Accrual of Older Breast Cancer Patients to Alliance Systemic Therapy Trials over Time: Protocol A15127

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Alliance Meeting
May 2016

Accrual of Older Patients to Clinical Trials is Persistent Challenge

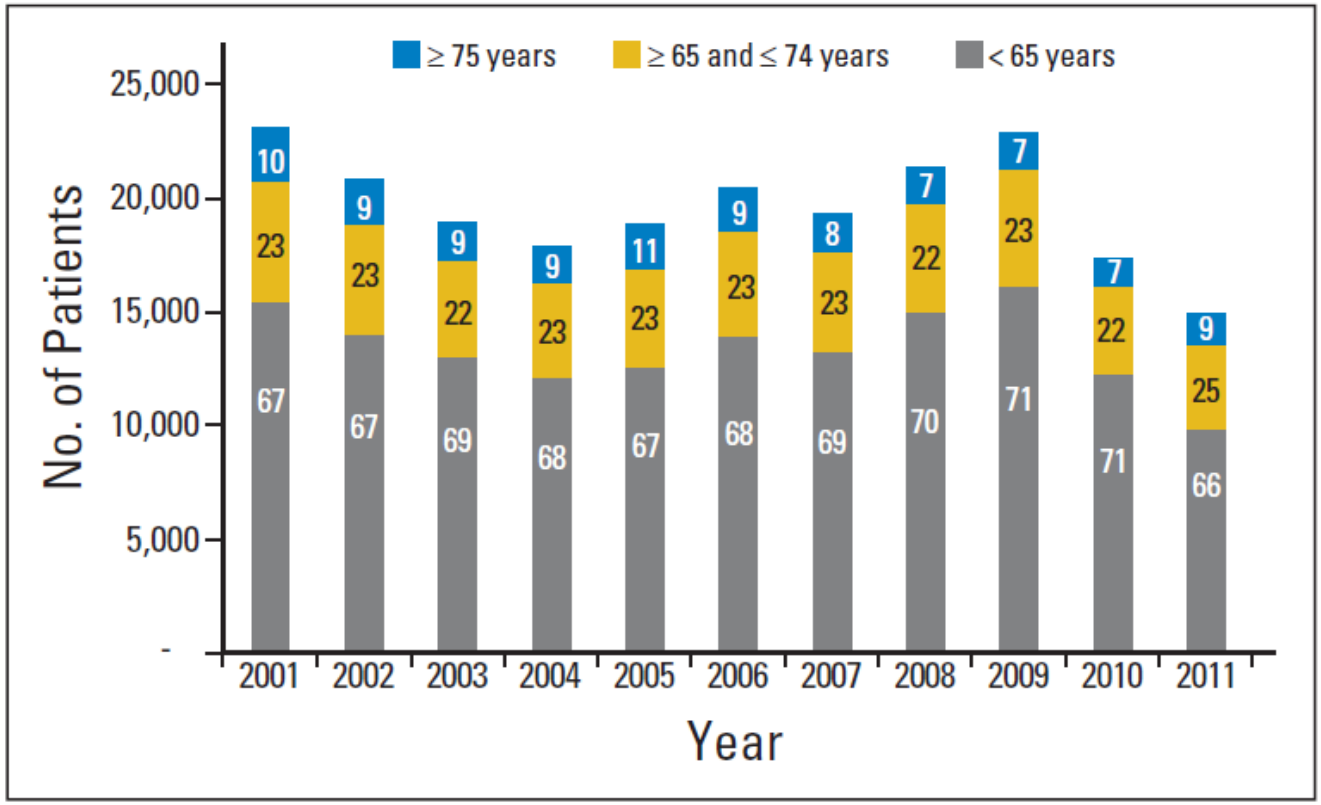


Fig 1. Age distribution for patients enrolled onto National Cancer Institute (NCI) adult cooperative group phase II and III treatment trials (all diseases) from 2001 to 2011. Percentage of patients enrolled in each age group is shown for each year, as reported by cooperative groups to the NCI Clinical Data Update System database (NCI Division of Cancer Treatment and Diagnosis) as of May 2012.

Hurria et al JCO 2014; U13 conference recommendations

Study Objectives

- To describe the proportion of patients 65+ and 70+ enrolled to breast cancer systemic therapy clinical trials within the Alliance during 1985-2012

- To compare disease characteristics of older vs. patients enrolling on Alliance studies

- To compare the reasons for protocol therapy cessation for older vs. younger trial participants

Methods (1)

- Reviewed Alliance trial portfolio for adjuvant, neoadjuvant, metastatic trials
- Focused on systemic treatment trials (not supportive care)

Neo/Adjuvant Trials Included

Clinical Trial	Agents given
Adjuvant Trials	
CALGB 40101	AC vs. T (4 vs. 6 cycles)
CALGB 49907	AC/CMF vs. capecitabine
N9831	ACT vs. ACTH
CALGB 9344	AC with 3 different doses of A (60, 75, 90 mg/m2) x 4 cycles +/- T
CALGB 9741	ACT on q2 vs. q3 week schedule vs. sequential ATC
NCCTG 89-30-52	Tam +/- fluoxymesterone
CALGB 8541	CAF dosing
Neoadjuvant trials	
CALGB 40603	ACT +/- carbo +/- bev
CALGB 40601	TH vs. THL vs. TL
ACOSOG Z1041	Preop FEC-->TH vs. TH-->FEC+H
ACOSOG Z1031	Preop exemestane, letrozole, anastrozole in postmenopausal pts.

Metastatic Trials Included

Clinical Trial	Agents given
Metastatic trials	
CALGB 40503	Let/tam +/- bev
CALGB 40502	Weekly paclitaxel vs. nab-paclitaxel vs. ixabepilone
CALGB 40302	Fulvestrant +/- lapatinib for Postmenopausal patients
CALGB 9342	Paclitaxel dosing
CALGB 9840	Paclitaxel schedules (q1 vs. q3 week) + trastuzumab

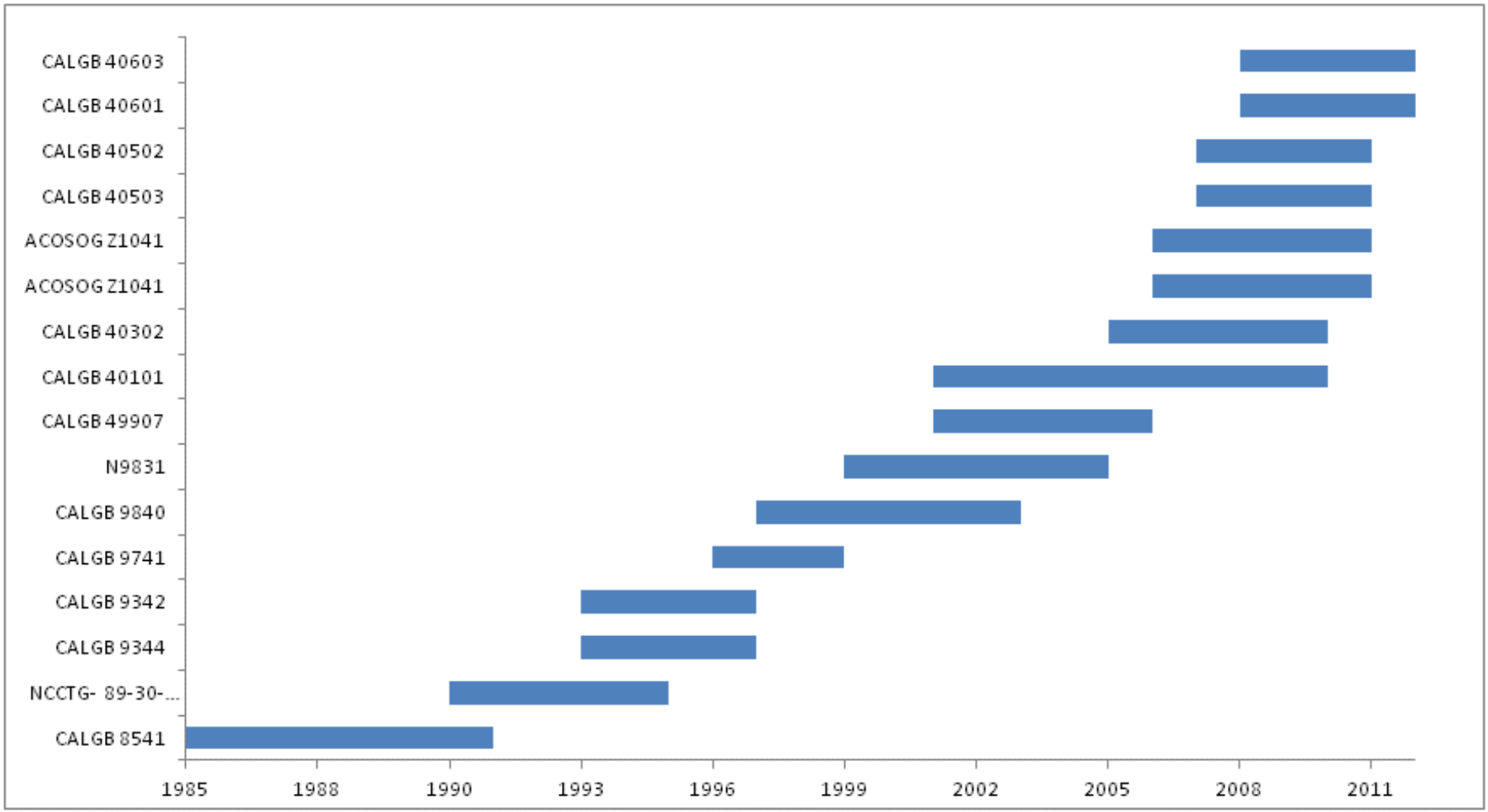
Methods (2)

- Primary endpoint
  - Proportion of older patients enrolled onto studies over time, using the date of protocol registration for each patient
    - Overall and by trial type (adjuvant/neoadjuvant/ metastatic)
    - By age 65+ and 70+
- Secondary endpoints
  - Disease characteristics and ECOG PS by age
  - Reasons for cessation of treatment by age

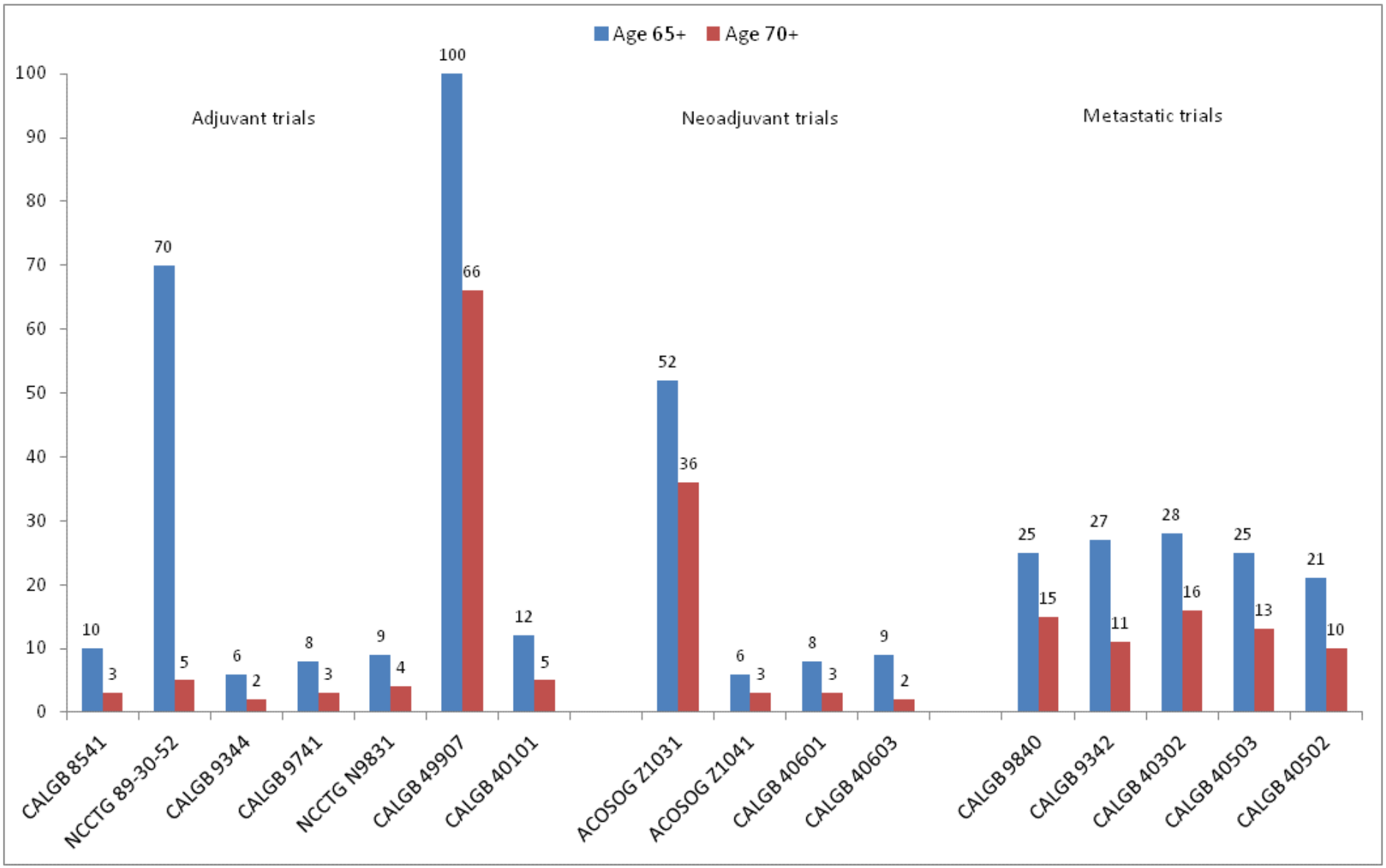
Statistical Analysis

- Modeled age as a function of time using logistic regression for age ≥65 (vs. <65) and age ≥70 (vs. <70)
  - Separate models for adjuvant, neoadjuvant, and metastatic trials
  - Sensitivity analysis after excluding CALGB 49907, NCCTG 89-30-52, ACOSOG Z1031 because these trials enrolled patients age ≥65 at rates of 100%, 70%, and 52%
- Compared ER/PR/HER2 status, mean tumor size, number of nodes involved on adjuvant studies
  - Chi-squared tests for comparisons of receptor status
  - Paired t-tests for comparisons of tumor size and nodes
- Compared ECOG PS by age using chi-square tests (when info available)
- Compared reasons for therapy cessation by age (chi-squared tests) for all studies combined and for each trial type separately

Dates of Accrual for Each Study

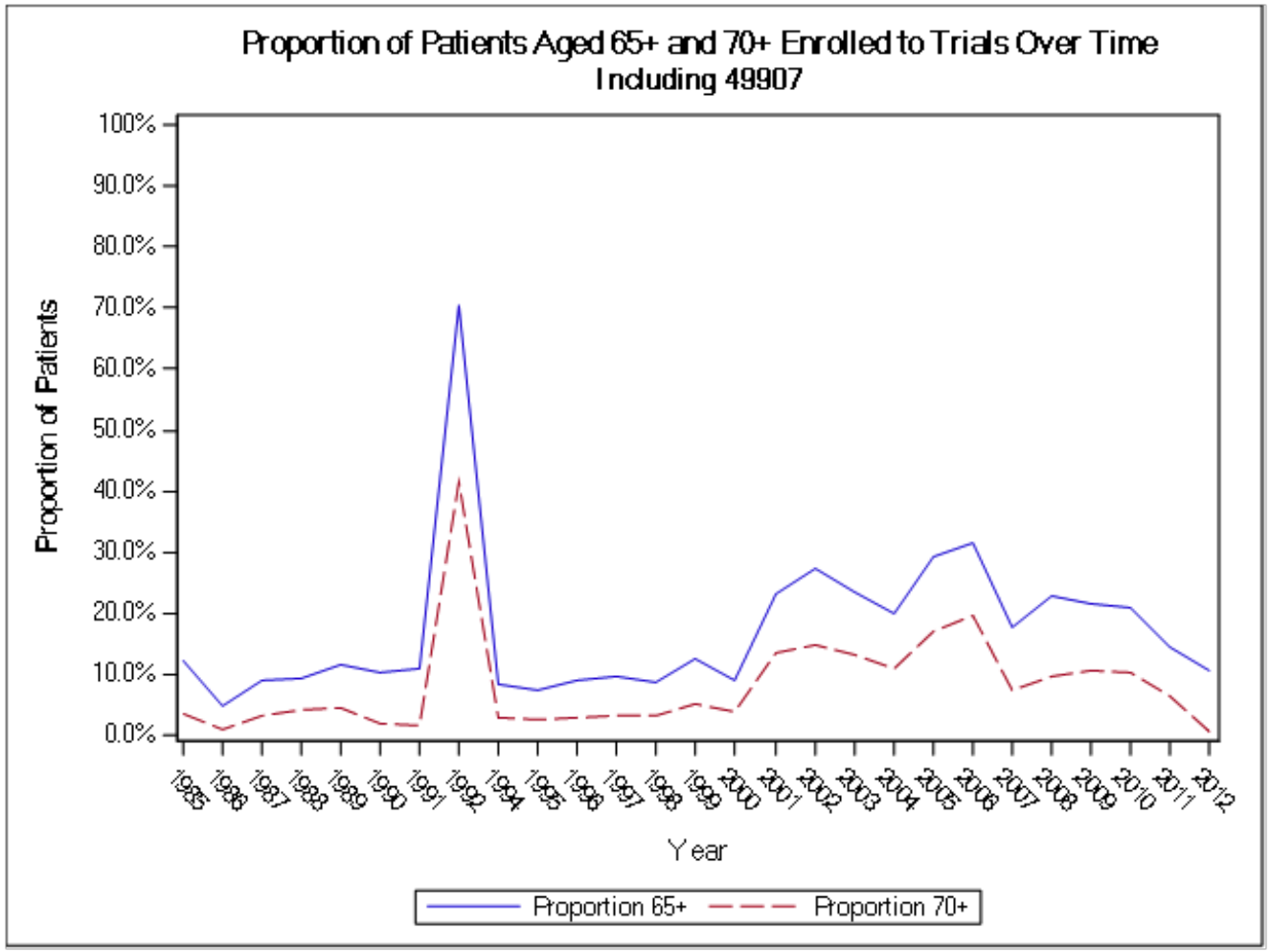


Proportion (%) of those Age 65+ (blue bars) and 70+ (red bars) Enrolled to Clinical Trials by Trial Type

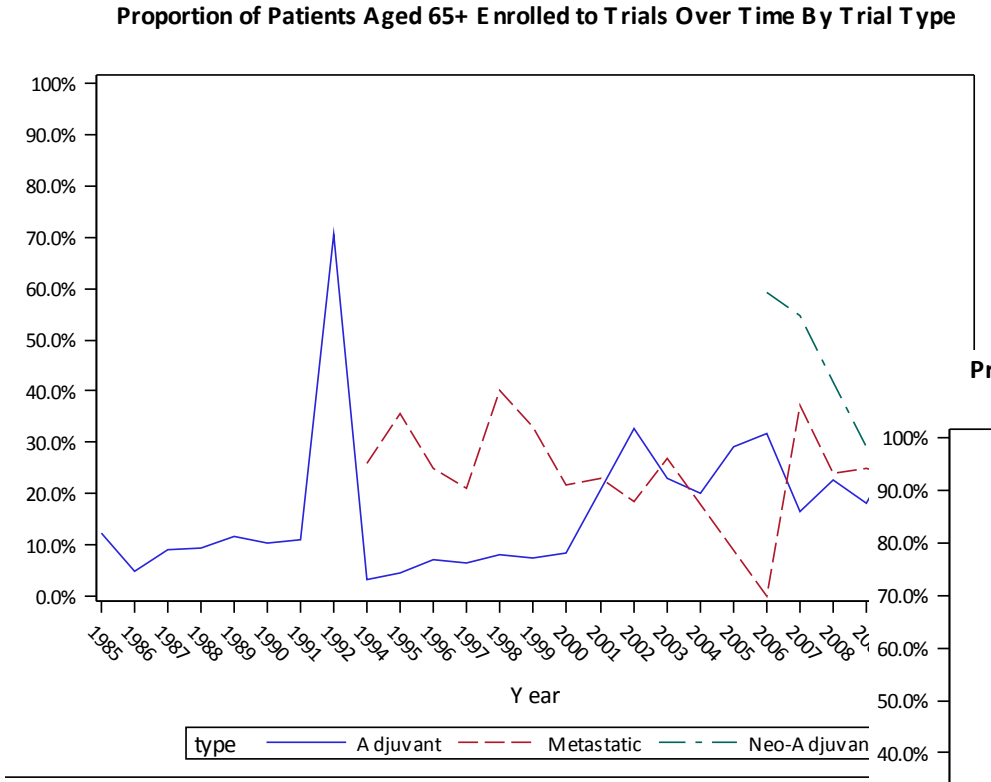


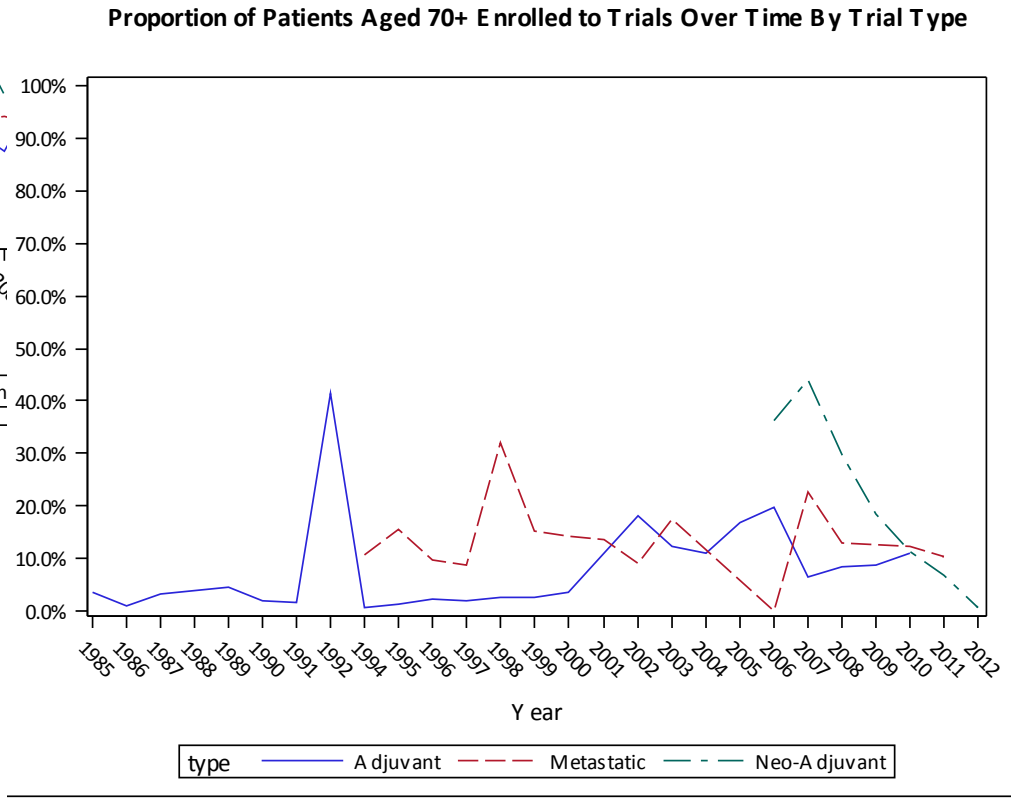
Unadjusted % of older patients enrolled over time for 65+ and 70+

(Overall, across all trials)

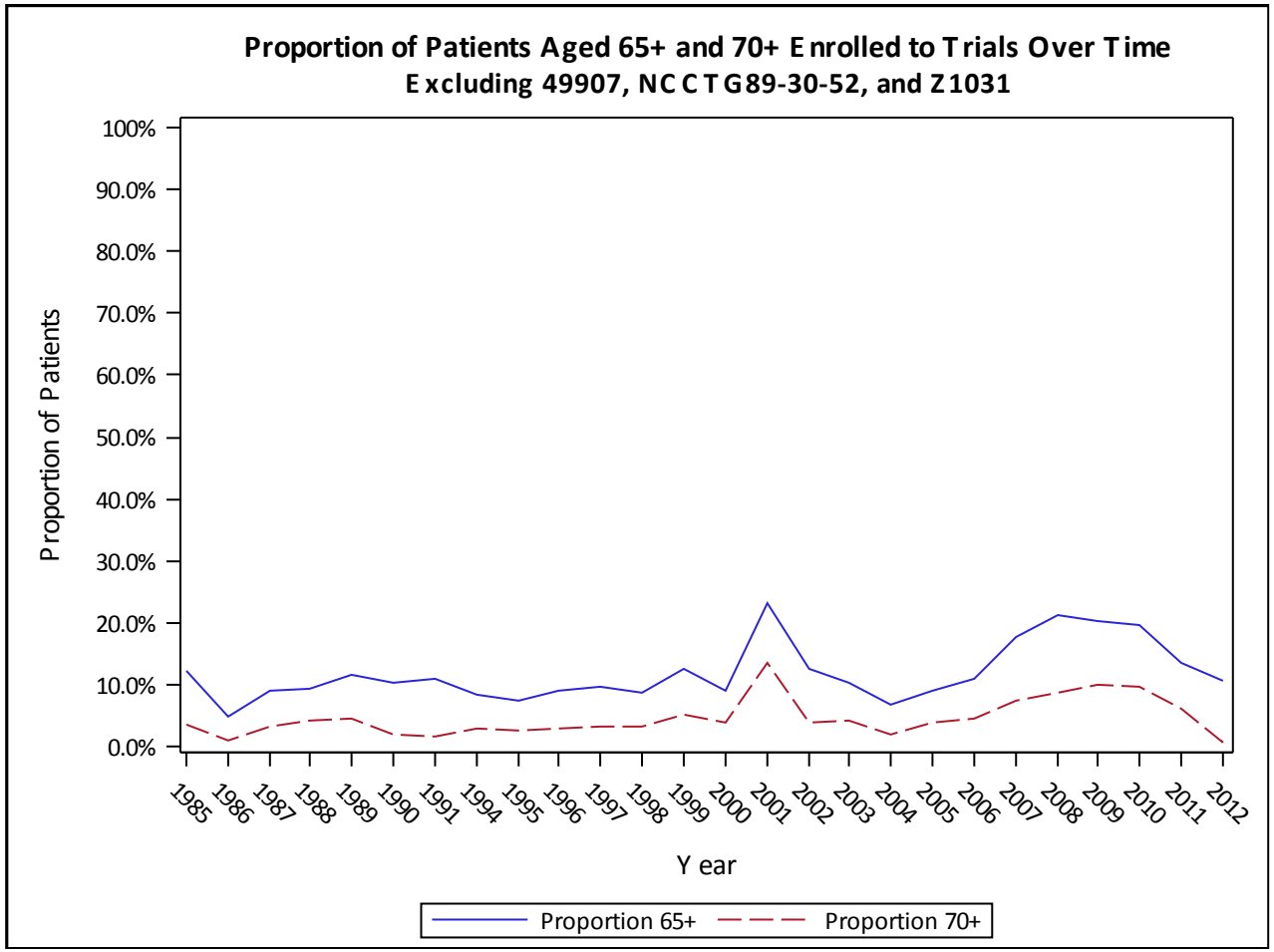


Unadjusted % of older patients enrolled over time for 65+ and 70+ by Trial Type





Accrual After Exclusion of 49907, NCCTG 89-30-52, and Z1031



Results from Models: OR for Enrollment

OR for enrolling for age ≥65 vs. age <65:

- Significant increase by year in adjuvant trials
  - OR=1.04 (95% CI=1.04-1.05;p<.0001)
- Significant decrease by year in neoadjuvant and metastatic trials
  - OR=0.62, 95% CI=0.58-0.67; p < 0.0001 (neoadjuvant)
  - OR=0.98, 95% CI=0.97-1.00; p=.03 (metastatic)
- Similar trends for age ≥70, but were statistically significant for adjuvant and neoadjuvant trials only
  - OR=1.05, 95% CI=1.04-1.07 (adjuvant)
  - OR=0.57, 95% CI=0.52-0.62 (neoadjuvant)
- After exclusion of 49907, NCCTG 89-30-52, and ACOSOG Z1031, results were similar for adjuvant and metastatic trials, but not significant for neoadjuvant trials

Secondary Endpoints (Summary)

- In general, mean number of nodes was statistically higher across all adjuvant studies for older vs. younger patients
- For ECOG PS, those age ≥65 and ≥70 had higher proportions of participants with ECOG PS 1 (vs. 0) on CALGB 40101, 40302, 40503, and 40603 compared with younger women

Reasons for Therapy Cessation by Age

Reason for going off study	Total N (%) (all ages)	Age <65 (n, %)	Age >=65 (n, %)	p-value
All studies combined	(N=13763)	(N=11336)	(N=2427)	<0.0001[1]
Adverse event	911 (6.6)	720 (6.4)	191 (7.9)	
Completed per protocol	8481 (61.6)	7267 (64.1)	1214 (50.0)	
Death	43 (0.3)	19 (0.2)	24 (1.0)	
Disease progressed/new primary	1274 (9.3)	994 (8.8)	280 (11.5)	
Never started	245 (1.8)	208 (1.8)	37 (1.5)	
Other disease	56 (0.4)	46 (0.4)	10 (0.4)	
Other therapy	84 (0.6)	71 (0.6)	13 (0.5)	
Other/Missing	2053 (14.9)	1517 (13.4)	536 (22.1)	
Refused further treatment	616 (4.5)	494 (4.4)	122 (5.0)	

[a] excluding NCCTG 89-30-52, CALGB 8541, CALGB 9344, and CALGB 9342 where this information was not available

[b] excluding CALGB 9342 where this information was not available

*Note: 22 deaths were in the metastatic setting and 65% of pts in neoadjuvant setting were other/missing for reason

*In adjuvant setting: 80.1% younger pts completed tx as planned vs. 77.4 in age 65+

Summary and Implications

- We observed small increases in accrual of older patients to adjuvant trials but a decrease in accrual to trials in the neoadjuvant and metastatic setting
- Overall, the proportion of patients enrolling to clinical trials age ≥65 and ≥70 remained low throughout the study period, with the exception of rare, selected trials
  - i.e. 40% of all breast cancer occurs in age 65+ but only 20% and 10% of accruals were for ages 65+ and 70+
- In general, % of older adults on neoadjuvant/metastatic trials was numerically higher than adjuvant trials, perhaps because of higher disease burden or symptomatic state
  - Older patients on adjuvant studies had more nodal involvement →perhaps a higher threshold to treat

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Study Limitations

- No information on the numbers of women approached, not approached, and why patients did not enroll on studies
- Analyses limited to Alliance Trials only
- We did not have complete disease characteristics, ECOG PS for some trials

Next Steps

- Poster presentation at ASCO 2016
- Paper in progress
- Draft to co-authors soon

Acknowledgements

- Jared Foster
- Drew Seisler
- Jeff Sloan
- Arti Hurria

- Hy Muss
- Gretchen Kimmick
- Jacqueline Lafky
- Aminah Jatoi
- Harvey Cohen
- Jeanne Mandelblatt
- Eric Winer and Cliff Hudis
- Constance Cirrincione
- Alvaro Moreno-Aspitia
- Whole committee!