Results from ChronEx: a Phase 2 multicenter, prospective, randomized, placebo controlled, adaptive design study performed to evaluate the safety and efficacy of Bromelain-based enzymatic debridement agent (BBD) in debridement of Venous Leg Ulcers

Dr. John Lantis, MD[1], Dr. Ram Avrahami, MD[2], Dr. Alexander Reyzelman, DPM[3], Dr. Robert J Snyder, DPM[4], Dr. Yael Katz-Levy, PhD[5], Dr. Cyaandi R. Dove, DPM[6]

1 Mount Sinai New-York NY , 2 TLM Tel-Aviv Israel, 3 CCR San Francisco CA, 4 Barry University Miami FL, 5 MediWound Yavne Israel, 6 Advanced Foot & Ankle Center Las Vegas NV

Introduction: Debridement represents a key step in the management of chronic wounds and is considered a basic necessity to induce wound bed preparation that leads to tissue repair. Use of novel therapies that specifically remove the non-viable tissues is a promising strategy for improving patient outcomes. Bromelain-based enzymatic debridement agent (BBD) named EscharEx, is currently in clinical development for debridement of chronic wounds. ChronEx study objectives were to assess safety and efficacy of BBD in patients with venous leg ulcers (VLUs).

Methods: 120 patients with 2-100cm^2 VLUs with ≥50% non-viable tissue were treated up to 8 daily applications with either BBD, Gel Vehicle (GV, placebo) or Non-surgical standard of care (NSSOC, commercially approved products) at a ratio 3:3:2, and then continued follow-up for up to 12 weeks. Wounds were clinically assessed for complete debridement, percentage of granulation tissue and wound status, wound size (measured by eKare™ Planimetry system) in each clinic visit.

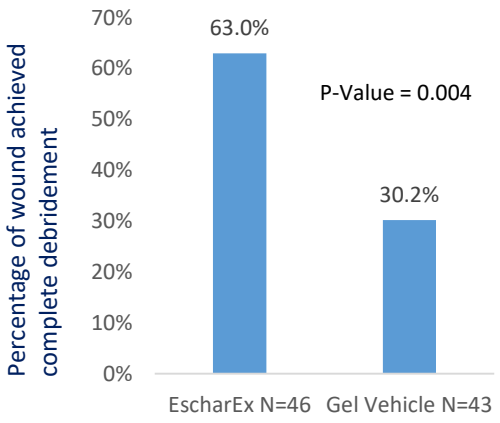
Results: Primary EP: Patients treated with BBD had a statistically significant higher incidence of complete debridement within up to 8 applications compared to GV (BBD=63% vs. GV=30%, p=0.004), and to NSSOC (13%, p<.001, post hoc). **Secondary EPs**: The estimated median time to complete debridement was shorter: BBD=9 vs. NSSOC=59 days (p=0.016) and vs. GV=63 days (p=0.004, exploratory EP). Patients treated with BBD demonstrated higher incidence of ≥75% granulation tissue at the end of treatment compared to GV (p<0.0001). No significant differences could be detected in changes in pain, wound size and wound-QoL.

Patients treated with BBD demonstrated lower incidence of superficial bio-burden (measured by NERDS scale) during the daily treatments and one week later compared to GV (p=0.0524, post hoc).

Safety EPs: BBD was safe and well tolerated. Rates of wound closure achieved with BBD were not inferior to those of GV & NSSOC; 32.6%, 27.9% (p=0.0056) and 26.7% (p=0.0094), respectively. Time to wound closure was 64 days, 63 days and 78 days respectively.

Conclusion: BBD is significantly more effective and faster than NSSOC and GV in debridement of VLU and in encouraging the formation of granulation tissue, that promote wound bed preparation. BBD is safe and well tolerated in VLU patients and has no deleterious effect on occurrence or time to wound healing.

Incidence of wounds achieved complete debridement (during daily application period)



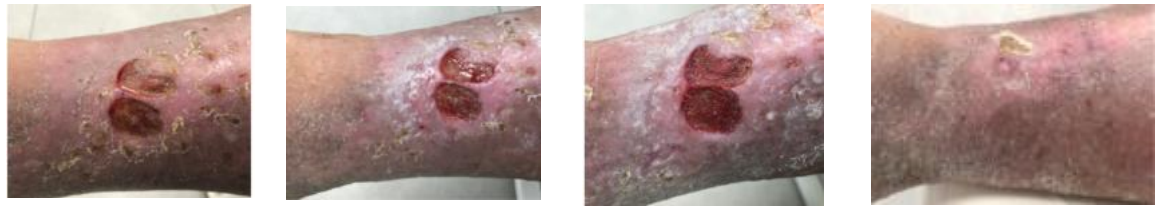
Incidence of wounds with at least 75% granulation (at the end of daily application period), n (%)

EX-02 (N=46)	Gel Vehicle (N=43)	P-Value
42 (93.3%)	24 (55.8%)	<.0001

Incidence of increased superficial bacterial burden (NERDS) during daily application period and 1 week later, n (%)

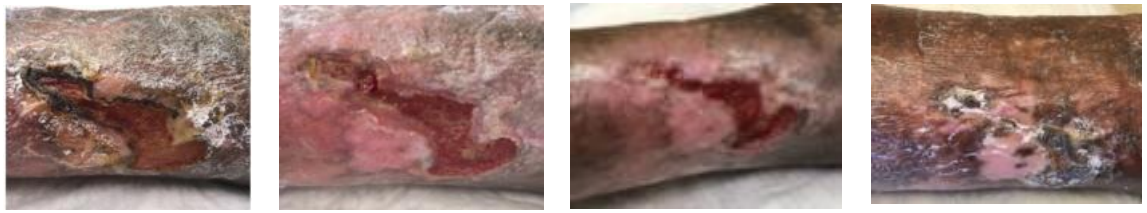
EX-02 (N=46)	Gel Vehicle (N=43)	P-Value
22 (47.8%)	30 (69.8%)	0.0524

Case Study (Pt. 107-015), VLU pre-existing 9 months, treated with EX-02, 24h daily treatments



Before treatment | After 1st treatment | After 3rd & last treatment | Wound closed (post autograft)

Case Study (Pt. 204-013), VLU pre-existing 8 months, treated with EX-02, 24h daily treatments



Before treatment | After 1st treatment | After 2nd & last treatment | Wound closed