### Clinical Assessment of AK following Levulan and BLU-U Photodynamic Therapy after Pre-treatment with a Sterile, Plastic Microneedle Device (MSS™)

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#### Abstract

A small-scale clinical study was conducted whereby the use of a sterile, plastic microneedle device (Microchannel Skin System – MSS™) was investigated for pretreatment prior to photodynamic therapy for the treatment of actinic keratosis (AK) lesions. Over the 30 day study lesions that were pretreated with the MSS were cleared at a significantly higher rate than those that were not pretreated with the MSS. MSS pretreatment of AK lesion may enhance photodynamic therapy by increasing the absorption of the photosensitizing agent prior to blue light treatment.

#### Background

A previous passive microneedle arrays that, when applied by hand, disrupt the stratum corneum and epidermis creating microchannels in the skin. Testing was conducted to characterize the microchannels, test the durability of the microchannels, and demonstrate enhanced delivery of topically applied formulations of lidocaine hydrochloride and methylprednisolone.

3M Microchannel Skin System (MSS) arrays were applied to human skin using controlled force to create microchannels and enhance delivery of the photosensitizing agent (BLU-U®) to the skin that was not pretreated to enhance delivery of the photosensitizing agent to the skin. The clinical study was conducted to analyze the effectiveness of MSS pretreatment for AK lesions.

#### Local Tissue Concentrations of Methylprednisolone and Lidocaine following Application and Pretreatment with the MSS

<table>
<thead>
<tr>
<th>Substance</th>
<th>100%</th>
<th>80%</th>
<th>60%</th>
<th>40%</th>
<th>20%</th>
<th>0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>

#### Tissue Levels of methylprednisolone following application on skin that was not pretreated with an MSS array, pre-treated one time with an MSS array or pre-treated two times in succession with an MSS array.

Application time of the formulation, indicated on the graph, was either 15min or 30min.

#### MSS Pre-treatment for AK

In a clinical study, three subjects with at least 10 AK lesions distributed on each side of their face, were pretreated for photodynamic therapy with Levulan® (aminolevulinic acid, 3% solution).

On Day 1, an AK count was conducted. The left side of each subject’s face was pretreated with the MSS device immediately prior to application of Levulan®. The right side of the face was not pretreated prior to Levulan® application. After 1 hour (typical treatment time is 6 – 24 hours), the subject’s faces were cleansed and placed in a Blue Light Photodynamic Therapy Illuminator (BLU-U®). Subjects returned for reassessment on Day 30 following treatment and the AK count was repeated.

#### Conclusions

The Microchannel Skin System (MSS) is the first microneedle product launched from 3M’s Microstructured Transdermal System (MTS) platform. The MSS array demonstrates consistent penetration of the stratum corneum with as little as 1.3 lbf applied by hand. The depth of penetration varies from about 60 – 150µm depending upon the force of application and upon the firmness of the underlying tissue. MSS pretreatment creates hydrophilic channels in the skin. Following pretreatment with the MSS device, some drug formulations may be absorbed faster or to a greater extent than when they are applied to skin without microchannels.

Clinical study results indicate the potential for pretreatment of the skin with the MSS to enhance the therapeutic effects of photodynamic therapy for the treatment of AK.

#### References
