Bibliography:


Technical Specifications:

Combat Medical leading the current investigation in thermotherapy device assisted therapies for NMIBC

Combat Medical is committed over the next 5 years to creating a new clinical investigation in the field of intravesical hyperthermia as an adjuvant therapy in select patients. The goal is to achieve a reduction in recurrence and progression rates in patients with NMIBC.

Combat Medical is committed to improving outcomes without healthcare providers having to significantly alter their treatment model or adding additional resources, in fact they believe that we will be able to reduce the overall treatment cost due to our streamlined approach and through the reduction in recurrence and progression rates.

We have demonstrated the potential in a phase II clinical trial and through clinical use over the last 3 years. During this time Combat BRS has shown itself to be easy to use and self-tolerated by the patient with minimal side effects to standard MMC instillations, but importantly, with little impact in terms of time and effort for the healthcare professional in delivering Combat's new HIVEC™ treatment.

HIVEC I & II trials are already underway

Prospective, Randomized International Multicentre Clinical Trials in 693 NMIBC Intermediate Risk Patients.

For more information please contact Combat Medical

www.combat-medical.com

Technical Specifications:

Physical characteristics

**COMBAT BRS System**

- **Equipment external dimensions:** Height 500 mm
  Width 250 mm
  Depth 255 mm

- **Equipment weight:** BRS system 48 kg plus portable stand

- **Safety alarms:** High & Low temperature alarms
  High pressure alarms
  Auto safety cut off
  End of treatment alarm & auto stop

- **Electrical risk classification:** Type II

- **Fluid ingress protection:** IPX2

- **Function mode:** Continuous delivery at set temperature between 40 – 44°C ± 1°C

- **Certification:** UL 60601-1; IEC 60601-1; IEC 60601-2; EN 55011; CAN/CSA-C22.2; 0120

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Visit: www.combat-medical.com
Solvent Content %
94.2
89.7
94.9

Content %
87.3
90.6
90.4

1 hr
40mg MMC 60 min
100.0
100.0
91.0

Comarcal de Monforte, Galicia (Spain)
Alfonso Piñeiro, Urology Nurse, Hospital
the treatment.”
and dispose of the drug after
that you are able to safely remove
system doesn’t require continuous
treatment I am able to continue my
or BCG. During the 60 minute
5 minutes more to set up compared
To USB drive in csv
Data can be stored
USB Port
and graphical
Continuous monitoring
checking procedure.
Automated setup
Simple user interface.
Touch Screen

The Combat BRS system harnesses accurate and effective heat control and the
precision operation of chemo-hyperthermia to ensure MMC’s toxicity is
maximally reduced while allowing for consistent patient comfort and ease.

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Simplicity
The Combat BRS system is portable, reliable and easy to use. Simple to
transport into current treatment rooms or regimes simulated at all, its
continuous monitoring and therefore omission of additional resources either physically
logistically or financially. Both the BRS system and disposable sets are
affordable and through improving patient outcomes, the overall treatment cost can be reduced.

Synergy
The Combat BRS system features accurate and effective heat control and the
precision operation of chemo-hyperthermia to ensure MMC’s toxicity is
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"Our mission is to drive change
in the treatment of bladder cancer in a
cost effective way that helps ease of insertion.
Catheter
In line fluid temperature
Temperature Probe Port
Pressure Sensor
invasive catheterisation.
Pressure sensor detects overpressure
and accurate temperature
and flow rates.
Continuous recirculation
Peristaltic Pump

Temperature Probe Port
In line fluid temperature

Effect of Hyperthermia on Mitomycin C

Mitomycin C (MMC) exposure at higher temperatures.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Mitomycin C Concentration (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>40 mg dose of Mitomycin C</td>
</tr>
<tr>
<td>40</td>
<td>50 mg dose of Mitomycin C</td>
</tr>
<tr>
<td>43</td>
<td>60 mg dose of Mitomycin C</td>
</tr>
<tr>
<td></td>
<td>100 mg dose of Mitomycin C</td>
</tr>
</tbody>
</table>

Mitomycin C remains stable at higher temperatures.

Clinical hyperthermia is defined as the therapeutic use of temperature between 42°C to 44°C. The introduction of thermal energy to the treatment site causes the cancer cells to undergo a change in their structure and function, making them more vulnerable to the effects of chemo-hyperthermia. Mitomycin C (MMC) is an alkylating chemotherapy agent that binds to DNA and inhibits DNA synthesis, thus inducing cell death. Hyperthermia increases the efficacy of MMC by increasing its cytotoxic effects, leading to a higher tumor cell kill. The Combat BRS system harnesses accurate and effective heat control and the precision operation of chemo-hyperthermia to ensure MMC’s toxicity is maximally reduced while allowing for consistent patient comfort and ease.

Synergistic effects of hyperthermia
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