

AFT-16: Phase II Trial of Induction Immunotherapy with Atezolizumab for Patients with Unresectable Stage IIIA and IIIB NSCLC Eligible for Chemoradiotherapy with Curative Intent

**ALLIANCE
FOUNDATION TRIALS, LLC**

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KIOSK MENU

Helen J. Ross, MD, Mayo Clinic Arizona

rationale/
objective

study
schema

treatment plan/
intervention

key eligibility
criteria

endpoints

text 2

follow up

- Immuno-oncology (IO) therapeutics including the PD-L1 checkpoint inhibitor atezolizumab have been shown to improve the survival of patients with metastatic NSCLC compared to second-line chemo-therapy, e.g., docetaxel.^{1,2}
- Over 40,000 US patients/year present with stage III NSCLC. Most have unresectable disease and only ~25% are cured by conventional chemoradiation.
- This, together with the generally better health of this cohort compared to patients with metastatic NSCLC, makes these patient ideal candidates for IO studies to increase cure rates.
- The combination of checkpoint inhibition to counter tumor related immuno-suppression along with standard chemo-radiation that depletes T-regulatory cells should create immunologic “space” to facilitate clonal expansion of effector T-cells in an environment that fosters improved tumor immunogenicity by blocking PD-L1.
- Responses to IO therapeutics seem to be higher in patients for whom significant cytoreduction can be achieved such as with radiation of all known disease.
- Both chemotherapy and radiation may expose otherwise hidden antigens that can present additional targets to the reconstituting immune system.

- Disease control rate (DCR = CR + PR + SD) after 12 weeks induction atezolizumab
- 90% power to detect H0:DCR ≤ 0.5 vs. H1:DCR ≥ 0.67
- DCR > 35/60 pts. will warrant further investigation

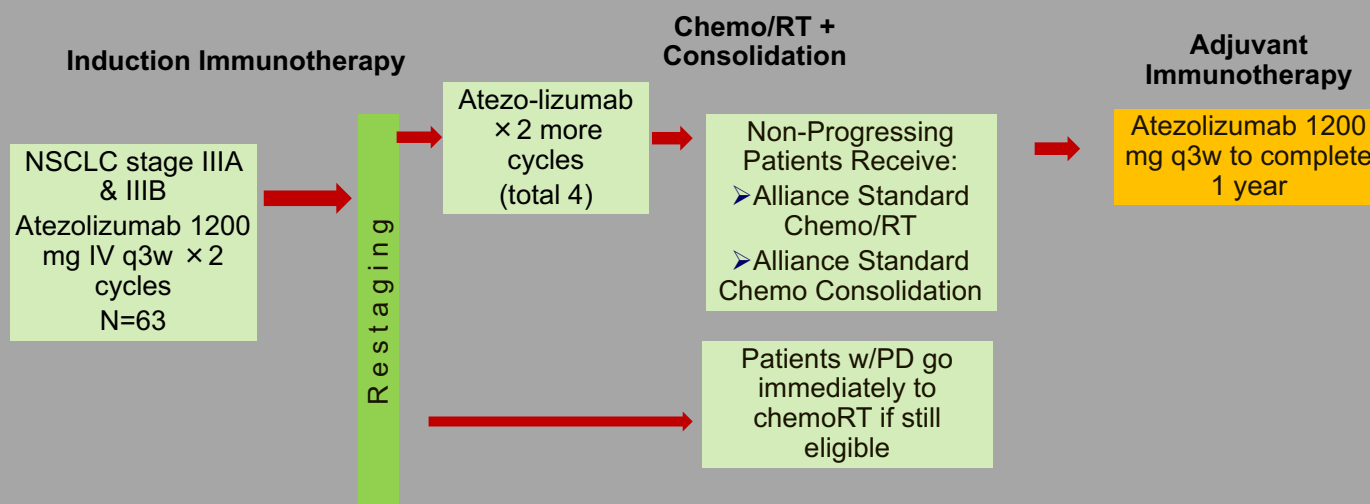
RATIONALE

PRIMARY ENDPOINT

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- follow up



STUDY SCHEMA

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Tumor

- At study entry and, where possible, at progression
- Role of PD-L1 biomarker testing
- Multiplex immunofluorescence/ immunohistochemistry
- Gene expression profiling by Nanostring, RNAseq or RT-PCR
- Whole exome and T cell receptor sequencing

Blood

- ACD, BCT and heparin tubes
- At six timepoints: baseline, post-induction atezolizumab, post-chemoRT, during adjuvant atezolizumab q 3 months x 2, at study completion/progression
- Flow cytometry immunophenotyping
- T cell function analysis
- Circulating tumor DNA analysis
- Cytokine/chemokine analysis

TREATMENT PLAN / INTERVENTION

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- Pathologically proven stage IIIA-IIIB NSCLC
- Tissue available for PD-L1 testing
- ECOG PS 0-1
- No active autoimmune disease
- Adequate cardiopulmonary function
- No underlying organ dysfunction

KEY ELIGIBILITY CRITERIA

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- Response rates to neoadjuvant atezolizumab and to the overall treatment regimen
- Progression-free survival
- Overall survival at 12 and 18 months
- Safety
- Quality of life by the EORTC QLQ-30

SECONDARY ENDPOINTS

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- 15+ Alliance sites activated or near-activation
- 15+ patients screened
- 11+ patients started treatment
- No serious adverse events to date

CURRENT STATUS

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This trial (AFT-16) is funded by
Genentech, Inc.

1. POPLAR: Fehrenbacher L et al. *Lancet* 2016 Apr 30;387(10030):1837-46.
2. OAK: Rittmeyer A et al. *Lancet* 2017 Jan 21;389(10066):255-65.

FUNDING SUPPORT

REFERENCES