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Phase III Trial of Enzalutamide (NSC# 766085) Versus Enzalutamide, Abiraterone and Prednisone for Castration Resistant Metastatic Prostate Cancer

ClinicalTrials.gov Identifier: NCT01949337

Study Background

Trial Description

This randomized phase III trial studies enzalutamide to see how well it works compared to enzalutamide, abiraterone, and prednisone in treating patients with castration-resistant metastatic prostate cancer. Androgens can cause the growth of prostate cancer cells. Drugs, such as enzalutamide, abiraterone acetate, and prednisone, may lessen the amount of androgens made by the body.

Arms:

Arm A: (enzalutamide): (Experimental): Patients receive enzalutamide 160 mg PO QD. Treatment will continue until confirmed disease progression or unacceptable toxicity.

Arm B: (enzalutamide, abiraterone, prednisone): (Experimental): Patients receive enzalutamide 160 mg PO QD, abiraterone 1000 mg PO QD, and prednisone 5 mg PO BID. Treatment will continue until confirmed disease progression or unacceptable toxicity.

Objectives:

Patients are randomized to one of two treatment groups: enzalutamide or enzalutamide, abiraterone and prednisone. Treatment will continue until disease progression or unacceptable toxicity. Patients are followed for clinical outcomes for a maximum of 5 years post study treatment. The primary and secondary objectives are described below.

1. Primary Objective: To compare the overall survival of patients with progressive metastatic castration-resistant prostate cancer (CRPC) treated with either enzalutamide only or enzalutamide with abiraterone and prednisone
2. Secondary Objectives:

- To assess the grade 3 or higher toxicity profile and compare safety by treatment arm.

- To assess and compare post-treatment prostate-specific antigen (PSA) declines by treatment arm.
- To compare radiographic progression free survival defined by Prostate Cancer Working Group 2 (PCWG2), and objective response rate, by treatment arm.
- To test for radiographic progression free survival (rPFS) treatment interaction in predicting overall survival.
- To assess pre- and post-treatment measures of tumor burden and bone activity using sodium fluoride (NaF) positron emission tomography (PET)/computed tomography (CT) and technetium (Tc) methylene diphosphonate (MDP) bone scintigraphy and correlate these measures with overall survival.
- To develop and validate prognostic and predictive models of overall survival that include baseline clinical and molecular markers.

Study Milestones:

Start date: January 22, 2014

Primary Completion Date: November 2, 2018

Publication Information:

Analysis Type: Primary

PubMed ID: 36996380

Citation: J Clin Oncol. 2023 Jun 20;41(18):3352-62. doi: 10.1200/JCO.22.02394. Epub 2023 Mar 30.

Associated Datasets: NCT01949337-D1-Dataset.csv (master), NCT01949337-D2-Dataset.csv (adverse_events), NCT01949337-D3-Dataset.csv (pk_abi), NCT01949337-D4-Dataset.csv (pk_enza)

Dataset Information:

Dataset Name: NCT01949337-D3-Dataset.csv (pk_abi)

Description: Dataset NCT01949337-D3-Dataset.csv (pk_abi) is one of 4 datasets associated with PubMed ID 36996380. This dataset contains abiraterone based PK data that can be input into Pumas PK software to produce PK results.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

Blank values indicate data not applicable or missing, except where otherwise noted.

NCT01949337-D3-Dataset.csv (pk_abi) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient ID	id		
Time since first recorded dose (hours)	time		
Abiraterone dose (mg daily p.o.)	Abi_Dose	0, 10, 40, 80, 100, 120, 150, 160, 250, 500, 750, 975, 1000, 7000	
Compartment of model drug is initially dosed to	cmt	1=depot compartment	
Event ID	EVID	0=observation row, 1=dosing event	
Number of additional doses at the same dose level	addl		
Interdose interval (hours)	ii	0, 24	Needed for dosing rows with addl>0
Observed plasma concentration of parent (ug/L)	dv		
Observation Occasion (days)	occasion		Used for Between Occasion Variability

LABEL	NAME	ELEMENTS	COMMENTS
Cycle Number	pkcycle	2, 3, 4, 5, 6	

There have been two changes made to the pharmacokinetic (PK) analyses published in our manuscript. First, the apparent clearance estimates for the drugs in the combination treatment have changed, using the Pumas AI PK model following a software update. The revised clearance estimates are 0.347 L/h for Enzalutamide and 3388.1 L/h for Abiraterone as compared to 0.367 L/h for Enzalutamide and 3429 L/h for Abiraterone in the manuscript.

The second modification pertains to an error in the patient count used for calculating the apparent clearance estimates for Enzalutamide in both arms of the study. For Enzalutamide clearance as a monotherapy, the corrected patient count is 458, and for Enzalutamide clearance in the combination therapy, the corrected patient number is 445. The patient counts were 440 and 420 in the manuscript, respectively. There were a total number of 903 evaluable patients for this analysis (not the 916 noted in manuscript).