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 recurrence
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 $3 \text{ cm}^2$

• 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)
- Vacuum assisted closure therapy (VAC) 5 days prior to application.
- AlloDermis applied for 1 week prior to application.
- The ulcer was covered with Tiscover and kept in place with bandages.
- Weekly treatment (cleaning, silversulfadiazin, petrolatum gauzes, bandage) and examination in the outpatient clinic.

Outpatient treatment (33 ulcers)
- - safety
- - number of healed ulcers
- - size reduction
- - recurrence

1) Woundbed preparation
2) Single Tiscover application
3) Follow-up ≥ 24 wks
4) Endpoint
## Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>(arterio-)venous</th>
<th>post-operative</th>
<th>pressure (grade 3-4)</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>number ulcers</td>
<td>49</td>
<td>9</td>
<td>8</td>
<td>66</td>
</tr>
<tr>
<td>age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range)</td>
<td>79 (45-91)</td>
<td>62 (39-87)</td>
<td>62.5 (36-92)</td>
<td>76 (36-92)</td>
</tr>
<tr>
<td>gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>14</td>
<td>4</td>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td>female</td>
<td>35</td>
<td>5</td>
<td>4</td>
<td>44</td>
</tr>
</tbody>
</table>
Ulcer size and duration before treatment with Tiscover

<table>
<thead>
<tr>
<th></th>
<th>(arterio-)venous</th>
<th>post-operative</th>
<th>pressure</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ulcer size (cm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range)</td>
<td>5.6 (0.75-150)</td>
<td>35 (2-147)</td>
<td>3.1 (1.2-13)</td>
<td>5.7 (0.75-150)</td>
</tr>
<tr>
<td>ulcer duration (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range)</td>
<td>2 (0.33-32)</td>
<td>2.5 (0.5-14)</td>
<td>1.7 (1-7)</td>
<td>2 (0.33-32)</td>
</tr>
</tbody>
</table>
Application Tiscover

Woundbed before application: debridement

Tiscover on the wound

1 week after Tiscover application
Application: Venous Ulcus

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
Pressure ulcers

- Sacral ulcer – 1.5 yrs open
- Heel ulcer – 2 yrs open
- Ulcer toe – 7 yrs open
- Heel ulcer – 1 yr open
- Heel ulcer – 2 yrs open
- 9 wk
- wk 9
- wk 24
- 6 wk
- 9 wk
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 recurrence
- 32 of 36 closed ulcers available for follow-up 1 yr later
- 27: still closed (84%)
- 5: recurrence
- 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
Laboratorium
Melanie Breetveld
Taco Waaijman
Maria Thon
Sander Spiexstra
Chantal Blok
Sue Gibbs

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)
- Ziekenhuis Groep 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: 

Past financers: 
Oproep:

Patienten insturen voor onze studie?

Triallocatie worden?

Informatie aanvragen?

Neem contact met ons op via:

Tiscover@vumc.nl