

Supplementary Data

Pulmonary Stereotactic Body Radiation Therapy of Oligometastatic Head-and-Neck Squamous Cell Carcinoma - A Multicenter Retrospective Study

Fig E1. Cumulative Incidence of Local and Distant Failures After Pulmonary Stereotactic Body Radiotherapy (SBRT) in Patients With Oligometastatic Head and Neck Squamous Cell Carcinoma (HNSCC). The cumulative incidence of local failures (A) was computed for each treated lung metastasis (n=284), while the cumulative incidence of distant failures (B) including progression of the primary HNSCC was calculated for each patient since the first pulmonary SBRT (n=178). Death was considered as a competing event for both analyses.

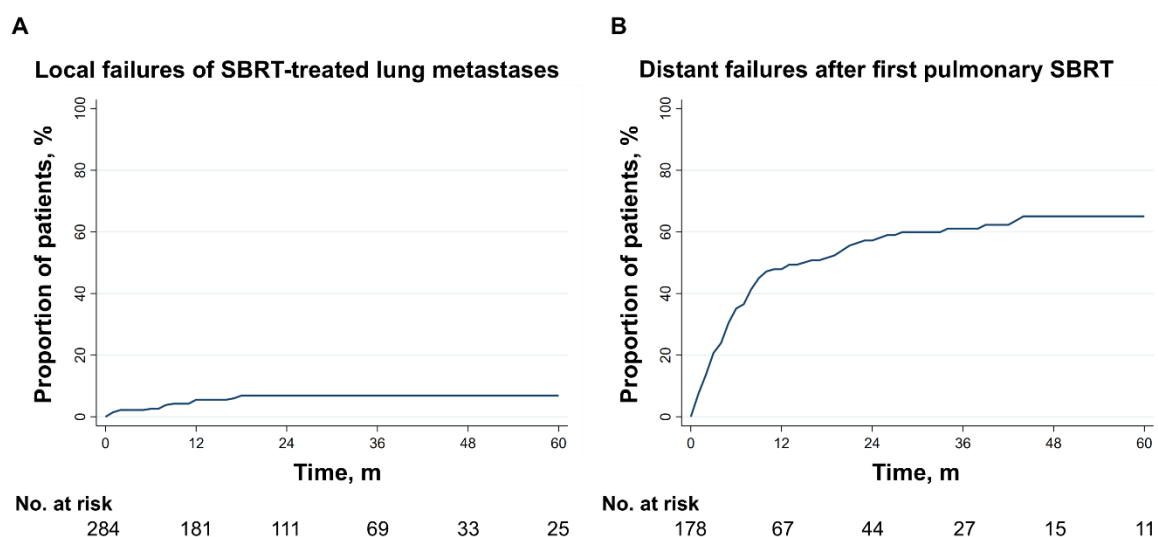


Fig. E2. Cumulative Incidence of Local Failures After Pulmonary Stereotactic Body Radiotherapy (SBRT) in Patients With Oligometastatic Head and Neck Squamous Cell Carcinoma (HNSCC) Stratified For the Biologically Effective Dose (BED). Death was considered as a competing event. A Fine-Gray subdistribution hazards regression analysis was performed regarding an association of a BED ≥ 100 Gy at the planning target volume (PTV) encompassing isodose with the incidence of local failures. The subdistribution Hazard Ratio (sHR) value with the corresponding 95% confidence interval (95% CI) is presented.

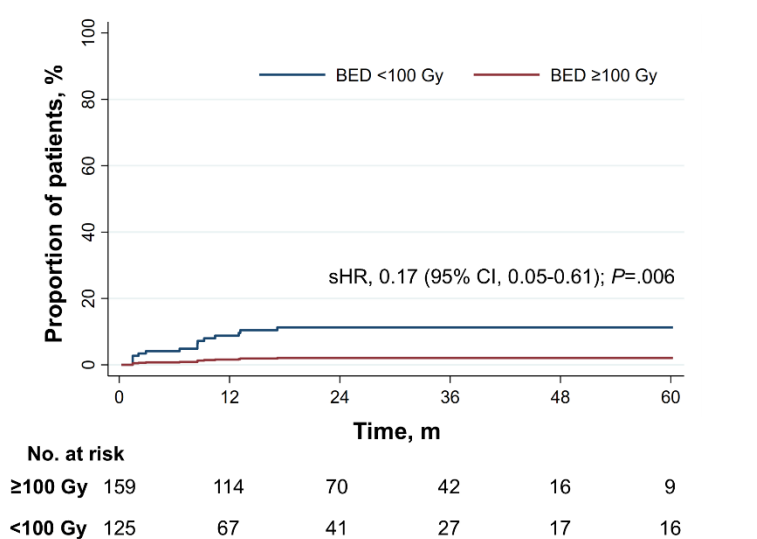


Fig. E3. Cumulative Incidence of Local Failures After Pulmonary Stereotactic Body Radiotherapy (SBRT) in Patients With Oligometastatic Head and Neck Squamous Cell Carcinoma (HNSCC) Stratified For Prior Histological Confirmation. Death was considered as a competing event. A Fine-Gray subdistribution hazards regression analysis was performed. The subdistribution Hazard Ratio (sHR) value with the corresponding 95% confidence interval (95% CI) is presented.

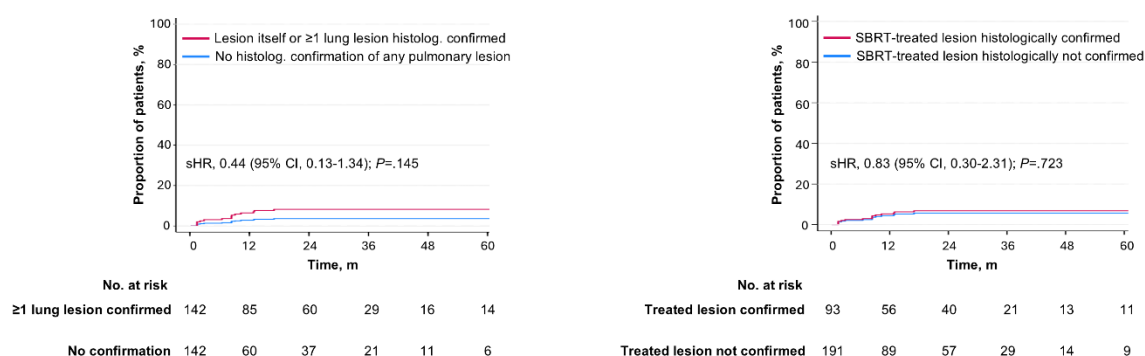


Fig. E4. Overall Survival in Patients With Oligometastatic Head and Neck Squamous Cell Carcinoma (HNSCC) Undergoing Pulmonary Stereotactic Body Radiotherapy (SBRT) Stratified for Type of Oligometastatic Disease at the Time of First SBRT. Hazard ratios (HR) with 95% confidence intervals (95% CI) are reported for survival times, calculated in months.

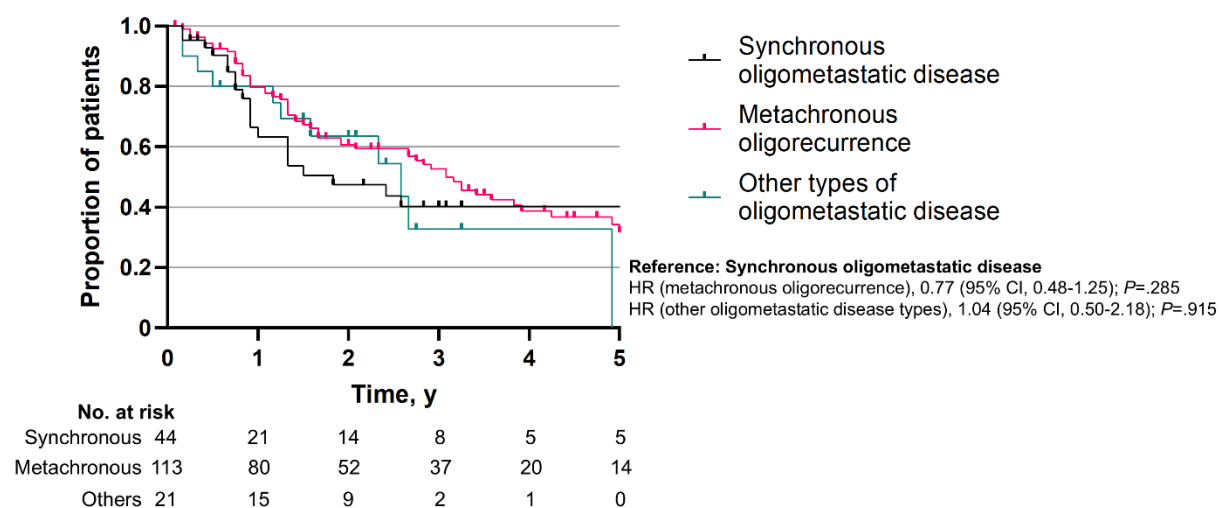


Fig. E5. Overall Survival in Patients With Oligometastatic Head and Neck Squamous Cell Carcinoma (HNSCC) Undergoing Pulmonary Stereotactic Body Radiotherapy (SBRT) Stratified for Histological Confirmation of at Least One Pulmonary Lesion Prior to SBRT. Hazard ratios (HR) with 95% confidence intervals (95% CI) are reported for survival times, calculated in months.

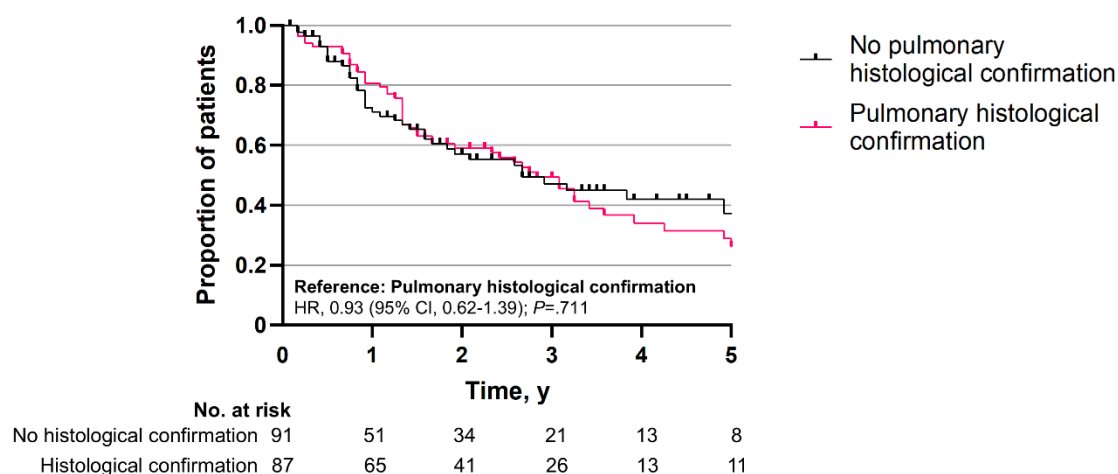


Table E1. Institutional Follow-up Schedule After Pulmonary SBRT for Oligometastatic Head and Neck Squamous Cell Carcinoma (HNSCC) of the 16 Participating Study Centers.

Study center	Follow-up after pulmonary SBRT of oligometastatic HNSCC patients
Center 1	3-monthly imaging and clinical consultation
Center 2	3-monthly imaging and clinical consultation
Center 3	First imaging and clinical consultation at 4-6 weeks after SBRT, then 3-monthly in the first year, and 6-monthly from the second year onward
Center 4	3-monthly imaging and clinical consultation
Center 5	First clinical consultation at 4-6 weeks after SBRT, followed by 3-monthly imaging and clinical consultation
Center 6	First clinical consultation at 2-4 weeks after SBRT, followed by imaging and clinical consultations every 3 months for the first 18 months, every 6 months until 3 years post-SBRT, and annually thereafter
Center 7	3-monthly imaging and clinical consultation
Center 8	3-to-4-monthly imaging and clinical consultation
Center 9	3-monthly imaging and clinical consultation
Center 10	3-monthly imaging and clinical consultation
Center 11	3-monthly imaging and clinical consultation
Center 12	2-to-3-monthly imaging and clinical consultation
Center 13	First imaging and clinical consultation at 3 months after SBRT, followed by 6-monthly intervals with imaging and clinical consultation thereafter
Center 14	3-monthly imaging and clinical consultation including functional pulmonary tests for the first 2 years, followed by 6-monthly intervals with imaging and clinical consultations thereafter
Center 15	3-monthly imaging and clinical consultation
Center 16	3-monthly imaging and clinical consultation

Table E2. Classification of Oligometastatic Disease at the Time of First SBRT According to Guckenberger et al. 2020¹.

	No (%)
De-novo oligometastatic disease	
Synchronous oligometastatic disease	44 (24.7)
Metachronous oligorecurrence	113 (63.5)
Metachronous oligoprogression	6 (3.4)
Repeat oligometastatic disease	
Repeat oligorecurrence	8 (4.5)
Repeat oligopersistence	1 (0.6)
Repeat oligoprogression	4 (2.2)
Induced oligometastatic disease	
Induced oligorecurrence	0 (0.0)
Induced oligopersistence	0 (0.0)
Induced oligoprogression	2 (1.1)

¹Guckenberger M, Lievens Y, Bouma AB, et al. Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation. *Lancet Oncol.* 2020;21(1):e18-e28.

Table E3. Details of the 15 Local Recurrences Including the Methods Used to Confirm Local Recurrence After Pulmonary SBRT. The Biologically Effective Dose (BED) was calculated using the formula $BED = n \times d \times (1 + \frac{d}{\alpha})$ with n = number of fractions, d = dose per fraction, and $\frac{\alpha}{\beta} = 10$ Gy.

Lesion	Number of fractions	BED [Gy]	Type of Confirmation
1	5	107.6	PET-CT
2	3	95.2	PET-CT
3	5	72.0	Histological confirmation
4	8	68.2	Histological confirmation
5	3	95.2	PET-CT
6	10	96.0	PET-CT
7	10	96.0	PET-CT
8	3	112.5	High-risk CT features
9	1	93.6	High-risk CT features
10	3	112.5	Histological confirmation
11	1	93.6	High-risk CT features
12	5	72.0	Histological confirmation
13	5	72.0	Histological confirmation
14	5	72.0	Histological confirmation
15	5	72.0	Histological confirmation

Table E4. Multivariable Cox Proportional Hazard Regression Analysis for Progression-Free Survival in Patients With Oligometastatic HNSCC Undergoing SBRT for Lung Metastases between 2010-2022. AaCCI, age-adjusted Charlson Comorbidity Index; BED, Biologically Effective Dose; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; SBRT, Stereotactic Body Radiotherapy; PTV, planning target volume; UICC, Union for International Cancer Control.

Characteristic	HR (95% CI)	<i>p</i>
Age, y		
≤65	Reference	
>65	1.13 (0.77-1.66)	.522
Sex		
Male	Reference	
Female	1.53 (0.96-2.45)	.072
ECOG status		
0	Reference	
1	1.10 (0.72-1.68)	.671
2-3	1.01 (0.55-1.85)	.982
aaCCI	0.98 (0.90-1.07)	.664
Smoking		
Never smoker	Reference	
Former or active smoker	1.06 (0.61-1.84)	.834
Primary localization		
Oropharynx	Reference	
Oral cavity	1.16 (0.60-2.23)	.666
Nasopharynx	1.82 (0.70-4.74)	.221
Hypopharynx	1.30 (0.74-2.28)	.368
Larynx	0.97 (0.57-1.65)	.903
Oro-/Hypopharynx (multi-level)	0.65 (0.08-4.98)	.677
p16 status		
Positive	Reference	
Negative/unknown	0.96 (0.54-1.73)	.903
Immune checkpoint inhibitor treatment within 60 days before or after the first SBRT		
Yes	Reference	
No	1.54 (0.56-4.22)	.404
Chemotherapy administration within 30 days before or after the first SBRT		
Yes	Reference	
No	0.62 (0.30-1.28)	.198
No. of metastases at the time of first SBRT	1.00 (0.79-1.26)	.996
No. of affected organs at the time of first SBRT		
1	Reference	
2	2.93 (1.27-6.80)	.012
Type of oligometastatic disease		
De-novo oligometastatic disease	Reference	
Repeat oligometastatic disease	1.79 (0.87-3.71)	.114
Induced oligometastatic disease	2.00 (0.22-18.19)	.539
BED at PTV periphery of the first SBRT, Gy	1.00 (0.99-1.01)	.563
Time between initial diagnosis and first SBRT, m	0.99 (0.98-1.00)	.065