

Masivet®

Targeted Therapy for Inflammatory Diseases

MASIVET® TARGETS MAST CELLS

Masivet® selectively targets mast cells and regulates their activity.

- The specific targets of Masivet® are stem cell factor receptor (c-Kit), PDGFR α and β , and Lyn.
- By merit of a combined inhibition of c-Kit and Lyn, Masivet® is particularly efficient in controlling the proliferation, differentiation and degranulation of mast cells (MC).

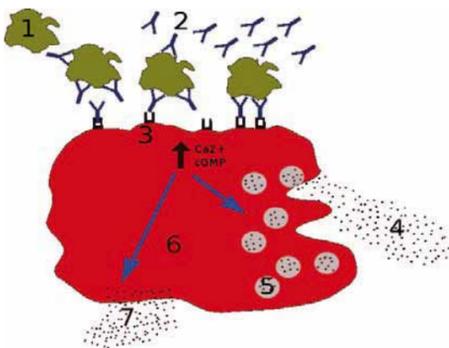
Inhibition (%) of human mast cell degranulation; cytokine production; and migration of murine bone marrow mast cells.

Assay	10 μ M	1.0 μ M	0.1 μ M
Degranulation (β -hexosaminidase release)	35%	18%	7%
Cytokine production (TNF- α release)	68%	40%	16%
BMMC migration	-	80%	-

- Masivet® therefore, has potential in the treatment of MC dysfunctions and related complications; for example, rheumatoid arthritis (Arthritis Res Ther, 11:R95 doi:10.1186/ar2740, 2009), and asthma (Allergy, 64: 1194-1201, 2009).
- The following clinical development program for Masivet® in inflammatory diseases has been implemented:
 - Phase 3 pivotal study in canine atopic dermatitis
 - Phase 2 in canine arthritis
 - Phase 2 in canine inflammatory bowel disease
 - Phase 2 in feline asthma

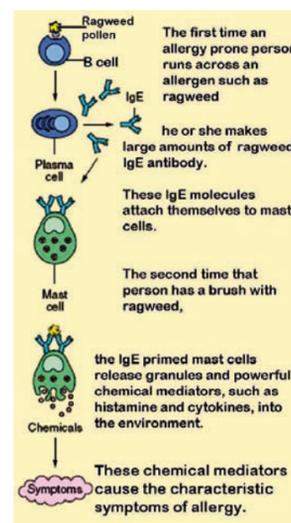
Mast cells play a key role in chronic inflammatory diseases.

- MCs are part of the body's immune system that can respond very rapidly to a stimulus by producing an array of chemical mediators or messengers.
- MCs can be stimulated to degranulate by direct injury (e.g. physical or chemical), cross-linking of Immunoglobulin E (IgE) receptors or by activated complement proteins.
- It is well established that MCs play a key role in chronic inflammatory diseases such as allergy, atopic dermatitis, asthma and arthritis.
- Thus, MCs present a promising therapeutic target to address unmet medical needs.



The degranulation process in a mast cell.

1 = antigen; 2 = IgE; 3 = Fc ϵ RI; 4 = preformed mediators (histamine, proteases, chemokines, heparin); 5 = granules; 6 - mast cell; 7 - newly formed mediators (prostaglandins, leukotrienes, thromboxanes, platelet-activating factor).



The role of mast cells in the development of allergy

MASIVET® IN CANINE ATOPIC DERMATITIS: A PILOT STUDY

- Study objective: To evaluate the potential response and safety of Masivet® administered orally for 28 days, in dogs diagnosed with canine atopic dermatitis (CAD) in accordance to the Willemse/Prélaud criteria.
- Study design: Prospective, uncontrolled, open label, multicentre study. Dogs of any breed or sex were eligible and stayed under their usual living conditions throughout the study.
- Masivet® improved CAD with a mean reduction in mCADESI of 50.7 \pm 29.8% (95% C.I. = 29.4 - 72.0; p = 0.0004) at day 28 relative to baseline, with 8/10, 8/10 and 4/10 dogs showing improvement of 33%, 40% and 50%, respectively.
- Improvement was most significant for subscores of erythema (p = 0.0005), lichenification (p=0.0371), excoriation (p=0.0177) and scraping alopecia (p=0.0137).
- Surface area of lesions decreased between D0 and D28;
 - <25% of body surface in 70% subjects at D28 vs. 20% subjects at D0.
 - >75% of body surface in 0% subjects at D28 vs. 20% subjects at D0.
- Pruritus score was improved at D28: 50% subjects had their pruritus score decrease 50%.



Example of improvement in CAD symptoms after Masivet® treatment



Example of improvement in CAD after Masivet® treatment

- Masivet® was relatively well tolerated with 6/11 dogs (55%) reporting mild to moderate drug-related adverse events. No serious or severe adverse events occurred during this trial.
- Conclusion: CAD is a potential indication for Masivet®.
- Phase 3 pivotal study involving 300 subjects was initiated (now closed to enrolment).

USING MASIVET®

- Currently Masivet® is officially authorised for the treatment of non-resectable mast cell tumours grade II and III, with confirmed mutation of c-Kit in dogs. AB Science is actively developing knowledge in other oncology and non-oncology indications for both dogs and cats.
- Masivet® is simple to use, with a once daily oral administration. Treatment can be administered every day directly by the owner. Tablets must be administered whole and should not be divided, broken or ground.
- Masivet® is supplied as round, film-coated tablets at two doses (50 or 150mg) in bottles of 30 tablets.
- Common side effects with Masivet® are diarrhoea, vomiting and alopecia. These reactions are usually mild to moderate in severity and typically last less than a few weeks.
- Dogs must be regularly monitored by the veterinarian (bi-weekly during the first 3 months, then at least monthly) for side effects including possible protein loss syndrome.

