Superiority of Bone Marrow derived-Osteoblastic Cells (ALLOB®) over Bone Marrow derived-Mesenchymal Stromal Cells

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SUMMARY

Bone Therapeutics is a bone cell therapy company addressing high unmet medical needs in the field of bone fracture repair, more specifically in non-union and delayed-union fractures – and spinal fusion - where the bone repair process is impaired. The company has developed a unique allogeneic osteoblastic cell product (ALLOB®) derived from bone marrow which is currently tested in three Phase I/IIa proof of concept clinical trials. The purpose of the study was to directly compare ALLOB® *vs*. non-differentiated mesenchymal stromal cells (MSC) for their *in vitro* osteogenic characteristics and their *in vivo* osteogenic potential in order to determine which cellular type would be the most adapted for bone repair.

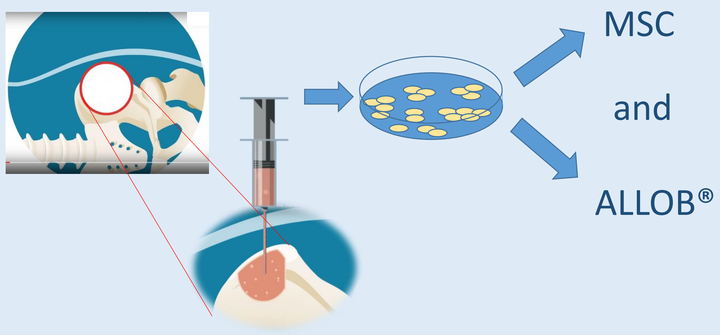
Declaration of Conflict of Interest: *All authors have no potential conflict of interest to declare*

METHODS

1. Culture and expansion of MSC and ALLOB® cells (n=7 Bone Marrow)

Bone marrow aspirate from iliac crest

In vitro culture process



2. *In vitro* characterization (n=7)

Cells were characterized *in vitro* by morphology, immunophenotype (FACS), gene expression (qRT-PCR) and differentiation potential.

3. *In vivo* assessment of efficacy (n=6)

Subcutaneous injection over the calvaria of nude mice of

- MSC cells
- ALLOB® cells
- excipient (control -)

Bone formation evaluated by

- Radiology (Faxitron®)
- Histomorphometry

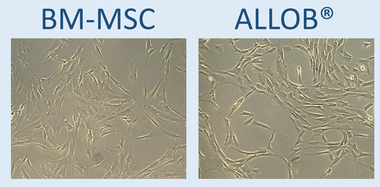
RESULTS

1. Cells immunophenotype, ALP activity and morphology (n=7)

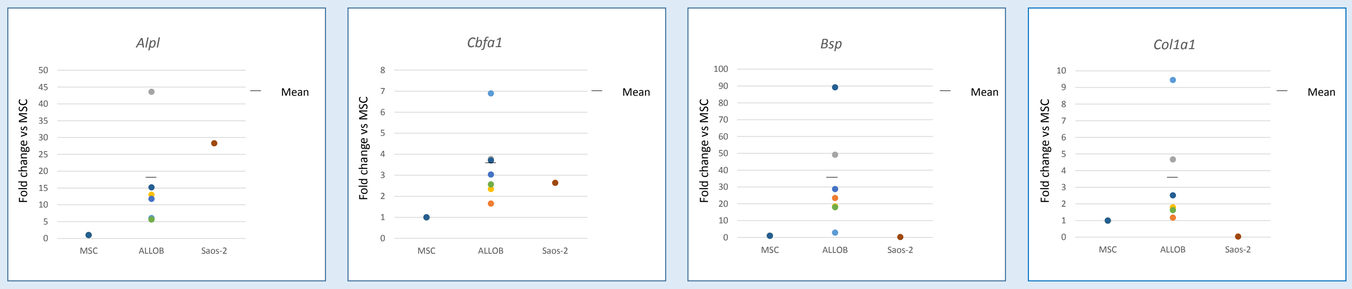
Cell population	Mesenchymal markers	Hematopoietic markers		Osteoblastic markers	
	FACS analysis				Enz. act. analysis
	CD73/CD90/CD105	CD3	CD45	ALP	ALP enz. (mU/mg tot. prot.)
MSC	99 ± 1 (n=7)	3 ± 1 (n=7)	2 ± 0 (n=7)	15 ± 7 (n=7)	108 ± 86 (n=7)
ALLOB®	100 ± 0 (n=7)	7 ± 0 (n=7)	1 ± 1 (n=7)	75 ± 7 (n=7)	495 ± 266 (n=7)

Cell morphology

BM-MSC ALLOB®



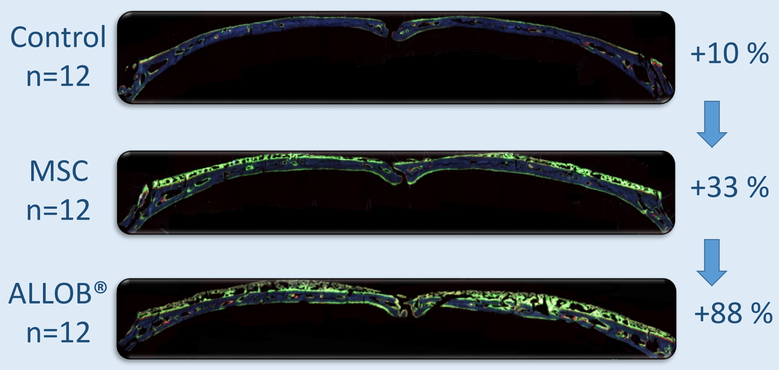
2. Analysis of chondro- and osteoblastic markers gene expression (n=7)



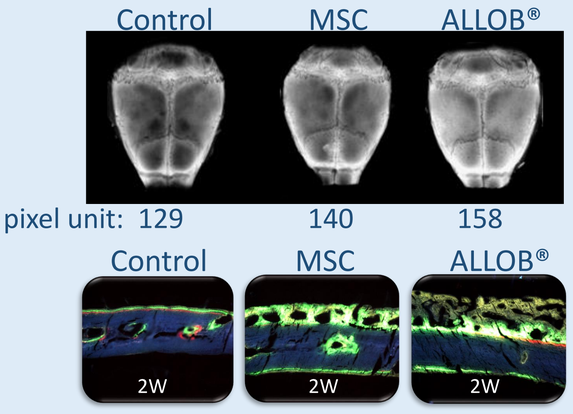
ALLOB® also expressed significantly higher levels of *Sox9* (fold change (FC) >5), *Ctsk* (FC > 200), *Bglap* (FC > 16), *Bmp2* (FC > 120) compared to MSC.

3. Bone Formation in NMRI-Nude mice

Histomorphometrical evaluation of the bone formation



Radiological evaluation of the bone formation



CONCLUSIONS

ALLOB® displays superior osteogenic capacity over BM-MSCs in vitro and in vivo, and is therefore a good clinical candidate.