CLINICAL AND SCIENTIFIC LITERATURE ABOUT NOBEL BIOCARE BIOMATERIALS

CREOS™ REGENERATIVE PRODUCTS

creos™ xenogain

creos™ xenogain is a bovine bone mineral matrix for bone grafting in periodontal, oral and maxillofacial surgery. This bone graft material is a hydroxyapatite derived from bovine bone and it has a wide application in bone regeneration. creos™ xenogain is a class III medical device (Europe), it is CE marked and approved by GMED notified body. creos™ xenogain is US class II cleared by the FDA federal agency of the United States Department of Health and Human Services. The material used for creos™ xenogain has been on the market for more than 15 years.

Type	Reference	Description	Extract (verbatim)
Clinical study	Maxillary sinus floor augmentation using deproteinized bovine bone-derived bone graft material (OCS-B). Clinical and histologic findings in humans. Jun-Beom Park et al. The Journal of the Korean Dental Association. 2007;45(8):491 – 499.	Clinical study with 10 patients. Up to 9 months follow-up. creos™ xenogain is named OCS-B in the article.	"From the results, it is believed that maxillary sinus augmentation with OCS-B® can achieve excellent level of bone mass gain before implant insertion."
Clinical study	Periodontal Repair on Intrabony Defects treated with Anorganic Bovine-derived Xeonograft. Young-Taek Kim et al. J Korean Acad Periodontol. 2007;37(3):489 – 496.	Clinical study with 10 patients, 6 months follow-up.	"On the basis of these results, anorganic bovine-derived xenograft improves probing depth and clinical attachment level in periodontal defects."
Clinical study	A radiographical study on the changes in height of grafting materials after sinus lift: a comparison between two types of xenogenic materials. Pham-Duong Hieu. J Periodontal Implant Sci 2010;40:25-32	Clinical study with 21 patients, 4 years follow-up. creos™ xenogain is named OCS-B in the article.	"No significant difference in height change was observed between the Bio-Oss® and the OCS-B® groups."
Clinical study	Long-term results of new deproteinized bovine bone material in a maxillary sinus graft procedure. Seung-Yun Shin et al. Periodontal Implant Sci 2014;44:259-264	Clinical study with 12 patients, 2-6 years follow-up.	"Our results show that the new DBBM is useful for a maxillary sinus graft procedure. Good healing responses as well as reliable results were obtained for an average follow-up period of 43.3 months."
Clinical study	A multicenter clinical investigation demonstrates bone regeneration in severe horizontal defects in the posterior mandible using creos xenoprotect: Interim results [PR546]. Aleksic Z. et al. J Clin Periodontol 2018;45(S19):306.	Clinical study with 46 patients, 8 months follow-up.	"GBR led to robust bone regeneration after 8 months of healing."

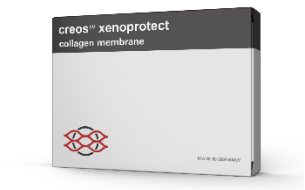
Clinical study	Histomorphometric analysis of regenerated bone in sinus lift by deproteinized bovine bone particles. De Santis D. et al. Clinical Oral Implants Research 2018 Volume 29, Issue S17.	Histomorphometric analysis of regenerated bone in sinus lift by deproteinized bovine bone particles, 18 months follow-up	"The histologically observed integration of deproteinized bovine bone particles (creos xenogain) and the good clinical results support bovine apatite as valid bone substitute where sinus floor elevation precedes implant insertion. Bovine apatite acts as spacer and conducting structure for the new bone formation. Mesenchymal stem cells, osteoblasts and capillaries are able to enter the macropores of the xenograft particles, promoting the healing process."
Clinical study	Peri-implantitis surgical treatment with xenograft and L-PRF. Orlando Martins & Sérgio M Matos. Clinical Oral Implants Research Volume 29, Issue S17. November 2018	Peri-implantitis surgical treatment, 6 months follow-up	"PI treatment depends on defect configuration (Schwarz et a. 2010) and the L-PRF/xenograft block allows a higher biomaterial stability and also their application on more demanding peri-implant defects."
Clinical study	Alveolar Crestal Approach for Maxillary Sinus Membrane Elevation with <4mm of Residual Bone Height: A Case Report. Jae Won Jang et al. International Journal of Dentistry. Volume 2018, Article ID 1063459, 7 pages. Published 28 June 2018	Clinical study with 10 patients, up to 3 years follow-up	"The mean residual bone height before implant placement was 3.41 ± 0.53 mm; no complications, including membrane perforation, severe postoperative pain, or discomfort, occurred either during or after surgery."
Clinical study	Horizontal Ridge Augmentation and Contextual Implant Placement with a Resorbable Membrane and Particulated Anorganic Bovine Bone-Derived Mineral September. Ferdinando Attanasio et al. Case Reports in Dentistry 2019(1):1-6 Follow journal. DOI: 10.1155/2019/6710340	Horizontal ridge augmentation, 6 months follow-up	"Within the confines of this case report, we can consider the GBR technique to be successful in the preprosthetic surgical treatment of horizontally deficient alveolar ridges [...]"

Table 1

Type	Reference	Description	Extract (verbatim)
 In-vivo	A study on the safety and efficacy of bovine bone-derived bone graft material OCS-B. Ho-Nam Park et al. J Korean Acad Periodontol Vol. 35, No. 2, 2005	Histology in-vivo in rabbits and mouses. creos™ xenogain is named OCS-B in the article.	"It is concluded that newly developed inorganic bovine bone mineral (OCS-B) is a flourishing bone-forming material and biocompatible material."
 In-vitro	Effect of Heat-Treatment Temperature on the Osteoconductivity of the Apatite Derived from Bovine Bone. Sang-Hoon Rhee et al. Key Engineering Materials Vols. 309-311 (2006) pp 41-44Online available since 2006/May/15 at www.scientific.net© (2006) Trans Tech Publications, Switzerland doi:10.4028/www.scientific.net/KEM.309-311.41	In-vitro study.	"The apatite granules heat-treated at 600°C showed much better osteoconductivity comparing to that heat-treated at 1000°C."
 In-vivo	Bone reaction to human hydroxyapatite grafted in the mandibular defects of beagle dogs. Jun-Beom Park et al. Article in The Journal of the Korean Academy of Periodontology – January 2006. DOI: 10.5051/jkape.2006.36.1.39	In-vivo in dogs.	"New bovine hydroxyapatite was proved to be an excellent osteoconductive agent in grafted sites, which biologically incorporate with newly formed osseous tissue."
 In-vitro	Evaluation on the bone regenerative capacity of deproteinized bovine bone-derived bone graft material (OCS-B). Park, Jun-Beom et al.	In-vitro study. creos™ xenogain is named OCS-B in the article.	"It is concluded that newly developed deproteinized bovine bone (OCS-B) is biocompatible material showing excellent regenerative potential."
 In-vivo	The comparative study - the regenerative effect depends on size of bone graft material in bone loss site. Hong-kyun O et al. J Korean Acad Periodontol 2008;38:493-502.	Investigation on the regenerative capacity in rabbits.	"Small grafting material size has great influence on bone regeneration."

Table 2

creos™ xenoprotect



creos™ xenoprotect is a biodegradable barrier membrane for use in Guided Tissue Regeneration (GTR) and Guided Bone Regeneration (GBR) procedures. In these procedures, creos™ xenoprotect can be used as a resorbable membrane for the containment of bone grafts in bone repair procedures during treatment of periodontal bone defects (GTR) and for bone augmentation procedures (GBR). creos™ xenoprotect is a highly purified membrane produced from porcine collagen using controlled and standardized manufacturing processes. creos™ xenoprotect is a class III medical device (Europe), it is CE marked and approved by ECM notified body. creos™ xenoprotect is US class II cleared by the FDA federal agency of the United States Department of Health and Human Services.

Type	Reference	Description	Extract (verbatim)
Clinical study	Horizontal ridge augmentation with a novel resorbable collagen membrane: a retrospective analysis of 36 consecutive patients. B. Wessing et al. Int J Periodontics Restorative Dent 2016;36(2):179–187.	Horizontal ridge augmentation, 6-29 months follow-up	"These early data demonstrate a low dehiscence rate and excellent potential of this new noncross-linked collagen membrane for use with horizontal ridge augmentation."
Clinical study	A multicenter randomized controlled clinical trial using a new resorbable non-cross-linked collagen membrane for guided bone regeneration at dehisced single implant sites: interim results of a bone augmentation procedure. B. Wessing et al. Clin. Oral Impl. Res. 28, 2017, e218–e226 doi: 10.1111/clr.12995	Clinical study with 24 patients, 6 months follow-up	"The new resorbable non-cross-linked collagen membrane facilitates bone gain to support implant placement in expected dehiscence defects. The observed trend toward higher mean bone gain and lower exposure rate with creos™ xenoprotect compared to Bio-Gide should be further investigated."
Clinical study	Guided bone regeneration using collagen membranes simultaneous to implant placement at compromised sites leads to reproducible results and high success rates. B. Wessing et al. Musculoskelet Regen 2017; 3: e1537. doi: 10.14800/mr. 1537	24 patients, 6 months follow-up.	"The new creos™ xenoprotect membrane was statistically non-inferior to the reference Bio-Gide membrane with respect to mean difference in bone defect height between implant insertion and reentry surgery (p <0.001). Moreover, there was no difference in patient pain or quality of life between the two treatment arms. However, there were trends in improved outcomes, namely higher bone gain and lower membrane exposure rates, when creos™ xenoprotect was used compared with Bio-Gide, though not statistically significant. Together, the study confirms that, even using a simultaneous surgical approach, the creos xenoprotect collagen membrane supports bone regeneration at dehisced implant sites with few complications. This demonstrates that new barrier membrane materials with improved properties, such as creos™ xenoprotect, can provide clinical benefits to patients."

Clinical study	A multicenter randomized controlled trial using a novel collagen membrane for guided bone regeneration at dehisced single implant sites: Outcome at prosthetic delivery and at 1-year follow-up. I. Urban et al. Clin Oral Implants Res. 2019 Jun;30(6):487-497. doi: 10.1111/clr.13426.	24 patients, 1-year follow-up.	"The use of creos™ xenoprotect and Bio-Gide for simultaneous implant placement and GBR at dehisced implant sites similarly reduced defect height and improved secondary measures, indicating non-inferiority."
Clinical study	A randomized controlled study comparing guided bone regeneration with connective tissue graft to reestablish buccal convexity at implant sites: A 1-year volumetric analysis. Thomas De Bruyckere at el. PMID: 32686234 DOI:10.1111/cid.12934	21 patients, 1-year follow-up	"GBR as well as CTG are effective in reducing horizontal alveolar defects for aesthetic purposes."

Table 3

Type	Reference	Description	Extract (verbatim)
In-vitro	GBR with a mechanically stable resorbable membrane as a potential alternative to the use of autogenous bone block grafts. B. Wessing et al. October 2013. Clinical Oral Implants Research 24(2):153. Conference: European Association for OsseointegrationAt: DublinVolume: 22.	In-vitro for mechanical tests. creos™ xenoprotect is named Remaix in the article.	"The evaluation of the different membranes in the first part of the study showed a significantly higher mechanical stability of the Remaix membrane than of all other membranes tested, even the PTFE membrane."
In-vitro	Resorbable Collagen Membranes Expansion In Vitro. Arrighi et al. J Dent Res 93, 2014	In-vitro + clinical case	"The clinical results achieved with the creos xenoprotect membrane demonstrated easy fixation, perfect containment of the graft material and excellent wound healing. The significantly lower surface expansion of creos xenoprotect provides for more accurate trimming of the membrane to the defect dimensions in a dry stage. In addition, the lower surface expansion compared to Bio-Gide may potentially reduce strain on the primary wound closure."
In-vivo	Differences in degradation behavior of two non-cross-linked collagen barrier membranes: an in vitro and in vivo study. Bozkurt A et al. Clin. Oral Impl. Res.25, 2014, 1403–1411 doi: 10.1111/clr.12284	In-vitro + in-vivo in rats. creos™ xenoprotect is named Remaix in the article.	"after 20 weeks, the thickness of Remaix decreased only slightly, whereas Bio-Gide showed a thickness loss of around 50% and stronger degradation than Remaix."

In-vitro	Mechanical stability of collagen membranes: an in vitro study. Gasser A et al. J Dent Res 2016;95 (Spec Iss A):1683 (www.iadr.org)	In-vitro & clinical	"• creos™ xenoprotect demonstrated the highest force at break wet (21.2 N; interquartile range [IQR]: 13 –23.7). • creos™ xenoprotect showed the highest stress at break wet (14.2 N/mm2; IQR: 9.1-16.3). • creos™ xenoprotect had the highest suture retention wet (6.1 N; IQR: 5.9-6.5). • In general, NXL membranes had a higher force at break wet and a higher stress at break wet in comparison to XL membranes."
In-vivo	Tissue dynamics and regenerative outcome in two resorbable non-cross-linked collagen membranes for guided bone regeneration: A preclinical molecular and histological study in vivo. Omar O et al. Clin Oral Implants Res 2018;29(1):7–19.	In-vivo in rats	"[...] the creos™ xenoprotect group demonstrated significantly higher de novo bone formation in the central portion of the defect. This increase in bone formation was reflected by triggered expression of potent osteogenic growth factor, Bmp2, in the defect. These findings suggest that the creos™ xenoprotect membrane may have a more active role in regulating the bone healing dynamics."
In-vitro	Tensile Properties of Three Selected Collagen Membranes. Perry Razet al. BioMed Research International 2019(3):1-8	In-vitro, creos™ xenoprotect is named Remaix in the article.	"Among the 3 tested membranes, Remaix exhibited higher performance results in all the mechanical tests."

Table 4

creos™ syntoprotect

creos™ syntoprotect is a dense PTFE membrane that exists in two version: non-titanium-reinforced and titanium-reinforced. Dense PTFE was designed to withstand exposure in the oral environment, which represents an improvement to earlier versions of expanded PTFE in applications such as socket preservation where deliberate membrane exposure offers several advantages. creos™ syntoprotect is CE marked, cleared by the FDA federal agency of the United States Department of Health and Human Services.

creos™ syntoprotect has over 30 clinical publications available. Here are some of those:

Type	Reference	Description	Extract (verbatim)
Clinical study	Alveolar Bone Preservation in Extraction Sockets Using Non-Resorbable dPTFE Membranes: A Retrospective Non-Randomized Study. O. Hoffmann et al. j Periodontol. 2008;79:1355-1369.	276 extraction sockets in 276 patients, measurements taken 12 months after surgery.	"a significant regeneration of the volume of sockets could be noted by histologic evaluation, indicating that the newly formed tissue in extraction sites was mainly bone [...]. The use of dPTFE membranes predictably led to the preservation of soft and hard tissue in extraction sites."
Clinical study	Soft tissue enhancement using non-expanded PTFE membranes without primary closure. Barboza EP et al. Annual Meeting of the American Academy of Periodontology (AAP) in Seattle, WA, September 6-9, 2008.	15 lower posterior extraction selected to receive PTFE membranes.	"Non-expanded PTFE membrane utilized over extraction sockets, without primary closure, can be predictably used to promote soft tissue enhancement."
Clinical study	Comparison of Dermal Matrix and Polytetrafluoroethylene Membrane for Socket Bone Augmentation: A Clinical and Histologic Study. Paul D. Fotek et al. J Periodontol 2009;80:776-785.	Clinical study with 20 patients, measurements after 16 weeks of healing.	"All sites evaluated showed minimal ridge alterations, with no statistical difference between the two treatment modalities with respect to bone composition and horizontal and vertical bone loss, indicating that both membranes are suitable for alveolar ridge augmentation."
Clinical study	Guided Bone Regeneration Using Nonexpanded Polytetrafluoroethylene Membranes in Preparation for Dental Implant Placements – A Reports of 420 Cases. E. Barboza et al. Implant Dentistry Volume 19, Number 1, 2010	420 cases of alveolar ridge maintenance, of single molars (286) and bicuspids (134), using intentionally exposed PTFE membranes.	"Exposed nonexpanded PTFE membranes positioned over fresh extraction sockets associated or not with bone graft, provide tissue both hard and soft formation suitable for implant placement."

Table 5

creos™ mucogain

creos™ mucogain is a resorbable matrix intended to provide support during coverage procedures of localized gingival recessions and for local soft tissue augmentation. creos™ mucogain is designed to provide an off-the-shelf alternative to autogenous soft tissue grafts. The open, interconnecting porous structure of creos™ mucogain provides a matrix for the migration of proliferating cells and vascular structures. As the healing process advances, creos™ mucogain is degraded whilst a new soft tissue matrix is regenerated inside the creos™ mucogain structure. creos™ mucogain is composed of highly purified porcine collagen and elastin fibers. creos™ mucogain is a class III medical device (Europe), it is CE marked and approved by ECM notified body.

Type	Reference	Description	Extract (verbatim)
Clinical study	Soft tissue augmentation with a new regenerative collagen 3-d matrix with oriented open pores as a potential alternative to autologous connective tissue grafts [329]. Wessing B, Vasilic N. Clin Oral Implants Res 2014;25(s10):342.	Clinical study with 7 patients, 5 months follow-up	"The initial results obtained after clinical application of the new 3-D collagen matrix in closed-healing procedures are very encouraging. All treatments with closed healing procedures were able to reach a satisfying outcome, both for the surgeon and the patient, without having to perform any connective tissue harvesting."
Clinical study	Soft tissue augmentation at immediate implants using a novel xenogeneic collagen matrix in conjunction with immediate provisional restorations: A prospective case series. Sanz-Martin I. et al. Clin Implant Dent Relat Res. 2018;1–9.	Clinical study, 1-year follow-up	"[...] this case series has shown that a surgical implant protocol consisting of immediate implants in the anterior maxillary region and premolar area, in conjunction with hard and soft tissue grafting with xenogeneic substitutes, together with immediate provisionalization, resulted in high aesthetic scores and patient satisfaction [...]."
Clinical study	Soft tissue augmentation with a collagen-based 3D matrix with directed pore channels. B. Wessing et al. Clinical Oral Implants Research 30, 401-401. 2019	Clinical study with 45 patients, 1.8 ± 1.3 years follow-up	"This retrospective analysis demonstrated that creos mucogain promotes soft tissue health and maintains adequate soft tissue thickness when used simultaneously with implant placement. The histological findings demonstrate excellent biocompatibility of creos mucogain and indicate this matrix as a valid alternative to autologous grafts."
Clinical study	Treatment Of Multiple Gingival Recessions With Tunnel Procedure And A New Xenogeneic Collagen Matrix. Gaudard M. et al. Clinical Oral Implants Research 30, 401-401 and OBJECTIF PARO #50 - September 2019	Clinical study with 10 patients, 6 months follow-up	"The new creos mucogain matrix would lead to satisfactory clinical results and would make it possible to have a large amount of material available without additional surgical site. The operating time is reduced for the practitioner as for the patient."

Table 6

Type	Reference	Description	Extract (verbatim)
 **In-vivo**	Soft tissue volume augmentation in the oral cavity with a collagen-based 3D matrix with orientated open pore structure. Leon Olde Damink et al. Current Directions in Biomedical Engineering 2018;4(1) [conference paper]	In-vitro + in-vivo with pigs	"The in-vitro studies show that the mechanical properties (e.g. suture retention, volume recovery after cyclic compression) and the observed active cell migration into the open porous structure of the matrix fulfil essential design requirements. The in-vivo pig animal study shows that the matrix is well integrated into the surrounding tissue and replaced by newly formed autogenous soft tissue without a significant loss in tissue volume."

Table 7