ONENESS

Macrophage-regulation drug (ON101) In treating difficult Diabetic Foot Ulcer Real-World Cases Study

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Director of Department of Medical Science

ON101 (Fespixon®)

- ON101 is the only Phase 3 IND for DFU approved by US FDA achieving statistical significance (P=0.0001) since 1997.
- The DFU new drug, FESPIXON® has been granted a new drug approval by Taiwan FDA in 2021, with indication " Diabetic Foot Ulcer. "
- Novel Mechanism to Promote Healing by Regulating M1/M2 Macrophages and Rebalancing the Wound Microenvironment.
- Phase 3 MRCT results and mechanism of action have been published in the《JAMA Network Open》,《JID Innovations》, and 《Pharmaceutics》.
- After launching, FESPIXON® achieves good wound healing in treating difficult diverse Wagner grade 1-4 DFUs, long-term dialysis patients, lower extremity venous ulcers, pressure ulcers, burns ,and surgical wounds.

ON101 (Fespixon®) Entering Markets after 15 years of R&D

2008 — ONENESS Founded

2016 — PIC/s GMP Plant

2020 — Phase 3 MRCT Study Completed

2021 — New Drug Licenses in Taiwan and Macao

2022 — NDA Submissions in Multiple SEA Countries

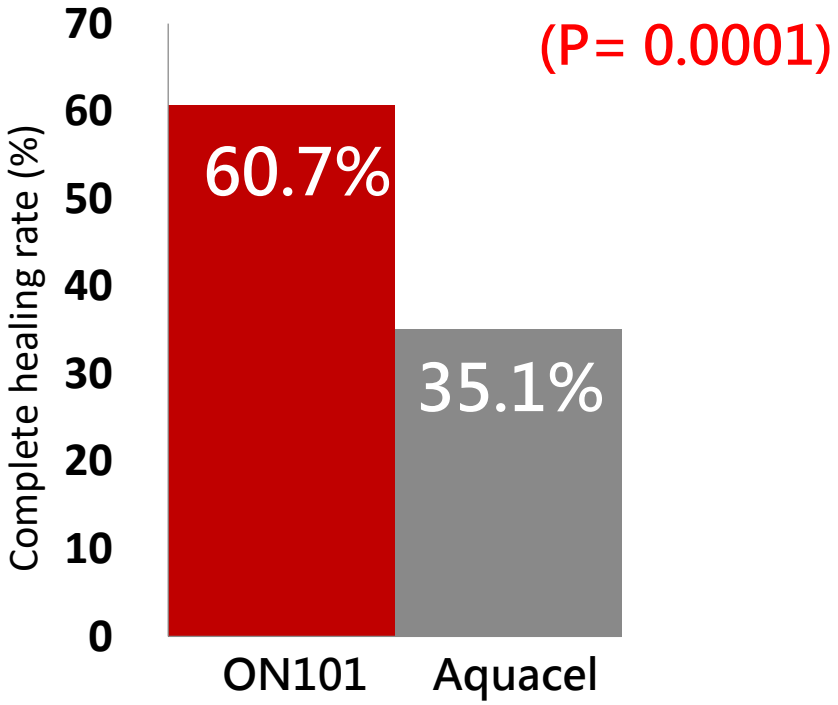
2023

- ✓ In 2021, U.S. FDA granted fast track designation and expanded access (compassionate use)
- ✓ NDA was submitted to NMPA in China and is under review

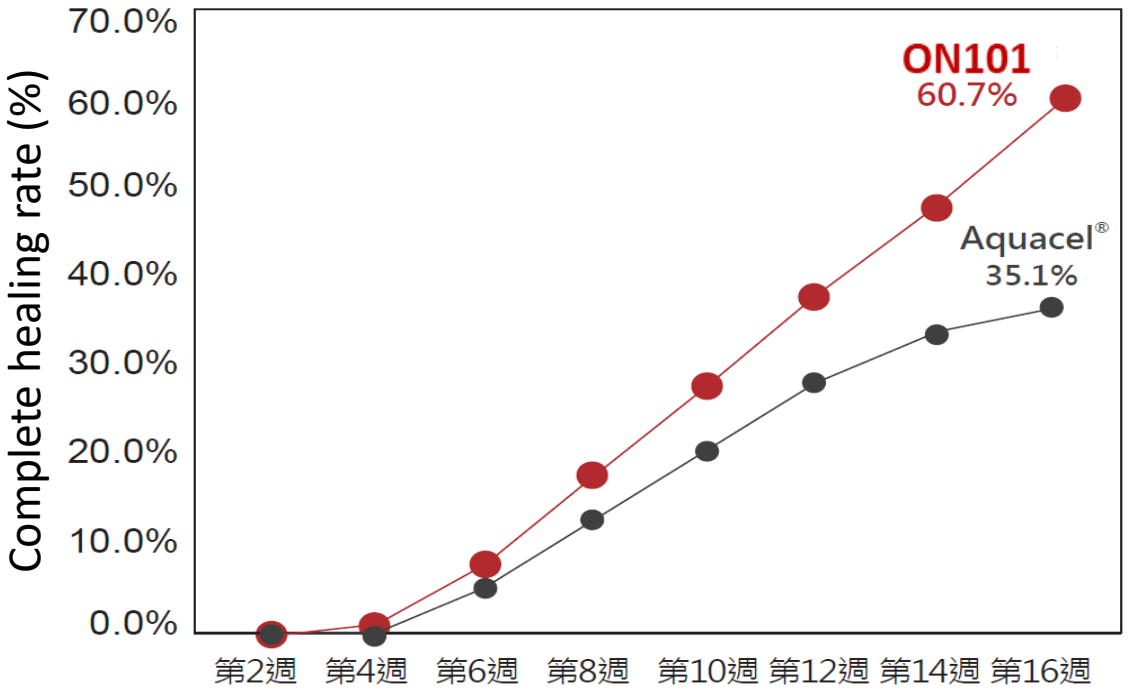
Primary Endpoint - Complete Healing Rate

- N=236 subjects (China, Taiwan and US)

Complete Healing Rate

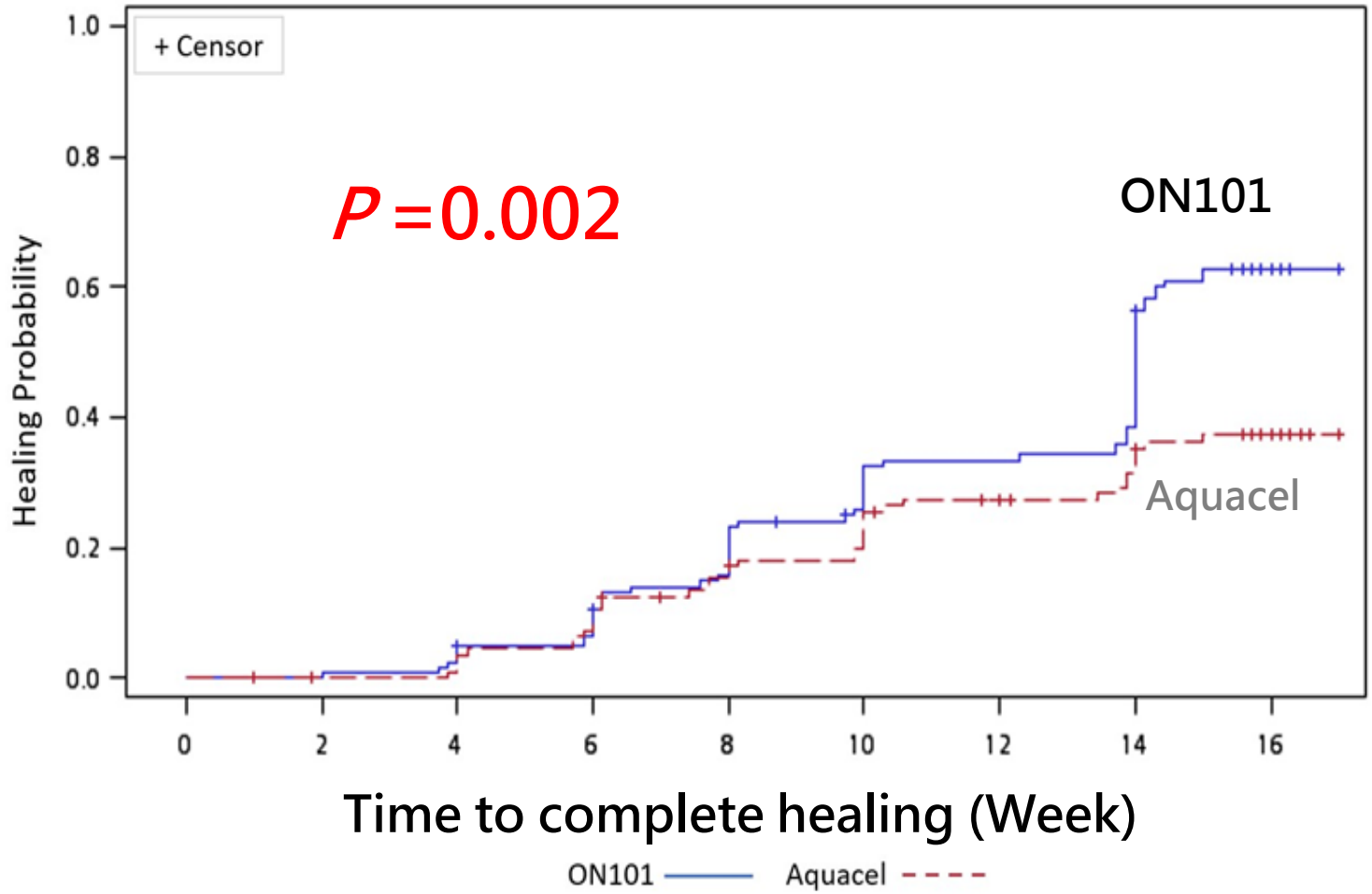


Cumulative Rate of Complete Healing



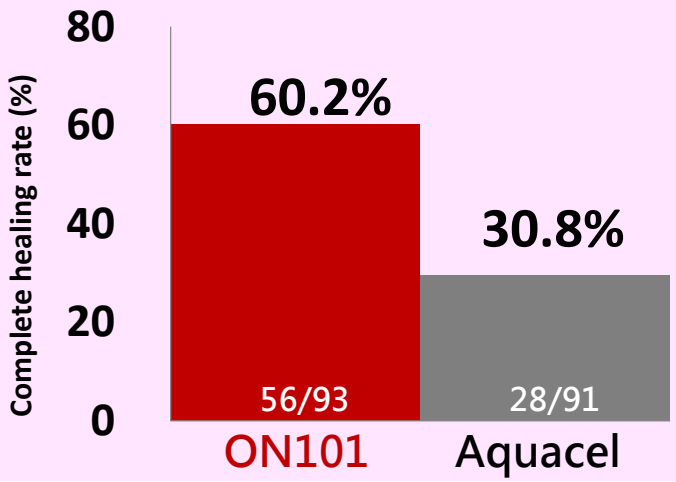
Secondary Endpoint - Time to complete healing

Ulcer complete healing time is faster in ON101 group

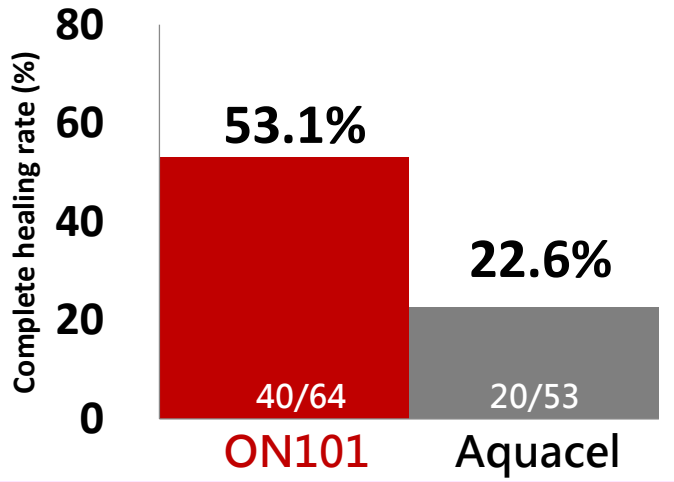


Hard-to-Heal Subgroup Analysis-1

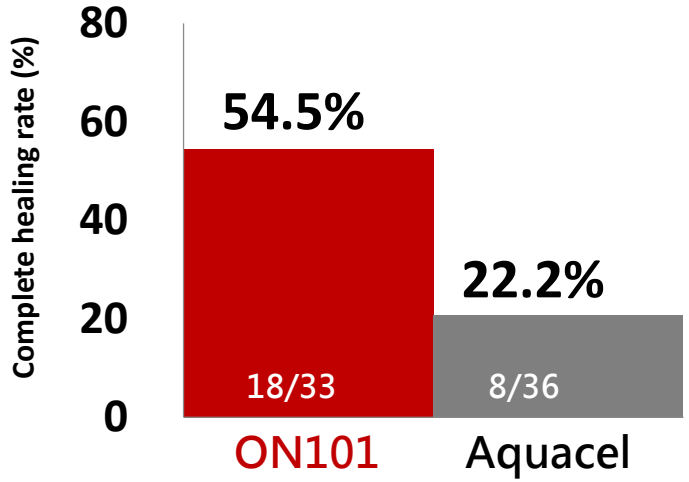
Wagner Grade 2 Ulcers (P < 0.0001)



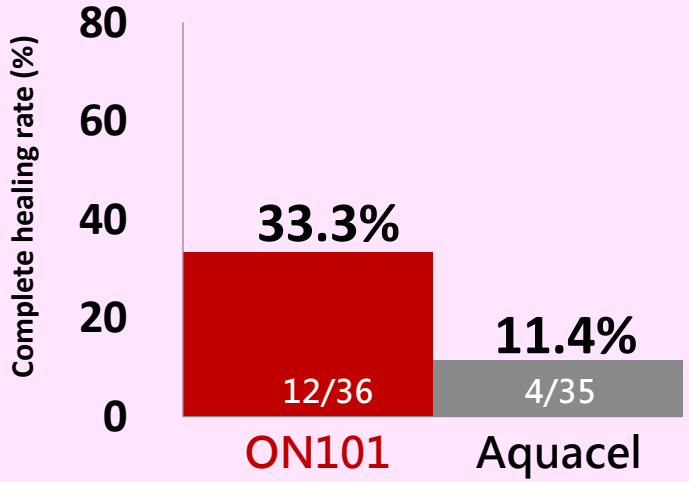
Plantar Ulcers (P = 0.0008)



Ulcers > 5 cm^2 (P = 0.0056)

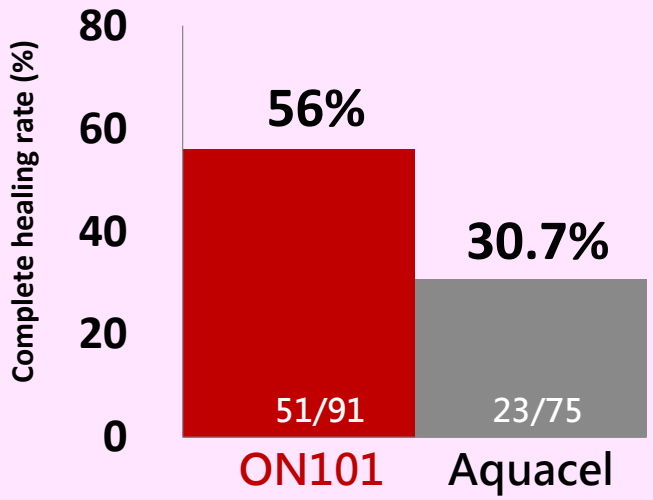


Durationn ≥ 6 month (P = 0.0272)

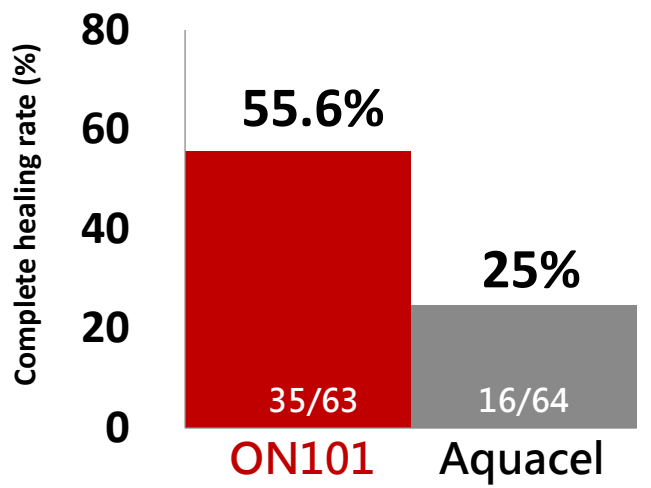


Hard-to-Heal Subgroup Analysis-2

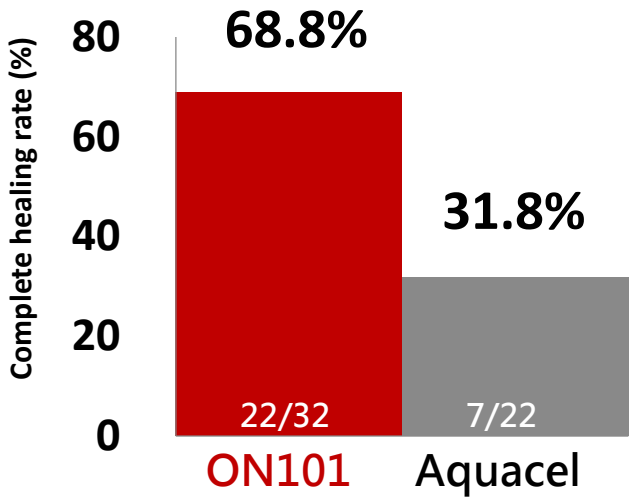
HbA_{1c} >7% (P = 0.0011)



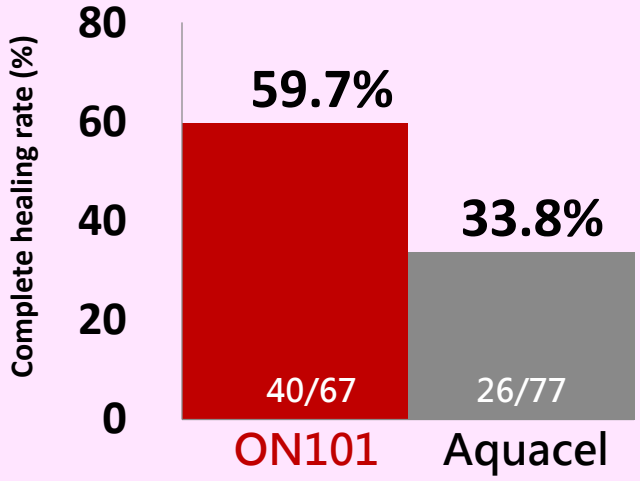
BMI ≥ 25 (overweight) (P = 0.0004)



Current Smokers (P = 0.0075)



DM > 10 years (P = 0.0018)



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Phase 3 study - Efficacy and Safety

ClinicalTrials.gov Identifier: NCT01898923

JAMA Network | Open™

Impact factor: 13.366

Original Investigation | Diabetes and Endocrinology

Effect of a Novel Macrophage-Regulating Drug on Wound Healing in Patients With Diabetic Foot Ulcers

A Randomized Clinical Trial

JAMA Netw Open. 2021;4(9):e2122607 | MRCT : Multi-center randomized clinical trial

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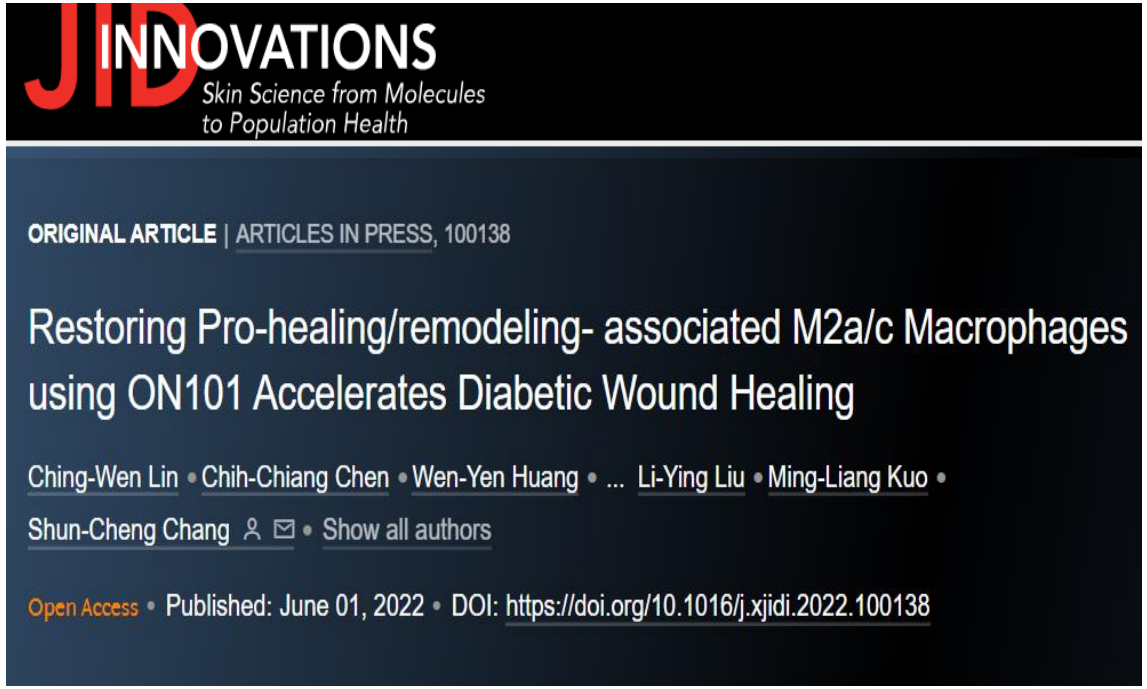
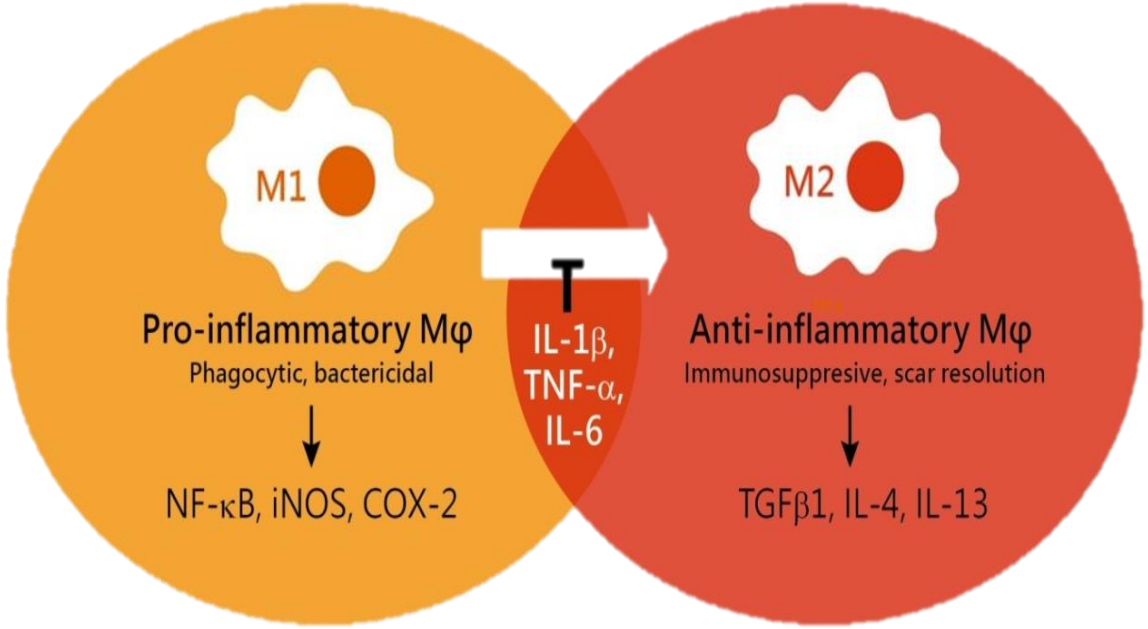
Novel Mechanism Promotes Healing by Regulating M1/M2 Macrophages and Rebalancing the Wound Microenvironment





JID Innovations (2022), doi: https://doi.org/10.1016/j.xjidi.2022.100138.

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ON101 Proved Macrophage Modulation Therapies Improving the Effectiveness of Diverse DFUs Treatment

pharmaceutics

MDPI

Review

New Horizons of Macrophage Immunomodulation in the Healing of Diabetic Foot Ulcers

Ching-Wen Lin [1], Chien-Min Hung [2], Wan-Jiun Chen [2], Jui-Ching Chen [1], Wen-Yen Huang [2], Chia-Sing Lu [1], Ming-Liang Kuo [2,*] and Shyi-Gen Chen [1,3,*]

Difficult DFU Real-World Cases Study

American Diabetes Association. | 82ND SCIENTIFIC SESSIONS | HYBRID | NEW ORLEANS | JUNE 3-7, 2022

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Published at 82nd

American Diabetes Association (ADA), 2022

Author Block: SHYI-GEN CHEN, YUN-NAN LIN, JUI-CHING CHEN, YUK-KEN KUO, *Taipei, Taiwan, Kaohsiung,*

Abstract:

A 53-year-old female with type 2 DM (HbA_{1c} 11.7%), peripheral artery disease (PAD), hypertension, and hyperlipidemia was sent to the emergency room of K
an infected DFU with exposed tendon and ischemic necrosis (Figure 1a). Ankle brachial index of her right leg was 0.8 and angiography revealed severe sten
downgraded from Wagner grade IV to II after a 10-day treatment by broad-spectrum antibiotics and angioplasty for infection and ulcer severity control. Ho
inflammation and ischemia (Figure 1b). The growth of granulation tissue was limited despite using fat grafting to boost mesenchymal tissues. Pseudomonas
artificial dermis after further debridement and intravenous antibiotics but noted poor ingrowth of cells. The patient declined the recommended surgical re
macrophage-regulating drug, was applied twice a day. The ulcer area measured digitally by imitoMeasure, was 7.23cm^2 before treated by ON101 (Figure 1c)
healing is often hindered by DM or PAD despite of multiple interventions. Macrophage-regulation can be deemed as a novel approach to promote

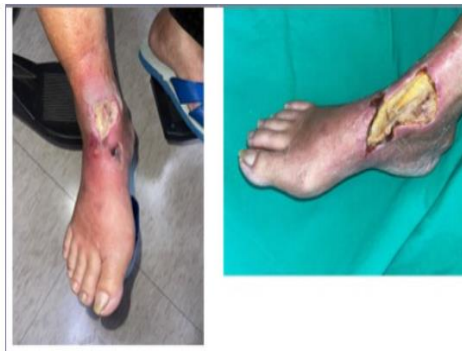

Figure 1.
The DFU was presented with complicated skin and soft tissue infection and diagnosed as **Wagner grade IV.**

Figure 2.
The ulcer was downgraded to Wagner grade II after ag treatment but persistent inflammation and ischemia pr the tissue proliferation.

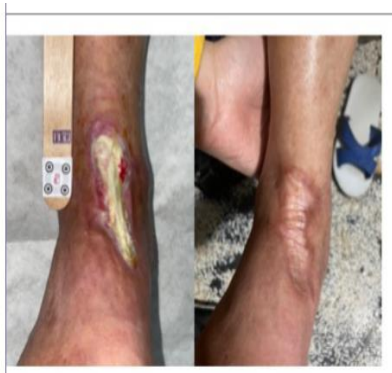

Figure 3.
Wound picture before **ON101 topical use.**

Figure 4.
The ulcer healed uneventfully after 16 weeks.

Macrophage-regulating Drug Healed a Diabetic foot Ulcer with Gangrene and Osteomyelitis

Shun-Cheng Chang, MD[1]; Shyi-Gen Chen, MD, MPH[2]; Jui-Ching Chen, PhD[2]; Yi-Hsin Wu[2]

1 Division of Plastic Surgery, Department of Surgery, Integrated Burn and Wound Care Center, Taipei Medical University-Shuang Ho Hospital, Taiwan
2 Department of Medical Science, Oneness Biotech Co., Ltd., Taiwan

Introduction

ON101 is a topical macrophage-regulating new drug for diabetic foot ulcers (DFUs). With its mechanism by inhibiting pro-inflammatory M1 macrophages and promoting GCSF and CXCL3 to increase pro-healing M2 macrophages (figure 1A), ON101 has been demonstrated with superior efficacy to the standard care dressing in a large Phase 3 multicenter random
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Materials and methods

The presented case in figure 1B is a 77-year-old male with type 2 DM (Hb A_{1c} 7.2%), peripheral artery disease (PAD), chronic kidney disease (CKD) stage 3, coronary artery disease, and a persisted DFU for 8 months. Deep infection was presented on the left first toe amputated stump with exposed bone, and extensive ischemic necrosis in the surrounding wound

Published at 51st

Annual ESDR Meeting, 2022

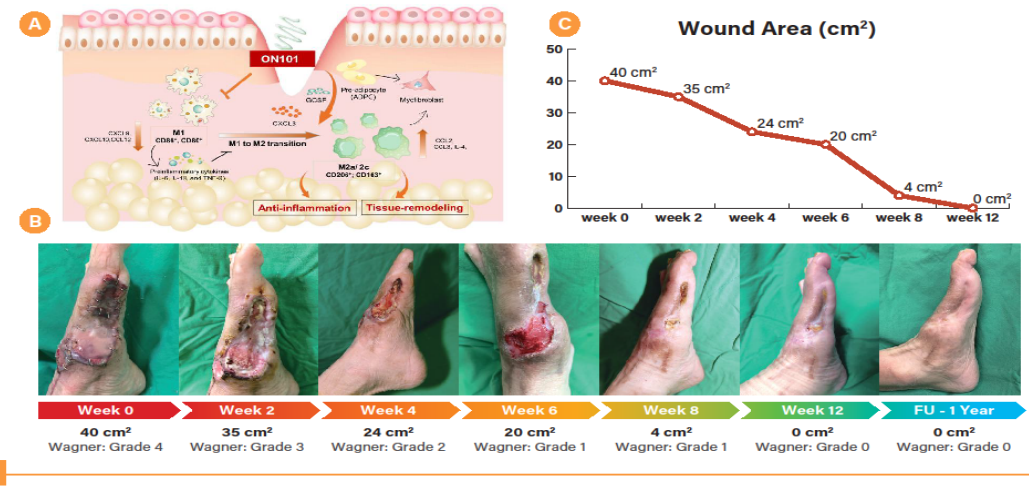
Results

The unresponsive ulcer to artificial dermis measured 40 cm^2 (figure 1C), prior to the treatment with ON101 and reached complete closure after 12 weeks. There is no treatment-related adverse event. The patient was able to walk wearing protective shoes without crutches or assistive devices, and can return to work. After a one-year follow-up (FU), the patient reminded ulcer-free. This has demonstrated the healing durability by ON101 treatment.

Discussion

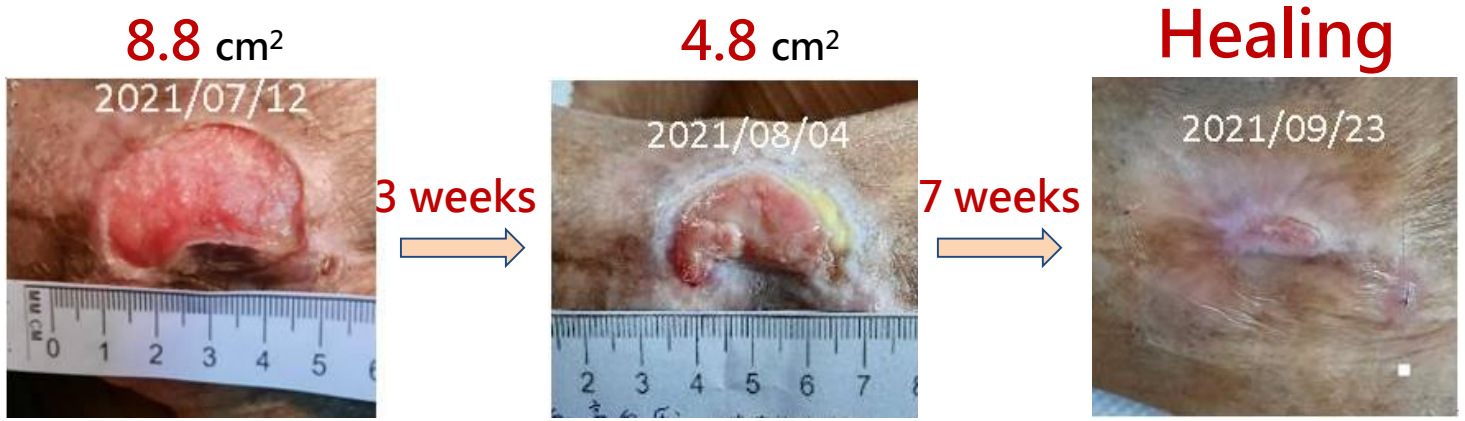
The finding of this case study is in alignment with the previously-reported randomized, multi-regional phase 3 clinical trial on ON101, where a macrophage-regulator is different from moisture-retaining dressings can provide treatments with an active-healing ability for patients with chronic DFUs at an out-patient setting. This also provides an evidence-based approach in the proposed new treatment flow. Healing of full-thickness ulcers is commonly hindered by DM, PAD, or CKD despite of multiple interventions, and macrophage-regulation can be deemed as a novel approach to promote tissue repair on full-thickness skin ulcers, and suitable for routine care.

Figure 1



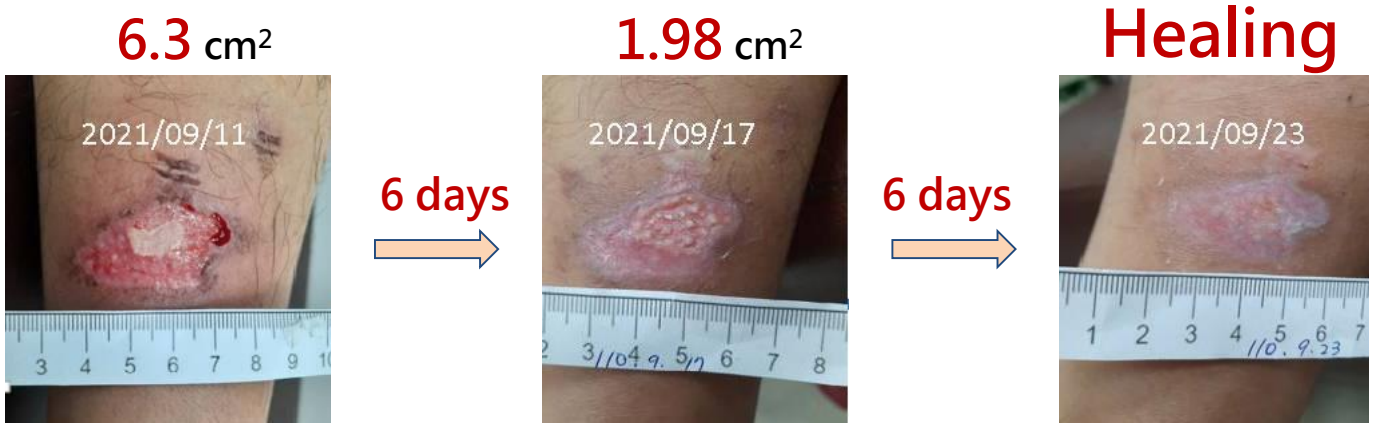
Pressure Ulcer - NPUAP Grade2

- Male aged 92 with anemia and hypertension.
- Existence of pressure ulcers for many years in lower back and lower extremity.
- ON101 accelerated healing (45% ulcer size reduction after 3 weeks) and ulcer was healed in 10 weeks.



Burn injury

- Male aged 41
- Burn injury while working
- 69% wound size reduction after ON101 application for 6 days.
- Significant and rapid healing in 2 weeks with ON101 treatment.



ON101 (Fespixon®)

- Kick off global launch plan, with NDA Submissions in China, Singapore, Malaysia, Thailand, Indonesia, and Vietnam since 2021.
- Simultaneously conduct second phase 3 clinical trial in US.
- Global launch by 2026, with total target population of 30 million per year.

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