NEW EVIDENCES AND PRACTICE CHANGING TREATMENTS IN OLIGOMETASTATIC TUMORS

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OLIGOMETASTATIC TUMORS: definition

1995: *Hellman and Weichselbaum*: «oligometastatic theory»: there is a spectrum of intermediate states between localized and systemic disease, where radical local treatment of the primary cancer and all metastatic lesions might have a curative potential.

TREATMENT APPROCHES

- **LOCAL CONSOLIDATIVE THERAPY OF THE PRIMARY TUMOR**
- **METASTASES DIRECTED THERAPY**
- **SYSTEMIC, TARGET and IMMUNOTHERAPY**

Cancer-specific dose and fractionation schedules in stereotactic body radiotherapy for oligometastatic disease: An interim analysis of the EORTC-ESTRO E^2-RADIatE OligoCare study

Radiotherapy and Oncology (2024)

«The OligoCare cohort enrolls patients with oligometastatic NSCLC, breast cancer (BC), CRC, and PC treated with metastasis-directed radiotherapy. The primary objective of Oligo-Care is to identify patient, tumor, staging and treatment characteristics impacting overall survival. The secondary objective is to identify patterns of care of SBRT for OMD and to determine factors influencing outcomes.»

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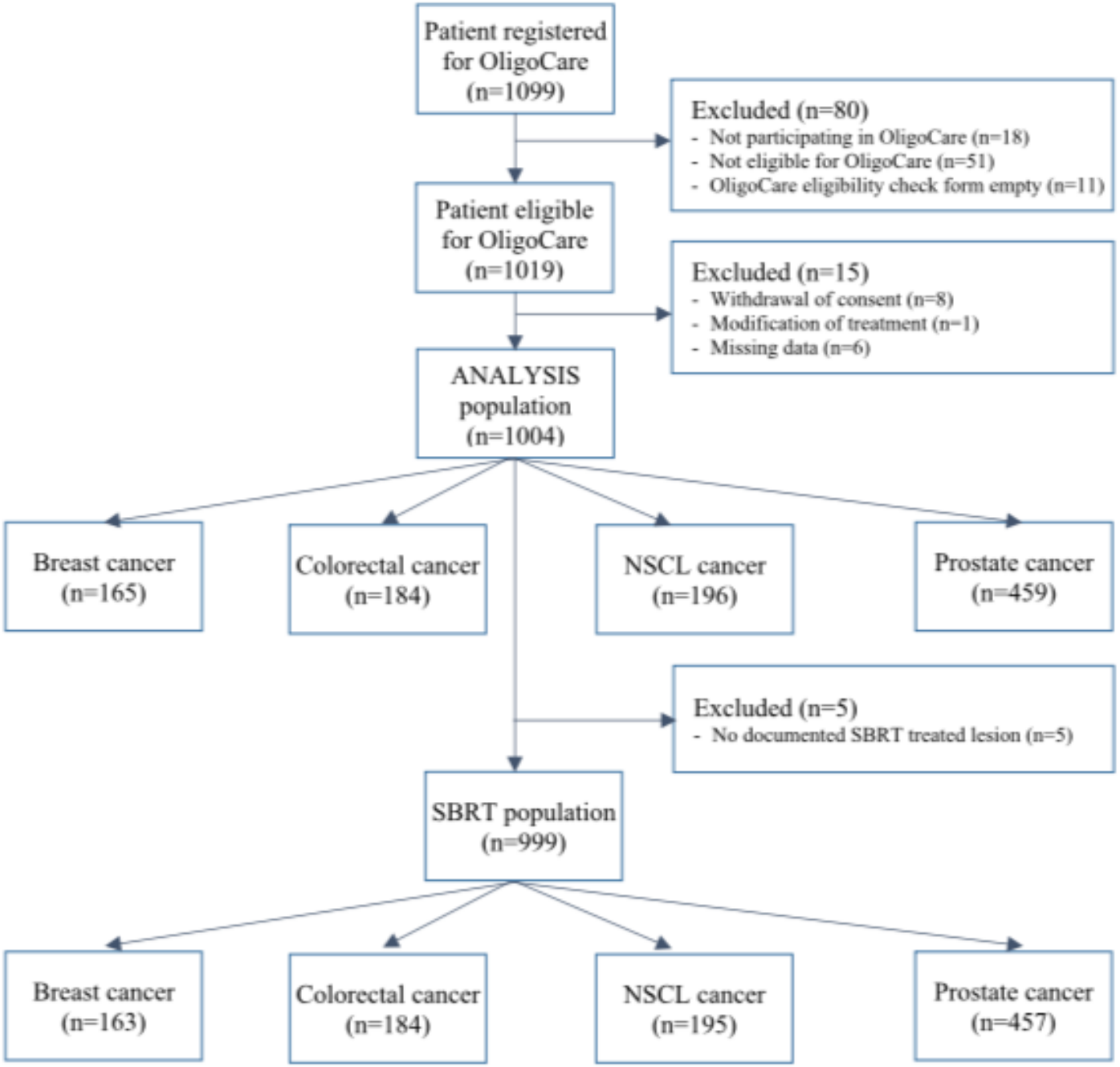

OLIGOMETASTATIC PROSTATE CANCER

The application of RT in OMPC typically involves two main strategies: targeting the primary tumor and treating metastatic lesions. Clinical studies suggest that primary prostate radiotherapy (PPR) in OMPC may confer survival benefits. Additionally, metastasis-directed RT, often involving stereotactic body radiation therapy (SBRT) to all metastatic sites following the radical treatment of the primary tumor, can slow further metastatic progression and delay the initiation of ADT

The Role of Local Prostate and Metastasis-Directed Radiotherapy in the Treatment of Oligometastatic Prostate Cancer

S.H. Choi, *Cancers* **2024**

«This study highlights the potential survival benefits of early OMDRT in patients with OMPC, in both synchronous and metachronous cases. While our findings suggest that a timely and aggressive RT approach, possibly in combination with primary prostate treatment, could improve outcomes, additional data are needed to fully validate this conclusion».

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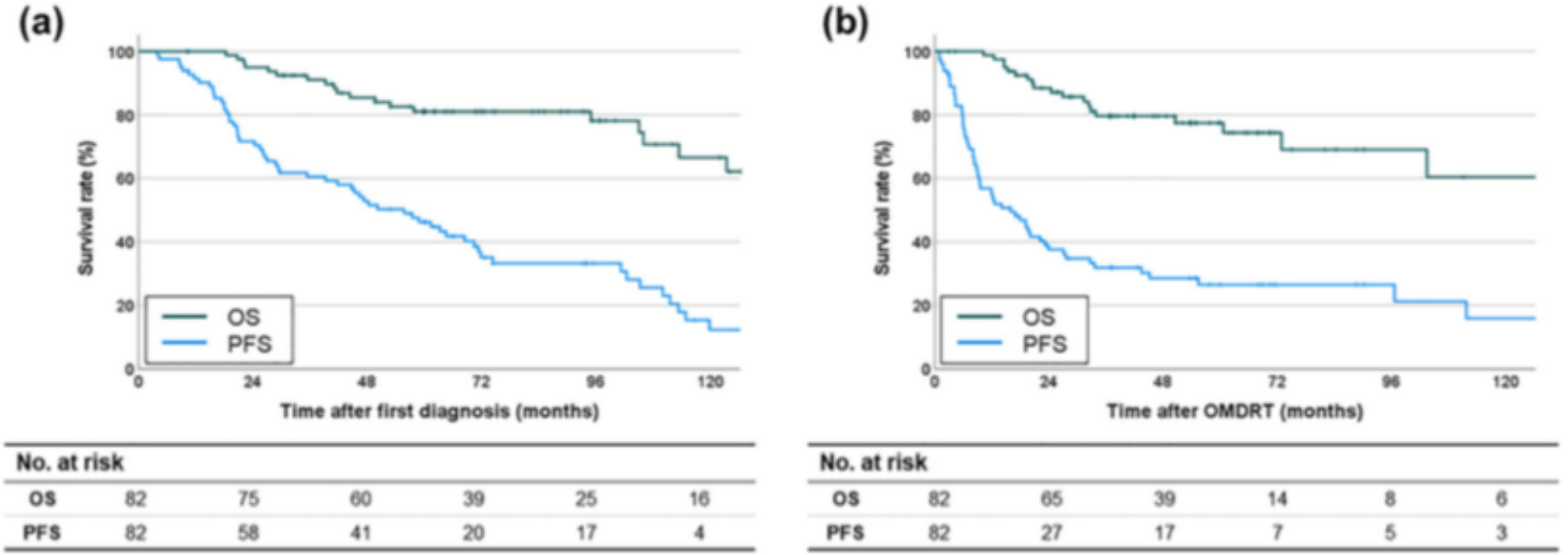
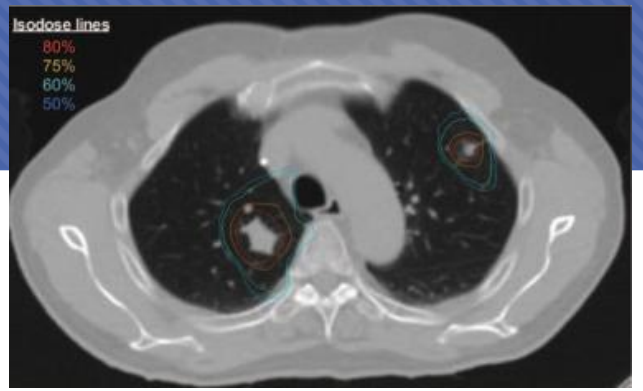


No. at risk						
OS	82	75	60	39	25	16
PFS	82	58	41	20	17	4

No. at risk						
OS	82	65	39	14	8	6
PFS	82	27	17	7	5	3

Curves for (a) OS and PFS rates after the first diagnosis of prostate cancer and (**b**) OS and PFS rates after OMDRT

OLIGOMETASTATIC LUNG CANCER



The Role of Stereotactic Body Radiotherapy in Oligometastatic Non-Small Cell Lung Cancer

«Published phase II-III trials show clear role for LCT techniques such as SBRT in attaining local control in OM-NSCLC patients. This has been demonstrated to be beneficial in improving survival in patients, cost-effective, and generally well tolerated.»

B. Wan et al. *Curr. Oncol.* **2024**

Highlighted trials with preliminary data and other trials discussing the role of SBRT/LCT in OM-NSCLC.

Study	Sample Size	Inclusion/Exclusion Criterion	Dose and fx	Results	Pertinent Treatment-Related Toxicities (Pneumonitis, Grade ≥ 3 Toxicities)
NRG LU002 Iyengar et al., 2024 [19] Randomized, phase II/III	A total of 215 patients; 134 LCT, 81 in no LCT	Metastatic NSCLC, 3 or fewer extracranial sites upon restaging after 4 cycles of first-line therapy	A total of 24 Gy in 1 fx, 30 Gy in 3 fx, 34 Gy in 5 fx A total of 45 Gy in 15 fx to primary	1-year PFS: 51.5% vs. 48% 2-year PFS: 40.1% vs. 35.9% 1 year OS: 76.5% vs. 75.8% 2 year OS: 54.1% vs. 58.1%	LCT: 84% with grade ≥ 2 events, 10% grade 3 pneumonitis, 15% grade 4 events, 8% grade 5 events No LCT: 73% with grade ≥ 2, 1% grade 3 pneumonitis, 15% grade 5 events, 6% grade 5 events
NCT03275597 Bassetti et al., 2021 [20] Phase 1b study—Abstract	A total of 17 patients; 15 non-squamous	Metastatic NSCLC, 1–6 extracranial metastatic sites, no actionable driver mutation, no prior immunotherapy	A total of 30–50 Gy in 5 fx to all sites of disease, followed by Durvalumab + Tremelimumab	OS and PFS not reached	12% grade ≥ 3 hepatitis or pancreatitis, 29% grade 3 event, 6% grade 4 event

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Study	Sample Size	Inclusion/Exclusion Criterion	Dose and fx	Results	Pertinent Treatment-Related Toxicities (Pneumonitis, Grade ≥ 3 Toxicities)
Rashdan et al., 2024 [21] Single-arm, phase II, non-randomized—Abstract	A total of 43 patients; 29 received SBRT	NSCLC, EGFR mutant, no prior treatment, no limit on number of mets, SBRT delivered to persisting lesions after 8 weeks of Osimertinib	Not reported	PFS 32.6 months OS 45.7 months Mean duration osimertinib 31.5 months	2% Grade ≥ 3 pneumonitis 2% Grade ≥ 3 pain, 2% Grade ≥ 3 paronychia, transaminitis, fatigue, hyponatremia and diarrhea
Bestvina et al., 2020 [22] Randomized, phase I	A total of 37 patients; 18 concurrent SBRT with nivolumab and ipilimumab, 19 with sequential SBRT then immunotherapy	Metastatic NSCLC, treatment naïve, no limit to number of metastases	A total of 30 Gy in 3 fx, 45 Gy in 3 fx, or 50 Gy in 5 fx	Median PFS 5.8 months Median OS not reached	Concurrent: 3% grade 5 pulmonary hemorrhage, 5% grade 3 pneumonitis, 3% grade 3 esophageal stenosis and esophagitis Sequential: 8% grade 3 pneumonitis

OLIGOMETASTATIC BREAST CANCER

While the standard treatment for metastatic disease includes systemic therapy with or without palliative radiotherapy (RT), recent studies are evaluating the role of ablative therapies to metastases and locoregional treatment to the primary tumor site in oligometastatic breast cancer

Ongoing prospective trials of Metastasis directed-therapy for oligometastatic and oligoprogressive breast cancer

Trial	Phase	Study completion	Primary endpoint	Tumor histology	# of metastasis allowed	Local tx
Oligometastasis						
STEREO-SEIN (NCT02089100)	III	2023	PFS	Breast (HR+/any HER2)	5	SBRT
CLEAR (NCT03750396)	II, single arm	2025	PFS	Breast (HR+/HER2-)	2	Surgery, SBRT, RFA
EXTEND (NCT03599765)	II, single arm	2025	PFS	Various	5	SBRT
LARA (NCT04698252)	II, randomized	2031	PFS	Breast (HR+/HER2-)	4	Surgery, SBRT, RFA
OMIT (NCT04413409)	III	2025	OS	Various	3	Surgery
SABR-COMET-10 (NCT03721341)	III	2029	OS	Various	10	SBRT
OLGIOMA (NCT04495309)	III	2025	PFS	Various	5	SBRT
TAORMINA (NCT05377047)	III	2027	OS	Various	5	SBRT
Oligoprogression						
AVATAR (ACTRN 12620001212943)	II, single arm	2024	Time to change of sys tx	Breast (HR+/HER2-)	5	SBRT
EXTEND (NCT03599765)	II, single arm	2025	PFS	Various	5	SBRT
COSMO (NCT05301881)	II, single arm	2040	PFS	Various	2	Surgery, SBRT, RFA

Navigating Breast Cancer Oligometastasis Current Landscape and Future Directions

S. M. Yoon ;J.G. Bazan

Current Oncology Reports (2024)

Prospective studies evaluating SBRT in oligometastatic breast cancer

Author, year	# patients	# metastasis	Dose fractionation	Prior/concurrent systemic tx use	LC	PFS	OS	Toxicity
Trovo et al., 2018 [105]	54	92	30–45 Gy/3 fx; 60 Gy/25 fx	89%	2-year, 95%	2-year, 53%; median, 28 months	2-year, 95%; median, not reached	Grade 2, 3.7%; grade 3+, 0%
Milano et al., 2019 [106]	48	102	Various; 3–17 Gy/fx for majority	91%	10-year, 100% (bone only), 73 (non-bone)	NR	10-year, 83% (bone only), 31% (non-bone); median, 3.2 years (bone only)	NR
David et al., 2020 [107]	15	19^	20 Gy/1 fx	87%	2-year, 100%	2-year, 65%	2-year, 100%	Grade 2, 27%; grade 3+, 0%
Franceschini et al., 2022 [108]	64	90	75 Gy/3 fx (liver); various for lung (location dependent)	84%	NR	NR	NR	Grade 2, 3%; grade 3+, 0%

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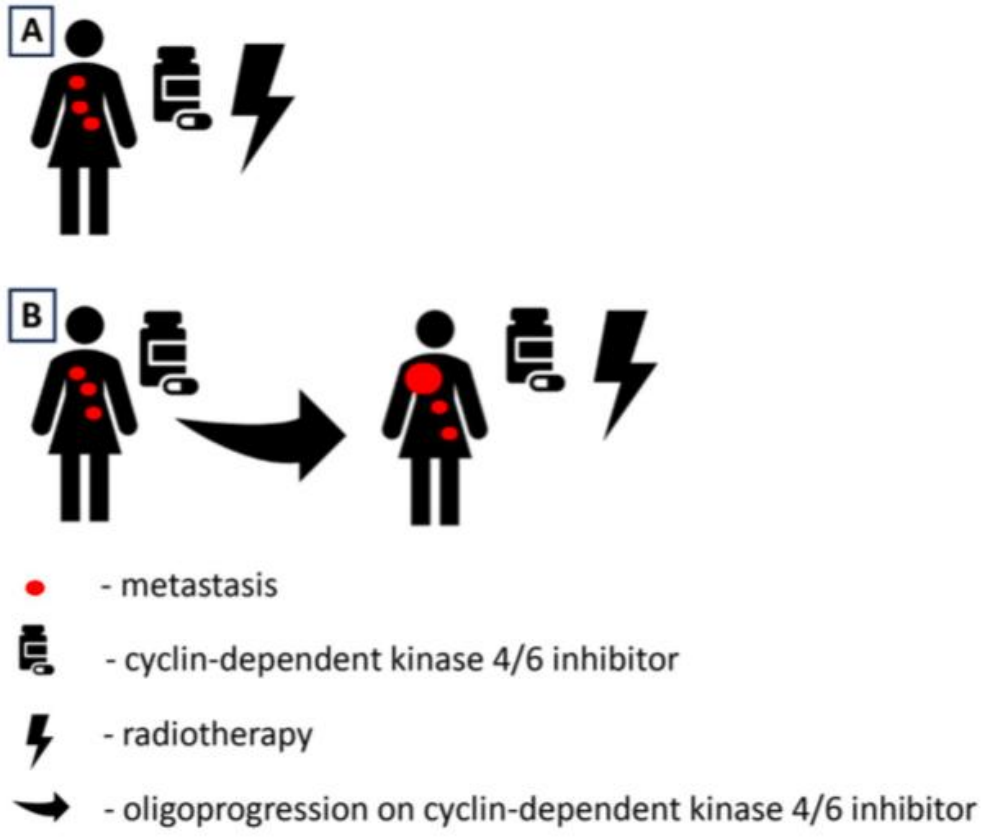
Current Oncology Reports (2024)

Cyclin-dependent kinase 4/6 inhibitors combined with stereotactic ablative radiotherapy in oligometastatic HR-positive/HER2-negative breast cancer patients

M. Kubeczko et al.
BJR 2024

«Overall survival and PFS of ABC patients treated with stereotactic ablative radiation therapy added to cyclin-dependent kinase 4/6 inhibitors is relatively high in oligometastatic patients. The addition of SABR to CDK4/6i seems to be safe and effective. Whether it is a bias of patient selection or an actual synergistic effect requires further validation in prospective studies.»



BIR British Institute of Radiology

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Thank you for your attention!

Prof. Mattia Falchetto Osti