ChronEx Phase II Study Results

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Conflict of Interest Disclosure

Dr. Snyder is Senior Vice President, Global Medical Affairs at MediWound Ltd.

No other relevant conflicts of interest.

Bromelain Based Enzymatic Debridement (BBD)

A fully controlled process - from plant to a sterile pharmaceutical-grade product

Pineapple stem harvest

Protein extraction

Purification, enrichment, stabilization

Bottling and distribution

Bromelain enriched mixture of proteolytic enzyme derived from pineapple stems

BBD Products

Acute Injuries

NexoBrid® (8.8%)

Approved therapy for burn care

Indication: Eschar removal in deep partial and full-thickness thermal burns in adults and pediatric (US/EU/JP/AUS)

Target users: Hospitalized patients

Treatment: Single application for 4 hours

Clinical Evidence: Post marketing experience in >16,000 patients since 2012

Planned studies: Blast injuries and Friction Burns

Chronic Wounds

EscharEx® (5%)

Investigational enzymatic therapy for wound care

Targeted Indication: Debridement and facilitation of wound closure for chronic/hard-to-heal wounds

Target users: Chronic wound care settings

Treatment: up to 8 daily applications

Clinical evidence: Phase II studies in VLU, DFU, Traumatic ulcers

Planned and Ongoing studies: Ongoing Phase 3 VLU, Planned phase 2 DFU, proof of concept in Pressure Ulcers

ChronEx – Multicenter, Randomized, Controlled Phase II Study

[1] A standardized selection of non-active dressings to be applied according to their approved label or investigator discretion. Compression wraps were mandatory

[2] Non-Surgical Standard of Care - a standardized selection of non-active dressings or enzymatic debridement to be applied according to their approved label or investigator discretion. Compression wraps were mandatory

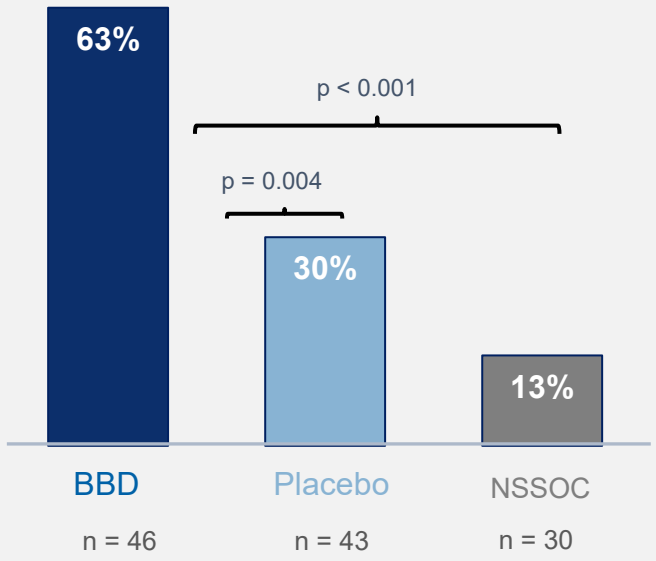
Baseline Characteristics

Parameter	BBD (n=46)	Gel vehicle (N=43)	NSSOC (N=30)	All (N=119)
Age (years) - Mean (SD)	65.5 (12.2)	61.4 (12.6)	65.5 (12.7)	64.0 (12.5)
Female Gender - n (%)	20 (43.5)	16 (37.2)	19 (63.3)	55 (46.2)
Wound age (weeks) - Mean (SD)	26.8 (20.5)	39.5 (27.6)	25.7 (20.7)	31.1 (24.0)
Wound size (cm2) - Mean (SD)	13.3 (20.4)	18.9 (18.1)	14.7 (20.1)	15.7 (19.5)
Non-viable tissue (%) - Mean (SD)	72.2 (13.7)	77.7 (14.8)	68.4 (16.7)	73.2 (15.2)

BBD's baseline characteristics were balanced between treatment arms
Wounds treated with Gel Vehicle tended to be older and larger in size (NSS)

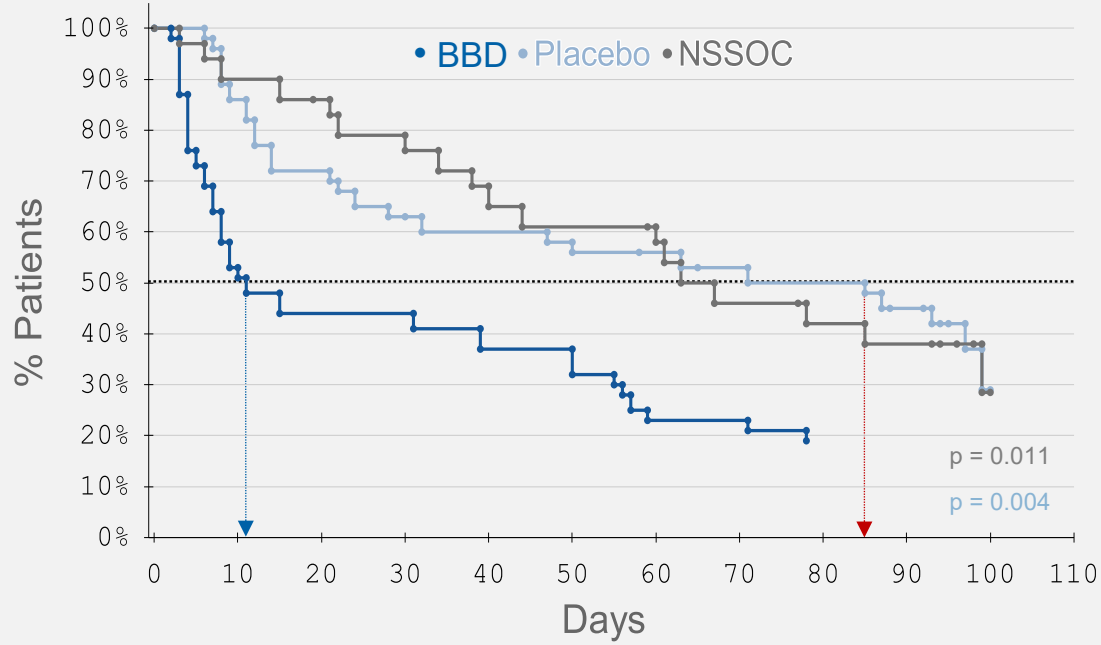
BBD Superiority vs. Placebo and Standard of Care

Complete debridement within 2 weeks
(primary endpoint)



BBD 63% vs. placebo 30%

Time to wound bed prepared
(complete debridement + healthy granulation tissue)



Median time: BBD 11 days vs. placebo 85 days

1. Shoham et al. 2024; LANCET's eClinicalMedicine

Adverse Events

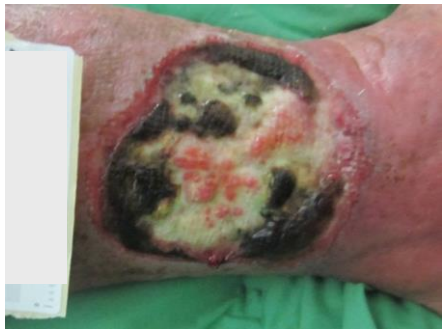
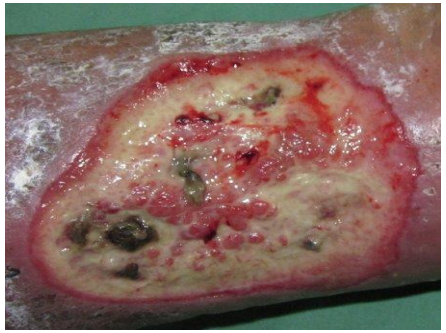
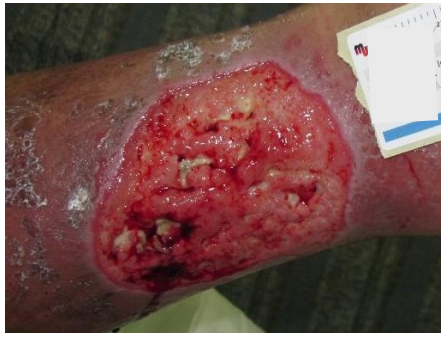
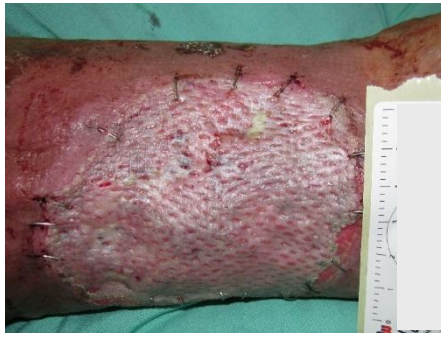
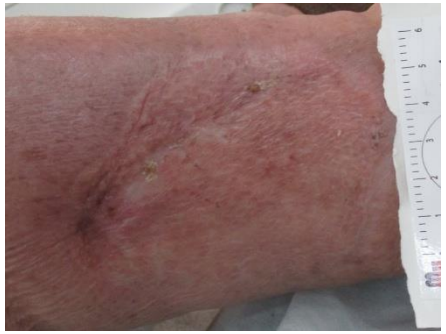
- Most common AEs (≥ 5%) in any treatment arm by decreasing order of frequency

Preferred Term	BBD (N=46) n (%)	Gel Vehicle (N=43) n (%)	NSSOC (N=30) n (%)
At least one AE	24 (52.2%)	27 (62.8%)	14 (46.7%)
Cellulitis	4 (8.7%)	10 (23.3%)	5 (16.7%)
Skin maceration	4 (8.7%)	4 (9.3%)	1 (3.3%)
Skin exfoliation	4 (8.7%)	3 (7.0%)	1 (3.3%)
Wound infection	4 (8.7%)	2 (4.7%)	2 (6.7%)
Skin ulcer	3 (6.5%)	0	2 (6.7%)
Erythema	2 (4.3%)	1 (2.3%)	2 (6.7%)
Blood glucose increase	1 (2.2%)	0	2 (6.7%)
Chest pain	0	0	2 (6.7%)
Skin erosion	0	0	2 (6.7%)

- **BBD** was safe and well tolerated
- Reduced frequency of cellulitis in **BBD** vs. NSSOC
- Increased frequency of skin maceration in **BBD** vs. NSSOC; **BBD** comparable to Gel Vehicle
- No related SAEs

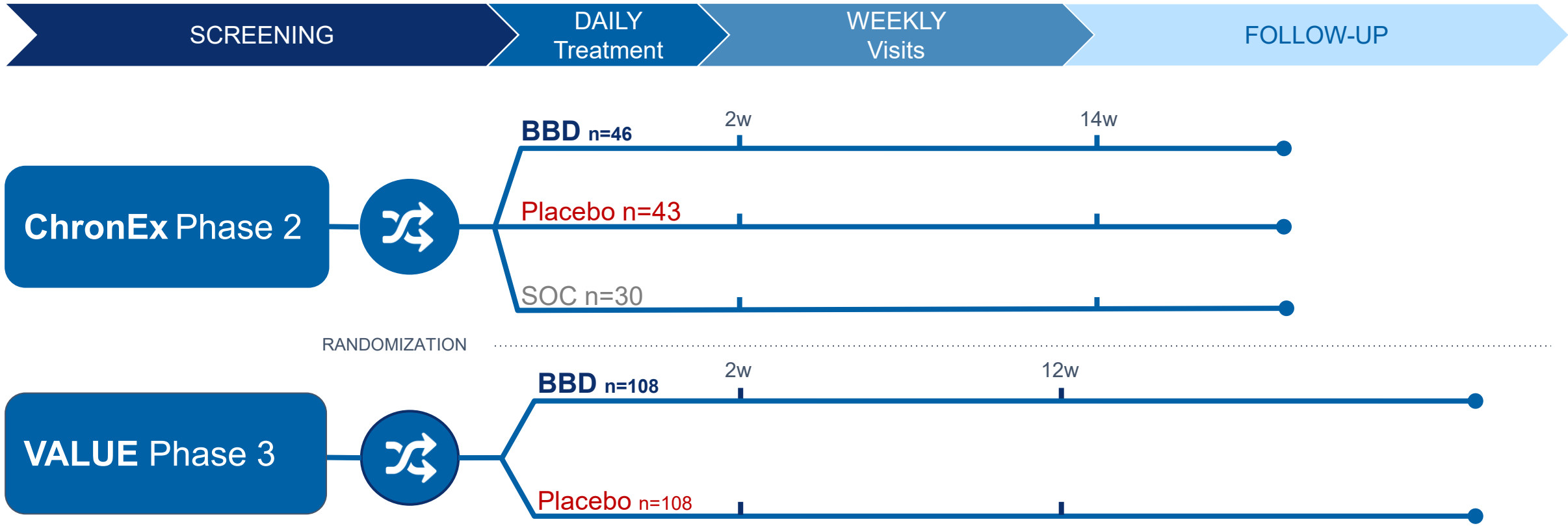
Case Study

Patient: 80-years-old female
Clinical presentation: 68cm² VLU on left lower leg
Treatment: Debridement with BBD; autograft placed week 1

Screening	Post 1st Tx	Post 7th Tx	Week 1	3 Months
				

Treatment timeline

Phase 3 Study: Proven Phase 2 Design + Key Enhancements



- ✓ Sample size based on ChronEx data vs placebo
- ✓ Interim analysis for sample size re-assessment
- ✓ Mandatory active wound closure (CTP/autograft)
- ✓ Standardized dressings

VALUE Phase 3 Trial

STUDY OBJECTIVES

Assess safety and efficacy of **BBD** compared to placebo in VLU patients

STUDY DESIGN

A global (US, EU, ROW), randomized, double blind, adaptive design study in VLU patients

Two arms: BBD vs. placebo, 1:1 ratio

Sample size: 216 VLU patients

Study design:

- Up to 8 applications over 2 weeks, followed by 12 weeks of standardized wound management
- Advanced wound closure (Autograft/CTP) for patients reaching wound bed prepared (WBP)
- 3-month patient follow-up

ENDPOINTS

Co-Primary:

Incidence of complete debridement

Facilitation of wound closure, as measured by time to wound closure

Summary and Conclusions

- BBD was superior to standard of care in the incidence and time to complete debridement
- BBD demonstrated efficacy beyond debridement
  - *Promotion of healthy granulation tissue was achieved faster than standard of care*
  - *Healthy granulation tissue is the aim of WBP, leading to complete wound closure (Shultz, 2003)*
- Comparable safety profile to gel vehicle and standard of care

BBD's advantage in facilitation of active wound closure, is being assessed in an ongoing, global, Phase 3 randomized controlled study (VALUE)

Thank You!