LOW LEVEL LASER THERAPY IN THE TREATMENT OF CHEMOTHERAPY AND TARGETED THERAPY INDUCED PALMAR-PLANTAR ERYTHRODYSESTHESIA (PPE)

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### Faculty Disclosure

<table>
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<tr>
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<th>No, nothing to disclose</th>
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Yes, please specify:
PPE: grades

Grade 1: Minimal skin changes or dermatitis (e.g., erythema, edema or hyperkeratosis) without pain

Grade 2: Skin changes (e.g., peeling, blisters, bleeding, edema or hyperkeratosis) with pain; slightly limiting instrumental activities of daily living (IADLs)

Grade 3: Severe skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting self-care ADL

*CTCAE Version 4.0, June 2010, National Institutes of Health, National Cancer Institute*
PPE: histology and pathogenesis

- First described in 1984 by Lokich and Moore during a 5FU infusion
- Pathogenesis – unclear
- Histology is not specific but shows:
  - interface dermatitis, keratinocyte necrosis, dilated blood vessels, edema, hyper or parakeratosis, perivascular lymphohistiocytic infiltration in the dermis, and possible eccrine squamous syringometaplasia

- **PPE etiology**: antimetabolites, antracyclines, TKI, dermatologic diseases, infections, denutrition, GVH

- **Standard treatment**: dose reduction or discontinuation of anticancer treatment, symptom control and local treatment

- **Bio-photomodulation (LLLT)**: active for mucositis and radiodermatitis
Methods

- N patients: 32 included and 31 evaluated
- Random allocation of treatment was done to determine the site to be treated with LLLT: left or right
- The other site had to be treated with sham laser
- The patient was his « own-control »
- Dose: 2 J/cm², 500 mW, 3 x week and with minimum 2 weeks blinded
- Total of 6 weeks
- Evaluation
  - blinded assessor 1 x week
  - treating nurse on every session
  - photos 1x week
Study design

32 patients

< 2 weeks

Bilateral progression

Stop

Unilateral progression

Stop blind
LLLT active

No

Yes

stop

Bilateral LLLT

Inclusions criteria

• Bilateral PPE grade 1, 2 et 3
• Patients on undergoing anti-cancer treatment: chemo and/or targeted treatment

Statistics

• Expectations: response in 57% for treated sites and 25% for sham treated sites; statistical power 90%
# Results

<table>
<thead>
<tr>
<th>Patients characteristics</th>
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<tbody>
<tr>
<td>N patients</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>- excluded</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- female</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>- male</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>58 years (34-80)</td>
<td></td>
</tr>
<tr>
<td>Tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- solid</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>- hematology</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
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</tr>
<tr>
<td>- chemotherapy</td>
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</tr>
<tr>
<td>- TKI</td>
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</tr>
<tr>
<td>- combination</td>
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<tr>
<td>Treatment body side</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- right</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>- Left</td>
<td>15</td>
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</tr>
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</table>

### Frequency of PPE according to cancer type and treatment

**Cancer type**

- Breast cancer
- Kidney cancer
- GIST
- Ovarian cancer
- Hematology

### Anticancer treatment

![Bar chart showing frequency of anticancer treatments](chart.png)
Results

• There was no evidence that the severity of the lesions, at baseline, was different according to the body site:
  Hand : p=0.25  Foot : p=1

• This first main assessment was done before unblinding (T1)
  - median 21 days (from 2 to 61 days)
  - median number of sessions 10 (from 2 to 18)

• At that point the results of the treatment for 27 patients with available data (median and range) show that the overall median difference is 0 (-5;5) and the p value is 0.42

<table>
<thead>
<tr>
<th>ScoreT0LT</th>
<th>ScoreT1LT</th>
<th>Difference T1-T0</th>
<th>ScoreT0SL</th>
<th>ScoreT1SL</th>
<th>Difference T1-T0</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 (4;21)</td>
<td>8 (2;17)</td>
<td>-2 (-15;6)</td>
<td>10.5 (3;25)</td>
<td>8 (2;16)</td>
<td>-2 (-18;5.5)</td>
</tr>
</tbody>
</table>
Results

- Mean number of 28.5 sessions (range: 3-160)
- 15 patients reported a decreased pain (40% of them with a grade benefit at T1)
- PPE grade decrease in 19 patients (11 of them at T1)
- 72% of the patients were satisfied with the LLLT treatment
Conclusions

• Our study indicates that photo-biomodulation was not significantly beneficial for the control of treatment induced PPE

• Nevertheless pain was decreased or stabilized and patients satisfaction was greater with LLLT

• Caveats:
  - small number of patients
  - investigator dependent subjectivity

• Future:
  - prospective data needed in larger cohorts
  - reevaluation of LLLT dosage, duration and frequency