Pooled survival analysis of first-line carboplatin doublet chemotherapy for advanced non-small cell lung cancer in elderly patients vs. younger patients enrolled in CALGB trials

Josephine Feliciano, Jared Foster, Ajeet Garja, Aminah Jatoi

Background

- Median age 70 y.o. for advanced lung cancer
- Population based analyses demonstrate about 25% elderly receive chemotherapy
- Elderly under-represented in trials
  - ≈ 30% clinical trial participants are elderly
  - ECOG 4599 (47.9% > 65; 27.1% >70)
  - Scagliotti (35% > 65)

Elderly "specific" phase III trials for chemotherapy

Study	Ages	Regimen	Results	comments
ELVIS (n=191)	>70	Vinorelbine Vs. BSC	28 w. 21 w.	Improved EORTC subscales
IFCT-0501 (n=451)	70-89	Carbo + pac Vs. Vin or gem	10.3m. 6.2 m.	↑neutropenia, asthenia
MILES (n=698)	>70	vin + gem Vs. Vin or gem	30 w. 36 w. or 28 w.	↑ toxicity

Meta-analysis: doublet vs. singlet

- 11 studies (n=2,782)
- Subgroup analyses of elderly (>65)

Results

Group	H.R doublet vs. singlet	95% CI
Overall	**0.89**	0.83, 0.95
Non-Asian	**0.89**	0.83, 0.95
Asian	0.87	0.66, 1.16
Non-platinum doublet	0.93	0.86, 1.01
Platinum doublet	**0.71**	0.60, 0.84

Elderly vs. younger

- Retrospective and secondary analyses
- Various regimens used (i.e. carbo vs. cisplatin)

Studies with elderly vs. younger subset analyses

Study	Ages	Regimen	Results	Comments
ECOG 1594	≥ 70 (n=227) Vs. <70	**Cis** + pac **Cis** + gem **Cis** + doc Carbo + pac	8.25 m. 8.15 m.	Similar completion and grade 4 toxicity
SWOG 9308 SWOG 9509	≥ 70 (n=122) Vs. <70	**Cis** + vin Carbo + pac	7 m. 9 m.	Similar toxicity

Hypotheses:

- Elderly patients fit for clinical trial will derive similar survival benefit from carboplatin doublet chemotherapy compared to younger patients.
- Elderly patients will receive reduced intensity chemotherapy (more frequent dose reductions, lower completion rates) than younger patients.
- Elderly patients fit for clinical trial will experience similar toxicity with carboplatin doublet chemotherapy compared to younger patients.

Aims:

- Primary aim:
  - To compare progression free survival and overall survival in elderly participants compared to younger participants (≥65 vs. <65; ≥70 vs. <70) who have received carboplatin based doublet 1st line therapy for advanced NSCLC
- Secondary aims:
  - To compare the relative dose intensity (dose percentages, percent completion of therapy) in older vs. younger patients.
  - To compare adverse events in elderly patients compared to younger patients who receive carboplatin based doublet therapy.

Methods

- CALGB 9730 (N=584)
  - Carbo + pac vs. pac
- CALGB 30203 (N=134)
  - Carbo + gem ± zileuton or celecoxib
- CALGB 30801 (N=319)
  - Carbo + gem ± celecoxib
  - Carbo + pem ± celecoxib

Reported results

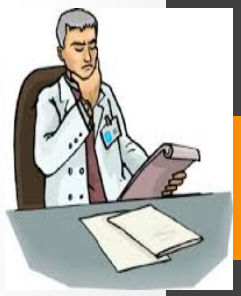
Study	Regimen	Response	Survival	Toxicity	Comments
9730 (N=584) 2005	Carbo + pac Vs. Pac	30% 17% (p<0.0001)	8.8 m. 6.7 m. (p=0.25)	↑cytopenias ↑N/V ↑any Gr 3/4	• <50% got 2nd line • 68% men
30203 (N=134) 2008	Carbo + gem ± Celecoxib and/ or zileuton	28%	10.3m. (p=0.75)	Similar toxicity	• 63% men • COX-2
30801 (N=319) 2014 a.	Carbo + gem Or Carbo + pem ± celecoxib	NR	9.03-14.85 m	Similar toxicity	• Study halted for futility • Analysis of 300 pt

Included studies – elderly subgroup

Study	#Elderly receiving doublet	Results	Comments
9730 (N=584) 2005	77 (>70 y.o.)	RR 38% OS 8 m. 1 y. 35%	50% in combo arm received 2nd line
30203 (N=134) 2008	31 (>65 y.o.)	RR 28% OS 10.3 m. 1 y. 42%	No diff in toxicity
30801 (N=319) 2014 a.	137 (>65 y.o.)	No results stratified by age available	Study halted for futility

Information Available
(All 3 studies)

- Demographic
  - Race/ Ethnicity
  - Age/ gender/ SS#
  - Type of Insurance
- Patient Characteristics
  - ECOG PS/ Stage/ Histology
  - Smoking history
  - Labs: CBC CMP incl Albumin
- Treatment
  - Doses and modification
  - Reason for discontinuation
- Efficacy
  - Response
  - Survival
    - PFS
    - OS



Statistical Analysis:

- Primary aim:
  - To compare progression free survival and overall survival in elderly participants compared to younger participants (≥65 vs. <65; ≥70 vs. <70) who have received carboplatin based doublet 1st line therapy for advanced NSCLC
- Statistical analysis:
  - Overall survival and progression free survival will be modeled as a function of age (separately for age ≥ 65 vs. < 65 and age ≥ 70 vs. < 70) adjusted for specific type of therapy given, and any other baseline patient characteristics we feel have the potential to confound

Statistical Analysis:

- Secondary Aim #1
  - To compare the relative dose intensity (dose percentages, percent completion of therapy) in older vs. younger patients.
- Statistical Analysis
  - Dose percentages and percent completion of chemotherapy will be modeled as a function of binary age and specific chemotherapy given using linear regression and again adjusted for any other baseline potential patient confounders
- Secondary Aim #2:
  - To compare adverse events in elderly patients compared to younger patients who receive carboplatin based doublet therapy.
- Statistical Analysis
  - The probability of experiencing at least one adverse event will be compared across age using logistic regression. These models will be adjusted for specific therapy received and any other potential baseline patient confounders.

Potential limitations

- Role of histology with chemotherapy combinations
- Second line therapy?

Questions?