WOUND BED PREPARATION IS A PREREQUISITE FOR WOUND CLOSURE

POST-HOC ANALYSIS FROM THE CHRONEX MULTICENTER RCT

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Overview

INTRODUCTION

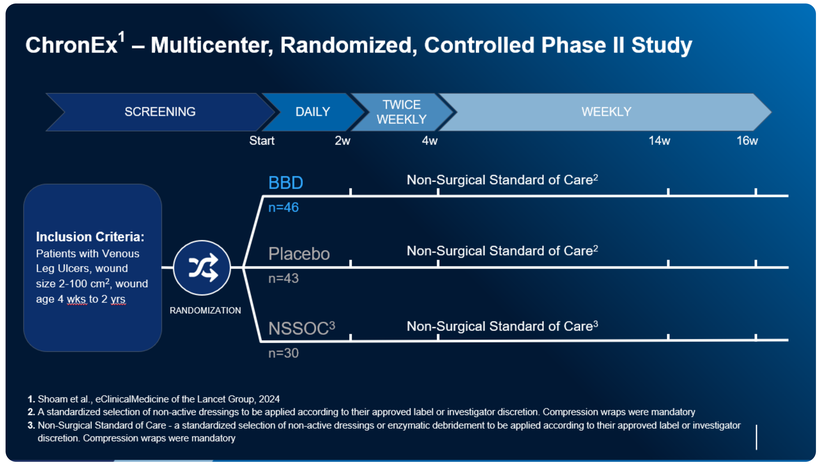
Wound bed preparation (WBP) is a critical step in transitioning chronic wounds from a disrupted to a healing state. It involves removal of non-viable tissue, reduction of infection and inflammation, maintenance of a moist environment, and promotion of keratinocyte migration from wound edges, all supportive of healing. Schultz et al. (2003) identified healthy granulation tissue as the ultimate goal of WBP. The ChronEx randomized controlled trial (RCT), which assessed a novel bromelain-based enzymatic debridement (BBD) in venous leg ulcers (VLUs), provided a unique opportunity to evaluate the relationship between achieving WBP and wound closure (WCL).

METHODS

Patients with chronic VLUs were randomized (3:3:2) to receive BBD, placebo gel, or non-surgical standard of care (NSSOC) for up to 2 weeks or until complete debridement, followed by 12 weeks of standardized NSSOC. WBP was defined as complete debridement with full granulation tissue coverage; WCL as full re-epithelialization without drainage, confirmed at two consecutive visits. The incidence of WCL was compared between patients who did or did not achieve WBP at any point. Additionally, WCL incidence during the 12 weeks follow-up was compared based on whether WBP was achieved by Day 14. The correlation between time to WBP and time to WCL was assessed using a time-dependent Cox proportional hazards model.

The ChronEx Phase II Study

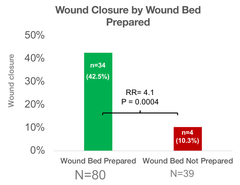
Of the 119 patients randomized, 46 were treated with BBD, 43 with placebo, and 30 with NSSOC. The mean age was 64 years (SD 12.5), with 46% females. The average wound size was 15.7 cm² (SD 19.5), average non-viable tissue was 73.2% (SD 15.2), and average wound age was 31.1 weeks (SD 24.0). Overall, 80 patients (67%) achieved WBP, among whom 34 (42.5%) achieved WCL.



Shoham et al. 2024; LANCET's eClinicalMedicine

Results

Correlation – WBP to WCL Anytime During Study



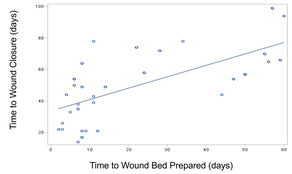
WBP and Wound Closure Matrix

		Wound Closure	
		Yes (n=38)	No (n=81)
Wound Bed Prepared	Yes (n=80)	34	46
	No (n=39)	4	35

Negative Predictive Value (NPV) - 35/39 = 89.7%
Positive Predictive Value (PPV) - 34/80 = 42.5%

WBP is essential for wound healing
Wound bed not prepared – very low probability to heal

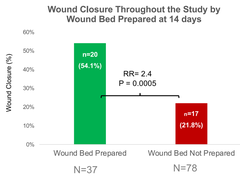
Time to WBP vs. Time to WCL



Spearman correlation = 0.66
p-value < 0.0001

Time to WBP is correlates with Time to Wound Closure

Landmark Analysis: WBP at 14 Days and Odds of Wound Closure



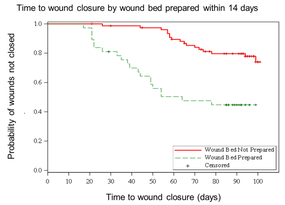
WBP and Wound Closure Matrix

		Wound Closure	
		Yes (n=37)	No (n=78)
Wound Bed Prepared	Yes (n=80)	20	17
	No (n=39)	17	61

Negative Predictive Value (NPV) - 61/78 = 78.2%
Positive Predictive Value (PPV) - 21/37 = 54.1%

Wound Bed Preparation within 14 Days Could Predict Wound Closure
Wound bed not prepared within 14 days decrease likelihood to heal

Landmark Analysis: WBP at 14 days and Time to Wound Closure



Estimated Median time to WCL:
- Wound bed prepared – 64 days
- Wound bed not prepared – not applicable

(P<0.0001)

WBP within 14 Days Associated with Faster Time To Wound Closure

At any timepoint during the study, an unprepared wound bed is associated with a 12-fold increase in the risk of non-healing compared to a prepared wound bed

Hazard Ratio (HR) of WBP indicator for achieving wound closure: 11.96 (95% CI= 4.236 to 33.787 , p<0.0001)

Conclusions

- Wounds that failed to achieve WBP had a 90% probability of not healing (Negative Predictive Value = 90%)
- Wounds that achieved WBP were 4.1 times more likely to close compared to those that did not (p = 0.0004)
- Early achievement of WBP (within 14 days) was associated with a significantly increased likelihood of healing (Relative Risk = 2.4, p =0.0005)
- At any time point, a wound that has failed to reach WBP had a 12-fold higher risk of remaining unhealed throughout the 14 weeks study period (Hazard Ratio = 12, p < 0.0001)

- This analysis confirms that wound bed preparation (complete debridement and full granulation tissue coverage) is a prerequisite for wound closure in VLUs
- The data further validates BBD therapeutic potential to improve healing outcomes by accelerating wound bed preparation in patients with venous leg ulcers
- These data validate the design and outcomes of the ongoing Phase III VALUE study with EscharEx in VLU