5.1 Indication for Use: Natural History and Alternate Practices and Procedures

It was postulated that the use of OP-1 Putty could prove beneficial as a substitute for autograft in the treatment of patients requiring primary decompression and lumbar spinal fusion, because it could stimulate the new bone growth needed for a successful fusion, while eliminating the pain and morbidity associated with surgical harvesting of autograft bone from the iliac crest. Stryker Biotech therefore pursued extensive pre-clinical and clinical research to investigate whether OP-1 Putty is a safe and effective alternative to autograft for primary spinal fusion surgery. A recent pre-clinical study in a primate model of posterolateral fusion demonstrated the safety and efficacy of the OP-1/collagen matrix combination in promoting spine fusion over a broad dose range. Clinical fusion with bridging bone was observed at all dose levels, including a subclinical dose of 0.33 mg/ml OP-1 (4 mg per level) with 3 out of 4 animals fused at 4 months. All animals in the 1 mg/ml (equivalent concentration used in the clinical study), 2 mg/ml and 4 mg/ml groups were completely fused at 4 months with no safety observations. Fusion in the clinical equivalent dose group to the pivotal trial was better than the autograft group at 3 months and fusion was never observed in the matrix only control group. Safety and efficacy of other BMPs in spinal applications have also been reported in animal models.8,9,10,11,12

References

8 Sandhu HS. Spinal applications for recombinant bone morphogenetic protein: early experimental results. 1996.
5.1 Indication for Use: Natural History and Alternate Practices and Procedures
(Content from P060021/A011, November 2007 Amendment, Section V, Clinical, Section 1.1, Page 11)

Rationale for Indication and Population Studied

It has been estimated that up to 70% of the adult population suffers from some form of low back (lumbosacral) pain, which is usually attributed to a degenerative disease process within the vertebral spine. Degenerative spondylolisthesis, a condition characterized by a slipping of one vertebral segment on the one below in the presence of an intact neural arch, is one of the diagnoses attributed to the degenerative disc disease process. It is more prevalent in women and the incidence increases with age. Spinal stenosis is often associated with the spondylolisthesis, due to facet hypertrophy, ligamentum flavum thickening, and osteophyte formation. If patient pain, neurological deficits, and instability do not respond to conservative management, decompression and lumbar spinal fusion are the most common surgical treatments of choice for degenerative spondylolisthesis and spinal stenosis.

Spinal fusion is a surgically created bony union across the involved vertebrae and approximately 70,000 posterolateral lumbar spinal fusions are performed annually. The use of bone graft to stimulate bone growth is a standard surgical technique in spinal fusion with and without instrumentation. Bone graft stimulates new bone formation and acts as a matrix or scaffold into or over which new bone can grow. Currently, autologous bone (autograft) is considered the most successful bone grafting material and it is preferred over allograft bone. The most common site for harvesting autograft material is the iliac crest. However, this increases operative time, blood loss, and the morbidity associated with spinal fusion.

In recent years, there has been focus on BMPs as osteoinductive agents. OP-1 is one such BMP. Implants containing OP-1 and collagen matrix have been shown to be osteoinductive and osteoconductive, to speed the rate of bone healing and to improve the performance of autograft in animals. Implants containing OP-1 and collagen matrix have also been shown to promote stable spinal fusions in a significantly more rapid fashion than autograft. Safety and efficacy of other BMPs in spinal applications have also been reported in animal models.

It was therefore postulated that OP-1 Putty could substitute for iliac crest autograft for the treatment of patients requiring decompression and lumbar spinal fusion, thereby eliminating the pain and morbidity associated with harvesting autograft bone from the iliac crest. A clinical study program was therefore designed to evaluate the safety and effectiveness of OP-1 Putty as a replacement to autograft in posterolateral fusion of the lumbar spine in patients with degenerative spondylolisthesis with spinal stenosis.

Reference