A031201

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-D1-Dataset.csv (master)

Description: Dataset NCT01949337-D1-Dataset.csv (master) is one of 4 datasets associated with PubMed ID 36996380. This dataset contains data for the baseline characteristics table, primary analysis and secondary analyses minus adverse event and PK analyses.

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-D1-Dataset.csv (master) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient ID	id		
Bone Metastasis	METSITEBONE	No, Yes	Patients will have a value of “Yes” if there were bone metastases noted at baseline.
Liver Metastasis	METSITELIV	No, Yes	Patients will have a value of “Yes” if there were liver metastases noted at baseline.
Lung Metastasis	METSITELUNG	No, Yes	Patients will have a value of “Yes” if there were lung metastases noted at baseline.
Nodal Metastasis	METSITENOD	No, Yes	Patients will have a value of “Yes” if there were nodal metastases noted at baseline.
Other Site of Metastasis	METSITEOTH	No, Yes	Patients will have a value of “Yes” if there were other sites of metastases noted at baseline.

LABEL	NAME	ELEMENTS	COMMENTS
Treatment of primary tumor	PRITXPRMTUM	No, Yes	Value of “Yes” indicates receipt of prior therapy to treat the primary tumor.
Treatment Arm	ARM	Enzalutamide, Enzalutamide+AAP	Treatment arm to which the patient was randomized.
Baseline PSA (ng/mL)	bslpsaval		
Baseline ECOG Performance Status	ecogps	0, 1	
Prior Chemotherapy	prior_ct	No, Yes	Value of “Yes” indicates prior receipt of chemotherapy.
Gleason Score	gleascat	Greater than or equal to eight, Less than or equal to six, Missing, Seven	Gleason grade of primary tumor.
Halabi Risk Group	nomo_strat	High, Intermediate, Low, Missing	Risk group categorization using the Halabi nomogram.
Visceral Metastasis	metvis	No, Yes	Patients will have a value of “Yes” if there were visceral metastases noted at baseline.
Race	racecat	Black, Other, White	
Bone-only Metastasis	boneonly_mets	No, Yes	Indicator if only site of metastases noted at baseline was bone.
Baseline Bone lesions	bsl_boneles	No, Yes	Indicator for assessable bone lesions per Prostate Cancer Working Group 2 criteria.

LABEL	NAME	ELEMENTS	COMMENTS
Brief Pain Inventory (BPI)	bpi03_med	< 1, >= 1	Patient-reported severity of pain as measured by Brief Pain Inventory.
Baseline LDH (U/L)	bsl_ldh_med	< 195, >= 195	
Baseline ALP (U/L)	bsl_alkphos_med	< 90, >= 90	
Age (Years)	ageyears		Patient age at registration.
PSA Decline (%)	maxdeclinepct		Maximum decline in PSA from baseline, measured as percent decline from the baseline measure.
Treatment duration (Months)	trtdur		Duration in months of therapy received.
Non-Protocol Therapy Docetaxel	docetaxel	No, Yes	Indicator if patient received off-protocol Docetaxel after the completion of protocol therapy.
Non-Protocol Therapy Cabazitaxel	cabazitaxel	No, Yes	Indicator if patient received off-protocol Cabazitaxel after the completion of protocol therapy.
Non-Protocol Therapy Enzalutamide	enza	No, Yes	Indicator if patient received off-protocol Enzalutamide after the completion of protocol therapy.

LABEL	NAME	ELEMENTS	COMMENTS
			completion of protocol therapy.
Non-Protocol Therapy Abiraterone	abiraterone	No, Yes	Indicator if patient received off-protocol Abiraterone after the
Non-Protocol Therapy Olaparib	olaparib	No, Yes	Indicator if patient received off-protocol Olaparib after the completion of protocol therapy.
Non-Protocol Therapy Pembrolizumab	pembro	No, Yes	Indicator if patient received off-protocol Pembrolizumab after the completion of protocol therapy.
Non-Protocol Therapy Sipuleucel	sipuleucel	No, Yes	Indicator if patient received off-protocol Sipuleucel after the completion of protocol therapy.
Non-Protocol Therapy Radiation therapy	rt	No, Yes	Indicator if patient received off-protocol radiation therapy after the completion of protocol therapy.
Other Non-Protocol therapy	othertx	No, Yes	Indicator if patient received other off-protocol therapy beyond Cabazitaxel, Enzalutamide, Abiraterone, Olaparaib, Pembrolizumab, Sipuleucel, or radiation therapy after the completion of protocol therapy.

LABEL	NAME	ELEMENTS	COMMENTS
Enzalutamide Dose Reduced	enzreduc	No, Yes	Indicator if prescribed enzalutamide dose was reduced over course of therapy.
Abiraterone Dose Reduced	abireduc	No, Yes	Indicator if prescribed abiraterone dose was reduced over course of therapy. Missing for patients randomized to Enzalutamide alone arm.
Prednisone Dose Reduced	predreduc	No, Yes	Indicator if prescribed prednisone dose was reduced over course of therapy. Missing for patients randomized to Enzalutamide alone arm.
Bone Progression	bone_prog	No, Yes	Indicator for progression of bone lesions.
Time to Death (Days)	fu_time		
Reasons for Discontinuation	endreason	Adverse Events, Alternate TX, Clinical progression only, Comorbid Disease, Death, Other, rPFS and clinical progression, rPFS criterion only, Study Termination, Withdrawal before Treatment, Withdrawal during treatment	Reason for protocol therapy discontinuation.

LABEL	NAME	ELEMENTS	COMMENTS
CONSORT Status	consort_stat	Alternate Treatment; Comorbid Disease; Other reasons; Study Termination; Treated until Clinical Outcome; Withdrawal, AE; Withdrawal, Patient Decision; Withdrawal before Treatment	Holds patient status used for CONSORT diagram.
Soft Tissue Progression	softprog	No, Yes	Indicator for progression of soft tissue lesions.
Overall survival status	death	Alive, Dead	
Radiographic Progression Status	rprog	Censor, Event	Progression status: Event=progression.
rPFS Status	rpfs	Censor, Event	Radiographic Progression-Free Survival Status. Event=progression or death.
Clinical Progression (UCP) Status	ucpdurtx	Censor, Event	Clinical progression of symptoms status. Event=clinical progression.
UCP with Decline in ECOG Performance Status	ucp_declineps	No, Yes	Indicator of clinical progression of disease due to decline in performance status by ECOG.
UCP with Failure to Thrive	ucp_failuretothrive	No, Yes	Indicator of clinical progression of disease due to failure to thrive.

LABEL	NAME	ELEMENTS	COMMENTS
UCP with Fatigue	ucp_fatigue	No, Yes	Indicator of clinical progression of disease due to fatigue.
UCP with Pain worsening	ucp_pain	No, Yes	Indicator of clinical progression of disease due to worsening pain.
UCP with Weight Loss	ucp_weightloss	No, Yes	Indicator of clinical progression of disease due to weight loss.
UCP with Other reason for progression	ucp_other	No, Yes	Indicator of clinical progression of disease due to symptom beyond those listed above.
RUCP Status	rucp	Censor, Event	Radiographic and Clinical Progression-free survival status. Event=progression by radiographic or clinical symptom, or death.
Time to rPFS (Days)	t2rpfs		
Time to RUCP (Days)	t2rucp		
Extended rPFS Status	extended_rpfs	Censor, Event	Radiographic progression-free survival under 'extended' definition to include progression events occurring after termination of protocol therapy. Event=progression or death.
Time to Extended rPFS (Days)	t2extended_rpfs		

LABEL	NAME	ELEMENTS	COMMENTS
Time to Progression (Days)	t2rprog		