Sn-117m Homogeneous Colloid is a Disease-Modifying Device in the Treatment of Osteoarthritis

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AIM/INTRODUCTION

Radionuclides have been used to treat human rheumatoid (RA), osteoarthritis (OA) and other arthritides for decades outside of the United States. The procedure, radiosynoviorthesis (RSO), is the intra-articular injection of an isotope, either as a non-homogeneous microparticle (Er-169 and Y-90) or a colloid (Re-186), that is engulfed by synovial macrophages. This results in thickening of the synovium and sclerosis and fibrosis resulting in decreased joint pain. Sn-117m, used in the manufacture of a homogeneous Sn-117m colloid (HTC) for RSO procedures, is generated in nuclear reactors via 117Sn(n,n'γ)117mSn. Although radionuclide drug injections for RSO are approved in Europe, in the US the HTC device is available only for the treatment of canine elbow OA. Our aim was to investigate whether the HTC demonstrated an OA disease modifying effect (defined here as a treatment that delays or slows the progression of a disease by targeting its underlying cause[1]), and we report here the data from cGMP/GLP rodent trials which suggest the existence of that effect.

MATERIALS AND METHODS

Adult rats (n=109) were studied using the surgical meniscal tear OA model. The trial consisted of rats divided into 5 arms including 2 control arms, 1 safety arm, and 2 treatment arms using RSO dosages of 2µCi (low dose) and 10µCi (high dose) HTC. Rats were sacrificed at 1, 4, 6 and 10 weeks (Table 1). Sacrificed study knees received histopathology analysis. Sn-117m was produced in the BR2 nuclear reactor followed by manufacturing of HTC.

RESULTS

Generally, animals treated with 2 or 10 µCi had lesion severity that was slightly to significantly reduced compared to non-injected OA controls. Based on substantial cartilage degeneration widths with support from other cartilage degeneration parameters (scores, depth ratios, osteophyte measures), there is evidence of beneficial effects of treatment at week 1, and trends toward at 4 and 6 weeks on some parameters (Figure 1).

CONCLUSION

To our knowledge, this is the first time that a medical device has provided evidence of an OA disease modifying effect. Our rat data translates to and provides validation for the Phase 1 human clinical trial of OA and RA therapy that is authorized to begin in Canada. Although OA contributors include obesity, malalignment, acute and repetitive joint injuries, generalized disease, heredity, and muscle weakness, OA ultimately progresses to include a rheumatologic component which also is well known to respond to RSO treatments.

We anticipate that HTC will produce a disease modifying effect in the planned human OA/RA trials, similar to that seen in the rat trials.

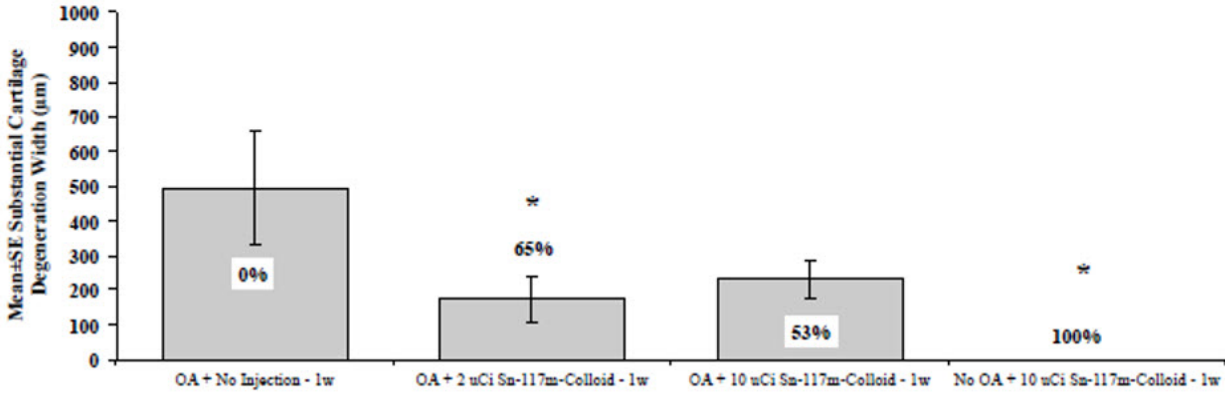
REFERENCES

Oo, W. M. et al. (2021). The development of disease-modifying therapies for osteoarthritis (DMOADs): The evidence to date. *Drug Design, Development and Therapy* 15, 2921-2945.

Table 1 Schemata of the GLP rat trial using the meniscal tear model of OA

Rat OA GLP							
Date of procedure/sacrifice		1 wk	0 wk	1 wk	4 wk	6 wk	10 wk
Group							
OA Lewis male	# animals						
Group 1 (Model Control)	**15**	Surgery	None	4	4	4	3
Group 2--2uCi	**31**	Surgery	HTC	10	10	11	
Group 3--10uCi	**36**	Surgery	HTC	11	11	11	3
Group 4--10uCi (no disease)	**8**	No Surgery	HTC	2	2	2	2
Group 5 (Control)	**20**	Surgery	cold Sn colloid	5	5	5	5
Total OA study	**110**						

Figure 1



Substantial Cartilage Degeneration Width (1 wk) – All Rats
n = 4-10/group
*$p \leq 0.050$ Student's t-test *vs*. OA + No Injection

Substantial cartilage degeneration width as an example of an analyzed study parameter demonstrating reduced lesion severity following intra-articular injection of 2 µCi Sn-117m colloid