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Simultaneous Integrated Dose Reduction Intensity-Modulated Radiotherapy Effectively Reduces Cardiac Irradiation Dose in Limited-Stage Small-Cell Lung Cancer

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Purpose/Objective(s): To assess the clinical survival outcomes and toxicities of simultaneous dose reduction with intensity-modulated radiotherapy (SIR-IMRT) versus conventional IMRT (C-IMRT) in patients with limited-stage small cell lung cancer (LS-SCLC).

Materials/Methods: After propensity score matching (PSM), a retrospective analysis of 320 patients with LS-SCLC who were treated using SIR-IMRT or C-IMRT from January 1, 2013 to December 31, 2018 was conducted. The prescribed irradiation dose in the SIR-IMRT cohort was 60 Gy to the planning gross tumor volume (PGTV) and 54 Gy to the planning target volume (PTV); in the C-IMRT cohort, the radiation dose was 60 Gy to both PGTV and PTV. Treatment-related toxicities, short-term effects, and survival outcomes were observed.

Results: Of the 320 patients (n = 160 patients in each group) included in the study, 196 (61.3%) were male, and the median patient age was 60 years. The median survival time (MST) was 31.3 (95% CI, 29.5−33.2) months, and the median progression-free survival (PFS) and locoregional recurrence-free survival (LRFS) were 18.1 (95% CI 13.6−23.5) months and 26.9 months, respectively. The MST in the two cohorts were 32.3 (95% CI, 29.8−34.8) months (SIR-IMRT) and 29.3 (95% CI 26.2−32.4) months (C-IMRT), respectively ($\boldsymbol{P} = 0.048$). No differences in PFS and LRFS and no treatment failure were found between the two groups. Compared with the C-IMRT cohort, obviously lower radiation-related toxicities were observed in the SIR-IMRT cohort. In addition, the underlying dose was minimized in the SIR-IMRT treatment plans through critical thoracic organs at risk (OAR), and the percentage of Vheart20 − Vheart50 was obviously lower in the SIR-IMRT group (all $\boldsymbol{P} < 0.05$). Further, the cardiac dose dosimetric parameter Vheart40 was found to have a negative association with survival ($r = -0.21$, $P = 0.011$). The ROC curve of Vheart40 was plotted by identifying 15.04% as a cut-off point, which that yielded 54.0% sensitivity and 69.2% specificity for predicting survival loss, and the area under the ROC curve was 0.612 (95% CI 0.538−0.686, $\boldsymbol{P} = 0.004$).

Conclusion: Compared with C-IMRT, SIR-IMRT minimizes the underlying dose to critical thoracic OARs. Lower radiation-related toxicity was observed in the SIR-IMRT group, without compromising local control and disease control. In addition, cardiac dose exposure was negatively associated with survival. Thus, 15.04% of Vheart40 is recommended as the cut-off point, and a value above 15.04% predicts survival loss.

Abstract 2970 − Table 1

		Patients, n (%)	MST, months	*P*
Age, y	≥60	109	27.0	0.06
	< 60	211	32.9	
Gender	Male	196	31.3	0.61
	Female	124	31.3	
KPS	≥80	308	31.4	0.92
	< 80	12	30.0	
Clinical stage	II(a/b)	13/12	54.7/28.2	0.003
	III(a/b/c)	123/155/17	32.1/28.7/20.1	

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Phase 3 Study of Pembrolizumab With Concurrent Chemoradiation Therapy Followed by Pembrolizumab With or Without Olaparib vs. Concurrent Chemoradiation Therapy in Patients With Newly Diagnosed Limited-Stage Small-Cell Lung Cancer: KEYLYNK-013

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Purpose/Objective(s): Concurrent chemoradiotherapy (CCRT) with etoposide and platinum (carboplatin/cisplatin) plus the anti−PD-1 antibody pembrolizumab (pembro) has shown antitumor activity and acceptable safety in patients (pts) with limited-stage small-cell lung cancer (LS-SCLC). The poly (ADP-ribose) polymerase (PARP) inhibitor, olaparib, has shown activity in combination with checkpoint inhibitors in SCLC. KEYLYNK-013 (NCT04624204) is a randomized, placebo-controlled, double-blind phase 3 trial of pembro plus CCRT followed by pembro with or without olaparib in pts with newly diagnosed LS-SCLC.

Materials/Methods: Eligible pts are those aged ≥18 years with previously untreated LS-SCLC, ECOG PS 0/1, and adequate pulmonary function. Pts are randomized 1:1:1 to receive pembro 200 mg Q3W (groups A and B) or pembro placebo (saline) Q3W (group C) during the chemoradiation phase. All pts also receive 4 cycles of chemotherapy (etoposide 100 mg/m^2 on days 1, 2, and 3 of each cycle and investigator's choice of carboplatin AUC 5 mg/mL/min or cisplatin 75 mg/m^2 on day 1 of each cycle) with definitive thoracic radiotherapy (total dose of 45 Gy in 30 fractions twice daily over 3 weeks or 66 Gy in 33 fractions once daily over 6.5 weeks starting on day 1 of cycle 2). After chemoradiation, prophylactic cranial irradiation is strongly recommended for pts with CR/PR or at investigator's discretion for pts with SD. Postchemoradiation pts receive pembro 400 mg Q6W plus olaparib placebo (group A), or pembro 400 mg Q6W plus olaparib 300 mg BID (group B), or pembro placebo plus olaparib placebo (group C) for 9 cycles/12 months. Randomization is stratified by ECOG PS (0 vs 1), SCLC stage (I/II vs III), radiation fractionation (twice vs once daily), and region (east Asia vs North America/western Europe/UK/Australia vs rest of world). Tumor imaging occurs at baseline, within 12 weeks of cycle 1 day 1, followed by Q9W to the end of year 2, Q12W in year 3, Q16W in year 4, every 6 months in year 5, and annually thereafter. Imaging is assessed per RECIST v1.1 by blinded independent central review. AEs are made per NCI-CTCAE v5.0. Health-related quality of life is assessed using EORTC-QLQ-C30 and QLQ-LC13. Primary endpoints are OS and PFS per RECIST v1.1 by blinded independent central review. OS and PFS are estimated by the Kaplan-Meier method. Between-group differences will be evaluated with stratified log-rank tests and Cox proportional hazard models with Efron's method of tie handling. Secondary endpoints include ORR, duration of response, safety, and pt-reported outcomes. Enrollment began in Dec 2020 and is ongoing at 43 sites in 11 countries as of Feb 24, 2021.

Results: TBD

Conclusion: TBD

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Limited Stage Small Cell Lung Cancer Patients With Complete Response After Thoracic Chemoradiotherapy Still Benefit From Prophylactic Cranial Irradiation in the MRI Era

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Purpose/Objective(s): Currently prophylactic cranial irradiation (PCI) is recommended for limited stage small cell lung cancer (LS-SCLC) patients with good response after thoracic chemoradiotherapy. However, the role of PCI for LS-SCLC was doubted after Japanese study published, which PCI was not superior to magnetic resonance imaging (MRI) follow up for extensive stage of SCLC. This study was aimed to investigate the role of PCI for LS-SCLC in the MRI era.

Materials/Methods: We retrospectively evaluated patients with LS-SCLC who without brain metastasis (BM) confirmed by MRI, and had complete response (CR) or partial response (PR) after initial chemoradiotherapy in our Center between 2007 and 2018. The overall survival (OS), progression-free survival (PFS), and cumulative incidence of BM were estimated by Kaplan−Meier method between patients received PCI or not.

Results: There were 121 patients enrolled in this study. The median age was 59 years old. Ninety-six patients were male, and 25 patients were female. After initial chemoradiotherapy, 55 patients achieved CR, and 66 patients achieved PR. Eighty-six patients received PCI, and 35 patients did not. For the whole group, patients received PCI had lower 2-year BM (10.8% vs 31.9%, $P = 0.02$), and better median PFS (58.0 [95% CI: 7.4 - 108.6] months vs 18.0 [95% CI: 11.0 - 25.0] months, $P = 0.002$) than those did not. However, the difference of median OS between two group was not statistically significant (95.0 [95% CI: 56.5 - 133.5] months vs 56.0 [95% CI: 13.8 - 98.2] months, $P = 0.08$). For the CR subgroup, patients received PCI had lower 2-year BM (8.6% vs 47.1%, $P = 0.04$), better median PFS (93.0[95% CI: 54.7 - 131.3] months vs 66.0 [95% CI: 0.0 - 141.6] months, $P = 0.04$), and better median OS (117.0 [95% CI: 85.4 - 148.6] months vs 68.0 [95% CI: 0.0 - 143.3] months, $P = 0.049$) than those did not. For the PR subgroup, patients received PCI had better median PFS (31.0 [95% CI: 17.0 - 44.9] months vs 16.0 [95% CI: 5.8 - 26.2] months, $P = 0.012$) than those did not. However, the difference of median OS between two group was not statistically significant (45.0 [95% CI: 28.4 - 61.7] months vs 56.0 [95% CI: 9.2 - 102.8] months, 2-year BM between two group was not statistically significant (12.8% vs 20.6%, $P = 0.53$).

Conclusion: In the MRI era, LS-SCLC patients with CR after thoracic chemoradiotherapy still benefited from PCI. However, PCI should not be recommended to patients achieved only PR after initial treatment.

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A Comparison of Hypofractionated and Twice Daily Thoracic Irradiation in Limited-Stage Small Cell Lung Cancer: An Overlap Weighted Analysis

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Purpose/Objective(s): Despite evidence for the superiority of twice daily (BID) radiotherapy schedules, their utilization in practice remains logistically challenging. Hypofractionation (HFRT) is a commonly implemented alternative. We aim to compare the outcomes and toxicities in limited stage small cell lung cancer (LS-SCLC) patients treated with hypofractionated versus BID schedules.

Materials/Methods: A bi-institutional retrospective cohort review was conducted of LS-SCLC patients treated with BID (45Gy/30 fractions) or HFRT (40Gy/15 fractions) schedules from 2007-2019. Overlap weighting using propensity scores were performed to balance observed covariates between the two radiotherapy schedule groups. Effect estimates of radiotherapy schedule on overall survival (OS), locoregional recurrence (LRR) risk, thoracic response, any grade 3+ (including lung, and esophageal) toxicity were determined using multivariable regression modelling. E-values were used to assess the sensitivity of effect estimate to unobserved confounding.

Results: A total of 173 patients were included in the overlap weighted analysis, with 110 patients having received BID treatment, and 63 treated by HFRT. The 5-year OS for the overlap weighted cohort was 24.3% (95% CI, 16.1-36.6), and specifically 22.1% (95% CI, 12.7-38.5) and 26.6% (95% CI, 14.4-49.0%) when stratified by BID and HFRT cohorts specifically. The 5-year LRR risk for the same cohorts after overlap weighting were 68.9% (95% CI, 59.2-80.1), 68.9% (95% CI, 56.6-83.8),