Abstract #TPS9145: FoRT 05-BEAT: a Phase II randomized trial comparing atezolizumab versus atezolizumab+bevacizumab as first-line treatment in patients with PD-L1 high advanced/metastatic NSCLC

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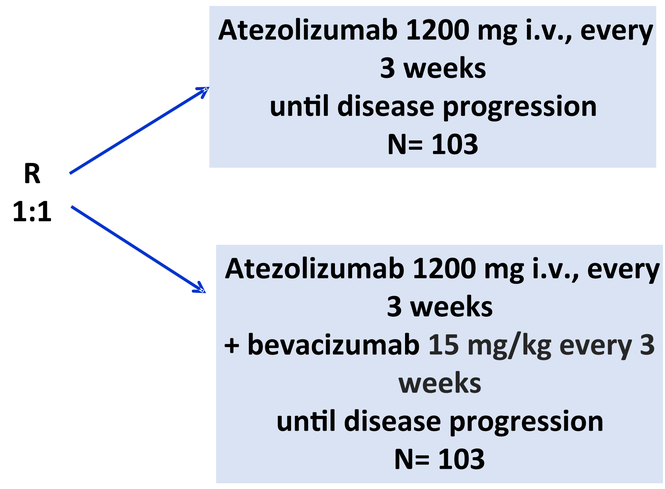
Background/Methods:

- Phase III studies evaluated the efficacy of first-line atezolizumab in combination with chemotherapy in patients with non small-cell lung cancer (NSCLC).[1,2]
- Among angiogenesis inhibitors, bevacizumab is approved as first-line therapy in combination with chemotherapy or in combination with erlotinib in patients with NSCLC harboring activating EGFR mutations.[3]
- Wallin et al suggested that the combination of atezolizumab and bevacizumab increases intra-tumoral CD8+T cells, suggesting that dual VEGF and PD-L1 inhibition improves antigen-specific T-cell migration.[4]
- In addition, preliminary clinical data suggested a strong synergistic effects of bevacizumab with immune checkpoint inhibitors.[5-7]
- There is therefore a strong rationale for investigating the combination of atezolizumab and bevacizumab in patients with advanced/metastatic NSCLC.

Key Inclusion criteria

- Histologically confirmed diagnosis of stage IV non-squamous NSCLC
- No evidence of *EGFR* sensitizing mutations or *ALK* or *ROS1* rearrangements
- Availability of tumor tissue
- PD-L1 expression ≥50%
- No previous chemotherapy
- ECOG Performance status 0-1
- Measurable disease RECIST v1.1
- Asymptomatic stable brain metastases allowed



Primary end point:

- Overall Survival (OS) at 18 months

Secondary end points:

- Response rate (RR); Progression-free survival (PFS); Safety; Correlation with tumor biomarkers in tumor tissue

Statistical plan

The primary endpoint of this study is 18 months Overall Survival rate (18mOS). Considering a 12-month PFS rate of 28-37% for pembrolizumab [8], 48% in patients with high PD-L1 expression levels [9] and considering that with atezolizumab the 2-year PFS rate was 21% with a median PFS of about 7.5 months[10], we assumed a 18mOS rate of a 50% in the arm A. Then, a total of 186 patients is needed to detect an absolute improvement of 20% (thus obtaining a 18mOS of 70% in the arm B) with a power of 80% at a significance level of 5% (two tail). According to loss to follow-up reported in the OAK study[11] , the sample size will be increased by 10% for a total of 206 patients (103 in each arm) to be enrolled. Chi-square test will be used to compare these two rates.

Study update

The study is currently recruiting at 28 Italian centers. From February, 2020, 56 of planned 206 patients have been enrolled

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BEAT

FoRT

Registration number

EudraCT Number: 2018-003973-82

NCT03896074

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Supported by

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