Current Concepts & Controversies in Locally Advanced NSCLC, Case 1:
Multidisciplinary Management of Stage IIIA N2 Disease

Dr. George Blumenschein
Medical Oncologist
Associate Professor,
Thoracic & Head/Neck Oncology
MD Anderson Cancer Center
Houston, TX

Dr. Walter Curran
Radiation Oncologist
Executive Director
Winship Cancer Center
Emory University
Atlanta, GA

with Howard (Jack) West, MD
Medical Oncologist
President & CEO
GRACE

This program is made possible through an educational grant from OSI Pharmaceuticals, who had no input in the development of its content.

We deeply appreciate their support.
Stage IIIA N2 NSCLC, Background

- 54 year-old male aerospace mechanic with excellent performance status just diagnosed with stage IIIA, N2 NSCLC
- Previously smoked 1 ppd x 10 years, quit 25 yrs ago
- Noted dry cough x 1 month, mentioned to primary MD
- CXR: right upper lobe mass, confirmed on chest CT, also modest right hilar +/- mediastinal adenopathy
- Referred to pulmonologist: bronch/EBUS:
  - 4R node shows adenocarcinoma, TTF-1 positive
PET/CT and Pulmonary Function Tests

- PET/CT: 4.4 x 4.1 cm RUL mass, mSUV 12.6, abnormal uptake in right hilum as well, 4R 1 cm, SUV 3.5

- Pulmonary function tests: FEV1 2.9 L, DLCO 85% predicted

Would you pursue an upfront mediastinoscopy to more definitively determine stage, or would you defer it until after induction therapy?
Heterogeneity within the Stage IIIA N2 LN-Positive Population

N= 702

Andre, JCO 18: 2981-9, 2000

Induction Chemo +/- RT for Resectable Stage IIIA N2 NSCLC: Schema

IIIA N2+ NSCLC “non-bulky”
N = 574

Randomize

Cis/Taxotere x 2 cycles
if no PD
Surgery
Taxotere x 3 cycles

Cis/Taxotere + Chest RT (50.4 Gy)
if no PD
Surgery
Taxotere x 3 cycles

Stratification:
#LN (1 vs >1)
Gender
Clin/Micro N2
T stage (T1 vs 2/3)

PD = progressive disease
How do you decide who is an which patients with stage IIIA N2 NSCLC are appropriate candidates for a surgical vs. non-surgical approach?

Do you/physicians at MD Anderson pursue induction chemotherapy or chemo/radiation before surgery?

What chemotherapy regimen(s) do you recommend?
Intergroup 0139: Definitive CT/RT vs. Induction CT/RT → Surgery for Stage IIIA NSCLC

Stage IIIA N2 NSCLC: Pre-operative therapy

- He is felt to be a very good candidate for chemo/radiation prior to surgery.

- He receives cis/etoposide x 2 cycles, concurrent with thoracic radiation to 50.4 Gy, tolerating it with essentially no side effects.

- Unfortunately, his cancer shows only minimal radiographic response 3 weeks later.
No radiographic response after induction chemo/radiation. Would you still recommend surgery? Would you use mediastinoscopy results to shape recommendations?

SWOG 8805: Chemoradiation Followed by Surgery for Stage IIIA/IIIB NSCLC


N=126, Path-staged N2 or N3 IIIA/IIIB NSCLC

Cisplatin/Etoposidex2 w/concurrent chest RT 45 Gy

Surgery

Cis/Etop x2, RT to 60 Gy
Intergroup 0139: Definitive CT/RT vs. Induction CT/RT → Surgery for Stage IIIA NSCLC

III A pN2
N = 439

Cis/Etoposide x 2 cycles w/concurrent XRT 45 Gy

if no prog.
Surgery

Cis/Etoposide x 2 cycles w/concurrent XRT 45 Gy

if no prog.
XRT to 61 Gy (cont.)

Cis/Etoposide x 2 cycles

Post-Induction Surgery/Pathology Results

- Undergoes mediastinoscopy/dissection and right upper lobectomy (pneumonectomy felt unlikely to have been necessary)
- Residual viable tumor in primary mass, and in nodes in 2R and 4R (4L, station 7 negative)
- Recovers from surgery extremely well

Albain, Lancet 2009
What post-operative chemotherapy, if any, would you recommend after induction cisplatin/etoposide and concurrent chest irradiation?

Would you order molecular marker tests (EGFR mutations, ERCC1, etc.) on the tumor tissue and use these results to guide your systemic therapy recommendations?
Is there any value in additional post-operative radiation in a higher risk patient who previously received induction radiation to ~45 Gray?
RTOG 0229: Chemotherapy with Concurrent Definitive RT, followed by Planned Surgery

Primary Investigator: M. Suranthalingam, Univ. of Maryland

N = 60, Path-staged N2 or N3 IIIA/IIIB NSCLC

Carboplatin/Paclitaxel weekly w/concurrent chest RT 60 Gy

(if felt to be resectable)

Surgery

Carbo/Paclitaxel Q3wks x 2

We depend on your support to continue GRACE educational programs like these.

PLEASE contribute at http://cancergrace.org/donate/