AUGMENT Injectable Surgical Technique Guide

November 2018

AUGMENT Injectable is a device/drug combination product for use in bone fusion of the foot/ankle.

AUGMENT Injectable is indicated for use as an alternative to autograft in arthrodesis (i.e., surgical fusion procedures) of the ankle (tibial/talar joint) and/or hindfoot (including subtalar, talonavicular, and calcaneocuboid joints, alone or in combination), due to osteoarthritis, post-traumatic arthritis, rheumatoid arthritis, psoriatic arthritis, avascular necrosis, joint instability, joint deformity, congenital defect, or joint arthropathy in patients with preoperative or intraoperative evidence indicating the need for supplemental graft material.

AUGMENT Injectable combines recombinant human platelet-derived growth factor B homodimer (rhPDGF-BB) with a bioreorbable composite matrix comprised of 80% beta tricalcium phosphate (β-TCP) in granule particulate form (nominal particle size 100-300μm) and 20% bovine Type I collagen. The rhPDGF-BB functions as a chemo-attractant and mitogen for cells involved in wound healing and through its promotion of angiogenesis at the site of healing. The β-TCP acts as a bone void filler and as a scaffold for new bone growth. When mixed at the time of surgery, the three components combine to create a flowable gel-like consistency that allows the surgeon to place the product at the fusion site, using a 14 gauge blunt tip needle attached to a 10 ml syringe (included).

KIT COMPONENTS
• The components of AUGMENT Injectable are provided as two sterile secondary packaging configurations:
  • The matrix secondary packaging (tray or pouch) contains a 10 ml polypropylene syringe containing either 0.5 or 1.0 grams of a milled β-TCP/bovine Type I collagen (ratio=4:1) matrix. Also included are an empty polypropylene syringe, one 14 gauge blunt tip needle for administration of the combination product, one 18 gauge needle (to draw up the rhPDGF-BB from the vial), and female/female luer connector for mixing of the two components. The package is sterilized by gamma irradiation.
  • The vial tray contains one vial, dependent on the kit configuration, of aseptically filled with either 1.5 ml or 3.0 ml of rhPDGF-BB solution (0.3mg/ml). The vial tray is sterilized by ethylene oxide.

STERILITY
• The contents within each kit are supplied sterile and are for single use only
• The contents of the kit are sterile until the expiration date printed on the package and must be used before this date.
• The kit is not to be used in the event that any of kit seals are breached. Notify your sales representative or BioMimetic Therapeutics, LLC directly.
• The sterile β-TCP/collagen syringe is contained within a sterile secondary package (tray or pouch).
• The rhPDGF-BB vial is contained in a sterile tray.
• Both the sterile β-TCP/collagen syringe and the rhPDGF-BB vial can be handled in the sterile field.
• AUGMENT Injectable cannot be reused, and components of AUGMENT Injectable must not be re-sterilized by any method.

PREPARATION NOTES
• Familiarization with the device and its handling properties, proper sterile surgical grafting techniques, and thorough surgical preparation of the host bone surfaces intended for arthrodesis and all associated bony defects are extremely important when using AUGMENT Injectable.

AUGMENT INJECTABLE PREPARATION
1. Completely withdraw the contents of the vial containing the rhPDGF-BB solution using the empty syringe and the 18 gauge needle. After all of the fluid has been extracted from the vial, remove the needle and dispense any air remaining in the syringe.
2. Remove the cap from the syringe containing the β-TCP/collagen matrix.
3. Pull the plunger to the 10 ml mark and tap the syringe to loosen the matrix.
4. Connect the syringe containing the rhPDGF-BB solution with the syringe containing the matrix using the female-to-female luer-lock connector.
5. Transfer the rhPDGF-BB solution into the syringe containing the matrix. After transferring all of the rhPDGF-BB solution, pull the plunger on the syringe containing the hydrated matrix past the 10 ml mark.

Note: The liquid is infused into the dry matrix, allowed to soak for at least 90 seconds, and then forced back and forth three times.

AUGMENT Injectable is then prepared by completely saturating the β-TCP/collagen matrix with the rhPDGF-BB solution, as shown in the following diagram:

Shredded Matrix is shipped in one syringe. rhPDGF-BB and Matrix are drawn into a second syringe.

6. Release the plunger of the syringe containing the hydrated matrix. Let the syringes sit undisturbed for a minimum of 90 seconds.
7. AUGMENT Injectable is then prepared by completely saturating the β-TCP/collagen matrix with the rhPDGF-BB solution, as shown in the following diagram:

Shredded Matrix is shipped in one syringe. rhPDGF-BB and Matrix are drawn into a second syringe.

8. After hydrating the matrix, transfer the contents back and forth between the two syringes for no less than (20) twenty cycles. Note: A cycle is defined as passing the matrix to the empty syringe and back. Upon completion, the matrix should form a homogenous paste.
9. Transfer all of the paste to one of the syringes, and relieve any pressure built up during the mixing process by gently pulling the plunger containing the matrix.
10. Disconnect the empty syringe and female-to-female luer-lock connector from the syringe that contains the paste. Displace any air remaining in the syringe and connect the 14 gauge blunt needle. The syringe is now ready to dispense the hydrated matrix into the surgical void as described below in the “Recommended Surgical Technique” section.

RECOMMENDED SURGICAL TECHNIQUE

NOTE: Always complete proper surgical preparation of all host articular surfaces intended for arthrodesis prior to implanting any graft material to these sites.

Preparation of the Joint
1. In standard fashion for arthrodesis surgery, debride and denude all articular surfaces by exposing viable host bone and decorticating these surfaces. This will maximize an osteous healing response. Following exposure of the joint(s) intended for arthrodesis, all remaining cartilage should be removed. The opposing bony surfaces should be adequately prepared to optimize the osteous healing response and allow apposition of healthy, vascularized bone.

Preparation of the Bone Interface
2. Debridement
Debridement should be performed by feathering and/or perforating the subchondral plate of all exposed articular surfaces intended for arthrodesis. This can be accomplished by using any standard technique and preferred combination of curettes, drills, burr, drill bits, and/or osteotomes as a means of maximizing the surface area of exposed bleeding bone (see below 2A and 2B).

2A. Perforation
Some surgeons may prefer to perforate the cortical bone with drilling prior to placement of the AUGMENT Injectable material. Drilling of the bone surface helps to create a bleeding bone environment to promote fusion.

2B. Feathering
Alternatively, other surgeons may choose to create subchondral exposure by using a burr, osteotome and/or curette to roughen and “feather” the joint surface to maximize the surface area of bleeding bone. It does not matter which method is chosen (2A or 2B), as long as one of these two joint preparation techniques is employed subsequent to denuding all remaining joint cartilage and prior to implantation of any AUGMENT Injectable.

Tip: In more severe deformities, portions of the talar head may need to be resected to reduce the deformity and create a good bone-on-bone interface.
Application of the Graft to the Implant Site

3. Using the prepared syringe (see AUGMENT® Injectable Preparation section, above), dispense the hydrated matrix into the void. Note: It may require an initial force to get the paste to flow through the 14 gauge needle. However, once the paste starts to flow, the force required to maintain a flow will be reduced.

4. Carefully apply the hydrated matrix to the surgical site (i.e. the subchondral voids, and surface irregularities visualized throughout the entire joint) such that the graft material is in contact with the entire osseous surfaces to be fused/repaired while allowing rigid fixation and primary bone contact to occur between the osseous surfaces. Immediately after joint reduction and hardware fixation of the fusion site, any remaining (unused) AUGMENT® Injectable should be applied around the external perimeter of the fusion construct.
   - Because AUGMENT® Injectable does not harden or “set”, standard hardware implantation to ensure rigid fixation is necessary.
   - In order to enhance the formation of new bone, AUGMENT® Injectable should be placed in direct contact with well-vascularized bone. Cortical bone may be perforated prior to placement of the AUGMENT® Injectable material.

Remember: It is important to ensure that all bony defects are grafted. Adequate graft fill is needed to optimize results with any grafting material.

5. Once AUGMENT® Injectable has been applied to the defect site, carefully layer periosteal and overlying soft tissue to enclose and contain the graft material.

6. Care should be taken not to irrigate the graft site following implantation of AUGMENT® Injectable.
   - To guard against ectopic bone formation, take care to prevent AUGMENT® Injectable extrusion beyond the desired fusion regions, especially during hardware placement and joint reduction.

7. Any remaining graft material should be discarded.

Fixation of the Joint

8. Reduce the joint and apply rigid fixation.

Closure of the Site

9. Following reduction and fixation, perform a carefully layered periosteal and capsular closure with the overlying soft tissues to enclose and contain all graft material in its intended joint space(s). Employ standard surgical technique to complete any remaining portion of the procedure.

10. Apply the self-adhesive labels that indicate the lot number of each device to the patient’s permanent records and discard any remaining AUGMENT® Injectable.

Please see the AUGMENT® Injectable Package Insert for information regarding contraindications, warnings, precautions and storage instructions.
The safety and effectiveness of repeat applications of rhPDGF-BB in patients with end-stage osteoarthritis of the knee (OSA) undergoing arthroplasty for knee pain may be misguiding.

Women of childbearing potential should avoid pregnancy during the period of rhPDGF-BB treatment.

is a prisoner, known or suspected transient or a history of drug/alcohol abuse within the 12 months prior to screening.

Subject evaluation consisted of a series of clinical and radiographic assessments. These were collected at up to 21 days pre-op (if available for all assessments at 52 weeks. For the autograft group, the 52 week follow up rate for all assessments was 91.0%.

The primary effectiveness endpoint was defined as the percent of subjects achieving fusion (FFI) and radiographic (x-rays with secondary assessments using CT scans to demonstrate presence of fusion) endpoints for structural graft.

The presence of a milled chain. rhPDGF-BB supports angiogenesis by upregulating vascular endothelial growth factor formation and facilitates bone growth by stimulating osteoinductive activity. The product is intended to be used as an osteoconductive scaffold to promote bone formation and to support the in-growth or angiogenesis of bone from the host bone.

It is not known if any component of AUGMENT™ Injectable may impair wound healing, particularly in the presence of infection. Potential for bleeding complications are: e.g. endocrine-induced bone disease, renal disease, neoplastic disease, immunosuppressive therapy, anticoagulant therapy, e.g. platelet aggregation, or aspirin therapy. Subjects who tested positive or had a known hypersensitivity to any of the components of the product or the yeast used in the production of rhPDGF-BB should not receive AUGMENT™ Injectable.

The summary of adverse events by MedDRA class through 52 weeks follow-up is presented in Table 1. Variable AE definitions were utilized by the study sites. The assessment of whether or not an event constituted an AE was made by the investigators, for example, radiologic measurements or laboratory parameter changes were not considered AEs unless associated with symptoms or changes in patient status.

The criteria for fusion success were based on the independent radiographic review of bone formation (fusion) across the treated joints. Greater than 90% bone on the baseline CT scan was the criterion for fusion. Fusion was defined as a minimum of 50% bone formation across the treated joints at the 24 weeks post-op visit.

The safety and effectiveness of rhPDGF-BB was assessed in the pivotal Phase III randomized, controlled clinical trials (BMTI-2006-01 and BMTI-2009-01) and the investigational study (BMTI-2010-01) as compared with targeted autograft control.

Subjects were also monitored over the course of the study for the loss of reduction, infection, non-union, need for additional procedures, any serious AEs possibly related to treatment, and any serious AEs possibly related to device. Safety and effectiveness results were measured in the randomized groups and compared with those in the autograft control group.

Table 1: Study Withdrawals Pre-randomization

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The safety and effectiveness of AUGMENT Injectable in patients with an active infection at the operative site.

The two sub-assemblies are consisting of different components – a two-part matrix and a recombinant human platelet derived growth factor-BB (rhPDGF-BB) -TCP component. The matrix combines with the bone.

The stratum corium is processed until an acid soluble slurry is produced. At this point the collagen is combined with the TCP granules and rhPDGF-BB.

Injectable are provided as two sterile secondary packaging configurations: a combination product bone graft material consisting of multiple components – a two-part matrix with pre-fracture neuromuscular or musculoskeletal deficiency which limits ability to perform objective functional measurements and may be at risk for complications. For the purpose of this protocol, diabetics not sensitive to insulin are included.

The stratum corium is processed until an acid soluble slurry is produced. At this point the collagen is combined with the TCP granules and rhPDGF-BB.

The following clinical and radiographic evaluations were performed:

- Subject evaluation consisted of a series of clinical and radiographic assessments. These were collected at up to 21 days pre-op (if applicable), 7-21 days post-op and at 6, 12 and 24 weeks post-op for all subjects.

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The stratum corium is processed until an acid soluble slurry is produced. At this point the collagen is combined with the
removal of calcium. The collagen complies with ASTM F2212 (human cancellous bone). The granules have a nominal diameter of 100-300μm. Injectable is identical to the rhPDGF-BB contained in AUGMENT® Injectable.

Injectable should only be used by surgeons who are familiar with the product. The sponsor defined a series of primary and secondary effectiveness and safety endpoints that consisted of clinical and radiographic assessments. Safety was assessed by comparing the type and rate of adverse events (AEs) between the investigational AUGMENT Injectable graft material from the surrounding tissue. AEs were classified as serious or non-serious, and were tracked by type and severity. The assay for anti-rhPDGF-BB or anti-bovine Type I collagen antibodies was tested for neutralizing activity. Subjects who tested positive for anti-rhPDGF-BB or anti-bovine Type I collagen antibodies were tested for neutralizing activity. Subjects who tested positive for anti-rhPDGF-BB or anti-bovine Type I collagen antibodies were tested for neutralizing activity. The sponsor defined a series of primary and secondary radiographic and clinical effectiveness endpoints.

Subject evaluation consisted of a series of clinical and radiographic assessments. These were collected at up to 21 days pre-op (if available) and up to 21 days post-op then annually until the last subject enrolled had returned for their 104 week evaluation. Serum was collected at baseline (prior to grafting procedure), the 7-21 day post-op visit and at 6, 12, 24, 36, 52 and 104 weeks post-op. Serum was assessed for the presence of neutralizing antibodies. The data from the control population of this study were used to supplement the control population data from the clinical study that evaluated AUGMENT® Injectable. The study encompassed triple arthrodesis (subtalar, talonavicular and calcaneocuboid joints) OR double fusions (talonavicular and calcaneocuboid joints). Subject evaluation consisted of a series of clinical and radiographic assessments. These were collected at up to 21 days pre-op (if available) and up to 21 days post-op then annually until the last subject enrolled had returned for their 104 week evaluation. Serum was collected at baseline (prior to grafting procedure), the 7-21 day post-op visit and at 6, 12, 24, 36, 52 and 104 weeks post-op. Serum was assessed for the presence of neutralizing antibodies. The data from the control population of this study were used to supplement the control population data from the clinical study that evaluated AUGMENT® Injectable. The study encompassed triple arthrodesis (subtalar, talonavicular and calcaneocuboid joints) OR double fusions (talonavicular and calcaneocuboid joints).

The sponsor defined a series of primary and secondary radiographic and clinical effectiveness endpoints.

- Clinical (pain using a Visual Analog Scale (VAS) and function using the Foot Function Index (FFI)) at 6, 12, 24, 36, 52 and 104 weeks post-op.
- Time to radiographic healing as determined by the independent radiologist.
- Fusion site pain (via VAS) at 24 weeks.
- Subject determined to have union or progressive evidence of healing (as per the Investigator assessment).
- Quality of life assessments included SF-12, AOFAS Outcomes Scores (Ankle-Hindfoot Scale) and the Foot Function Index (FFI) at 6, 12, 24, 36, 52 and 104 weeks.

The sample size calculation was based on the primary endpoint, a comparison of the clinical and radiographic outcomes at 24 weeks. The study included 132 patients, 66 in the AUGMENT Injectable group and 66 in the autograft bone control group. The primary endpoint was evaluated using Fisher's exact test for categorical variables, and two-sample t-test for continuous variables.

Safety endpoints included:
- Incidence of infections
- Incidence of bone non-unions
- Incidence of other complications
- Incidence of serious complications
- Incidence of other medically important events

Serious Complications:
- Any event that resulted in persistent or significant disability/incapacity
- Death
- Life-threatening event
- Required hospitalization or prolongation of existing hospitalization
- Required use of any life-saving intervention that was not a surgical procedure for an accident or drug effect
- A medical event or condition that required medical or surgical intervention to prevent one of the outcomes listed above

Other medically important events that in the opinion of the investigator may have jeopardized the patient or may have

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AUGMENT® INJECTABLE PACKAGE INSERT

II only

October 2018

1. PRODUCT DESCRIPTION

1.1. Component Components

AUGMENT Injectable Package contains Bone Graft and AUGMENT Injectable in a single carton. The AUGMENT Injectable contains: 1) a Collagen Bone Graft Substitute (CGB) bone matrix and 2) a TCP/collagen mixture. The AUGMENT Injectable Package also contains an empty 10ml syringe which is utilized during the procedure. Consequently, the AUGMENT Injectable Package is intended to be used separately.

1.2. Device Components

The device consists of a container containing the Bone Graft and AUGMENT Injectable, a 10ml polypropylene syringe and polypropylene needle syringe, and a tip cap. Use a new device for subsequent applications.

1.3. Purpose

The safety and effectiveness of AUGMENT Injectable has been established in adult patients. The device is intended to stimulate bone formation following surgical procedures, including, but not limited to fusions of the ankle (tibiotalar joint) and/or hindfoot (including subtalar, talonavicular, calcaneocuboid) or any other joints.

2. CONTRAINDICATIONS

2.1. Use AUGMENT Injectable in physically or mentally compromised, non-cooperative, non-compliant, or withdrawn patients.

2.2. Use AUGMENT Injectable in patients requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

2.3. Use AUGMENT Injectable in patients who should not use AUGMENT Injectable (e.g., patients who are allergic to yeast-derived products or bovine collagen or other bovine-sourced products).

3. PRECAUTIONS

3.1. Use AUGMENT Injectable in subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

3.2. Use AUGMENT Injectable in subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

3.3. Use AUGMENT Injectable in subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

3.4. Use AUGMENT Injectable in subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

4. ADVERSE REACTIONS

4.1. The matrix secondary packaging (tray or pouch) contains a 10ml polypropylene syringe containing the Bone Graft for Surgical Implants and Substrates for Medical Purposes. The Bone Graft for Surgical Implants and Substrates for Medical Purposes is indicated for use in converting porcine tissues to human tissues. The Bone Graft for Surgical Implants and Substrates for Medical Purposes is derived from the connective tissues of the pig. The Bone Graft for Surgical Implants and Substrates for Medical Purposes is a human and veterinary diagnostic product.

4.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

4.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

4.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

4.5. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

5. CLINICAL STUDIES

5.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

5.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

5.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

5.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

6. INDICATIONS

6.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

6.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

6.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

6.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

7. PATIENTS' INSTRUCTIONS

7.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

7.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

7.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

7.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

8. SAFETY AND EFFECTIVENESS

8.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

8.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

8.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

8.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

9. SUPPORTING STUDIES

9.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

9.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

9.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

9.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

10. PATIENTS' INFORMATION

10.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

10.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

10.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

10.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

11. PATIENT SAFETY

11.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

11.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

11.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

11.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

12. SUMMARY OF QUALITATIVE AND QUANTITATIVE RESULTS

Table 1: Summary of Quantitative and Qualitative Results

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Event Category</th>
<th>Event</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

13. REFERENCES

13.1. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

13.2. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

13.3. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)

13.4. Subjects requiring less than 3 cc of graft material substantially benefit by two intermolecular disulfide bonds at Cys 25 (12.9%)
## Table 1: Foot Function Index*

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>22.1 (9.3)</td>
<td>23.3 (10.0)</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>19.5 (9.1)</td>
<td>21.3 (10.1)</td>
<td>0.23</td>
</tr>
<tr>
<td>24</td>
<td>16.5 (9.1)</td>
<td>18.6 (11.1)</td>
<td>0.25</td>
</tr>
<tr>
<td>36</td>
<td>14.0 (7.4)</td>
<td>16.4 (10.0)</td>
<td>0.32</td>
</tr>
<tr>
<td>52</td>
<td>11.0 (6.4)</td>
<td>12.8 (9.4)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).

## Table 2: Secondary Surgical Interventions

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>0%</td>
<td>0%</td>
<td>0.23</td>
</tr>
<tr>
<td>24</td>
<td>0%</td>
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<td>0.25</td>
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<tr>
<td>36</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>52</td>
<td>0%</td>
<td>0%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).

## Table 3: Upper Extremity Injury (klas) Number

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>0%</td>
<td>0%</td>
<td>0.23</td>
</tr>
<tr>
<td>24</td>
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<td>0%</td>
<td>0.25</td>
</tr>
<tr>
<td>36</td>
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<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>52</td>
<td>0%</td>
<td>0%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).

## Table 4: Lower Extremity Femur Fracture (klas) Number

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>0%</td>
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<td>0.23</td>
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<tr>
<td>24</td>
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<td>0.25</td>
</tr>
<tr>
<td>36</td>
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<td>0%</td>
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</tr>
<tr>
<td>52</td>
<td>0%</td>
<td>0%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).

## Table 5: Lower Extremity Femur Fracture (klas) Number

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>0%</td>
<td>0%</td>
<td>0.23</td>
</tr>
<tr>
<td>24</td>
<td>0%</td>
<td>0%</td>
<td>0.25</td>
</tr>
<tr>
<td>36</td>
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<td>0%</td>
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</tr>
<tr>
<td>52</td>
<td>0%</td>
<td>0%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).

## Table 6: Lower Extremity Femur Fracture (klas) Number

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>0%</td>
<td>0%</td>
<td>0.23</td>
</tr>
<tr>
<td>24</td>
<td>0%</td>
<td>0%</td>
<td>0.25</td>
</tr>
<tr>
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</tr>
<tr>
<td>52</td>
<td>0%</td>
<td>0%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).

## Table 7: Lower Extremity Femur Fracture (klas) Number

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>0%</td>
<td>0%</td>
<td>0.23</td>
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<tr>
<td>24</td>
<td>0%</td>
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<tr>
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<td>0.32</td>
</tr>
<tr>
<td>52</td>
<td>0%</td>
<td>0%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).

## Table 8: Lower Extremity Femur Fracture (klas) Number

<table>
<thead>
<tr>
<th>Week</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>0.32</td>
</tr>
<tr>
<td>12</td>
<td>0%</td>
<td>0%</td>
<td>0.23</td>
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<td>24</td>
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<tr>
<td>52</td>
<td>0%</td>
<td>0%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are based on generalized linear model with factors: baseline value, treatment (AUGMENT Injectable vs autograft) and week. The values of x and n represent the observed data without adjustment. Actual success rates are computed based on a logistic regression with factors treatment (AUGMENT Injectable minus autograft) between the means and the confidence limit should be greater than the negative of the desired delta. In this case, the desired delta is 10.3 (95% confidence interval 0.8-7.4) in the becaplermin treated group receiving 3 or more tubes of REGRANEX Gel had a statistically significant increased rate of mortality, i.e., a 5.2 fold greater rate, secondary to malignancy, for the comparators. Adjusted for several possible confounders, the rate ratio was 1.2 (95% confidence interval 0.7-1.9).
### Table 1: Surgical Procedures of Concern During Baseline

<table>
<thead>
<tr>
<th>Procedure</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>Non-Union</th>
<th>Deep vein thrombosis</th>
<th>Renal and urinary tract infection</th>
<th>Psychiatric disorders</th>
<th>Tooth abscess</th>
<th>Connective tissue reaction</th>
<th>Sepsis</th>
<th>Wound infection</th>
<th>Device related infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Union</td>
<td>22.9%</td>
<td>10.7%</td>
<td>2.3%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connective tissue reaction</td>
<td>13.6%</td>
<td>3.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound infection</td>
<td>1.3%</td>
<td>0.2%</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Device related infection</td>
<td>1.9%</td>
<td>1.2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Sepsis</td>
<td>0.8%</td>
<td>0.2%</td>
<td></td>
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</tbody>
</table>

### Table 2: Average Change in Foot Function Score and Pain (mm) at 52 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>12.4 ± 1.2</td>
<td>16.3 ± 1.2</td>
</tr>
</tbody>
</table>

### Table 3: Safety Discussion

The study results showed that AUGMENT Injectable had non-inferiority of AIBG relative to autograft at all time points. The effectiveness measurements for AUGMENT Injectable vs autograft and propensity score quintiles to adjust for possible confounding factors. In the pharmacovigilance mechanism, patient outcomes are not actively researched.

### Table 4: Safety of AUGMENT Injectable

- **Non-Union**: 22.9% of AUGMENT Injectable vs 10.7% of autograft
- **Connective tissue reaction**: 13.6% of AUGMENT Injectable vs 3.8% of autograft
- **Wound infection**: 1.3% of AUGMENT Injectable vs 0.2% of autograft
- **Device related infection**: 1.9% of AUGMENT Injectable vs 1.2% of autograft
- **Sepsis**: 0.8% of AUGMENT Injectable vs 0.2% of autograft
- **Tooth abscess**: 0.55% of AUGMENT Injectable vs 0.60% of autograft
- **Psychiatric disorders**: 0.67% of AUGMENT Injectable vs 1.6% of autograft
- **Renal and urinary tract infection**: 0.85% of AUGMENT Injectable vs 2.1% of autograft

### Table 5: Effectiveness of AUGMENT Injectable

- **Pain Reduction**: 12.4 ± 1.2 at 52 weeks
- **Foot Function Index**: 16.3 ± 1.2 at 52 weeks

### Table 6: Average Change in Foot Function Score and Pain (mm) at 24 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>11.8 ± 1.0</td>
<td>15.7 ± 1.0</td>
</tr>
</tbody>
</table>

### Table 7: Average Change in Foot Function Score and Pain (mm) at 36 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>11.2 ± 1.1</td>
<td>15.1 ± 1.1</td>
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</tbody>
</table>

### Table 8: Average Change in Foot Function Score and Pain (mm) at 52 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>12.4 ± 1.2</td>
<td>16.3 ± 1.2</td>
</tr>
</tbody>
</table>

### Table 9: Average Change in Foot Function Score and Pain (mm) at 97 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>97</td>
<td>12.0 ± 1.0</td>
<td>16.0 ± 1.0</td>
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</tbody>
</table>

### Table 10: Average Change in Foot Function Score and Pain (mm) at 108 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>108</td>
<td>11.6 ± 1.1</td>
<td>15.6 ± 1.1</td>
</tr>
</tbody>
</table>

### Table 11: Average Change in Foot Function Score and Pain (mm) at 122 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>122</td>
<td>11.2 ± 1.0</td>
<td>15.2 ± 1.0</td>
</tr>
</tbody>
</table>

### Table 12: Average Change in Foot Function Score and Pain (mm) at 97 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>97</td>
<td>12.0 ± 1.0</td>
<td>16.0 ± 1.0</td>
</tr>
</tbody>
</table>

### Table 13: Average Change in Foot Function Score and Pain (mm) at 108 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>108</td>
<td>11.6 ± 1.1</td>
<td>15.6 ± 1.1</td>
</tr>
</tbody>
</table>

### Table 14: Average Change in Foot Function Score and Pain (mm) at 122 Weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Pain Reduction (via VAS)</th>
<th>Foot Function Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>122</td>
<td>11.2 ± 1.0</td>
<td>15.2 ± 1.0</td>
</tr>
</tbody>
</table>
Table 12: Odds Ratio Estimates for Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism and mediastinal bleeding</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 13: Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis</td>
<td>1.8%</td>
<td>2.1 (0.8, 5.6)</td>
<td>0.158</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>1.2%</td>
<td>0.89 (0.65, 1.2)</td>
<td>0.497</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 14: Osteoarthritis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>5%</td>
<td>1.2 (0.7, 2.1)</td>
<td>0.497</td>
</tr>
<tr>
<td>Other distant</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other adjacent</td>
<td>3%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 15: Fusion Site Pain

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fusion site pain</td>
<td>5%</td>
<td>1.2 (0.7, 2.1)</td>
<td>0.497</td>
</tr>
<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures adjacent</td>
<td>3%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 16: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures adjacent</td>
<td>3%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 17: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures adjacent</td>
<td>3%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 18: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures adjacent</td>
<td>3%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 19: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures adjacent</td>
<td>3%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 20: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures adjacent</td>
<td>3%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 21: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
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<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
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<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 22: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
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<th>p-Value</th>
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</thead>
<tbody>
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<tr>
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<td>0.363</td>
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Table 23: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
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<tbody>
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<tr>
<td>Other procedures</td>
<td>2%</td>
<td>1.5%</td>
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</tr>
<tr>
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<td>0.363</td>
</tr>
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Table 24: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
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</thead>
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<td>0.363</td>
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<tr>
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<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
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<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 25: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
<th>Odds Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
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<td>1.5%</td>
<td>0.363</td>
</tr>
<tr>
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<td>0.363</td>
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<td>1.5%</td>
<td>0.363</td>
</tr>
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</table>

Table 26: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
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<th>p-Value</th>
</tr>
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<tbody>
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</tr>
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Table 27: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
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</thead>
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<td>0.363</td>
</tr>
</tbody>
</table>

Table 28: Table 10 Subsequent Analyses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate</th>
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<th>p-Value</th>
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<td>0.363</td>
</tr>
<tr>
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<td>1.5%</td>
<td>0.363</td>
</tr>
</tbody>
</table>
A summary of the subsequent secondary surgical interventions recorded through the 52 week post-op follow-up period is presented in Table 1. The incidence of surgical procedures was balanced across treatment groups. The most common procedures included wound debridement and wound closure, skin grafting, and fasciotomy.

### Secondary Surgical Interventions

<table>
<thead>
<tr>
<th>Procedure</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound debridement</td>
<td>12 (9.1%)</td>
<td>12 (7.7%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Wound closure</td>
<td>9 (6.9%)</td>
<td>10 (6.1%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Skin grafting</td>
<td>5 (3.8%)</td>
<td>6 (3.7%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Fasciotomy</td>
<td>3 (2.3%)</td>
<td>4 (2.4%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Surgical Procedures

- Wound debridement
- Wound closure
- Skin grafting
- Fasciotomy

### Table 1: Secondary Surgical Interventions

<table>
<thead>
<tr>
<th>Procedure</th>
<th>AUGMENT Injectable</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0.99</td>
</tr>
<tr>
<td>Fasciotomy</td>
<td>3 (2.3%)</td>
<td>4 (2.4%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>