TH-138: Phase II Randomized Trial of Carboplatin + Pemetrexed + Bevacizumab, With or Without Atezolizumab, in Patients With Stage IV Nonsquamous NSCLC Who Harbor a Sensitizing *EGFR* Mutation or Have Never Smoked

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Condition: Stage IV nonsquamous non-small cell lung cancer

Institution: Fox Chase Cancer Center

Patients with non-small cell lung cancer (NSCLC) who harbor an *EGFR* mutation or are never-smokers generally do not benefit from single-agent immunotherapy. Subgroup analyses from the recent phase III IMpower150 trial suggested that immunotherapy-chemotherapy with vascular endothelial growth factor inhibition may overcome immunotherapy resistance in patients with *EGFR*-mutated tumors. Further prospective research is needed to explore the checkpoint inhibitor-VEGF inhibitor combination. None of the checkpoint inhibitors are currently approved in first-line treatment for patients with *EGFR* mutations after failure of tyrosine kinase inhibitor therapy. This phase II study proposes to exclusively examine a population of patients with stage IV nonsquamous NSCLC who either harbor a sensitizing *EGFR* exon 19 or 21 mutation or are never-smoker wild-types to determine whether adding the PD-L1 inhibitor atezolizumab in combination with pemetrexed/carboplatin/bevacizumab can improve outcomes. *Never-smoker wild-type* is defined as smoking <100 cigarettes in a lifetime and without any *EGFR* mutation or *ALK* or *ROS1* rearrangement.

Primary Objective:

- Compare progression-free survival (PFS) in patients receiving atezolizumab in addition to pemetrexed/carboplatin/bevacizumab (Arm A) versus those receiving pemetrexed/carboplatin/bevacizumab without atezolizumab (Arm B)

Secondary Objectives:

- Perform a safety analysis in all treated subjects
- Compare the overall response rate of Arm A versus Arm B
- Compare the duration of response of Arm A versus Arm B
- Compare the time to response of Arm A versus Arm B
- Compare PFS and overall survival of Arm A versus Arm B in the subset of patients with tumors with a known *EGFR* exon 19 or 21 mutation

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ClinicalTrials.gov Identifier: NCT03786692

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This feature highlights an NCCN study funded through the grant mechanism.

doi: 10.6004/jnccn.2020.0034

For more information on specific trials, including patient selection criteria, use the contact information listed with each study.

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