NCI National Clinical Trials Network

EA5182

ECOG-ACRIN cancer research group

For Patients with Metastatic EGFR-Mutant NSCLC

Please Enroll Your Eligible Patients!

EA5182 Available Through ECOG-ACRIN Cancer Research Group

Randomized Phase III Study of Combination Osimertinib (AZD9291) and Bevacizumab versus Osimertinib (AZD9291) Alone as First-Line Treatment for Patients with Metastatic EGFR-Mutant Non-Small Cell Lung Cancer (NSCLC)

Patient Population

See Section 3 for complete eligibility criteria

- Age ≥ 18 years, ECOG PS 0-2, adequate lab values
- Pathologically-confirmed diagnosis of non-squamous NSCLC; must have advanced disease, defined as either stage IV disease, stage IIIB disease not amenable to definitive multi-modality therapy, or recurrent disease after a prior diagnosis of stage I-III disease (AJCC 8th ed.)
- Must have somatic activating sensitizing mutation in EGFR (see protocol for details)
- Must not have received prior treatment with an anti-VEGF agent; note: prior treatment with an EGFR TKI is not allowed, however if a study candidate has already started osimertinib within 21 days of randomization, per protocol, the patient will be eligible
- Must not have risk factors for anti-VEGF administration (see protocol)
- Patients that received prior radiation therapy are eligible per protocol; must not have had any prior systemic treatment for metastatic disease (prior osimertinib allowed per protocol)
- Must have measurable disease per protocol
- Patients with treated brain metastases or untreated brain metastases/leptomeningeal disease: eligible per protocol
- Patients with known history/current symptoms of cardiac disease must be NYHA class 2B or better
- Must not be receiving strong inducers of CYP3A4
- No refractory nausea and vomiting, chronic GI diseases, the inability to swallow tablets or previous significant bowel resection that would preclude absorption
- No medical history/evidence of clinically active interstitial lung disease, drug-induced interstitial lung disease, or radiation pneumonitis which required steroid treatment
- No clinically important abnormalities in rhythm, conduction or morphology of resting ECG
- No factors that increase the risk of QTc prolongation or risk of arrhythmic events (see protocol)

Treatment Plan

See Section 5 for complete treatment details

Cycle = 21 days

Arm A– Osimertinib:

- 80 mg by mouth once daily on days 1-21

Arm B– Osimertinib with Bevacizumab:

- Osi 80 mg by mouth once daily on days 1-21
- Bev 15 mg/kg IV once every 3 weeks on day 1

Note: If a patient started on osimertinib prior to study randomization, it is allowed if osimertinib was initiated within 21 days of randomization, the exact start date is known, and the required baseline imaging was completed prior to the start date

Patients will continue treatment until disease progression, treatment interruption/discontinuation for toxicity and/or patient/physician desire to discontinue

- If patients on Arm B discontinue bevacizumab, they will continue treatment on Arm B and continue to receive osimertinib alone.
- If patients on Arms A or B discontinue osimertinib, they will come off study treatment and will be followed for disease progression and survival

Notes:

- *Osimertinib should be taken at the same time every day (+/- 4 hours), with or without food. Missed doses of osimertinib should not be made up. In addition to dose interruptions, dose reductions will be utilized to manage toxicity for osimertinib*
- *Bevacizumab is based on actual weight; there are no dose reductions (treatment can be interrupted)*
- *The initial dose of bevacizumab (cycle 1) should be administered over a minimum of 90 minutes, the second dose (cycle 2) over 60 minutes, and if no adverse reactions occur, all subsequent doses (cycle 3+) should be administered over a minimum of 30 minutes*

Study Chair:
Helena Yu, MD

Co-Chair:
Balazs Halmos, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open

1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login)

1-857-504-2900

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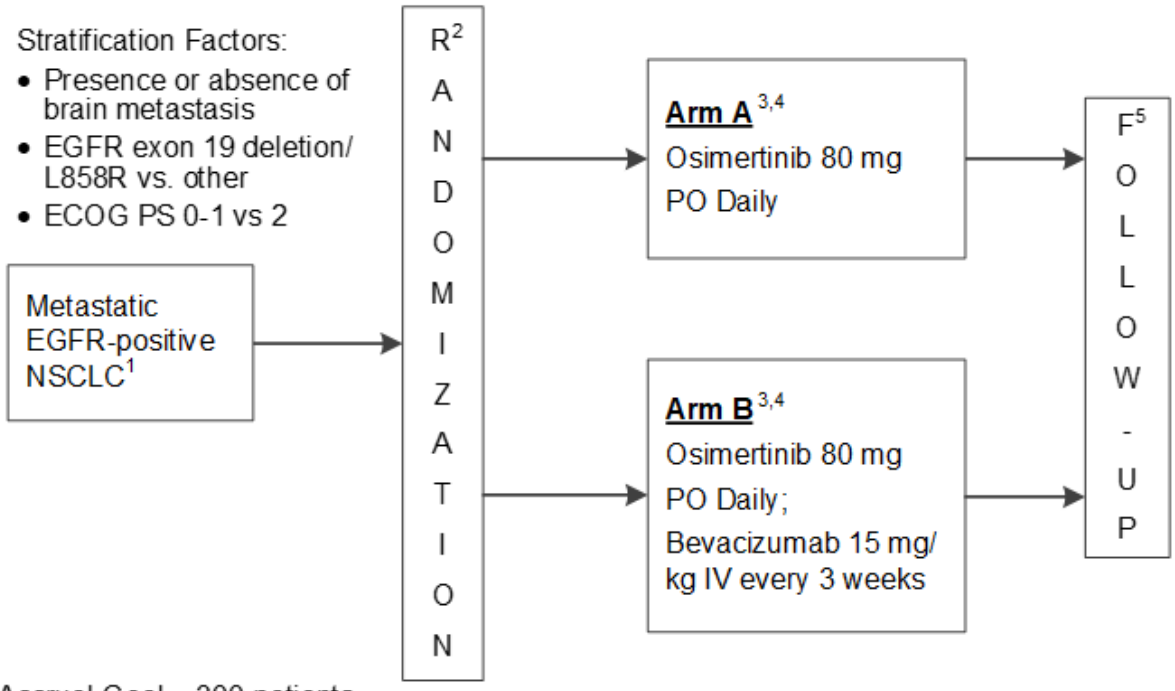
Schema



Accrual Goal = 300 patients
Cycle = 3 weeks (21 days)

1. Patients are eligible to enroll if they are within their first 3 weeks of osimertinib and are registered prior to 3 weeks on treatment.
2. Randomization is 1:1 for Arms A and B.
3. Imaging will be obtained every 3 cycles (9 weeks).
4. Patients will continue on study treatment until progressive disease or unacceptable toxicity.
5. All patients, including those who discontinue protocol therapy early, will be followed until progression, even if non-protocol therapy is initiated, and for survival for 10 years from date of registration.