CALGB-30801

A Randomized Phase III Double Blind Trial Evaluating Selective COX-2 Inhibition in COX-2 Expressing Advanced Non-Small Cell Lung Cancer

ClinicalTrial.gov Identifier: NCT01041781

Study Background

Trial Description

RATIONALE: Drugs used in chemotherapy, such as gemcitabine hydrochloride and carboplatin, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing. Pemetrexed disodium and celecoxib may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. It is not yet known whether giving gemcitabine hydrochloride or pemetrexed disodium together with carboplatin is more effective with or without celecoxib in treating non-small cell lung cancer. PURPOSE: This randomized phase III trial is studying gemcitabine hydrochloride, pemetrexed disodium, and carboplatin to compare how well they work when given together with celecoxib or a placebo in treating patients with advanced non-small cell lung cancer.

Arms:

Arm I: (Experimental): Patients receive gemcitabine hydrochloride IV on days 1 and 8 OR pemetrexed disodium IV on day 1. Patients also receive carboplatin IV on day 1 and oral celecoxib twice daily on days 1-21.

Arm II: (Active Comparator): Patients receive gemcitabine hydrochloride OR pemetrexed disodium and carboplatin as in arm I. Patients also receive oral placebo twice daily on days 1-21.

Objectives:

- Primary
  - To confirm the beneficial effect of gemcitabine hydrochloride or pemetrexed disodium in combination with carboplatin with or without celecoxib in patients with advanced non-small cell lung cancer that expresses COX-2.
- Secondary
  - To describe the response rate in patients treated with these regimens.

  - To describe the distribution of progression-free survival (PFS) and overall survival of patients treated with these regimens.
  - To compare the PFS of patients with COX-2 index 2 (adjusting for CYP2C9 genotype and celecoxib trough concentrations as covariates) treated with these regimens.
  - To correlate urinary PGE-M level with COX-2 expression, COX-2 inhibition, and outcome.
  - To evaluate the association between the -765G/C polymorphism in PTGS2 and COX-2 expression in non-small cell lung cancer specimens.
  - To characterize a trough plasma celecoxib concentration which will be used as a measure of patient adherence to study treatment and which may be used in future studies for correlations with genotype and pharmacodynamic outcomes.
- OUTLINE: This is a multicenter study. Patients are stratified according to gender, disease stage (IIIB vs IV), histology (squamous cell carcinoma vs non-squamous cell carcinoma), smoking status (never/former light smoker [defined as 10 pack years AND quit 1 year ago] vs smoker), and COX-2 expression status (COX-2 index 4 vs COX-2 index 2 but < 4). Patients are randomized to 1 of 2 treatment arms.
  - Arm I: Patients receive gemcitabine hydrochloride IV on days 1 and 8 OR pemetrexed disodium IV on day 1. Patients also receive carboplatin IV on day 1 and oral celecoxib twice daily on days 1-21.
  - Arm II: Patients receive gemcitabine hydrochloride OR pemetrexed disodium and carboplatin as in arm I. Patients also receive oral placebo twice daily on days 1-21.
  - NOTE: Patients with squamous cell carcinoma receive gemcitabine hydrochloride; patients with non-squamous cell carcinoma receive pemetrexed disodium.
- In both arms, treatment repeats every 21 days for up to 6 courses in the absence of disease progression or unacceptable toxicity. After completion of 6 courses, patients with responding or stable disease may continue to receive celecoxib or placebo alone in the absence of disease progression or unacceptable toxicity.
- Patients may undergo blood and urine sample collection periodically for correlative laboratory studies.
- After completion of study therapy, patients are followed up every 2 months for 2 years and then every 6 months for 3 years.

Study Milestones:

Start date: February 2010

Primary Completion Date: November 2013

Publication Information:

Analysis Type: Primary

Pubmed ID: 28489511

Citation: J. Clin. Oncol vol 35 (19) 2184-2192 2017

Associated Datasets: NCT01041781-D1-Dataset.csv (c30801), NCT01041781-D2-Dataset.csv (c30801_ae)

Dataset Information:

Dataset Name: NCT01041781-D2-Dataset.csv (c30801_ae)

Description: Dataset NCT01041781-D2-Dataset.csv (c30801_ae) is one of 2 datasets associated with PubMed ID 28489511. This dataset contains information that will allow you to reproduce the adverse events analysis.

Due to further data cleaning subsequent to the JCO publication, there are slight discrepancies in the numbers of patients reporting various grade 3 adverse events from those reported in Table A3 in the publication.

NCT01041781-D2-Dataset.csv (c30801_ae) Data Dictionary:

LABEL	NAME	elements	comments
Treatment Arm	ARM	1 = Celecoxib 0 = Placebo	
AE Grade	GRADE	0, 1, 2, 3, 4, 5 -1 = Unknown	
AE Related to the Treatment	REL_SMED	-1 = Not Applicable 0 = Unknown 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	No value was given to an event with grade 0. This is indicated by missing values.
System Organ Class	SOC		
Adverse Event Code	TOXCODE		
Adverse Event Term	AE		
PATID	PATID		