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The Selective Personalized Radio-Immunotherapy for Locally Advanced NSCLC Trial (SPRINT)

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The Selective Personalized Radio-Immunotherapy for Locally Advanced NSCLC Trial (SPRINT)

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Purpose/Objective(s): Standard therapy for unresectable locally advanced non-small cell lung cancer (LA-NSCLC) is concurrent chemoradiotherapy (chemoRT), which is usually followed by adjuvant durvalumab. We performed a prospective trial testing sequential pembrolizumab and risk-adapted radiotherapy without chemotherapy for biomarker-selected LA-NSCLC patients.

Materials/Methods: Patients with AJCC version 8 stage III NSCLC or unresectable stage II NSCLC and ECOG performance status 0-1 were eligible for this trial. Subjects with PD-L1 tumor proportion score (TPS) ≥ 50% received three cycles of induction pembrolizumab (200 mg, every 21 days), underwent restaging FDG-PET/CT, received risk-adapted thoracic radiotherapy (55 Gy delivered to tumors or lymph nodes with metabolic tumor volume exceeding 20 cc and 48 Gy delivered to smaller lesions, all in 20 daily fractions), and then received up to 13 cycles of additional pembrolizumab. Subjects with PD-L1 TPS < 50% received concurrent chemoRT, and adjuvant durvalumab was recommended for patients without disease progression. The primary study endpoint was one-year progression-free survival (PFS) for subjects treated with pembrolizumab and radiotherapy (pembroRT), which we hypothesized would exceed 65%. Other study endpoints included 1-year overall survival (OS) and rates of clinician-scored (CTCAE v. 4.03) and patient-reported (PRO-CTCAE) adverse events observed over one year.

Results: Twenty-five subjects with PD-L1 TPS ≥ 50% and 12 subjects with PD-L1 TPS < 50% from three institutions were enrolled between August 2018 and November 2021. Median age was 70. Twenty-four subjects had stage II-IIIA disease, and 13 had stage IIIB-IIIC disease. Except for PD-L1 TPS, subject characteristics did not differ significantly across treatment groups. Ten out of the 12 subjects with ChemoRT received adjuvant durvalumab, and one received adjuvant osimertinib for EGFR mutation. The median follow-up duration is 15 months. Compared to patients treated with chemoRT, treatment with pembroRT has yielded numerically higher 1-year PFS (72% v. 46%, log rank p=0.232) and OS (91% v. 73%, log rank p=0.213) rates. Similar rates of grade 3 physician-scored adverse events have been observed with pembroRT (24%) and chemoRT (25%). Less severe patient-reported adverse events occurred with pembroRT compared to chemoRT (See Table).

Conclusion: Treatment with pembrolizumab and risk-adapted radiotherapy without chemotherapy is a promising approach for LA-NSCLC patients with PD-L1 TPS ≥ 50%. In addition to yielding high disease control rates, this strategy appears to reduce patient-reported adverse events compared to standard chemoRT and adjuvant therapy.

Abstract 147 − Table 1: Average PRO-CTCAE grades and t-test p-values

	PembroRT	ChemoRT	p-value
Dysphagia	1.5	2.3	0.056
Dyspnea	1.4	1.9	0.111
Cough	1.4	2.4	0.005
Wheezing	1.2	2.1	0.017
Dermatitis	0.9	1.9	0.028
Dizziness	0.7	1.5	0.051
Fatigue	0.7	2.5	0.051
Anxiety	1.2	1.9	0.047
Depression	1.0	1.8	0.022

Author Disclosure: N. Ohri: Consultant; Merck, AstraZeneca, Genentech. S. Jolly: Honoraria; Varian. Consultant; AstraZeneca, Varian. B.T. Cooper: None. R. Kabarriti: None. W.R. Bodner: None. J. Klein: None. S. Viswanathan: None. R. Kaufman: None. E. Shum: Research Grant; Delfi Diagnostics. Consultant; Janssen, Genentech. Travel Expenses; AstraZeneca, Boehringer Ingelheim, Nektar. J.K. Sabari: Consultant; AstraZeneca, Janssen, Navire, Pfizer, Regeneron, Medscape, Takeda. H. Cheng: Research Grant; Roche/Genentech, Spectrum, Vaccinex. Consultant; AstraZeneca, Bayer. R. Gucalp: None. E. Castellucci: None. A. Qin: Research Grant; Takeda, Clovis, Merck, Xencor, AstraZeneca, Roche. S.M. Gadgeel: Honoraria; Merck. Consultant; Genentech/Roche, AstraZeneca, Bristol-Myers Squibb, Takeda, Daiichi Sankyo, Novartis, Blueprint Medicines, Lilly, Pfizer, Janssen Oncology, Mirati Therapeutics. Travel Expenses; Merck. B. Halmos: Consultant; AstraZeneca, Boehringer Ingelheim, Genentech/Roche, Pfizer, Lilly, Foundation Medicine, Guardant Health, Takeda, Novartis, Merck, Bristol-Myers Squibb, Spectrum, Turning Point Therapeutics, Apollomics, Janssen, Veracyte, BeiGene.

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Validation of the Prognostic Utility of ESTRO/EORTC Oligometastatic Disease Classification: A Secondary Analysis from the Population-Based Phase II SABR-5 Trial

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Purpose/Objective(s): The recently developed ESTRO/EORTC oligometastatic disease (OMD) classification has not been validated in terms of its prognostic significance. This study stratified patients from the phase II SABR-5 trial based on ESTRO/EORTC criteria, and compared progression-free survival (PFS) and overall survival (OS) to determine the prognostic significance of the classification scheme.

Materials/Methods: The SABR-5 trial was a single arm phase II study conducted at the 6 regional cancer centers across British Columbia, where SABR for oligometastases was only offered on trial. Patients with up to 5 oligometastases (total or not controlled by prior treatment, and including induced oligometastatic disease) underwent SABR to all lesions. Patients were 18 years of age or older, ECOG 0-2, and life expectancy ≥ 6 months. PFS and OS were calculated using the Kaplan-Meier method and differences between OMD groups were assessed with log-rank tests. Univariable and multivariable analyses were performed using Cox regression modelling.

Results: Between November 2016 and July 2020, 381 patients underwent SABR on trial. Prostate was the most frequent primary tumor histology (32%), followed by colorectal (17%) and breast (11%). Most patients (69%) underwent SABR to one metastasis and 10% received SABR to 3 or more lesions. Median follow-up was 27 months (IQR 18−36). The most frequent OMD group was de-novo oligometastatic disease (69%), followed by repeat (16%) and induced (13%). In total, 62 patients received SABR to oligoprogressive lesions. OMD groups differed significantly in PFS (p<0.001) but not OS (p=0.069). The OMD classification was an independent predictor of both PFS (p=0.005) and OS (p=0.002). Of the five classification factors, only chronicity (synchronous, HR=0.54, p=0.027) and oligoprogression (HR=2.05, p=0.004) were