What to Know About Anti-NGF Monoclonal Antibody Injections

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KEY POINTS:

- Recently, the US Food and Drug Administration (FDA) approved species-specific, monoclonal antibody (mAB) drugs for the treatment of osteoarthritis (OA) pain in cats and dogs. The FDA refused to approve similar drugs for human use; the drug approval process for humans requires more evidence of safety and effectiveness.
- These compounds, i.e., "frunevetmab" for cats and "bedinvetmab" for dogs, bind to a biologically significant neurotrophin called nerve growth factor (NGF).
- Drug companies have targeted NGF because its concentration increases in arthritic joints; excess levels of NGF may worsen pain problems.[1]
- AntiNGF mAB drugs may induce severe side effects over time; more research needs to be done to adequately assess safety. Ideally, investigators would not have financial conflicts of interest with the manufacturer.

PROBLEMS WITH ANTI-NGF MONOCLONAL ANTIBODY DRUGS:

- Human pharmaceutical companies spent billions of dollars for decades of research, seeking to bring to market a safe and non-addictive alternative to NSAIDs.[2] The FDA denied approval. Per the FDA, "[T]he treatment effect size is modest, and there is no convincing evidence of a superior efficacy of tanezumab over NSAIDs." Additionally, the panel expressed concern about the risks of developing peripheral neuropathy from the drug as well as "rapidly progressing osteoarthritis" (RPOA)".[3] [4]
- Osteonecrosis may result, as well. "[NGF blockade] may also promote more rapid cartilage degeneration, synovitis, and possibly subchondral bone changes, particularly when treatment starts in the earlier stages of disease."[5]
- Will RPOA affect veterinary patients? What about other serious side effects? Insufficient research exists; most studies reveal financial ties to the manufacturer.
- We do know that cats receiving frunevetmab, compared to controls, were at risk of worsened renal insufficiency, anorexia, lethargy, dermatitis, dehydration, lameness, pruritus, scabbing on the head/neck, bacterial skin infection, gingival disorder, otitis externa, alopecia, vomiting, abnormal behavior or behavioral disorders, and diarrhea.[6]

WHY OUR PATIENTS NEED NGF AND WHY IT'S HARMFUL TO BLOCK IT:

- NGF exists in every peripheral tissue and organ supplied by sensory or sympathetic efferent fibers, including immune cells.[5]
- NGF also helps to *resolve* inflammation and may serve a protective role for joint health.[7,8] Interfering with NGF signaling may impair bone repair processes.
- NGF supports the survival and function of neurons typically afflicted by neurodegenerative disorders. Could lower levels invite or worsen cognitive decline?
- NGF supports pancreatic beta-cell survival and function; It also balances autonomic responses to stress.[9] Are diabetic patients at increased risk of negative outcomes?
- NGF supports tissue healing in epithelial cells, fibroblasts, myofibroblasts, endothelial cells, smooth muscle cells, glial cells, astrocytes, and hepatocytes.[7] It already has several ophthalmic and dermatologic clinical applications.[10] [11] How do antiNGF mABs affect veterinary patients with comorbidities affecting the eye, skin, and nervous system?
- Integrative medical approaches such as acupuncture and photomedicine treat arthritis by supporting the nervous system instead of potentially harming it. [12] [13] [14]

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