ALLIANCE FOUNDATION TRIALS, LLC

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

Helen J. Ross, MD, Mayo Clinic Arizona

TAP TO RETURN TO KIOSK MENU

rationale/ objective
study schema
treatment plan/ intervention
key eligibility criteria
endpoints
text 2
follow up

RATIONALE

- 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.

PRIMARY ENDPOINT

- 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

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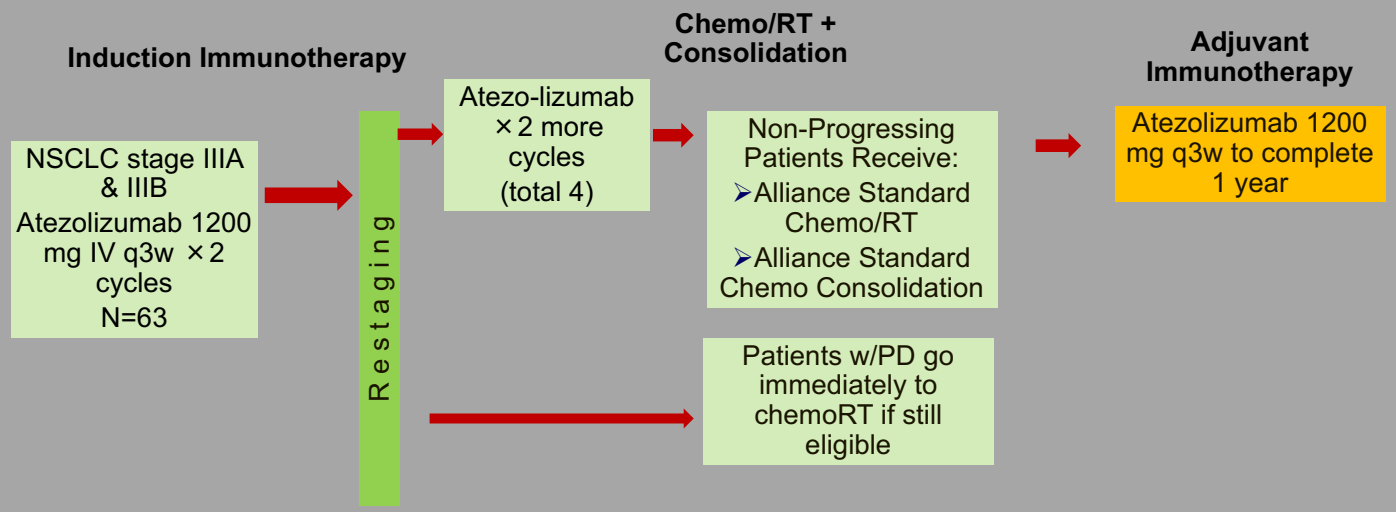

STUDY SCHEMA

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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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FUNDING SUPPORT

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

REFERENCES

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.