

From Research to Reality:

**Practical Perspectives on
Advanced Wound Healing
with Intact Fish Skin**

Supported by an educational grant from Kerecis

Faculty

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Faculty Disclosures

- **Cyaandi R. Dove, DPM**
Advisory Board, Consultant: MediWound Ltd.; **Consultant:** Alira; **Speakers Bureau:** Advanced Oxygen Therapy Inc.; Engineered Tissue Solutions
- **Caroline Fife, MD**
Executive Director of US Wound Registry (USWR), a 501(c)(3) non-profit organization recognized by CMS as a Qualified Clinical Data Registry (QCDR) – uncompensated position. No conflicts in relation to this activity.
- **John C. Lantis II, MD, FACS**
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Grant/Research Support: Biotissue; MediWound Ltd.; Organogenesis Inc.; Polarity TE

Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration)
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Learning Objectives

- Investigate the role of clinical evidence in shaping the proposed LCD changes, highlighting how data and research inform policy decisions
- Examine the clinical evidence supporting the use of intact fish skin grafts in wound healing and tissue regeneration
- Summarize key findings from the largest RCT focused on complex diabetic foot ulcers (DFUs) with exposed bone, tendon, or joint capsule, emphasizing the implications for clinical practice

Randomized, Controlled Trials, Coverage Policy, and the Real World

Caroline Fife, MD

Chief Medical Officer, Intellicure, LLC

The Woodlands, TX

Study Type in Local Coverage Determination (LCD) Evidence Review for DFUs (by product)

RCT = prospective randomized, controlled trial (12-16 wks)

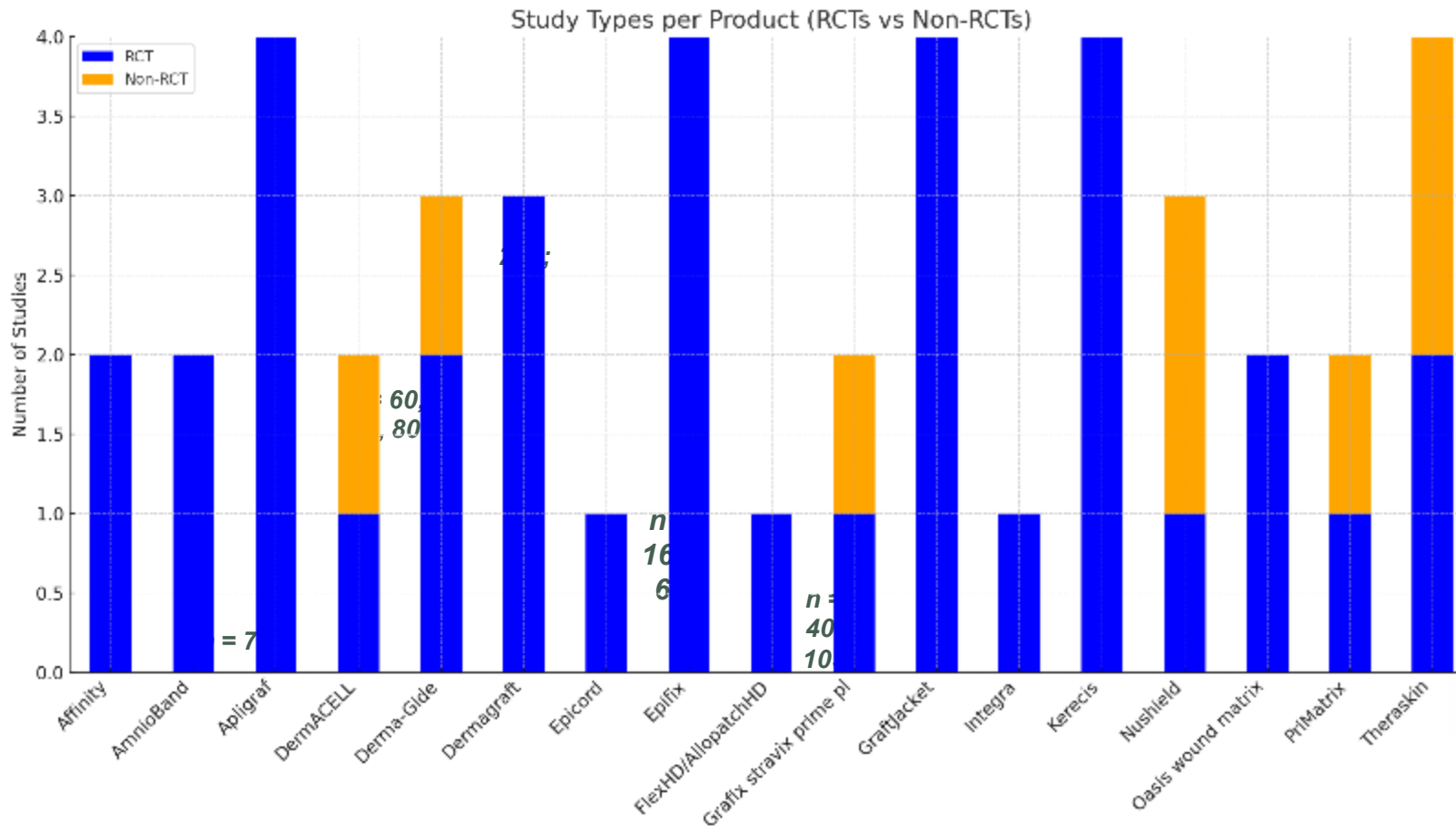


Table 3: Evidence for Non-Covered Products

Skin Substitutes (Per sq cm unless otherwise stated)	Evidence (Published, peer reviewed literature to support use in chronic DFUs/VLU)
	No literature found
	No literature found
	No literature found
	Evidence in breast surgery and hernia repair
	No literature found
	Evidence in burn and orthopedics
	Literature in hand, foot, forearm, ankle, spine, neck, and torso
	Small RCT ¹⁰⁰
	No literature found
	No literature found
	No literature found
	Case report ¹⁰⁰
	No literature found
	No literature found
	No literature found
	No literature found
	Retrospective comparative study of 47 wounds ¹⁰⁰ , case series ¹⁰⁰
	No literature found
	No literature found

Product names redacted

No literature found

Evidence and Coverage Policy

- The Medicare Administrative Contractors (MACs) appear to have required at least 1 prospective RCT to include a product in the “covered” list for the Diabetic Foot Ulcer (DFU) and Venous Leg Ulcer (VLU) LCD(s)
- Unfortunately, most CTP/CAMP prospective RCTs are highly non-generalizable
 - Most enroll only superficial ulcers
 - Most exclude patients with serious comorbid disease
- Why are non-generalizable trials a problem?
 - They provide evidence of “efficacy” in a perfect world, BUT
- They have little relevance to actual patients (ie, we know nothing about real-world EFFECTIVENESS from them)



The happy land of RCTs.

Comorbid Disease in Real-World Patients with DFU, VLU

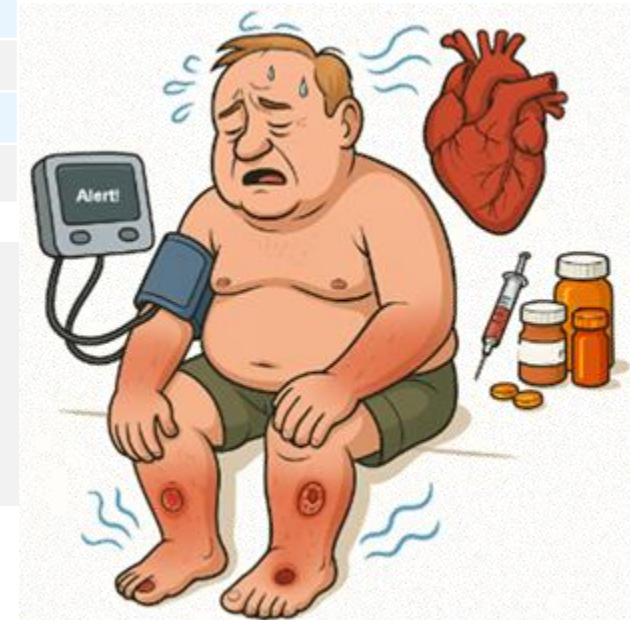
Patients with DFUs

Rank	Comorbidity	% of DFU Pts
1	Diabetes	10,966 (100.0)
2	Hypertension	7,964 (72.6)
3	Obesity	6,469 (59.0)
4	Edema	4,059 (37.0)
5	Peripheral Arterial Disease	3,817 (34.8)
6	Osteomyelitis	2,837 (25.9)
7	Hyperlipidemia	5,323 (48.5)
8	Venous insufficiency	2,130 (19.4)
9	Cellulitis	1,839 (16.8)
10	Autoimmune Disease	1,762 (16.1)
11	Neuropathy	1,762 (16.1)

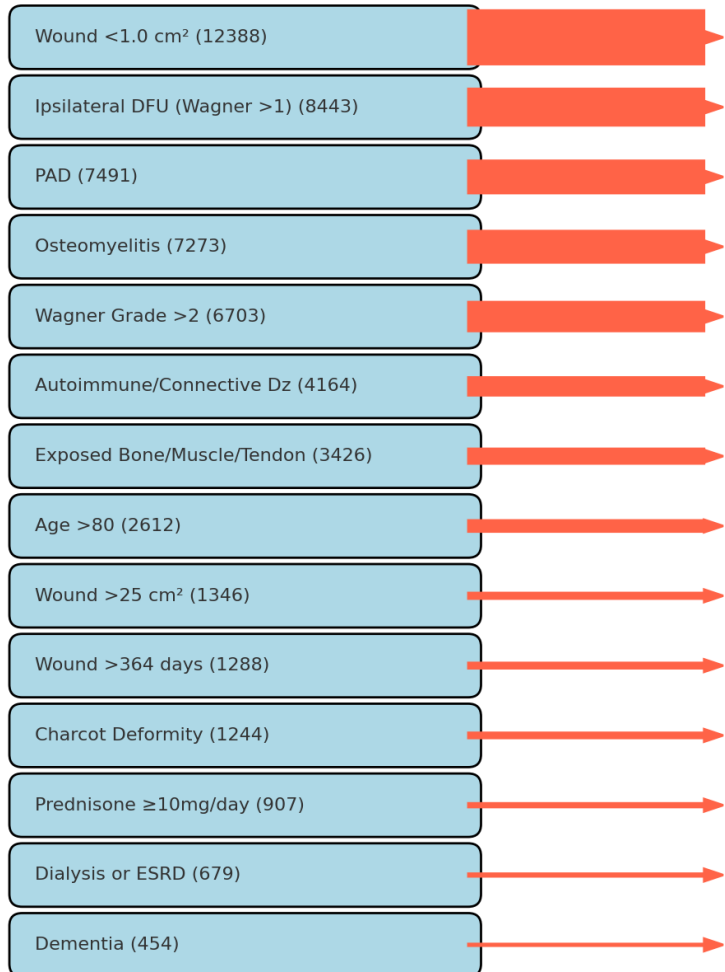
Patients with VLUs

Rank	Comorbidity	% of VLU Pts
1	Edema	8,757 (78.2)
2	Venous insufficiency	7,367 (65.8)
3	Hypertension	7,159 (63.9)
4	Obesity	7,150 (63.0)
5	Diabetes	4,850 (43.3)
6	Lymphedema	2,702 (24.1)
7	Cellulitis	2,252 (20.1)
8	Peripheral Arterial Disease	2,471 (22.1)
9	Hyperlipidemia	3,972 (35.5)
10	Congestive Heart Failure	1,535 (13.7)
11	Autoimmune Disease	1,533 (13.7)

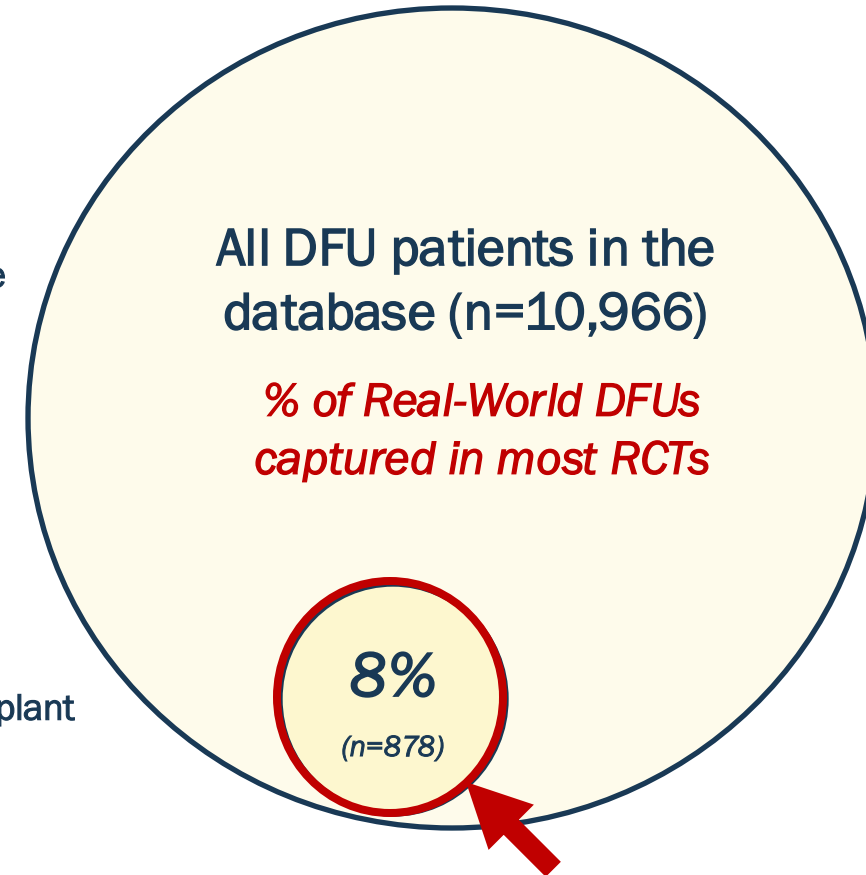
- Of the top 30 medications taken by patients with DFUs, 80% were in the top 30 taken by patients with VLUs
- 43% of patients with VLUs have diabetes
- Autoimmune disease is present in 16% of patients with DFUs and 13.7% of patients with VLUs



Non-Generalizability of Prospective RCTs for DFUs



- No tendon, muscle, joint capsule exposed
- Venous stasis for DFU trial
- Alcohol/drug abuse
- Anticoagulant treatment
- Cellulitis or local wound infection
- Cancer or recent cancer treatment
- Collagen vascular disease/connective tissue disease
- Rheumatoid arthritis/autoimmune disease any type
- Scleroderma/lupus, any autoimmune disease
- Charcot foot changes in DFU
- Corticosteroid treatment any reason
- Deep venous thrombosis/pulmonary embolus
- Gastrointestinal disease any kind/any liver disease/hepatitis
- Renal impairment/ESRD/renal dialysis/renal transplant
- Any organ transplant
- In diabetics, HbA1c >8-10
- Nutritional impairment/albumin <3.0 mg/dl
- Osteomyelitis
- Peripheral arterial disease/ischemia



DFU patients eligible for participation in most RCTs

Real DFU Patients Are Sicker, and DFUs Are Worse than Subjects in Most RCTs

- Consortium of 6 wound clinics performing clinical research
 - Compared actual patients seen to patients enrolled in CTP trials
 - 244 DFU subjects enrolled in 4 RCTs vs 2,634 DFUs seen in same clinics
- Real patients differed from RCT subjects
 - **12.2% had renal failure** (excluded from all RCTs)
 - **4.3 DFUs per patient** (not 1 DFU per patient as in typical trial)
 - **43.6% had Wagner 3 or worse ulcers** (RCTs enrolled Wagner 1, 2)
 - **Initial DFU surface area was 3x larger than ulcers in the RCTs**
- Estimated mean Wagner Healing Index (WHI) of real DFUs is much worse, meaning they are less likely to heal than an RCT ulcer (68.6 vs 88.1)



PERSPECTIVE ARTICLE

A new approach to clinical research: Integrating clinical care, quality reporting, and research using a wound care network-based learning healthcare system

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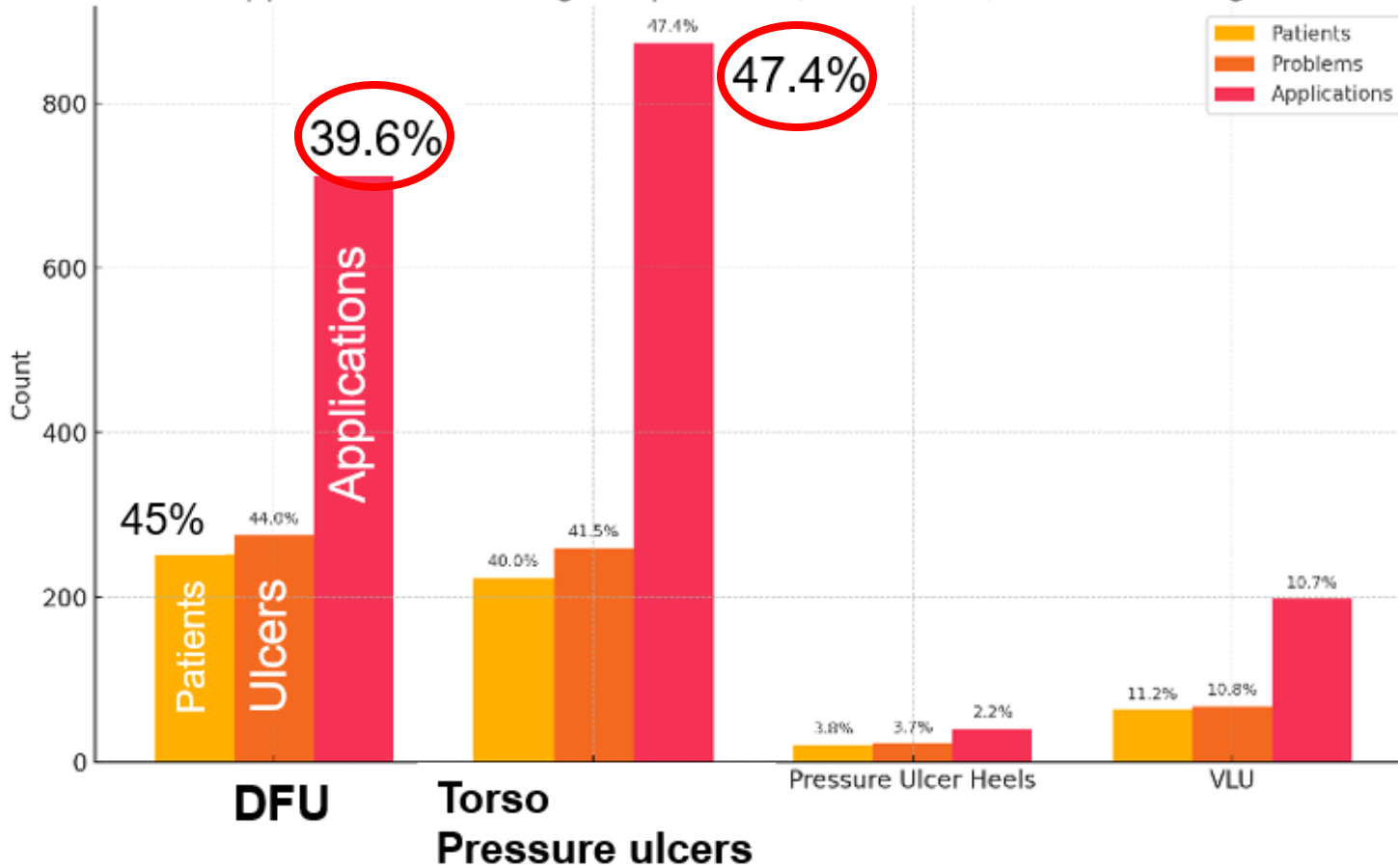
DOI:10.1111/wrr.12538

ABSTRACT

The disparity between ideal evidence from randomized controlled trials and real-world evidence in medical research has prompted the United States Food and Drug Administration to consider the use of real-world data to better understand safety and effectiveness of new devices for a broader patient population and to prioritize real-world data in regulatory decision making. As the healthcare system transitions from volume- to value-based care, there is a growing need to harness the power of real-world data to change the paradigm for wound care clinical research and enable more generalizable clinical trials. This paper describes the implementation of a network-based learning healthcare system by a for-profit consortium of wound care clinics that integrates wound care management, quality improvement, and comparative effectiveness research, by harnessing structured real-world data within a purpose-built electronic health record at the point of care. Centers participating in the consortium submit their clinical data and quality measures to a qualified clinical data registry for wound care, enabling benchmarking of their data across this national network. The common definitional framework of the purpose-built electronic health record and the 21 wound-specific quality measures help to standardize the potential sources of bias in real-world data, making the consortium data useful for comparative effectiveness research. This consortium can transform wound care clinical research and raise the standards of care, while helping physicians achieve success with the Merit-Based Incentive Payment System.

Real-World Use of All CTPs/CAMPs Applications Involving Deep Tissue (2020–2024)

Applications Involving Deep Tissue (2020–2024) with Percentages



(unpublished data, USWR, 2025)

“Deep Tissue” = muscle, tendon, bone

Problem Type	Patients	Ulcers	Applications
DFU	252	276	729
Pressure Ulcer Torso	224	260	874
Pressure Ulcer Heels	21	23	41
VLU	63	68	198
Total	554	627	1,842

Data from Jan 1, 2020 – Dec. 31, 2024

Depth of Tissue Exposed in DFUs Treated with Intact Fish Skin (n=104)

Tissue Exposed	Problems	Percentage
Partial thickness	18	17.3%
Subcutaneous	44	42.3%
Adipose	1	0.9%
Muscle	11	10.5%
Tendon	2	1.9%
Bone	15	14.4%
Unknown	52	0.5%
TOTAL	104	100%

} **26.8%**

In the real world, more severe ulcers are treated than in a clinical trial.

Depth of Tissue Exposed in VLUs Treated with Intact Fish Skin (n=122)

Tissue Exposed	Problems	Percentage	
Partial thickness	24	14.29%	
Subcutaneous	73	43.45%	
Adipose	1	0.60%	
Fascia	1	0.60%	} 9% Are these VLUs?
Muscle	8	4.76%	
Tendon	1	0.60%	
Bone	1	0.60%	
Unknown	59	35.12%	
TOTAL	122	72.62%	

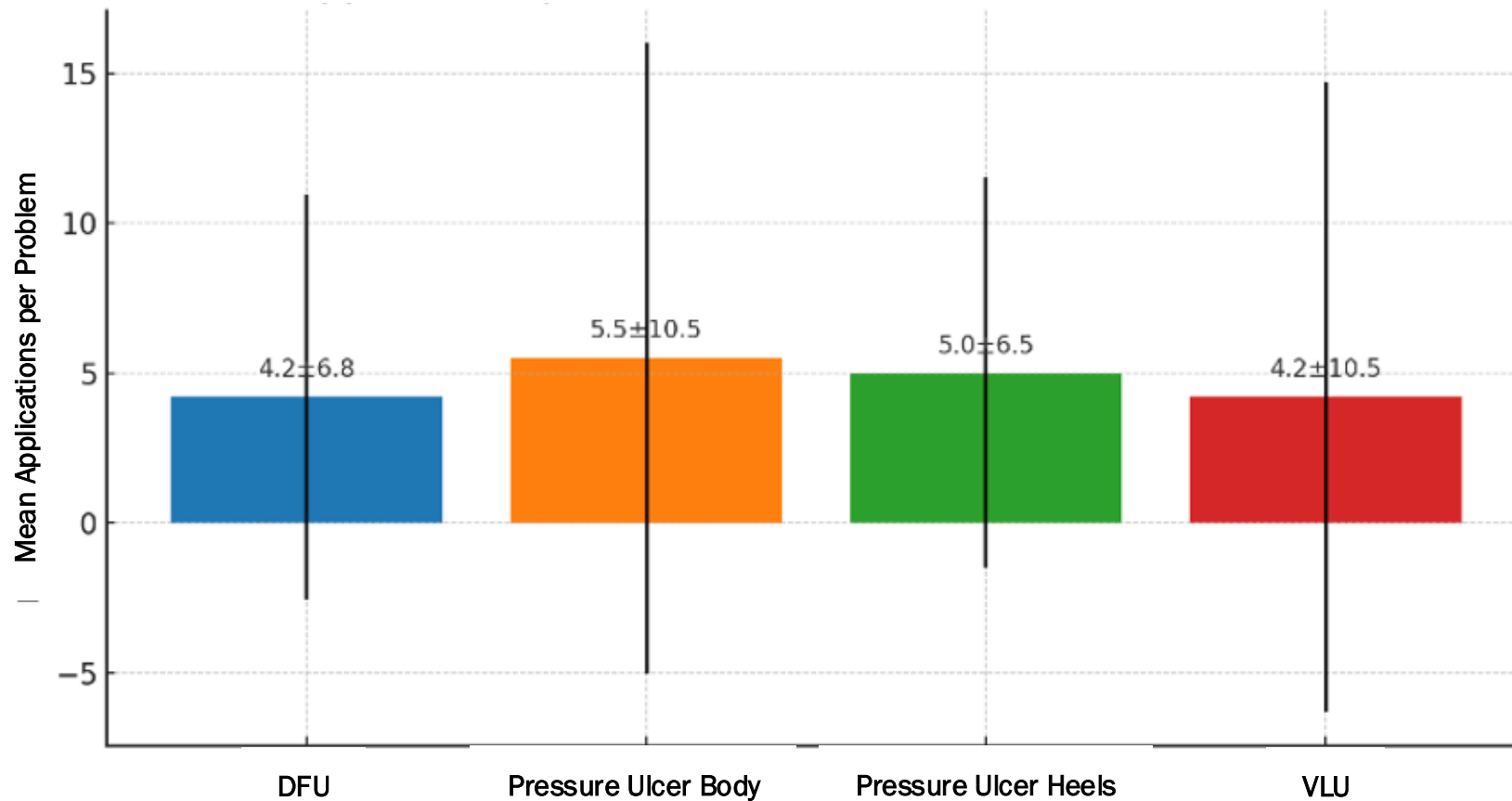
Intact Fish Skin in Pressure Ulcers Treated with Intact Fish Skin (n=68 Ulcers)

Stage	Count	Percentage
NPIAP Stage II	9	13.2%
NPIAP Stage III	24	35.3%
NPIAP Stage IV	30	44.1%
Unstageable	4	5.9%
DTI	1	1.5%
TOTAL	68	100.00%

Real-World Use of All CTPs/CAMPs

Mean Applications per Ulcer

Applications per Problem (Mean \pm Estimated Std Dev)



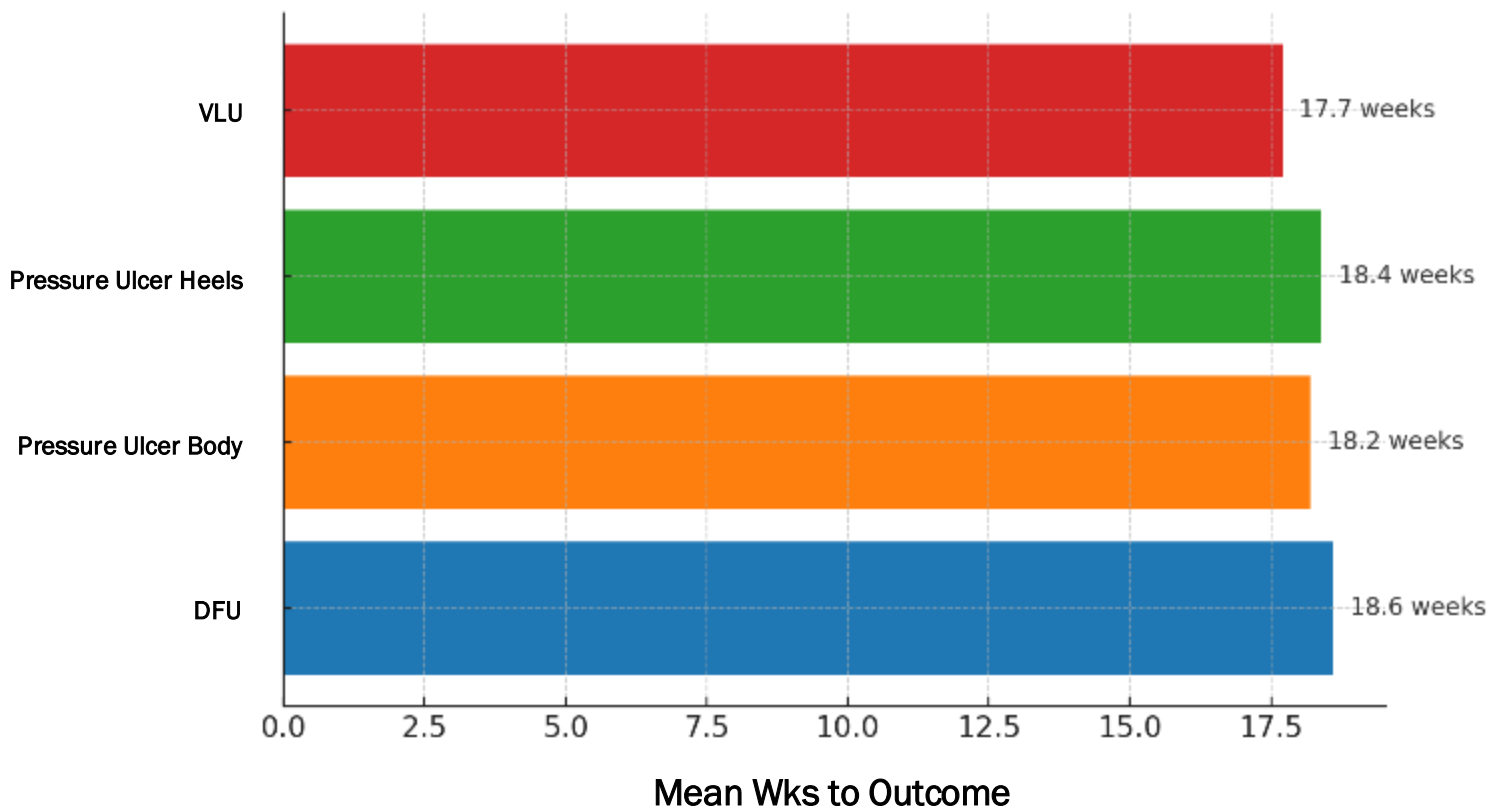
The mean is <5 but look at the standard deviation!

Problem Type	Min	Max	Mean
DFU	1.0	28.0	4.2
Pressure Ulcer Body	1.0	43.0	5.5
Pressure Ulcer Heels	1.0	27.0	5.0
VLU	1.0	43.0	4.2
Total	1.0	43.0	4.5

Data from Jan 1, 2020 – Dec. 31, 2024

Mean Weeks to Outcome by Ulcer Type (After Initial CTP/CAMP Application)

Mean Wks to Outcome by Problem Type



The mean is not far from the “episode of care,” but some ulcers will remain unhealed for months after the final application.

Problem Type	Min	Max	Mean
DFU	0.9	185.0	18.6
Pressure Ulcer Body	0.1	158.9	18.2
Pressure Ulcer Heels	1.0	126.0	18.4
VLU	1.0	205.0	17.7
Total	0.1	205.0	18.1

Data from Jan. 1, 2020 – Dec. 31, 2024

Death and Major Amputation Rates by Ulcer Type Among Real-World Ulcers Treated with CTPs/CAMPs



2%-3% of (all) chronic ulcer patients treated with CTPs/CAMPs die in treatment

What Can We Learn from the Real World?

- Most CTP/CAMP RCTs are relatively healthy patients with superficial ulcers, which is not representative of real-world patients/ulcers
- Most real-world patients have complex comorbid diseases
- A high percentage of real-world ulcers that get CTPs/CAMPs expose deep tissue
- Serious complications (eg, major amputation, death) are surprisingly common among real-world patients who get CTPs/CAMPs
- What we need are prospective studies that are more generalizable to the real world (both to understand clinical effectiveness and to inform coverage policy)
 - Sicker patients
 - More serious ulcers



Intact Fish Skin in High-Risk Wounds

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Director of Clinical Research, UT Health San Antonio

San Antonio, TX

Objectives

- 1) The importance of biologics in limb salvage in real-world scenarios
- 2) Optimal selection of biologics in a resource-challenged setting
- 3) Proactive, not reactive, use of intact fish in at-risk patient populations



Building on the Evidence

Dr. Fife showed us the critical gap between clinical trial populations and real-world patients.

Dr. Lantis demonstrated that fish skin grafts succeed in challenging, comorbid patients—where it matters most.

Now, let's talk about how we put this evidence into practice to drive remission, mobility, and survival.

I. The Importance of Biologics: Our Real-World Patients

Patients with chronic
DFUs post amputation

Individuals in safety-
net hospitals, VAs, IHS,
or rural health centers

Disproportionate
burden among racial
minorities



Biologics in the Real World: Who Are Our Patients?

Typical Patient Profile

Poor perfusion (PAD/CLI)

Chronic kidney disease

Limited mobility

Poor adherence to offloading

The Importance of Biologics: High Stakes

What Matters Most?

- Closure
- Durability
- Remission



Real-World Use of Biologics: Preventing an Unfortunate Series of Events

Initial Procedure

- Transmetatarsal amputation (TMA)
- Partial calcaneotomy

Downstream Consequences

- 25%-40% of TMAs lead to proximal amputation
- Loss of mobility
- Loss of independence

Biologics in RWS — The Clock is Ticking

Critical Turning Point

30%–50% of TMA patients may require additional revision surgery

Biologics in RWS: Major Foot Amputations

Are we following our own protocols?

- Fife CE, Carter MJ, Walker D, Thomson B, Eckert KA. Diabetic foot ulcer offloading: the gap between evidence and practice. *Adv Skin Wound Care*. 2014;27(7):310-316.

The Importance of Biologics in RWS: Calcanectomy

Functional and Emotional Toll

- Limited mobility, loss of independence
- Higher rates of depression and caregiver strain
- **Healing drives remission**
- Supports long-term limb stability and quality of life



Early Use of Biologics Can Shift the Trajectory of Healing

- Act early with effective biologics
 - Remission, coupled with durability and functionality
 - Tettelbach, et al
 - Optimal use of debridement coupled with adj. use of skin substitutes significantly improves outcomes
 - Can lower the use of healthcare resources
 - Medicare data analysis shows that wound care providers have not applied skin substitutes early enough

Why Intact Fish Skin? The Pace and Durability of Healing Matter

- Acellular, natural scaffold with native ECM
- Preserved molecular content reduces inflammation
- Supports cell migration and angiogenesis
- No need for special storage or rehydration



Evidence Check-In

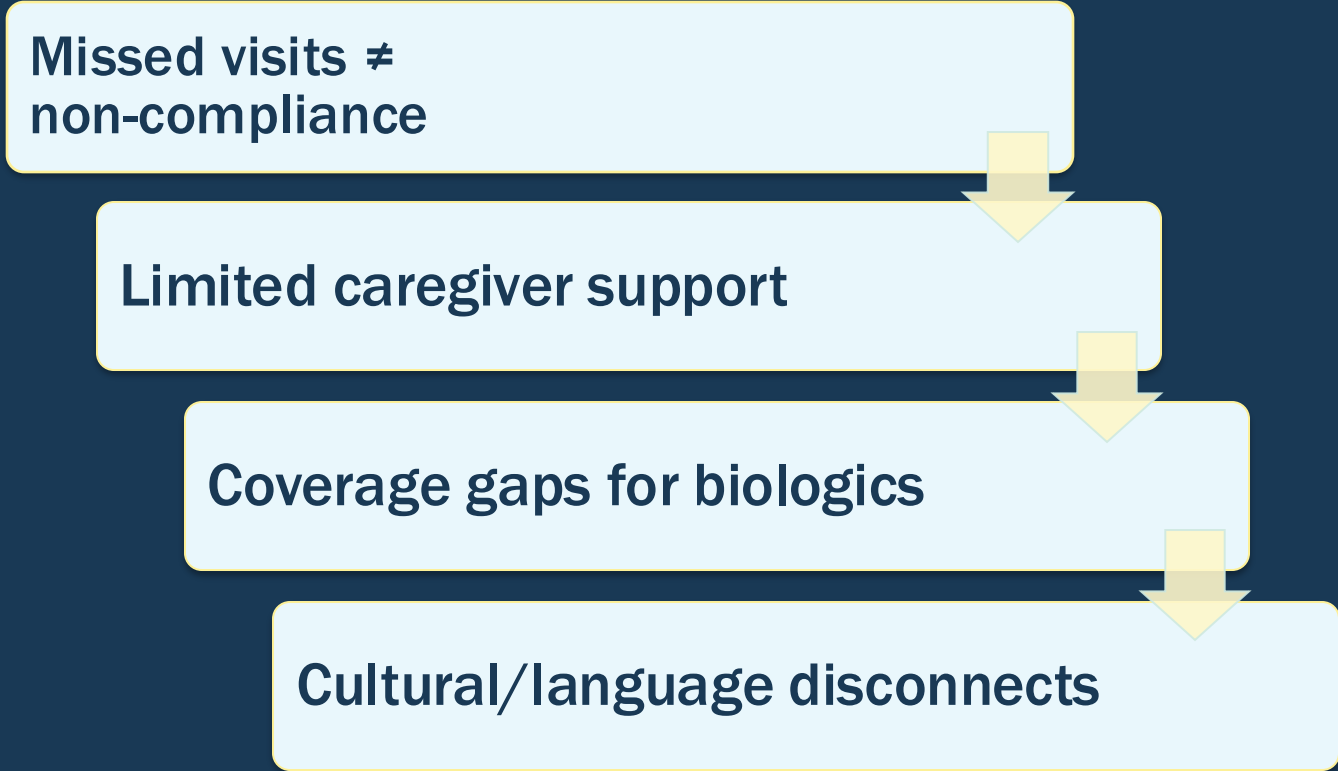
- What evidence do we have?
 - There is a need for more inclusive trials that reflect our actual patient populations

Importance of Biologics

- ODINN trial
 - Difficult truly real-world patients
 - 44% of UT Grade 2/3 patients healed at 16 wks
 - Findings can be translated directly into clinical practice

II. Optimal Selection of Biologics RWS: Resource-Challenged Settings

Missed visits \neq
non-compliance



```
graph TD; A[Missed visits ≠ non-compliance] --> B[Limited caregiver support]; B --> C[Coverage gaps for biologics]; C --> D[Cultural/language disconnects]
```

Limited caregiver support

Coverage gaps for biologics

Cultural/language disconnects

Selecting the Best Biologic: Practical, Real-World Determinants

Healing beyond the wound bed

- 1 application can be billed with standard CPT codes
- Less dependence on complex wound care center infrastructure
- Easy to store, apply, and teach in remote or resource-limited settings





Integration of Biologics Into a Healthcare Practice: High-Tech Lab

Practical Integration In Clinics

- Easily integrate into routine clinic workflows
- No refrigeration/specialty devices
- Avoid secondary costs of refrigeration
- Suited to a spectrum of healthcare settings
- Learning curve is not steep

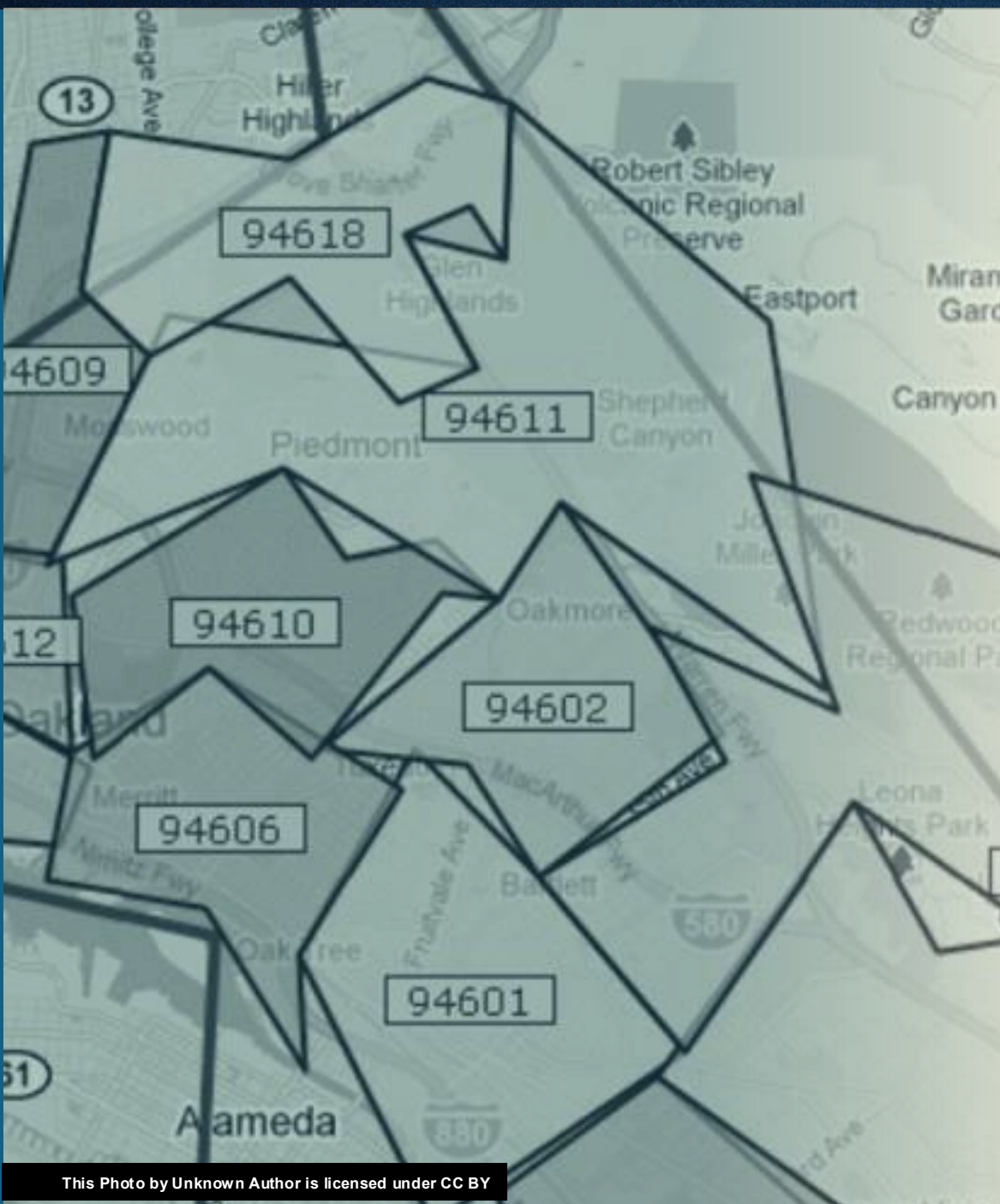
**III. Proactive,
Not Reactive,
Use of Biologics**

IT IS ABOUT ACCESS

Geography

Race

Comorbidities



III. Structural Barriers to Limb Preservation

Black and Hispanic patients are 2-4x more likely to undergo lower extremity amputation than White patients

Creager MA, et al. 2021 – AHA Scientific Statement




III. Structural Barriers to Limb Preservation

These disparities persist even after adjusting for comorbidities like diabetes and PAD.


Zip code matters — geography, poverty, and healthcare access strongly influence outcomes.

III. Proactive, Not Reactive, Use of Intact Fish Skin in RWS: Disproportionate Amputation Rates Identified

Delayed referral to vascular specialists or limb preservation teams



Fewer advanced therapies (eg, revascularization, grafts) offered to minority patients



Limited access to post-acute care, durable offloading, and wound surveillance

Key Factors for Using Intact Fish Skin Graft

Speed and durability

Adaptability to multiple settings

Biologics are SOC, not rescue therapy

From Evidence to Action: Key Principles

1

Act Early: Proactive use of biologics changes outcomes.

2

Simplify Access: Choose solutions that fit resource-challenged clinics.

3

Address Disparities: Recognize and dismantle barriers to limb salvage.

4

Save Lives, Not Just Limbs: Limb preservation is a public health mandate.

**Limb Salvage
Is a Mandate**

**Saving limbs.
Saving lives.
Acting now.**

The Odinn Trial

“The trial you asked for!”

John C. Lantis II, MD, FACS

Site Chief, Professor of Surgery

Mount Sinai West Hospital and Icahn School of Medicine

New York City, NY

So, This Is What You Wanted!

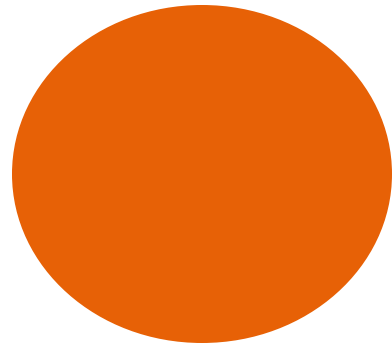
- Renal dysfunction (not on HD)
- Big wounds
- Deep wounds
- >75 % visits in the community
- Closer to the real world!!!!!!

ORIGINAL ARTICLE | SYMPOSIUM ON ADVANCED WOUND CARE

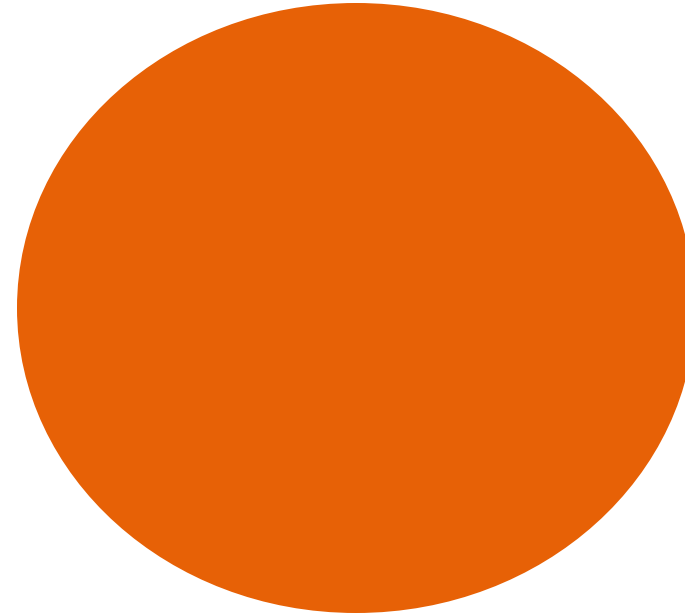
Intact Fish Skin Graft to Treat Deep Diabetic Foot Ulcers

Dured Dardari, M.D, Ph.D.,^{1,2} Alberto Piaggese, M.D.,³ Louis Potier, M.D.,^{4,5} Ariane Sultan, M.D.,^{6,7} Holger Diener, M.D.,⁸ Maude Francois, M.D.,⁹ Bernhard Dorweiler, M.D.,¹⁰ Benjamin Bouillet, M.D.,^{11,12} Jocelyne M'Bemba, M.D.,¹³ Lucy Chaillous, M.D.,¹⁴ Giacomo Clerici, M.D.,^{15,16} Laurence Kessler, M.D.,¹⁷ Walter Wetzels-Roth, M.D.,¹⁸ Martin Storck, M.D.,¹⁹ Olafur Birgir Davidsson, Ph.D.,²⁰ Baldur Baldursson, M.D.,²¹ Hilmar Kjartansson, M.D.,²¹ John C. Lantis II, M.D.,²² and Guillaume Charpentier, M.D.²³

The Wounds Are Bigger! (2.5x)



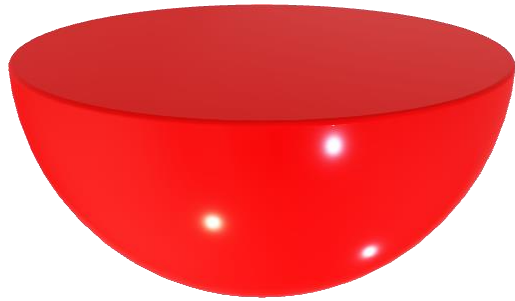
3.69 cm²



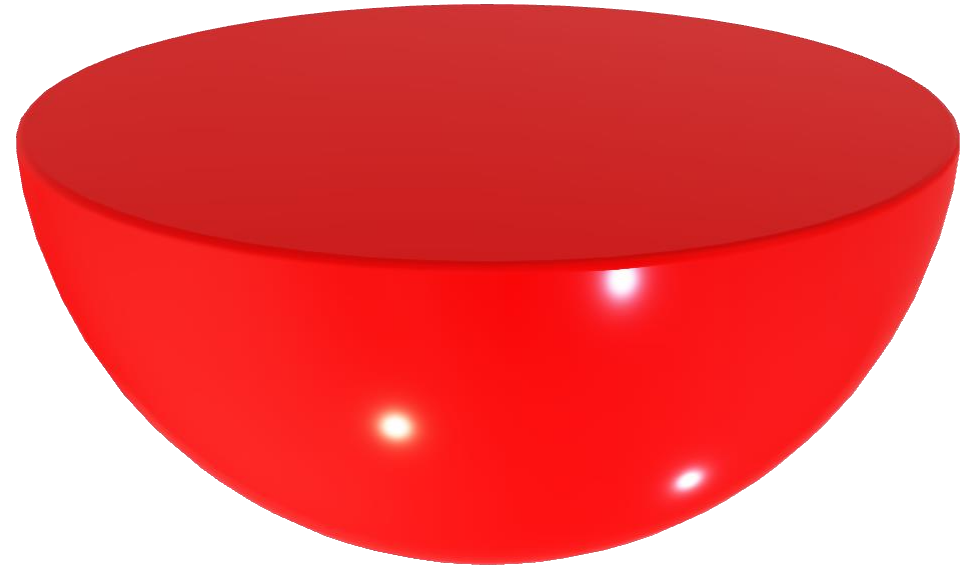
10.48 cm²

The Wounds Were Deeper!

- UT 1



- UT 2 and 3



The French KereFish Study

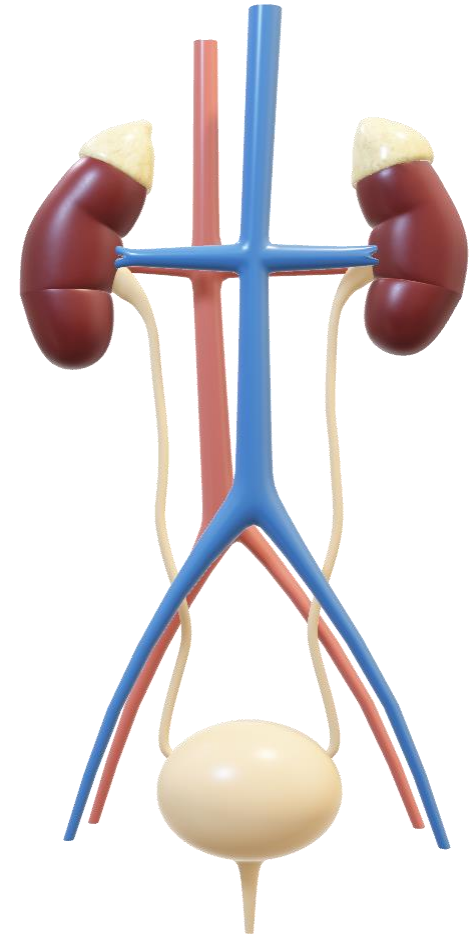
- 179 patients (of 252 total)
- Almost all patients (97.2%; N=175) had at least 1 diabetic complication or comorbidity
- Half (50%; N=86) had retinopathy, 11.2% (N=15) had associated maculopathy
- 53.3% of patients (N=90) had abnormal renal function
- 90.3% (N=158) had neuropathy
- 73.6% (N=128) had macroangiopathy

KereFish – French Cohort

- 51.1%; N=92 had a wound UT score 2 (“Wound is penetrating to tendon or capsule”)
- 48.3% had a score 3 (“Wound is penetrating bone or joint” N=87)

Renal Failure (The Patients Are Sicker!)

- 53.3% of French cohort (179 patients) had renal dysfunction
- 39% of the entire cohort (98 patients)
- 24% had an MI within 6 months
- HgBA1c was 8.2%-8.5%



The Entire Cohort

- 61 patients had a recent MI (24%)
- 98 patients had renal dysfunction (39%)
- HBA1c was 8.2 in the intact fish skin graft (IFSG) and 8.5 in the standard of care (SOC)

Not Easy Ulcers (KereFish)

- The majority of patients (N=108; 60.7%) were included in the study for the treatment of a chronic diabetic foot wound
- 58 patients (32.6%) were included for a recent bone resection/amputation
- 12 patients (6.7%) were included for an old bone resection/amputation

Perfusion Status

ABPI		
Normal	54 (42%)	60 (48%)
0.91 to 0.99	25(20%)	21 (17%)
0.60 to 0.90	50(39%)	45(36%)

ODINN

Interventional multi-center post market randomized controlled open-label clinical trial comparing IFSG vs standard of care in hard-to-heal diabetic foot wounds

ID RCB : 2018-A01743-52

NCT04537520

Coordinating Investigator: Dured Dardari, MD, PhD
Centre Hospitalier Sud francilien Corbeil Essonne France,
Clinique la prairie Clarens Switzerland

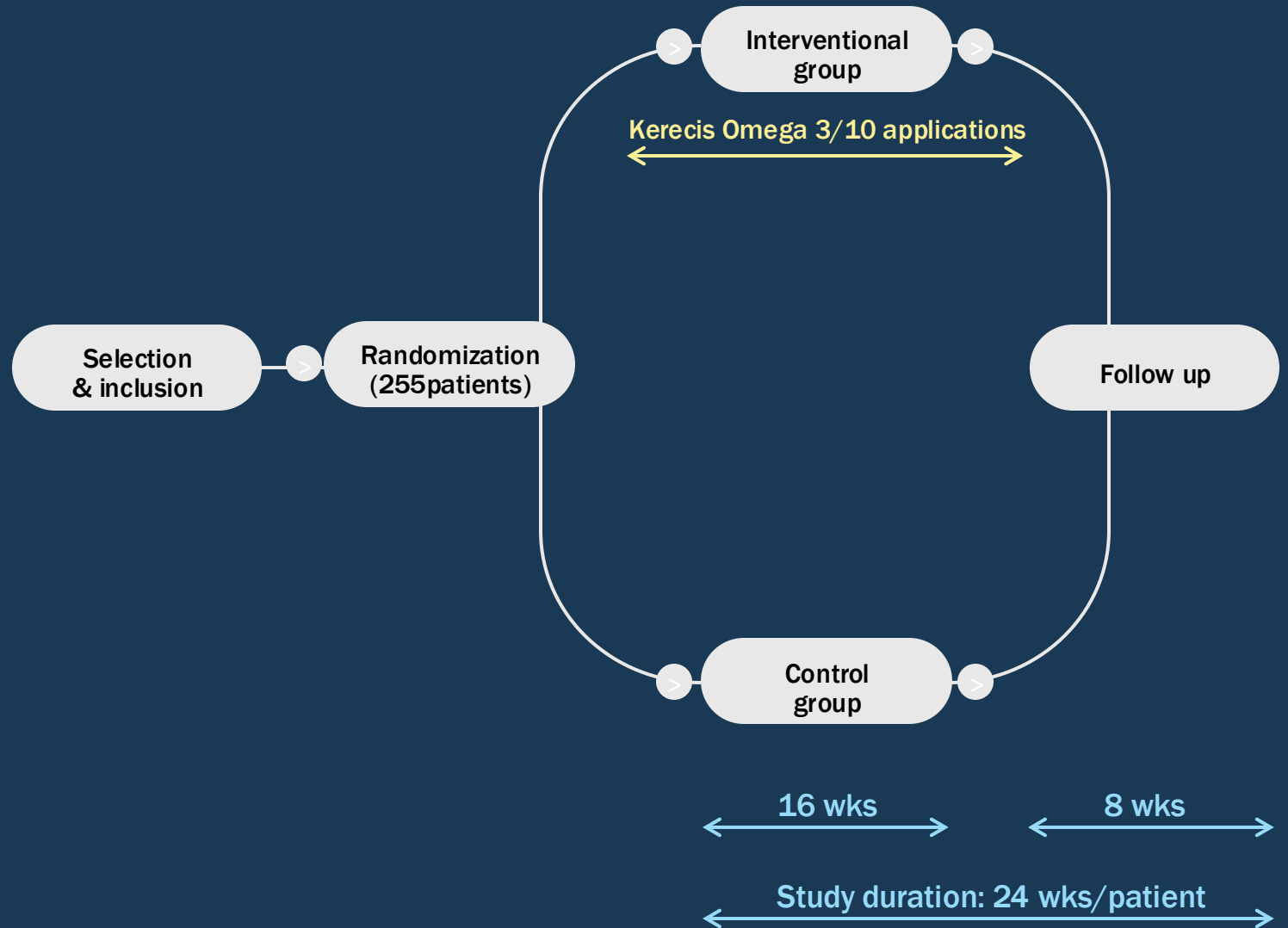
Sponsor: KERECIS



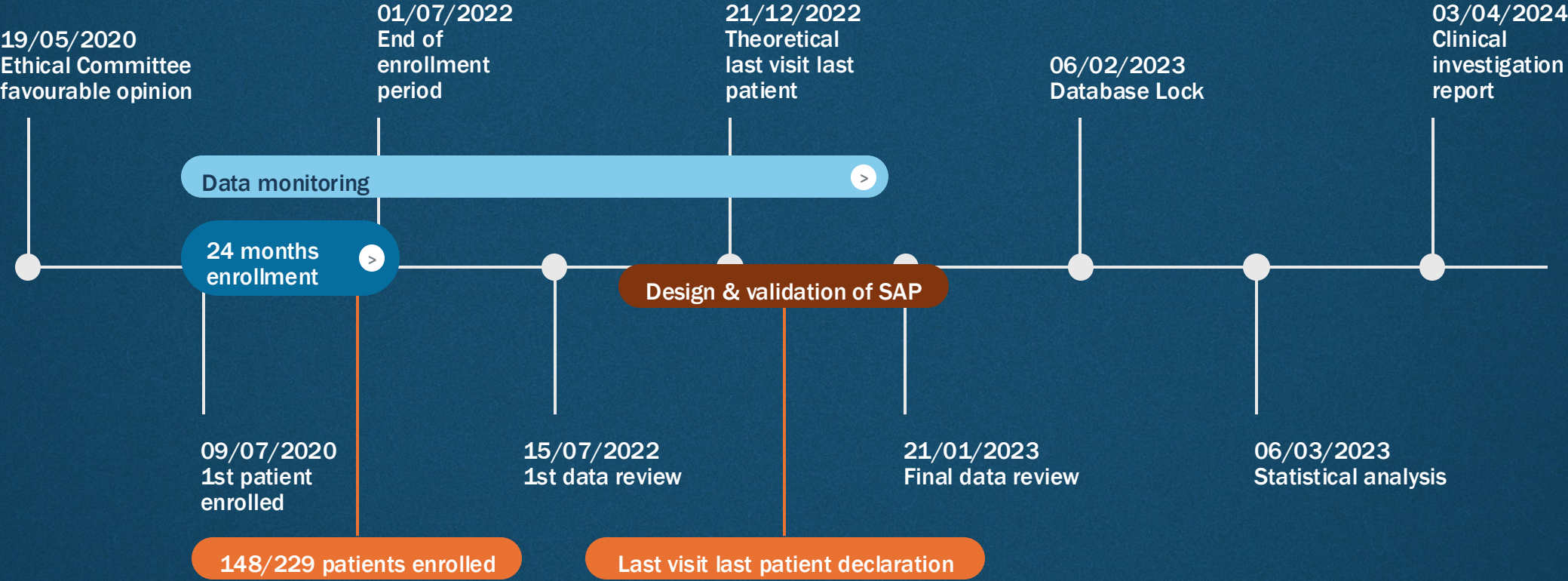
Study Design

Multinational multicenter trial, controlled, randomized, and open comparing 2 parallel treatment groups

- Wound treatment with **IFSG wound device** vs conventional treatment



Clinical Trial Schedule



Primary Objective

To demonstrate the effect of wound treatment with IFSG over conventional treatment.

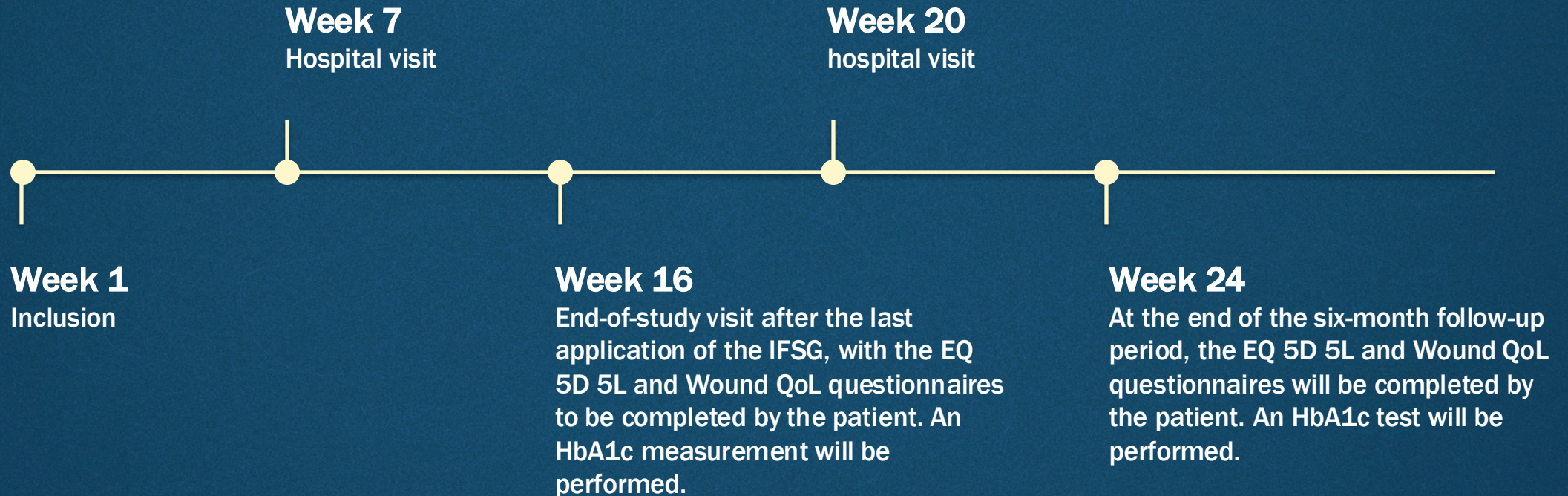
> Primary endpoint

Percentage of healed wounds with complete epithelialization at 16 wks



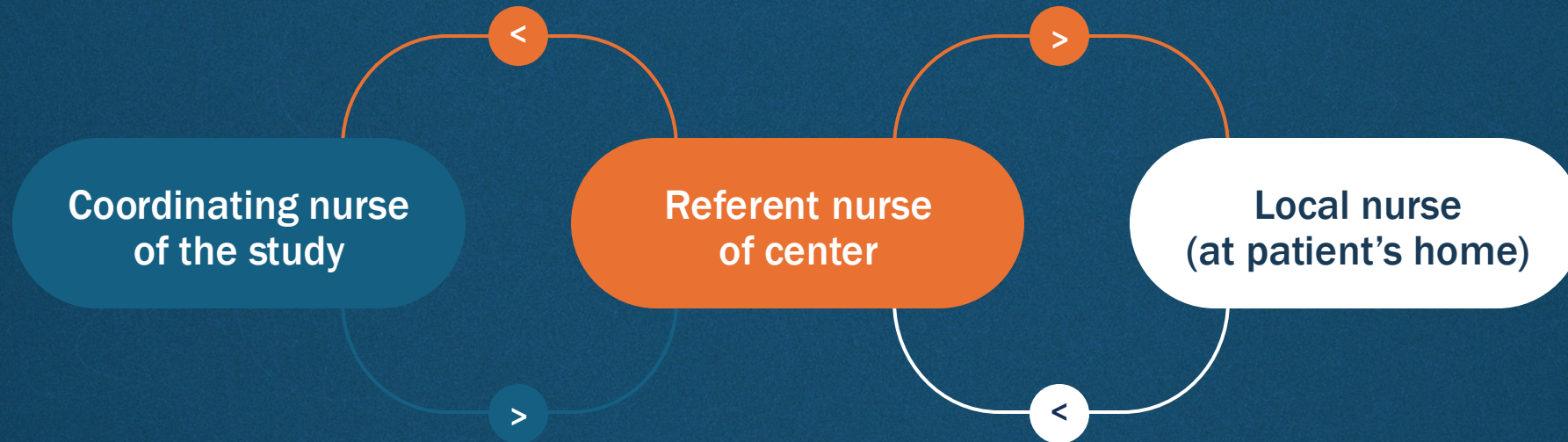
Methodology: Follow-up hospital visits study in the real world

The investigator assesses the wound condition of patients in both groups during hospital visits:





Methodology: Communication follow-up process





Methodology: IFSG applications (sheet only/NO NPWT)

Intervention group: Treatment with IFSG (maximum 10)

2nd matrix:

Applied either in hospital by IR or at home by RN with local nurse (LN) (W2)

4th matrix:

Applied in patient's home by LN (alone or under RN supervision) (S4)

1st matrix:

Applied at the hospital by the center's referral nurse RN (W1)

3rd matrix:

Applied at home by RN with LN (1st LN training period at home) or by LN if already trained (under RN supervision) (S3)

5th, 6th, 7th, 8th, 9th and 10th matrices:

At patient's home, IFSG will be applied every wk until wk 6 (W5 and W6), then every 2 wks until wk 14 (W8, W10, W12 and W14)





Methodology:

Follow-up visits at home

Perception of pain

- Completion of a VAS (patient)
- Pain experienced during the week
- Pain at the time of wound care

3 photos will be taken by the nurse and sent to the coordinating centre

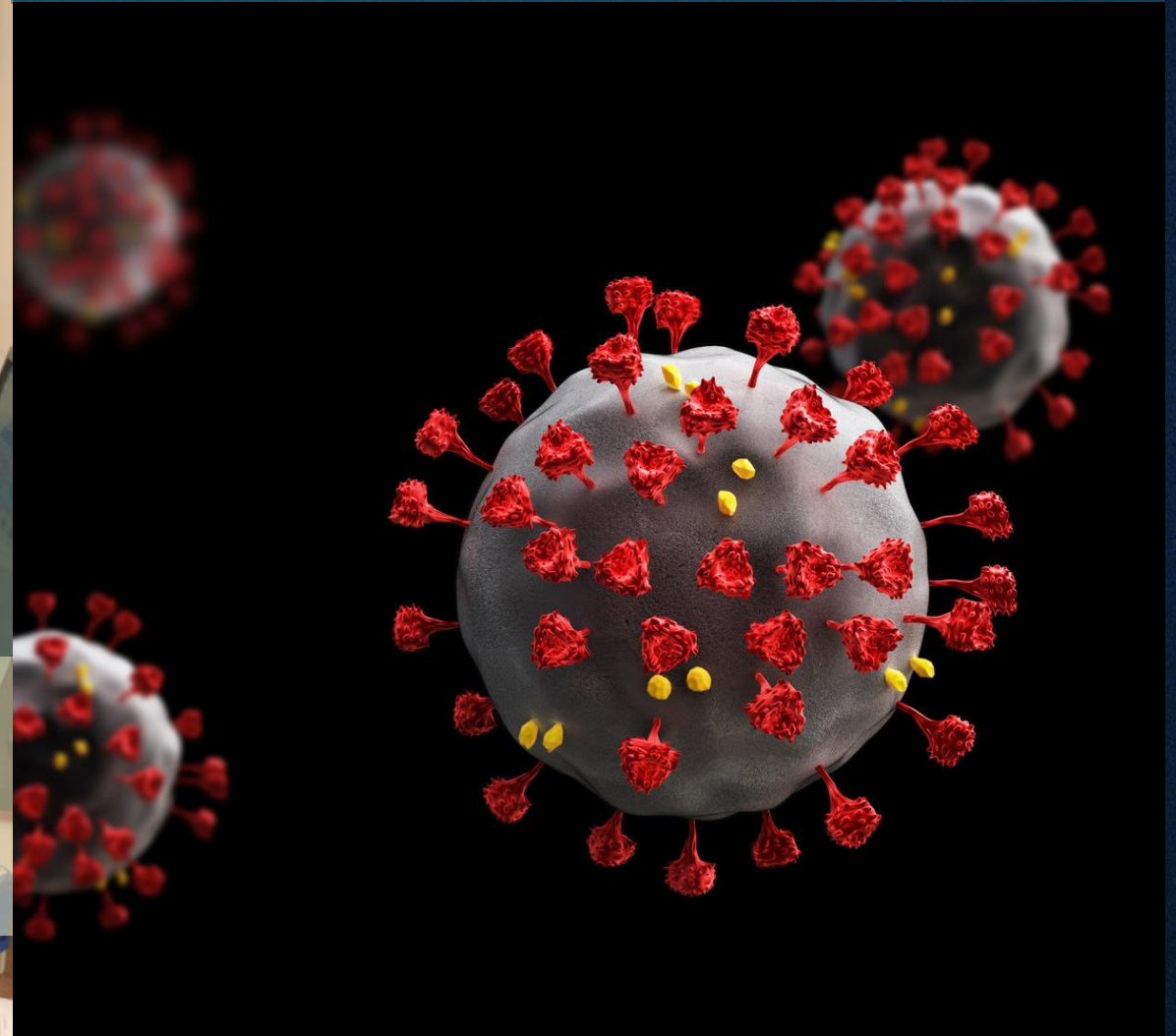
- Before debridement
- After debridement
- After application of IFSG (experimental group)



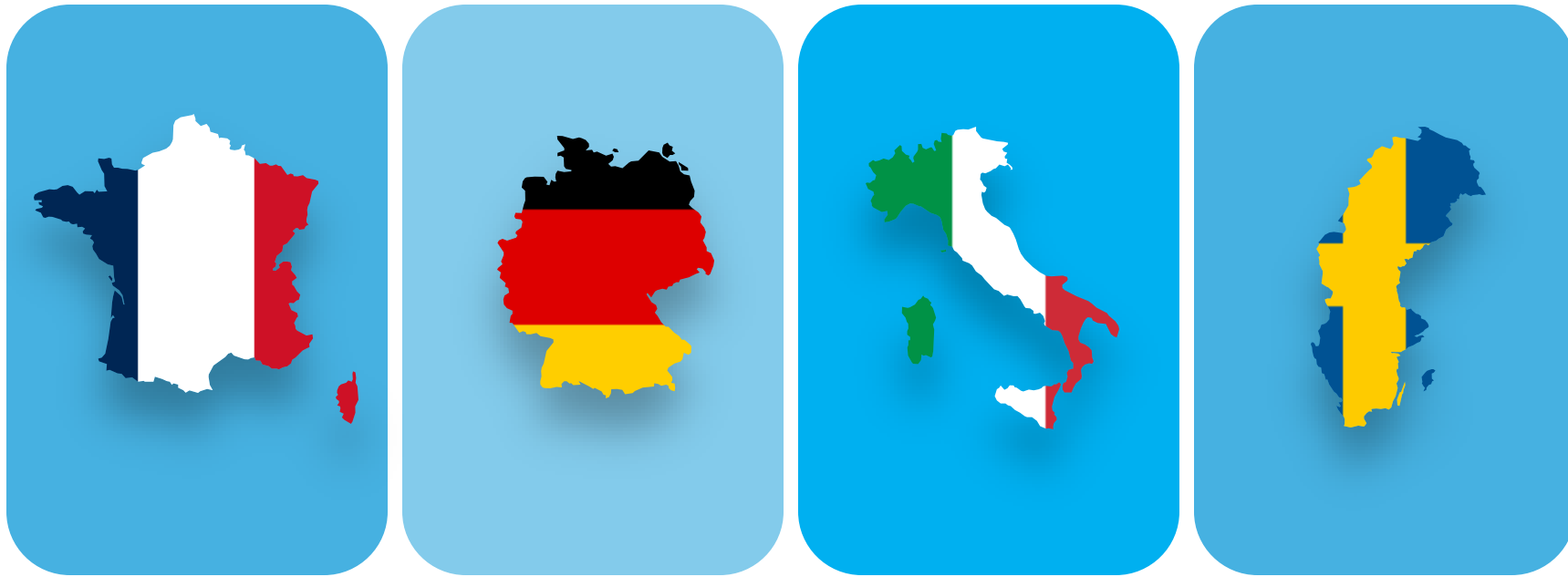
3 Lockdown COVID +



**Enrollment
from day 0**

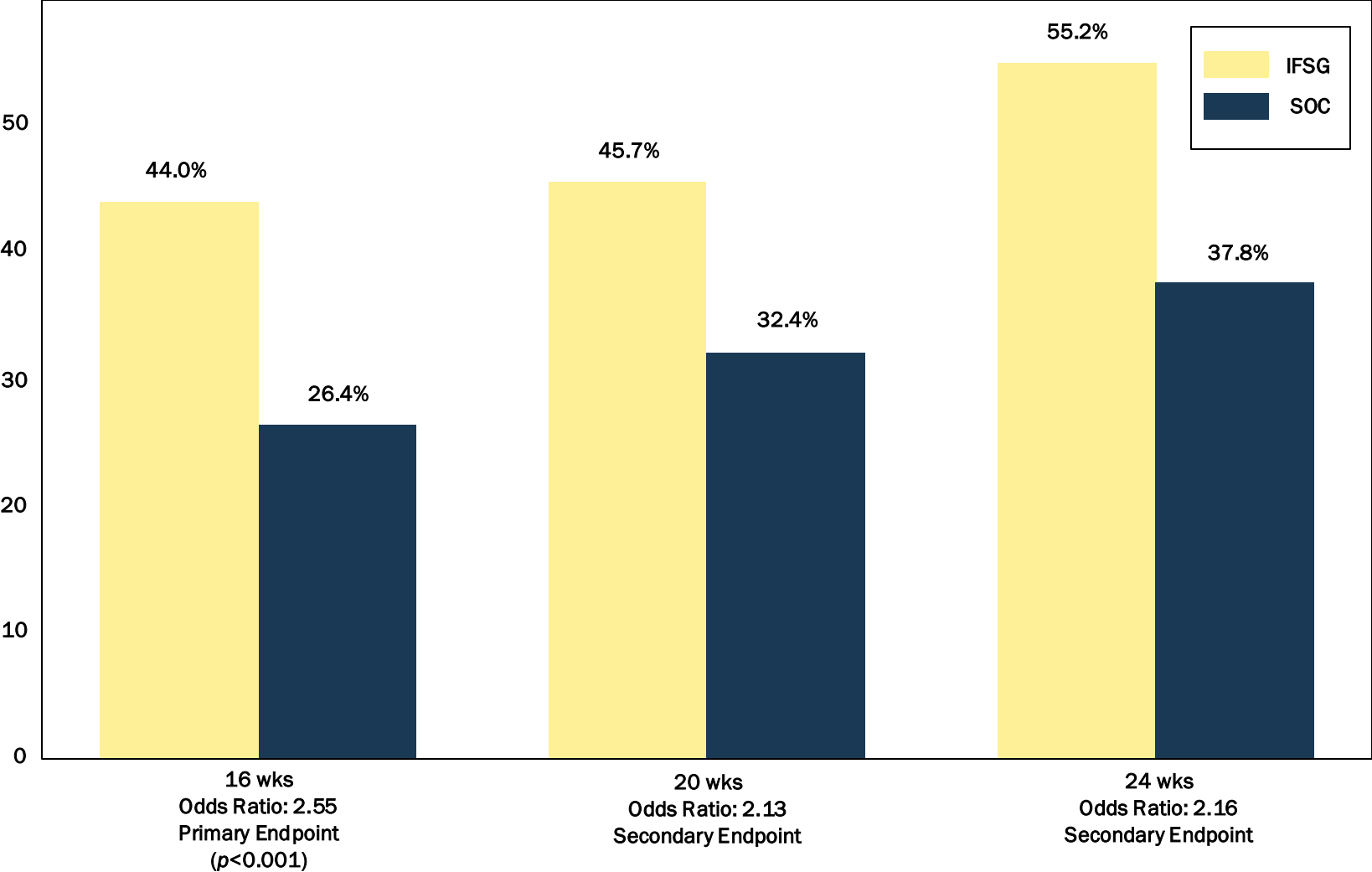


Enrollment: A multinational, multicentric RCT



Absolute Closure Rate: 44% in IFSG group vs 26.4% in SOC group

Proportion of Wound Closure: IFSG vs SOC

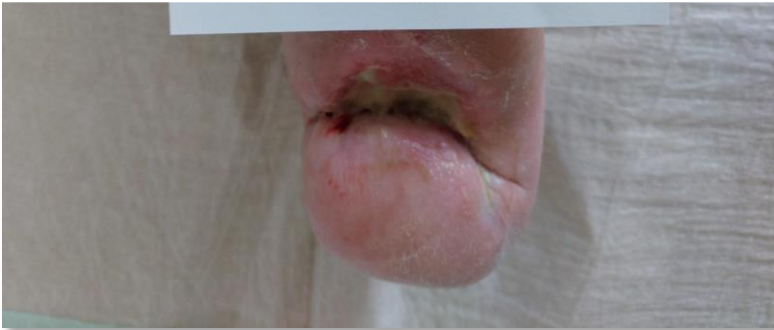


Absolute Closure Rate: 44% in IFSG group vs 26.4% in SOC group

Baseline (Grade 3): Post-Surgical
Debridement



10 wks



23 wks (Healed)



Baseline (Grade 3)



4 wks

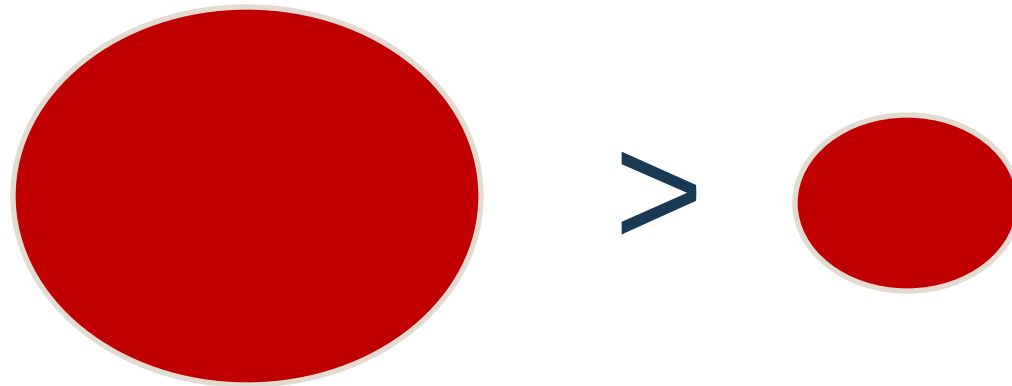


8 wks (Healed)



Wound Size (not $4\text{cm}^2 > 10\text{cm}^2$)

- Median for the IFSG was 10.48cm^2
 - Median for the SOC was 9.76cm^2
 - 2.5-3x larger than all other DFU trial
- } almost significant



Median 7 applications to close the wound

Secondary Endpoints

Title —

*Wound Closure, Wound Area Reduction,
Pain, and Quality of Life:*

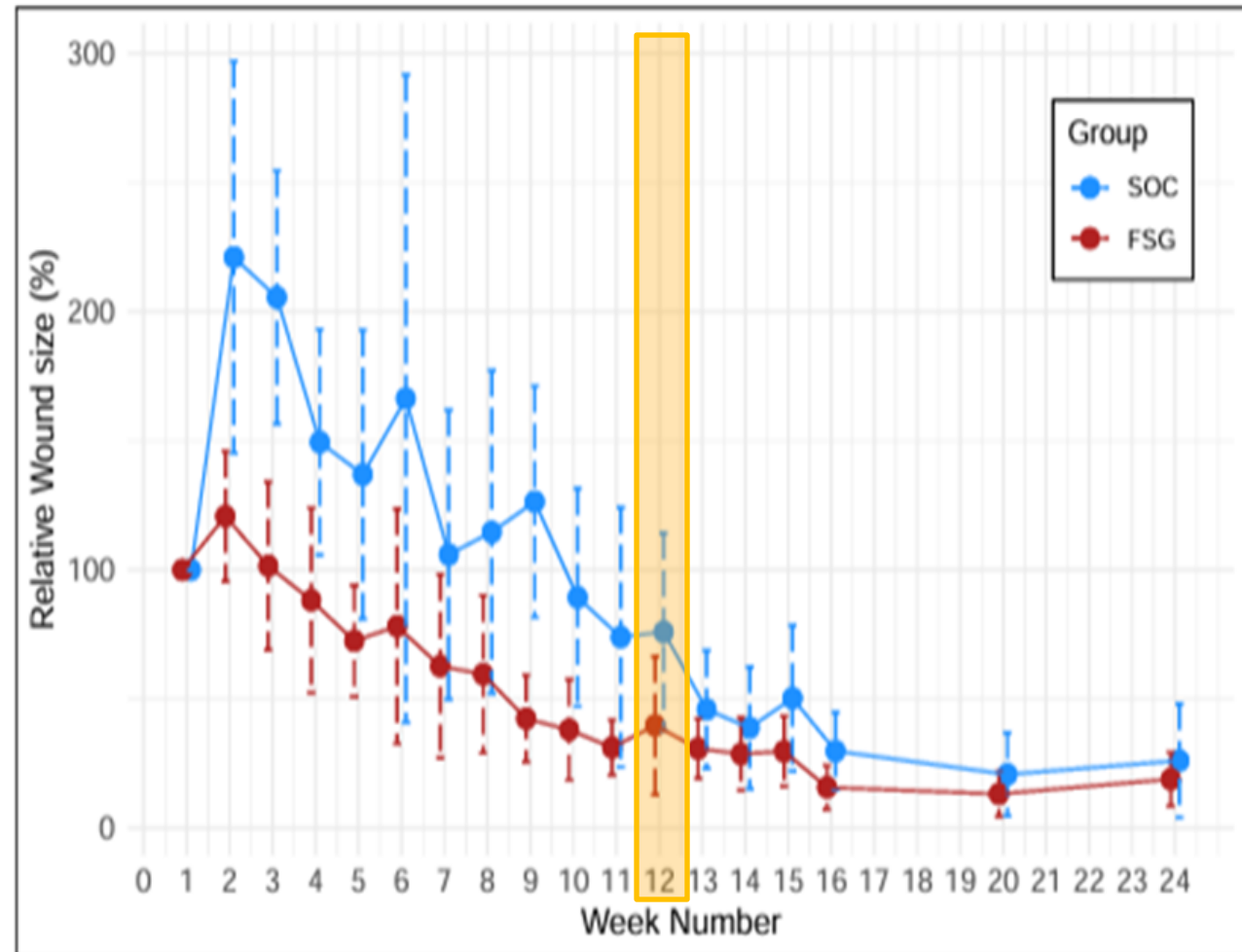
***Secondary Outcomes for the
Odinn Intact Fish Skin Graft
for Deep Diabetic Foot Wounds Trial***

Dured Dardari MD, Alberto Piaggese MD, Louis Potier MD, Ariane Sultan MD,
Holger Diener MD, Maud Francois MD, Bernhard Dorweiler MD, Benjamin Bouillet
MD, Jocelyne M'Bemba MD, Lucy Chaillous MD, Giacomo Clerici MD, Laurence
Kessler MD, Walter Wetzel-Roth MD, Martin Storck MD, Baldur Baldursson MD,
Hilmar Kjartansson MD, Guillaume Charpentier MD, John C Lantis II, MD



Percentage of ulcers healed 50% or more at 12 wks

50% wound area reduction (PAR) at 12 wks (65.53%) was statistically significant ($p=0.007$) between IFSG and SOC (30.82%)



Effect of UT Grade on Healing

- There were 75 UT grade 2 DFUs in each group, with a closure rate of 47% vs 23% at 16 wks for IFSG vs SOC ($p=0.0033$)
- There were 54 UT grade 3 ulcers in the IFSG group with a closure rate of 33.3% at 16 wks vs 19.6% in the SOC arm
- This represented a relative improvement in healing in the UT 2 group of 104%,
- And in the UT 3 group a 70% improvement in healing

Quality of Life and Pain

Quality of Life

Assessed at 3 timepoints in the study, (wks 1, 16 and 24)

- At wk 24, the IFSG group showed a trend toward better global quality of life compared to SOC ($p=0.095$)
- Analysis of change scores (delta, calculated as the difference from baseline), indicated a trend favorable towards IFSG in almost all areas, with notable subsets close to significance in Body (baseline to wk 16, $p=0.179$) and Psyche (baseline to wk 24, $p=0.08$)
- Financial score, analyzed separately, had a statistically significant difference, in favor of IFSG, in the change

Pain

- Pain was reported by study participants in both groups. There were no significant differences in the distribution of pain at 0 ($p=0.8795$), 16 ($p=0.784$), or 24 wks ($p=0.414$)

Time to Healing

- The time to healing for the IFSG in restricted mean survival time:
- (Weeks) was **17.31** wks (95% CI 15.5, 18.67) compared to SOC,
- Which was **19.37 wks** (95% CI, 18.09, 20.66)
- Overall, healed patients treated with IFSG healed **2 wks faster** than those treated with SOC
- The patients that closed – closed with a median of 7 applications of IFSG

Status Post Amputation

- A total of 93 patients enrolled after an amputation were evaluated
- These amputations/bone resections (including partial calcaneotomy)
 - *Were performed to treat an ulcer which had been present for greater than 30 days*
- At wk 16, amputees demonstrated
 - 31.1% wound healing for IFSG treated wounds in comparison
 - 16.7% wound healing in the SOC patients
- At wk 20
 - 37.8% wound healing in the IFSG group
 - 23.4% wound healing in the SOC group
- At 6 months
 - 44.2% wound healing in the IFSG group
 - 29.8% wound healing in the SOC group

Effect of Limited Perfusion

- ABPI was stratified as >0.6 , <0.9 , and >0.9 among the various treatment groups (IFSG vs SOC)
(Although this study was not powered for this level of stratification, we presented descriptive statistics)
- At 16 wks, the overall closure rate in those with an ABPI of >0.9 was 39% vs 0.6 to 0.9, which was 19%
 - When stratified by ABPI and both treatment groups, the IFSG group demonstrated a higher proportion of wound closure than the SOC group
- ABPI >0.9 IFSG treatment was associated with a $>100\%$ improvement in wound closure at 16 wks
 - In those treated with IFSG with an ABPI 0.6 to 0.9, there was a relative improvement of 50% in the number of wounds closed at 16 wks

*As the study was not originally designed or powered for this level of stratification, p -values derived may not necessarily reflect an accurate comparison. Thus, these results are presented as descriptive only.

In Closing

First DFU with Exposed Structure Prospective Randomized Trial Done

- Relative closure improvement of 66% at 4 months
- Wounds 2.5 to 4.5 times larger than any other study
- Wounds 2.5 x deeper
- Differences in closure were greater in UT 2 than in UT 3
- In those that closed, they closed 2 wks sooner
- IFSG worked very well after amputation and showed a strong clinical effect in those with limited ABPI
- Those that closed required a median of 7 applications