

Community Counts: Exploring Transcription Regulation & Immunotherapy for ES-SCLC

Clinical Case #2

References

Atrafi F, Groen HJM, Byers LA, et al. A phase I dose-escalation study of veliparib combined with carboplatin and etoposide in patients with extensive-stage small cell lung cancer and other solid tumors. *Clin Cancer Res*. 2019;25(2):496-505. doi:10.1158/1078-0432.CCR-18-2014

Baize N, Monnet I, Greillier L, et al. Carboplatin plus etoposide versus topotecan as second-line treatment for patients with sensitive relapsed small-cell lung cancer: an open-label, multicentre, randomised, phase 3 trial. *Lancet Oncol*. 2020;21(9):1224-1233. doi:10.1016/s1470-2045(20)30461-7

Chung HC, Piha-Paul SA, Lopez-Martin J, et al. Pembrolizumab after two or more lines of previous therapy in patients with recurrent or metastatic SCLC: results from the KEYNOTE-028 and KEYNOTE-158 studies. *J Thorac Oncol*. 2020;15(4):618-627.

ClinicalTrials.gov. Study in patients with advanced cancers associated with expression of DLL3 who have failed standard available therapy. NCT04471727. Updated August 30, 2021. Accessed October 8, 2021. <https://clinicaltrials.gov/ct2/show/NCT04471727>

ClinicalTrials.gov. Clinical trial of lurbinectedin (PM01183)/doxorubicin versus CAV or topotecan as treatment in patients with small-cell lung cancer (ATLANTIS). NCT02566993. Updated March 10, 2020. Accessed October 25, 2021. <https://clinicaltrials.gov/ct2/show/NCT02566993>

ClinicalTrials.gov. Study evaluating safety, tolerability and PK of AMG 757 in adults with small cell lung cancer. NCT03319940. Updated October 15, 2021. Accessed October 27, 2021. <https://www.clinicaltrials.gov/ct2/show/NCT03319940>

de Bono J, Ramanathan RK, Mina L, et al. Phase I, dose-escalation, two-part trial of the PARP inhibitor talazoparib in patients with advanced germline BRCA1/2 mutations and selected sporadic cancers. *Cancer Discov*. 2017;7(6):620-629. doi:10.1158/2159-8290.CD-16-1250

Farago AF, Yeap BY, Stanzione M, et al. Combination olaparib and temozolomide in relapsed small-cell lung cancer. *Cancer Discov*. 2019;9(10):1372-1387. doi:10.1158/2159-8290.CD-19-0582

Knelson EH, Patel SA, Sands JM. PARP inhibitors in small-cell lung cancer: rational combinations to improve responses. *Cancers (Basel)*. 2021;13(4):727. doi:10.3390/cancers13040727

Krebs M, Ross K, Kim S, et al. P1.15-004 An open-label, multitumor phase II basket study of olaparib and durvalumab (MEDIOLA): results in patients with relapsed SCLC. *J Thorac Oncol*. 2017;12(11):S2044-S2045. doi:10.1016/j.jtho.2017.09.1040

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Small Cell Lung Cancer (v1.2022). Updated August 9, 2021. Accessed September 29, 2021. https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf

O'Brien MER, Ciuleanu TE, Tsekov H, et al. Phase III trial comparing supportive care alone with supportive care with oral topotecan in patients with relapsed small-cell lung cancer. *J Clin Oncol*. 2006;24(34):5441-5447. doi:10.1200/JCO.2006.06.5821

Owonikoko TK, Park K, Govindan R, et al. Nivolumab and ipilimumab as maintenance therapy in extensive-disease small-cell lung cancer: CheckMate 451. *J Clin Oncol*. 2021;39(12):1349-1359. doi:10.1200/JCO.20.02212

Paz-Ares L, Ciuleanu T, Navarro A, et al. PL02.03 - Lurbinectedin/doxorubicin versus CAV or topotecan in relapsed SCLC patients: Phase III randomized ATLANTIS trial. Presented at: World Conference on Lung Cancer; September 8 to 14 2021; Virtual. https://library.iaslc.org/conference-program?product_id=24&author=&category=&date=&session_type=&session=&presentation=PL02.03&keyword=&cme=undefined&

Pietanza MC, Waqar SN, Krug LM, et al. Randomized, double-blind, phase II study of temozolomide in combination with either veliparib or placebo in patients with relapsed-sensitive or refractory small-cell lung cancer. *J Clin Oncol*. 2018;36(23):2386-2394. doi:10.1200/JCO.2018.77.7672

Ready N, Farago AF, de Braud F, et al. Third-line nivolumab monotherapy in recurrent SCLC: CheckMate 032. *J Thorac Oncol*. 2019;14(2):237-244. doi:10.1016/j.jtho.2018.10.003

Rudin CM, Awad MM, Navarro A, et al. Pembrolizumab or placebo plus etoposide and platinum as first-line therapy for extensive-stage small-cell lung cancer: randomized, double-blind, phase III KEYNOTE-604 Study. *J Clin Oncol*. 2020;38(21):2369-2379. doi:10.1200/JCO.20.00793

Subbiah V, Paz-Ares L, Besse B, et al. Antitumor activity of lurbinectedin in second-line small cell lung cancer patients who are candidates for re-challenge with the first-line treatment. *Lung Cancer*. 2020;150:90-96. doi:10.1016/j.lungcan.2020.10.003

Thomas A, Vilimas R, Trindade C, et al. Durvalumab in combination with olaparib in patients with relapsed SCLC: results from a phase II study. *J Thorac Oncol*. 2019;14(8):1447-1457. doi:10.1016/j.jtho.2019.04.026

Trigo J, Subbiah V, Besse B, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. *Lancet Oncol*. 2020;21(5):645-654. doi:10.1016/s1470-2045(20)30068-1

ZEPZELCA™ (lurbinectedin) [prescribing information]. Jazz Pharmaceuticals, Inc. Approved 2020. Revised June 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213702s000lbl.pdf

Glossary

1L, first line
AE, adverse event
ALT, alanine aminotransferase
AST, aspartate transaminase
BSC, best supportive care
Carbo, carboplatin
CAV, cyclophosphamide/doxorubicin/vincristine
CE, cisplatin/etoposide
Chemo, chemotherapy
CHK1, checkpoint kinase 1
CI, confidence interval
CNS, central nervous system
CR, complete response
CT, computed tomography
CTFI, chemotherapy-free interval
DCR, disease control rate
DLL3, delta-like ligand 3
DOR, duration of response
ES-SCLC, extensive-stage small-cell lung cancer
Etop, etoposide
HR, hazard ratio
IO, immunotherapy
IV, intravenous
Ipi, ipilimumab
LS-SCLC, limited-stage small-cell lung cancer
Lurbi, lurbinectedin
mDOR, median duration of response
Mets, metastases
mOS, median overall survival
mPFS, median progression-free survival
MTD, maximum tolerated dose
NCCN, National Comprehensive Cancer Network
Nivo, nivolumab
NR, not reported
OS, overall survival
ORR, overall response rate
PARP, poly ADP ribose polymerase
PCI, prophylactic cranial irradiation
Pembro, pembrolizumab
PD-L1, programmed death-ligand 1
PFS, progression-free survival
PO, by mouth
PR, partial response

RR, response rate

RNA pol II, ribonucleic acid polymerase II

SCLC, small-cell lung cancer

TMZ, temozolomide

Topo, topotecan

TRAE, treatment-related adverse event

w/, with