MEASUREMENT OF ADHERENCE, HEALTH-RELATED QUALITY OF LIFE, AND HEALTH-CARE RESOURCE UTILIZATION DURING ANTICOAGULATION THERAPY IN CANCER-RELATED VENOUS THROMBOEMBOLISM

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CONTENT

- Brief background review
- Study problem and objectives
- Study design and activities
- Timeline and updates
Cancer-related venous thromboembolism (VTE) is a prevalent problem that occurs in 20-25% of patients with malignancy.

For cancer related-VTE, consensus guidelines (ASCO, ACCP, NCCN) recommend treatment with parenteral low molecular weight heparin (LMWH) for the initial and long term therapy (at least 6 months).

Recommendations in VTE guidelines are based on efficacy and safety data, but scant (to none) information on quality of life, patient’s preference and adherence to therapy outside clinical trials.

Although LMWH are effective agents for the treatment of cancer-related VTE, they are often difficult to tolerate and might be inconvenient for long-term use by cancer patients.


U.S. PRESCRIPTION PATTERNS FOR CANCER-VTE

Anticoagulation prescription patterns (2009-2014)

- Warfarin: 50%
- LMWH: 40%
- DOAC: 10%

n = 105,399

U.S. PRESCRIPTION PATTERNS FOR CANCER-VTE

Anticoagulation prescription patterns (2013-2014)

- Warfarin: 28%
- LMWH: 23%
- DOAC: 49%

Proportion of patients on anticoagulation from cancer-VTE diagnosis

< 1 month
1 to 3 months
3 to 6 months

LMWH  Warfarin  DOAC

Some reports based on expert experience have described that reasons for non-adherence to guidelines might be:

- Reluctance to impose daily injections on fragile patients
- The complexity of the medical care organization and pathway (cost related issues, patient’s preference, level of awareness, etc.)
- Strength of habit
- Lack of knowledge or confidence in treatment guidelines
- Concerns about bleeding, dose adjustments in specific circumstances (i.e.: thrombocytopenia, concurrent coagulopathy, drug interactions)

PROBLEM

- There is a need for further investigation of the treatment adherence, health related quality of life (QoL) and health care resources utilization during long term anticoagulation for cancer-related VTE.

- Knowledge gap in the impact of QoL and treatment adherence in cancer-thrombosis related outcomes:
  - Recurrent venous thromboembolism
  - Clinical relevant bleeding
PROBLEM: TARGET POPULATION

- Adult (≥ 18 years) female or male subjects
- Confirmed symptomatic proximal or distal lower extremity deep venous thrombosis with or without pulmonary embolism or other venous thromboses
- Active cancer or diagnosed within 2 years prior to VTE
- Intention for long-term treatment (at least 3 months) with anticoagulation
- Setting: Hospital/outpatient clinic/anticoagulation clinic
STUDY OBJECTIVES

- **PRIMARY**
  - To assess self-reported adherence to long term anticoagulation treatment for cancer related-venous thromboembolism

- **SECONDARY**
  - To assess anticoagulation self-reported adherence changes over time, by the anticoagulant type used (parenteral versus oral)
  - To assess if other patient, tumor and anticoagulation-related outcomes are associated with self-reported adherence to anticoagulation treatment
  - To assess the QoL variables in patients for cancer-related VTE treated with anticoagulation
  - To measure the number of outpatient visits, emergency center visits and hospitalization episodes related to the management of anticoagulation complications during the study period
### STUDY DESIGN

<table>
<thead>
<tr>
<th>Assessments</th>
<th>Completed by</th>
<th>Time 1</th>
<th>Follow-up at 30 day</th>
<th>Follow-up at 3 months</th>
<th>Follow-up at 6 months</th>
<th>Follow-up at 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent</td>
<td>Patient</td>
<td>X</td>
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<tr>
<td>Screening Questionnaire</td>
<td>Research coordinator</td>
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<tr>
<td>QoL variables</td>
<td>Patient</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Adherence report</td>
<td>Patient</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Documentation of visits for anticoagulation</td>
<td>Research coordinator</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>complications</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- Prospective observational (non-interventional) study
- Multiple centers will be participating
- 260 patients
- Potential participants in the study will be identified through a list of daily diagnostic doppler ultrasonography and computerized tomography studies.
STUDY OUTCOMES MEASUREMENT

- SELF –REPORTED ANTICOAGULATION ADHERENCE

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you ever forget to take your medicine?</td>
<td></td>
</tr>
<tr>
<td>Are you careless at times about taking your medicine?</td>
<td></td>
</tr>
<tr>
<td>When you feel better, do you sometimes stop taking your medicine?</td>
<td></td>
</tr>
<tr>
<td>Sometimes if you feel worse when you take the medicine, do you stop taking it?</td>
<td></td>
</tr>
</tbody>
</table>

The Morisky scale is a validated, self-reported measure that can be integrated in a medical visit.

It is composed of four dichotomized item/questions with good predictive validity for medication adherence (alpha reliability=0.6)

This adherence scale has been previously used in patients on oral long term anticoagulation and shown to provide correlation with anticoagulation control.


STUDY OUTCOMES MEASUREMENT

- HEALTH CARE RELATED QoL: DVTQOL TOOL

- A questionnaire that includes a total of 29 questions.

- For each question, responses are arranged on a seven-point Likert scale:
  - Severity of the degree of distress
    not at all, minor, mild, moderate, moderate severe, severe, extremely severe
  - Frequency of the problem
    never, hardly ever, occasionally, sometimes, frequently, most of the time, all of the time

- The item-questions are grouped in six domains: Emotional distress, symptoms, limitations in physical activity, hassle with monitoring, sleep disturbance, and dietary problems.

- The DVTQOL has a good internal consistency reliability (alpha, 0.79 to 0.93) and it correlates well with other well validated tools for the evaluation of health related QoL, such as SF-36 and EQ-5D

TIMELINE & UPDATES

- Protocol approved at MD Anderson Cancer Center (USA) in October 2017
- Applied for local Survivorship Program funding
- Screening and enrollment of participants started in November 2017
- At May 31, 2018:
  - A total of 339 patients screened for eligibility
  - 12 subjects are currently participating
  - 6 subjects have completed surveys for 30-day follow-up visits
  - 2 subjects have withdrawn from the study
## TIMELINE & UPDATES

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>%</th>
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<tbody>
<tr>
<td>Female</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>Age [min., max]</td>
<td>[43, 78]</td>
<td></td>
</tr>
<tr>
<td>Type of malignancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>Hematologic</td>
<td>2</td>
<td>17</td>
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<tr>
<td>Active cancer therapy</td>
<td>9</td>
<td>75</td>
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<tr>
<td>Anticoagulation of choice</td>
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<td></td>
</tr>
<tr>
<td>LMWH</td>
<td>9</td>
<td>75</td>
</tr>
<tr>
<td>DOAC</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>Location of index DVT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal lower extremity</td>
<td>7</td>
<td>58</td>
</tr>
<tr>
<td>Distal lower extremity</td>
<td>5</td>
<td>42</td>
</tr>
<tr>
<td>Concurrent pulmonary embolism</td>
<td>7</td>
<td>58</td>
</tr>
</tbody>
</table>
TIMELINE & UPDATES

- At 30-day follow up: 100% self-reported adherence to treatment (6 subjects)

- Health related QoL features:
  - Frequent moderate to moderate-severe distress in the domains of physical symptoms and limitation to physical activity
  - Frequent moderate emotional distress related to anxiety about own health
TIMELINE & UPDATES

- Sites initiating IRB approval and activation (2018):
  - Mitchell Cancer Institute (Alabama, USA): Dr. Butler
  - Hospital Clinic (Barcelona, Spain): Dr. Font
  - Virgen del Rocio Hospital (Seville, Spain): Dr. Jara-Palomares
  - Valle del Lili Clinic (Cali, Colombia): Dr. Chavarro-Dominguez
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