AUTOLOGOUS OSTEOBLASTIC CELLS VS. CONCENTRATED BONE MARROW IMPLANTATION IN OSTEONECROSIS OF THE FEMORAL HEAD: A RANDOMIZED CONTROLLED SINGLE BLIND STUDY

THU0540

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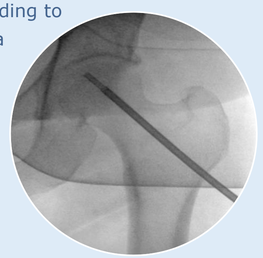
Introduction

Non traumatic osteonecrosis of the femoral head (ONFH) is characterized by epiphyseal necrosis leading to femoral head collapse and hip replacement. ONFH pathogeny appears to be related to local ischemia and to mesenchymal and bone cellular deficiency[1].



Earlier interventions showed that implantation of bone marrow concentrate **(BMC)** containing mesenchymal stem cells (MSCs) could delay ONFH progression and improve symptoms[2]. Then, the possibility was raised that a cell-based medicinal product consisting in a population of **autologous osteoblastic (OB) cells (PREOB®)** could be more efficacious than BMC in early stages ONFH.

Objectives: This study was undertaken to evaluate the efficacy of OB cells implantation in a randomized comparison with BMC implantation in early stages ONFH.

Methods

Subjects (hips) with ARCO stage 1 or 2 ONFH were included in the trial, and randomized to receive a core decompression procedure followed by either BMC or OB cells single percutaneous injection.

From 82 subjects (hips) enrolled,

- **63 were treated** and
- **60 were assessable** and analyzed as the efficacy cohort.

Baseline demographics, risk factors, location/size of ON & symptoms were not statistically different between groups (post-hoc analysis).

In the BMC group, 410.6 ± 84.9 ml of bone marrow (BM) was harvested from the iliac crest and concentrated to 41.8 ± 10.9 ml.

In the OB group, MSCs were isolated from BM aspirate (56.8 ± 36.3 ml), expanded and differentiated *ex vivo* under autologous conditions to obtain a population of OB cells (target of 20.10^6 cells).

ARCO stage (as assessed by X-Rays), **hip pain** (visual analog scale) and WOMAC® index were assessed at 3, 6, 12, 24 and 36 months.

Primary endpoint was the **proportion of responders at 24 months.** A responder was defined as the absence of progression to fractural stage (3 or 4) & a clinically significant pain improvement.

N=30 per group	BMC group	OB group
Age* (Y)	51.1 ± 10.6	50.8 ± 13.2
Male:Female	21:9	20:10
Ethnic Origin		
White European	30 (100.0%)	29 (96.7%)
Black/Afro American	0 (0.0%)	1 (3.3%)
BMI*	26.3 ± 4.4	26.1 ± 4.5
ON risk factors		
Corticosteroids	20 (66.7%)	17 (56.7%)
Alcohol abuse	12 (40.0%)	7 (23.3%)
Other	6 (20.0%)	10 (33.3%)
Idiopathic	2 (6.7%)	3 (10.0%)
ARCO stage		
Stage I	10 (33.3%)	11 (36.7%)
Stage II	20 (66.7%)	19 (63.3%)
Size of ON		
Minimal A<15%	5 (16.7%)	1 (3.3%)
Moderate B 15-30%	9 (30%)	11 (36.7%)
Extensive C>30%	16 (53.3%)	18 (60.0%)
VAS pain (mm)*	34.6 ± 31.3	43.1 ± 30.2
WOMAC® (pts)*	33.3 ± 25.7	38.3 ± 24.2

** Expressed as mean ± standard deviation*

Efficacy Results

Primary Endpoint – Treatment Response

At 24 months, responder rate to treatment was 37% in the BMC group *vs.* 70% in the OB group (p=0.011; Fisher's exact test)

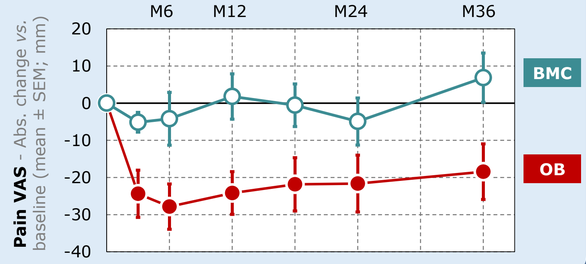
At 24 months, the proportion of hips that progressed to fracture in the BMC and OB groups was respectively 40% and 20%, corresponding to a **50% reduction in fracture risk.**

N=30 per group	BMC group	OB group
Responder		
24 months	36.7% (11/30)	70.0% (21/30)
36 months	33.3% (10/30)	60.0% (18/30)
Prog. to fracture		
24 months	40.0% (12/30)	20.0% (6/30)
36 months	50.0% (15/30)	20.0% (6/30)
THA		
24 months	16.7% (5/30)	6.7% (2/30)
36 months	20.0% (6/30)	10.0% (3/30)

Clinical Improvement

Patients treated with OB cells had a **clinically and statistically significant improvement in joint pain and symptoms** (WOMAC®) at all timepoints up to 36 months, and as early as 3 months.

No clinically relevant improvement was observed in patients treated with BMC.



Safety Results

Overall, 553 treatment emergent AE (TEAEs, of which 121 TESAEs) were reported, of which 2.7% (15 TEAEs) were possibly related to the procedure or the cell therapy products. The AEs reported as possibly related to study treatment were **in accordance with the possible risks linked to study procedures (in particular bone marrow aspiration)** as described in the literature.

During the trial, 61.9% of subjects experienced at least 1 SAE.

Conclusion

This study showed that a single OB cells (PREOB®) implantation in ON lesion could be more efficacious than BMC treatment

- **to delay the evolution to subchondral fracture and**
- **to reduce pain in ON of the femoral head.**

REFERENCES

[1] Hernigou P *et al*. Decrease in the mesenchymal stem cell pool in the proximal femur in corticosteroid-induced osteonecrosis. J Bone Joint Surg Br 1999; 81: 349–55

[2] Gangji V *et al*. Treatment of osteonecrosis of the femoral head with implantation of autologous bone marrow cells. A pilot study. J Bone Joint Surg Am 2004; 86-A(6): 1153-60

*Poster (THU0540) presented at the Annual European Congress of Rheumatology EULAR congress 2016 on 8th June 2016, and will be available for download on the website: **http://www.bonetherapeutics.com/en/investors/presentations.***

Safety data displayed herein differ from those in the EULAR abstract (THU0540). Please note that the correct safety data are displayed on this poster.