

Roundtable document

Expert Roundtable Recommendations on Wound-Bed Optimization in Difficult-to-Heal Wounds: Clinical Positioning of ON101 From a U.S. Multidisciplinary Roundtable

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Background: Diabetic foot ulcers (DFUs) remain a major clinical and economic challenge and may persist within a dysregulated wound microenvironment characterized by persistent inflammation, impaired cellular signaling, microbial biofilm burden, and failure to progress through normal healing pathways. ON101 is a provider-directed topical wound-bed optimization matrix developed to support progression toward closure in difficult-to-heal DFUs.

Objective: To review the available evidence and develop structured expert roundtable recommendations regarding the role of ON101 as an adjunctive wound-bed optimization approach for difficult-to-heal DFUs. Potential applications beyond DFUs were considered separately as emerging research contexts. Discussion focused on patient selection, treatment timing, integration with standard care, administration, implementation, economic considerations, and research priorities.

Methods: A multidisciplinary structured expert roundtable was convened in April 2026 in Charlotte, North Carolina, involving 11 panelists, including 10 clinical experts and one wound-care research statistician and healthcare/research executive, representing wound care, surgery, podiatry, and related clinical specialties. Panel members reviewed preclinical, clinical, real-world, health-economic,

regulatory, and emerging evidence and discussed key questions regarding integration of ON101 into wound management. Draft statements were developed from discussion themes and areas of broad agreement and reviewed by participants. No formal voting or prespecified agreement threshold was used, and the recommendations should not be interpreted as formal clinical practice guidelines.

Results: The panel identified difficult-to-heal wounds characterized by persistent inflammation, biofilm burden, delayed closure progression, and wound microenvironment dysfunction as clinical features of interest for ON101 consideration, while recognizing that predictors of differential treatment response have not been established. Emphasis was placed on difficult-to-heal DFUs, where the strongest evidence currently exists. In physician-directed DFU care, early wound-area reduction at four weeks may serve as a prognostic reassessment marker to identify wounds requiring continued optimization or escalation; it does not establish the optimal timing of ON101 initiation. Preliminary U.S. real-world evidence reported greater early wound-area reduction, shorter time to complete closure and lower direct cost per wound with ON101 compared with matched standard-care controls; these findings are hypothesis-generating. The panel conditionally supported consideration of ON101 during active

wound-bed optimization, although optimal timing has not been prospectively established.

Roundtable recommendations emphasized that ON101 should be integrated with established standards of care, including etiology-appropriate wound-bed preparation, infection and vascular management, offloading or compression as indicated, and systemic optimization. While the strongest evidence currently exists for diabetic foot ulcers, applications in radiation-associated wounds, pressure injuries, venous leg ulcers, post-surgical wounds, and other difficult-to-heal wound types were considered emerging or research-only applications requiring prospective evaluation.

Limitations: The recommendations reflect a structured expert roundtable informed by available

evidence and clinical experience rather than formal evidence-based guidelines or standards of care. Evidence is strongest in DFUs; evidence in other wound types remains limited or preliminary.

Conclusions: The panel concluded that ON101 may be considered as an adjunct to comprehensive wound care, particularly for difficult-to-heal DFUs, during active wound-bed optimization. Priority outcomes for future evaluation include complete closure, time to closure, early wound-area reduction, subsequent interventions, healthcare encounters, and total cost of care. Further research should address comparative effectiveness, patient selection, dosing, biomarkers, implementation, and health-economic outcomes, particularly beyond DFUs.

Forward

Written by Chair Dr Serena

Wound management continues to evolve as understanding of wound biology advances. Although comprehensive standard care remains foundational, persistent inflammation, impaired immune responses, biofilm, and altered cellular signaling may contribute to chronic wound persistence.

ON101 has been evaluated for the management of diabetic foot ulcers, with randomized and observational evidence summarized in this article. The objectives of this roundtable were to review the current evidence, identify patient populations most likely to benefit, explore optimal timing of therapy, consider integration into established standards of care, and identify priorities for future clinical investigation.

The recommendations presented in this manuscript reflect a structured expert roundtable informed by published evidence and clinical experience. Further clinical, mechanistic, and real-world studies are needed.

Table of Contents

Executive Summary	1
Foreword	3
Table of Contents	4
1. Introduction	5
1.1 <i>Chronic Wound Burden and Dysregulated Wound Microenvironment</i>	5
1.2 <i>ON101 Overview</i>	5
1.3 <i>Purpose of this Roundtable</i>	5
2. Reported Clinical Experience with ON101	6
2.1 <i>Biological Rationale for ON101</i>	6
2.2 <i>Clinical Trial Experience in Diabetic Foot Ulcers</i>	6
2.3 <i>Real-World Clinical Experience</i>	7
2.4 <i>Emerging Applications Across Wound Types</i>	7
3. Methods	8
3.1 <i>Panel Composition</i>	8
3.2 <i>Materials Reviewed</i>	10
3.3 <i>Roundtable Process</i>	11
3.4 <i>Statement Development</i>	11
4. Roundtable Recommendations	12
4.1 <i>Patient and Wound Selection</i>	12
4.2 <i>Timing of Intervention</i>	13
4.3 <i>Integration with Standard Care</i>	14
4.4 <i>Administration and Dosing</i>	14
4.5 <i>Clinical Settings</i>	15
4.6 <i>Economic Considerations</i>	16
4.7 <i>Research Priorities</i>	17
5. Clinical Algorithm	18
6. Discussion	20
6.1 <i>Clinical Implications</i>	20
6.2 <i>Implementation Considerations</i>	20
6.3 <i>Limitations</i>	20
6.4 <i>Future Directions</i>	21
7. Conclusion	22
References	25

1. Introduction

1.1 Chronic Wound Burden and Dysregulated Wound Microenvironment

Diabetic foot ulcers (DFUs) represent one of the most severe manifestations of chronic wounds and are associated with substantial risks of infection, hospitalization, lower-extremity amputation, and mortality. Despite advances in multidisciplinary care, recurrence and long-term complications remain common, and difficult-to-heal wounds continue to impose substantial clinical and economic burden.^{1–6} This supports the need for therapies that address biological factors contributing to impaired wound closure.

Chronic wound persistence is associated with a dysregulated wound microenvironment characterized by persistent inflammation, impaired angiogenesis, altered cellular activity, excessive protease burden, microbial biofilm formation, and disrupted signaling pathways. These processes may delay progression through normal healing and reduce responsiveness to conventional wound management, providing a biological rationale for therapeutic approaches directed at the wound microenvironment.^{7–9}

1.2 ON101 Overview

ON101 is a semi-solid, provider-directed topical wound management matrix formulation developed to support wound-bed optimization in wounds with delayed closure progression. Its formulation includes defined botanical fractions derived from *Plectranthus amboinicus* (also known as Mexican mint) and *Centella asiatica* with preclinical and clinical evidence suggesting activity within the wound microenvironment. In the United States, ON101 has received FDA 510(k) clearance (K251093) for healthcare-professional-directed management of partial- and full-thickness wounds, post-surgical wounds, first- and superficial second-degree burns, DFUs, venous stasis ulcers, and pressure ulcers.¹⁰ Clearance establishes substantial equivalence for the specified wound-management indications and should not be interpreted as evidence of clinical effectiveness across each wound type. Preclinical evidence suggests effects on inflammatory and reparative pathways associated with chronic wound persistence.^{11,12} Randomized clinical evidence supports improved closure outcomes in selected patients with DFUs,¹⁰ whereas evidence in other wound types is preliminary and does not establish clinical effectiveness.

1.3 Purpose of this Roundtable

Comprehensive SOC remains foundational to successful wound management^{13–16}; however, clinicians frequently encounter wounds that fail to respond adequately despite adherence to accepted SOC. While emerging clinical and real-world evidence has expanded interest in ON101, questions remain regarding optimal patient selection, timing of intervention, integration with SOC, administration strategies, and implementation across clinical settings.

To address these questions, a multidisciplinary panel of wound care experts convened to review the available evidence, discuss emerging clinical experience, and develop structured expert roundtable recommendations regarding the role of ON101 in modern wound management. This manuscript summarizes the evidence reviewed by the panel and the resulting roundtable recommendations.

2. Reported Clinical Experience with ON101

2.1 Biological Rationale for ON101

Persistent inflammatory signaling and failure of the normal transition to tissue repair are particularly important in diabetic wounds.^{17–19} ON101 was developed to address biological processes associated with chronic wound persistence.^{11,12} In cellular and diabetic wound models, ON101 has been associated with changes in wound-closure progression, inflammatory signaling, pro-inflammatory macrophage activity, and macrophage populations associated with tissue repair and remodeling.^{12,20} These findings provide biological plausibility for clinical investigation, although the mechanisms underlying clinical effects remain incompletely understood.

2.2 Clinical Trial Experience in Diabetic Foot Ulcers

The strongest clinical evidence for ON101 is in patients with difficult-to-heal DFUs.^{21–25}

The pivotal clinical evaluation of ON101 was a multicenter, evaluator-blinded, randomized controlled trial (ClinicalTrials.gov NCT01898923) involving patients with Wagner grade 1 or 2 DFUs. In this study, ON101 was associated with superior closure outcomes compared with an absorbent dressing control when used in conjunction with SOC. Complete wound closure rates were significantly higher among patients treated with ON101, supporting the potential role of wound microenvironment modulation as a therapeutic strategy in chronic diabetic wounds.¹¹

Post hoc analyses further evaluated ON101 in difficult-to-heal DFU subgroups with adverse prognostic characteristics and reported treatment effects across several of these subgroups.²⁶

In the randomized trial, treatment-emergent adverse events were reported in 76 of 122 patients (62.3%) receiving ON101 and 77 of 114 patients (67.5%) receiving the comparator. Events considered treatment related occurred in 7 patients (5.7%) and 5 patients (4.4%), respectively; no serious adverse event was considered related to ON101 [10]. Complete and durable wound closure and time to closure are clinically meaningful DFU outcomes, given the risks of recurrence, infection, hospitalization, and amputation.^{21,25} Given the substantial clinical and economic burden associated with diabetic foot complications, therapies that improve wound-bed preparation may have implications extending beyond wound closure alone.

The panel members noted that treatment effects appeared to become increasingly apparent over time, consistent with the concept that restoration of a more favorable wound microenvironment may require sustained therapy before clinically meaningful differences in wound closure emerge. These observations contributed to subsequent discussions regarding patient selection, timing of intervention, and the potential role of ON101 earlier in the wound management pathway. This temporal pattern informed discussion of patient selection and treatment timing but does not establish the optimal timing of ON101 initiation.

Collectively, clinical trial evidence in difficult-to-heal DFUs provides the primary evidence base for the roundtable recommendations.

2.3 Real-World Clinical Experience

Real-world evidence provides complementary evidence from routine clinical practice, although interpretation should account for patient and wound characteristics, adherence, care setting, and continued standard care.^{5,21,22}

Chang et al.²⁷ reported favorable outcomes among patients with Wagner grade 1 to 3 DFUs treated with ON101 in routine clinical practice and observed evidence of a dose-response relationship associated with treatment exposure. These findings provide real-world evidence complementary to the randomized clinical trial.¹¹ Ng et al.²⁸ described favorable outcomes in patients with complex wounds who had failed to progress with conventional management, including successful limb salvage in selected cases. Interpretation is limited by the observational case-series design and absence of a comparator group.

Published experience from Taiwan and Singapore provides information on ON101 implementation, access, healthcare utilization, and reimbursement in routine care.^{29–31} Health-economic findings are summarized in Section 4.6; their transferability to other healthcare systems, including the US, remains uncertain because of differences in reimbursement, care pathways, resource use, and model assumptions.

A recent Bayesian network meta-analysis of 51 randomized controlled trials involving 6,161 patients suggested that ON101 ranked among the higher-performing topical interventions for wound closure compared with standard care.³² Because network rankings depend on the included evidence network and assumptions of transitivity and consistency, this indirect comparison should be interpreted cautiously and does not establish superiority over every alternative.

A preliminary US real-world analysis in mildly infected Wagner grade 2 DFUs reported greater wound-area reduction at Week 4, shorter median time to complete closure, and lower direct cost per wound closed with ON101 compared with matched SOC controls.³³ Because this analysis was small and non-randomized, these findings should be interpreted as hypothesis-generating. These findings should not be interpreted as evidence of reduced hospitalization, amputation, or total healthcare utilization, which require prospective evaluation.

2.4 Emerging Applications Across Wound Types

Although the strongest evidence supporting ON101 has been generated in DFUs, panel discussions identified several additional wound types in which the biological rationale and early clinical experience suggest potential use. Evidence in these settings remains preliminary and should be interpreted as research context rather than established clinical effectiveness.

Inflammatory and Difficult-to-Heal Wounds: Beyond DFUs, inflammatory or biologically stalled wound phenotypes remain research considerations rather than established ON101 applications. The biological rationale for investigation in these phenotypes derives from literature on persistent inflammation and wound-microenvironment dysfunction.^{17–19}

Emerging Chronic Wound Applications: Emerging evidence has been reported in venous leg ulcers (VLUs), referred to as venous stasis ulcers in the U.S. regulatory labeling. Conference presentations and retrospective analyses have suggested potential use in selected patients with chronic VLUs, particularly those demonstrating prolonged inflammation and delayed healing despite appropriate compression therapy and SOC. However,

robust prospective evidence remains limited, and further evaluation is required before conclusions regarding clinical effectiveness can be drawn.³⁴

Pressure injuries and deep tissue injuries were identified as research priorities because direct clinical evidence remains limited.

Specialized Clinical Settings: Conference presentations describe early clinical experience in acute radiation dermatitis, but peer-reviewed evidence remains limited.³⁵ Whether these findings extend to chronic radiation-associated wounds requires prospective evaluation.

Preliminary observational evidence suggests that ON101 can be incorporated with negative pressure wound therapy in difficult-to-heal DFUs, but prospective evaluation is required before routine use can be recommended.³⁶

FDA 510(k) clearance encompasses full- and partial-thickness wounds, post-surgical wounds, burns, DFUs, VLU and pressure ulcers.³⁷ Clearance defines intended use but does not establish clinical effectiveness for every wound category.

Wound-Bed Optimization Prior to Advanced Therapies: The panel identified ON101 use before cellular and tissue-based products, skin substitutes or other biologic interventions as a treatment-sequencing hypothesis requiring prospective evaluation.

Panel members reported that ON101 was readily incorporated into existing wound-care pathways, but these observations are experiential rather than comparative evidence.

3. Methods

3.1 Panel Composition

A multidisciplinary expert panel consisting of 11 participants—10 clinical experts and one wound-care research statistician and healthcare/research executive—convened in Charlotte, North Carolina, US, in April 2026 to discuss the clinical application of ON101 in wound management. The panel included clinicians and investigators with expertise in wound care, DFU management, surgery, advanced wound therapies, clinical research, and healthcare delivery. The meeting was co-chaired by Dr. Thomas Serena and Dr. Daniel Kapp.

Emily Cook, MS, attended the meeting in a medical writing capacity and was not a member of the expert panel. Sasha Frade, PhD, provided medical writing support during manuscript development and did not attend the roundtable.

Panelists were selected based on relevant clinical expertise and experience in wound care, with the aim of incorporating perspectives across specialties, practice settings, and geographic regions. Invitations were based on subject-matter expertise and experience relevant to the discussion topics; no formal geographic or stakeholder quotas were established. Because the meeting was designed as a multidisciplinary expert roundtable discussion, participation focused on clinicians. Patients, payers, and other stakeholder groups were not included, and these representation limitations should be considered when interpreting the recommendations. Broader stakeholder input should be incorporated into future roundtable work or external validation. Differences in opinion were discussed openly; when agreement was not immediate, panelists reviewed the available evidence and considered differing clinical perspectives. No formal statement-level voting was conducted. No recommendation-specific recusal process was applied.

Table 1. Panel Description

Name	Specialty/ Professional Background	Practice Setting/ Affiliation	Geographic Location	Meeting Attendance	Role
Thomas E Serena, MD	Founder, CEO, and Medical Director	SerenaGroup, Inc.	MA, USA	Yes	Co-Chair
Daniel L. Kapp, MD	Chief of Plastic Surgery; Plastic and Reconstructive Surgeon	Palm Beach Plastic Surgery Center	FL, USA	Yes	Co-Chair
John C Lantis, MD, FACS	Chief of Vascular/Endovascular Surgery	Mount Sinai Hospital	NY, USA	Yes	Panel
Michael N Desvigne, MD, FACS, CWS, FACCWS	Director Wound Reconstruction	Wound Care Specialists	AZ, USA	Yes	Panel
Laura Pfendler, PT, DPT, CWS	Director of Advanced Wound Care	Dr. Daniel L. Kapp Advanced Wound Care	FL, USA	Yes	Panel
Mark Suski, MD, FACS	Plastic Surgeon	Los Robles Hospital and Medical Center,	CA, USA	Yes	Panel
Greg Bohn, MD	Medical Director	SerenaGroup, Inc.	MA, USA	Yes	Panel
Zwelithini Tunyiswa, BA	Statistical Data Scientist	Open Wound Research	WA, USA	Yes	Panel
Mervin Low, MD	Plastic Surgeon and CEO	Newport Wound	CA, USA	Yes	Panel
Abigail E Chaffin, MD, FACS, CWSP, MAPWCA	Professor of Surgery; Medical Director, Wound Healing Institute	Division of Plastic Surgery, Tulane University School of Medicine	LA, USA	Yes	Panel
Brock A Liden, DPM, FAPWCA	Podiatrist	Wound, Ankle, Foot, and Leg	OH, USA	Yes	Panel
Emily Cook, MS	Chief Quality Officer	SerenaGroup, Inc.	MA, USA	Yes	Medical Writer
Sasha Frade, PhD	Senior Research Consultant	Open Wound Research	WA, USA	No	Medical Writer

3.2 Materials Reviewed

Prior to and during the roundtable discussion, panel members were provided with background materials relevant to ON101 and contemporary wound management. Materials considered included peer-reviewed preclinical studies, randomized clinical trial evidence, post hoc analyses, observational and real-world studies, health-economic analyses, regulatory documentation, and case-based clinical materials. Clinical experience shared by panel members during the roundtable was also considered as a distinct source of expert input. Conference presentations and posters were considered where relevant, with non-peer-reviewed evidence distinguished from published peer-reviewed evidence. A detailed summary of the evidence materials is available upon author request.

The evidence review was conducted as a narrative background review rather than a systematic review. Background materials were assembled by sponsor personnel; Oneness Biotech proposed and selected evidence for inclusion. A prespecified systematic literature search, duplicate independent screening, systematic risk-of-bias assessment, or GRADE-based certainty assessment was not undertaken.

Evidence considered during subsequent manuscript development was distinguished from materials available at the time of the April 2026 roundtable. During manuscript development, an independent targeted literature search was conducted using PubMed and Google Scholar between 18 June and 20 July 2026 to identify additional relevant evidence and assess the completeness of the evidence base. Search terms included combinations of keywords relating to ON101 and its components; diabetic foot ulcers, chronic wounds, wound healing and wound-bed preparation, wound-microenvironment biology, inflammation, clinical and real-world outcomes, health-economic outcomes, and the wound types and clinical applications addressed in the manuscript. Reference lists of relevant publications were also reviewed to identify additional sources.

Evidence was considered for inclusion when directly relevant to ON101, its biological rationale, clinical outcomes in DFUs, standard wound-care principles underpinning the roundtable recommendations, health-economic or implementation considerations, or the emerging applications discussed by the panel. Eligible evidence included peer-reviewed preclinical and mechanistic studies, randomized and observational clinical studies, real-world evidence, health-economic analyses, relevant clinical guidelines, regulatory documentation, and relevant conference abstracts or posters. Duplicate reports and sources without clear relevance to the roundtable questions were excluded. Evidence published or presented after the roundtable was incorporated, where relevant, to update and contextualize the manuscript but did not retrospectively inform the roundtable discussion or the development of the initial roundtable themes and statements.

For purposes of evidence characterization, sources were categorized using a descriptive hierarchy based on study design and evidence type: Level 1, randomized prospective clinical evidence; Level 2, post hoc analyses and peer-reviewed observational or real-world clinical evidence; Level 3, peer-reviewed mechanistic/preclinical and health-economic evidence; Level 4, conference abstracts or posters and regulatory documentation; and Level 5, expert clinical experience or opinion. The evidence hierarchy was used to distinguish evidence-supported principles from conditional, hypothesis-generating, and research-only roundtable recommendations; it was not intended to constitute a formal assessment of certainty or risk of bias.

3.3 Roundtable Process

The structured expert roundtable was conducted as part of a 4.5-hour meeting. The agenda included a 45-minute Round Table Discussion followed by a 45-minute Roundtable Statement Development Session, in addition to presentations on clinical evidence, clinical experience and case review, and implementation considerations. The meeting was recorded to facilitate accurate documentation of the discussion and identification of areas of agreement.

Discussion was guided by predefined questions and case-based clinical scenarios designed to explore practical considerations regarding ON101 use in routine clinical practice. Key topics included appropriate patient and wound selection, timing of intervention within the treatment pathway, integration with SOC practices, debridement considerations, administration and dosing strategies, positioning relative to existing wound care products, economic and operational considerations, and future research priorities.

Panel members reviewed available preclinical, clinical trial, real-world, regulatory, and emerging evidence relating to ON101 and shared their individual clinical experiences. Areas of agreement, disagreement, and uncertainty were explored through open discussion, with particular emphasis on practical implementation and integration into existing wound care pathways.

Representatives of Oneness Biotech were present during the meeting and presented a slideshow but did not participate in the expert roundtable discussion or statement-development session.

Following the meeting, the recorded discussion, predefined questions, and major areas of agreement were synthesized and organized into draft roundtable statements. These statements were subsequently circulated to and reviewed by all panelists during manuscript development to ensure they accurately reflected the discussion and the evidence reviewed by the panel. Voting status was not applicable, as no formal vote was conducted and no prespecified agreement threshold was applied.

3.4 Statement Development

The final statements represent expert recommendations informed by the evidence and collective clinical experience rather than formal clinical practice guidelines. Recommendations were intended to reflect expert opinion informed by available preclinical, clinical, and real-world evidence. Where evidence was limited or emerging, statements were deliberately framed as areas of potential clinical interest or future research priorities rather than as established clinical recommendations. Representatives of Oneness Biotech were present during the meeting and presented a slideshow but did not participate in the expert roundtable discussion or statement-development session.

4. Roundtable Recommendations

4.1 Patient and Wound Selection

Roundtable Statement 1 (Conditional recommendation; strongest evidence in DFUs):

ON101 may be considered for DFUs characterized by delayed closure progression; its use in other chronic wound types requires prospective evaluation.

Evidence basis: Level 1 randomized clinical evidence in DFUs,¹¹ supported by Level 2 post hoc and real-world evidence^{26,27} Application to non-DFU chronic wound types is based primarily on Level 3 mechanistic evidence^{12,20} and Level 5 expert clinical opinion.

The strongest ON101-specific evidence is in difficult-to-heal DFUs. Persistent inflammation, recurrent biofilm, excessive exudate, delayed granulation, and failure to progress despite appropriate care were identified as clinical features of interest; applications beyond DFUs require prospective evaluation.

Wound chronicity alone should not determine treatment selection; clinicians should consider biological indicators of impaired healing and the overall closure trajectory.

Roundtable Statement 2 (Conditional recommendation; DFU evidence with extrapolation to other high-risk populations):

ON101 may be considered in selected high-risk patients with difficult-to-heal DFUs, although subgroup-specific benefit in patients at increased risk for impaired wound healing, including individuals with diabetes, end-stage renal disease (ESRD), poorly controlled metabolic disease, multiple comorbidities, or other factors associated with delayed wound progression, remains unconfirmed

Evidence basis: Level 1 and Level 2 DFU evidence supports ON101 use in difficult-to-heal DFUs.^{11,26,27} while identification of ESRD, poor metabolic control, vascular disease, and other high-risk characteristics is supported by established prognostic literature.^{21,24,38} Extension of ON101-specific benefit to these broader high-risk subgroups remains conditional and is partly based on Level 5 expert opinion.

Diabetes, end-stage renal disease, poor metabolic control, vascular disease, and multiple comorbidities increase healing risk but are not established predictors of differential response to ON101. Subgroup-specific benefit requires prospective evaluation.

ON101 may be incorporated within comprehensive care while modifiable systemic factors are addressed, although this sequencing has not been prospectively evaluated in the broader high-risk populations discussed.

4.2 Timing of Intervention

Roundtable Statement 3 (Evidence-supported prognostic principle):

Clinicians can often identify wounds at high risk for delayed healing early in the treatment course using clinical, patient, and wound-related prognostic factors.

Evidence basis: Evidence-supported prognostic principle based on prospective and observational DFU literature demonstrating that early wound-area reduction predicts subsequent closure.^{24,38} This evidence supports early risk stratification but does not establish ON101-specific efficacy or optimal treatment timing.

Clinicians can often recognize wounds at risk for delayed healing before complete treatment failure by integrating wound trajectory, patient risk factors, and indicators of wound biology.

Relevant warning signs include persistent inflammation, biofilm burden, prolonged wound duration, poor metabolic or vascular status, multiple comorbidities, and inadequate wound-area or granulation response despite appropriate care.

During the first weeks of care, wound assessment and response to optimization provide information that can trigger reassessment or escalation. Early risk recognition should intensify comprehensive care rather than replace it.

Within this framework, 4-week percentage area reduction (PAR) may serve as a pragmatic prognostic marker for clinical decision-making. In DFU care, 4-week PAR can inform reassessment, continued optimization, or escalation.^{24,38} This prognostic association does not establish the optimal timing of ON101 initiation. ON101-specific use of 4-week PAR as a treatment-response marker requires prospective validation, particularly in high-risk populations.

Roundtable Statement 4 (Conditional expert recommendation; optimal timing not prospectively tested):

ON101 may be incorporated during the early wound management period as part of active wound-bed optimization rather than being reserved only after complete failure of standard care.

Evidence basis: Conditional expert recommendation informed by the prognostic literature on early wound trajectory,^{23,38} Level 2 preliminary ON101 real-world evidence,³³ and Level 5 expert opinion. No prospective study has directly compared early versus delayed ON101 initiation.

The panel favored reassessment and active wound-bed optimization before complete treatment failure, while recognizing that standard care remains essential.

ON101 may be considered as an adjunct during active wound-bed management in wounds showing inflammation, delayed progression, or other indicators of impaired healing.

Considering that available studies did not yet prospectively compare early versus delayed initiation, the optimal timing of ON101 remains to be determined. The panel considered earlier incorporation during active wound-bed management a conditional clinical strategy requiring prospective evaluation.

4.3 Integration with Standard Care

Roundtable Statement 5 (Evidence-supported standard-care principle):

ON101 should be used as an adjunct to, and not a replacement for, established wound care principles.

Evidence basis: Evidence-supported standard-care principle based on established wound-management guidance.^{13–17,22} ON101-specific integration is supported by Level 1 DFU trial evidence in which treatment was used alongside standard wound care,¹¹ with implementation considerations additionally informed by Level 5 expert opinion.

ON101 should complement comprehensive wound management directed at wound etiology and patient-specific barriers to closure. For DFUs, comprehensive care includes offloading, glycemic optimization, infection management, vascular assessment, and monitoring; corresponding etiologic care includes compression for VLU and pressure redistribution for pressure injuries.

Treatment should be individualized according to wound etiology, comorbidities, care setting, and patient risk.

Roundtable Statement 6 (Evidence-supported standard-care principle; ON101 integration conditional):

Appropriate wound-bed preparation, including debridement when clinically indicated, remains foundational to successful ON101 use.

Evidence basis: Evidence-supported wound-care principle based on established wound-bed preparation literature^{17,18} and contemporary DFU management guidance.²² The positioning of ON101 within this framework is supported by Level 1 DFU evidence¹¹ and Level 5 expert clinical experience.

Wound-bed preparation should be ongoing and individualized, with cleansing and debridement performed when clinically appropriate. Pain, ischemia, tissue fragility, and patient tolerance may limit debridement intensity. Clinicians should also reassess alternative causes of nonhealing, including infection, inadequate perfusion, and malignant transformation where clinically suspected.

4.4 Administration and Dosing

Roundtable Statement 7 (IFU-aligned administration; panel implementation considerations identified):

ON101 should be applied as a thin layer, and clinicians should avoid excessive product utilization.

Evidence Basis: Label-supported administration based primarily on the current U.S. Instructions for Use and FDA regulatory documentation.^{37,40} Practical application observations from the panel represent Level 5 expert experience and should be distinguished from formal product labeling.

Practical administration considerations emerged as an important component of the discussion. Panel members consistently emphasized ON101 as being applied in a thin layer directly to the wound-bed by cotton swab or tongue depressor, with careful attention to achieving adequate coverage without unnecessary product use.

Consistent with the current U.S. Instructions for Use (IFU), ON101 is for topical use in adults as directed by a physician or healthcare professional. After cleansing the wound, the product should be applied evenly based on clinical assessment, with the amount varying according to wound size.³⁹ Following application, the wound should be covered with an appropriate secondary dressing, such as gauze.³⁹ The IFU does not specify use of a cotton swab, tongue depressor, or applicator-disposal procedure; these are panel implementation considerations rather than labeled directions. The tube is for a single patient use.³⁹

The panel emphasized using only the amount necessary for appropriate wound coverage to reduce unnecessary variation in product use. The panel also emphasized adherence to the product's current safety instructions. The IFU contraindicates use in patients with known sensitivity or allergy to any ingredient and use for third-degree burns or control of heavy bleeding. If infection is present, ON101 should be used concurrently with systemic antibiotic therapy as directed; observed signs of infection require appropriate physician- or healthcare-professional-directed treatment.³⁹

Clinician education should distinguish panel application practices from the IFU, which directs single-patient use, storage and transport at 15°C to 30°C away from sunlight, no freezing, and disposal with domestic waste after sealing.³⁹

Roundtable Statement 8 (Research-only recommendation):

Standardized dosing guidance based on wound surface area would facilitate consistent implementation across care settings.

Evidence basis: Research-only recommendation derived primarily from Level 5 expert discussion regarding dosing consistency and implementation. No validated wound-surface-area dosing framework has yet been established for ON101; current use should follow the U.S. IFU.

The current IFU suggests clinical assessment of wound size for dosing and does not provide a surface-area dosing formula.³⁹ Future research should evaluate whether wound-size-based dosing can reduce variation in product use and support consistent education and implementation.

Potential frameworks, such as gram-per-square-centimeter guidance, require validation before clinical use.

4.5 Clinical Settings

Roundtable Statement 9 (Conditional implementations consideration):

ON101 may be considered for implementation across different provider-directed care settings where appropriate wound assessment, monitoring, and comprehensive standard care can be maintained; evidence regarding implementation and outcomes across individual care settings remains limited.

Evidence basis: Conditional implementation recommendation informed primarily by Level 2 real-world clinical evidence in outpatient practice^{27,28,33} and Level 5 expert experience. Direct comparative evidence across hospitals, skilled nursing facilities, home health, and mobile wound-care settings is limited.

Implementation across care settings remains primarily an expert-experience consideration. Skilled nursing, home-health, and mobile-care settings warrant further study because staffing, assessment practices, access, and patient complexity may influence implementation and outcomes.

4.6 Economic Considerations

Roundtable Statement 10 (Hypothesis-generating recommendation):

Earlier intervention may have the potential to reduce downstream healthcare utilization associated with prolonged wound closure.

Evidence basis: Hypothesis-generating recommendation informed by Level 2 preliminary U.S. real-world economic evidence³³ and Level 3 health-economic analyses from Taiwan and Singapore.^{29–31} Transferability across healthcare systems is uncertain, and prospective U.S.-based economic evaluation is required.

Economic evaluation should focus on complete closure, time to closure, early wound-area reduction, subsequent interventions, healthcare encounters, and total cost of care rather than acquisition cost alone.

The most directly applicable U.S. evidence currently available is a preliminary real-world analysis of mildly infected DFUs managed in an outpatient setting, in which ON101 was used with physician-directed wound care and appropriate infection management.³³ In that non-randomized analysis of 12 cases, ON101 was associated with faster 4-week wound improvement and an approximately 19% lower direct cost per wound closed compared with matched standard-care controls selected in 1:1 prioritized matching approach based, in order, on wound location and ulcer natural history, wound size, comorbidities potentially affecting wound healing (particularly peripheral arterial disease and its treatment status), and age. ON101 was associated with significantly greater wound-area reduction and a higher normalized healing slope at Week 4.

In a separate exploratory cost-minimization analysis of nine evaluable wounds, direct cost per wound healed was approximately 19% lower with ON101 than with SOC. The direct-cost model included healing duration, evaluation-and-management visits, wound dressing or treatment costs per application, dressing-change frequency, and debridement procedures; professional-service unit costs were based on 2025 Centers non-randomized for Medicare & Medicaid Services Physician Fee Schedule national averages. Given the small sample, design, and U.S. outpatient cost inputs, the result is hypothesis-generating and may not be transferable to other settings; larger prospective studies are required to confirm generalizability, durability, and cost impact.

Model-based economic evaluations from Taiwan and Singapore projected potential clinical and economic outcomes associated with ON101 when used with general wound care.^{29,31} These are model-derived estimates rather than demonstrated benefits, and differences in reimbursement, care pathways, resource use, unit costs, and model assumptions limit direct transferability to U.S. settings.

4.7 Research Priorities

Roundtable Statement 11 (Research-only recommendation):

Future research should evaluate ON101 in wound populations beyond diabetic foot ulcers, including radiation-associated wounds, pressure injuries, ischemic wounds, and other inflammatory wound phenotypes.

Evidence basis: Research-only recommendation informed by Level 3 mechanistic/biological rationale,^{12,20} Level 4 emerging conference evidence in venous stasis ulcers and acute radiation dermatitis,^{34,35} and Level 5 expert clinical opinion. Clinical effectiveness outside DFUs has not been established prospectively.

These non-DFU applications remain research priorities rather than established clinical indications.

Future studies should identify clinical phenotypes, biological characteristics, and risk profiles associated with treatment response.

Roundtable Statement 12 (Research-only recommendation):

Future studies should investigate comparative effectiveness, dosing optimization, health-economic outcomes, implementation strategies, and mechanistic biomarkers associated with ON101 therapy.

Evidence basis: Research-only recommendation derived from gaps identified across the Level 1–4 evidence base, including limited comparative effectiveness data, emerging combination-therapy evidence,³⁶ incomplete dosing evidence, mechanistic uncertainty,^{12,20} and evolving health-economic evidence.^{29–31,33} Prioritization of these research areas additionally reflects Level 5 expert opinion.

Future research should address comparative effectiveness, dosing and duration, biomarkers, treatment sequencing, implementation, adherence, resource use, and total cost of care. Comparative studies against commonly used topical, debridement, and advanced wound-care approaches may help clarify treatment positioning within multidisciplinary pathways.

5. Clinical Algorithm

Based on the structured expert roundtable discussion and available evidence, the panel developed a conceptual clinical algorithm illustrating the potential integration of ON101 into modern wound management pathways (**Figure 1**). The principal pathway focuses on DFUs, for which the ON101 evidence base includes randomized clinical trial and real-world evidence. The algorithm emphasizes comprehensive assessment, risk stratification, identification and management of potentially reversible contributors to delayed closure, and continuation of standard wound care throughout.

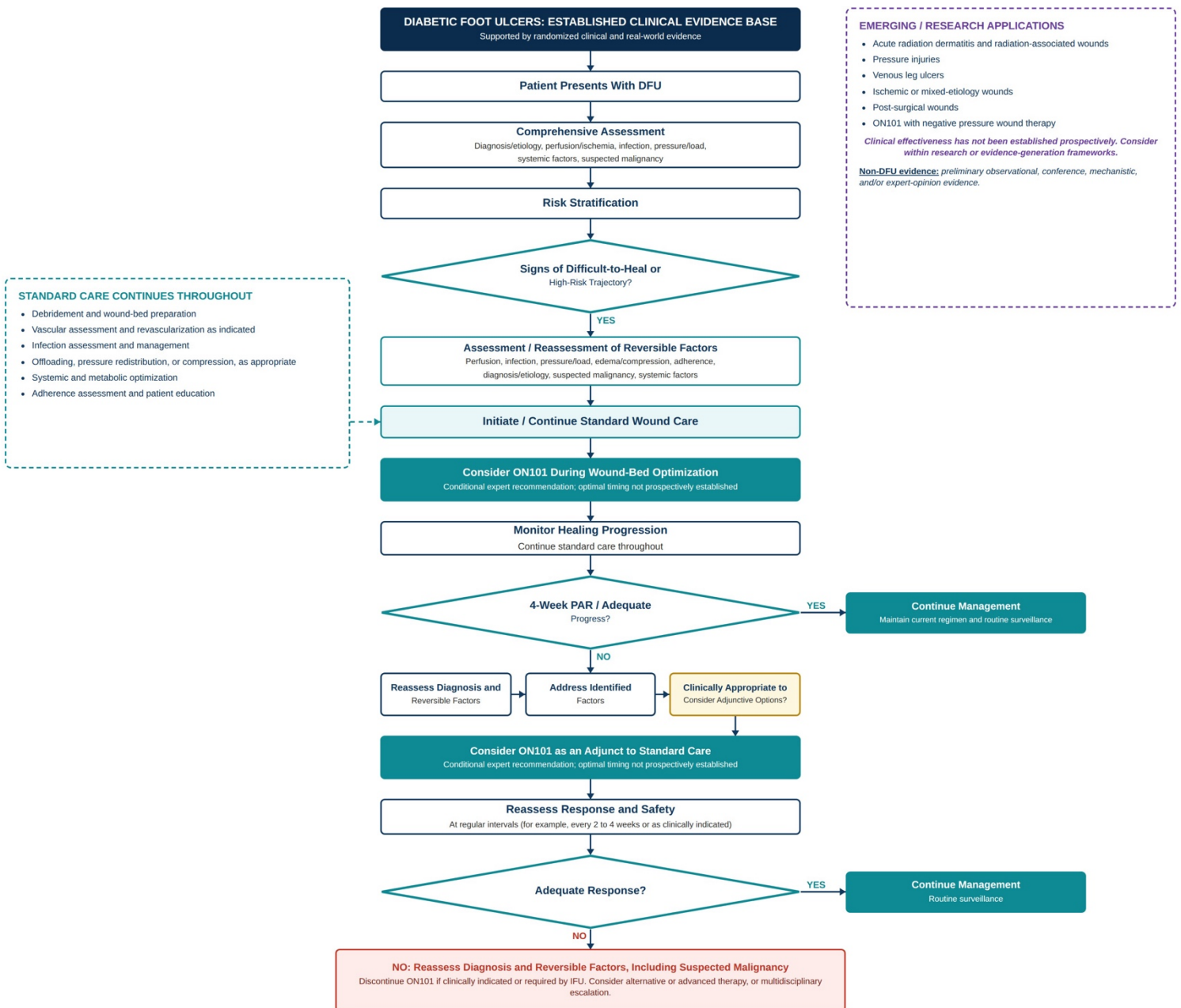
Wound progression should be reassessed at clinically appropriate intervals. In DFUs, 4-week percentage area reduction (PAR) is presented as a prognostic reassessment marker, not as a criterion for ON101 initiation. Where progress is inadequate, clinicians should first reassess the diagnosis and reversible contributors to delayed closure and address identified factors. Following reassessment and optimization of standard care, ON101 may be considered as an adjunct during wound-bed optimization when clinically appropriate. This represents a conditional expert recommendation, as the optimal timing of ON101 initiation has not been prospectively established. Ongoing assessment of response and safety should guide continuation, discontinuation, or escalation of treatment.

The algorithm separately identifies emerging and research applications outside the established DFU evidence pathway, including radiation-associated wounds, pressure injuries, venous leg ulcers, ischemic or mixed-etiology wounds, post-surgical wounds, and ON101 use with negative pressure wound therapy. Evidence in these settings remains preliminary, and clinical effectiveness has not been prospectively established. The algorithm is therefore intended as a conceptual framework to support clinical reasoning rather than a validated clinical guideline and should be interpreted alongside the current U.S. Instructions for Use (IFU), applicable clinical guidance, and individual clinical judgment.

Figure 1. Expert Roundtable-Derived Conceptual Algorithm for Integration of ON101 into the Wound Care Pathway.

Chronic Wound Management: Clinical Treatment Pathway

Assessment → Standard Care → ON101 Optimization → Escalation



Eligibility, exclusions, contraindications, warnings, and discontinuation should follow the current U.S. IFU and individual clinical judgment.

Note: The algorithm distinguishes the evidence-supported DFU pathway from emerging or research-only applications. Eligibility, exclusions, contraindications, warnings, administration, and discontinuation should follow the current U.S. IFU and individual clinical judgment

6. Discussion

6.1 Clinical Implications

Early wound trajectory, including four-week percentage area reduction in DFUs, supports timely reassessment and escalation decisions.^{23,38} It does not establish the optimal timing of ON101 initiation.

Importantly, the panel consistently emphasized that ON101 should be viewed as an adjunctive therapy rather than a replacement for established wound care principles. This position is consistent with modern guideline recommendations, including those of the International Working Group on the Diabetic Foot, which continue to emphasize offloading, infection management, vascular assessment, debridement, and optimization of systemic risk factors as the foundation of care.²² Similarly, wound-bed preparation remains central to successful management of chronic wounds regardless of the advanced therapies employed.¹⁷ The roundtable recommendations therefore support integration of ON101 within established wound management frameworks rather than the creation of parallel treatment pathways.

Future prospective studies should assess whether improved closure and time to closure are accompanied by fewer interventions, encounters, hospitalizations, or escalations to advanced therapy.

6.2 Implementation Considerations

Successful implementation of ON101 will likely depend on its integration within existing wound care pathways rather than adoption as a standalone intervention. Throughout the discussion, panel members consistently emphasized that ON101 should complement established SOC, including wound-bed preparation, debridement when indicated, infection management, vascular assessment, offloading, compression therapy, and optimization of systemic risk factors. Within SOC, the panel hypothesizes that ON101 might help address a potential early wound-bed optimization gap by providing an earlier topical intervention before escalation to more complex advanced therapies. This positioning may be particularly relevant in physician-directed outpatient and hospital-based wound programs, where early wound trajectory can inform continued management, reassessment, and escalation decisions. This perspective is consistent with current wound management frameworks, which recognize that advanced therapies are most effective when incorporated within comprehensive multidisciplinary care programs.^{13,15}

Clinician education should address patient selection, wound assessment, application technique, and integration with comprehensive care.

Overall, the panel concluded that successful implementation of ON101 will depend upon appropriate patient selection, integration with established wound care practices, standardized administration, clinician education, and continued evaluation within real-world clinical settings. These considerations will be important as evidence continues to evolve and broader clinical experience is accumulated.

6.3 Limitations

Several limitations should be considered when interpreting the findings of this structured expert roundtable. The recommendations reflect expert opinion informed by available evidence and clinical experience rather than a formal evidence-based guideline process. No formal voting, prespecified agreement threshold, Delphi process, or systematic guideline methodology was used; the recommendations should therefore be viewed as expert guidance rather than prescriptive SOC.

The strength of evidence also varies substantially across wound types and applications. The most robust evidence currently exists in DFUs, where randomized controlled trial data, subgroup analyses, and emerging

real-world evidence are available. Evidence for radiation-associated wounds, pressure injuries, VLU, ischemic wounds, mixed-etiology ulcers, and other wound populations is based primarily on biological rationale, early clinical experience, observational evidence, conference presentations, or expert opinion. These, therefore, remain emerging areas of investigation rather than established indications.

Several topics—including optimal timing of intervention, comparative effectiveness, treatment sequencing, dosing strategies, health-economic impact, and biomarker-guided patient selection—remain incompletely characterized and require prospective evaluation. Generalizability may also be limited by heterogeneity in wound etiology, comorbidities, vascular and infection status, care setting, reimbursement environment, and access to multidisciplinary care.

The findings are also influenced by panel composition and may have differed with other specialties, geographic representation, healthcare delivery models, or clinical experience. The structured expert roundtable and associated manuscript development were funded by Oneness Biotech Co., Ltd., the manufacturer of ON101. Although the authors retained responsibility for the scientific interpretation and final manuscript content, manufacturer sponsorship represents a potential source of perceived bias and should be considered when interpreting the roundtable recommendations.

A related limitation is the absence of a formal conflict-management or recusal procedure during statement development, despite the financial relationships between several panelists and Oneness Biotech disclosed in the Conflicts of Interest section. No panelist was recused from any statement on that basis, which should be considered when interpreting the roundtable statements.

The roundtable did not include patients or caregivers, payer representatives, nurses without prescribing authority, or dedicated roundtable methodologists. Their absence may limit representation of patient-centered, implementation, reimbursement, and methodological perspectives.

Accordingly, the roundtable should not be interpreted as independently establishing comparative clinical improvement, reduced healthcare utilization, or economic benefit. Rather, it provides clinical context for interpreting the relevance of these outcomes when considered alongside comparative clinical evidence.

6.4 Future Directions

Research priorities are summarized in Statements 11 and 12 and include non-DFU populations, comparative effectiveness, treatment timing and sequencing, dosing, biomarkers, implementation, and health-economic outcomes.

A prospective, multicenter randomized controlled trial (clinicaltrials.gov #NCT07779239) is planned in the United States to further evaluate ON101 in patients with diabetic foot ulcers. If initiated, the study could provide additional evidence regarding the comparative clinical effectiveness of ON101 and its potential role within multidisciplinary wound care pathways in the United States.

7. Conclusion

This multidisciplinary expert roundtable considered ON101 a potential adjunct to comprehensive care for difficult-to-heal DFUs during wound-bed optimization.

The strongest evidence remains in DFUs, while effectiveness in other wound types and the optimal timing of treatment require prospective study. Continued evidence generation is needed to define patient selection, clinical positioning, and outcomes across modern wound-care pathways.

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