The Impact of Full Body Weight-Based Chemotherapy Dosing on Adverse Events and Outcome in Older Breast Cancer Patients: Results from Cancer and Leukemia Group B (CALGB) Trial 49907

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Cancer in the Elderly Committee – 13 May 2016
Introduction

- American Society of Clinical Oncology (ASCO) clinical practice guideline for appropriate chemotherapy dosing for obese cancer patients (J Clin Oncol 2012; 30:1553-1561)
  - Cytotoxic therapy – not targeted agents
  - No evidence that short-/long-term toxicities increased in obese pts receiving full weight-based doses
  - Full weight-based dosing be considered for obese patients, especially in potentially curative setting

- Cancer and Leukemia Group B (CALGB) 49907 – 633 women >65 years w/early stage (stages I-IIIB) breast cancer
  - Superiority of standard chemotherapy c/w capecitabine
  - Full-dose weight-based dosing utilized, except as follows: IBW used if actual weight was >30% IBW; dose adjustments for renal insufficiency made for methotrexate and capecitabine
Objectives

● Toxicities
  ● Grade 3/4 hematologic and non-hematologic
  ● Study entry BSA (quartiles)
  ● Study entry BMI (underwt-normal, overwt, obese)
  ● Treatment arm
  ● Age (65-69, 70-80, ≥80 years)

● Outcome – RFS, OS
  ● BSA / BMI subgroups
## Frequency of Grade $\geq 3$ Toxicities in the Study Population (n=615)

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Any gr $\geq 3$ toxicity</td>
<td>281 (45.7)</td>
</tr>
<tr>
<td>Gr $\geq 3$ non-heme toxicity</td>
<td>370 (60.2)</td>
</tr>
<tr>
<td>Gr $\geq 3$ heme toxicity</td>
<td>441 (71.7)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr $\geq 3$ anemia</td>
<td>13 (2.1)</td>
<td>602 (97.9)</td>
</tr>
<tr>
<td>Gr $\geq 3$ neutropenia</td>
<td>100 (16.3)</td>
<td>515 (83.7)</td>
</tr>
</tbody>
</table>
BSA and BMI Categories

- BSA category (n=615)
  - <25th Percentile (≤1.663)
  - 25th-50th Percentile (1.663-1.801)
  - 50th-75th Percentile (1.801-1.956)
  - >75th Percentile (>1.956)

- BMI category (n=615)
  - Normal or Underweight (≤25) (n=160)
  - Overweight (25-30) (n=200)
  - Obese (>30) (n=255)
BSA and Grade ≥3 Toxicities

No significant differences

No impact by chemotherapy regimen
BMI and Grade ≥3 Toxicities

Grade 3+ Heme AE’s, $p=0.048$
- Normal/underweight

Grade 3= anemia, $p=0.019$
- Normal/underweight – only 13 pts anemic

Grade 3= neutropenia, $p=0.043$
- Normal/underweight
- Impacted by chemotherapy regimen ($p=0.027$)
- More gr 3+ neutropenia with standard chemotherapy
Age and Grade ≥3 Toxicities

Age subgroups

- Age 65-69, n=213
- Age 70-79, n=362
- Age ≥80, n=40

No significant differences

No impact of chemotherapy regimen
RFS by BSA Category
OS by BSA Category

% Alive vs Time (years)

- <25th percentile
- 25th-50th percentile
- 50th-75th percentile
- >75th percentile

Time (years)

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

% Alive

0 10 20 30 40 50 60 70 80 90 100
RFS by BMI Category

- Normal or Underweight (≤25)
- Overweight (25-30)
- Obese (>30)
OS by BMI Category

% Alive

Time (years)

Normal or Underweight (≤25)
Overweight (25-30)
Obese (>30)
Limitations of the Study

- Retrospective analysis
- Predominantly Caucasian, PS 0-1 population
- Small subsets
  - Underweight pts
  - Pts ≥80 yrs old
  - Pts with grade 3+ anemia, thrombocytopenia
- No PK studies done
Conclusions

- Findings support ASCO guidelines that full weight-based dosing should be used in obese pts, esp in setting of curative intent
- No increased toxicities or poorer outcome with full dose therapy in obese pts
- Do underweight pts tolerate full dose chemotherapy more poorly?
- No increased toxicities by age
- Unique study – geriatric population