

363

VACTOSERTIB AND DURVALUMAB AS SECOND OR LATER LINE TREATMENT FOR PD-L1 POSITIVE NON-SMALL CELL LUNG CANCER: INTERIM RESULT

¹Byoung Chul Cho*, ²Ki Hyeong Lee, ³Ji-Youn Han, ⁴Byoung Yong Shim, ¹Hye Ryun Kim, ¹Kyoung-Ho Pyo, ¹Jae-Hwan Kim, ¹Chung-Feng Xin, ⁵Jin Kyung Lee, ⁵Jiyeon Ryu, ⁵Bitna Oh, ⁵Sunjin Hwang, ⁵Ki Baik Hahm, ⁵Seong-Jin Kim. ¹Yonsei Cancer Center, Seoul, Korea, Republic of; ²Chungbuk National University Hospital, Cheongju, Korea, Republic of; ³National cancer center, Goyang, Korea, Republic of; ⁴ST. Vincent's Hospital, Suwon, Korea, Republic of; ⁵MedPacto, Inc, Seoul, Korea, Republic of

Background Targeting transforming growth factor- β (TGF- β) is reported to augment the efficacy of immune checkpoint inhibitors (ICIs) through either enhanced anti-tumor immunity or the correction of tumor microenvironment (TME). Therefore, the combination of vactosertib, a highly selective TGF- β RI kinase inhibitor, and durvalumab is anticipated to improve anti-tumor activity of the ICI. A phase 1b/2a study was conducted to evaluate the combination of vactosertib and durvalumab in patients with advanced NSCLC who progressed after platinum-based chemotherapy.

Methods Patients were treated with vactosertib at a dose of 200 mg twice daily (five days on and two days off) and durvalumab at a dose of 1500 mg every four weeks. Eligible patients were ≥ 19 years old with good performance status (ECOG 0–1) and have no prior exposure to immune checkpoint inhibitors or other TGF- β R1 kinase inhibitors. The objectives of this analysis were to evaluate the safety, antitumor activity including objective response rate (ORR), duration of response (DOR), and time to response (TTR) as well as circulating pharmacodynamic biomarkers related to TGF- β signaling. Response was assessed per RECIST (v1.1).

Results By August 4 2020, twenty-six PD-L1 positive (SP263 assay) patients were analyzed. Median age was 61.5 years (range 48–83), 69.2% were male, median number of previous lines of chemotherapy was 1 (range 1–4), and all patients were PD-L1 positive (15 patients with PD-L1 $\geq 25\%$ and 11 patients with PD-L1 1–24%). The most frequently reported treatment-related adverse events (TRAE) were itching (38.5%) and skin rash (34.6%), but no Gr ≥ 3 itching and rash were observed. Each case of the following was reported as Grade 3 TRAEs: adrenal insufficiency, anemia, and pneumonitis; Grade 4 TRAE, CPK increase, was observed in one patient. Objective response rate was 30.8% and 40.0% in patients with PD-L1 $\geq 1\%$ and $\geq 25\%$ respectively. Circulating PAI-1 and CTGF evaluated in 15 patients decreased significantly on Cycle 1 day 5. Ongoing biomarker results will be presented.

Conclusions The combination of vactosertib and durvalumab has demonstrated a manageable safety profile and encouraging anti-tumor activity as a potential therapeutic strategy in patients with advanced NSCLC. The efficacy outcomes of this combination in a larger number of patients with advanced NSCLC will be followed.

Trial Registration NCT03732274

Ethics Approval The study was approved by Ethics Board of Severance Hospital (4-2018-0892), National Cancer Center (NCC2019-0057), St. Vincent's Hospital (VC19MDDF0205), and Chungbuk National University Hospital (2019-08-015).

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0363>

364

A PERSONAL NEOANTIGEN VACCINE NEO-PV-01 IN COMBINATION WITH CHEMOTHERAPY AND PEMBROLIZUMAB INDUCES BROAD DE NOVO IMMUNE RESPONSES IN FIRST LINE, NON-SQUAMOUS NSCLC

¹Mark Awad*, ²David Spigel, ³Edward Garon, ⁴Saiama Waqar, ³Aaron Lisberg, ⁵Melissa Moles, ⁵Jennifer Tepper, ⁵April Lamb, ⁵Amy Wanamaker, ²Zakaria Khondker, ⁵John Srouji, ⁵Jesse Dong, ⁵Asaf Poran, ⁵Kristen Balogh, ⁵Meghan Bushway, ⁵Mark DeMario, ⁵Lakshmi Srinivasan, ⁵Richard Gaynor, ⁴Ramaswamy Govindan. ¹Dana Farber Cancer Research Institute, Boston, MA, USA; ²Sarah Cannon Cancer Institute, Nashville, TN, USA; ³UCLA Medical Center, Santa Monica, CA, USA; ⁴Washington University, St Louis, MO, USA; ⁵BioNTech US, Cambridge, MA, USA

Background Neoantigens arising from mutations in cancer cell DNA are important targets for T cell mediated anti-tumor immunity. NEO-PV-01 is a personal neoantigen vaccine of up to 20 peptides (14–35 amino acids) based on a patient's HLA profile and bioinformatic analysis of tumor neoantigens. We report here clinical and immune data for NT-002, a Phase 1b study of NEO-PV-01 with pemetrexed, carboplatin, and pembrolizumab as first-line therapy for advanced non-squamous NSCLC.

Methods Patients received 12 weeks of pembrolizumab (Q3W) plus carboplatin and pemetrexed. NEO-PV-01 was then given subcutaneously in a prime-boost format spanning 12 weeks, followed by pembrolizumab for up to 2 years. The primary objective was safety; secondary objectives included overall response rate (ORR), clinical benefit rate (CBR), progression-free survival (PFS), and overall survival (OS). Comprehensive immune assessments were performed with peripheral blood mononuclear cells and biopsies collected at weeks 0, 12, and 24.

Results A total of 38 patients initiated study treatment (ITT population); 21 patients received at least 1 dose NEO-PV-01 (vaccinated group, VAX). The demographics included 61% women and 82% with a smoking history. The regimen was well tolerated consistent with the pembrolizumab plus pemetrexed/carboplatin safety profile, with transient low-grade injection site reactions present in VAX (29%). Treatment-related study discontinuations were rare (2/38). The ORR/CBR for the ITT and VAX were 37%/69% and 57%/95%, respectively. Median PFS was 7.2 months (95% CI: 5.6,16.8) for both the ITT and VAX, and median OS 16.8 months (95% CI: 11.6, NR) for both groups. Interim immune analysis on 8 patients revealed neoantigen-specific CD4+ and CD8+ T cell responses against 48% of vaccine peptides. T cell responses were durable at 52 weeks and exhibited a memory phenotype with cytolytic potential. Epitope spread was observed in 3 of 5 patients analyzed thus far. Further, assessments of immune and molecular correlates of clinical response identified both tumor mutation burden and baseline levels of T cell infiltration in tumor as highly predictive of durable PFS ($p = 0.005$ and $p = 7.2e-07$ (for CD8), respectively). Additional correlates of clinical outcomes with molecular and immunologic responses will be presented.

Conclusions NEO-PV-01 in combination with pembrolizumab and carboplatin/pemetrexed is feasible, has a good safety profile, and induces de novo immune responses in first line non-squamous NSCLC. The association of baseline disease characteristics to prolonged PFS suggests future patient enrichment strategies for evaluation of this novel regimen in a phase 2 trial.

Trial Registration NCT03380871