Clinical Trials Completed

329 EARLY BLOOD CELL COUNT TEST (BCT) FOR SURVIVAL PREDICTION FOR NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH ATEZOLIZUMAB: INTEGRATED ANALYSIS OF 4 MULTICENTER CLINICAL TRIALS

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Background Immune checkpoint inhibitor (ICI) therapy is a major breakthrough for non-small cell lung cancer (NSCLC) treatment given its high efficacy and tolerable toxicity. Although pre-treatment PD-L1 expression levels and tumor mutation burden (TMB) may serve as prognostic biomarkers for patient stratification, effective predictive biomarkers are lacking. Blood cell count test (BCT) is a routine, regular blood test conducted before and during treatment to provide a direct overview of the immune landscape based on the counts of various types of immune cells (ICs). For instance, previous studies showed that neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) both indicate poor treatment outcomes of ICI therapy of NSCLC patients.

Methods This study analyzed relevant combinations of IC counts from four international, multi-center clinical trials of OAK, BIRCH, POPLAR and FIR to conduct post-hoc analysis of NSCLC patients undergoing atezolizumab (anti-PD-L1) single-agent treatment (n = 1,479), while docetaxel single-agent treatment (n = 707) was used as control. BCT was conducted at three timepoints, T1 to T3, during pre-treatment and on the first day of treatment cycles 3 and 5, which correspond to baseline, 6, and 12 weeks on-treatment, respectively. Univariate and multivariate Cox regression analysis was conducted to identify NLR_T3, PLR_T3 and neutrophil-to-monocyte (NMR) at T2 as early BCT biomarkers that may predict ICI efficacy. Next, univariate and multivariate Cox proportional hazards regression analysis were used to identify any effective combination of BCT biomarkers and their absolute cutoff values that may serve as predictive biomarkers to predict atezolizumab treatment outcomes. Lastly, combinations of these BCT biomarkers were tested to optimize BCTscore model for clinical evaluation.

Results The final BCT biomarker combination, comprising of the BCT biomarkers of NLR and PLR at 12 weeks on-treatment (T3) and NMR at 6 weeks on-treatment (T2), was identified to be a strong predictive biomarker for atezolizumab (Ate)-treated NSCLC patients in comparison to docetaxel (Dtx)-treated patients regarding overall survival (OS) (BCTscore low-risk: HR Ate vs Dtx = 1.54 (95% CI: 1.04–2.27), P = 0.036; high-risk: HR Ate vs Dtx = 0.84 (95% CI: 0.62–1.12), P = 0.236). Our BCTscore model consistently exhibited better OS AUC in the OAK (AUC12month=0.696), BIRCH (AUC12month=0.672) and POPLAR+FIR studies (AUC12month=0.727) than that of each of the three BCT biomarkers in these three studies.

Conclusions The BCTscore of NLR at 12 weeks, PLR at 12 weeks and NMR at 6 weeks is a strong efficacy predictive biomarker for atezolizumab-treated NSCLC patients.

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Trial Registration Deidentified individual participant data from the single-arm phase II studies of FIR study (NCT01846416; as of Janurary 7, 2015) [Spigel2018] and BIRCH (NCT02031458; as of May 28, 2015) [Peters2017], and the two-arm randomized controlled trials (RCT) of the POPLAR phase II study (NCT01903993; as of May 8, 2015) [Fehrenbacher2016] and the OAK phase III study (NCT02008227; as of July 7, 2016) [Rittmeyer2017] were made available by Genentech Inc. and accessed through the secure Vivli online platform.

Ethics Approval Both studies were approved by the respective national ethics committees and institutional review boards and written informed consent was obtained from all patients.

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