Clinical trial enrollment among older cancer patients

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2002: Cancer killed more than 6.7 million people around the world.
By 2020, cancer could kill 10.3 million people per year unless we act.

Percentage Increase in cancer deaths since 2002:
- 0-25%
- 25-50%
- 50-75%
- 75-100%

Source: IARC, Globocan 2002
Incidence of breast cancer

Incidence [1/100,000/y]

Age

35 40 45 50 55 60 65 70 75 80 85+
Background

- Breast Cancer is the second most common cause of cancer death among women in the U.S.

<table>
<thead>
<tr>
<th>Age</th>
<th>In situ</th>
<th>Invasive</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 40</td>
<td>1,780</td>
<td>11,330</td>
<td>1,160</td>
</tr>
<tr>
<td>Under 50</td>
<td>14,240</td>
<td>50,430</td>
<td>5,240</td>
</tr>
<tr>
<td>50-64</td>
<td>23,360</td>
<td>81,970</td>
<td>11,620</td>
</tr>
<tr>
<td>65+</td>
<td>20,050</td>
<td>98,080</td>
<td>22,660</td>
</tr>
<tr>
<td>All ages</td>
<td>57,650</td>
<td>230,480</td>
<td>39,520</td>
</tr>
</tbody>
</table>

35% of the in situ carcinoma; 43% of the invasive breast cancer, 57% of the breast cancer deaths occur among patients >65
Clinical trials, cancer and the elderly

• Advances in cancer care derive from clinical trials.
  - Crucial step evaluating new treatments.
  - Access and participation are essential to establish treatment guidelines that are applicable to the general population.

• Despite the fact that older patients account for the greatest proportion of those with cancer, they are disproportionately underrepresented in clinical trials.

• Change in Medicare policy in 2000 to include coverage of routine care costs of clinical trials.

• NCCN senior oncology guidelines/ ASCO
  – Recognize paucity of data to make strong recommendations.
  – Patients >65 are underrepresented and therefore how to extrapolate results from clinical trials to this patient population can be difficult.
  – Older patients should be encouraged to participate in clinical trials.
Clinical trials, cancer and the elderly

• 16,396 patients enrolled in 164 SWOG clinical trials 1993-1996 according to age.
• Rates compared with rates in the general population US Census and SEER data.
  • Similar proportion on women and blacks in trials as in the general population.
  • Statistically significant underrepresentation of patients >65 (25% vs 63% p<0.001)
  • Underrepresentation was particularly notable in breast cancer trials (9% vs 49%, p<0.001)
    – Similar findings after exclusion of trials designed specifically for premenopausal patients.

Hutchins, NEJM 1999.
Clinical trials, cancer and the elderly

• Retrospective review of 495 NCI-sponsored clinical trials 1997-2000

• Phase II, III clinical trials
  • 32% of patients were >65 compared with 61% in general population.
  • Degree of underrepresentation was more pronounced for trials for early stage cancer. Strict eligibility criteria were associated with lower enrollment of patients >65yo.

Clinical trials, cancer and the elderly

- The FDA experience
- Retrospective review of demographic data of patients enrolled on 55 registration trials of new therapies (n=28,766).
- 36 vs 60%.
- Breast clinical trials – 38% hormonal trials
Clinical trials, cancer and the elderly - After 2000

- Evaluate the change of the Medicare reimbursement coverage policy on enrollment of older cancer patients.
- CTEP-database NCI-sponsored lung, colon, breast, prostate.
  - 39% of patients were older than 65 before the policy change vs. 33.5% after policy change
  - Breast cancer 21.7% vs 23% (p=0.18)

Clinical trials, cancer and the elderly
- After 2000

- Proportion of enrollment of patients >65 in SWOG clinical trials overtime.

- 31% of patients >65 before the policy change vs 38% after the policy change

The new kids on the block

- **TDM1** - median age 53 (range 24-84)
  - 11% (65-74)
  - 2.5% (>75)
- **Pertuzumab** - median age 54 (range 27-89)
  - 15% (>65)
  - 2% (>75)
- **Everolimus** - median age 62 (range 93)
  - 26% >65

Verma, NEJM 2012.
Baselga NEJM, 2011.
Baselga NEJM, 2011.
Why elderly patients are not enrolled?

- Barriers for enrollment
  - Protocol design
  - Inclusion criteria
  - Performance status
  - Comorbidities
  - Education and income level
  - Distance to center with clinical trials
  - Perception
    - of patient
    - of physician
    - of family & friends
  - More risks
  - More cost
  - More visits
  - “experimental”
  - Randomization
Who is enrolled in clinical trials?

- Snapshot of patients enrolled in NCI-sponsored clinical trials (n=24,000)
- Strong accrual of children (0-10 yo)
- Poor accrual among the elderly
  - 60-66: 17.4%
  - 70-79: 14.3%
  - >80: 2.9%
- Lower numbers of asians and hispanics. Black men 30-59 have lower accrual
- Patients enrolled in clinical trials are less likely to be uninsured
- Areas of high socioeconomic status had higher rates of participation
- Number of ASCO member per 1,000 cancer patients was associated with clinical trial participation

*Sateren J Clin oncol 2002.*
Barriers to clinical trial enrollment

- Patient survey via an internet-based treatment decision tool to assess clinical trial participation (77,752 sent; 6,259 answered, 5499 successful surveys)
  - 22% of responders >65
- Was a clinical trial discussed? 40%
- Was a clinical trial offered? 45%
- Did you participated? 51%
- Perceptions regarding a clinical trial:
  - Better treatment
  - Are more difficult to tolerate
  - Represent a gamble
  - Are inconvenient
  - Were more difficult to pay for

Unger, J Clin Oncol 2013.
Barriers to clinical trial enrollment

- SES associated with enrollment in multivariable model.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Sample Size</th>
<th>OR</th>
<th>P</th>
<th>Line of Equal Odds (OR = 1.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 65</td>
<td>964</td>
<td>0.79</td>
<td>.06</td>
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<tr>
<td>&lt; 65</td>
<td>3,625</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Female</td>
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<tr>
<td>Male</td>
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<td>0.69</td>
<td>.13</td>
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<tr>
<td>Race</td>
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</tr>
<tr>
<td>African American</td>
<td>125</td>
<td>1.51</td>
<td>.49</td>
<td></td>
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<tr>
<td>White/other</td>
<td>4,454</td>
<td>0.67</td>
<td>&lt;.001</td>
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<tr>
<td>Education</td>
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<td></td>
</tr>
<tr>
<td>&lt; College</td>
<td>1,595</td>
<td>0.66</td>
<td>.02</td>
<td></td>
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<tr>
<td>≥ College</td>
<td>2,984</td>
<td>0.74</td>
<td>.06</td>
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<tr>
<td>Comorbidities</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 or 1</td>
<td>2,711</td>
<td>0.76</td>
<td>.07</td>
<td></td>
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<tr>
<td>≥ 2</td>
<td>1,868</td>
<td>0.65</td>
<td>.03</td>
<td></td>
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<tr>
<td>Distance to clinic, miles</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 13</td>
<td>2,266</td>
<td>0.64</td>
<td>.005</td>
<td></td>
</tr>
<tr>
<td>≥ 13</td>
<td>2,274</td>
<td>0.73</td>
<td>.08</td>
<td></td>
</tr>
</tbody>
</table>

Odds of Clinical Trial Participation for Lower Income Patients: ← Lower Odds  Higher Odds →

Unger, J Clin Oncol 2013.
ICD coding for clinical trial participation

- 9/19/2000 CMS introduced **QV** modifier (item or service provided as routine care a Medicare qualifying clinical trial)
- Diagnostic code **V70.5** to identify clinical trial items
- 1/2/2002 V70.5 was discontinues, leaving only QV modifier.
- New code **V70.7** (examination of participant in clinical trial

SEER Medicare study evaluating clinical trial participation among prostate cancer patients (2000-2002)
- n= 37217 (only 211 clinical trial participants)
- Participants were not representative of the rest of the population
  - Age, SES associated with participation. Comorbidities and tumor characteristics were not associated.
Possible aims

• To evaluate the rates and predictors of clinical trial enrollment among older persons with cancer
• To assess toxicity associated with clinical trial enrollment
• To determine the costs associated with clinical trial participation (vs resource utilization: tests, md visits, etc)
Grant proposal discussion

- Validation
  - Using V codes to identify trial enrollment?
  - MDACC data—can get sensitivity and specificity
  - SWOG-Medicare linked data-only sensitivity
  - Need to assess multiple tumor types?
  - Other ideas?
Possible Data Sources

• 100% Medicare: breast cancer
• SEER-Medicare, TCR-Medicare: several cancers
• Marketscan? Probably not-focus on older patients
100% Medicare Data

• National rates of clinical trial enrollment
• Geographic distribution
• Access to care—use clinicaltrials.gov to map centers and distance
  • For trials initiated after 9/27/07 or still ongoing as of 12/26/07, using drugs, biologics or devices, NOT all phase 1
  • How much due to poor access?
• Survey—probably not or next step?
• Breast purchased, others expensive
SEER-Medicare/TCR Medicare

- Advanced disease versus early stage
- Toxicity
  - Hospital admissions
  - ER visits
- Costs/charges
- Or could look at resource utilization: days in hospital, tests performed, number of doctor visits, etc
Both datasets

- Patient characteristics
  - Age, ethnicity, SES, male vs female
- Physician characteristics
  - Type of practice, years in practice, gender
  - ASCO membership
Limitations

• Can’t identify type of clinical trial
• Can’t tell if trial related to cancer or other condition
• Patient selection confounding
• What if trials are more expensive or more toxic?
• Clinicaltrials.gov missing phase 1
• Costs of 100% Medicare data
Possible aims

• To evaluate the rates and predictors of clinical trial enrollment among older persons with cancer
  – 100% Medicare breast, lung, colon, prostate?
  – Patient and provider characteristics
  – Geographic analysis
  – clinicaltrials.gov: distance from closest center

• To assess toxicity associated with clinical trial enrollment
  – SEER-Medicare
  – Hospitalizations, ER visits, specific diagnoses

• To determine the costs associated with clinical trial participation (vs resource utilization: tests, md visits, etc)
  – SEER-Medicare
Thank you