, neither the prior US Food and Drug Administration (FDA)-approved vaccine nor the one currently in clinical trials would be expected to reduce tick bites per se or to reduce infections caused by tick-borne pathogens other than *B. burgdorferi*.

The isoxazoline class of ectoparasiticide drugs, that includes fluralaner, sarolaner, afoxolaner, and lotilaner, can cause paralysis and death of ticks feeding on dogs.^{4,5} Although all drugs in this class are not equally effective, many of those that have been evaluated have been found to be safe and effective, and consequently, have been approved for use in dogs. In dogs they have been shown to interrupt tick feeding and rapidly kill ticks from multiple different species, including *I. scapularis*, with efficacy potentially extending to ≥ 1 month following a single oral dose.^{4,5}

In addition, a Phase 2 clinical trial is in progress to assess the safety and efficacy of oral administration of lotilaner for interruption of *I. scapularis* tick bites in humans, with

apparently promising safety and efficacy results, although no data from this study have been published in the scientific literature so far.^{6,7} An ophthalmic solution of lotilaner has, however, been approved by the FDA to treat *Demodex* blepharitis (an infection caused by mites) in humans.

If lotilaner, or perhaps other drugs in this class, can be shown to be safe for humans, then it might be a promising approach to use this agent prophylactically for humans at risk for tick bites in order to interrupt tick feeding should a tick bite occur, which would be especially helpful in preventing both Lyme disease and babesiosis, because both of these infections usually require at least 36 hours of uninterrupted tick feeding for the respective pathogens, *B. burgdorferi* and *B. microti*, to be transmitted.⁸

However, of particular importance and not previously discussed is that lotilaner, or other drugs in this class, should also be considered for experimental studies in white-tailed deer in order to interfere with successful feeding by adult *I. scapularis* ticks. The most likely route of administration for deer would be by oral administration, as is routinely done for dogs. Of course, safety in humans is an important prerequisite for use of drugs in deer, because humans might be exposed to the drug when ingesting deer meat. An initial experimental approach might be to target deer in geographic areas where deer hunting does not take place. Targeting deer with an oral ectoparasiticide has already been evaluated experimentally for the drug moxidectin in order to reduce effective tick feeding on deer,⁹ although this particular study was focused on a different tick species, *Amblyomma americanum*. Moxidectin is a drug that also potentially interferes with tick feeding but is structurally different from an isoxazoline. Preceding the moxidectin study were several studies evaluating the impact of oral administration of ivermectin to deer to reduce tick feeding,¹⁰⁻¹³ including one study that evaluated the impact on *I. scapularis* ticks.¹⁰

If adult *I. scapularis* ticks can be effectively prevented from completing their blood meal on deer in a particular geographic area, then this tick species might be eliminated from that location. The reason for this is that adult *I. scapularis* ticks feed almost exclusively on deer, and without a successful blood meal that requires several days of feeding, there would be no reproduction of the tick, and therefore this tick

Funding: None.

Conflicts of Interest: GPW reports receiving research grants from Biopeptides, Corp. and Pfizer, Inc. He has been an expert witness in malpractice cases involving Lyme disease and is an unpaid board member of the non-profit American Lyme Disease Foundation. TNM and SMR are supported in part by the New England Center of Excellence in Vector-borne Diseases (NEWVEC), which is made possible by a grant from the Centers for Disease Control and Prevention (U01CK000661).

Authorship: All authors had access to the data and participated in writing the manuscript. GPW and TNM: Conceptualization, Writing – review & editing; SMR: Writing – review & editing.

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species would be greatly reduced in number and potentially completely eliminated from that geographic area.

Studying the oral use of lotilaner (or other isoxazolines) for free-ranging deer, however, will pose many challenges. Initial studies to evaluate the best approach for providing lotilaner for oral consumption and to assess the safety, blood levels, and pharmacokinetics (including the serum half-life) of this drug in white-tailed deer, however, could be done using captive deer.¹² Also, such studies could be used to assess the impact of lotilaner on the duration of tick attachment for those deer that were treated. With regard to both ivermectin and moxidectin, each medication was provided to deer orally when mixed with corn,⁹⁻¹² which might be tried for lotilaner as well. An alternative food item that could potentially serve as bait is molasses.¹⁴ The next phase of the investigation would be to provide lotilaner for oral consumption in feeding stations placed at locations with free ranging deer. If a high level of oral consumption were achieved, then a final phase of the investigations would be to determine if all life stages of *I. scapularis* ticks in that geographic area were reduced in number over time, as would be the expected and desired outcome of the study. If this medication is successful in regard to this objective, it would also likely reduce or eliminate certain other tick species, such as *A. americanum* (the lone star tick), which depend on deer for a blood meal. Bites from *A. americanum* ticks can also transmit infections to humans (such as human monocytic ehrlichiosis, which is caused by *Ehrlichia chaffeensis*), and in addition are thought to potentially cause red meat allergy.¹⁵

It is past time to develop newer approaches to reduce or eliminate not only Lyme disease, but also all of the other *I. scapularis*-transmitted pathogens. Evaluation of a targeted tick-killing approach involving deer that is potentially doable, but of course must be unequivocally not harmful for the deer or for the humans consuming deer meat, is clearly desirable, and if successful, could substantially improve the health status of the many humans at risk for certain tick-borne infections.

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