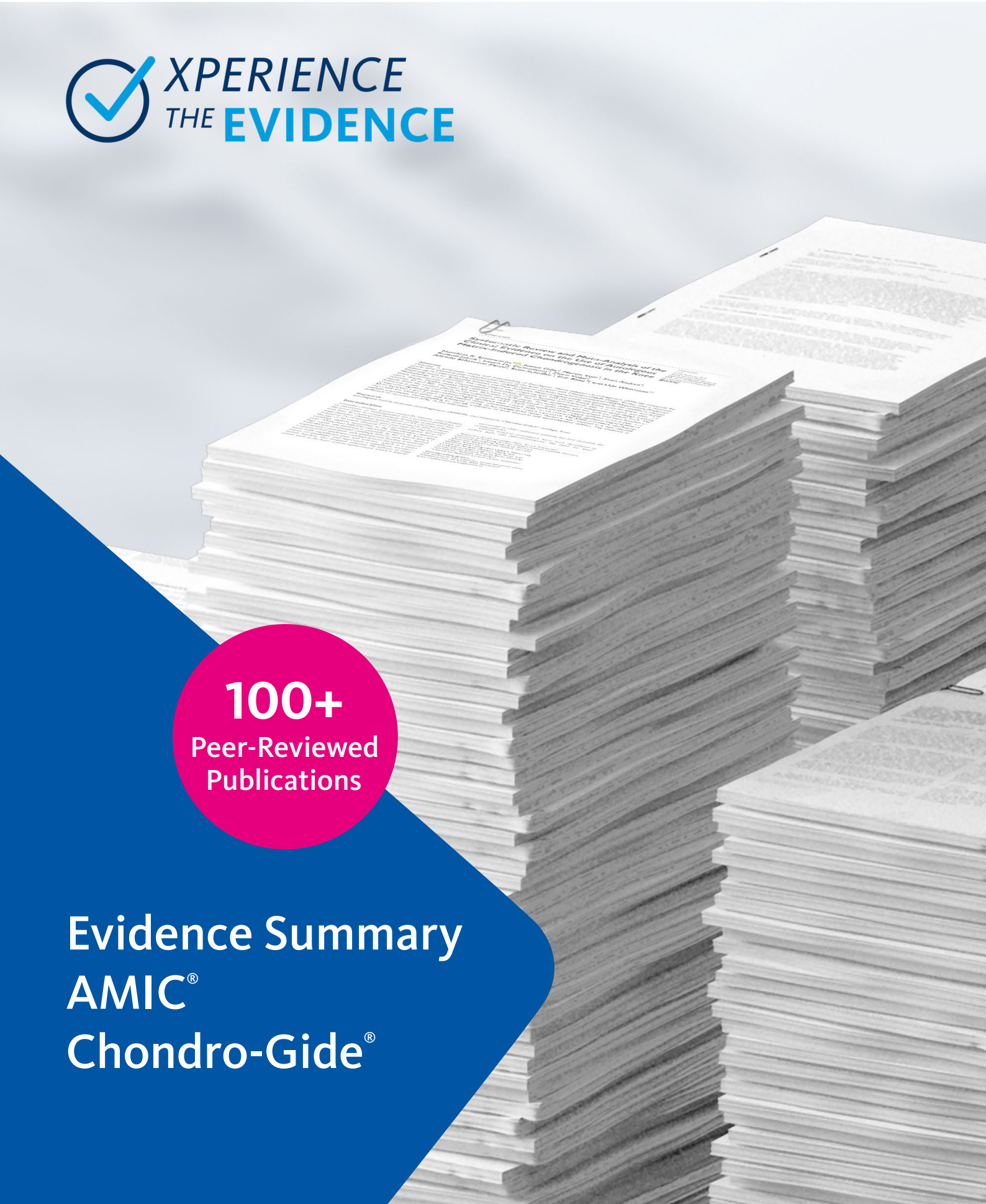
Geistlich
Surgery

XPERIENCE
THE EVIDENCE



100+
Peer-Reviewed Publications

Evidence Summary AMIC® Chondro-Gide®

CONTENTS

What's in it for you?

From levels of evidence
to levels of confidence

FOLLOW-UP

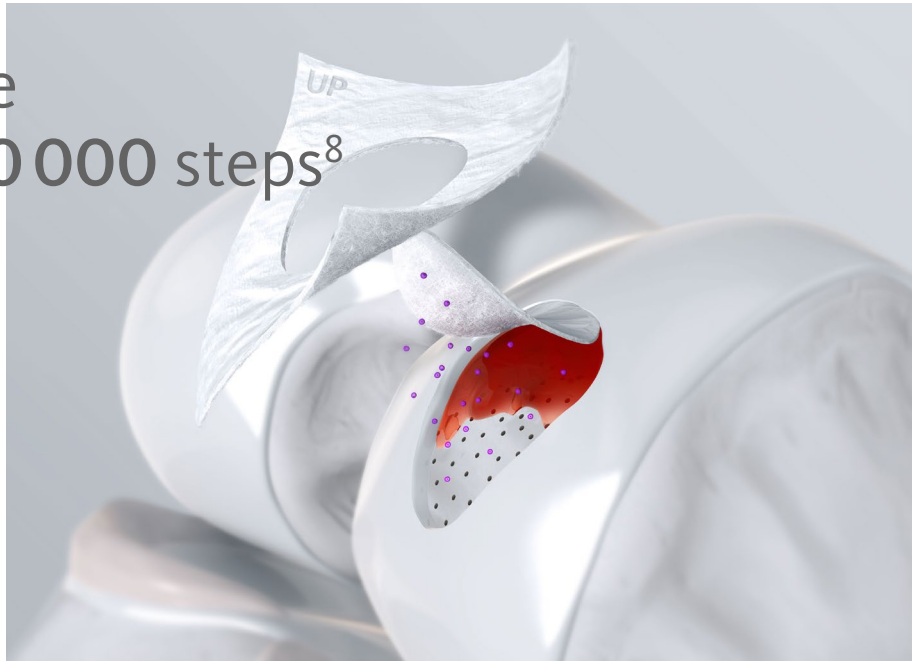
10 years and counting

AMIC® Chondro-Gide® was developed to support regenerative approaches in cartilage treatment. It is a one-step procedure that meets the requirements of surgeons and patients alike:

› Minimally invasive one-step procedure[1]
› Positive long-term outcome[2,3,4,5,6]
› cost efficient[6,7]

Data collected for the treatment of cartilage defects in the knee, ankle and hip have demonstrated that AMIC® Chondro-Gide® provides stable results for up to 10 years post-op[2]. Patients regain joint function and more invasive procedures can be postponed, possibly avoided altogether.

1-Step procedure wins **15 000 000** steps[8]



15+ Years AMIC®

AMIC® Chondro-Gide® was developed in collaboration with leading surgeons in Europe to stimulate and support the body's potential to heal itself. Because the self-healing ability of the avascular and aneural articular cartilage is limited, AMIC® recruits cells from bone marrow to the defect.

Bone marrow stimulation (BMS) induces the cascade of events needed to form new tissue. Chondro-Gide®, a collagen membrane, is used to cover the defect to keep cells in place and protect them from forces in the joint. The techniques for BMS may vary, but clinical data indicates that the defect preparation should include the removal of the calcified layer until petechial bleeding occurs[9, 10,11]. This step may be enough to jumpstart the regeneration cascade.

Such minimally invasive treatments, which reduce stress to the subchondral bone, are currently being tested.

1 Schagemann et al. 2019 (Clinical study)
2 Kaiser et al. 2020 (Clinical study)
3 De Girolamo et al. 2019 (Clinical study)
4 Walther et al. 2020 (Meta - analysis)
5 Walther et al. 2014 (Clinical study)
6 Gille et al. 2021 (Clinical study)
7 Fossum et al. 2019 (Clinical study)
8 Althoff et al 2017 (Data analysis)
9 Steadman et al. 1997 (Clinical study)
10 Frisbie et al. 2006 (Pre-clinical study)
11 Steadman et al. 2010 (Clinical study)

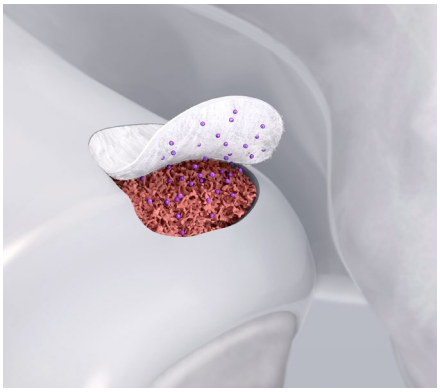
100+ PEER-REVIEWED AMIC® PUBLICATIONS*

We invest in evidence to win your confidence

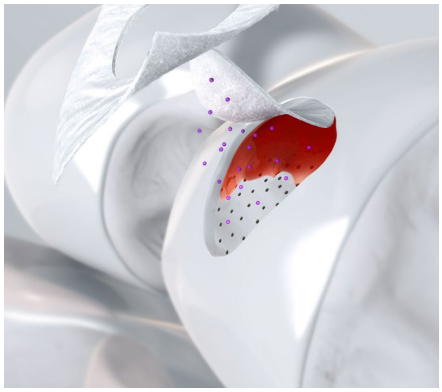
The application and outcomes using Chondro-Gide® in the treatment of knee, ankle joint, hip and MTP defects in 3671 patients were studied by

› 257 researchers
› 117 institutions in
› 12 countries

AMIC® and Chondro-Gide® have been included in national and international consensus recommendations[1,2,3,4].



The International Society on Cartilage Repair of the Ankle (ISCRA) defined the ideal size guidelines for bone marrow stimulation (BMS) as a diameter of < 10 mm, an area of < 100 mm², and a depth of < 5 mm. Bone grafting may already be considered for a depth of > 3 mm[5].



Matrix augmented BMS recommended for chondral and osteochondral defects 1 cm²–4.5 cm² by the DGOU in 2021[6].

Your choice – **AMIC® works**

› Knee
Ankle
Hip
Metatarsal

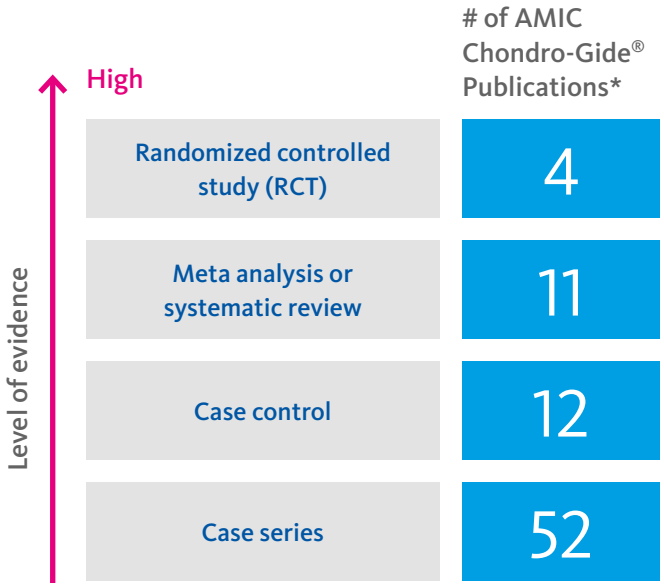
› Glue or suture
› Mini-open or arthroscopic
› Arthroscopic with or without AMIC® arthroscopic instruments

› AMIC® or AMIC®+ biological factors
› Bone marrow stimulation: MFx, drilling, removal of the calcified layer

1 Niemeyer et al. 2018 (Guidelines)
2 Aurich et al. 2017 (Guidelines)
3 Fickert et al. 2017 (Guidelines)
4 The International Society on Cartilage Repair of the Ankle (ISCRA) Consensus Meeting 2018 (Consensus meeting)
5 Hannon et al. 2018 (Consensus meeting)
6 Guideline announcement July 2021: https://youtu.be/nhPgL9otI7I

* You can download the full list here: Reference List Chondro-Gide®

LEVELS OF EVIDENCE



* Overview by Geistlich Pharma AG 2021
Download the list of publications here.

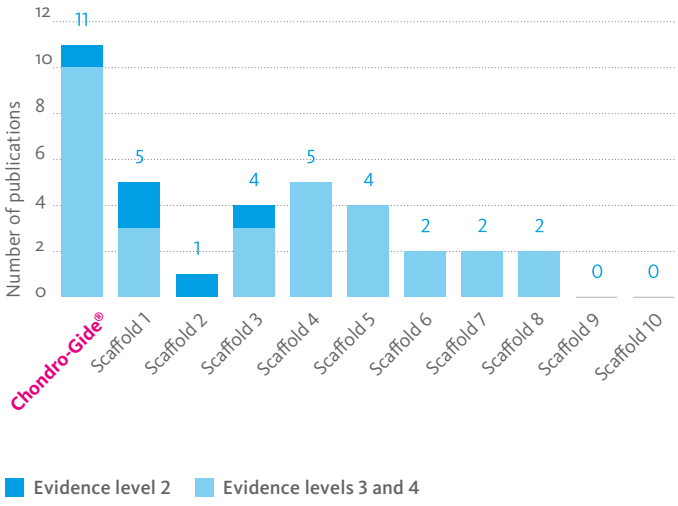
In 2018 the German Orthopaedic and Trauma Society (DGOU) Working Group on Tissue Regeneration released their consensus statement for cartilage treatment with matrix-augmented bone marrow stimulation. They compared 11 products and concluded that there was considerable variation in the quality of the studies about them (Fig. 1)[1]. Chondro-Gide® had the highest number of peer-reviewed publications and also higher level evidence such as randomized control trials.

Since 2018, 66 new peer reviewed papers on Chondro-Gide® were published in international journals, among them two meta-analyses on AMIC® in the knee and ankle joint.

In 2021 the DGOU announced an update of the consensus statement, with input from more than 30 cartilage experts. You can watch the announcement in German here[2].

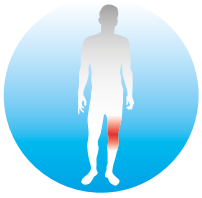
The new recommendations[2] include matrix augmented BMS for chondral and osteochondral defects ranging from 1 cm²–4.5 cm².

FIG. 1: OVERVIEW OF PRODUCTS AND NUMBER OF PUBLICATIONS PER PRODUCT[1]



1 Niemeyer et al. 2018 (Guidelines)
2 https://youtu.be/nhPgL9otI7I (Guideline announcement)

META ANALYSIS MEANS MEGA CONFIDENCE



AMIC® in the knee joint

The first meta-analysis of a one-step cartilage repair procedure in the knee using the Chondro-Gide® membrane demonstrated significant improvement in pain (VAS 4.8 points) and functional scores (Lysholm, and IKDC) compared to pre-operative values over a follow-up period of more than 3 years[1].

The meta-analysis identified 66 publications through systematic searches performed in the PubMed & Embase databases as well as in other sources using the search terms: "Chodro-Gide®", "AMIC®", "cartilage", and "knee". The following inclusion criteria were applied: clinical study with a minimum of 6 patients, cartilage defects in the knee, and primary endpoints of pain and function.

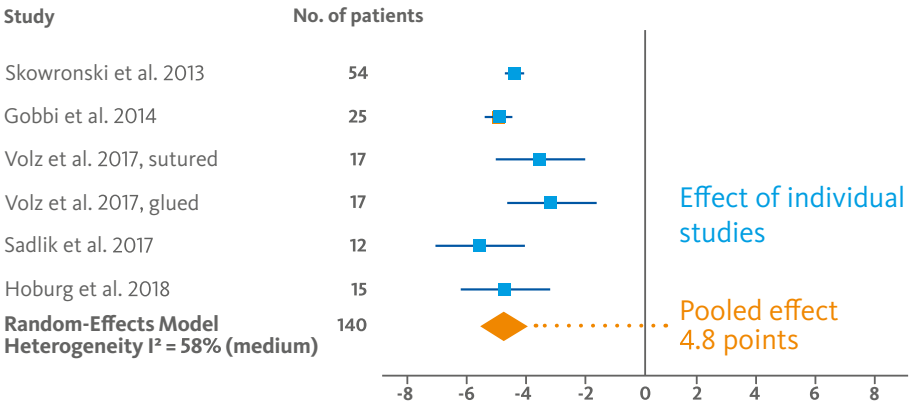
12 publications met the criteria.

These studies included **375** patients, **mean age: 36.2 years (14–70 years), with chondral and osteochondral defects Outerbridge Grade III & IV** with a minimum follow-up of 2 years.

The improvement was maintained for more than 5 years which confirms the longterm success of AMIC® Chondro-Gide® in the treatment of Outerbridge grade III & IV lesions with an average size of **4.2 cm²**.

Less than 1% (3/375) of the cases required conversion to arthroplasty.

FOREST PLOT FOR PAIN VAS AFTER > 3 YEARS



1 Steinwachs et al. 2019 (Meta-analysis)

AMIC® in the Ankle Joint

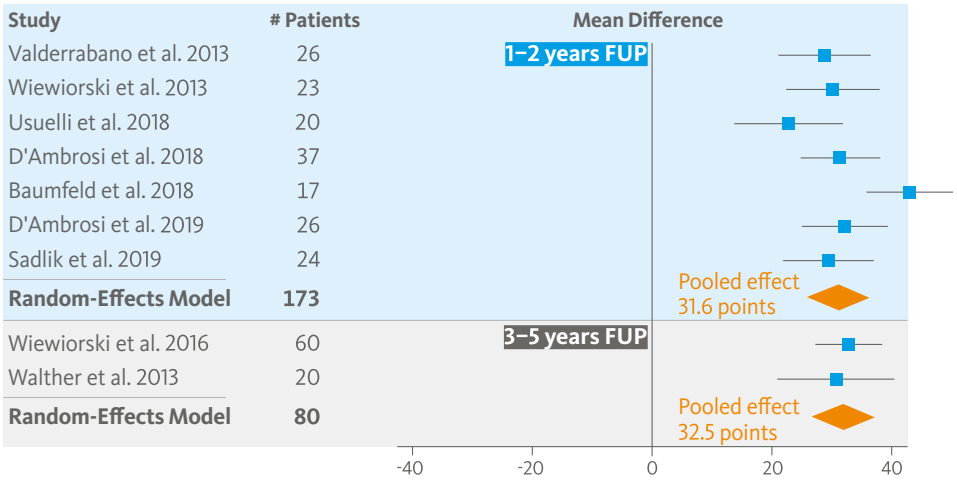
The first meta-analysis of pain and functional outcomes following AMIC® Chondro-Gide® treatment of osteochondral lesions of the talus (OCL) demonstrated significant improvement compared to the baseline.

The meta-analysis compared the pain VAS, the American Orthopedic Foot and Ankle Score (AOFAS), and the Foot Function Index (FFI) between baseline and follow-up of 1–2 and 3–5 years[1].

48 publications were identified in systematic searches in PubMed and Embase databases. Studies were included (PRISMA guidelines) if they had primary measures of clinical outcomes, a minimum of 1-year follow-up, and included more than 5 patients.

- Qualitative analysis: **15 studies** / **492 patients**
- Quantitative analysis: 12 studies / 323 patients
- Mean age: 36 (range, 12–68) years
- OCL size **1–2.4 cm²**
- Different surgical approaches and bone marrow stimulation techniques
- Mean follow-up: 33 (range, 12–60) months

IMPROVEMENT IN AOFAS COMPARED TO BASELINE



Improvement in joint function following AMIC

- From baseline to 1–2 year FUP, the forest plot shows a significant improvement in mean AOFAS of 31.6 points (light blue area).
- From baseline to 3–5 year FUP, significant improvement was observed for the mean AOFAS by 32.5 points (light grey area) and for the mean FFI by 31 points (not shown).

The AMIC® Chondro-Gide® procedure for treatment of OCL of the talus provided clinically relevant and significant improvement in ankle joint pain and functional outcome scores up to **5 years** after surgery.

None of the patients required conversion to ankle fusion or arthroplasty.

1 Walther et al. 2020

WE'VE GOT YOU COVERED

The Collagen Membrane: Chondro-Gide®

It's BI & BIO

BI is for BILAYER

Chondro-Gide® is a porcine bilayer Collagen I/III membrane. It has a unique structure, being compact and smooth on one side and rough and porous on the other[1].

BIO is for BIOCOMPATIBLE

The collagen bilayer is compatible with the tissues at the site of the defect[1].

BIO is for BIOFUNCTIONAL

The rough, porous layer faces the defect. Cells that are released through BMS techniques attach themselves to this layer, where they proliferate and support the growth of new tissue[1].

The compact top layer protects the cells and newly forming tissue from forces in the joint. It functions as the roof of a biological chamber that forms over the defect. Overall the 3D structure and material of the membrane provide a bio-functional environment that fosters cell growth and differentiation[1,2].

BIO is also for BIODEGRADABLE

The collagen membrane is naturally resorbed without any negative side-effects and is slowly replaced by the newly forming tissue[1].

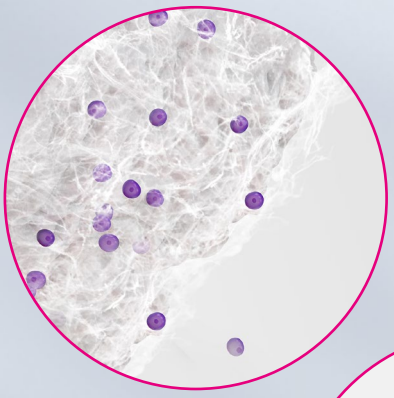
Don't lose your investment.

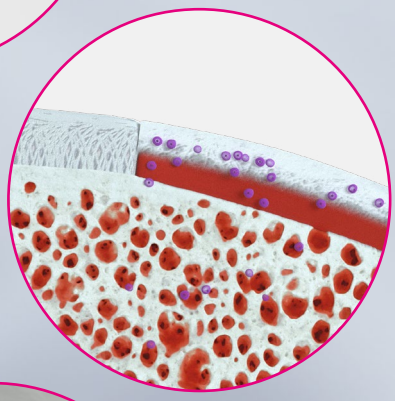
1 Geistlich Pharma AG data on file (Bench test)
2 Gille et al. 2010 (Pre-clinical study)

Chondro-Gide® is not approved for sale and usage in all countries or regions by the relevant authorities. Indications of use may also vary by country and region. Please contact your country representative of Geistlich Pharma AG for product availability and information.

Chondro-Gide® is VERSATILE

You can cut, wrap, pull, stretch and suture the membrane.[1]





CARRIER

Initially designed as a carrier for autologous chondrocyte implantation (ACI), Chondro-Gide® is an established product for cartilage therapies with >20 years of proven clinical use[1,2].

A recent tissue engineering study including Chondro-Gide ® is in BIO-CHIP, a Horizon2020 project that uses nasal chondrocytes cultured on Chondro-Gide® for cartilage regeneration[3,4].

COVER

Chondro-Gide® has been successfully used for over 15 years in AMIC®⁴ to cover cartilage defects[5,6]. Recent studies explore new approaches where AMIC® is augmented with additional cells (minced cartilage, adipose cells...) or bioactive components to enhance the regeneration process[7,8,9].

WRAP

The intended use of Chondro-Gide ® has been extended to augment meniscal repair by wrapping the membrane around the sutured meniscus[10,11,12]. The corresponding meniscus wrapping technique is registered as Arthroscopic Matrix based Meniscus Repair (AMMR®).

Gain function and time for your patients.

1 Geistlich Pharma AG data on file (Bench test)
2 Steinwachs 2008 (Clinical study)
3 Mumme et al. 2016 (Clinical study)
4 BIO-CHIP – researching a new regenerative therapy (biochip-h2020.eu)
5 Steinwachs et al. 2019 (Meta-analysis)
6 Walther et al. 2020 (Meta-analysis)
7 DeGirolamo et al. 2019 (Clinical study)
8 Gobbi et al. 2011 (Clinical study)
9 Gobbi et al. 2014 (Clinical study)
10 Steinwachs et al 2014 (Clinical study)
11 Sciaretta et al. 2017 (Clinical study)
12 Piontek et al 2012 (Clinical study)
13 Piontek et al. 2016 (Clinical study)
14 Ciemniewska-Gorzela et al. 2020 (Clinical study)

A VERSATILE METHOD

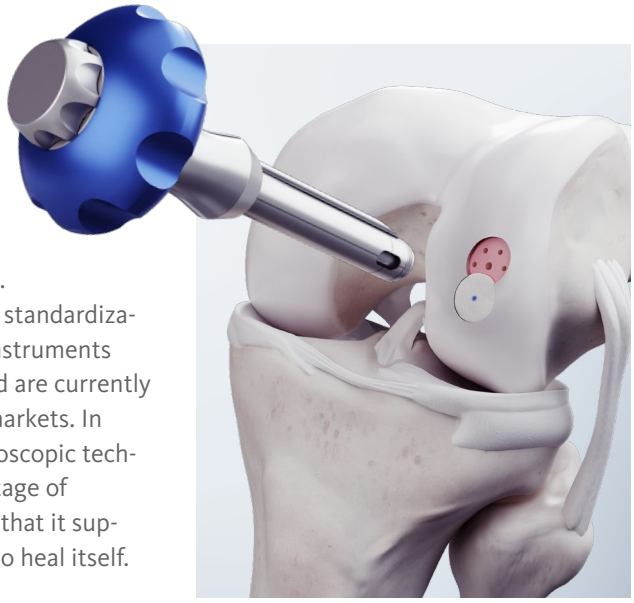
Mini-Open or arthroscopic? – AMIC® works

Arthroscopic technique is as equally positive as mini-arthrotomy with AMIC Chondro-Gide

In a retrospective study, Schagemann et al. compared the clinical outcomes of AMIC® Chondro-Gide® procedures that were performed as either arthroscopic or mini-open surgeries. The study followed patients for 2 years[1].

Both surgical approaches yielded equally positive results, according to the patients' Visual Analog Scale (VAS) pain scores, Lysholm scores, and Knee injury and Osteoarthritis Outcome Scores (KOOS).[1]

The arthroscopic approach can also be carried out with the help of the AMIC® Arthroscopic Instruments. These instruments offer a standardization of the process. The instruments were launched in 2021 and are currently available in selected EU markets. In both mini-open and arthroscopic techniques, the unique advantage of AMIC® Chondro-Gide® is that it supports the body's potential to heal itself.



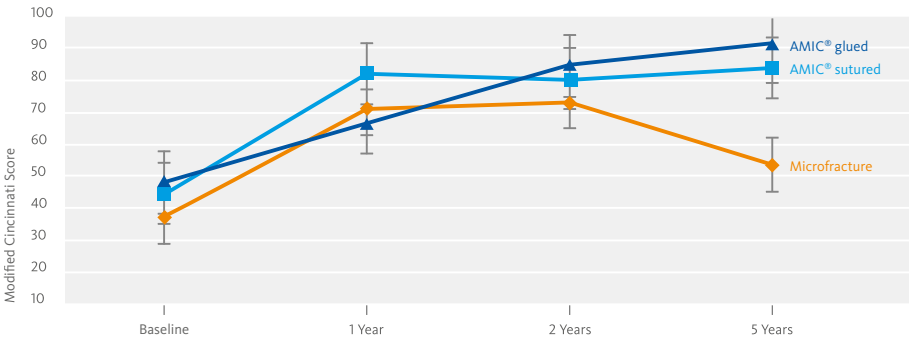
MFx or AMIC®? AMIC® Glue or suture? – Your choice

A multi-center, randomized, controlled 3-arm study by Volz et al. 2017 reported a significant deterioration in results after 2 years when microfracture (MFx) was used alone without Chondro-Gide®.

All treatment groups in the study showed significant improvement in the first year, followed by stabilization at 2 years, regardless of whether the membrane was glued or sutured[2].

At 5 years, however, results of the AMIC® Chondro-Gide® patients were markedly better than those from patients treated with MFx alone. Overall, the results of this study are consistent with observations from other published studies that show positive mid-to long-term clinical results for AMIC®, while clinical outcomes for patients treated with MFx alone show a decline in performance after 2 years.

FUNCTIONAL STATUS OVER TIME



1 Schagemann et al. 2018 (Clinical study)
2 Volz et al. 2017 (Clinical study)

AMIC® VS ACI

Chondro-Gide® was initially developed for Autologous Chondrocyte Implantation (ACI) and subsequently became the basis for the one-step treatment approach with AMIC®. The membrane is still successfully used in both approaches.
In view of regulatory hurdles and the need for cost-efficient cartilage treatments, AMIC® could provide the more efficient and economical choice according to a recent study by Fossum et al. 2019.

The group compared the outcomes of ACI covered with Chondro-Gide (ACI-C) and AMIC® in a randomized controlled clinical study (Level 2) for the treatment of chondral or osteochondral defects in the knee. Clinical outcomes at 2 years, showed no significant superiority of either ACI-C or AMIC®.

Both cartilage repair methods resulted in significant improvement of average KOOS and Lysholm scores as well as a significant reduction in pain VAS at 1- and 2-year follow-up, when compared to baseline values.

Fossum et al. 2019 concluded that if the results of the study can be confirmed after 5- and 10-year follow-up, AMIC® could be considered an equal alternative to techniques based on chondrocyte transplantation for treatment of knee cartilage defects.

AMIC®+

Combines current trends in cartilage regeneration with AMIC® regeneration therapy

The benefit of AMIC®, an established, successful cartilage repair technique is that it provides the foundation for attempting variation and inspiring new developments.

AMIC® is a biological procedure that combines bone marrow stimulation (BMS) with Chondro-Gide®, a collagen membrane. Here is a selection of approaches that are labeled as AMIC®+ because they combine BMS with additional biological components. The addition of some of the biological materials is subject to regulations, which vary from country to country. Further research and long-term results are needed to assess the clinical benefit of adding biological material (AMIC®+) beyond that produced in AMIC® approaches. Geistlich continues to support collaborations with regeneration experts and the exploration of new approaches in cartilage repair therapies.

AMIC+	Additional Biological Components	References
	Minced Cartilage (MC)	Massen et al. 2019 (Clinical study)
	MC + Platelet Rich Plasma (PRP)*	Steinwachs technique – see video. (Link to video)
	Bone Marrow Aspirate (BMA) or Bone Marrow Aspirate Concentrate (BMAC)	De Girolamo et al. 2019 (Clinical study); Gobbi et al. 2011 (Clinical study); Gobbi et al. 2014 (Clinical study)
	PRP	Dhollander 2010 (Clinical study); Richter et al. 2019 (Clinical study); Richter et al. 2020 (Clinical study)
	BMA + PRP	Steinwachs et al. 2014 (Clinical study)
	Lipoaspirate	Sciaretta et al. 2017 (Clinical study)

* There are several techniques available for preparing platelet concentrates; each method leads to a different product with different biological properties. See source for exact preparation.

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swiss made

COLLAGEN EXPERTS

Geistlich is a family owned Swiss company with a 160-year history of processing materials into a variety of different products.

Geistlich was among the first pharmaceutical companies to introduce collagen for medical use in the 1990s. We applied our extensive knowledge of collagen and its biofunctionality to develop the first collagen membrane to foster regeneration by providing a protective environment for cells and other factors that are essential for regrowth.

A recent endeavor in the orthoregeneration field is a EU funded Horizon2020 project «MEFISTO» for meniscus regeneration, where Geistlich contributes towards the development of a meniscus implant[1]. (MEFISTO – Driving meniscus health forward; mefisto-project.eu)

All in the family

As an integrated company Geistlich controls all steps of the product development, production and distribution from the material source to the surgeon's operating room.

MORE QUESTIONS?

For more information contact your local representative.

1 MEFISTO – Driving meniscus health forward (mefisto-project.eu); This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 814444

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