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Durvalumab ± tremelimumab + platinum-etoposide in first-line extensive-stage SCLC (ES-SCLC): 3-year overall survival update from the phase III CASPIAN study

L. Paz-Ares[1], Y. Chen[2], N. Reinmuth[3], K. Hotta[4], D. Trukhin[5], G. Statsenko[6], M.J. Hochmair[7], M. Ozguroglu[8], J.H. Ji[9], O. Voitko[10], A. Poltoratskiy[11], F. Verderame[12], L. Havel[13], I. Bondarenko[14], G. Losonczy[15], N.V. Conev[16], H.L. Broadhurst[17], T. Dalvi[18], H. Jiang[19], J.W. Goldman[20]

[1] Medical Oncology Department, Hospital Universitario 12 de Octubre, H12O-CNIO Lung Cancer Clinical Research Unit, Universidad Complutense & Ciberonc, Madrid, Spain, [2] Oncology Department, Cancer & Hematology Centers of Western Michigan, Grand Rapids, MI, USA, [3] Thoracic Oncology Department, Asklepios Lung Clinic, Munich-Gauting, Germany, [4] Center for Innovative Clinical Medicine, Okayama University Hospital, Okayama, Japan, [5] Outpatient Chemotherapy, Odessa Regional Oncological Dispensary, Odessa, Ukraine, [6] Ministry of Health, Omsk Regional Cancer Center, Omsk, Russian Federation, [7] Respiratory Oncology Unit, Department of Respiratory and Critical Care Medicine, Karl Landsteiner Institute of Lung Research and Pulmonary Oncology, Vienna, Austria, [8] Cerrahpaşa School of Medicine, Istanbul University–Cerrahpaşa, Istanbul, Turkey, [9] Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, Republic of Korea, [10] Thoracic Surgery, Kyiv City Clinical Oncological Centre, Kiev, Ukraine, [11] Department of Clinical Trials, N.N. Petrov National Medical Research Center of Oncology, St. Petersburg, Russian Federation, [12] Medical Oncology, AO Ospedali Riuniti PO Vincenzo Cervello, Palermo, Italy, [13] Thomayer Hospital, First Faculty of Medicine, Charles University, Prague, Czech Republic, [14] Oncology and Medical Radiology, Dnipropetrovsk Medical Academy, Dnipro, Ukraine, [15] Department of Pulmonology, Semmelweis University, Budapest, Hungary, [16] Clinic of Medical Oncology, UMHAT St Marina, Varna, Bulgaria, [17] Statistics, Plus-Project Ltd, Alderley Park, UK, [18] Late Oncology R&D, AstraZeneca, Gaithersburg, MD, USA, [19] Clinical Development, Oncology R&D, AstraZeneca, Gaithersburg, MD, USA[20] Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Background

In CASPIAN, the Phase 3 study of etoposide + cisplatin/carboplatin (EP) ± durvalumab (D) ± tremelimumab (T) as first-line treatment of ES-SCLC, D + EP demonstrated a statistically significant improvement in OS vs EP alone (data cut-off [DCO]: 11 Mar 2019; HR 0.73 [95% CI 0.59–0.91; p=0.0047]). In a subsequent analysis after a median follow-up of 25.1 mo (DCO 27 Jan 2020), OS benefit with D + EP vs EP was sustained (HR 0.75 [95% CI 0.62–0.91; nominal p=0.0032]), and D + T + EP numerically improved OS vs EP (HR 0.82 [95% CI 0.68–1.00; p=0.0451]), but did not reach statistical significance (p≤0.0418). Here we report updated OS after a median follow-up of >3 years, the longest reported to date for a phase 3 trial of EP + PD(L)1 in this disease setting.

Methods

Pts with treatment-naïve ES-SCLC were randomised 1:1:1 to D 1500 mg + EP q3w, D 1500 mg + T 75 mg + EP q3w, or EP q3w. Pts in the IO arms received 4 cycles of EP + D ± T, followed by maintenance D 1500 mg q4w. Pts in the EP arm received up to 6 cycles of EP. The two primary endpoints were OS for D + EP vs EP and for D + T + EP vs EP. Serious AEs (SAEs) were assessed during long-term follow up.

Results

268, 268 and 269 pts were randomized to D + EP, D + T + EP and EP, respectively. At a DCO of 27 Mar 2021, median follow-up was 39.4 mo, 86% maturity. D + EP continued to demonstrate improved OS vs EP: HR 0.71 (95% CI 0.60–0.86; nominal p=0.0003). Median OS was 12.9 vs 10.5 mo; 22.9% vs 13.9% of pts were alive at 24 mo; and 17.6% vs 5.8% of pts were alive at 36 mo with D + EP vs EP, respectively. D + T + EP continued to numerically improve OS vs EP: HR 0.81 (95% CI 0.67–0.97; nominal p=0.02); median OS was 10.4 mo, and 15.3% of pts were alive at 36 mo. 46 pts remained on treatment with D at DCO (27 in the D + EP arm and 19 in the D + T + EP arm). In D + EP, D + T + EP and EP arms, respectively, incidences of SAEs (all cause) were 32.5%, 47.4% and 36.5%; and AEs leading to death (all cause) were 5.3%, 10.9% and 6.0%.

Conclusions

D + EP demonstrated sustained OS benefit over EP with a well-tolerated safety profile after >3 years of median follow-up, consistent with previous analyses. 3 times more pts were estimated to be alive at 3 years when treated with D + EP vs EP alone, further establishing D + EP as standard of care for first-line treatment of ES-SCLC.

Clinical trial identification

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Disclosure

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