Clinical Application of Osteoblastic Cell-based Therapy in Spinal Fusion

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BACKGROUND

Spinal fusion is the gold standard procedure for treating a broad spectrum of spine disorders, such as degenerative disc disease.

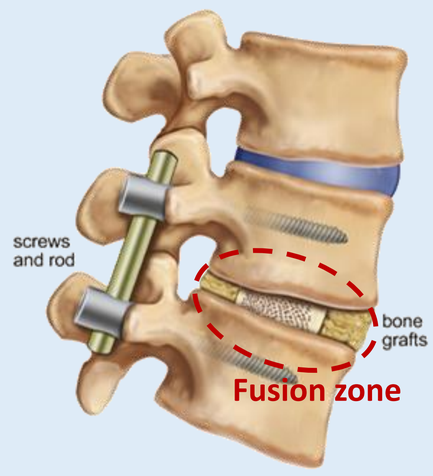
Globally, around one million spinal fusion procedures are performed in Europe, the US and Japan, of which half at the level of the lumbar spine. It is estimated that the spinal fusion market will continue to grow with approximately 5% per year.

Spinal fusion aims to:

- Immobilize a painful vertebral segment
- Relieve pain
- Improve function in daily life

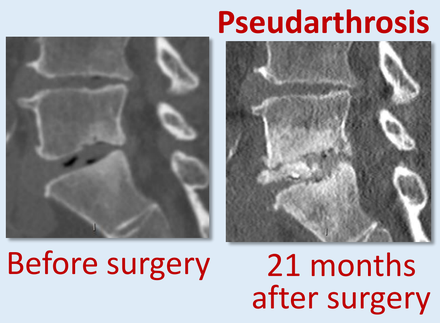
The procedure consists of bridging two or more vertebrae with the use of:

- Instrumentation (e.g. screws, rods) to provide mechanical stabilization
- Bone graft (e.g. autograft or synthetic bone graft) to promote bone formation and spinal fusion



VALUE PROPOSITION

Limitations of standard spinal fusion



Despite the fact that spinal fusion is a routine procedure, this surgery often results in lack of fusion and continuing pain, leaving up to 30% of patients unsatisfied with their surgery.

Among the concerns are:

- Clinical and radiological success rates are highly variable (no fusion in 5% to 25% of cases)
- Slow progression to fusion (6 to 24 months)

To improve fusion rates and time to fusion, various bone grafts (e.g., autograft, DBM, BMP) have been developed. However, none of these present simultaneously all the required properties for bone formation (i.e. osteogenic, osteoinductive and osteoconductive properties) as well as a good safety profile.

Bone Therapeutics is seeking to improve spinal fusion procedures through the inclusion of its allogeneic bone cell therapy product, ALLOB®, combined with a TCP ceramic scaffold in the procedure:

ALLOGENEIC OSTEOBLASTIC CELLS + **CERAMIC SCAFFOLD**

Advantages over mesenchymal stromal cells:

- More potent (faster and better bone-forming capacity)
- Safer (no unwanted cells or activity)

Biocompatible
Bioresorbable
Synthetic

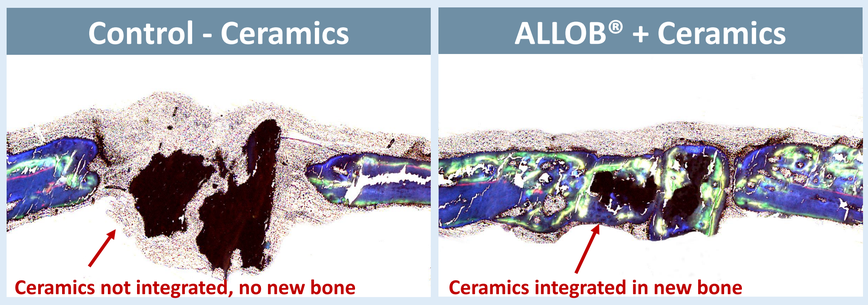
RESULTS

Preclinical proof-of-concept studies

Based on *in vivo* regulatory studies, no safety issues have been observed in cell biodistribution, tumorigenicity, safety pharmacology and GLP long-term toxicity.

Preclinical proof-of-concept studies show increased bone fusion when combining ALLOB® cells with ceramic granules:

- Sub-critical circular cranial bone defect in Nude mice
- Administration of ceramic scaffold alone or combined with ALLOB®, mimicking a fusion procedure
- Analysis of bone fusion by imaging (µCT), histomorphometry, ALP and TRAP staining (indication of bone remodeling)



Absence of continuity between bone edge and ceramics
→ No fusion

Continuity between bone edge and ceramics
→ Fusion

Ongoing Pilot Phase IIA, Multicentre, Open, Proof-of-concept Study on the Safety and Efficacy of Allogeneic Osteoblastic Cells (ALLOB®) Implantation in Lumbar Spinal Fusion

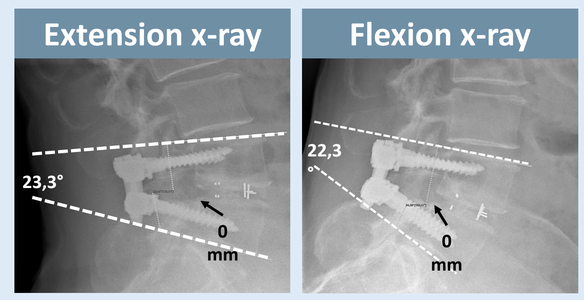
The pilot Phase IIA study will enrol a total of 16 patients with symptomatic degenerative lumbar disc disease who require interbody fusion surgery. An interbody cage is implanted according to the standard-of-care surgical approach, supplemented with ALLOB® in combination with bioceramic granules. Safety and efficacy of this treatment is assessed over 12 months, using clinical and radiological evaluations.

Safety: Twelve patients out of 16 have now been treated with ALLOB® in combination with ceramics in the spinal fusion trial without any treatment-related safety concerns.

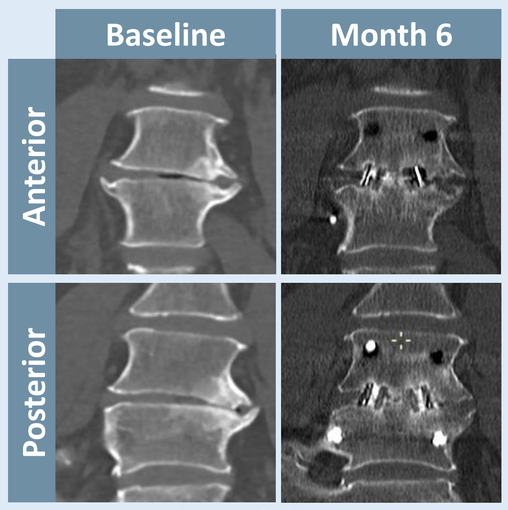
Efficacy: Today, one patient has completed the 12-months follow-up, this patient (treated between L4&L5):

- Regained function in daily life
- Experienced back and leg pain relief

Radiologically, dynamic x-rays and CT-scans showed, starting from 6 months, no intervertebral mobility and an interbody fusion at the treated level, respectively. More precisely, trabecular bridging bone can be observed in the segment in the disc space occupied by the interbody cages in both anterior and posterior view of the spine.



Dynamic x-rays



Coronal CT scans

CONCLUSION

ALLOB® combined product displays a target product profile of choice for spinal fusion procedures:

- All the required properties for bone formation and fusion
- An excellent safety profile both preclinical and clinical
- Strong preclinical efficacy results
- Encouraging clinical efficacy data