Background
The standard treatment for good PS pts with inoperable Stage III NSCLC is concurrent chemoradiation (CRT) followed by consolidation docetaxel. However, SWOG 0533 failed to show a survival benefit compared to CRT followed by consolidation docetaxel, primarily due to intolerance of the chemotherapy dose. Bevacizumab, an anti-VEGF antibody, was evaluated in combination with CRT and docetaxel in a Phase III trial.

Methods - Treatment Plan
Stratification by High Risk vs Low Risk (See definition below)

First registration

Concurrent Chemoradiation

Bevacizumab Schedule during Chemoradiation

Cohort 1: No Bevacizumab

Cohort 2: Bevacizumab 15mg/kg Days 1, 22, 43

Cohort 3: Bevacizumab 15mg/kg Days 1, 22, 43

Consecutive Chemo/RT

Bevacizumab 50 mg/m² Days 1 and 8

Etoposide 50 mg/m² Days 15, 22, 43

Chemo/RT

Days 1

Days 2

G-CSF required

36 (51%)

13 (64%)

5 (45%)

7 (69%)

13 (7)

77 (53)

Patient Characteristics

Low Risk - No squamous histology or mixed histology with < 50% squamous cell; primary tumor with no cavitation and not within 1 cm of a major vessel; no hemoptysis

High Risk - Does not fulfill all 3 criteria for low risk

Pts not registered to Cohort 2 until all pts on Cohort 1 have safely finished tx

Pts not registered to Cohort 3 until all pts on Cohort 2 have safely finished tx

Toxicities

Conclusions

SWOG 0533: A Pilot Trial of Cisplatin (C)/Etoposide (E)/Radiotherapy (RT) followed by Consolidation Docetaxel (D) and Bevacizumab (B) (NSC-704865) in Three Cohorts of Patients with Inoperable Locally Advanced Stage III Non-Small Cell Lung Cancer (NSCLC)

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Methods - Patient Eligibility

Histologic/cytologic proof of unresectable Grade 4G histologic toxicities from the addition of early to late B therapy in patients with inoperable Stage III-stage NSCLC (NSC-704865) followed by consolidation docetaxel. Stratified by high and low risk pts

Assess PS and OS

Assess RR

Evaluate the frequency and severity of all toxicities

Evaluate molecular correlations including EGFR, MVG, CEACs and CEsPs on pt specimens and investigate potential predictors of efficacy

Statistical Design

Accrual occurred separately for the low risk and high risk strata

Planned accrual was 50 pts to each stratum for the first cohort. For each stratum 28 pts to each cohort were planned of whom 22 were randomized random

This design was sufficient to distinguish between the null hypothesis of an unacceptable rate (≥ 20%) of Grade 4/5 hemorrhage and the alternative hypothesis of an acceptable rate (≤ 5%) with 84% exact power, using a one

Within each stratum, if 4 (14%) or more pts experienced Grade 4/5 hemorrhage within 3 cycles of Cohort hole, the trial would be stopped. If that stratum had 4/10 of pts of pts completed in the low risk stratum accrued would stop for the high risk stratum as well

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References


1) Adenocarcinoma, central tumor. Grade 5 hemoptysis - 29 days after cycle 2
2) Squamous Ca, cavitation, grade 5 hemoptysis - 13 days after cycle 2