Supplementary Materials 1. Study protocol summary

Title

Objective
This split-face study objectively compared the efficacy and safety of 532 nm PS and QSND lasers for the treatment of solar lentigines.

Study institution/primary investigator
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Client
Wontech corporation (CEO: Jong Won Kim, Jung Hyun Kim)
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Monitor
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Subjects
Female patients with Fitzpatrick skin types III∼V and more than 5 clinically obvious solar lentigines observed on both sides of the face

Number of subjects
20 Patients (considering a drop-out rate of 10%)

Clinical trial device
■ Investigational device: Picocare 450 (Picocare; Wontech Co., Ltd., Daejeon, Korea)
■ Control device: Pastelle (Pastelle; Wontech Co., Ltd., Daejeon, Korea)

Study design
This is a prospective, randomized, split-face, controlled trial study.

Method
1. Females (27∼72 years) with Fitzpatrick skin types III∼V and more than 5 clinically obvious solar lentigines observed on both sides of the face will be consulted for the clinical trial.
2. Subjects who have satisfied the inclusion criteria and signed the written consent form will be given a patient number and registered as a trial subject.
3. The faces of the enrollees were divided into halves (right and left sides with a line down the middle) with the halves randomly allocated for 532 nm PS laser or 532 nm QSND laser treatment in a 1:1 fashion.
4. All patients received one laser treatment for each side of the face.
5. The subjects will be evaluated on the efficacy and safety of the treatment 2 week, 4 weeks, 8 weeks, and 12 weeks after the laser therapy.
6. All follow-up evaluations will be completed 12 weeks after the laser therapy. If no adverse event had occurred or if such event had been solved, the clinical trial will be completed.

Table 1. Conditions of the laser therapy

<table>
<thead>
<tr>
<th>Treatment conditions</th>
<th>① Picocare 450</th>
<th>② Pastelle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluence (J/cm²)</td>
<td>0.3~0.5</td>
<td>0.6~0.8</td>
</tr>
<tr>
<td>Pulse Width (ps, ns)</td>
<td>450 ps</td>
<td>10 ns</td>
</tr>
<tr>
<td>Spot Size (mm)</td>
<td>3~4</td>
<td>3~4</td>
</tr>
<tr>
<td>Pulse Rate (Hz)</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Duration of the clinical trial
After gaining the approval of the Ministry of Food and Drug Safety and the IRB, a total of 15 months will be needed for the trial, including 9 months for subject enrollment and 3 months for treatment and follow-up. After the clinical trial is completed, 3 months will be needed for data processing, statistical analysis, results reporting, and IRB approval.
### Supplementary Materials 1. Continued

#### Inclusion criteria
The subjects must satisfy the following inclusion criteria in order to be registered in this trial.

1. Females between the ages of 19 and 74
2. Has Fitzpatrick Skin Type III–V
3. Agreed to have their face photographed
4. Agreed to the prohibition of the use of local/systemic corticosteroids or retinoids and other local/systemic lightening medications, and willing to abide by such instructions
5. Agreed to use the same facial skin care products during the clinical trial period (including the follow-up period), and willing to abide by such instructions
6. Agreed to the daily use of an over SPF 50 sunblock on their face during the clinical trial period (including the follow-up period), and willing to abide by such instructions
7. Agreed not to undergo any other procedure on their face during their participation in the clinical trial
8. (In case of fertile women) Tested negative in the pregnancy test and agreed to use birth control contraceptives during the clinical trial period
   - Oral contraceptives are forbidden as they may influence the results of the clinical study.
9. Voluntarily agreed to sign the written consent form and willing to follow the instructions of the study protocol

#### Exclusion criteria
Subjects who satisfy any of the following exclusion criteria cannot be enrolled in this trial.

1. Has a history of convulsive disorder caused by light
2. Has an infection, dermatitis, or rash on their face
3. Has a history of keloid scarring, hypertrophic scarring, or abnormal would healing
4. Has a history of leukoplakia, eczema, or psoriasis
5. Has a history of connective tissue diseases such as systemic lupus erythematosus or scleroderma
6. Has a history of diseases irritated by heat on their face (e.g., herpes simplex or herpes zoster)
7. Has a history of radiotherapy or anticancer chemotherapy on their face
8. Has a history of malignant tumors on their face
9. Has a history of allergic reaction to local anesthesia
10. Has a history of use of a lightening medication (hydroquinone, tranexamic acid), isotretinoin (or retinoid), light-sensitive medication, or steroids in the last 6 months
11. Received a cosmetic treatment such as laser, light therapy, or surgery in their facial area in the last 6 months, or have a history of filler treatments using collagen, hyaluronic acid, or any other material
12. Currently diagnosed with uncontrolled diabetes or a cardiac disorder such as resistant hypertension
13. Currently diagnosed with anticoagulant disease or taking anticoagulants
14. Has a history of immunodeficiency or intake of immunosuppressants
15. Has excessive facial tanning
16. Pregnant or breastfeeding
17. Participated in another medical device or medication clinical trial in the last 3 months, or planning to participate in another trial during this trial
18. Other subject assessed as inadequate for the clinical trial by the investigators

#### Outcome measures

<table>
<thead>
<tr>
<th>Primary outcome measures</th>
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</thead>
<tbody>
<tr>
<td>■ Clearance rate of treated areas according to quartile improvement scale (12 week after the treatment)</td>
</tr>
<tr>
<td>■ Subjective satisfaction</td>
</tr>
<tr>
<td>■ Assessment of the pain caused by the laser therapy</td>
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<table>
<thead>
<tr>
<th>Safety outcome measure</th>
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<tr>
<td>All adverse events that occurred in the subjects during the clinical trial period</td>
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Early outcome measures and criteria

Primary outcome measures

■ Clearance rate of treated areas according to QIS (12 week after the treatment)

Table 2. Evaluation index of melasma improvement according to the QIS

<table>
<thead>
<tr>
<th>Grade (score)</th>
<th>Improvement rate of melasma</th>
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<tbody>
<tr>
<td>Excellent (4)</td>
<td>76% ~ 100%</td>
</tr>
<tr>
<td>Good (3)</td>
<td>51% ~ 75%</td>
</tr>
<tr>
<td>Fair (2)</td>
<td>26% ~ 50%</td>
</tr>
<tr>
<td>Poor (1)</td>
<td>1% ~ 25%</td>
</tr>
<tr>
<td>No improvement (0)</td>
<td>0%</td>
</tr>
</tbody>
</table>

● Measurement of the QIS

The overall facial pigmentation of each patient before and 12 week after treatment was assessed by three dermatologists who were blinded to the treatment specifics and operated independently of this study. A digital camera and specialized imaging system (Dermavision 1; Optobiomed Inc., Gangwon, Korea) were used to record full face images to assist in the evaluation and assessment of skin pigmentation.

Secondary outcome measures

■ Subjective satisfaction

The subjects in the test and control groups are asked to answer 5-point scale questionnaires on their satisfaction. The results for each group are compared and evaluated.

■ Assessment of the pain caused by the laser therapy (0=no pain, 10=intolerable pain)

The subjects are asked to answer a questionnaire (10-point NRS pain scale) on the pain caused by the laser therapy after each treatment session.

● NRS pain assessment questionnaire

Safety evaluation methods and criteria

Observational items

Expected adverse events

All adverse effects after treatment and PIH were observed and recorded throughout the study, and the occurrence of PIH was evaluated at 12 weeks post-treatment.

See the “Study Schedule.”

1. Burn
2. Pain
3. Dyspigmentation
4. Hyperpigmentation
5. Mottled hypopigmentation
6. Urticaria
7. Acneiform eruption
8. Petechiae
9. Leukoderma
10. Erythema