Neoadjuvant atezolizumab in resectable non-small cell lung cancer (NSCLC): Interim analysis and biomarker data from a multicenter study (LCMC3).

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Background:
Small pilot studies (e.g., N Engl J Med. 2018;378:1976) have shown that preoperative immune checkpoint inhibitor therapy may be of benefit in early-stage NSCLC. This large multicenter trial assesses the benefit of neoadjuvant treatment with atezolizumab (atezo; NCT02927301).

Methods:
Patients (pts) with stages IB to selected IIIB resectable NSCLC receive 2 cycles of atezo 1200 mg (days 1, 22) then undergo resection (day 40 ± 10). Primary tumor +/- node biopsies and blood samples are obtained before atezo and at surgery for biomarker studies. The primary endpoint is major pathological response (MPR), defined as ≤ 10% viable tumor cells in the resection specimen. Secondary endpoints include safety and correlation of response with PD-L1 expression, tumor mutation burden (TMB) and gene expression signatures.

Results:
For this interim efficacy analysis (5 Sep 2018 data cut), we report on the first 101 of 180 planned pts: 47 males, median age, 64 y; all ECOG PS 0-1; 23 current and 68 former smokers; 66 non-squamous NSCLC; clinical stages IB/IIA/IIIB/IIIA/IIIB n = 11/16/28/39/7. There were 2 treatment-unrelated Gr 5 AEs (cardiac death post surgical resection; death due to disease progression), 29 Gr 3-4 AEs (6 [6%] treatment related). 90 pts had surgery. Excluding 8 pts who had driver mutations (7 EGFR, 1 ALK, no MPR), MPR rate was 15/82 (18%, 95% CI 11%-28%), 4 pts had pathological complete response (pCR). By RECIST, 6/82 pts had PR, 72 had SD.
and 4 had PD. Two of 26 (8%) PD-L1− (TC0 and IC0, clone SP142) and 10 of 35 (29%) PD-L1+ had MPR (P= 0.055). Five of 44 (11%) TPS < 50 (PD-L1 clone 22C3) and 7 of 20 (35%) TPS > 50 had MPR (P= 0.040). Exome sequencing data was available for 47/101 pts. Median TMB was 10.4 (range, 1.5-46.5) mutations per Mb and was not different in those with MPR compared with those without MPR. Further analysis of TMB, mutation signatures, and gene expression profiling is ongoing.

Conclusions:

Atezo in the neoadjuvant setting was well tolerated, and pCR and MPR rates are encouraging in this large multicenter trial. Efficacy interim analysis passed its futility boundary, and study enrollment continues. Safety, efficacy results and ongoing correlative analyses will be presented. Clinical trial information: NCT02927301

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Meeting: 2019 ASCO Annual Meeting

Session Type: Oral Abstract Session

Session Title: Lung Cancer—Non-Small Cell Local-Regional/Small Cell/Other Thoracic Cancers

Track: Lung Cancer—Non-Small Cell Local-Regional/Small Cell/Other Thoracic Cancers

Subtrack: Local-Regional Non-Small Cell Lung Cancer

Abstract #: 8503

Clinical Trial Registry Number:NCT02927301

Citation: J Clin Oncol 37, 2019 (suppl; abstr 8503)