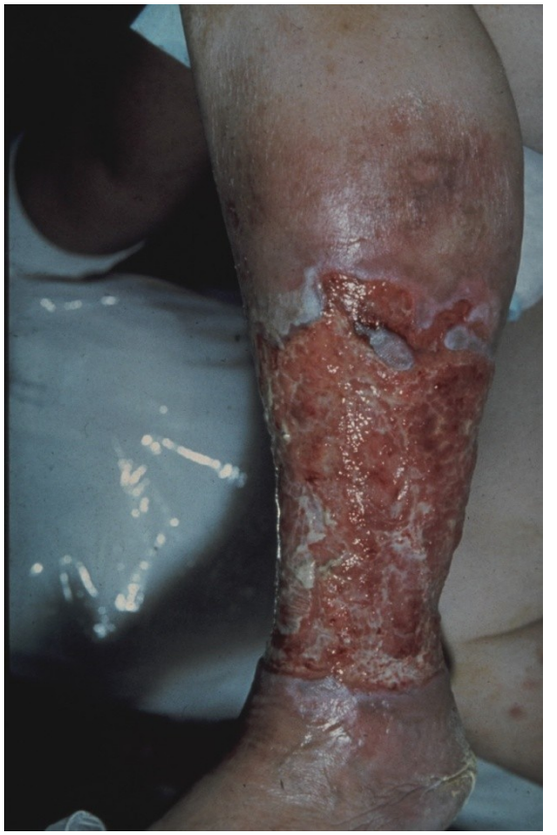
Retrospective analysis of treating therapy resistant ulcers with a full thickness skin substitute (Tiscover)

- Dr. E.M de Boer, dermatoloog
- Dr. C. van Montfrans, dermatoloog
- Prof. Dr. S. Gibbs, hoofd research dermatologie lab
- Drs. C. Blok, clinical trial management
- Drs. M. Breetveld, cleanroom manager

Disclosure: Prof. Gibbs is co-founders of university spin-off company A-SkinBV

Chronic wounds

- Leg ulcers, diabetic foot ulcers, pressure ulcers, chronic wounds occurring after major surgery
- Leg ulcers: 1% of the population;
  4-5% of individuals ≥ 80 years
- High costs (>1% total budget)
- Can exist for many years



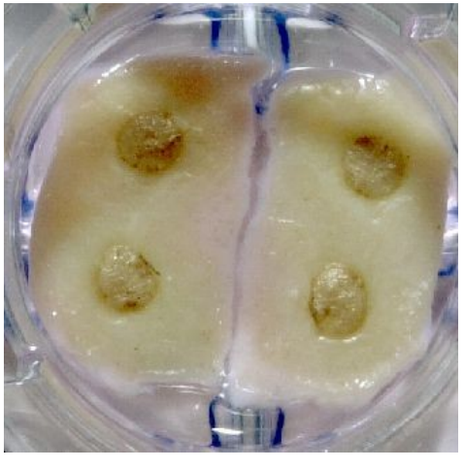
Autologous skin substitute: Tiscover

advantages:

- Patient own cells, therefore no rejection
- Secretes many cytokines, chemokines and growth factors which stimulate wound healing

indication:

- Therapy resistant chronic wounds




TISSUE ENGINEERED SKIN
FOR WOUND HEALING

Advantage above split skin grafting

- Donor site is very small, results in fast healing with good scar
- direct release of cytokines and growth factors
- Full thickness skin, not fragile, less chance of recurance

Advantages above acellular dressing

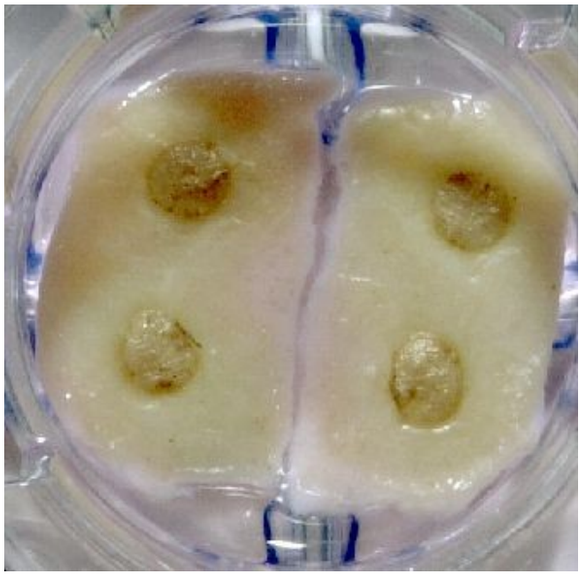
- Only one or 2 applications required
- Patient own skin cells
- Direct release of cytokines and growth factors
- Stimulates angiogenesis, granulation tissue and epithelialization

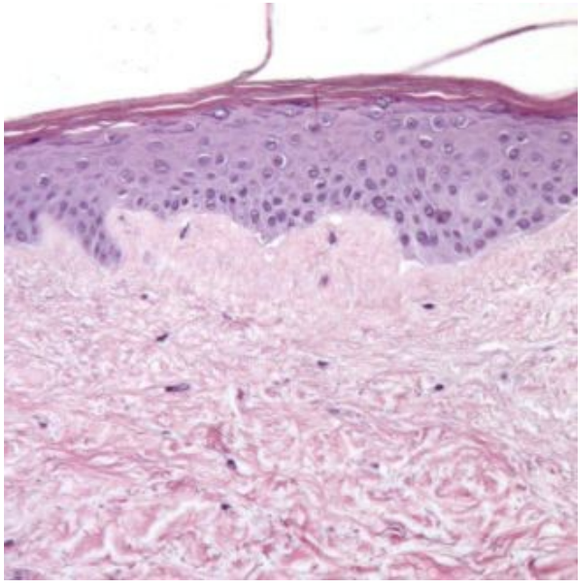
Aim of pilot-study

evaluate safety and efficacy of

Tiscover

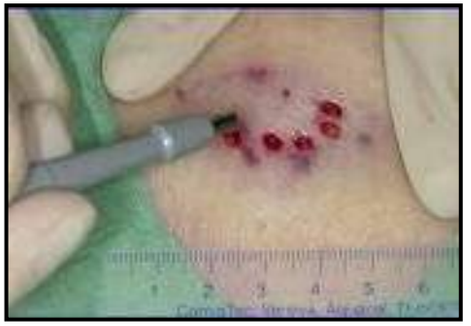
for treating therapy resistant ulcers



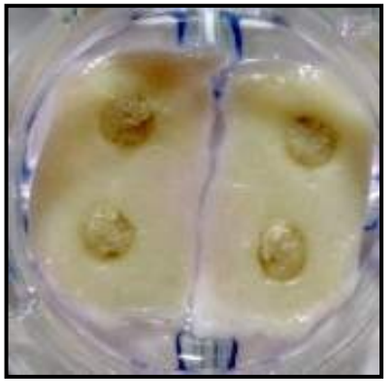


Background Tiscover

- 3 mm biopsies



- two 3 mm biopsies make 3 cm^2 Tiscover



- After 3 weeks Tiscover is ready to use

Material & methods

Retrospective study 2004–2010:

- Treatment Tiscover
- 5 studies:
  i. Pilot
  ii. Insurance initiated
  iii. Nursing home
  iv. Individual case studies
  v. Interim multicenter trial
- 7 Dutch Centers (VU medical center; hospitals; nursing homes etc)
- 83 patients (99 ulcers) treated in different studies
- Inclusion criteria for retrospective study:
  - ulcer duration > 12 wks (arterio-venous; post-traumatic; pressure)
  - no intention to heal using standard therapy
  - follow-up > 24 wks (at least)
  - no age limit
  - **66 ulcers**

Material & methods

	Hospitalized treatment (33 ulcers)	*Outpatient treatment* (33 ulcers)
1) Woundbed preparation	Vacuum assisted closure therapy (VAC) 5 days prior to application.	Allodermis applied for 1 week prior to application.
2) Single Tiscover application	The ulcer was covered with Tiscover and kept in place with bandages.	
3) Follow-up ≥ 24 wks	Weekly treatment (cleaning, silversulfadiazin, petrolatum gauzes, bandage) and examination in the outpatient clinic.	
4) Endpoint	- safety - number of healed ulcers - size reduction - recurrence	

Patient characteristics

	(arterio-)venous	post-operative	pressure (grade 3-4)	total
number ulcers	49	9	8	66
age				
median (range)	79 (45-91)	62 (39-87)	62.5 (36-92)	76 (36-92)
gender				
male	14	4	4	22
female	35	5	4	44

Ulcer size and duration before treatment with Tiscover

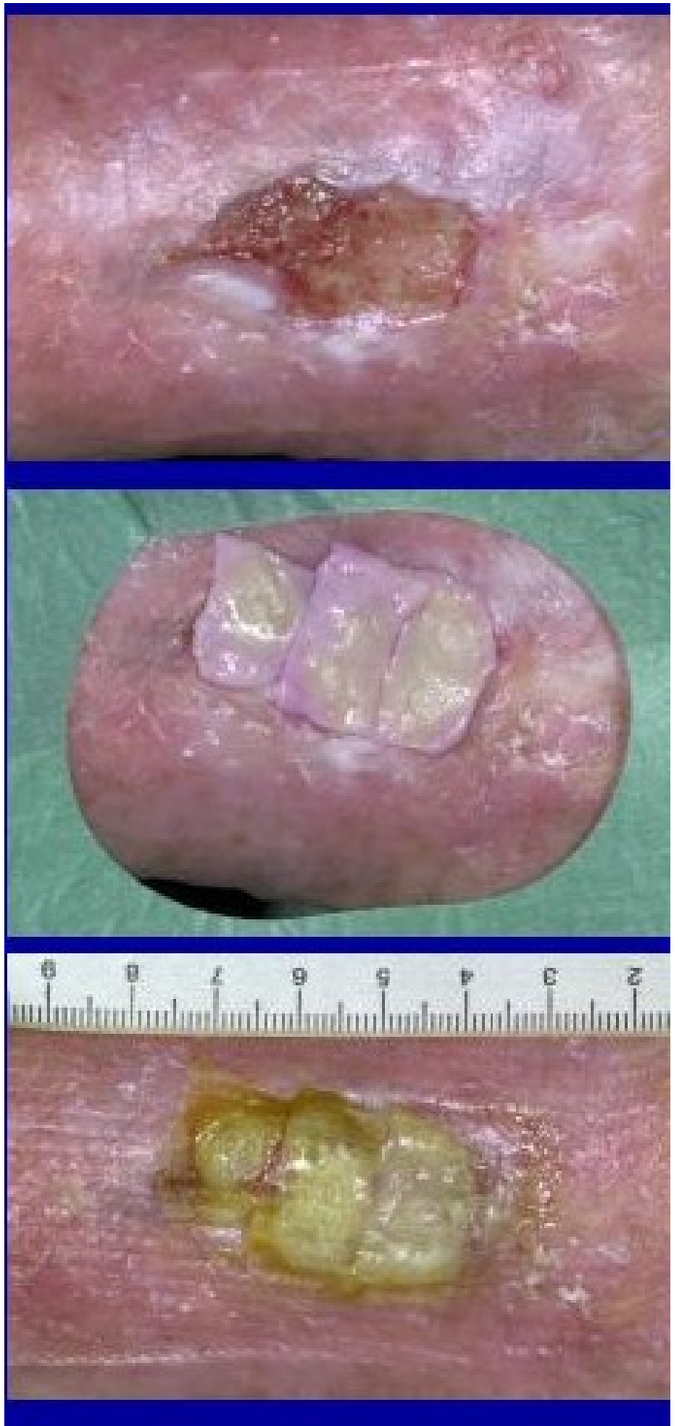
	(arterio-)venous	post-operative	pressure	total
ulcer size (cm^2)				
median (range)	5.6 (0.75-150)	35 (2-147)	3.1 (1.2-13)	5.7 (0.75-150)
ulcer duration (yrs)				
median (range)	2 (0.33-32)	2.5 (0.5-14)	1.7 (1-7)	2 (0.33-32)

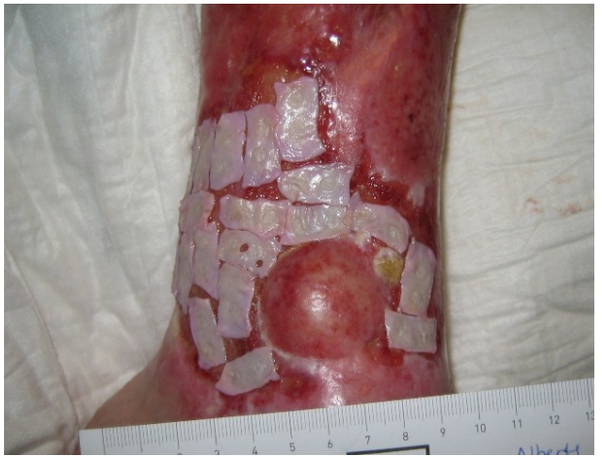
Application Tiscover

Woundbed before application: debridement

Tiscover on the wound

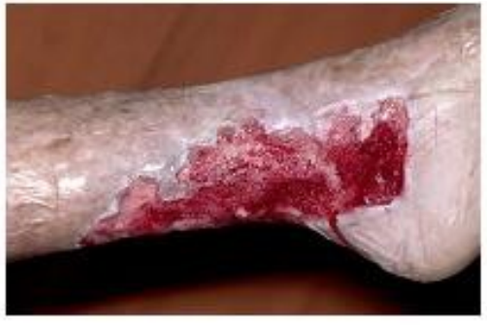
1 week after Tiscover application



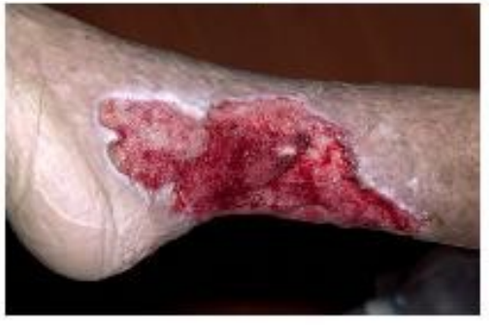


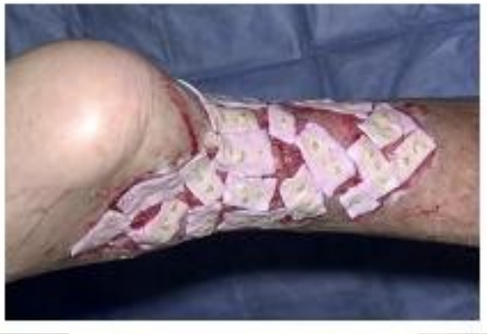
Application: Venous Ulcus

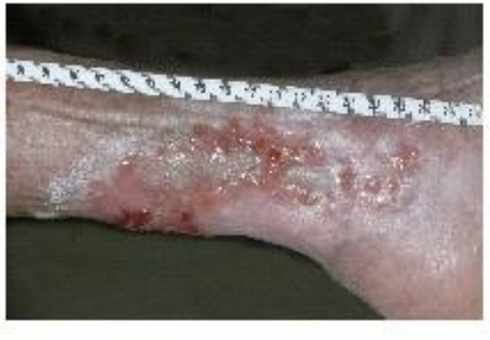
VU medisch centrum



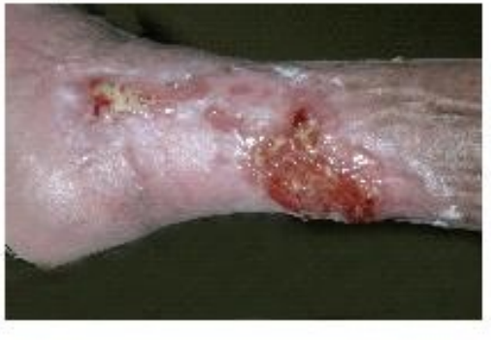
14 years open

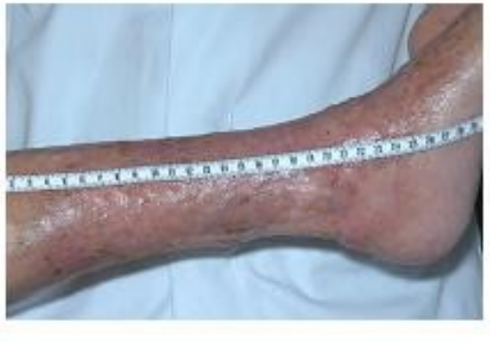




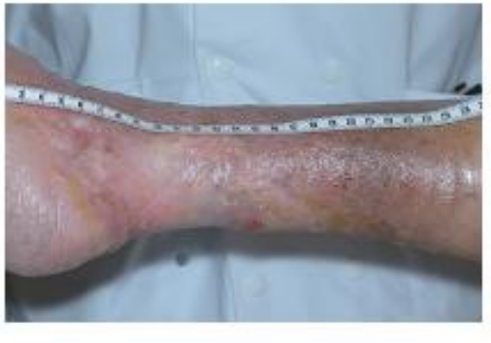


8 weeks later

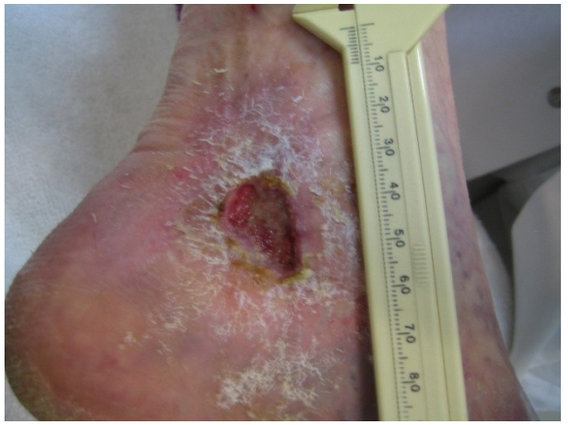




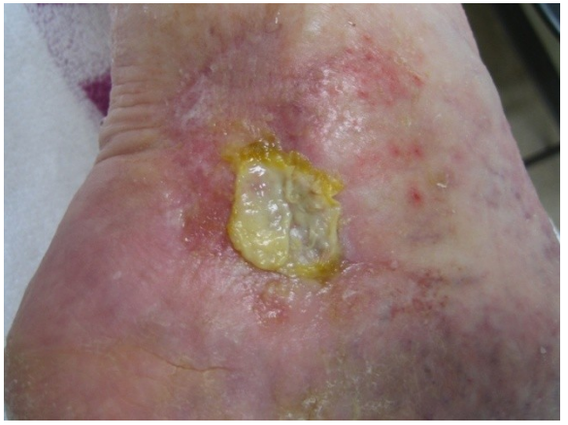
11 months later



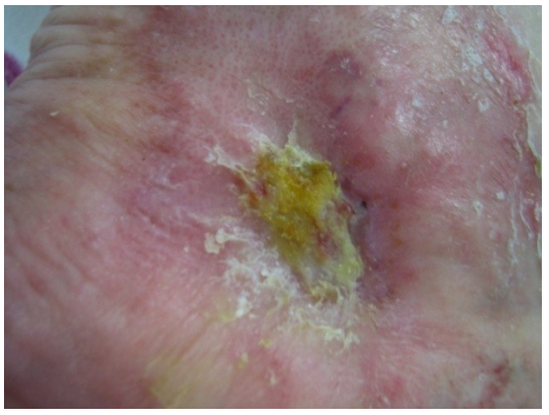
Application: Venous Ulcus



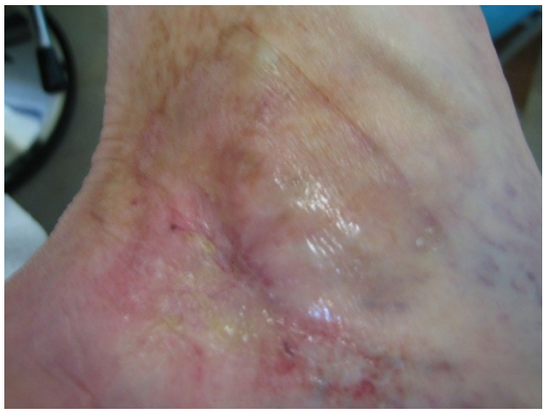
WK -3



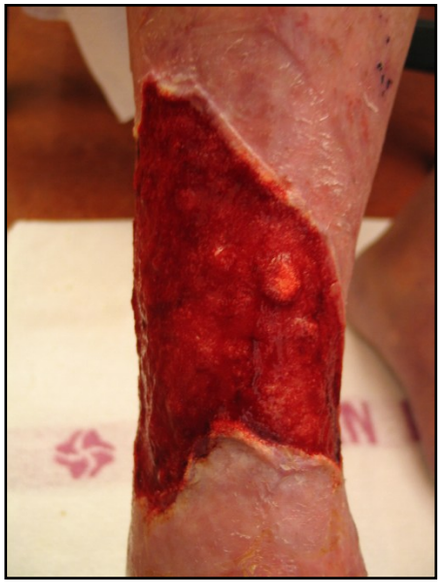
1 week after Tiscover application



WK 12

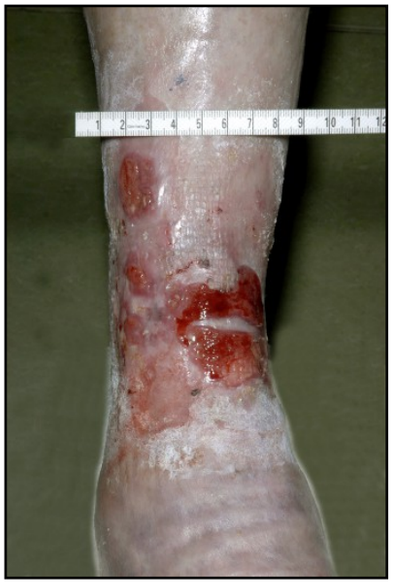


wound closed, week 24

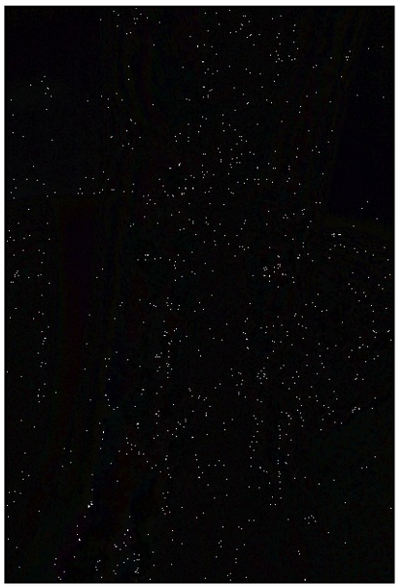


ulcus cruris

+ Tiscover



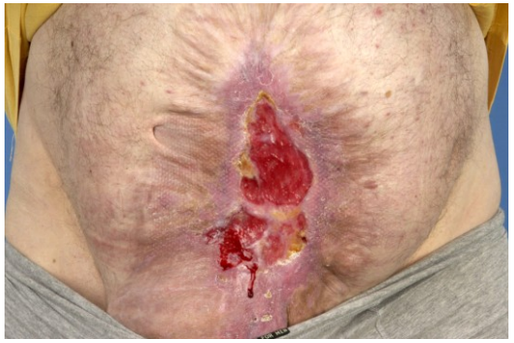
after 12 weeks



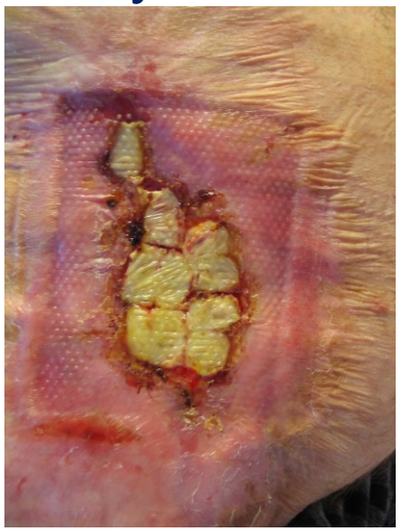
after 24 weeks

Abdomen post-operative wound

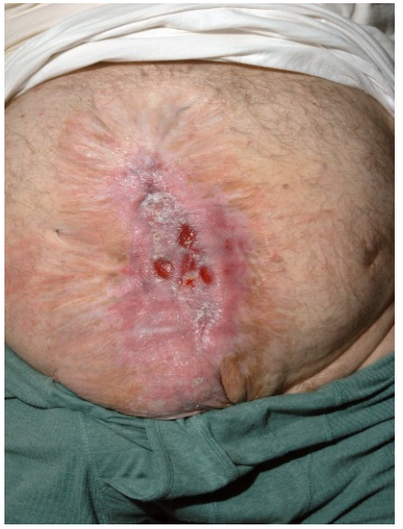
before



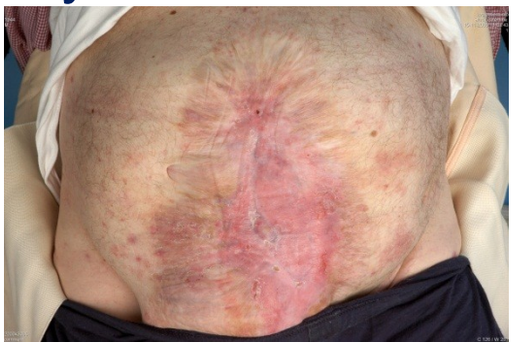
3 days



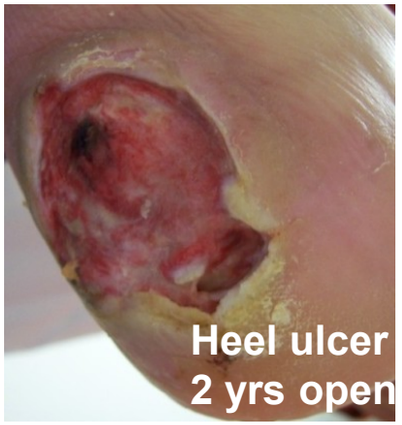
3 months

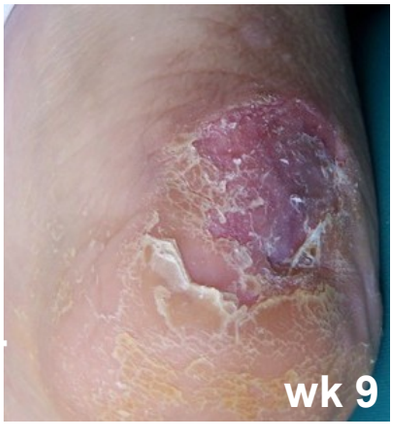


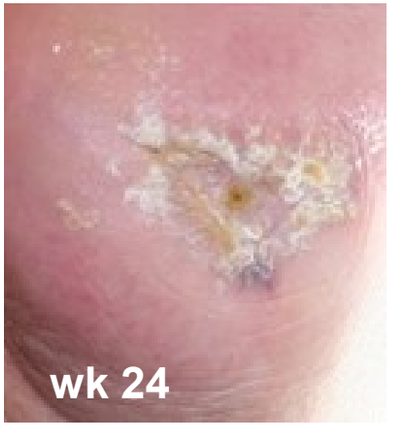
2 years

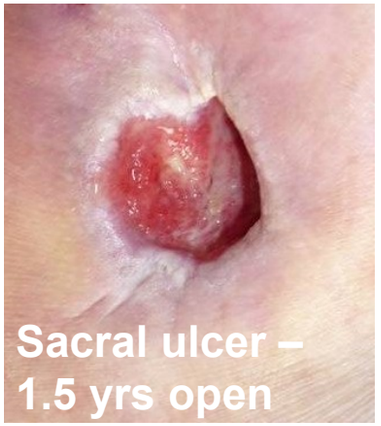


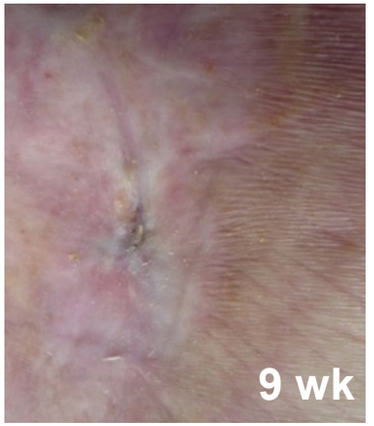
Pressure ulcers

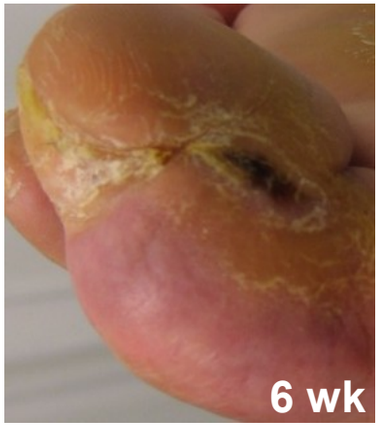








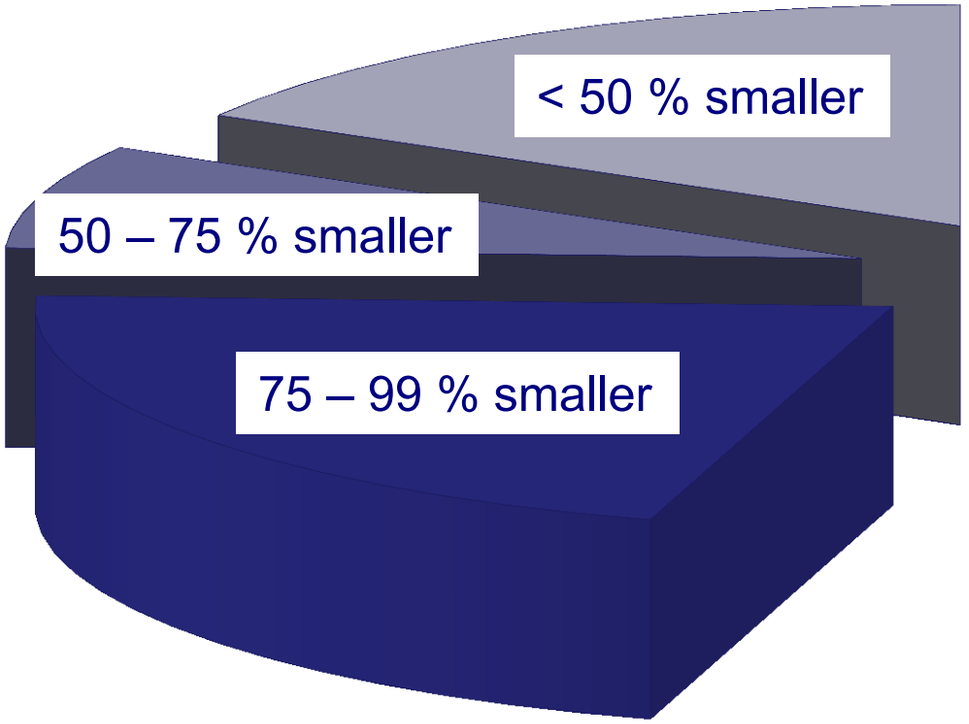


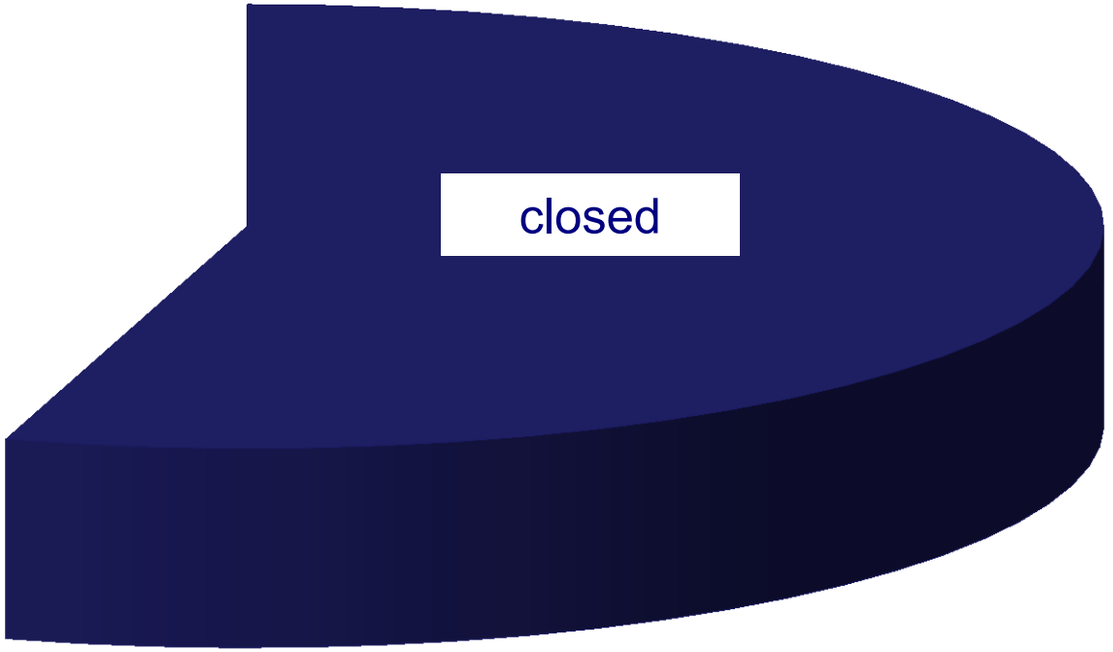


Retrospective analysis of ulcer healing with Tiscover

single application, 24 week follow-up, 66 ulcers

(arterio-)venous, decubitus, post-operative ulcers





55 % closed
29 % decreased in size between 50-99 %
Total healing = 84 % of ulcers

ulcer recurrance

- 32 of 36 closed ulcers available for follow-up 1 yr later
- 27: still closed (84%)
- 5: recurrance
- 3: not available for follow-up

Gibbs et al., British Journal Dermatology, 2006; Blok et al., Wound Repair and Regeneration 2013

Conclusion

- Multi-centre: 7 Dutch centres
- 83 patients (99 ulcers treated)
- 1 moderate possibly related adverse event: lymph node inflammation
- 1 minor possibly related adverse event:
  mild asymptomatic transient erythema

- Therefore Tiscover is safe to use

- Phase 2 multi-centre study underway
- VUmc, Centrum Oosterwal, Slotervaart Ziekenhuis en Flevo ziekenhuis,
- St. Fransiscus Gasthuis, Ziekenhuisgroep Twente
- Hospital exemption granted by IGZ for The Netherlands

VUmc Dermatology, Amsterdam

Laboratorium
Melanie Breetveld
Taco Waaijman
Maria Thon
Sander Spiekstra
Chantal Blok
Sue Gibbs

A-SKIN Nederland BV
Rik Scheper (CEO)
Sue Gibbs (CSO)
Edith de Boer
Michiel Haasjes

Dermatologists
Edith de Boer
Bibi van Montfrans
L. Vink (aio)
Menno de Rie
Rick Hoekzema

Tiscover Trial Locations:
- Centrum Oosterwal (drs. M. Mooij)
- Slotervaart Ziekenhuis (drs. J. Serrarens)
- Flevo Ziekenhuis (drs. W. Roest)
- ZiekenhuisGroep Twente (dr. C. Hebeda)
- St. Fransiscus Gasthuis (dr. M. Loots)
- Dermatologisch centrum Isala, Isala klinieken (drs. H.Y.Lam)
- Groene Hart Ziekenhuis (dr. I. Bruynzeel)
- Evean Zorg Waterland (A. van der Kraan)
- Vivium Zorggroep (G. van Brakel)
- Rode Kruis Ziekenhuis (dr. A. Vloemans)

Current financers:

ZonMw
Agentschap NL Ministerie van Economische Zaken, Landbouw en Innovatie
Euro Trans Bio
NIRM Netherlands Institute of Regenerative Medicine
Nederlandse Brandwonden Stichting

Past financers:

dpte
AGIS
biopartner
Agentschap NL Ministerie van Economische Zaken, Landbouw en Innovatie
Nederlandse Brandwonden Stichting
Askin

Oproep:

Patienten insturen voor onze studie?

Triallocatie worden?

Informatie aanvragen?

Neem contact met ons op via:
Tiscover@vumc.nl