Predictive Models for Chemo- and Radiotherapy

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Disclosures

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Brain metastases (BM) development after chemoradiation for stage III Non-Small Cell Lung Cancer: does the type of chemotherapy matter?


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Consort diagram study inclusion

- Retrospective multicenter study
  - Jan 1st 2006 - June 30th 2014
  - Last date of FU June 30th 2015

- Included
  - 18FDG-PET staged stage III NSCLC pts who completed CRT
  - Baseline CT/MRI brain without BM

- Primary endpoints
  - For different chemotherapy regimens:
    - BM development within 1st year of stage III NSCLC diagnosis;
    - BM as only site of first relapse
## Results

Percentage brain metastases development < 1 year

<table>
<thead>
<tr>
<th></th>
<th>BM &lt;1 year of NSCLC diagnosis</th>
<th>p-value</th>
<th>BM as only site of first relapse</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients (N)</strong></td>
<td>88/838 (11)</td>
<td></td>
<td>39/838 (5)</td>
<td></td>
</tr>
<tr>
<td><strong>CRT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Sequential</td>
<td>10/101 (10)</td>
<td>0.834</td>
<td>4/101 (4)</td>
<td>0.724</td>
</tr>
<tr>
<td>- Concurrent</td>
<td>78/737 (11)</td>
<td></td>
<td>35/737 (5)</td>
<td></td>
</tr>
<tr>
<td><strong>Concurrent CRT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Doublet CTx</td>
<td>37/346 (11)</td>
<td>0.927</td>
<td>14/346 (4)</td>
<td>0.399</td>
</tr>
<tr>
<td>- Daily LD cis</td>
<td>41/391 (11)</td>
<td></td>
<td>21/391 (5)</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** LD; low dose, cis; cisplatin.
## Logistic regression analysis

### Only concurrent chemoradiation patients (N=737)

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All brain relapses &lt;1 year</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (female vs male)</td>
<td>1.01 (0.67-1.51)</td>
<td>0.974</td>
</tr>
<tr>
<td>Age (continuous, older vs younger)</td>
<td>0.98 (0.96-0.99)</td>
<td><strong>0.037</strong></td>
</tr>
<tr>
<td>T-stage (T3-4 vs T0-2)</td>
<td>1.18 (0.78-1.77)</td>
<td>0.431</td>
</tr>
<tr>
<td>N-stage (N2-3 vs N0-1)</td>
<td>1.88 (0.90-3.93)</td>
<td>0.095</td>
</tr>
<tr>
<td>Treatment regimen (LD cis vs cyclic doublet)</td>
<td>0.96 (0.65-1.41)</td>
<td>0.819</td>
</tr>
<tr>
<td>Histology (SQCC vs AdC)</td>
<td>0.19 (0.10-0.36)</td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>Histology (NOS vs AdC)</td>
<td>0.73 (0.47-1.12)</td>
<td>0.153</td>
</tr>
</tbody>
</table>

**Abbreviations:** LD: low dose; cis: cisplatin; SQCC: squamous cell carcinoma, AdC: adenocarcinoma, NOS: not otherwise specified.
Results

• No differences in BM diagnosis < 1 year, as first site of relapse irrespective of
  • Concurrent versus sequential
• Within concurrent group:
  • Daily low dose cisplatin (N=391) versus cyclic dose taxane based (N=69) or non-taxane based Ctx (N=277)
  • Daily low dose cisplatin (N=391) versus cisplatin/etoposide (N=188), cisplatin/vinorelbin (N=65), weekly cisplatin/docetaxel (N=60)
Conclusions

- 11% of pts developed BM <1 year after stage III diagnosis despite no suspect brain imaging at initial diagnosis
- Results not dependent on type of chemotherapy regimen used within CRT treatment

Possible explanations and future directions:
- Microscopic BM present at initial diagnosis and ineffective Ctx due to inadequate blood-brain barrier (BBB) penetration
- BM development after CRT due to seeding of extracranial metastases
- Future: risk stratification tool & regular FU for high risk patients or PCI / BBB penetrating agents
Impact of KRAS mutation on response and outcome of patients with stage III non-squamous non-small cell lung cancer

Shigehiro Yagishita,1,2 Hidehito Horinouchi,1,3 Kuniko S. Sunami,1,3,5 Shintaro Kanda,1 Yutaka Fujiwara,1 Hiroshi Nokihara,1 Noboru Yamamoto,1 Minako Sumi,4 Kouya Shiraishi,5 Takashi Kohno,5 Koh Furuta,6 Koji Tsuta,7 Tomohide Tamura1 and Yuichiro Ohe1,3

1Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo; 2Department of Respiratory Medicine, Juntendo University Graduate School of Medicine, Tokyo; 3Advanced Clinical Research of Cancer, Juntendo University Graduate School of Medicine, Tokyo; 4Department of Radiation Oncology, National Cancer Center Hospital, Tokyo; 5Division of Genome Biology, National Cancer Center Research Institute, Tokyo; 6Departments of 6 Clinical Laboratories, Tokyo; 7Pathology, National Cancer Center Hospital, Tokyo, Japan
Overall results

- 119 patients were included in the analysis
- KRAS mutations were found at a frequency of 13%
- Patients with KRAS mutations had a shorter median relapse-free survival (6.1 vs 10.9 months) and a lower response rate (63% vs 81%)
- As for the first relapse site, patients with KRAS mutations had fewer local relapses (8% vs 23%) and more brain metastases (46% vs 12%)
- After disease progression, patients with KRAS mutations had a significantly shorter median survival post-progression (2.5 vs 7.3 months, P = 0.028) and median overall survival (15.1 vs 29.1 months, P = 0.022)
Median Relapse Free and Overall Survival

(a) Probability of relapse-free survival
- Wild-type KRAS: MRFS 10.9 (95% CI, 10.4–11.9) months
- Mutated KRAS: MRFS 6.1 (95% CI, 5.1–8.4) months

(c) Probability of overall survival
- Wild-type KRAS: MS 29.1 (95% CI, 26.3–33.1) months
- Mutated KRAS: MS 15.1 (95% CI, 8.7–25.9) months

Number at risk
- Wild-type KRAS: 103
- Mutated KRAS: 16

Number at risk
- Wild-type KRAS: 103
- Mutated KRAS: 16
Brain metastases after definitive concurrent chemoradiotherapy in patients with stage III lung adenocarcinoma: carcinoembryonic antigen as a potential predictive factor

Overall results

• In total, 116 patients were identified with a median (range) age of 57 (35-74) years

• Of these, 86 (74%) were men, all patients had platinum-based chemotherapy, and 100 (86%) received a total dose of 60 Gy in 30 fractions as definitive thoracic radiotherapy

• 95 patients had disease progression or recurrence
  • 19 (16%) developed brain metastases as the sole site of initial recurrence
  • 43 (37%) patients developed brain metastases at some time during follow-up

• Time to brain metastases was associated with the pretreatment carcinoembryonic antigen (CEA) value, with a hazard ratio = 2.64 (C.I. 1.39-5.02; P = 0.003)
PCI in operable stage III NSCLC treated with neoadjuvant chemoRt

Fig 1. Actuarial probabilities of brain relapse at first site of failure by intent-to-treat analysis.

Pottgen C et al, JCO 2007
Results

• PCI significantly reduced the probability of brain metastases as first site of failure (7.8% at 5 years v 34.7%; P = .02)

• the overall brain relapse rate was reduced comparably (9.1% at 5 years v 27.2%; P = .04)

• A slightly reduced neurocognitive performance in comparison with the age-matched normal population was found for patients in both treatment groups.
Figure A: Disease-free survival (probability) over time from randomization (months) for PCI and Control groups. The median disease-free survival is 28.5 months for PCI and 21.2 months for Control. The hazard ratio (HR) with 95% confidence interval (CI) is 0.67 (0.46 to 0.98) with a p-value of 0.037.

Figure B: Overall survival (probability) over time from randomization (months) for PCI and Control groups. The median overall survival is 31.2 months for PCI and 27.4 months for Control. The HR with 95% CI is 0.81 (0.56 to 1.16) with a p-value of 0.310.
Prophylactic Cranial Irradiation for Patients With Locally Advanced Non-Small-Cell Lung Cancer at High Risk for Brain Metastases

• A seer database analysis of 17852 patients showed no evidence of an overall survival benefit for PCI in this setting
Bevacizumab and pemetrexed versus pemetrexed alone as maintenance therapy for patients with advanced nonsquamous NSCLC:

Results of the expanded SAKK19/09 trial

Gautschi O, Li Q, Matter-Walstra K, Betticher D, Früh M, Rauch D, Pless M, Froesch P, Mach N, Ochsenbein AF; on behalf of the SAKK
Targeting VEGF can improve survival

**E4599: 1st line paclitaxel/carboplatin +/- bevacizumab in nonsquamous**


**E4599: adenocarcinoma subset**

Bevacizumab and Chemotherapy: Consistent increase in ORR

**E4599**

- CP (n=392)
- Avastin 15mg/kg + CP (n=381)

**ORR (%)**
- CP (n=392): 15
- Avastin 15mg/kg + CP (n=381): 35

**p<0.001**

**AVAiL**

- Placebo + CG (n=324): 22
- Avastin 15mg/kg + CG (n=332): 35
- Avastin 7.5mg/kg + CG (n=323): 38

**p=0.0002**

**p<0.0001**

Diagnosis

Tumour response or SD

First-line treatment
Platinum-doublet chemotherapy (4–6 cycles)

‘Watch and wait’ maintenance therapy

≥Second-line treatment

PD

PD
Maintenance therapy: Classification and Definition

- **Maintenance**
  - **Continuation**
    - The use of at least one of the agents given in first line, beyond 4-6 cycles in the absence of disease progression.
  - **Switch**
    - The initiation of a different agent, not included as part of the first-line regimen, in the absence of disease progression, after 4-6 cycles of initial therapy.

PARAMOUNT: study design

Study Treatment Period

Induction therapy (4 cycles) 21 to 42 Days Maintenance therapy (until PD)

Patients enrolled if:
• Nonsquamous NSCLC
• No prior systemic treatment for lung cancer
• ECOG PS 0/1

Stratified for:
• PS (0 vs 1)
• Disease stage (IIIB vs IV) prior to induction
• Response to induction (CR/PR vs SD)

CR, PR, SD

500 mg/m² pemetrexed + BSC, d1, q21d

2:1 Randomization

500 mg/m² pemetrexed + 75 mg/m² cisplatin, d1, q21d

PD

• Randomized, placebo-controlled, double-blind, phase III study
• Folic acid and vitamin B12 administered to both arms
• Objectives: primary: PFS; secondary: OS, RR, PRO, resource utilization, AEs

Paz-Ares et al. J Clin Oncol 29: 2011; (suppl; abstr CRA7510)
**PARAMOUNT: efficacy**

**PFS (investigator assessment)**
- PFS in all subgroups (stage, induction response, pre-randomization PS, smoking status, age, sex histology) favoured pemetrexed treatment
  - PFS from induction: 6.90 (pemetrexed) vs 5.59 months (placebo), HR 0.59 (0.47-0.74), p<0.0001

**PFS during maintenance therapy (investigator assessment)**
- Pemetrexed: median = 4.1 mos (3.2-4.6)
- Placebo: median = 2.8 mos (2.6-3.1)
  - Log-rank P=0.00006
  - Unadjusted HR: 0.62 (0.49-0.79)

**PFS during maintenance therapy (independent assessment):**
- 88% patients independently reviewed
- Median PFS: 3.9 (pemetrexed) vs 2.6 months (placebo), HR 0.64 (0.51-0.81), p=0.0002

**Response to maintenance therapy (independent assessment):**
- RR: 2.8% (pemetrexed) vs 0.6% (placebo), p=0.176
- DCR: 71.8% (pemetrexed) vs 59.6% (placebo), p=0.009

**PRO:**
- No statistical differences in EQ-5D index score or visual analogue scale observed between treatment groups

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Paz-Ares et al. J Clin Oncol 29: 2011; (suppl; abstr CRA7510)
Maintenance therapy: Classification and Definition

**Maintenance**
- **Continuation**: The use of at least one of the agents given in first line, beyond 4-6 cycles in the absence of disease progression.
- **Switch**: The initiation of a different agent, not included as part of the first-line regimen, in the absence of disease progression, after 4-6 cycles of initial therapy.
## Switch Maintenance: Overview of Chemotherapy Clinical Trials

### Efficacy Summary

<table>
<thead>
<tr>
<th>Study</th>
<th>Maintenance</th>
<th>Median TTP/PFS (p)</th>
<th>Median OS (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Westeel 2005</td>
<td>Vinorelbine 25mg/m²/w × 6m vs. Observation</td>
<td>5m vs. 3m (0.11)</td>
<td>12.3m vs. 12.3m (0.48)</td>
</tr>
<tr>
<td>Fidias 2008</td>
<td>Immediate docetaxel 75mg/m² q3w × 6 cycles vs. delayed docetaxel 75mg/m² q3w at first PD</td>
<td>5.7m vs. 2.7m (0.001)</td>
<td>12.3m vs. 9.7m (0.0853)</td>
</tr>
<tr>
<td>Ciuleanu 2009</td>
<td>ALIMTA® 500mg/m² q3w + BSC vs. BSC</td>
<td>4.0m vs. 2.0m (0.001)</td>
<td>13.4m vs. 10.6m (0.012)</td>
</tr>
</tbody>
</table>

NSCLC: Maintenance treatment

*Maintenance Pem plus BSC vs placebo plus BSC*

- **Design**
  - Pem 500 mg/m² on day 1 + BSC q3wk until PD
  - Placebo plus BSC q3wk until PD
  - 2:1 randomisation
  - 663 patients randomised

All pts received vitamin B12, folic acid and dexamethasone.
Overall Survival by Histology

Non-squamous (n=481)

HR=0.70 (95% CI: 0.56-0.88)  
\( P=0.002 \)

Squamous (n=182)

HR=1.07 (95% CI: 0.49-0.73)  
\( P=0.678 \)
PRONOUNCE: randomized, open-label, phase III study of first-line pemetrexed + carboplatin followed by maintenance pemetrexed versus paclitaxel + carboplatin + bevacizumab followed by maintenance bevacizumab in patients with advanced nonsquamous non-small-cell lung cancer

• PFS, OS, ORR, or DCR did not differ significantly between the arms

AVAPERL trial design

**First-line induction**
4 cycles, q3w

- Previously untreated stage IIIB–IV nsNSCLC

- Bevacizumab\(^b\) + pemetrexed\(^b\) + cisplatin\(^b\)

- CR/PR/SD per RECIST\(^c\)

- PD

- Follow-up

**Continuation maintenance**
q3w until PD

- Arm A: bevacizumab

- Arm B: bevacizumab + pemetrexed

Stratification factors:
- Gender
- Smoking status
- Response at randomization

nsNSCLC, nonsquamous non–small cell lung cancer
\(^a\)Randomized, open-label, phase III study; \(^b\)Dose of bevacizumab = 7.5 mg/kg; dose of pemetrexed = 500 mg/m\(^2\); dose of cisplatin = 75 mg/m\(^2\).
RECIST-related end points measured from the preinduction phase

Barseli et al. EJC: 2011; (suppl; abstr 34LBA)
Key results

PFS from induction

- Pem + BEV: 10.2 months (81 events)
- BEV: 6.6 months (104 events)
- HR: 0.50 (0.37–0.69); p<0.001

PFS subgroup analysis

- ITT population (n=253)
  - Age <65 y (n=178)
  - Age ≥65 y (n=77)
  - ECOG PS 0 (n=118)
  - ECOG PS 1 (n=126)
  - Never smoker (n=64)
  - Current/past smoker (n=188)
  - Adenocarcinoma (n=225)
  - SD prior to randomization (n=116)
  - CR/PR prior to randomization (n=137)

- Hazard ratios: 0.54 to 0.64

Pem + BEV maintenance treatment was associated with a marked increase in PFS over BEV alone

Positive effect on PFS was observed in all subgroups studied

Barselli et al. EJC: 2011; (suppl; abstr 34LBA)
SAKK 19/09 Trial Overview

**METASTATIC NSCLC:**
NON-SQUAMOUS BY CENTRAL PATHOLOGY
EGFR MUTATION CONFIRMED BY CENTRAL LABORATORY

**STRATUM A**
MUTATED EGFR
N = 20
N = 20
ERLOTINIB + BEVACIZUMAB UNTIL PROGRESSIVE DISEASE (PD)

**STRATUM B**
WILDC TYPE EGFR
N = 129

**COHORT 1**
N = 77
INDUCTION: BEV + PEM + CIS X4
MAINTENANCE: BEV + PEM

**COHORT 2**
N = 52
INDUCTION: PEM + CIS X4
MAINTENANCE: PEM

**PLASMA MARKERS AT BASELINE**
TUMOR PROFILING FROM DIAGNOSTIC BIOPSY

**PLASMA MARKERS DURING TREATMENT**

**PLASMA MARKERS AT PROGRESSION**
TUMOR PROFILING FROM TUMOR REBIOPSY
Aims and Methods

- Efficacy analysis of new cohort 2 (Pem alone)
- Comparison with updated cohort 1 (Bev+Pem; Gautschi, Clin Lung Cancer 2015)
- Identical population, Pem dose and follow up
- Primary endpoint: PFS by RECIST1.1
- Further outcomes of interest: survival, response, adverse effects, treatment costs
Main Results

- **EGFR mutant**: Bev+Erlotinib
  - PFS = 16.7m

- **EGFR wild type**
  - PFS = 6.9m for Bev+Pem
  - PFS = 5.6m for Pem
  - HR = 0.7 (0.5-1.0); P = 0.04

- **OS**
  - EGFR mutant: Bev+Erlotinib
    - OS = 26.7m
  - EGFR wild type
    - OS = 14.7 for Bev+Pem
    - OS = 14.6 for Pem
    - HR = 1.0 (0.7-1.6); P = 0.89
Conclusions

- Maintenance therapy with Bev+Pem increased PFS, but not OS, compared with Pem alone
- Treatment costs per month were $10,226 with Bev+Pem and $6,251 with Pem alone
- Translational research is ongoing, using rebiopsies at progression
- The ongoing ECOG 5508 phase III trial compares Bev versus Pem versus Bev+Pem (OS as primary endpoint)
“I hooked a real big one but it kept swimming around the boat.”
nab-Paclitaxel + Carboplatin (nab-P/C) in Advanced Non-small Cell Lung Cancer (NSCLC): Outcomes in Elderly Patients (pts) With Squamous (SCC) Histology

Cesare Gridelli, Tianlei Chen, Amy Ko, Mary O’ Brien, Teng Jin Ong, Mark A. Socinski, Pieter E. Postmus
Carboplatin and weekly paclitaxel doublet chemotherapy compared with monotherapy in elderly patients with advanced non-small-cell lung cancer: IFCT-0501 randomised, phase 3 trial.

Overall results

- 226 enrolled patients were randomly assigned monotherapy and 225 doublet chemotherapy
- Median age was 77 years and median follow-up was 30.3 months (range 8.6-45.2)
- Median overall survival was 10.3 months for doublet chemotherapy and 6.2 months for monotherapy (hazard ratio 0.64, 95% CI 0.52-0.78; p<0.0001)
  - 1-year survival was 44.5% (95% CI 37.9-50.9) and 25.4% (19.9-31.3), respectively
  - Toxic effects were more frequent in the doublet chemotherapy group than in the monotherapy group (most frequent, decreased neutrophil count (108 [48.4%] vs 28 [12.4%]; asthenia 23 [10.3%] vs 13 [5.8%])
Weekly nab-Paclitaxel in Combination With Carboplatin Versus Solvent-Based Paclitaxel Plus Carboplatin as First-Line Therapy in Patients With Advanced Non–Small-Cell Lung Cancer: Final Results of a Phase III Trial

Overall response rate: Primary end-point of the study

<table>
<thead>
<tr>
<th>Table 2. Response Rates for the Intent-to-Treat Population and Histologic Subset Based on Independent Radiologic Assessment</th>
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</thead>
<tbody>
<tr>
<td><strong>nab-PC</strong></td>
</tr>
<tr>
<td>Response Rates</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Intent-to-treat</td>
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<tr>
<td>Overall response</td>
</tr>
<tr>
<td>Complete response</td>
</tr>
<tr>
<td>Partial response</td>
</tr>
<tr>
<td>Stable disease†</td>
</tr>
<tr>
<td>Progressive disease</td>
</tr>
<tr>
<td>Squamous subset</td>
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<tr>
<td>Overall response</td>
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<tr>
<td>Nonsquamous subset</td>
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<tr>
<td>Overall response</td>
</tr>
</tbody>
</table>

NOTE: The Hommel procedure was used to adjust for the three comparisons related to tumor response (overall populations and two histology subgroups). The treatment and histology interaction was based on logistic regression.

Abbreviations: nab-PC, 130-nm albumin-bound paclitaxel + carboplatin; sb-PC, solvent-based paclitaxel + carboplatin.

*95% CIs for response rate ratios are calculated according to the asymptotic 95% CI of the relative risk of nab-PC to sb-PC.
†P values are based on the $\chi^2$ test.
‡Stable disease was defined as $\geq$ 16 weeks.
Safety and efficacy of weekly nab®-paclitaxel in combination with carboplatin as first-line therapy in elderly patients with advanced non-small-cell lung cancer

M. A. Socinski¹, C. J. Langer², I. Okamoto³, J. K. Hon⁴, V. Hirsh⁵, S. R. Dakhil⁶, R. D. Page⁷, J. Orsini⁸, H. Zhang⁹ & M. F. Renschler⁹
Kaplan–Meier curves in the elderly population:

(a) PFS (top) with 8.0 and 6.8 median months in the nab-P/C versus sb-P/C arms, respectively

(b) OS (bottom) with 19.9 and 10.4 median months in the nab-P/C versus sb-P/C arms, respectively

nab-P/C, 130-nm albumin-bound paclitaxel + carboplatin; sb-P/C, solvent-based paclitaxel + carboplatin
Survival, quality-adjusted survival, and other clinical end points in older advanced non-small-cell lung cancer patients treated with albumin-bound paclitaxel

C J Langer, V Hirsh, I Okamoto, F-J Lin, Y Wan, S Whiting, T J Ong, M F Renschler, and M F Botteman

1Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; 2Department of Oncology, McGill University, Montreal, Quebec, Canada; 3Department of Medical Oncology, Kinki University, Osaka-Sayama, Japan; 4Pharmerit International, Bethesda, MD, USA and 5Celgene Corporation, Summit, NJ, USA
**Overall results**

- Among patients aged $\geq 60$ years (N=546), nab-PC (N=265) significantly increased ORR and prolonged OS, despite a non-significant improvement in PFS, vs sb-PC (N=281).

- Nab-PC improved QoL
  - less neuropathy, arthralgia, and myalgia
  - more anaemia and thrombocytopenia

- Nab-PC yielded significant Q-TWiST (quality adjusted time without symptoms or toxicity) benefits (11.1 vs 9.8 months; 95% CI of gain: 0.2-2.6), with a relative Q-TWiST gain of 10.8% (6.4% to 15.1% in threshold analysis)

- In the $\geq 70$ years age group, nab-PC showed
  - similar, non-significant, ORR, PFS, and Q-TWiST benefits
  - significantly improved OS and QoL.
Partitioned survival plots (A) in patients > 60 years and (B) in patients > 70 years.
Efficacy Summary in Patients With SCC NSCLC by Age

<table>
<thead>
<tr>
<th>Outcome by Age</th>
<th>≥ 70 Years</th>
<th>≥ 65 Years</th>
<th>≥ 60 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nab-P/C</td>
<td>P/C</td>
<td>nab-P/C</td>
</tr>
<tr>
<td></td>
<td>n = 35</td>
<td>n = 30</td>
<td>n = 67</td>
</tr>
<tr>
<td>Overall Response Rate, %</td>
<td>46</td>
<td>20</td>
<td>46</td>
</tr>
<tr>
<td>Ratio of ORR (95% CI)</td>
<td>2.286 (1.025 - 5.095)</td>
<td>1.799 (1.120 - 8.892)</td>
<td>1.845 (1.251 - 2.721)</td>
</tr>
<tr>
<td>P value</td>
<td>0.029</td>
<td>0.012</td>
<td>0.001</td>
</tr>
<tr>
<td>Median Overall Survival, months</td>
<td>16.9</td>
<td>8.6</td>
<td>13.9</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>0.50 (0.275 - 0.896)</td>
<td>0.62 (0.411 - 0.928)</td>
<td>0.70 (0.510 - 0.961)</td>
</tr>
<tr>
<td>P value</td>
<td>0.018</td>
<td>0.019</td>
<td>0.027</td>
</tr>
<tr>
<td>Median Progression-Free Survival, months</td>
<td>5.7</td>
<td>5.7</td>
<td>5.7</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>0.68 (0.347 - 1.339)</td>
<td>0.70 (0.443 - 1.102)</td>
<td>0.71 (0.499 - 1.014)</td>
</tr>
<tr>
<td>P value</td>
<td>0.267</td>
<td>0.120</td>
<td>0.058</td>
</tr>
</tbody>
</table>

- ORR and OS outcomes were significantly better with nab-P/C vs P/C across all ages, including pts ≥ 70 years of age

*nab*-P/C, *nab*-paclitaxel/carboplatin; P/C, paclitaxel/carboplatin; SCC, squamous cell carcinoma.

**Survival in Patients ≥ 70 Years of Age With SCC**

**Overall Survival**

- \( \text{nab-P/C, median 16.9 mo} \)
- \( \text{P/C, median 8.6 mo} \)
- \( \text{HR 0.50 (95% CI 0.275 – 0.896)} \)
- \( P = 0.018 \)

**Progression-Free Survival**

- \( \text{nab-P/C, median 5.7 mo} \)
- \( \text{P/C, median 5.7 mo} \)
- \( \text{HR 0.682 (95% CI 0.347 - 1.339)} \)
- \( P = 0.267 \)

- \text{nab-P/C vs P/C treatment resulted in less grade 3/4 neutropenia (50% vs 63%) but more grade 3/4 thrombocytopenia (21% vs 10%) and anemia (21% vs 7%); this trend was observed in the phase III trial ITT population as well as the individual elderly and SCC subsets}
Best Change from Baseline in Target Lesions

Patients with SCC

Patients ≥ 70 Years of Age with SCC

- More pts with SCC, including those ≥ 70 years of age, treated with nab-P/C vs P/C had greater decreases from baseline in total length of target lesions

Conclusion: Treatment with nab-P/C vs P/C resulted in significant improvements in ORR and OS in patients ≥ 70 years of age with SCC; similar findings were observed in other age groups

Conclusions

• No firmly established predictor for development of brain metastases post chemoradiotherapy yet defined
  
  • KRAS and CEA promising but require further evaluation
  
  • Prophylactic cranial irradiation reduces relapse from brain metastases but overall survival benefit unproven
  
  • Bevacizumab does not appear to add significantly to pemetrexed in the maintenance treatment of non-squamous NSCLC
  
  • Nap-paclitaxel may have a role in selected elderly patients with NSCLC, both non-squamous and squamous