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

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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

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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, $\geq$80 years)

- Outcome – RFS, OS
  - BSA / BMI subgroups

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Frequency of Grade ≥3 Toxicities in the Study Population (n=615)

	Number of patients (%)			
	None	1	2-3	≥4
Any gr ≥3 toxicity	281 (45.7)	160 (26.0)	121 (19.7)	53 (8.6)
Gr ≥3 non-heme toxicity	370 (60.2)	150 (24.4)	69 (11.2)	26 (4.2)
Gr ≥3 heme toxicity	441 (71.7)	93 (15.1)	77 (12.5)	4 (0.7)

	Yes	No
Gr ≥3 anemia	13 (2.1)	602 (97.9)
Gr ≥3 neutropenia	100 (16.3)	515 (83.7)

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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)

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BSA and Grade ≥3 Toxicities

No significant differences

No impact by chemotherapy regimen

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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

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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

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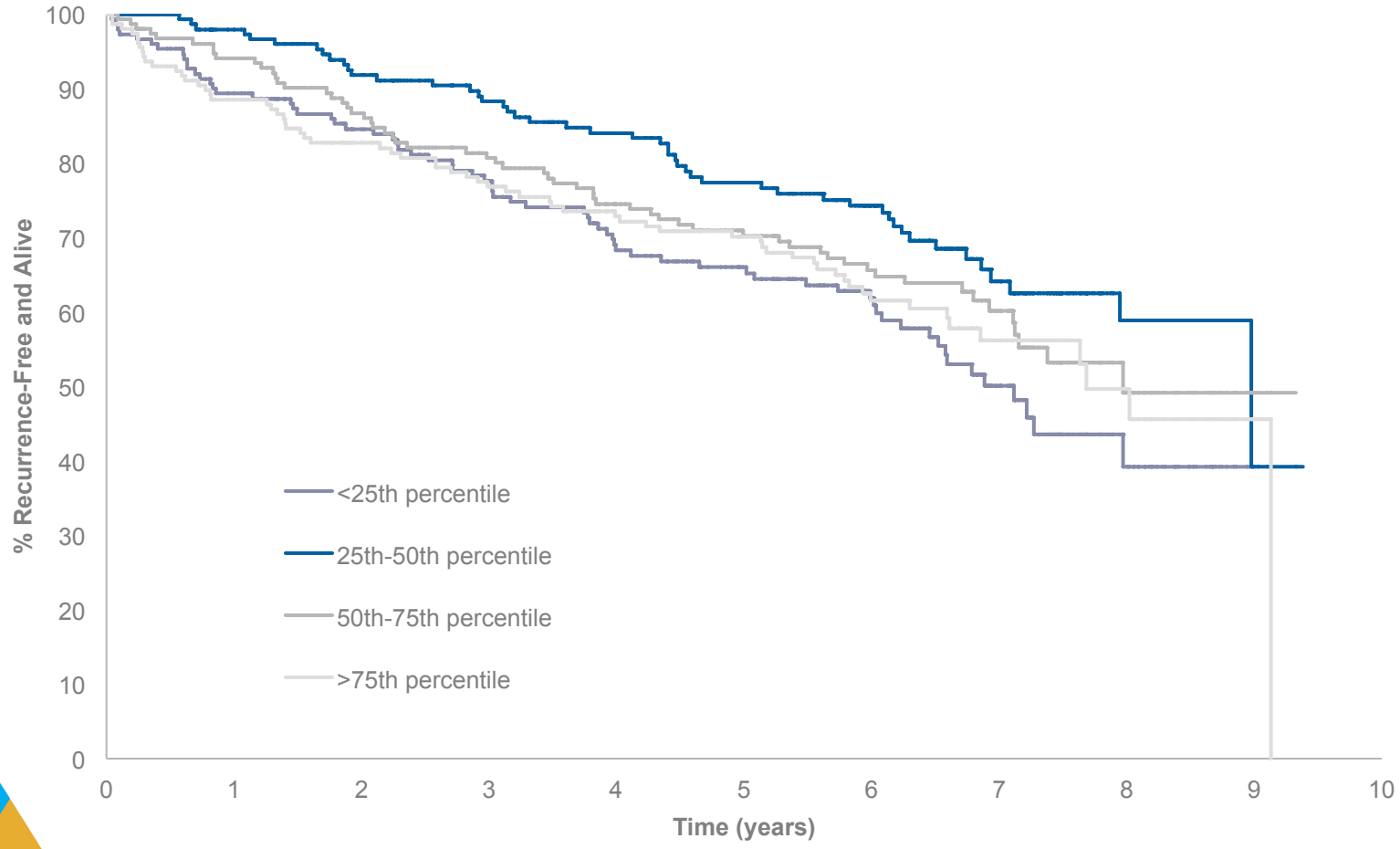
RFS by BSA Category



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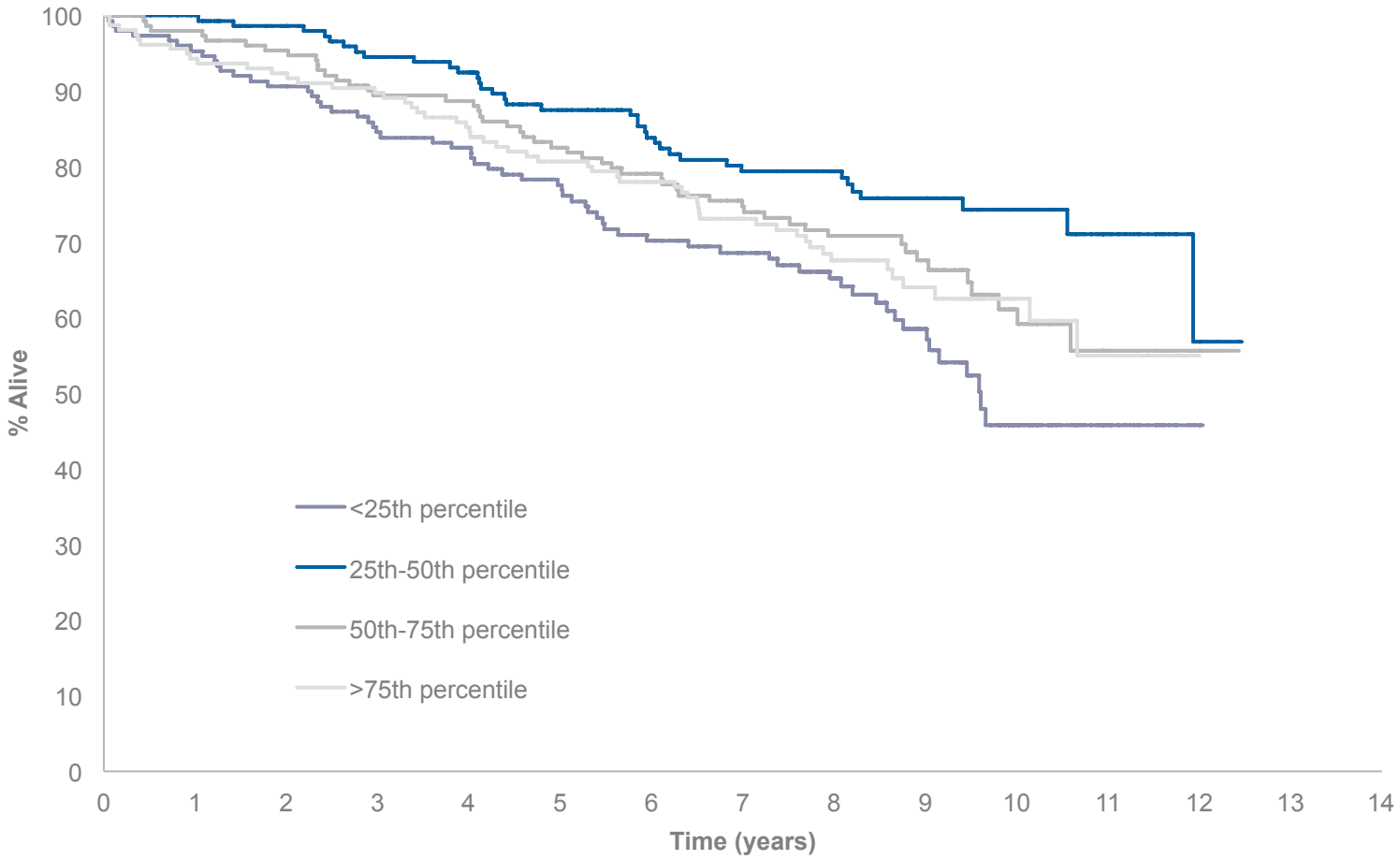
OS by BSA Category



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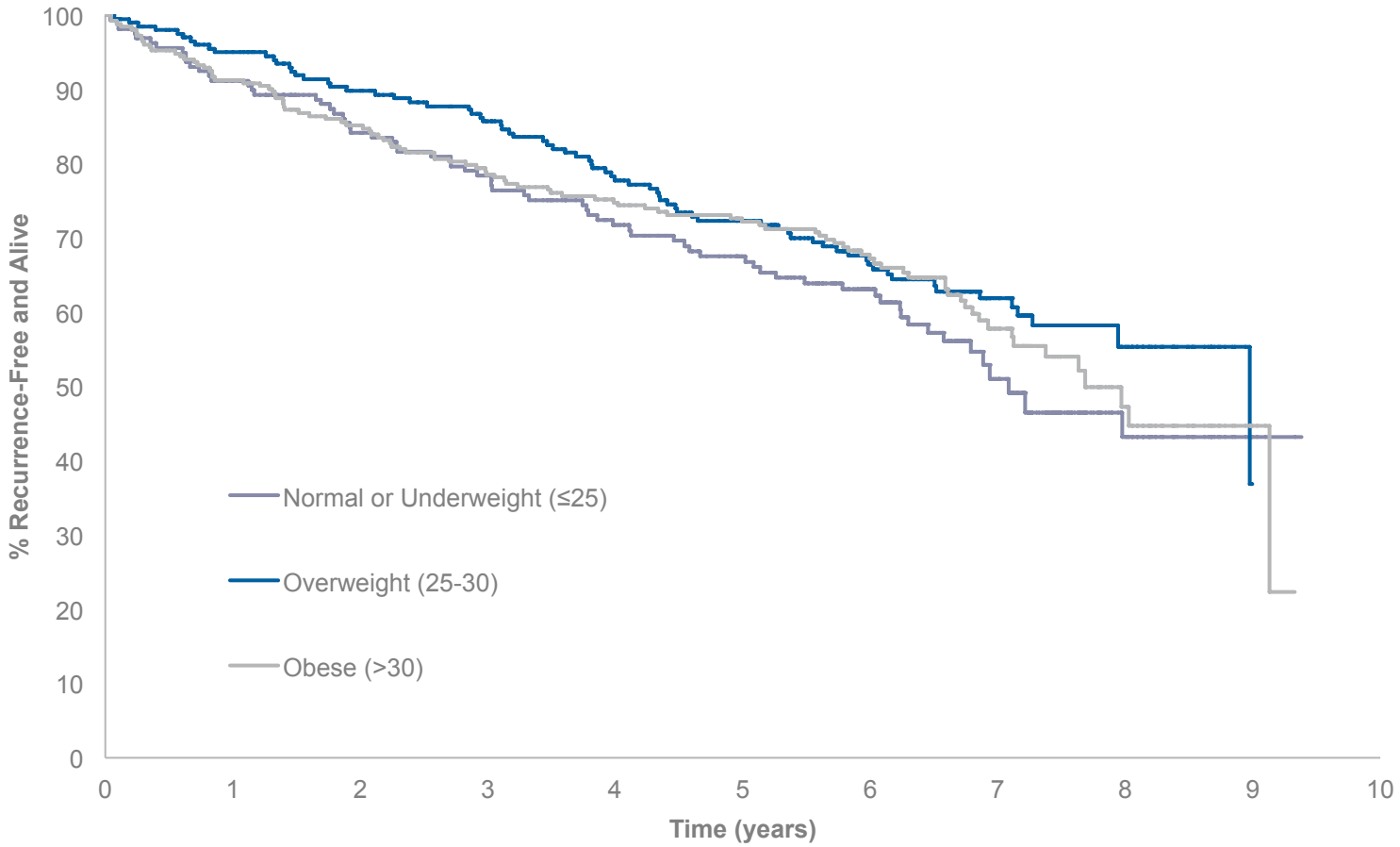
RFS by BMI Category



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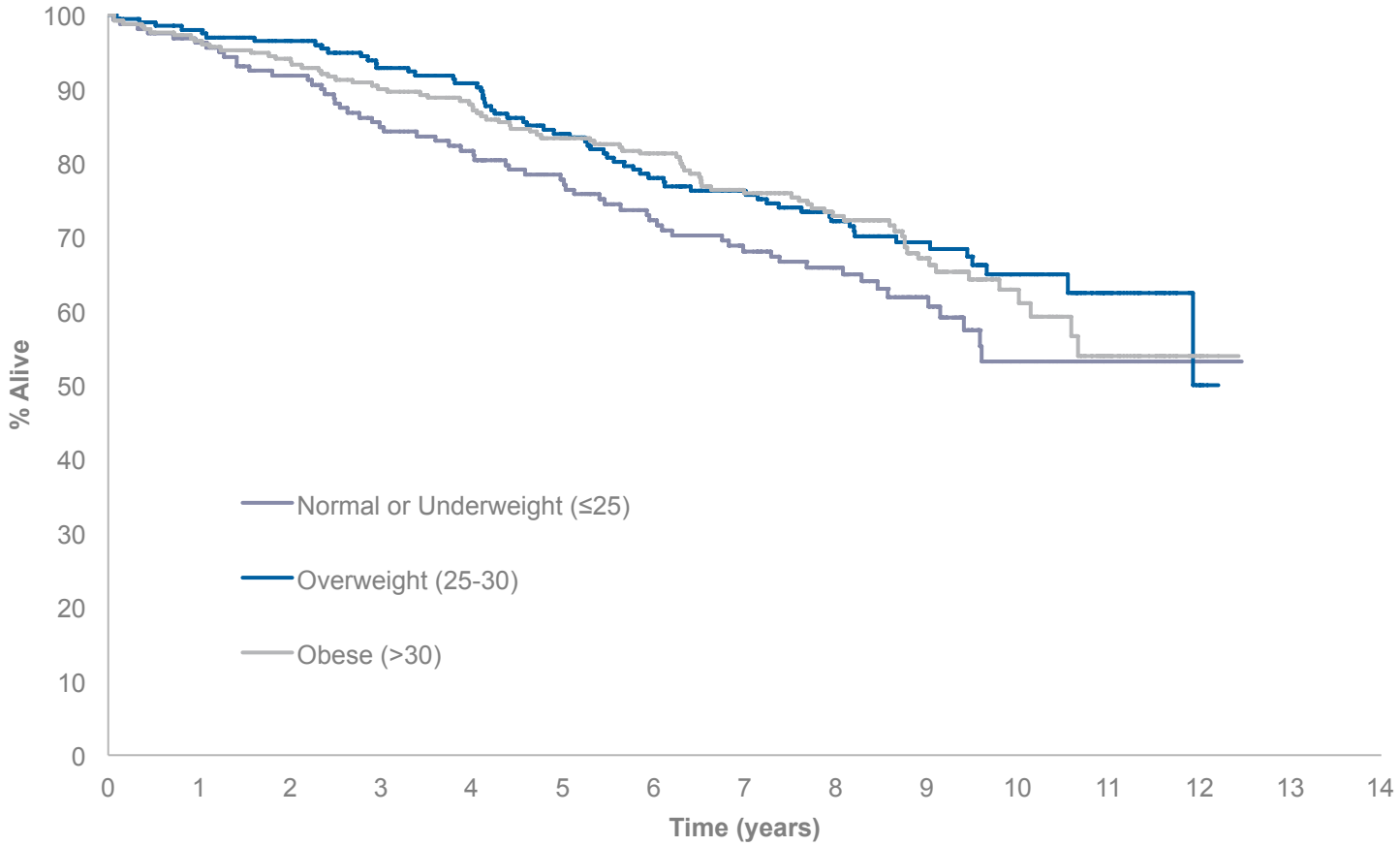
OS by BMI Category



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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

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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

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