EVALUATION OF THE SPECTRA OPTIA APHERESIS DEVICE FOR MONONUCLEAR CELL COLLECTION IN NON-MOBILIZED & MOBILIZED HEALTHY DONORS: RESULTS FROM A MULTICENTER TRIAL

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BACKGROUND
SPECTRA OPTIA: A NEWER APHERESIS DEVICE

- Cleared for use in Therapeutic Plasma Exchange (TPE) procedures (K071079) in the United States.

- Used to conduct a wide variety of therapeutic apheresis and cell therapy procedures, including mononuclear cell (MNC) collection outside of the U.S.
THE SPECTRA OPTIA VS. THE COBE SPECTRA:

• Spectra Optia has a smaller extracorporeal volume than the COBE Spectra
  • 191 mL vs. 285 mL
  • Accommodates patients with lower total blood volume (TBV) such as pediatric patients
• Minimizes the amount of operator interaction needed, allowing for more focused time with patients
• Automated Interface Management system produces consistent results through interface stability

Modified from http://advancingapheresis-emea.terumobct.com/protocols
MNC COLLECTION IN THE SPECTRA OPTIA

A. Intermediate collection chamber.

B. Blood separation in the connector.

Reinhardt et al, Transfusion, 2010
MNC COLLECTIONS

<table>
<thead>
<tr>
<th>Study Date</th>
<th>Study site</th>
<th>Study design</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>September, 2006</td>
<td>single site, U.S.</td>
<td>Software optimization feasibility study</td>
<td>5 healthy, nonmobilized subjects</td>
</tr>
<tr>
<td>May, 2007</td>
<td>single site, U.S.</td>
<td>Software optimization feasibility study</td>
<td>7 healthy, mobilized subjects</td>
</tr>
<tr>
<td>March, 2008</td>
<td>Europe</td>
<td>1st market acceptance study</td>
<td>100 procedures</td>
</tr>
<tr>
<td>March, 2009</td>
<td>U.S.</td>
<td>Clinical trial for U.S. 510(k) submission</td>
<td>7 clinical patients</td>
</tr>
<tr>
<td>October, 2009</td>
<td>single site, U.S.</td>
<td>Optimization feasibility study</td>
<td>6 healthy, mobilized subjects</td>
</tr>
<tr>
<td>May, 2010</td>
<td>Multi site, Europe</td>
<td>2nd market acceptance study (with optimized protocol)</td>
<td>36 patients</td>
</tr>
</tbody>
</table>

The optimized Spectra Optia MNC Protocol appeared ready for broad evaluation in a multisite U.S. clinical trial based on:

- Based on these studies’ outcomes
- CaridianBCT’s extensive experience outside of U.S.
STUDY OBJECTIVE

• To characterize the performance of the Spectra Optia Apheresis System’s MNC Protocol, when used to collect mononuclear cells from healthy blood donors.

• Complements a separate, historically controlled study, conducted in patients with multiple myeloma (Protocol No. BCT10-02).
METHODS
DESIGN:
A PROSPECTIVE OBSERVATION STUDY

Healthy Volunteer Donors (3 sites)

Donor Self-Selection

Mobilized with G-CSF
16 subjects

Non-mobilized
25 subjects
**Inclusion Criteria**

- Qualified blood donor & in general good health
- Age: 18-50 years
- Weight: 50-125 kg
- Male or non-pregnant, non-nursing female
- Acceptable lab values for eligibility & mobilization
  - Complete blood count, electrolytes, coagulation tests
  - Negative pregnancy test in female subjects
- Adequate peripheral venous access to allow for collection
**Apheresis Procedure**

- Dual-needle peripheral access
- Target the lesser of $12.5 \pm 0.5$ L or $2.0 \pm 0.2$ TBV processed
- Flow Rate: 30-125 mL/minute
- Target collect Hematocrit: < 5%
- Anticoagulant: ACD-A
- Inlet:AC Ratio: 6-15
- ACD-A Infusion Rate: 0.8 – 1.2mL/L TBV/min
- TUMs, IV calcium gluconate, or magnesium sulfate given to treat or prevent symptoms caused by citrate
OUTCOMES & ANALYSIS

• Collection Efficiencies (CE)
  • MNC counts (all subjects)
  • CD34 cell counts (mobilized subjects only)
• Cross-cellular contamination (stem cell product)
  • Granulocytes (% of WBCs)
  • Platelets (CE)
  • Red blood cells (Hct)
• CD34+ cell viability by 7-AAD staining
• Summary statistics: mean, standard deviation, median, range, and 95% confidence intervals
**Collection Efficiency**

\[
\left( \frac{C_{COL} \times V_{COL}}{C_{AV} \times V_{WB}} \right) \times 100\%
\]

- \( C_{COL} \): number of cells/mL in the collected product
- \( V_{COL} \): volume (mL) of the collected product
- \( C_{AV} \): \((\text{# of cells pre-apheresis} \ + \ \text{# of cells post-apheresis per mL})/2\)
- \( V_{WB} \): volume (mL) of whole blood processed
RESULTS
## Donor Demographics

<table>
<thead>
<tr>
<th>Study Protocol (n)</th>
<th>Gender (M/F)</th>
<th>Age (years)</th>
<th>TBV (mL)</th>
<th>Hct (%)</th>
<th>WBC (e³/uL)</th>
<th>Platelets (e³/uL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-mobilized Donors (15)</td>
<td>11/4</td>
<td>33 (29-47)</td>
<td>5149 (3887-6332)</td>
<td>44 (35-49)</td>
<td>5 (3-10)</td>
<td>244 (164-333)</td>
</tr>
<tr>
<td>Mobilized Donors (15)</td>
<td>12/3</td>
<td>25 (19-45)</td>
<td>5435 (3405-6705)</td>
<td>43 (38-50)</td>
<td>19* (10-34)</td>
<td>230 (161-390)</td>
</tr>
</tbody>
</table>

Reported as median (range) unless noted.

*Higher in mobilized arm ($P < 0.05$)
## Collection Conditions

<table>
<thead>
<tr>
<th>Study Protocol (N)</th>
<th>Blood Volume Processed</th>
<th>Inlet Flow Rate (mL/min)</th>
<th>Inlet:AC Ratio</th>
<th>Run time (min)</th>
<th>Product Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-mobilized Donors (15)</td>
<td>1.9 (1.8-2.0)</td>
<td>56 (40-70)</td>
<td>12 (9-15)</td>
<td>180 (150-241)</td>
<td>128 (81-207)</td>
</tr>
<tr>
<td>Mobilized Donors (15)</td>
<td>1.9 (1.6-2.1)</td>
<td>58 (40-80)</td>
<td>13 (12-15)</td>
<td>184 (162-259)</td>
<td>223* (150-345)</td>
</tr>
</tbody>
</table>

Reported as median (range) unless noted.

*Higher in mobilized arm ($P < 0.05$)
## Performance Characteristics

<table>
<thead>
<tr>
<th>Measure</th>
<th>Non-mobilized</th>
<th>Mobilized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Range</td>
</tr>
<tr>
<td>MNC collection efficiency (%)</td>
<td>57</td>
<td>27 to 92</td>
</tr>
<tr>
<td>CD34 collection efficiency (%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>WBC Viability (%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Platelet collection efficiency (%)</td>
<td>12</td>
<td>5 to 21</td>
</tr>
<tr>
<td>Product Hct (%)</td>
<td>4</td>
<td>2 to 5</td>
</tr>
<tr>
<td>Product granulocytes (%)</td>
<td>2</td>
<td>0 to 9</td>
</tr>
</tbody>
</table>
Adverse Events

• No serious adverse events or device malfunctions

• In total, there were 11 citrate reactions
  • One citrate reaction was Grade 3 (severe).
  • All other adverse events were mild to moderate.

• Other apheresis-related adverse events:
  • Venous access issues (4 subjects)
  • Arm numbness/stiffness (2 subjects)
  • Nausea (2 subjects)
  • Fatigue (1 subject)
SUMMARY
**Discussion**

- This study characterized the performance of the Spectra Optia MNC collection protocol in healthy donors.

- MNC collection efficiency was similar in both arms of the study and the presence of contaminating non-MNCs in the collected cell products was minimized.
**Conclusions**

- The Spectra Optia can be used for safe and efficacious collection of MNCs for donors.

- Adverse events were limited and similar to other collections systems.

- FDA 510(k) approval for use of the Spectra Optia device for MNC collection was achieved in the U.S. based partly on the results of this study.
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  • Scott Carter, MT(ASCP)
QUESTIONS