Safety profile of Mycobacterium cell wall fraction (IMMUNOCIDIN®) following multiple intravenous administrations in healthy dogs.

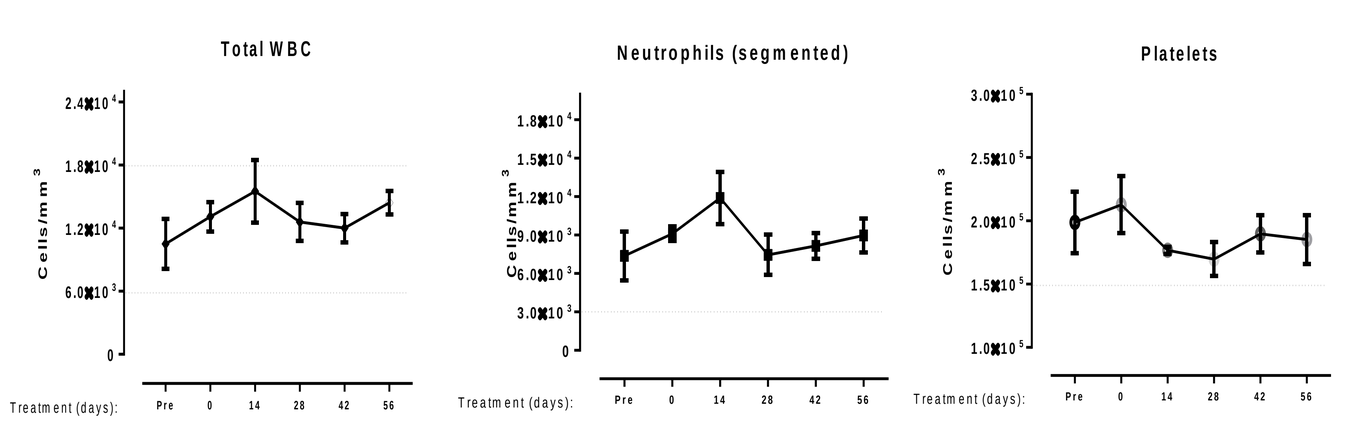
Juan Mangieri, Rodrigo de Haro, Lucas Rodrigues, Vladimir Kukolj, Bojana Prunic, Aleksandar Masic

Abstract:

Introduction: **IMMUNOCIDIN®** is a biological immunomodulator derived from mycobacterium cell wall fraction (MCWF). MCWF has potential in anticancer therapy and currently is USDA- and CFIA-approved for intralesional treatment of mammary tumors and mammary adenocarcinoma in dogs.

Study design: Two pilot studies in healthy dogs were conducted. MCWF was diluted in 20ml of 0.9%NaCl and administered as a slow bolus injection over a 3-5 min. period. One, two or four weeks following the last MCWF injection, dogs were euthanized and subjected to necropsies. Internal organs (lungs, spleen, kidneys, bone marrow, liver and heart) were subjected to histopathology evaluation.

Results:



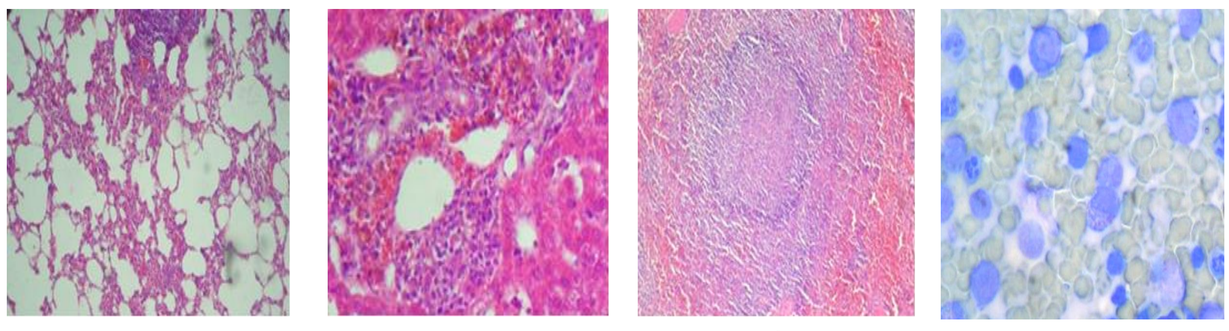


Table 1. Study design 1.

Day of study	-7	0	7	14	28	42	56
Acclimatization	X						
Physical exam	X	X	X	X	X	X	X
Clinical observation*	X	X	X	X	X	X	X
Body weight	X	X	X	X	X	X	X
Blood sampling	X	X		X	X	X	X
Urine sampling	X	X		X	X	X	X
1st injection		X					
2nd injection				X			
3rd injection					X		
4th injection						X	
Adverse reaction monitoring		X	X	X	X	X	
Necropsy							X

All dogs received 4 doses of MCWF every two weeks and 2 weeks following last MCWF injection and were subjected to necropsies; internal organs (lungs, spleen, kidneys, bone marrow, liver and heart) were subjected to histopathology evaluation.

Table2. Study design 2.

Day of study	-7	0	7	14	21	42
Acclimatization	X					
Physical exam	X	X	X	X	X	
Clinical observation*	X	X	X	X	X	
Body weight	X	X	X	X	X	
Blood sampling	X	X	X	X	X	
Urine sampling	X	X	X	X	X	
1st injection		X				
2nd injection			X			
3rd injection				X		
Adverse reaction monitoring		X	X	X	X	
Necropsy					X*	X*

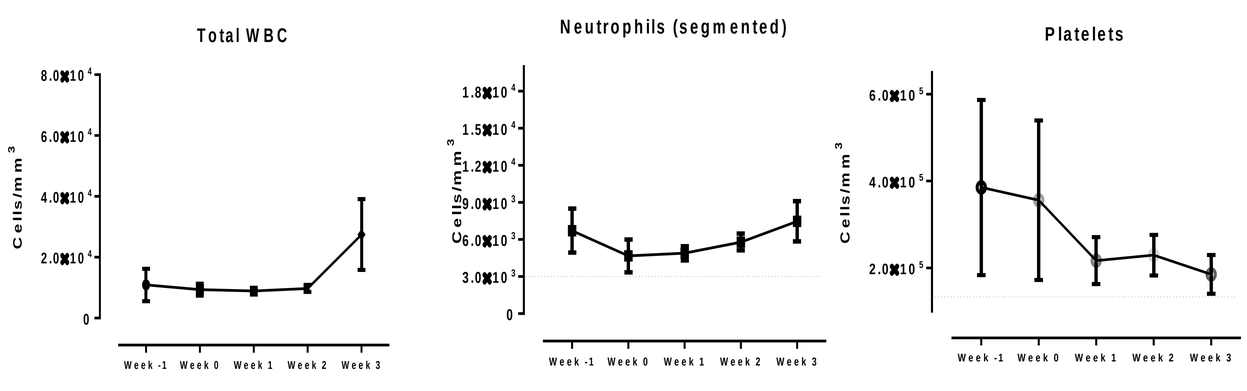
2 dogs were euthanized 7 days after last MCWF injection and 3 dogs were euthanized 4 weeks following last MCWF injection and subjected to necropsies ; internal organs (lungs, spleen, kidneys, bone marrow, liver and heart) were subjected to histopathology evaluation.

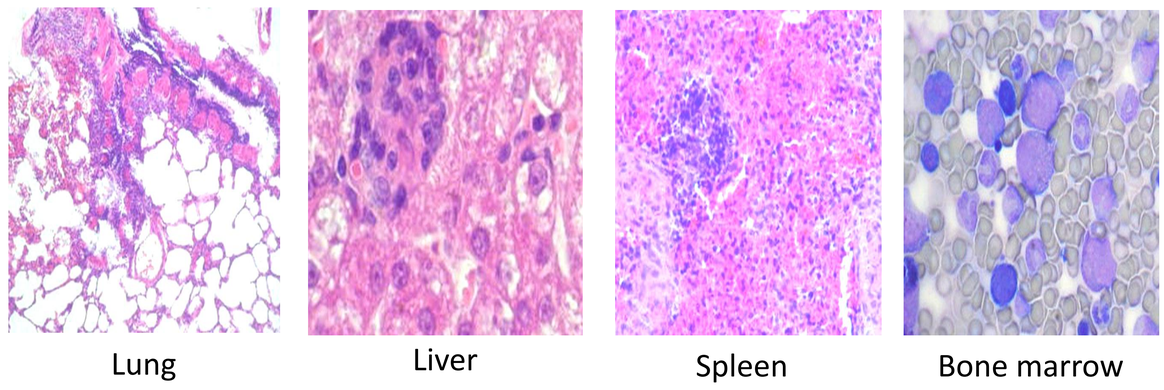
Study I (250 µg/dog)				
dogs	Age (yrs.)	sex	weight	dose
1	2	F	10 kg	100 µg (10 µg /kg)
2	3	F	18 kg	250 µg (14 µg /kg)
3	6	F	12 kg	250 µg (20.8 µg /kg)
4	2	M	15 kg	250 µg (16.7 µg /kg)

Study II-group A (500 µg/dog)				
dogs	Age (yrs.)	sex	weight	Dose
1	4	F	10 kg	500 µg (50 µg /kg)
2	2	M	8 kg	500 µg (62 µg /kg)
3	3	F	10 kg	500 µg (50 µg /kg)
4	1	M	10 kg	500 µg (50 µg /kg)
5	2	M	12 kg	500 µg (42 µg /kg)

Necropsy and histopathology observations:

No significant macroscopic changes were observed in any of the examined organs. Lungs: Infiltration of mononuclear cells and neutrophils into perialveolar and peribronchial interstitial space. Liver: Multifocal infiltration of mononuclear cells (Kupffer cells), neutrophils, lymphocytes and plasma cells. Spleen: Hyperplastic changes observed in lymphatic tissue. Diffuse inflammatory infiltrate of lymphocytes, plasma cells, histiocytes, megakaryocytes observed in the region of red pulp. Bone marrow: Presence of erythroid and myeloid immature cells, lymphocytes and neutrophils were the predominant population.





Necropsy and histopathology observations:

No significant macroscopic changes were observed in any of the examined organs. Lungs: Mild to moderate infiltration of mononuclear cells and neutrophils into perialveolar and peribronchial interstitial space. Liver: Multifocal infiltration of mononuclear cells (Kupffer cells), neutrophils, lymphocytes and plasma cells. Spleen: No significant histopathology changes were observed in the spleen. Bone marrow: High presence of immature cells (myeloids and erythroid), polynuclear cells and megacaryocites (neutrophils, lymphocytes and plasma cells).

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