# Clinical Trials Data ERBB2 - Document 5

# PD 0332991 and Anastrozole for Stage 2 or 3 Estrogen Receptor Positive and HER2 Negative Breast Cancer

## Clinical Trial: https://clinicaltrials.gov/study/NCT01723774

"eligibilityCriteria": "Pre-registration PIK3CA Mutant Inclusion\n\n\* Clinical T2-T4c, any N, M0 invasive ER+ (Allred Score of 6-8) and HER2 negative (0 or 1+ by IHC or FISH negative for amplification) breast cancer, by AJCC 7th edition clinical staging, with the goal being surgery to completely excise the tumor in the breast and the lymph node. Note: Patients with invasive ER+ (Allred Score of 6-8) HER2- breast cancer or DCIS in the contralateral breast the patient are eligible\n\* Female \u226518 years of age\n\* ECOG performance status of 0, 1 or 2\n\* Life expectancy \\> 4 months\n\* Premenopausal, patient must be willing to comply with pregnancy requirements\n\* Adequate organ and marrow function\n\n \* leukocytes \u2265 3,000/mcL\n \* absolute neutrophil count \u2265 1,500/mcL\n \* platelets \u2265 100,000/mcL\n \* total bilirubin \u2264 ULN\n \* AST(SGOT)/ and ALT(SGPT) \\< 2.5 X ULN\n \* Creatinine \u2264 ULN\n\* Able to understand and willing to sign an IRB-approved written informed consent document\n\nExclusion\n\n\* Prior treatment of this cancer including: surgery, radiation, chemotherapy, biotherapy, hormonal therapy, investigational agent prior to study entry\n\* Receiving any investigational agents\n\* Prior therapy with any Cdk4 inhibitor\n\* Any of the following in the previous 6 months: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident, transient ischemic attack, symptomatic pulmonary embolism\n\* Uncontrolled intercurrent illness including, but not limited to: ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, uncontrolled symptomatic cardiac arrhythmia, psychiatric illness/social situations that would limit compliance with study requirements\n\* Pregnant/nursing\n\* Unwilling to employ adequate contraception\n\* Known HIV-positive on combination antiretroviral therapy\n\* Evidence of inflammatory cancer\n\* Known metastatic disease\n\* Current use of anticoagulation therapy\n\* Previous excisional biopsy of the breast cancer or sentinel lymph node biopsy\n\* Any condition that impairs patient's ability to swallow PD 0332991 tablets (e.g., gastrointestinal tract disease resulting in an inability to take oral medication or a requirement for IV alimentation, prior surgical procedures affecting absorption)\n\* History of allergic reactions attributed to compounds of similar chemical or biologic composition to PD 0332991 or other agents used in the study\n\* Corrected QT interval \\>470 msec\n\nRegistration PIK3CA Mutant Inclusion The criteria below must be met in addition to the pre-registration criteria, except treatment with endocrine therapy for this cancer is allowed prior to registration\n\n\* PIK3CA mutant cohort: tumor PIK3CA mutation present\n\* Premenopausal women, serum estradiol level in postmenopausal range \u2264 7 days prior to registration\n\nExclusion Criteria below must be met in addition to the pre-registration criteria -Current use or anticipated need for food or drugs that are known strong CYP3A4 inhibitors (i.e. grapefruit juice, verapamil, ketoconazole, miconazole, itraconazole, posaconazole, erythromycin, clarithromycin, telithromycin, indinavir, saquinavir, ritonavir, nelfinavir, lopinavir, atazanavir, amprenavir, fosamprenavir, nefazodone, diltiazem, and delavirdine) or inducers (i.e. dexamethasone, glucocorticoids, progesterone, rifampin, phenobarbital, St. John's wort)\n\nPIK3CA Wild Type Inclusion\n\n\* Clinical T2-T4c, any N, M0 invasive ER+ (Allred Score of 6-8) and HER2 negative (0 or 1+ by IHC or FISH negative for amplification) breast cancer, by AJCC 7th edition clinical staging, with the goal being surgery to completely excise the tumor in the breast and the lymph node. Note: Patients with invasive ER+ (Allred Score of 6-8) HER2- breast cancer or DCIS in the contralateral breast the patient are eligible\n\* For the PIK3CA wild type cohort: tumor PIK3CA mutation absent. Note that if a patient did not have sufficient research tissue for PIK3CA sequencing at pre-registration or if PIK3CA sequencing result is delayed, she could be registered and enrolled on the PD991 trial without assigning to a particular cohort at the time of enrollment. PIK3CA sequencing will be performed in the future on tumors collected at subsequent time points to assign the treatment cohort or when the PIK3CA sequencing data is available\n\* For the endocrine resistant cohort: Ki67 \\> 10% by central testing at Washington University AMP laboratory from a tumor biopsy performed after at least 2 weeks on neoadjuvant endocrine therapy. Note that prior neoadjuvant endocrine therapy could include any endocrine therapy (including aromatase inhibitor, tamoxifen, fulvestrant) alone or in combination, or endocrine therapy in combination with any investigational agent that is not a Cdk 4/6 inhibitor\n\n \\\*Patients who had a Day 17 Ki67 \\> 10% from the NCI9170 trial are eligible for the endocrine resistant cohort\n\* Female \\>18 years of age\n\* ECOG performance status of 0, 1 or 2\n\* Life expectancy \\> 4 months\n\* If premenopausal, patient must be willing to comply with pregnancy requirements\n\* Adequate organ and marrow function:\n\n \* leukocytes \u2265 3,000/mcL\n \* absolute neutrophil count \u2265 1,500/mcL\n \* platelets \u2265 100,000/mcL\n \* total bilirubin \u2264 ULN\n \* AST(SGOT)/ and ALT(SGPT) \\< 2.5 X ULN\n \* Creatinine \u2264 ULN\n\* In premenopausal women, serum estradiol level in postmenopausal range \u2264 7 days prior to registration.\n\* Able to understand and willing to sign an IRB-approved written informed consent document\n\nExclusion\n\n\* Prior treatment of this cancer including: Surgery, Radiation therapy, Chemotherapy, Biotherapy, Hormonal therapy, Investigational agent prior to study entry\n\* Receiving any other investigational agents\n\* Prior therapy with any Cdk4 inhibitor\n\* Any of the following in the previous 6 months: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident, transient ischemic attack, symptomatic pulmonary embolism\n\* Uncontrolled intercurrent illness including, but not limited to: ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, uncontrolled symptomatic cardiac arrhythmia, psychiatric illness/social situations that would limit compliance with study requirements\n\* Pregnant/nursing\n\* Unwilling to employ adequate contraception\n\* Known HIV-positive on combination antiretroviral therapy\n\* Evidence of inflammatory cancer\n\* Known metastatic disease\n\* Current use of anticoagulation therapy\n\* Previous excisional biopsy of the breast cancer or sentinel lymph node biopsy\n\* Any condition that impairs patient's ability to swallow PD 0332991 tablets (e.g., gastrointestinal tract disease resulting in an inability to take oral medication or a requirement for IV alimentation, prior surgical procedures affecting absorption)\n\* History of allergic reactions attributed to compounds of similar chemical or biologic composition to PD 0332991 or other agents used in the study\n\* Corrected QT interval \\>470 msec\n\* Current use or anticipated need for food or drugs that are known strong CYP3A4 inhibitors (i.e. grapefruit juice, verapamil, ketoconazole, miconazole, itraconazole, posaconazole, erythromycin, clarithromycin, telithromycin, indinavir, saquinavir, ritonavir, nelfinavir, lopinavir, atazanavir, amprenavir, fosamprenavir, nefazodone, diltiazem, and delavirdine) or inducers (i.e. dexamethasone, glucocorticoids, progesterone, rifampin, phenobarbital, St. John's wort)\n\nEndocrine Resistant Inclusion\n\n\* Clinical T2-T4c at diagnosis or screening, any N, M0 invasive ER+ (Allred Score at least 3 or \\> 1% ER positivity) and HER2 negative (0 or 1+ by IHC or FISH negative or equivocal) breast cancer, by AJCC 7th edition clinical staging, with the goal being surgery to completely excise the tumor in the breast and the lymph node. Note: Patients with invasive breast cancer that is ER pos, HER2 neg or equivocal or DCIS in the contralateral breast are eligible; multi-focal diseases are not excluded. The dominant lesion will be followed per protocol\n\* Ki67 \\> 10% by central testing at Washington University AMP laboratory from a tumor biopsy performed after at least 2 weeks on neoadjuvant endocrine therapy. If Ki67 is \\> 10% by local testing, the Ki67 slide and H\\&E slide need to be reviewed by the study pathologist to confirm eligibility (discuss with Study Chair). For patients external to Washington University, please contact the Washington University coordinator by email so that a screening ID# can be assigned prior to shipment of the slides\n\* Female \u2265 18 years of age\n\* ECOG performance status of 0, 1 or 2\n\* Pre- or post-menopausal women are eligible. If premenopausal, patient must be willing to comply with pregnancy requirements and agrees with GnRH agonist therapy for ovarian suppression during the study\n\* Adequate organ and marrow function:\n\n \* Leukocytes \u2265 3,000/mcL\n \* Absolute neutrophil count \u2265 1,500/mcL\n \* Platelets \u2265 100,000/mcL\n \* Total bilirubin \u2264 ULN\n \* AST(SGOT)/ and ALT(SGPT) \\< 2.5 X ULN\n \* Creatinine \u2264 ULN\n\* Able to understand and willing to sign an IRB-approved written informed consent document\n\nExclusion\n\n\* Prior treatment of this cancer including: Surgery, Radiation, Chemotherapy\n\* Receiving any other investigational agents\n\* Prior therapy with Cdk4 inhibitor\n\* Any of the following in the previous 6 months: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident, transient ischemic attack, symptomatic pulmonary embolism\n\* Uncontrolled intercurrent illness including, but not limited to: ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, uncontrolled symptomatic cardiac arrhythmia, psychiatric illness/social situations that would limit compliance with study requirements\n\* Pregnant/nursing\n\* Unwilling to employ adequate contraception\n\* Known HIV-positive on combination antiretroviral therapy\n\* Known metastatic disease\n\* Current use of anticoagulation therapy\n\* Previous excisional biopsy of the breast cancer or sentinel lymph node biopsy\n\* Any condition that impairs patient's ability to swallow PD 0332991 tablets (e.g., gastrointestinal tract disease resulting in an inability to take oral medication or a requirement for IV alimentation, prior surgical procedures affecting absorption)\n\* History of allergic reactions attributed to compounds of similar chemical or biologic composition to PD 0332991 or other agents used in the study\n\* Corrected QT interval \\>470 msec\n\* Current use or anticipated need for food or drugs that are known strong CYP3A4 inhibitors (i.e. grapefruit juice, verapamil, ketoconazole, miconazole, itraconazole, posaconazole, erythromycin, clarithromycin, telithromycin, indinavir, saquinavir, ritonavir, nelfinavir, lopinavir, atazanavir, amprenavir, fosamprenavir, nefazodone, diltiazem, and delavirdine) or inducers (i.e. dexamethasone, glucocorticoids, progesterone, rifampin, phenobarbital, St. John's wort)\n\nAdjuvant Inclusion\n\n\* Derived benefit from PD 0332991 in the neoadjuvant setting in this trial. This includes the 26 patients who achieved complete cell cycle arrest only after the addition of PD 0332991 (C1D1 Ki67 \\>2.7% and C1D15 Ki67 \u2264 2.7%) from the main study (PIK3CA WT, mutant, or unknown cohorts) as well as any patients who have a Ki67 \u2264 10% on C1D15 biopsy in the endocrine resistant cohort\n\* ECOG performance status of 0, 1 or 2\n\* Premenopausal, patient must be willing to comply with pregnancy requirements laid out\n\* Adequate organ and marrow function\n\n \* leukocytes \u2265 3,000/mcL\n \* absolute neutrophil count \u2265 1,500/mcL\n \* platelets \u2265 100,000/mcL\n \* total bilirubin \u2264 ULN\n \* AST(SGOT)/ and ALT(SGPT) \u2264 2.5 X ULN\n \* Creatinine \u2264 ULN\n\* Underwent surgery of the breast and axilla for curative intent\n\* At least 4 weeks post completion of adjuvant chemotherapy and radiation therapy if indicated\n\* Patients who already started on adjuvant hormonal therapy are eligible under the following conditions:\n\n \* For the 26 patients who enrolled in the initial cohorts and derived benefit from neoadjuvant PD 0332991 (C1D1 Ki67 \\>2.7% and C1D15 Ki67 \u2264 2.7%), adjuvant PD 0332991 should be initiated as soon as possible if adjuvant hormonal therapy has been initiated and the patient has completed radiation if indicated\n \* For patients who enrolled in the endocrine resistant cohort and derived benefit from neoadjuvant PD 0332991 (C1D15 Ki67 \u2264 10%), adjuvant PD 0332991 should be initiated within 6 months or sooner after initation of adjuvant hormonal therapy\n\* Able to understand and willing to sign an IRB-approved written informed consent document\n\nExclusion\n\n\* Any of the following in the previous 6 months: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident, transient ischemic attack, symptomatic pulmonary embolism\n\* Uncontrolled intercurrent illness including, but not limited to: ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, uncontrolled symptomatic cardiac arrhythmia, ssychiatric illness/social situations that would limit compliance with study requirements\n\* Pregnant/nursing\n\* Unwilling to employ adequate contraception\n\* Known HIV-positive on combination antiretroviral therapy. -Known metastatic disease\n\* Any condition that impairs patient's ability to swallow PD 0332991 tablets (e.g., gastrointestinal tract disease resulting in an inability to take oral medication or a requirement for IV alimentation, prior surgical procedures affecting absorption)\n\* History of allergic reactions attributed to compounds of similar chemical or biologic composition to PD 0332991 or other agents used in the study\n\* Corrected QT interval \\>470 msec\n\* Current use or anticipated need for food or drugs that are known strong CYP3A4 inhibitors (i.e. grapefruit juice, verapamil, ketoconazole, miconazole, itraconazole, posaconazole, erythromycin, clarithromycin, telithromycin, indinavir, saquinavir, ritonavir, nelfinavir, lopinavir, atazanavir, amprenavir, fosamprenavir, nefazodone, diltiazem, and delavirdine) or inducers (i.e. dexamethasone, glucocorticoids, progesterone, rifampin, phenobarbital, St. John's wort)",  
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Question:  
Based on the following clinical trial information, would a patient with a ERBB2 gene mutation be eligible for the clinical trial?

Answer:  
Based on the provided eligibility criteria for the clinical trial, a patient with an ERBB2 (HER2) gene mutation would not be eligible. The trial requires that patients have ER+ (estrogen receptor positive) and HER2 negative breast cancer. Specifically, HER2 negative status is determined by "0 or 1+ by IHC or FISH negative for amplification." Since an ERBB2 gene mutation often implies HER2 positive status, such patients would not meet the HER2 negative requirement and thus would not be eligible for this trial.