A novel method for the treatment of osteonecrosis of the femoral head using allogenic osteoblasts with core decompression

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INTRODUCTION: This study presents a phase 1 clinical trial that investigates a novel approach for treating avascular necrosis (AVN) of the femoral head using allogenic osteoblasts in combination with core decompression. AVN is a progressive bone disease that primarily affects individuals aged between ages 20s and 50s, and previous attempts to preserve patients' own bone tissues have not been successful. This study aims to explore the potential of allogenic osteoblasts (CF-M801) to halt the disease progression of AVN and preserve patients' own bone tissues.

METHODS: Osteoblast Preparation: CF-M801 allogenic osteoblasts were prepared, and quality controlled according to regulatory guidelines. The study was approved by the Institutional Review Board (IRB number: EUMC 2019-11-030-009, KNUH202107015) and the Ministry of Food and Drug Safety (MFDS) (protocol ID, 100052, CRIS registration number, KCT0006627).
Patients Recruitment: Nine patients in the early stages of AVN (ARCO stage 1 and 2) underwent core decompression (CD), followed by transplantation of CF-M801 osteoblasts to the necrotic region.
Dosage Variation: The patients were divided into three groups, each group receiving a different dosage of CF-M801 osteoblasts. Three patients were assigned to each dosage group.
Outcome measurement: The study assessed the treatment's effectiveness through various outcome measures including immune response analysis, pain assessment using the Visual Analogue Scale (VAS), functional assessment using the Harris Hip Score (HHS) and Western Ontario and McMaster Universities Arthritis Index (WOMAC), and imaging evaluation using X-ray and MRI.

RESULTS SECTION: The study demonstrated significant improvements in patients-reported pain (VAS scores) and functional ability (WOMAC and scores). Positive changes in the necrotic angles were observed through X-ray and MRI analyses using the modified Kerboul method. Some patients also showed improvements in the Joint International Commission (JIC) stage. Importantly, no patient's AVN condition progressed to a more advanced stage (ARCO stage) during the study period. The treatment was deemed safe, as there were no indications of an immune reaction or the development of allo-antibodies.

DISCUSSION: This study's findings suggest that the utilization of allogenic osteoblasts (CF-M801) in combination with core decompression could hold promise as a novel approach for treating AVN. The observed improvements in symptoms and the potential to halt disease progression, along with the absence of adverse events and immune reactions, indicate the feasibility of this treatment strategy. Further research ad large-scale trials could provide deeper insights into the mechanisms and long-term effectiveness of this approach for AVN treatment.

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Dose	Enrollment #	[1]ARCO grade		[2]JIC Stage		[3]SAE (2023-03-31)	Comments
		Baseline (V1)	After 3M (V5)	Baseline (V1)	After 3M (V5)		
low dose	01-P1-R001	1	1	C1	C1	No	NO allogeneic immune response
	01-P1-R002	2	2	C2	C2	No	NO allogeneic immune response
	01-P1-R003	2	2	C2	B	No	NO allogeneic immune response
Medium dose	01-P1-R004	2	2	C2	C1	No	NO allogeneic immune response
	01-P1-R005	2	2	C1	C1	No	NO allogeneic immune response
	01-P1-S006	2	2	C1	C1	No	NO allogeneic immune response
High dose	01-P1-R007	2	2	C1	C1	No	NO allogeneic immune response
	01-P1-R008	2	2	C2	C2	No	NO allogeneic immune response
	01-P1-R009	1	1	C2	C1	No	NO allogeneic immune response

[1]ARCO : Association Research Circulation Osseous classification
[2]JIC : Japanese Investigation Committee classification
[3]SAE : Serious Adverse Event

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Dose	Enroll No.	Baseline	3M after IP	Necrotic Angle
				Baseline-3M
Low Dose	01-P1-R001	240.69	225.37	15.32
	01-P1-R002	305.3	305.32	-0.02
	01-P1-R003	579.23	563.39	15.84
	Average	375.07	364.69	10.38
Medium Dose	01-P1-R004	257.68	255.65	2.03
	01-P1-R005	277.95	270.51	7.44
	01-P1-R006	215.44	207.29	8.15
	Average	250.36	244.48	5.87
High Dose	01-P1-R007	290.85	285.43	5.42
	01-P1-R008	295.76	265.73	30.03
	01-P1-R009	329.95	299.69	30.26
	Average	305.52	283.62	21.90