Table SI Patient criteria

Inclusion criteria (venous leg ulcer wounds, Group A)
• Age 18 years or older
• Diagnosis of ulcus cruris venosum (verified by positive venous reflux testing, e.g. ultrasound)
• Ankle-brachial pressure index (ABPI) between 0.8 and 1.05
• Use of compression therapy before study inclusion and agreeing to continue to use compression therapy for the study duration
• Patient was mobile and able to walk to allow for effective compression therapy and ankle mobility was limited to fully mobile
• Target ulcer size was between 5 cm^2 and 50 cm^2
• Ulcer duration more than 3 and less than 36 months
• Wound surface was covered with yellow fibrin deposits by greater than 40% and required cleansing/wound bed preparation

Exclusion criteria (venous leg ulcer wounds, Group A)
• Female patients of childbearing age, pregnancy (suspected or confirmed), or breast-feeding
• Inability to follow the study protocol according to the physician's assessment, or a general condition that did not allow participation in the study for the treatment period of 12 weeks
• Known allergies or intolerance to any of the study product ingredients
• Hypertensive leg ulcers (Ulcus cruris hypertonicum Martorell characterized by superficial to deep, painful ulcers with a necrotic base, purple-reddish edges and episodes with enlargement, and satellite lesions[1]
• Acute septic phlebitis, acute severe deep vein thrombosis (phlegmasia cerulea dolens) or other conditions posing a contraindication for compression therapy
• Decompensated heart insufficiency (NYHA Class IV, ACC.AHA Stage D),
• Patients with poorly controlled diabetes mellitus (HbA1c <70 mmol/mol; < 8.6%)
• Severe dysfunction of liver or kidney (e.g. clinically relevant liver fibrosis, cirrhosis, prolonged prothrombin time, decreased albumin levels) and/or kidney disease (e.g. clinically relevant increase in serum creatinine, significant proteinuria, requirement for hemodialysis),
• Significant malnutrition with reduced serum albumin levels
• Active autoimmune disease requiring corticosteroid treatment (> 10 mg prednisolone equivalent/day) and/or other immunosuppressive and/or chemotherapy
• Wounds caused by a malign tumor (primary or metastasis).
Additional products in direct contact to wound surface apart from the study products were prohibited, as was the treatment of the target ulcer during the last four weeks before the study start

Inclusion criteria (split-thickness donor site wounds, Group B)
• Age 18 years or older
• Patient underwent a split-thickness skin harvesting procedure and needs dressing of the donor site wounds
• Split-thickness donor site wound size is between 5cm^2 and 50cm^2

Exclusion criteria (split-thickness donor site wounds, Group B)
• None

[1] Vuerstaek JDD, Reeder SWI, Henquet CJM, Neumann H a. M. Arteriolosclerotic ulcer of Martorell. J Eur Acad Dermatol Venereol 2010 Aug; 24:867–74.

Table SII Clinical endpoints

Clinical endpoints
• Wound area measurement was done from acetate tracings (Opsite Flexigrid®, Smith& Nephew, Hull, UK) digitization, and quantification (ImageJ software (ImageJ 1.50e, National Institutes of Health, USA) by two independent operators. Differences between both operators were 0.12% ± 0.93% and the mean of both measurements was used
• Absolute wound area was calculated from the digitized acetate tracings (cm^2)
• Absolute wound area reduction calculated from wound size t_0 - wound size t_{last} (cm^2)
• Relative wound area reduction (WAR) calculated as wound size t_0 - wound size t_{last})/wound size t_0*100 (%)
• Numbers of wounds with WAR ≥40 %, WAR ≥ 60% (N)
• Number of wounds healed (N)
• Physician estimated exudate levels (none=0, light=1, moderate=2, heavy=3)
• Perilesional skin (normal skin, vesicles, erythema, unspecific eczema, allergic reactions)
• Changes in wound pain, pain during dressing change as visual analog scale VAS score ranging from 0 mm (no pain) to 100 mm (maximal pain)
• Granulation tissue development (red granulation tissue as % of total wound surface area) was estimated by two independent investigators. In cases where estimation differed by more than 20%, resolution was achieved by reviewing the wound pictures jointly
• Epithelialization was judged as “absent”, “absent to beginning”, ”beginning”, ”beginning to robust”, ”robust” by two independent investigators. In cases where estimation differed, resolution was achieved by reviewing the wound pictures jointly
• Level of exudate as judged by the clinician as ”none”, ”minimal”, ”little”, ”heavy”

Table SIII Dressing regimens

Dressings before inclusion in venous leg ulcer wounds (Group A)	(N)	(%)
Foam dressings	24	42.1
Hydrofiber	12	21.1
Wound contact layer	12	21.1
Petrolatum gauze	5	8.8
Gauze compresses	5	8.8
Hydrocolloids	4	7.0
Amorphous gel	1	1.8
Others	21	36.8
Topical antiseptics		
Octenidine	7	35.0
Silver dressings	2	10.0
Iodine	1	5.0
(multiple entries allowed)		

Previous compression therapy in the venous leg ulcer cohort (Group A)	(N)	(%)
Compression stockings	9	15.8
Compression bandages	48	84.2

Table SIV Concomitant modication

Concomitant medication	Stat.	Category	Total	Missing data
Was any of the following medication taken during the trial?	N= (%)	Yes	42 (80.8%)	5 (8.8%)
		No	10 (19.2%)	
Antibiotics	N= (%)	Antibiotics	11 (26.2%)	0 (0.0%)
Corticosteroids	N= (%)	Corticosteroids	8 (19.0%)	0 (0.0%)
Immunosuppresives	N= (%)	Immunosuppressives	0 (0.0%)	0 (0.0%)
Chemotherapeutic agents	N= (%)	Chemotherapeutic agents	0 (0.0%)	0 (0.0%)
Anticoagulants	N= (%)	Anticoagulants	12 (28.6%)	0 (0.0%)
Analgesic	N= (%)	Analgesics	9 (21.4%)	0 (0.0%)
Other medication relevant to the wound	N= (%)		25 (59.5%)	0 (0.0%)
If other, specify	N= (%)	ASS, Calcium dobesilate, Vitamin B3	1 (4.0%)	0 (0.0%)
		Acenocumarol, Furosemide, Hesperidin, Ruscus Aculeatus, Vitamin C	1 (4.0%)	
		Acenocumarol	1 (4.0%)	
		Pentoxifyllin, Hesperidin, Ruscus Aculeatus, Vitamin C	1 (4.0%)	
		Pentoxifyllin, Sulodexide, Vitamin B3	1 (4.0%)	
		Cilostazol, Copidogrel, Pentoxifyllin	1 (4.0%)	
		L-arginine, Pentoxifyllin, Sulodexide, Spironolactone, Vitamin B3	1 (4.0%)	
		Copidogrel, Furosemide, Poly(O-2-hydroxyethyl)rutoside, Vitamin B3	1 (4.0%)	
		Bisoprolol, Sulodexide	1 (4.0%)	
		Calcium dobesilate, L-arginine, Pentoxifyllin, Sulodexide	1 (4.0%)	
		Hesperidin, Ruscus Aculeatus, Pentoxifyllin, Spironolactone, Vitamin C	1 (4.0%)	
		Hesperidin, Ruscus Aculeatus, Pentoxifyllin, Spironolactone, Vitamin C	1 (4.0%)	
		Hesperidin, Ruscus Aculeatus, L-arginine, Spironolactone, Vitamin C	1 (4.0%)	
		Hesperidin, Ruscus Aculeatus, Spironolactone, Sulodexide, Vitamin C	1 (4.0%)	
		Mometasone (topical preparation)	1 (4.0%)	
		Furosemide, Hesperidin, Ruscus Aculeatus, Sulodexide, Vitamin C	1 (4.0%)	
		Furosemide, Hesperidin, Ruscus Aculeatus, Spironolactone, Sulodexide, Vitamin C	1 (4.0%)	
		PVP-iodine	1 (4.0%)	
		ASS, Copidogrel, Hesperidin, Ruscus Aculeatus, Pentoxifyllin, Vitamin C	1 (4.0%)	
		Pentoxifyllin, Sulodexide	1 (4.0%)	
		ASS, Diosmin, Spironolactone	1 (4.0%)	
		Furosemide, Poly(O-2-hydroxyethyl)rutoside, Spironolactone	1 (4.0%)	
		Copidogrel, Gliclazide, Hesperidin, Ruscus Aculeatus, Spironolactone, Sulodexide, Vitamin C	1 (4.0%)	
		L-arginine, Pentoxifyllin, Spironolactone, Sulodexide	1 (4.0%)	
		ASS, Cilostazol, L-arginine	1 (4.0%)	

Table SV Wound parameters

Variable	Stat.	Venous leg ulcer			Acute wound		
		Base-line	Week 8	Week 12	Base-line	Day 4	Day 21
Wound area [cm2]	n	57	48	44	10	10	9
	mean (SD)	18.66 (12.25)	11.75 (11.39)	10.23 (11.76)	40.25 (30.88)	36.50 (30.63)	13.94 (12.67)
	median [IQR]	14.02 [10.09, 26.60]	7.83 [3.35, 15.30]	5.31 [2.08, 13.82]	33.45 [23.40, 40.51]	32.56 [19.96, 35.67]	9.27 [3.11, 23.49]
	min-max	5.8-59.1	0.0-45.4	0.0-47.8	11.4-121.2	11.5-117.9	0.0-35.4
Absolute WAR (wound area reduction) [cm2]	n	-	48	44	-	10	9
	mean (SD)	-	-7.54 (8.95)	-9.85 (10.58)	-	-3.75 (4.32)	-26.91 (27.73)
	median [IQR]	-	-6.10 [-12.66, -1.30]	-7.91 [-15.96, -2.77]	-	-3.30 [-6.26, -0.17]	-18.59 [-28.52, -14.63]
	min-max	-	-44.4-8.5	-44.4-8.5	-	-10.2-1.8	-97.7--5.9
Relative WAR (wound area reduction) [%] (LOCF for missing data)	n	-	57	57	-	10	10
	mean (SD)	-	38.52 (49.07)	48.93 (51.85)	-	10.78 (16.39)	61.22 (32.39)
	median [IQR]	-	47.49 [6.08, 75.00]	62.48 [13.80, 91.69]	-	7.21 [-1.74, 17.56]	62.31 [49.85, 84.41]
	min-max	-	-169.8- 99.6	-169.8-100.0	-	-7.8-47.2	6.1-100.0
Fibrin on the wound surface [%]	n	56	47	44			
	mean (SD)	71.70 (25.03)	28.62 (29.52)	23.30 (31.75)			
	median [IQR]	80.00 [55.00, 91.25]	15.00 [5.00, 55.00]	5.00 [0.00, 45.00]			
	min-max	15.0-100.0	0.0-95.0	0.0-100.0			
Granulation tissue on the wound surface [%] (LOCF for missing data)	n	57	57	57	10	10	10
	mean (SD)	38.82 (30.78)	65.18 (32.33)	63.33 (35.23)	0.00 (0.00)	85.00 (31.00)	88.00 (31.55)
	median [IQR]	35.00 [10.00, 60.00]	80.00 [45.00, 95.00]	80.00 [35.00, 95.00]	0.00 [0.00, 0.00]	100.00 [82.50, 100.00]	100.00 [100.00, 100.00]
	min-max	0.0-100.0	0.0-100.0	0.0-100.0	0.0-0.0	0.0-100.0	0.0-100.0
Necrotic tissue on the wound surface [%]	n	56	47	44			
	mean (SD)	1.25 (4.60)	0.21 (1.46)	0.34 (2.26)			
	median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]			
	min-max	0.0-25.0	0.0-10.0	0.0-15.0			
Maximum wound pain during the last 24 hours, VAS [mm] (LOCF for missing data)	n	57	57	57	10	10	10
	mean (SD)	34.9 (29.2)	18.9 (27.5)	14.6 (23.5)	4.0 (12.6)	30.2 (26.2)	2.6 (6.4)
	median [IQR]	36.0 [7.0, 53.0]	4.0 [0.0, 25.0]	1.0 [0.0, 22.0]	0.0 [0.0, 0.0]	33.5 [3.5, 43.5]	0.0 [0.0, 0.0]
	min-max	0-100	0-99	0-100	0-40	0-71	0-20
Pain at dressing changes, VAS [mm] (LOCF for missing data)	n	57	57	57	10	10	10
	mean (SD)	25.9 (27.2)	13.4 (21.1)	11.6 (21.5)	16.9 (20.3)	21.0 (34.2)	1.4 (4.4)
	median [IQR]	18.0 [0.0, 41.0]	4.0 [0.0, 20.0]	0.0 [0.0, 14.0]	12.0 [1.0, 24.8]	0.0 [0.0, 38.2]	0.0 [0.0, 0.0]
	min-max	0-92	0-96	0-90	0-66	0-100	0-14

Table SVI Local wound characteristics

Venous leg ulcer wounds (Group A)				
		Start	8 weeks	12 weeks
Clinical signs of infection				
• Reddening	N (%)	21 (36.8%)	6 (12.2%)	7 (12.7%)
• Edema	N (%)	12 (21.1%)	2 (4.1%)	2 (3.6%)
• Odor	N (%)	9 (15.8%)	4 (8.2%)	2 (3.6%)
• Friable granulation tissue	N (%)	8 (14.0%)	3 (6.1%)	2 (3.6%)
• No clinical signs of infection	N (%)	31 (54.4%)	40 (81.6%)	46 (83.6%)
Periwound color				
• livid/purple/blue/black	N (%)	6 (10.5%)	1 (2.1%)	2 (3.8%)
• red/pink	N (%)	49 (86.0%)	38 (79.2%)	39 (73.6%)
• white/hyper-hydrated	N (%)	2 (3.5%)	7 (14.6%)	10 (18.9%)
• other	N (%)	0 (0.0%)	2 (4.2%)	2 (3.8%)

Table SVII Adverse events

Adverse events	
#1	Persistent local wound infection without generalized signs of infection
#2	Occurrence of black-stained tissue of 1 cm x 1 cm which at the next visit was gently lifted off displaying healthy granulation tissue underneath