**RCT Demonstrating the Efficacy and Benefits of Sulodexide (GAGs) Treatment in Patients with VLU**

Joseph D. Raffetto MD  
VA Boston HCS, West Roxbury, MA; Harvard Medical School, Boston, MA; Brigham and Women’s Hospital  
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**Disclosures**

Nothing to Disclose  
No Conflicts of Interest

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**Sulodexide—What Is It?**

- **SDX** is a Glycosaminoglycan (GAG)-Sulfated polysaccharide  
- fast-moving heparin fraction (FMH, 80%) and dermatan sulfate (DS, 20%)  
- GAGs are naturally occurring anionic polycarbohydrates  
- negatively charged polysaccharides  
- MW 1–2,000 kDa

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**Glycosaminoglycan (GAG)**

- GAGs have disaccharide units  
- uronic acid  
- D-glucuronic acid [GlcA] or L-iduronic acid [IdoA]  
- acetylated amino sugar  
- N-acetylgalactosamine or N-acetylglucosamine  
- GAGs types:  
  - Sulfated: CS, DS, KS, HP, HS  
  - Non-sulfated: HA

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**Sulodexide—Properties**

- Highly purified GAG mixture  
- SDX is extracted from the porcine intestinal mucosa by a patented process  
- Pro-fibrinolytic and anti-thrombotic  
  - increases tPA and uPA, decreases PAI  
  - potentiates antiprotease activities of antithrombin III and heparin cofactor II  
  - inhibits FXa and thrombin  
- Anti-inflammatory and endothelial protective

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**SDX and VLU Healing**

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Outcome</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coccheri S, et al</td>
<td>235</td>
<td>Healing @ 3 mo 52% vs. 33%</td>
<td>1.44 (1.12-1.84) NNT 5 @ 3 mo</td>
</tr>
<tr>
<td>Scondotto G, et al</td>
<td>95</td>
<td>Healing @ 2 mo 58% vs. 35%</td>
<td>1.65 (1.06-2.7) NNT 4 @ 3 mo</td>
</tr>
<tr>
<td>Kasharawski M, et al</td>
<td>44</td>
<td>Healing @ 7 wks 70% vs. 35%</td>
<td></td>
</tr>
<tr>
<td>Zhu Y.X, et al</td>
<td>114</td>
<td>Healing @ 30 d 52% vs. 32%</td>
<td></td>
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</tbody>
</table>

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Randomised, Double Blind, Multicentre, Placebo Controlled Study of Sulodexide in the Treatment of Venous Leg Ulcers

Sergio Coccheri¹, Giacomo Scondotto², Giancarlo Ageni³, Daniele Alcolli³, Emesto Palazzetti³, William Zamboni⁴
for the venous arm of the SUAVE (Sulodexide Arterial Venous Italian Study) Group

- RCT multicenter double-blind placebo-controlled
- 31 Italian medical centers
- 120 pts SDX and 110 pts PLC with VLU
- 1° endpoint complete healing at 2 mo
- 2° endpoint healing at 3 mo, area reduction
- SDX 60 mg IM (20 d) and 100 mg PO (70d)
- Compression bandaging weekly


Similar baseline characteristics and type of compression

<table>
<thead>
<tr>
<th></th>
<th>Sulodexide (n=120)</th>
<th>Placebo (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>77.3±13.6</td>
<td>75.8±12.9</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.76±0.08</td>
<td>1.75±0.07</td>
</tr>
<tr>
<td>Physical activity</td>
<td>30 (25.0%)</td>
<td>31 (28.2%)</td>
</tr>
<tr>
<td>Work (y)</td>
<td>27 (22.5%)</td>
<td>26 (23.6%)</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>33 (27.5%)</td>
<td>32 (29.1%)</td>
</tr>
<tr>
<td>Percent VLU taken</td>
<td>60 (50.0%)</td>
<td>59 (53.6%)</td>
</tr>
</tbody>
</table>

VLU Surface Area Reduction (mean±sd)

<table>
<thead>
<tr>
<th>Day</th>
<th>SDX</th>
<th>PLC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12.25±23.12</td>
<td>13.38±26.00</td>
</tr>
<tr>
<td>20</td>
<td>8.81±19.84</td>
<td>10.59±25.25</td>
</tr>
<tr>
<td>60</td>
<td>7.19±21.11</td>
<td>9.97±26.16</td>
</tr>
<tr>
<td>90</td>
<td>5.39±14.91</td>
<td>8.35±24.21</td>
</tr>
</tbody>
</table>

Regression of area over time

0.004 ns


SDX NNT and Relative Rate

- The NNT to obtain one more healed patient on SDX was 7 at 2 months and 5 at 3 months
- The relative chance of healing SDX vs. PLC -1.37 (1.07,1.74) after 2 months -1.44 (1.12,1.84) after 3 months


Conclusions

- Clinical evidence in Europe that SDX and GAGs derivatives results in increased VLU healing
- Further studies to define duration of SDX treatment
- Longer follow up and ulcer free interval need to be determined
- Further RCT required in US before FDA approval and clinical use