Barriers to Enrollment in Phase I/II Clinical Trials for Patients >65 Years of Age: A Moffitt Experience

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University of Colorado Cancer Center Project

• To conduct a *survey* that characterizes the prevalence and magnitude of barriers to the participation of older patients in early phase clinical trials
• To utilize this data to *formulate* a patient-targeted intervention to enhance accrual
• To *conduct* a randomized clinical trial to assess the effects of the intervention on early clinical trial accrual
Incidence Rates of Invasive Neoplasms by Age

Source: SEER, 1996-1997
Persons aged 65+ years are underrepresented in clinical trials.
Referral from community to university → University MD Offers Trial → Patient Evaluates Therapy → Consent → Patient Evaluates Requirements for Study Participation

Model of the Process Leading to Participation in Early Clinical Trials at University
Proposed Barriers to Participation of Older Persons in Early Phase Trials

Community/academic oncologist barriers

- Loss of continuity
- Age-related bias re risks/benefits of RX
- Loss of revenue
- Comorbidity
- MD bias

- Age-related bias re risks/benefits
- Age-related ability to understand study
- Paperwork/time
- Knowledge of trials

Oncologist Refers Pt to Academic CA Center → University MD Offers Trial → Patient Evaluates Therapy
Proposed Barriers to Participation in Early Phase Trials

Patient Barriers

- Perceived risk/benefit ratio of therapy
- Lack of endorsements

- Logistics
- Insurance
- Perceived loss of continuity
- Protocol burden
- Perception of research
- Perception of academic centers

Patient Evaluates Therapy

Patient Evaluates Requirements for Study Participation

Consent

So- We focused on patient-related barriers
Primary Objectives of Survey

• To describe the *prevalence of perceived barriers* to participation in early phase clinical trials by older adults (i.e., aged ≥ 65 years)

• To identify factors considered *important to ≥ 20%* of older adults when deciding about clinical trial participation
Secondary Objectives of Survey

• To *compare* the prevalence of perceived barriers for the young old (aged 65-74 years) to that of the "old old" (aged 75+ years)

• To compare the prevalence of factors identified as *important* to the young old *versus* the old old when deciding whether to participate in an early phase clinical trial
A survey was Developed

• Patients were surveyed in their local oncologists office by a trained interviewer.
• Surveys were conducted in states of Colorado and Florida.
Proportion of subjects who reported facing at least 1 perceived barrier by age

N= 300 total community patients surveyed

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>65+</td>
<td>183 (61%)</td>
</tr>
<tr>
<td></td>
<td>(55.5-65.5)</td>
</tr>
<tr>
<td>65-74</td>
<td>83 (54%)</td>
</tr>
<tr>
<td>75+</td>
<td>100 (68%)</td>
</tr>
</tbody>
</table>

Any kind of barrier common, but not substantially different between age groups
### Results:
Prevalence of Perceived Barriers

<table>
<thead>
<tr>
<th>Perceived Barrier</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistics</td>
<td>102 (34%)</td>
</tr>
<tr>
<td>Unwilling to be treated at university cancer center</td>
<td>62 (21%)</td>
</tr>
<tr>
<td>Loss of continuity with primary oncologist</td>
<td>58 (20%)</td>
</tr>
<tr>
<td>Concern will be treated as “guinea pig”</td>
<td>56 (19%)</td>
</tr>
<tr>
<td>Insurance coverage</td>
<td>49 (16%)</td>
</tr>
</tbody>
</table>
# Prevalence of Barriers by Age

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Age 65-74</th>
<th>Age 75+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic</td>
<td>32%</td>
<td>36%</td>
</tr>
<tr>
<td>Unwilling to be treated at university cancer center</td>
<td>14%</td>
<td>27%</td>
</tr>
<tr>
<td>Loss of continuity with primary oncologist</td>
<td>15%</td>
<td>24%</td>
</tr>
<tr>
<td>Exploitation</td>
<td>14%</td>
<td>23%</td>
</tr>
<tr>
<td>Insurance</td>
<td>14%</td>
<td>19%</td>
</tr>
</tbody>
</table>
**Results: Factors rated very important when considering an experimental therapy**

<table>
<thead>
<tr>
<th>Possibility treatment results in...</th>
<th>Percent rated very important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better symptoms</td>
<td>94%</td>
</tr>
<tr>
<td>Shrink tumor</td>
<td>96%</td>
</tr>
<tr>
<td>Stabilize tumor</td>
<td>91%</td>
</tr>
<tr>
<td>Live Longer</td>
<td>92%</td>
</tr>
<tr>
<td>Need more care from family/friends</td>
<td>58%</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>57%</td>
</tr>
<tr>
<td>Unable to do things enjoy</td>
<td>51%</td>
</tr>
</tbody>
</table>
## Results:
Acceptability of an Experimental Treatment

<table>
<thead>
<tr>
<th>Endorsement Source</th>
<th>Percent rated very important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Oncologist</td>
<td>97%</td>
</tr>
<tr>
<td>Family</td>
<td>52%</td>
</tr>
<tr>
<td>Nurse who treats patients with experimental therapy</td>
<td>48%</td>
</tr>
<tr>
<td>Spouse/Partner</td>
<td>45%</td>
</tr>
<tr>
<td>Another patient who has received treatment</td>
<td>38%</td>
</tr>
<tr>
<td>Internet information</td>
<td>14%</td>
</tr>
</tbody>
</table>
A New Survey Instrument was created targeting the prevalent barriers

- A “navigator” was assigned to ½ of the patients to assist them in overcoming these barriers.
- Predominant barriers were identified as:
  - Side effects of treatment
  - Transportation to appointments
  - Financial worries
  - Communication with the healthcare team
  - Home care assistance
Proposed Intervention: Clinical research navigator

**Age-related bias re: risks/benefits**

- Navigator
  - prescreens patients
  - identifies trials
  - gives the investigator the consent, HIPPA, protocol summary

**University**
MD/Investigator Offers Phase I/II Trial

**Patient Evaluates Therapy**

**Navigator**
- consents for barriers study
- reviews Phase I/II consent with patient
- clarifies protocol requirements
- elicits questions for MD to address
- assess barriers with survey

**Patient** Evaluates Therapy
Proposed Intervention: Clinical research navigator

- Patient Evaluates Therapy
- Perceived risk/benefit ratio of therapy
- Navigator provides treatment-based information
- Patient Evaluates Requirements for Study Participation
- Protocol burden
- Navigator offers assistance with logistics and insurance questions
- Consent
A Randomized Trial of Navigators versus Usual Care for the Enrollment of Older Adults on Clinical Trials

• **Primary aim:**
  To assess whether the navigator intervention *increases* the proportion of older, clinical trial candidates who enroll on clinical trials (phase I, II or III). *(Patient barriers)*

• **Secondary aim:**
  To assess whether the navigator intervention *increases* the proportion of older, clinical trial candidates who are offered early phase clinical trials. *(Physician barriers)*
• **Inclusion Criteria**
  - Age ≥ 65 years
  - Clinical trial candidate
    - Normal end organ function (unless trial allows)
    - No active brain metastases (unless trial allows)
    - ECOG PS 0-2
    - Ability to provide informed consent

• **Exclusion Criteria**
  - Oncologist prefers to offer only standard therapy or a phase IV clinical trial
  - Patient enrolled in a phase I at age 65 or older previously
Recruitment Strategies

• Navigator/research associate attends all Phase I/II meetings to formulate a patient list of those patients over 65 who might qualify for the study.

• All patients charts reviewed for eligibility.

• Determination is made for next appointment time.
Study Schema (Original)

Patients enrolled in RCT

Research Navigator

Usual Care

MD offers

Phase II or III trial

Other (SOC)

Referral to Phase I

If offered phase I, II, III clinical trial, navigator assess barriers to participation

Navigator coordinates appointment with Phase I

Patient consents

Patient declines trial
## Barriers and Interventions

<table>
<thead>
<tr>
<th>Barriers Identified</th>
<th>Interventions Offered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation</td>
<td>Cab vouchers and Angel Flight</td>
</tr>
<tr>
<td>Lodging</td>
<td>Assistance with free hotel rooms through ACS</td>
</tr>
<tr>
<td>Concern regarding QOL/toxicity</td>
<td>Communicate concerns to MD</td>
</tr>
<tr>
<td>Treatment concerns</td>
<td>Arrange communication with another patient on trial or with RN who has treated patients on trial</td>
</tr>
<tr>
<td>Knowledge of trial</td>
<td>Communicate questions to research coordinator</td>
</tr>
</tbody>
</table>
Statistical analysis: Estimate of power

• With a sample size of 122 (61 patients randomized to the usual care arm and 61 randomized to the intervention arm):

• Achieves 80% power to detect a difference of 0.25 when the null hypothesis is that the proportion of subjects who enroll is identical (0.30) in both arms of the study - versus the alternative hypothesis that the prevalence is 0.30 in one group and 0.55 in the other group.
## Current Status

<table>
<thead>
<tr>
<th></th>
<th>Colorado</th>
<th>Florida</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients screened for Navigator Trial</td>
<td>107</td>
<td>111</td>
<td>218</td>
</tr>
<tr>
<td>Total enrolled in Navigator Trial</td>
<td>50</td>
<td>32*</td>
<td>82</td>
</tr>
<tr>
<td>Total patients who received Navigator</td>
<td>26</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>Total patients who received Usual Care</td>
<td>24</td>
<td>17</td>
<td>41</td>
</tr>
</tbody>
</table>

*One patient ineligible*
## Current Status

<table>
<thead>
<tr>
<th>Total of Navigator patients who enrolled in clinical treatment trial</th>
<th>Colorado</th>
<th>Florida</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22</td>
<td>8</td>
<td>30</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total that did not enroll in clinical treatment trial on Navigator Arm</th>
<th>Colorado</th>
<th>Florida</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total of Usual Care patients who enrolled in clinical treatment trial</th>
<th>Colorado</th>
<th>Florida</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
<td>11</td>
<td>31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total that did not enroll in clinical treatment trial on Usual Care Arm</th>
<th>Colorado</th>
<th>Florida</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
</tbody>
</table>

So: About 80% of patients on both arms have enrolled on clinical trials!
Conclusions: Were Objectives Met?

To conduct a survey that characterizes the prevalence and magnitude of barriers to the participation of older patients in early phase clinical trials

– 300 patients surveyed: manuscript in preparation

To utilize this data to formulate a patient-targeted intervention to enhance accrual

– Results of the survey suggested that a patient navigator would potentially help with logistical/informational barriers to clinical trials

• To conduct a randomized clinical trial to assess the effects of the intervention on early clinical trial accrual

– Results reflect the difficulty in translating the data obtained from community-based patients to an academic center

– Overall, patients that are seen in academic centers are highly motivated and patient navigators are seen as helpful, but not mandatory for participation

– Further data analysis is ongoing
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