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-D1-Dataset.csv (c30801)

Description: Dataset NCT01041781-D1-Dataset.csv (c30801) is one of 2 datasets associated with PubMed ID 28489511. This dataset contains information that will allow you to reproduce the baseline characteristics table and primary analysis.

In Table A5, there is a typo in the median number of OS months for Celecoxib patients with COX-2 >= 2. The correct numbers should be 15.73 (11.50-18.96) and they are the same as those present on this shared dataset.

NCT01041781-D1-Dataset.csv (c30801) Data Dictionary:

LABEL	NAME	elements	comments
Age (years)	AGE		
Race	RACE	1 = White 3 = Black or African American 4 = Asian 5 = Native Hawaiian or Pacific Islander 6 = American Indian or Alaska Native 13 = not reported	
Gender	SEX	1 = Male 2= Female	
ECOG performance status at registration	PS	0 = Fully active, able to carry on all pre-disease performance without restriction 1 = Restricted in physically strenuous activity but ambulatory 2 = Ambulatory and capable of selfcare, but unable to carry out any work activities	
Histology (Squamous vs Non-Squamous) Stratification Factor	HISTOLOGY	0 = Non-Squamous 1 = Squamous	

Stage Stratification Factor	STAGE	3.2 = Stage IIIB 4 = Stage IV	
Smoker Stratification Factor	SMOKER	0 = No 1 = Yes	
Patient raw COX-2 level	COX2		
COX-2 level stratification factor	COX2HIGH	0 = COX-2 level >=2 & <4 1 = COX >=4	
Treatment Arm	ARM	1 = Celecoxib 0 = Placebo	
Number of cycles patients received of study drug	CYCLENO	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 99 = Cycleno > 10	
Overall survival Status	SURVCENS	0 = alive or withdrawn consent to follow for survival 1 = death	
Overall survival (months)	SURVTIME		
Progression-free survival status	FAILCENS	0 = (progression) no or withdrawn consent to follow for survival 1 = (progression) yes	
Progression-free survival (months)	FAILTIME		
Baseline levels of prostaglandin E metabolite (Baseline PGE-M in pg/ml)	PGEM_BASE		Missing values indicate the data was not collected.
Baseline PGE-M first quantile (Q1) stratification factor	PGEM25	1 = PGE-M >= Q1 0 = PGE-M < Q1	Missing values indicate the data was not collected.
Baseline PGE-M median stratification factor	PGEM50	1 = PGE-M >= median 0 = PGE-M < median	Missing values indicate the data was not collected.
Baseline PGE-M third quantile (Q3) stratification factor	PGEM75	1 = PGE-M >= Q3 0 = PGE-M < Q3	Missing values indicate the data was not collected.

Day-8 PGE-M (pg/ml)	PGEM_DAY8		Missing values indicate the data was not collected.
De-Identified patient reference	PATID		