# EVIDENCE AND PRACTICE CHANGING TREATMENTS IN OLIGOMETASTATIC TUMORS

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IRCCS Humanitas Research Hospital

Humanitas University

ESTRO Institutional Member 2023

# AGENDA

- Where do we stand
- Large database
- Prospective trials (mixed histologies)
- Prospective trials (histology driven)
- More than the big killers
- Predictive models

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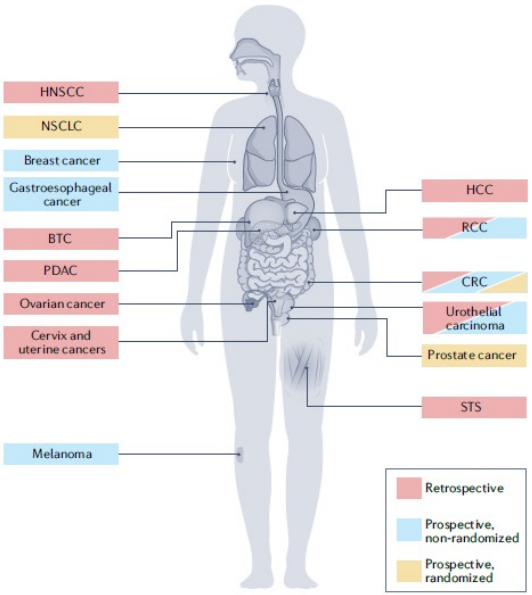
# The oligometastatic spectrum in the era of improved detection and modern systemic therapy

*Rohan R. Katipally, Sean P. Pitroda, Aditya Juloori, Steven J. Chmura and Ralph R. Weichselbaum*




## Key points

- Metastases remain the leading cause of cancer-associated mortality; however, the oligometastasis hypothesis postulates the existence of a spectrum of metastatic spread.
- In the context of modern systemic therapies and improved cancer detection, the oligometastatic phenotype is framed as a dynamic state within which local ablative therapies improve clinical outcome, including prolonging survival and achieving cure.
- The definition of the oligometastatic state should be expanded beyond the number or size of metastases, and incorporate clinical risk factors, tumour biology, host biology and novel biomarkers that intersect to define the metastatic spectrum.
- Blood-based biomarkers (such as circulating tumour DNA) might help select patients across the metastatic spectrum for systemic therapy and/or local therapy.
- As imaging modalities are improved and become more sensitive, it will become increasingly possible to detect and locally ablate all oligometastases (including those previously undetectable with less-sensitive imaging techniques), potentially facilitating the de-escalation of systemic therapy.
- In patients who are unable to be cured with ablative metastasis-directed therapies, cytoreduction might still improve the efficacy of systemic therapies via several mechanisms, such as elimination of subclones poised to confer resistance; thus, the integration of local therapies with evolving systemic treatments could result in long-term survival.

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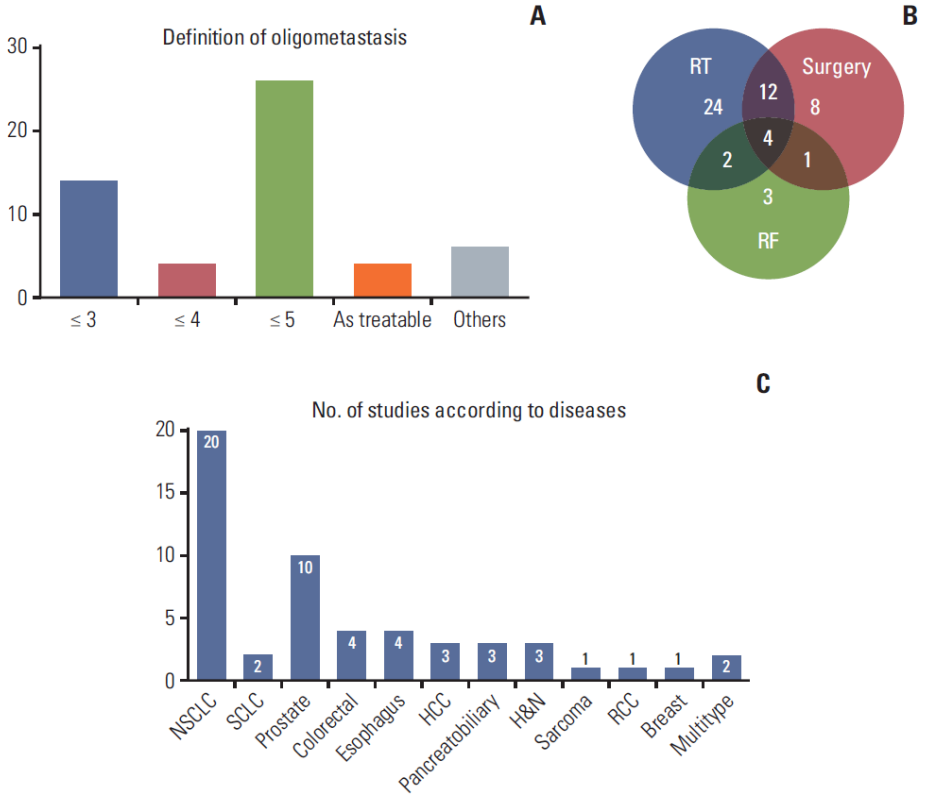
## Role of Local Treatment for Oligometastasis: A Comparability-Based Meta-Analysis

Chai Hong Rim[1], Won Kyung Cho[2], Jong Hoon Lee[3], Young Seok Kim[4], Yang-Gun Suh[5], Kyung Hwan Kim[6], Eui Kyu Chie[7], Yong Chan Ahn[2], The Oligometastasis Working Group, Korea Cancer Association




54 studies 7,242 patients

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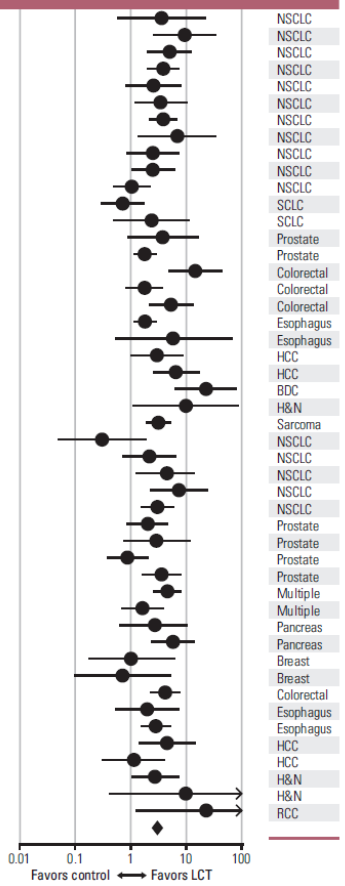
Overall survival

| Study name | Odds ratio | Lower limit | Upper limit | |
|---|---|---|---|---|
| He | 3.500 | 0.575 | 21.313 | NSCLC |
| Sheu (1 yr) | 8.984 | 2.481 | 32.529 | NSCLC |
| Yano | 4.902 | 2.013 | 11.937 | NSCLC |
| Frost | 3.732 | 1.974 | 7.058 | NSCLC |
| Gomez | 2.515 | 0.787 | 8.040 | NSCLC |
| Gray | 3.341 | 1.160 | 9.628 | NSCLC |
| Hu F | 3.734 | 2.132 | 6.540 | NSCLC |
| Song | 6.627 | 1.330 | 33.022 | NSCLC |
| Xu Q | 2.474 | 0.857 | 7.141 | NSCLC |
| Ni | 2.430 | 0.986 | 5.986 | NSCLC |
| Shang (1 yr) | 1.005 | 0.466 | 2.168 | NSCLC |
| Gore (1 yr) | 0.685 | 0.292 | 1.612 | SCLC |
| Xu | 2.316 | 0.476 | 11.261 | SCLC |
| Steuber (5 yr) | 3.661 | 0.893 | 15.014 | Prostate |
| Parker | 1.730 | 1.080 | 2.771 | Prostate |
| Giessen | 14.146 | 4.836 | 41.375 | Colorectal |
| Ruer (5 yr) | 1.742 | 0.819 | 3.706 | Colorectal |
| Ruo | 5.222 | 2.108 | 12.934 | Colorectal |
| Chen Y | 1.761 | 1.127 | 2.753 | Esophagus |
| Depypere | 6.000 | 0.532 | 67.649 | Esophagus |
| Chen J | 2.887 | 1.020 | 8.169 | HCC |
| Pan (1 yr) | 6.412 | 2.468 | 16.661 | HCC |
| Morino | 21.635 | 6.116 | 76.540 | BDC |
| Schulz | 9.480 | 1.089 | 82.555 | H&N |
| Falk | 3.066 | 1.873 | 5.021 | Sarcoma |
| Kagawa | 0.307 | 0.050 | 1.869 | NSCLC |
| Zhao Y | 2.144 | 0.732 | 6.274 | NSCLC |
| Li H | 4.406 | 1.242 | 15.621 | NSCLC |
| Gauvin | 7.211 | 2.234 | 23.274 | NSCLC |
| Chen XR | 2.951 | 1.474 | 5.909 | NSCLC |
| Yildirim | 1.953 | 0.849 | 4.497 | Prostate |
| Deek | 2.812 | 0.727 | 10.875 | Prostate |
| Boeri_RT (5yCSS) | 0.842 | 0.371 | 1.908 | Prostate |
| Boeri_OP (5yCSS) | 3.481 | 1.558 | 7.778 | Prostate |
| Hu X | 4.399 | 2.478 | 7.806 | Multiple |
| Palma | 1.598 | 0.672 | 3.798 | Multiple |
| Ji X (1 yr) | 2.607 | 0.644 | 10.559 | Pancreas |
| Shao Y (1 yr) | 5.581 | 2.342 | 13.298 | Pancreas |
| Lan_OP | 1.000 | 0.175 | 5.728 | Breast |
| Lan_LT | 0.695 | 0.096 | 5.037 | Breast |
| Moretto | 4.027 | 2.223 | 7.296 | Colorectal |
| Li J | 1.920 | 0.533 | 6.913 | Esophagus |
| Shi Z | 2.740 | 1.496 | 5.019 | Esophagus |
| Kim K | 4.397 | 1.410 | 13.710 | HCC |
| Wang H | 1.094 | 0.304 | 3.933 | HCC |
| Li W | 2.618 | 1.025 | 6.687 | H&N |
| Wright | 9.211 | 0.423 | 200.594 | H&N |
| Liu Y (2yCSS) | 21.634 | 1.228 | 381.129 | RCC |
| Pooled rate | 2.896 | 2.377 | 3.528 | |

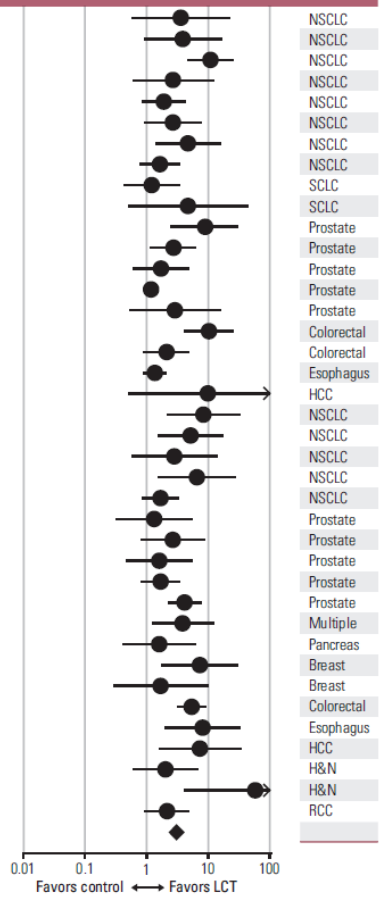
p (pooled analysis): < 0.001
p (heterogeneity): < 0.001, $I^2$=50.6%
n=6,759 (LCT=3,203, control=3,556)




Progression-free survival

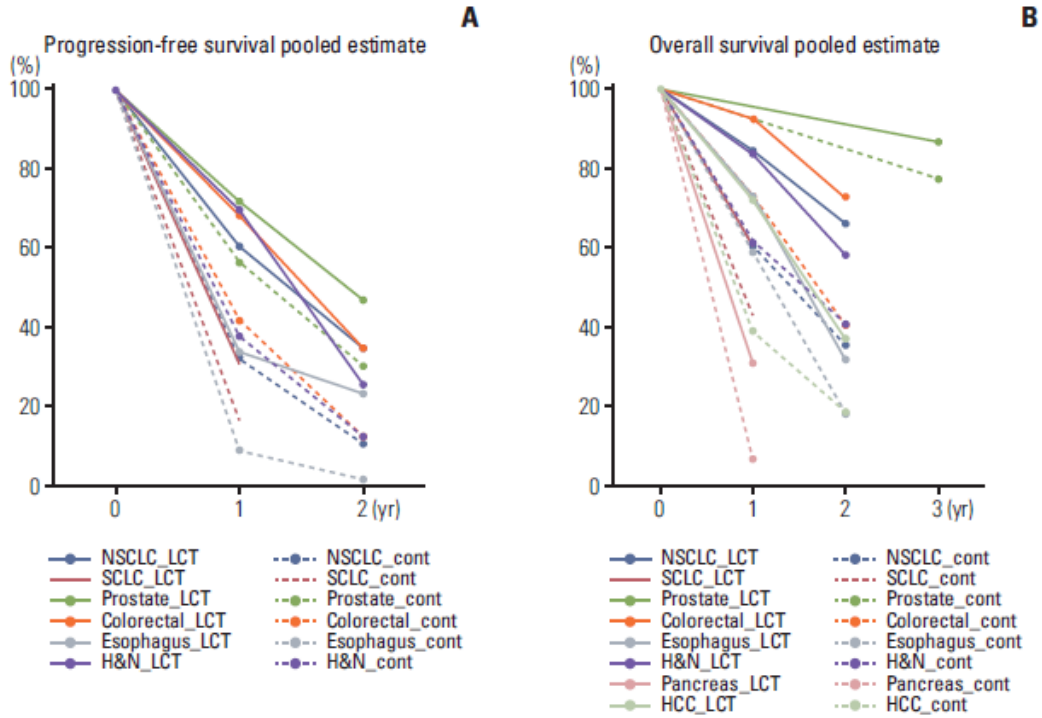
| Study name | Odds ratio | Lower limit | Upper limit | |
|---|---|---|---|---|
| Iyengar (1 yr) | 3.619 | 0.570 | 22.979 | NSCLC |
| Sheu (1 yr) | 3.938 | 0.924 | 16.775 | NSCLC |
| Frost | 11.178 | 4.849 | 25.768 | NSCLC |
| Gomez | 2.722 | 0.612 | 12.101 | NSCLC |
| Hu F | 1.887 | 0.853 | 4.175 | NSCLC |
| Xu Q (1 yr) | 2.636 | 0.919 | 7.562 | NSCLC |
| Ni (1 yr) | 4.679 | 1.435 | 15.261 | NSCLC |
| Shang (1 yr) | 1.630 | 0.781 | 3.404 | NSCLC |
| Gore (1 yr) | 1.218 | 0.440 | 3.375 | SCLC |
| Xu | 4.743 | 0.514 | 43.809 | SCLC |
| Bouman-Wammes (1 yr) | 8.850 | 2.556 | 30.640 | Prostate |
| Lan | 2.731 | 1.194 | 6.245 | Prostate |
| Ost | 1.729 | 0.615 | 4.857 | Prostate |
| Parker | 1.169 | 0.864 | 1.583 | Prostate |
| Tsumura | 2.917 | 0.538 | 15.828 | Prostate |
| Giessen | 10.615 | 4.347 | 25.923 | Colorectal |
| Ruer | 2.114 | 0.925 | 4.833 | Colorectal |
| Chen Y (1 yr) | 1.359 | 0.886 | 2.085 | Esophagus |
| Chen J (1 yr) | 10.211 | 0.528 | 197.396 | HCC |
| Hsu KH | 8.376 | 2.173 | 32.279 | NSCLC |
| Zhao Y (1 yr) | 5.127 | 1.515 | 17.354 | NSCLC |
| Li H | 2.796 | 0.564 | 13.854 | NSCLC |
| Gauvin | 6.544 | 1.509 | 28.374 | NSCLC |
| Wang | 1.693 | 0.865 | 3.317 | NSCLC |
| Yildirim | 1.332 | 0.312 | 5.679 | Prostate |
| Phillips (1 yr) | 2.672 | 0.835 | 8.543 | Prostate |
| Deek | 1.629 | 0.487 | 5.449 | Prostate |
| Boeri_RT (5ySSFS) | 1.715 | 0.870 | 3.378 | Prostate |
| Boeri_OP (5ySSFS) | 4.220 | 2.393 | 7.443 | Prostate |
| Palma | 3.920 | 1.244 | 12.353 | Multiple |
| Ji X (6 mo) | 1.605 | 0.416 | 6.199 | Pancreas |
| Lan_OP | 7.429 | 1.778 | 31.040 | Breast |
| Lan_LT | 1.714 | 0.301 | 9.773 | Breast |
| Moretto | 5.375 | 3.174 | 9.101 | Colorectal |
| Shi Z | 7.911 | 2.016 | 31.043 | Esophagus |
| Kim K | 7.479 | 1.657 | 33.754 | HCC |
| Li W | 2.070 | 0.630 | 6.794 | H&N |
| Wright (1 yr) | 58.586 | 4.253 | 806.971 | H&N |
| Liu Y | 2.108 | 0.901 | 4.931 | RCC |
| Pooled rate | 3.045 | 2.356 | 3.937 | |

p (pooled analysis): < 0.001
p (heterogeneity): < 0.001, $I^2$=62.1%
n=5,021 (LCT=2,454, control=2,567)




**OS pooled odds ratio 2.896**

**PFS pooled odds ratio 3.045**




**Conclusion** Pooled analyses results of all included studies, selected studies with reliable comparability, and RCT's demonstrated the survival benefit of LCT. These consistent results suggest that LCT was beneficial to the patients with oligometastasis.

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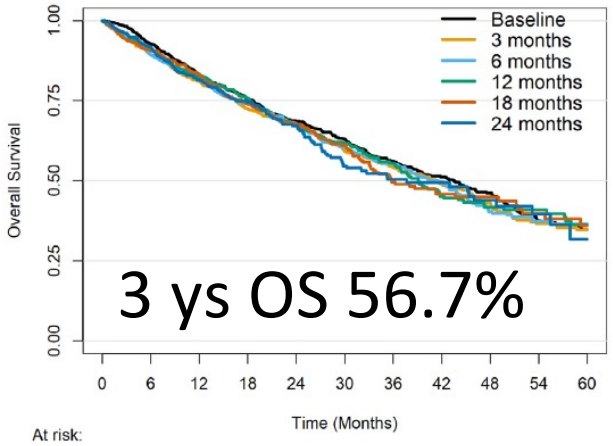
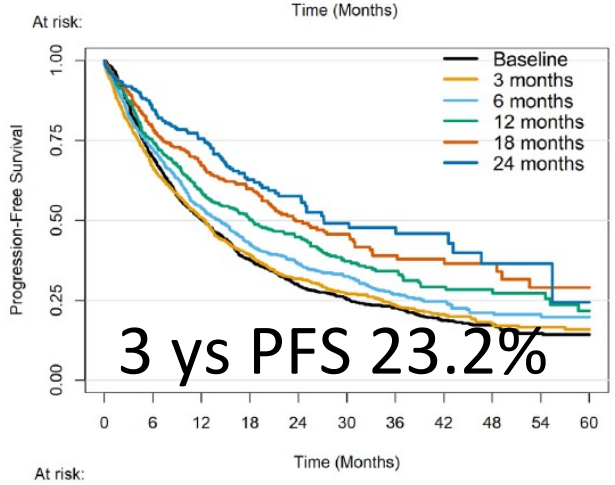
- Prospective trials (histology driven)
- More than the big killers
- Predictive models

## Conditional Survival of Patients With Extracranial Oligometastatic Treated With Stereotactic Body Radiation Therapy: An International Consortium Study

Hanbo Chen, MD, MPH,* Serena Badellino, MD,† Tithi Biswas, MD,‡ Roi Dagan, MD,§ Darby Erler, MRT(T),* Matthew Foote, MD,‖ Ian Poon, MD,* Kristin J. Redmond, MD,¶ Umberto Ricardi, MD,† Arjun Sahgal, MD,* and Alexander V. Louie, MD, MSc, PhD*

- Multi-institutional database
- 1033 patients with OM (≤5 metastases) treated with SBRT between 2006 and 2017
- The main outcomes of this study were conditional OS and PFS. These are defined as the OS and PFS probabilities in 3years' time conditional on having survived (OS) or survived without progression (PFS) for a given number of months

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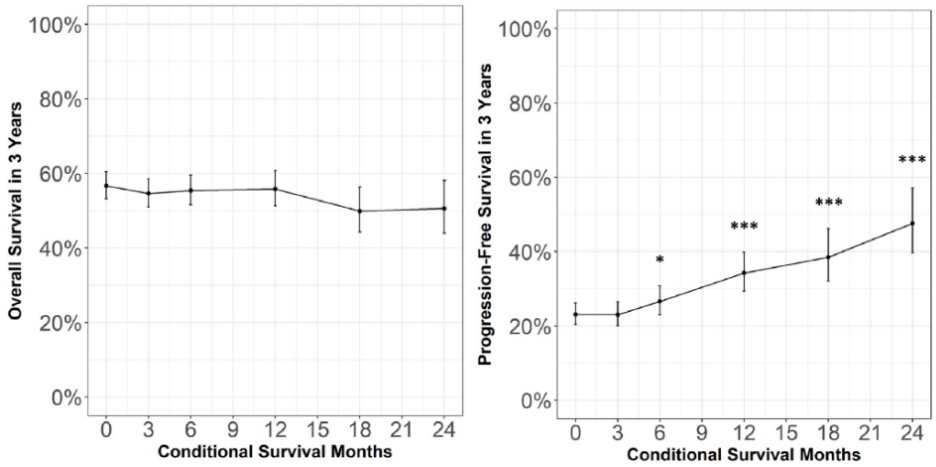
The conditional OS in 3 years did not significantly change over time (56.7%, 55.4%, 55.8%, and 50.6%, respectively; P = .60).

**The conditional PFS in 3 years significantly increased over time** (23.6%, 27.3%, 35.1%, and 48.8%, respectively; P < .001).

When stratified by primary site, conditional PFS significantly increased over time for patients with colorectal, breast, or kidney cancer.

Conditional OS remained stable for patients with non-small cell lung cancer or kidney cancer but significantly decreased over time for patients with prostate, breast, or colorectal cancer.




**Conclusions:** Analysis of conditional survival among patients with OM showed that as patients survived longer, their prognosis for further survival remained stable or decreased. However, patients who survived longer without disease progression had increased probability of PFS over time. 

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Patients' characteristics ($n$ = 620) (%).

| | |
|---|---|
| **Mean age (range) (years)** | 70 (31–90) |
| **Sex** | |
| Male | 223 (36) |
| Female | 397 (64) |
| **Primary site** | |
| Colon | 358 (57) |
| Rectum | 262 (43) |
| **Initial treatment** | |
| Surgery | 479 (78) |
| RCHT + surgery | 114 (18) |
| Systemic therapy | 27 (4) |
| **Adjuvant chemotherapy** | |
| Yes | 178 (28.5) |
| No | 419 (67.5) |
| Unknown | 23 (4) |
| **Histology** | |
| Adenocarcinoma | 588 (95) |
| Mucinous carcinoma | 32 (5) |
| **Initial stage** | |
| Stage I | 19 (3) |
| Stage II | 131 (21) |
| Stage III | 255 (41) |
| Stage IV | 176 (28.5) |
| Unknown | 39 (6.5) |
| **Tumor mutations (%)** | |
| EGFR | 3.21 |
| KRAS | 26.4 |
| NRAS | 3.21 |
| BRAF | 1.38 |
| MSI | 0.46 |
| **Median time to OMD (range)** | 24 (0–128) |
| **Systemic treatment before SABR** | |
| Chemotherapy | 330 (53) |
| TKI | 5 (0.8) |
| Antiangiogenetic | 40 (6.5) |
| Target therapy/immunotherapy | 8 (1.2) |
| No | 175 (28.5) |
| Unknown | 62 (10) |
| **Type of oligometastases** | |
| Synchronous | 148 (24) |
| Metachronous | 469 (75.5) |
| Unknown | 3 (80.5) |

A multicenter LArge retrospectIve daTabase on the personalization of stereotactic ABlative radiotherapy use in lung metastases from colon-rectal cancer: The LaIT-SABR study

L. Nicosia [a,*], D. Franceschini [b], F. Perrone-Congedi [c], F. Casamassima [d], M.A. Gerardi [e], M. Rigo [a], R. Mazzola [a], M. Perna [f], V. Scotti [f], A. Fodor [g], A. Iurato [h], F. Pasqualetti [i], G. Gadducci [i], S. Chiesa [j], R.M. Niespolo [k], A. Bruni [l], G. Alicino [l], L. Frassinelli [l], P. Borghetti [m], A. Di Marzo [n], A. Ravasio [o], B. De Bari [p,q], M. Sepulcri [r], D. Aiello [s], G. Mortellaro [t], C. Sangalli [u], M. Franceschini [u], G. Montesi [v], F.M. Aquilanti [w], G. Lunardi [x], R. Valdagni [u,y], I. Fazio [s], Giovanni Scarzello [r], L. Corti [r], V. Vavassori [o], E. Maranzano [n], S.M. Magrini [m], S. Arcangeli [k], Maria Antonietta Gambacorta [j,aa], V. Valentini [j,z], F. Paiar [i], S. Ramella [h], N.G. Di Muzio [g,aa], L. Livi [f], B.A. Jereczek-Fossa [e,ab], M.F. Osti [c], M. Scorsetti [b,ac], F. Alongi [a,ad]

Treatment characteristics ($n$ = 1090) (%).

| | |
|---|---|
| **Median lesion diameter (mm) (range)** | |
| **Total treated lesions** | |
| 1 | 437 (70.5) |
| 2 | 110 (17.7) |
| 3 | 39 (6) |
| 4 | 14 (2.3) |
| 5 | 20 (3.5) |
| **Median SUVmax (range)** | 5.1 (1–68) |
| **Lung lobe** | |
| SRL | 269 (24.5) |
| ML | 96 (9) |
| IRL | 251 (23) |
| SLL | 238 (22) |
| ILL | 236 (21.5) |
| **Median total dose (Gy) (range)** | 48 (18–75.2) |
| **Median dose per fraction (Gy) (range)** | 12 (4–42) |
| **Number of fractions** | |
| 1 | 280 (26) |
| 2 | 5 (0.5) |
| 3 | 295 (27.5) |
| 4 | 167 (15) |
| 5 | 193 (17.5) |
| 6 | 44 (4) |
| 8 | 75 (7) |
| 10 | 28 (2.5) |
| **Median BED (range)** | 105 (48–180) |
| **Mean GTV volume (cc)** | 2.6 (0.1–104) |
| **Mean PTV volume (cc)** | 11 (0.51–188) |
| **Lesion site** | |
| Central | 300 (27.5) |
| Peripheral | 790 (72.5) |

Patients with lung oligometastases from colorectal cancer treated with SABR over the decade 2009–2019

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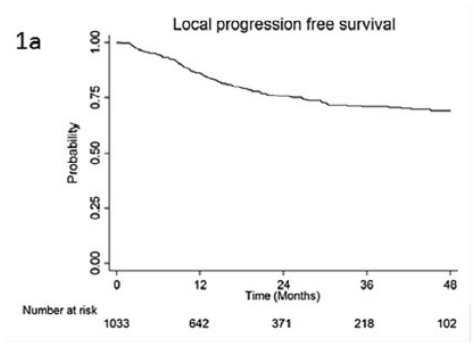
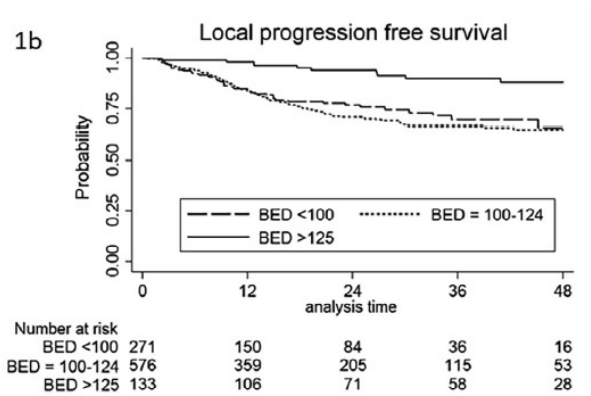
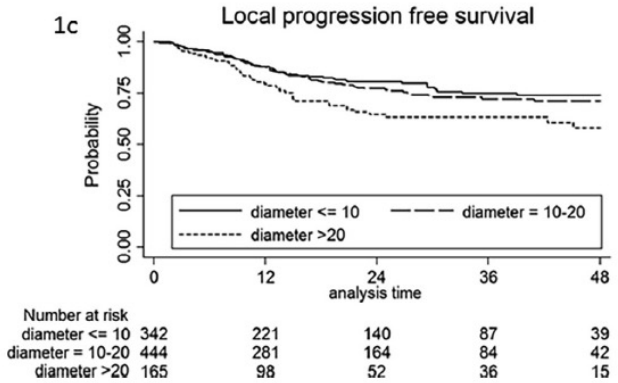
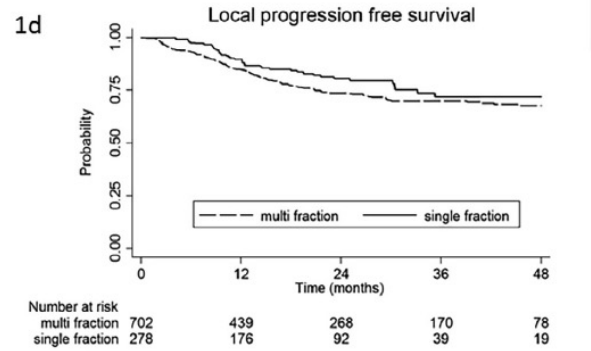


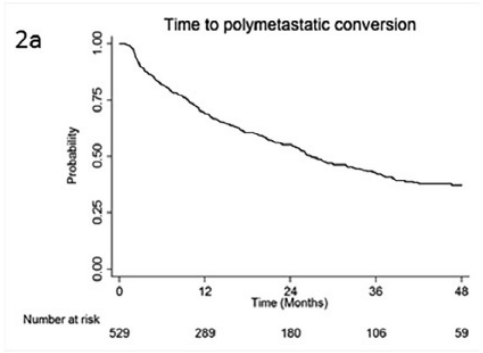



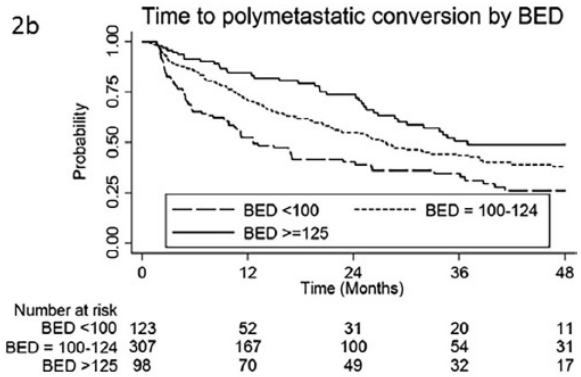



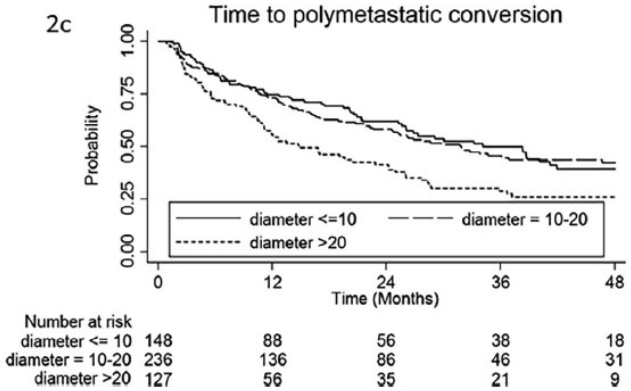



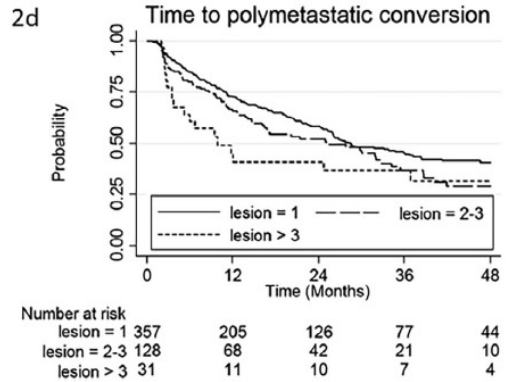

Two-year FLP was 75.4%.

At the multivariate analysis, a **BED > 125 Gy** significantly reduced the risk of local progression, while a **lesion diameter >20 mm** was significantly associated with an increased risk of local progression.




Median tPMC was 26.8 months.

At the multivariate analysis, **lesion diameter >20 mm** and having **4–5 metachronous lung metastases** were independently correlated with worse tPMC. Conversely, a **BED 125 Gy** significantly reduced that risk

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# SABR 5 trial

## Progression-Free Survival and Local Control After SABR for up to 5 Oligometastases: An Analysis From the Population-Based Phase 2 SABR-5 Trial

Sarah Baker, MD, PhD,[*,†] Will Jiang, MD,[*,†] Benjamin Mou, MD,[*,‡] Chad R. Lund, MD,[*,†] Mitchell Liu, MD, CM,[*,§] Alanah M. Bergman, PhD,[§] Devin Schellenberg, MD,[*,†] Abraham S. Alexander, MD,[*,‖] Hannah Carolan, MD,[*,§] Siavash Atrchian, MD,[*,‡] Nick Chng, PhD,[¶] Quinn Matthews, PhD,[¶] Gregory Arbour, MSc,[*] Alexander Benny, BSc,[*] Scott Tyldesley, MD,[*,§] and Robert A. Olson, MD, MSc[*,¶]

## Predictors of Early Polymetastatic Relapse After SABR for up to 5 Oligometastases: A Secondary Analysis of the Phase II SABR-5 Trial

Sarah Baker, MD, PhD,[*,†] Benjamin Mou,[*,‡] Will Jiang, MD,[*,†] Mitchell Liu, MD, CM,[*,§] Alanah M. Bergman, PhD,[§] Devin Schellenberg, MD,[*,†] Abraham S. Alexander, MD,[*,‖] Hannah Carolan,[*,§] Siavash Atrchian, MD,[*,‡] Tanya Berrang, MD,[*,‖] Andrew Bang, MD,[*,‖] Nick Chng, PhD,[¶] Quinn Matthews, PhD,[¶] Scott Tyldesley, MD,[*,§] and Robert A. Olson, MD, MSc[*,¶]

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

S. Baker, MD, PhD,[*,†] B. Mou, MD,[*,‡] W. Jiang, MD,[*,†] M. Liu, MD, CM,[*,§] A.M. Bergman, PhD,[§] D. Schellenberg, MD,[*,†] A.S. Alexander, MD,[*,‖] H. Carolan, MD,[*,§] S. Atrchian, MD,[*,‡] T. Berrang, MD,[*,‖] A. Bang, MD,[*,‖] N. Chng, PhD,[#] Q. Matthews, PhD,[#] S. Tyldesley, MD,[*,§] and R.A. Olson, MD, MSc[*,#]

## Treatment With Stereotactic Ablative Radiotherapy for Up to 5 Oligometastases in Patients With Cancer Primary Toxic Effect Results of the Nonrandomized Phase 2 SABR-5 Clinical Trial

Robert Olson, MD; Will Jiang, MD; Mitchell Liu, MD; Alanah Bergman, PhD; Devin Schellenberg, MD; Benjamin Mou, MD; Abraham Alexander, MD; Hannah Carolan, MD; Fred Hsu, MD; Stacy Miller, MD; Siavash Atrchian, MD; Elisa Chan, MD; Clement Ho, MD; Islam Mohamed, MD; Angela Lin, MD; Tanya Berrang, MD; Andrew Bang, MD; Nick Chng, PhD; Quinn Matthews, PhD; Sarah Baker, MD; Vicky Huang, PhD; Ante Mestrovic, PhD; Derek Hyde, PhD; Chad Lund, MD; Howard Pal, MD; Boris Valev, MD; Shilo Lefresene, MD; Scott Tyldesley, MD

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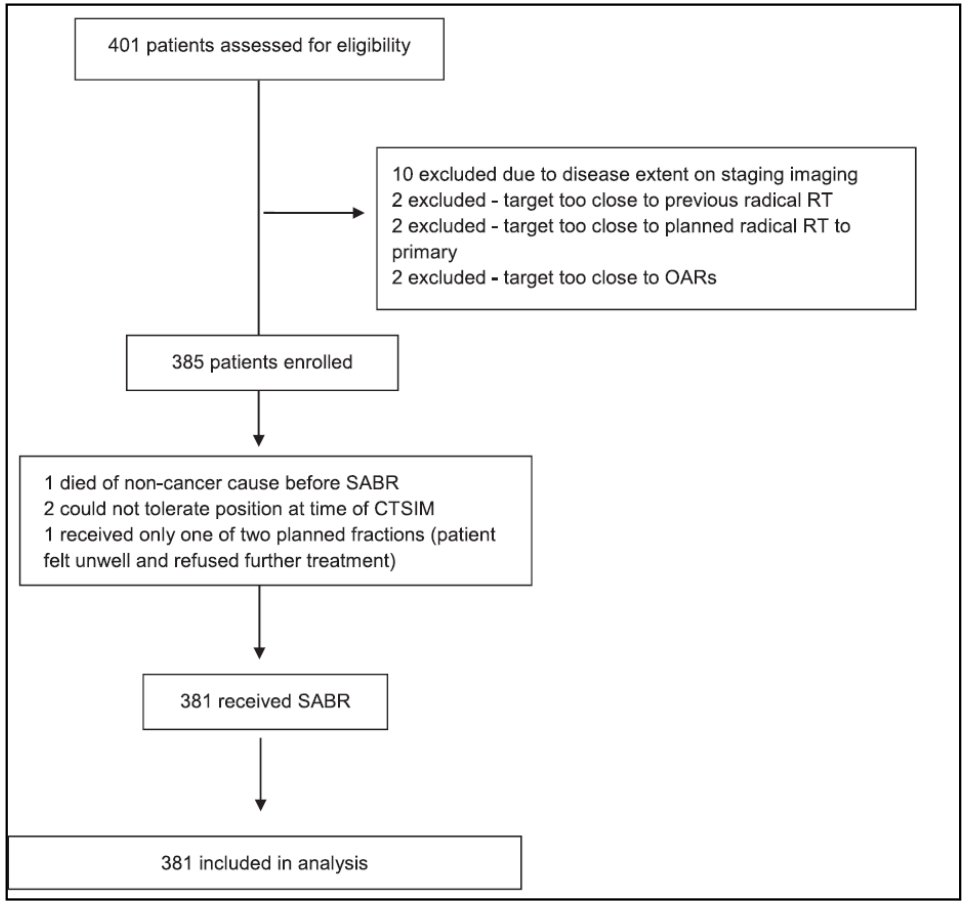
# SABR 5 trial

- single-arm phase 2 study
- primary endpoint toxicity
- Inclusion criteria:
  -up to 5 oligometastases, including induced oligo
  -SABR to all lesions
  -18 years of age or older
  -Eastern Cooperative Oncology Group score of 0 to 2,
  -life expectancy ≥ 6 months.




| Characteristic | Percentage (n) |
|---|---|
| Patient factors | |
| Sex: female | 32% (122) |
| ECOG PS: 0; 1; 2 | 60% (227); 37% (139); 4% (15) |
| Decline in ECOG PS in preceding 6 mo | 6% (23) |
| Current smoker | 9% (33) |
| Tumor factors | |
| Primary histology: prostate; colorectal; breast; lung; renal cell carcinoma; head and neck*; melanoma; other† | 32% (122); 17% (63); 11% (43); 9% (33); 9% (34); 5% (17); 5% (17); 14% (52) |
| Lesion site (total n = 549) | |
| Nonspine bone | 25% (136) |
| Spine | 15% (84) |
| Lung | 35% (190) |
| Adrenal | 3% (15) |
| Lymph node | 14% (78) |
| Liver | 5% (29) |
| Other‡ | 3% (17) |
| Extent of disease | |
| Number of metastases treated with SABR: 1; 2; 3; 4; 5 | 69% (262); 22% (83); 7% (26); 2% (7); 1% (3) |
| Induced oligometastatic disease | 13% (51) |
| Timing | |
| Synchronous; metachronous | 20% (77); 80% (304) |
| Disease-free interval: <18 mo; ≥18 mo | 45% (173); 55% (208) |
| Treatment factors | |
| Initiation or change in systemic treatment | 34% (129) |
| Oligoprogression | 16% (62) |

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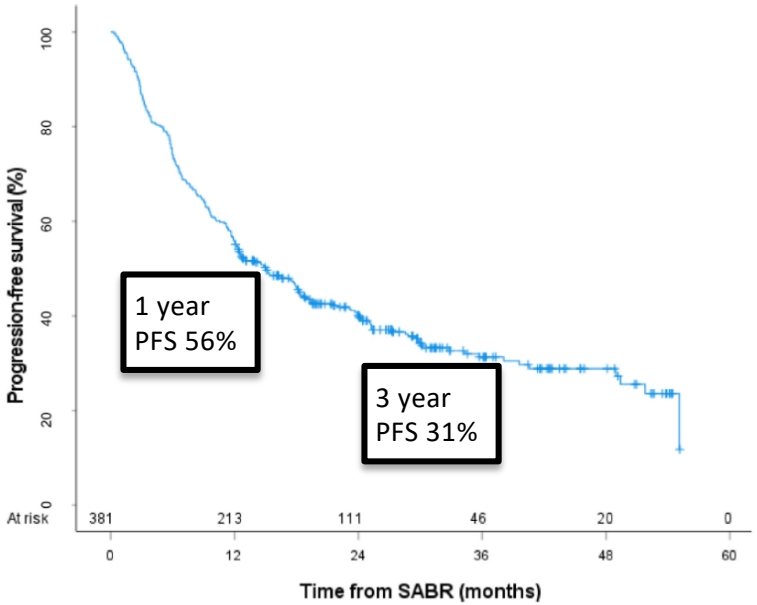
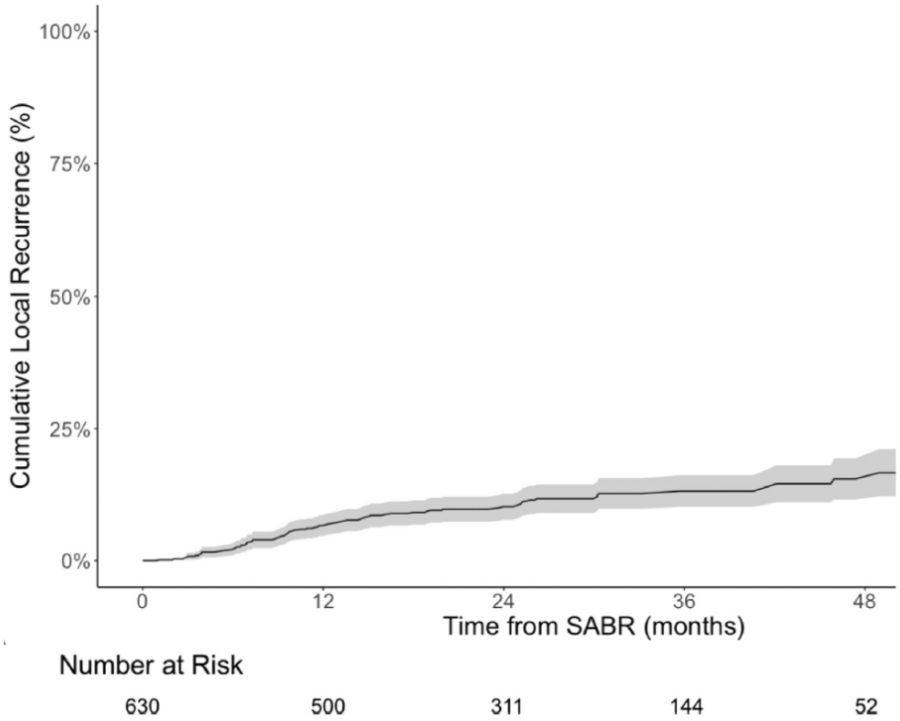



**Fig. 2.** Kaplan-Meier curve of progression-free survival.

Median PFS 15 months

Decline in **performance status**, greater **tumor diameter**, **4 or more metastases** at the time of SABR, **disease-free interval <18 months**, and **oligoprogression** were associated with greater risk of progression or death, while synchronous metastases and initiation or change in systemic treatment were associated with lower risk




Lesion control rate was 88%.

1- and 3-year LC 93% and 87%

Histology and tumor diameter were associated with LC

## Treatment With Stereotactic Ablative Radiotherapy for Up to 5 Oligometastases in Patients With Cancer Primary Toxic Effect Results of the Nonrandomized Phase 2 SABR-5 Clinical Trial

Robert Olson, MD; Will Jiang, MD; Mitchell Liu, MD; Alanah Bergman, PhD; Devin Schellenberg, MD; Benjamin Mou, MD; Abraham Alexander, MD; Hannah Carolan, MD; Fred Hsu, MD; Stacy Miller, MD; Siavash Atrchian, MD; Elisa Chan, MD; Clement Ho, MD; Islam Mohamed, MD; Angela Lin, MD; Tanya Berrang, MD; Andrew Bang, MD; Nick Chng, PhD; Quinn Matthews, PhD; Sarah Baker, MD; Vicky Huang, PhD; Ante Mestrovic, PhD; Derek Hyde, PhD; Chad Lund, MD; Howard Pai, MD; Boris Valev, MD; Shilo Lefresene, MD; Scott Tyldesley, MD

G2: 14,2%
G3: 4.2%
G4: 0%
G5: 0.3%

Table 2. Toxic Effects Associated With SABR by CTCAE Category per Patient

| | Grade, No./total No. (%) | | | | |
|---|---|---|---|---|---|
| Characteristic | ≥2 | 2 | 3 | 4 | 5 |
| Pain | 25/381 (7) | 20/381 (5) | 5/381 (1) | 0 | 0 |
| Diarrhea | 4/381 (1) | 3/381 (1) | 1/381 (0.3) | 0 | 0 |
| Constipation | 2/381 (1) | 2/381 (1) | 0 | 0 | 0 |
| Pneumonitis | 5/381 (1) | 5/381 (1) | 0 | 0 | 0 |
| Fracture | | | | | |
| Rib | 5/381 (1) | 5/381 (1) | 0 | 0 | 0 |
| Spine | 7/381 (2) | 3/381 (1) | 4/381 (1) | 0 | 0 |
| Neuropathy | 6/381 (2) | 6/381 (2) | 0 | 0 | 0 |
| Other | 39/381 (10) | 28/381 (7) | 10/381 (3) | 0 | 1/381 (0.3) |

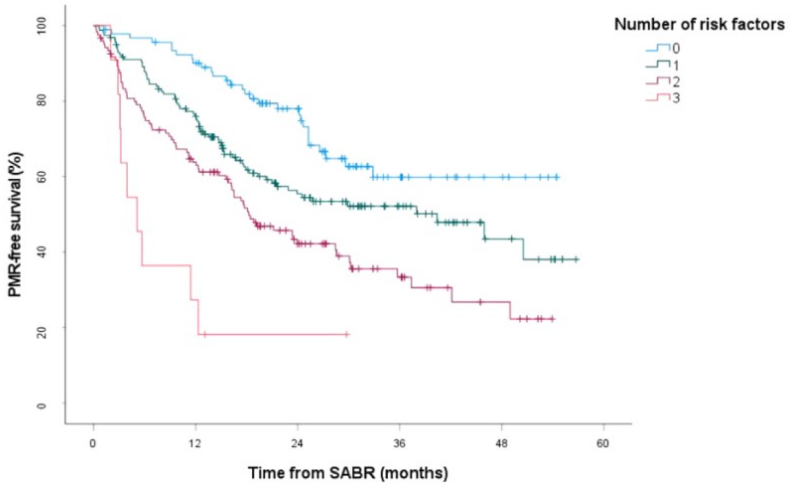
Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; SABR, stereotactic ablative radiotherapy.

**CONCLUSIONS AND RELEVANCE** This single-arm, phase 2 clinical trial found that the incidence of grade 3 or higher SABR toxic effects in this population-based study was less than 5%. Furthermore, the rates of grade 2 or higher toxic effects (18.6%) were lower than previously published for SABR-COMET (29%). These results suggest that SABR treatment for oligometastases has acceptable rates of toxic effects and potentially support further enrollment in randomized phase 3 clinical trials.

**Early Polymetastatic Relapse**: metastatic progression not amenable to further ablative therapy within 6 months of the start of SABR such that initiation or change in systemic treatment was warranted.

| Risk factor | Description | |
|---|---|---|
| ECOG performance status | 1-2 vs 0 | |
| Primary histology | Other than breast or prostate | |
| Oligoprogression | Progressive lesion on imaging while on systemic treatment | |
| Number of risk factors | Median PMR-free survival ($P$ <.001) | 3-y OS ($P$ <.001) |
| 0 | Not reached | 93% |
| 1 | 40 mo | 77% |
| 2 | 18 mo | 53% |
| 3 | 5 mo | 0% |

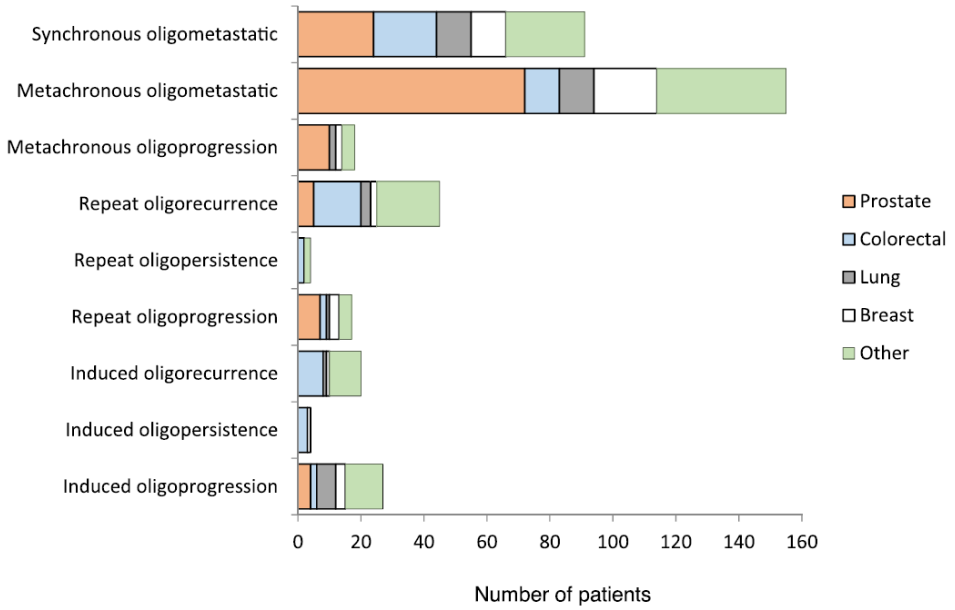
*Abbreviations*: ECOG = Eastern Cooperative Oncology Group; OS = overall survival; PMR = polymetastatic relapse.

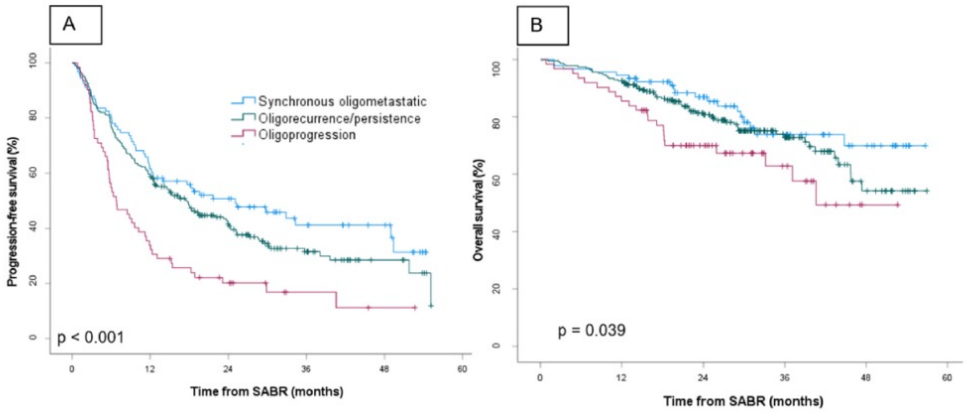



IJROPB 2022

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

S. Baker, MD, PhD,[*,†] B. Mou, MD,[*,‡] W. Jiang, MD,[*,†] M. Liu, MD, CM,[*,§] A.M. Bergman, PhD,[§] D. Schellenberg, MD,[*,†] A.S. Alexander, MD,[*,‖] H. Carolan, MD,[*,§] S. Atrchian, MD,[*,‡] T. Berrang, MD,[*,‖] A. Bang, MD,[*,‖] N. Chng, PhD,[#] Q. Matthews, PhD,[#] S. Tyldesley, MD,[*,§] and R.A. Olson, MD, MSc[*,#]




ESTRO/EORTC classification of OMD was an independent predictor of both PFS and OS

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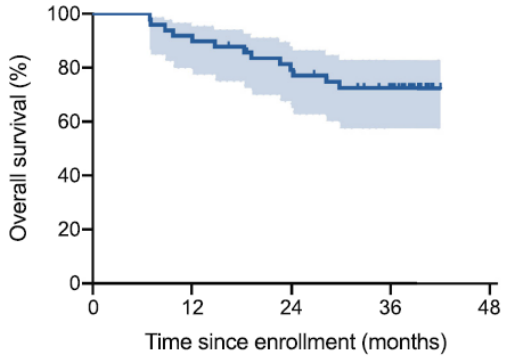
## Definitive Local Consolidative Therapy for Oligometastatic Solid Tumors: Results From the Lead-in Phase of the Randomized Basket Trial EXTEND

Alexander D. Sherry, MD,* Tharakeswara K. Bathala, MD, MBBS,† Suyu Liu, PhD,† Bryan M. Fellman, MS,‡ Stephen G. Chun, MD,* Nikesh Jasani, MD,§ B. Ashleigh Guadagnolo, MD, MPH,* Anuja Jhingran, MD,* Jay P. Reddy, MD,* Paul G. Corn, MD, PhD,‖ Amishi Y. Shah, MD,‖ Kelsey W. Kaiser, MS,* Amol J. Ghia, MD,* Daniel R. Gomez, MD,*,¶ and Chad Tang, MD*,#,**

EXTernal beam radiation to Eliminate Nominal metastatic Disease (EXTEND; NCT03599765)

Single arm "lead in" phase for a phase II randomized trial

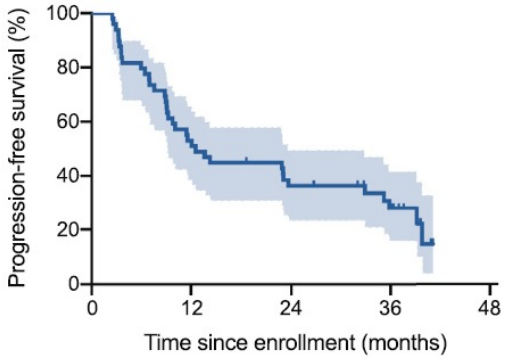
50 patients were enrolled and 49 received definitive LCT. Prostate, breast, and kidney were the highest enrolling histologies




Median PFS was 13 months

3-year overall survival rate was 73%

Two patients (4%) grade 3 toxic effects related to LCT; no patient had grade 4 or 5 toxic effects.

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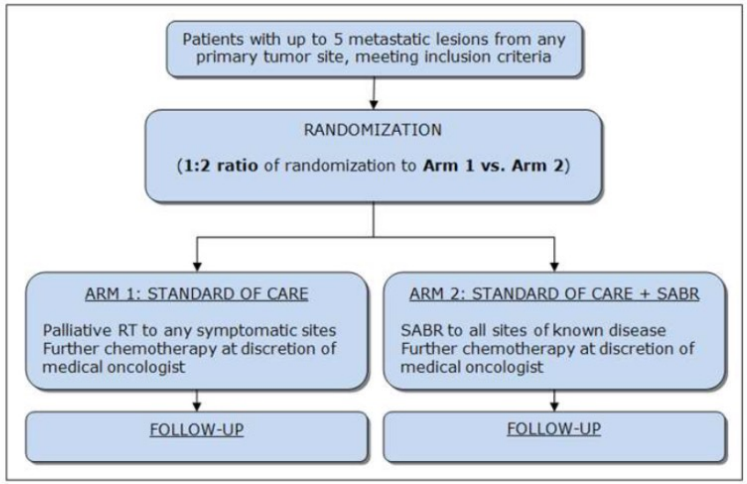
# Stereotactic Radiation for the Comprehensive Treatment of Oligometastases (SABR-COMET): Extended Long-Term Outcomes

Stephen Harrow, MBChB, PhD,* David A. Palma, MD, PhD,† Robert Olson, MD, MSc,‡ Stewart Gaede, PhD,† Alexander V. Louie, MD, PhD,†,§ Cornelis Haasbeek, MD, PhD,‖ Liam Mulroy, MD,¶ Michael Lock, MD,† George B. Rodrigues, MD, PhD,† Brian P. Yaremko, MD, MSc, PEng,† Devin Schellenberg, MD,# Belal Ahmad, MD,† Sashendra Senthi, MD, PhD,** Anand Swaminath, MD,†† Neil Kopek, MD,‡‡ Mitchell Liu, MD,§§ Roel Schlijper, MD,‡ Glenn S. Bauman, MD,† Joanna Laba, MD,† X. Melody Qu, MD, MPH,† Andrew Warner, MSc,† and Suresh Senan, MBBS, PhD‖




**Primary Endpoint**

- Overall Survival

**Secondary endpoints:**

- Progression-free survival
- Toxicity (CTC-AE 4.0)
- Quality of life (FACT-G)
- Lesional control rate
- Number of cycles of further systemic therapy
  - Changed to binary variable “Receipt of systemic therapy” (Y/N)

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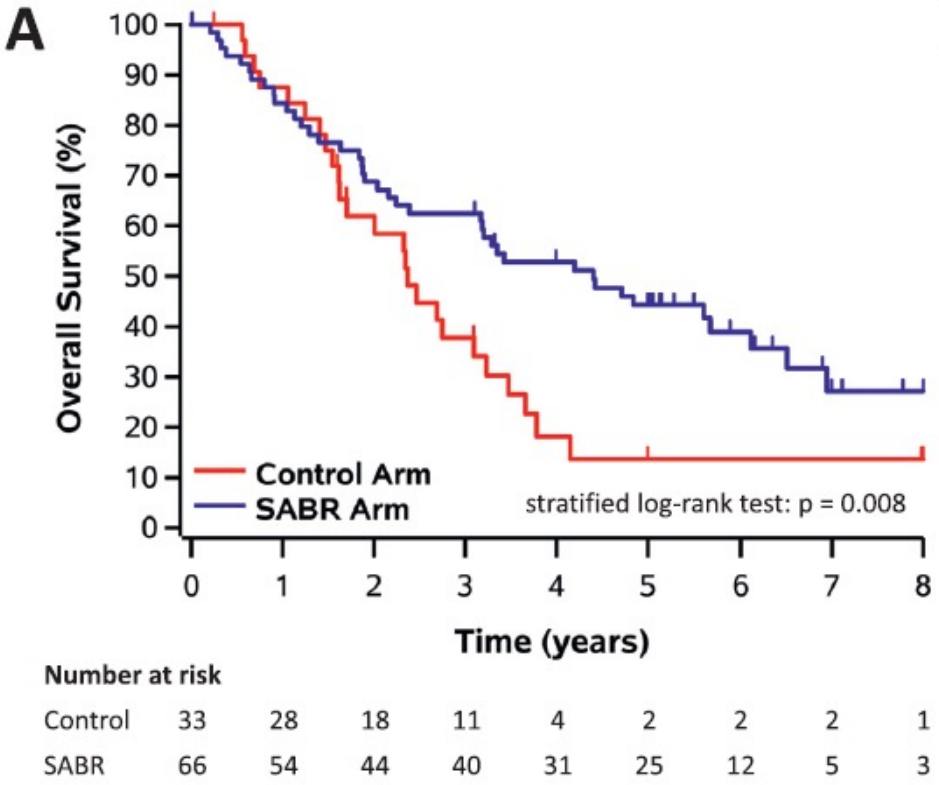


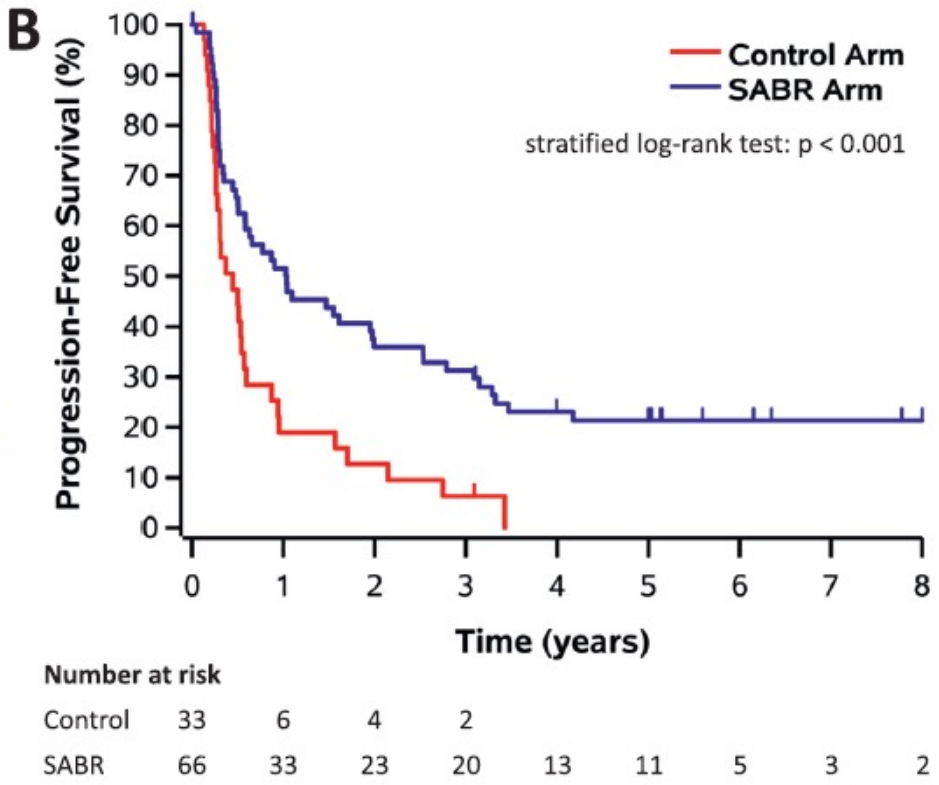


8-year OS 27.2% vs 13.6%

8-year PFS 21.3% vs 0.0%

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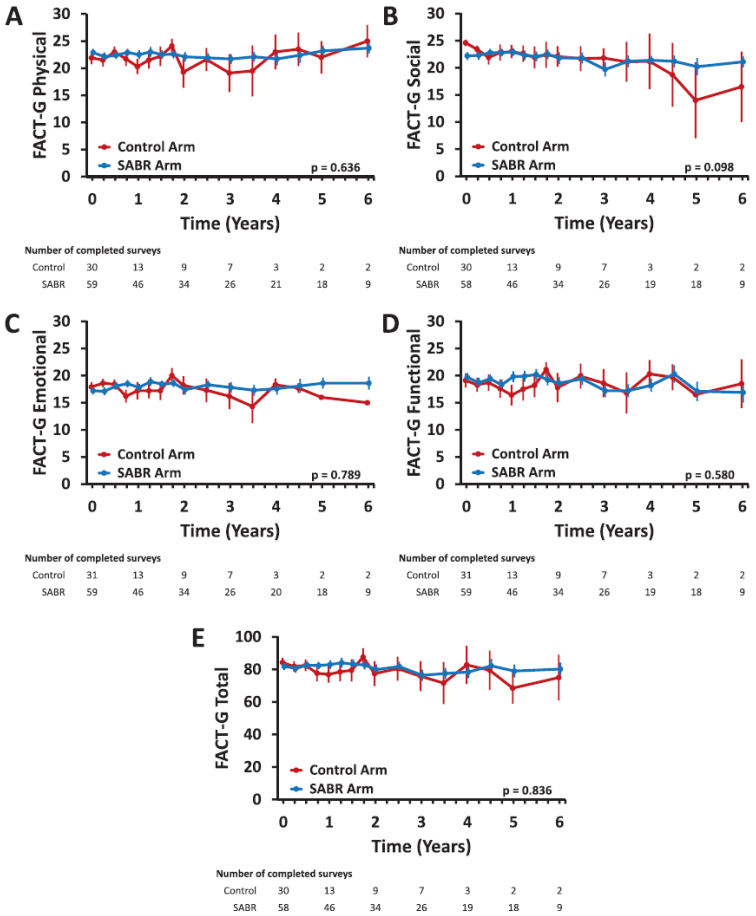


FACT-G **quality of life** scores declined over time in both arms, but there were no differences in quality of life scores between arms.

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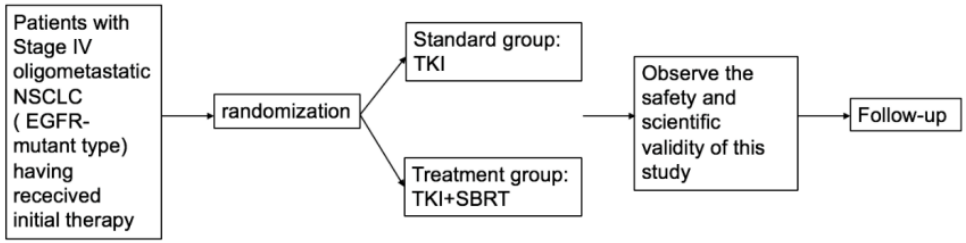
# AGENDA

- Where do we stand
- Large database
- Prospective trials (mixed histologies)
- Prospective trials (histology driven)
- More than the big killers
- Predictive models

## Randomized Trial of First-Line Tyrosine Kinase Inhibitor With or Without Radiotherapy for Synchronous Oligometastatic *EGFR*-Mutated Non-Small Cell Lung Cancer

Xiao-Shan Wang, MD,[1,‡] Yi-Feng Bai, MD,[1,‡] Vivek Verma, MD,[2] Rui-Lian Yu, MD,[1] Wei Tian, MS,[1] Rui Ao, MD,[1] Ying Deng, MD,[1] Jian-Ling Xia, MD,[1] Xue-Qiang Zhu, MD,[1] Hao Liu, MD,[1] Hai-Xia Pan, MD,[1] Lan Yang, MD,[1] Yang-Ke He, MD,[1] Han-Song Bai, MD,[3] Xing Luo, MD,[3] Yan Guo, MS,[3] Ming-Xiu Zhou, MD,[3] Yue-Mei Sun, MD,[4] Zi-Can Zhang, MD,[4] Si-Min Li, MD,[3,5] Xue Cheng, MD,[3] Bang-Xian Tan, MD,[3] Liang-Fu Han, MD,[6] Ying-Yi Liu, MD,[7] Kai Zhang, MD,[8] Fan-Xin Zeng, PD,[9] Lin Jia, MD,[10] Xin-Bao Hao, MD,[11] You-Yu Wang, MD,[1] Gang Feng, MD,[1] Ke Xie, MD,[1] You Lu, MD,[12] Ming Zeng, MD, PhD[1,*]




The **SINDAS** trial (NCT02893332) **evaluated first-line tyrosine kinase inhibitor (TKI) therapy** for **EGFR-mutated synchronous oligometastatic** NSCLC and randomized to **upfront RT vs no RT**

JNCI 2022

INCLUSION CRITERIA: biopsy-proven EGFR-mutated adenocarcinoma with synchronous (newly diagnosed, treatment naıve) oligometastatic (5 metastases; 2 lesions in any one organ) NSCLC without brain metastases.

PROCEDURES: All patients received a first-generation TKI (gefitinib, erlotinib, or icotinib), and **randomization was between no RT vs RT (25-40Gy in 5 fractions depending on tumor size and location) to all metastases and the primary tumor/involved regional lymphatics.**

ENDPOINTS: The primary endpoint (intention to treat) was **PFS**. Secondary endpoints included **OS** and toxicities.

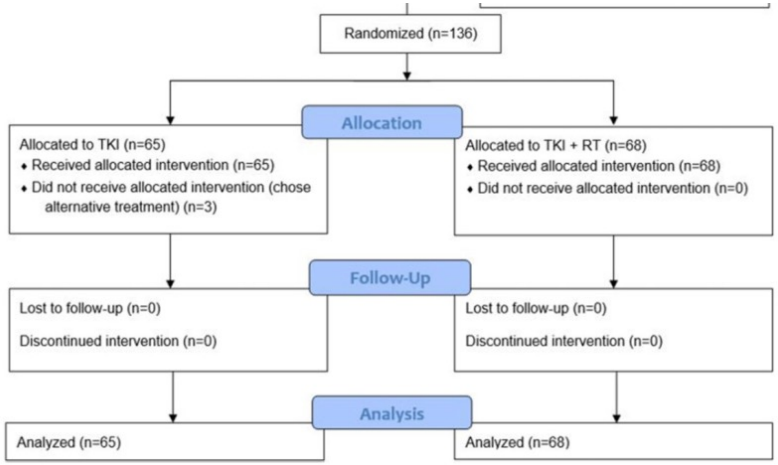



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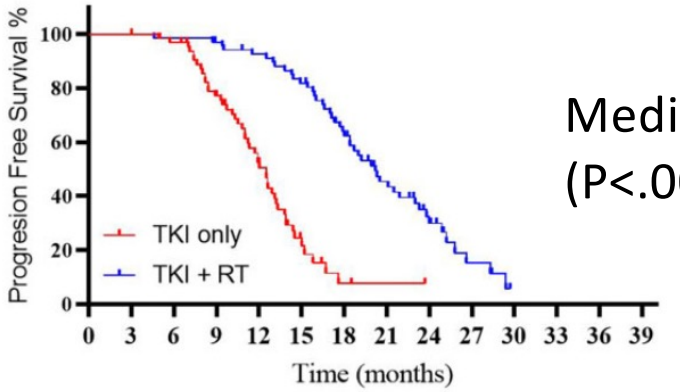
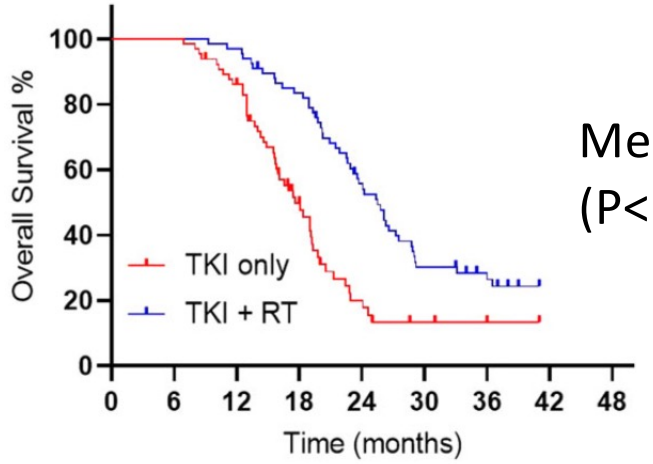
Table 1. Clinicopathologic characteristics of the study population[a]

| Parameter | TKI only (n = 65) | TKI + RT (n = 68) |
|---|---|---|
| Age, y | | |
| Mean (SD) | 63 (11) | 67 (10) |
| Sex, No. (%) | | |
| Male | 26 (40.0) | 25 (36.8) |
| Female | 39 (60.0) | 43 (63.2) |
| Zubrod performance status, No. (%) | | |
| 0 | 31 (47.7) | 36 (52.9) |
| 1 | 33 (50.8) | 32 (47.1) |
| 2 | 1 (1.5) | 0 (0.0) |
| Clinical T classification, No. (%) | | |
| 1 | 9 (13.8) | 5 (7.4) |
| 2 | 16 (24.6) | 17 (25.0) |
| 3 | 22 (33.8) | 20 (29.4) |
| 4 | 17 (26.2) | 23 (33.8) |
| Unknown | 1 (1.5) | 3 (4.4) |
| Clinical N classification, No. (%) | | |
| 0 | 8 (12.3) | 8 (11.8) |
| 1 | 23 (35.4) | 19 (27.9) |
| 2 | 24 (36.9) | 27 (39.7) |
| 3 | 10 (15.4) | 13 (19.1) |
| Unknown | 0 (0.0) | 1 (1.5) |
| *EGFR* mutation, No. (%) | | |
| Exon 19 | 47 (72.3) | 45 (66.2) |
| Exon 21 | 18 (28.7) | 23 (33.8) |
| Number of metastases, No. (%) | | |
| 1-2 | 38 (58.5) | 32 (47.1) |
| 3-4 | 23 (35.4) | 30 (44.1) |
| 5 | 4 (6.2) | 6 (8.8) |
| TKI, No. (%) | | |
| Gefitinib | 38 (58.5) | 32 (47.1) |
| Erlotinib | 23 (35.4) | 30 (44.1) |
| Icotinib | 4 (6.2) | 6 (8.8) |




Median PFS 20. 2 vs 12.5 months (P<.001)




Median OS 25.5 vs 17.4 months (P<.001)

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# Stereotactic Radiotherapy and Short-course Pembrolizumab for Oligometastatic Renal Cell Carcinoma—The RAPPORT Trial

Shankar Siva [a,b,*], Mathias Bressel [a], Simon T. Wood [c,d], Mark G. Shaw [a], Sherene Loi [a,b], Shahneen K. Sandhu [a,b], Ben Tran [a,b], Arun A. Azad [a,b], Jeremy H. Lewin [a], Katharine E. Cuff [c,d], Howard Y. Liu [c,d], Daniel Moon [a,e], Jeremy Goad [a], Lih-Ming Wong [e], Michael LimJoon [a], Jennifer Mooi [a], Sarat Chander [a], Declan G. Murphy [a,b], Nathan Lawrentschuk [a,e], David Pryor [c,f]

Single-arm multi-institutional phase I/II trial (NCT02855203)
Patients with two or fewer lines of prior systemic therapy and **one to five oligometastases from renal carcinoma**

A **single fraction of 20 Gy SABR** (or if not feasible, ten fractions of 3 Gy) was given to all metastatic sites, **followed by pembrolizumab** 200 mg administered Q3W for eight cycles

The endpoints were adverse events (AEs), disease control rate (DCR) for at least 6 mo, objective response rate (ORR), progression-free survival (PFS), and overall survival (OS)

**Table 1 – Baseline characteristics.**

| Characteristic | Total (*n* = 30) |
|---|---|
| Age (yr) | |
| Median (range) | 62 (47–80) |
| Sex, *n* (%) | |
| Female | 7 (23) |
| IMDC score, *n* (%) | |
| 0 | 17 (57) |
| 1 | 8 (27) |
| 2 | 5 (17) |
| ECOG, *n* (%) | |
| Status 0 | 20 (67) |
| Status 1 | 10 (33) |
| Prior treatments, *n* (%) | |
| No prior treatment | 1 (3) |
| Surgery | 22 (73) |
| Surgery + interleukin-2 | 5 (16) |
| TKI | 2 (7) |
| Prior surgery by type, *n* (%) | |
| Nephrectomy | 18 (67) |
| Nephrectomy + metastasectomy (body) | 7 (26) |
| Nephrectomy + metastasectomy (brain) | 2 (7) |
| Total number of metastases, *n* (%) | |
| 1 | 5 (17) |
| 2 | 8 (27) |
| 3 | 9 (30) |
| 4 | 5 (17) |
| 5 | 3 (10) |

ECOG = Eastern Cooperative Oncology Group; IMDC = International Metastatic RCC Database Consortium; RCC = renal cell carcinoma; TKI = tyrosine kinase inhibitor.

**Table 2 – Treatment characteristics.**

| Characteristic | Total (*n* = 30) |
|---|---|
| Lesion location, *n* (%) | |
| Adrenal | 8 (10) |
| Bone | 11 (13) |
| Lung | 43 (52) |
| Lymph node | 12 (14) |
| Soft tissue/muscle | 9 (11) |
| Radiotherapy modality per lesion, *n* (%) | |
| SABR | 64 (77) |
| CRT | 19 (23) |
| Radiotherapy dose per lesion, *n* (%) | |
| 20 Gy in 1 fraction | 64 (77) |
| 30 Gy in 10 fractions | 19 (23) |
| Number of cycles of pembrolizumab, *n* (%) | |
| 3 | 1 (3) |
| 5 | 1 (3) |
| 6 | 2 (7) |
| 7 | 2 (7) |
| 8 | 24 (80) |
| Reason for early discontinuation, *n* (%) | |
| Pneumonitis | 4 (67) |
| Progressive disease by RECIST 1.1 | 2 (33) |
| Delay in at least 1 cycle of pembrolizumab, *n* (%) | |
| Yes | 4 (13) |
| Reason for delay, *n* (%) | |
| Adverse event | 3 (75) |
| Patient vacation | 1 (25) |

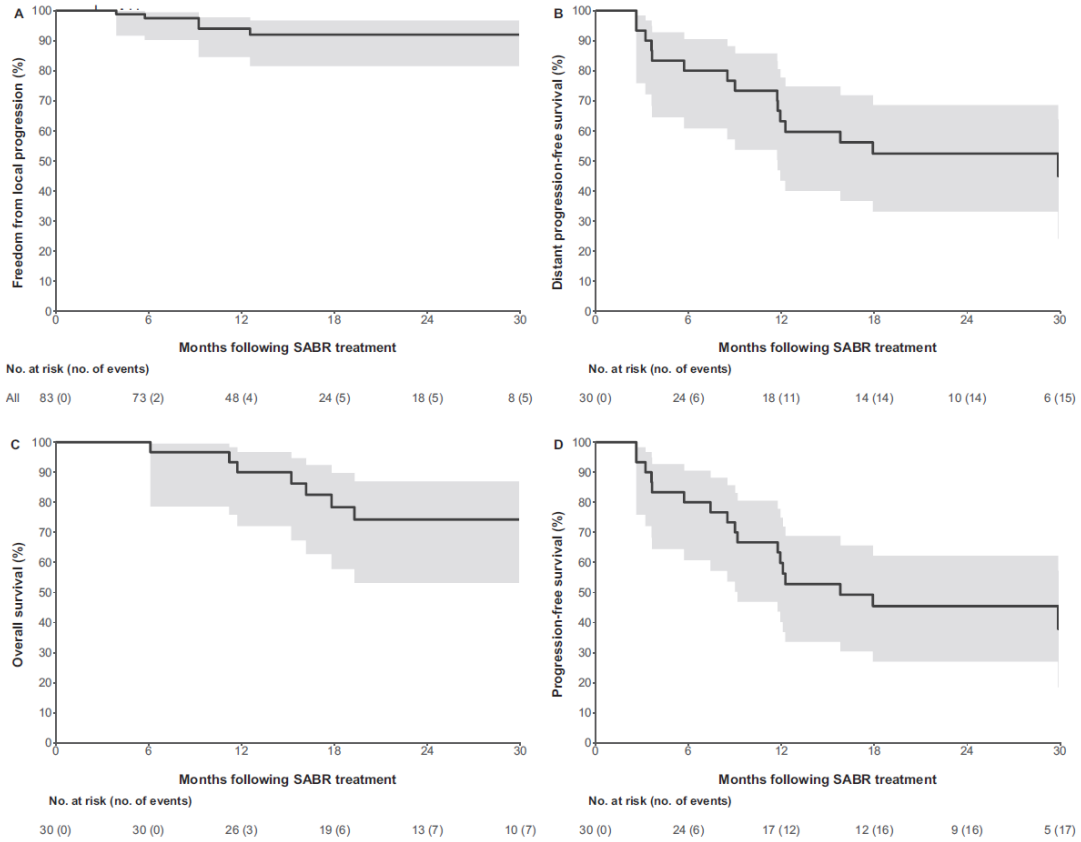
CRT = conventional radiotherapy; SABR = stereotactic ablative body radiotherapy.

**SAFETY:**

4 Grade 3 TRAEs

19 Grade 1-2 TRAEs

7 no TRAEs




2-yr FFLP 92%.
2-yr DPFS 52%
2-yr OS 74%
2-yr PFS 45%

Total metastatic ablation and pembrolizumab are associated with a tolerable AE profile in patients with one to five sites of oligometastatic disease from ccRCC. Excellent local control was observed. Durable responses to treated metastases, and encouraging PFS and distant disease control were observed with this approach, which warrants further investigation.

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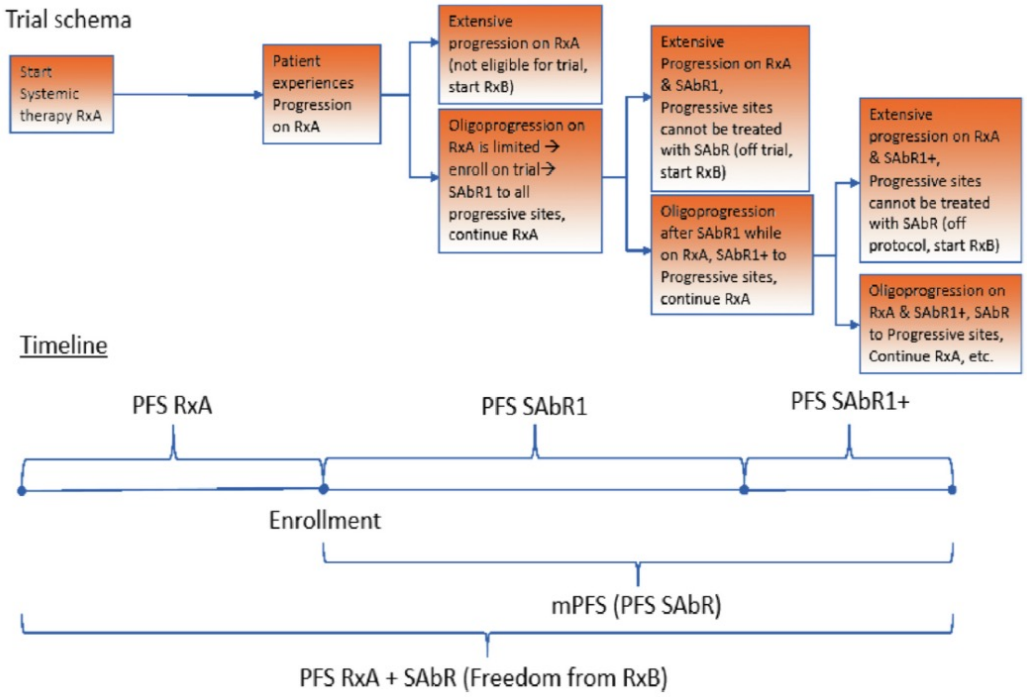


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**Phase II Trial of Stereotactic Ablative Radiation for Oligoprogressive Metastatic Kidney Cancer**

*Raquibul Hannan [a,b,*], Michael Christensen [a], Hans Hammers [b,c], Alana Christie [b], Brendan Paulman [a], Dandan Lin [a], Aurelie Garant [a,b], Waddah Arafat [b,c], Kevin Courtney [b,c], Isaac Bowman [b,c], Suzanne Cole [b,c], David Sher [a], Chul Ahn [c], Hak Choy [a], Robert Timmerman [a,b,*], James Brugarolas [b,c,*]*

Single-arm phase II clinical trial

**20 patients with mRCC** on first to fourth-line systemic therapy with three or fewer sites of progression (including new sites) involving 30% of all sites.

**SAbR to oligoprogressing metastases** at outset and longitudinally, while radiated sites remain controlled and overall disease oligoprogressive.

The primary objective was **to extend ongoing systemic therapy by >6 mo in >40% of patients**.

Secondary endpoints included overall survival, toxicity, and patient-reported quality of life.

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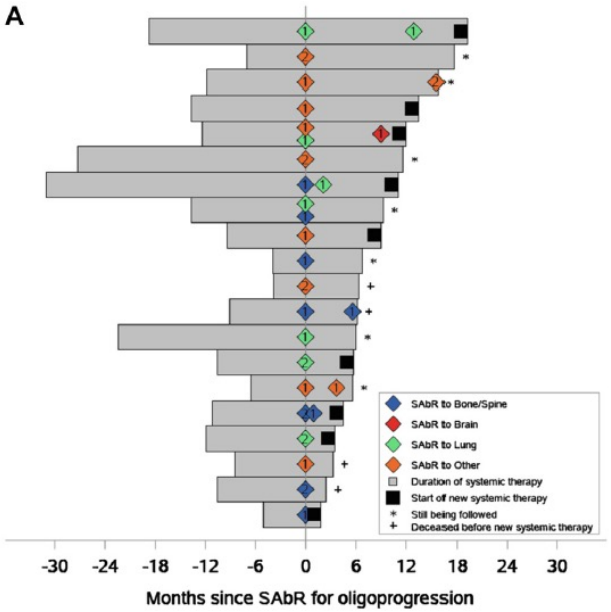


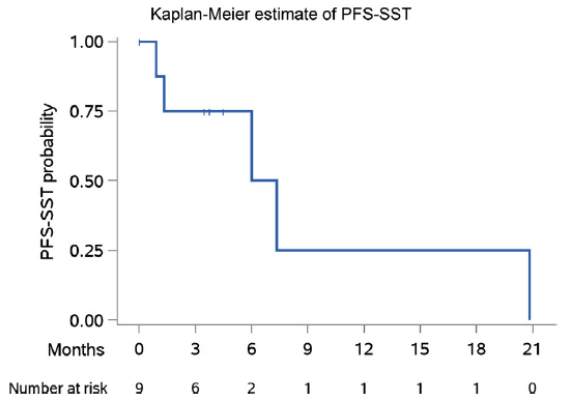


Fig. 3 – Kaplan-Meier estimate of PFS of subsequent systemic therapy. PFS = progression-free survival; PFS-SST = PFS of subsequent systemic therapy.

SAbR extended the duration of the **ongoing systemic therapy by >6 mo in 14 patients (70%).**

The median time from SAbR to the onset of new systemic therapy or death was 11.1 mo.

The median duration of SAbR-aided systemic therapy was 24.4 mo

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# Stereotactic Ablative Radiation for Systemic Therapy–naïve Oligometastatic Kidney Cancer

Raquibul Hannan[a,b,*], Michael Christensen[a], Alana Christie[b], Aurelie Garant[a,b], Ivan Pedrosa[b,d], Liliana Robles[a], Samantha Mannala[a], Chiachien Wang[a], Hans Hammers[b,c], Waddah Arafat[b,c], Kevin Courtney[b,c], Isaac A. Bowman[b,c], David Sher[a], Chul Ahn[b], Suzanne Cole[b,c], Hak Choy[a], Robert Timmerman[a,b,*], James Brugarolas[b,c,*]

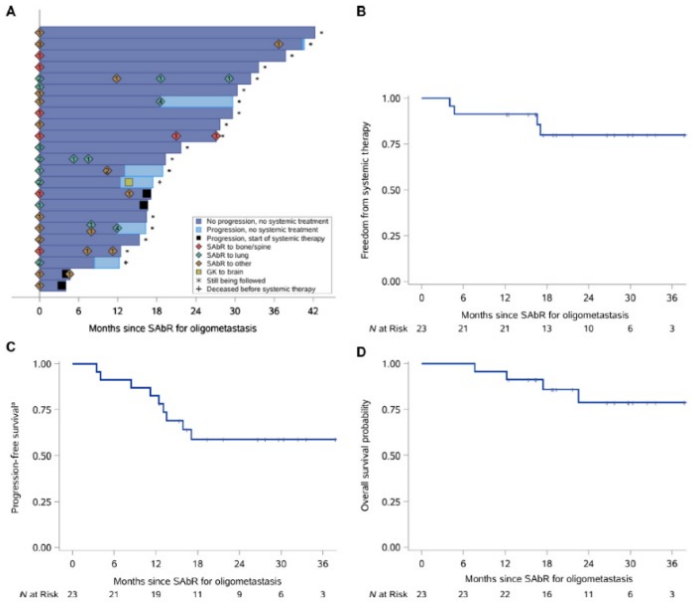
Phase II single-arm trial

Recurrent RCC patients with **three or fewer extracranial metastases**

**SAbR to all upfront** and, as applicable, subsequent metastases.

Primary objective of **freedom from systemic therapy for >1 yr in >60% of patients**.

Secondary endpoints included progression-free survival (PFS), defined as the time from first SAbR to progression not amenable to SAbR; patient reported QOL metrics; local control (LC) rates; toxicity; cancer-specific survival (CSS) and overall survival (OS).




**Freedom from systemic therapy at 1 yr was 91.3%**

One-year PFS was 82.6%

One-year OS was 95.7%

One-year CSS was 100%

*Conclusions:* SAbR for oligometastatic RCC was associated with meaningful longitudinal disease control while preserving QOL. These data support further evaluation of SAbR for systemic therapy–naïve oligometastatic RCC.

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# AGENDA

- Where do we stand
- Large database
- Prospective trials (mixed histologies)
- Prospective trials (histology driven)
- More than the big killers
- Predictive models

# Definition of oligometastatic esophagogastric cancer and impact of local oligometastasis-directed treatment: A systematic review and meta-analysis

Tiuri E. Kroese [a,b,*], Hanneke W.M. van Laarhoven [c], Magnus Nilsson [d], Florian Lordick [e], Matthias Guckenberger [f], Jelle P. Ruurda [a], Domenico D'Ugo [g], Karin Haustermans [h], Eric van Cutsem [i], Richard van Hillegersberg [a], Peter S.N. van Rossum [b]

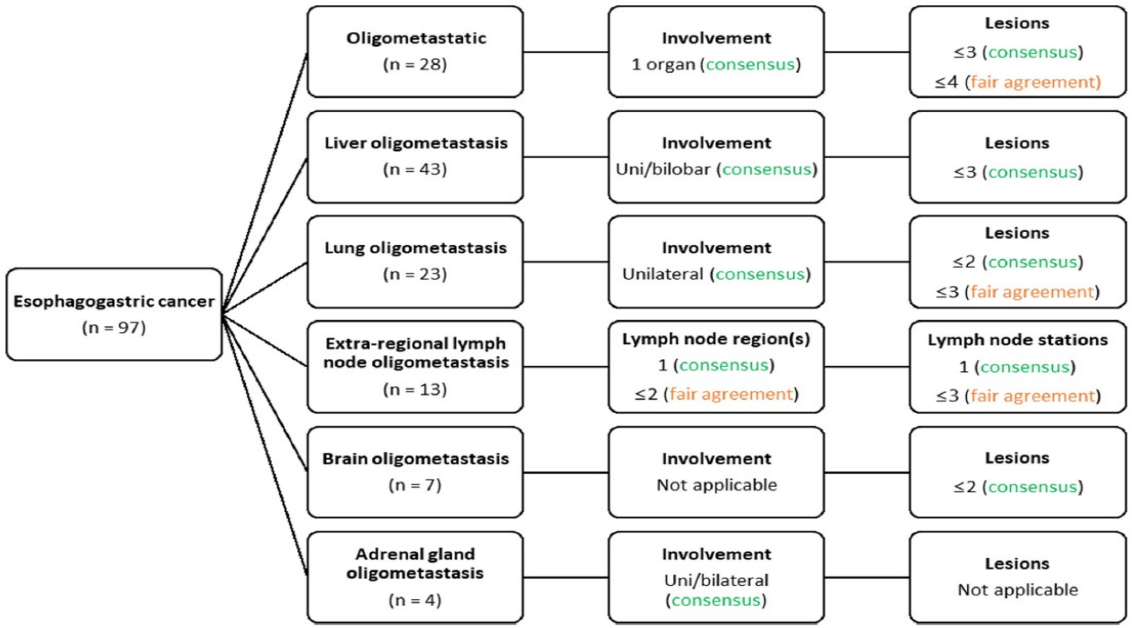
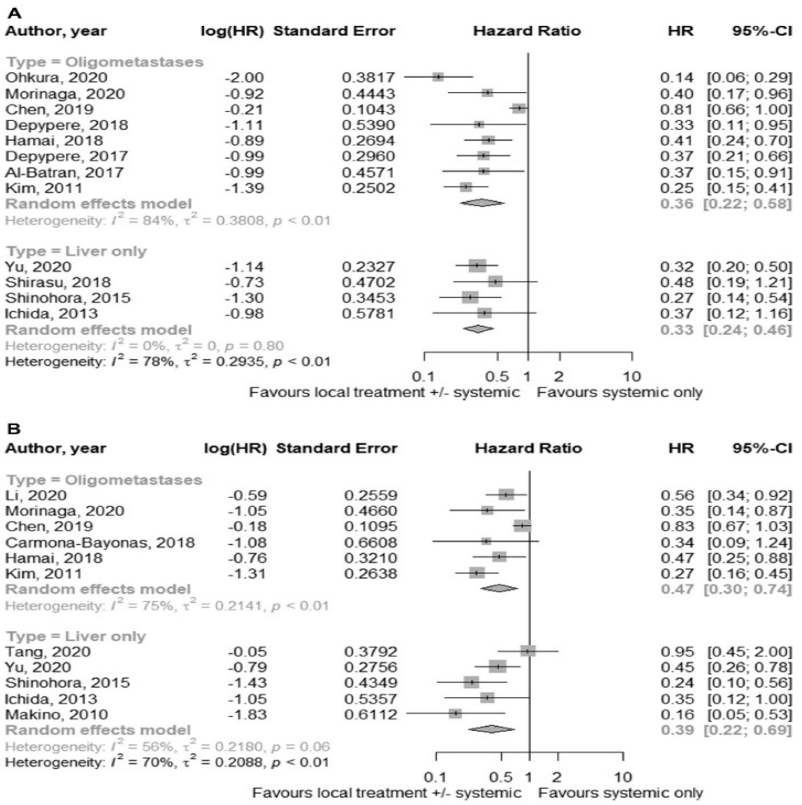



Fig. 2. Summary of definition of oligometastatic esophagogastric cancer according to literature and study protocols.

**OMD was considered in 1 organ with 3 metastases (consensus).**

'**Organ-specific**' OMD burden could involve bilobar 3 liver metastases, unilateral 2 lung metastases, 1 extra-regional lymph node station, 2 brain metastases, or bilateral adrenal gland metastases (consensus).




**Local treatment** for OMD was associated with **improved OS** compared with systemic therapy alone based on 6 non-randomized studies (pooled HR 0.47) and for liver oligometastases based on 5 non-randomized studies (pooled HR 0.39).

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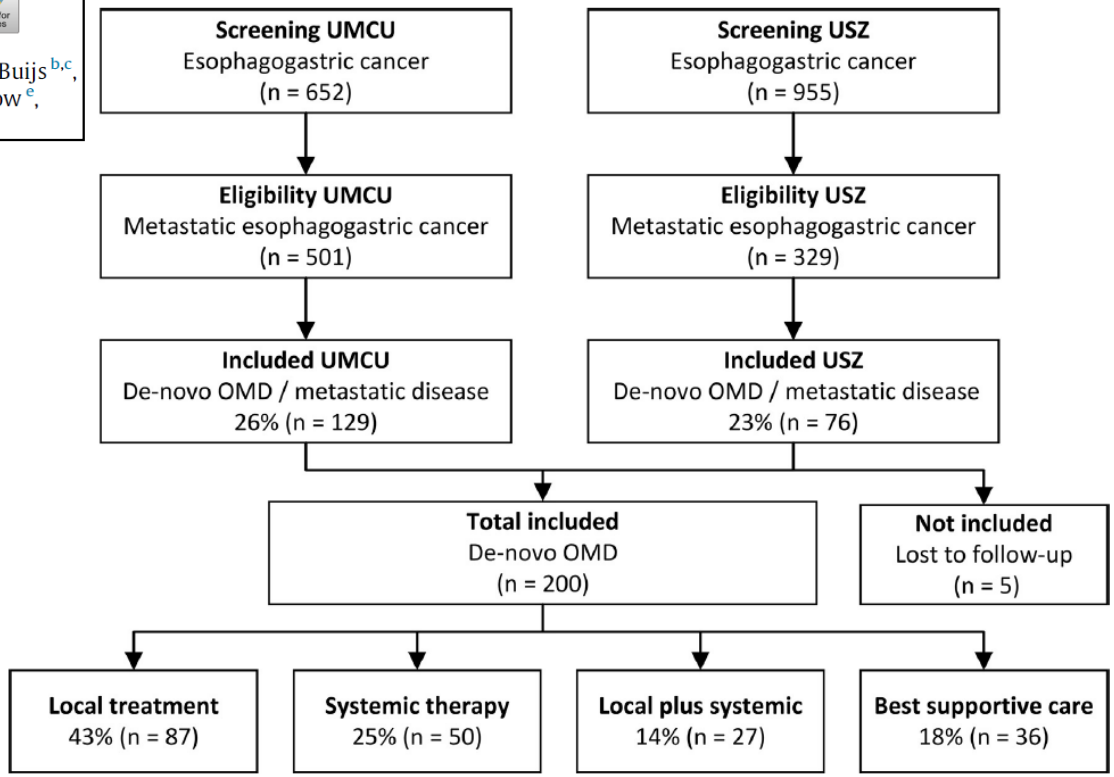
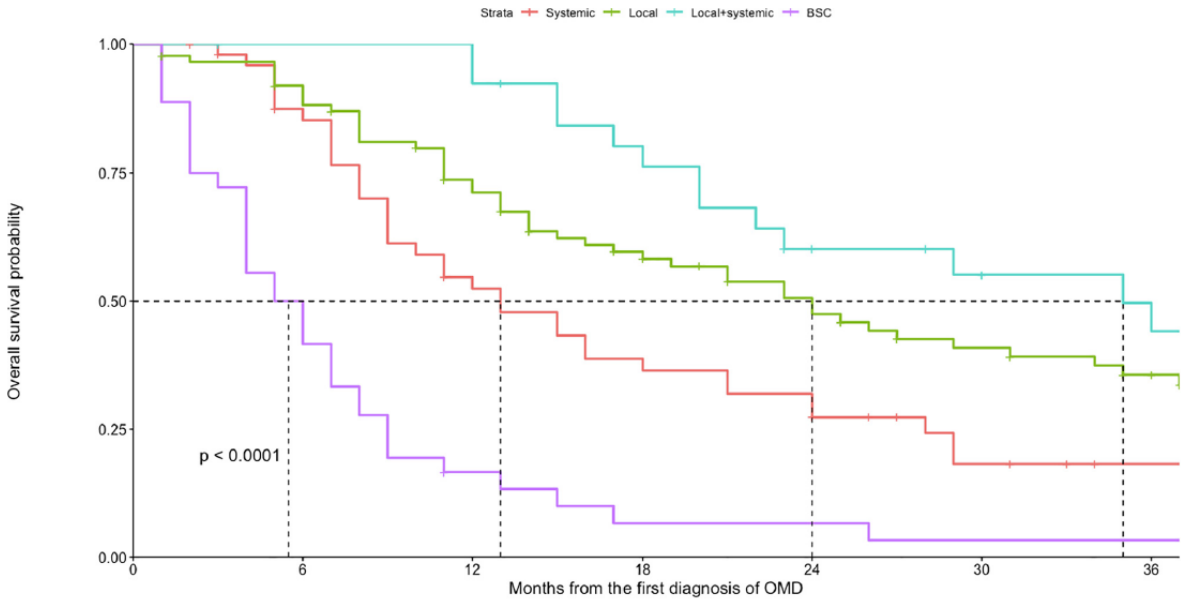
Incidence and survival of patients with oligometastatic esophagogastric cancer: A multicenter cohort study

Tiuri E. Kroese [a,b,c], Sebastian M. Christ [a], Peter S.N. van Rossum [b], Matthijs D.L. Burger [b,c], George S. Buijs [b,c], Urs Mühlematter [d], Nicolaus Andratschke [a], Jelle P. Ruurda [c], Martin Hüllner [d], Christian A. Gutschow [e], Richard van Hillegersberg [c], Matthias Guckenberger [a,*]

- Multi-centre study
- Between 2010 and 2021, patients with **metastatic esophagogastric cancer** were identified. Patients with **de-novo OMD** were included (first-time diagnosis of 5 distant metastases on 18FFDG-PET/CT).
- Treatment of OMD was categorized into (**1) systemic therapy**, (2**) local treatment** (stereotactic body radiotherapy or metastasectomy), (3) **local plus systemic therapy**, or (4) **best supportive care**.
- The primary outcomes were overall survival (OS) and independent prognostic factors for OS






**Median OS** after **local plus systemic therapy was 35 months** (95% CI: 22-NA) as compared with **13 months** (95% CI: 9–21,p < 0.001) after **systemic therapy alone**

*Conclusion:* Patients with metastatic esophagogastric cancer present in 25% with de-novo OMD. Local treatment of OMD plus systemic therapy was independently associated with long-term OS and independently improved OS when compared with systemic therapy alone. Randomized controlled trials are warranted to confirm these results.

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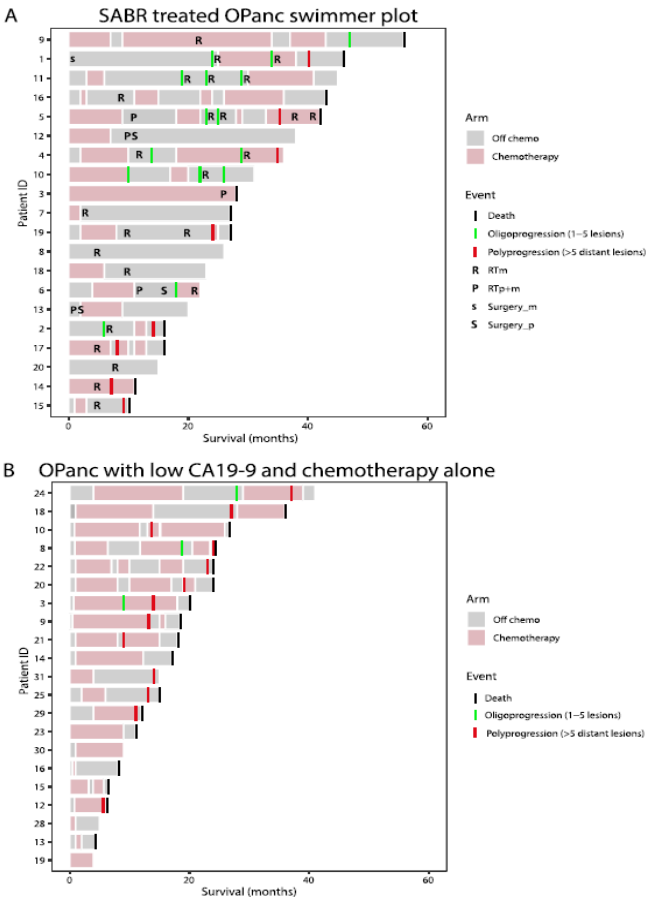
# Ablative Radiation Therapy in Oligometastatic Pancreatic Cancer to Delay Polyprogression, Limit Chemotherapy, and Improve Outcomes

Ahmed M. Elamir, MD,* John D. Karalis, MD,† Nina Niu Sanford, MD,* Patricio M. Polanco, MD,† Michael R. Folkert, MD, PhD,† Matthew R. Porembka, MD,† Syed Ali Kazmi, MD,§ Ravikanth Maddipati, MD,§ Herbert J. Zeh, MD,† Robert D. Timmerman, MD,* Song Zhang, PhD,‖ Matteo Ligorio, MD, PhD,† Muhammad Shaalan Beg, MD,§ and Todd A. Aguilera, MD, PhD*

Patients with synchronous or metachronous **Oligometastatic Pancreatic cancer** (1 to 5 metastases) who received **SABR to all active metastatic sites** was performed. **Propensity score** with similar patients who did not receive SABR

Out of the 20 SABR-treated OPanc patients, 17 (85%) had 6 or more months of time off chemotherapy, compared with 7 patients (33.3%) among the chemotherapy-treated group.

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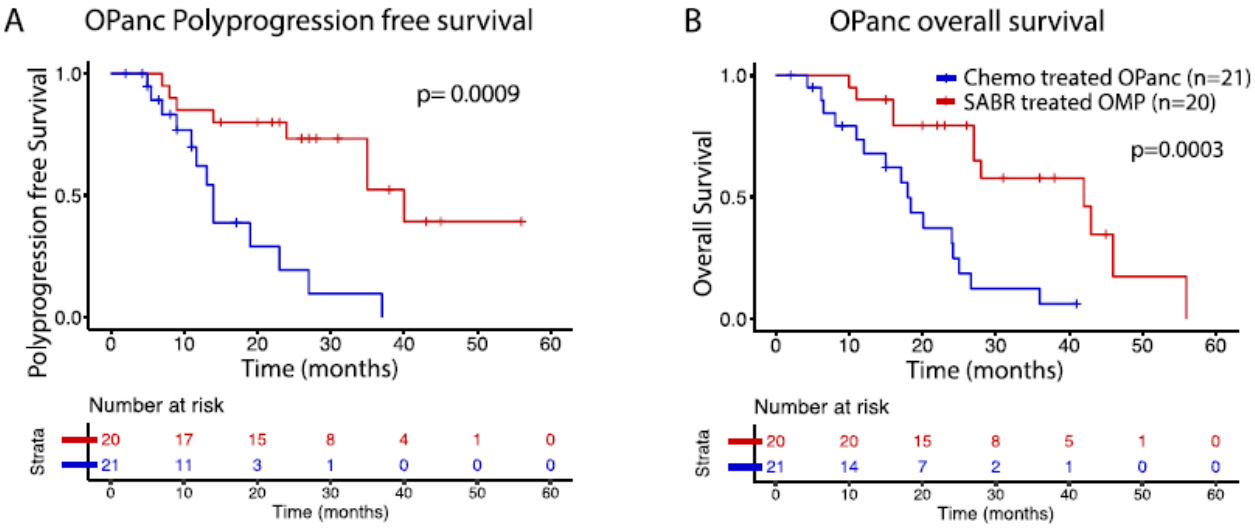


Median **polyprogression-free survival** was **40 vs 14 months** and **overall survival** was **42 vs 18 months** in SBRT vs systemic therapy arms, respectively.

**Conclusions:** Management of OPanc with SABR as local regional therapy could improve outcomes in a selected population and warrants prospective evaluation.

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# Stereotactic Body Radiation Therapy for Lung Metastases From Sarcoma in Oligometastatic Patients: A Phase 2 Study

Pierina Navarria, MD,* Davide Baldaccini, MD,* Elena Clerici, MD,* Beatrice Marini, MD,* Luca Cozzi, PhD,* Davide Franceschini, MD,* Alexia Francesca Bertuzzi, MD,‡ Vittorio Quagliuolo, MD,§ Valter Torri, MD,‖ Piergiuseppe Colombo, MD,¶ Ciro Franzese, MD,*,† Luisa Bellu, MD,* and Marta Scorsetti, MD*,†

Prospective phase 2 study

Adult patients with **up to 4 lung metastases (LMs) ≤5 cm** in diameter and **unsuitable for surgery** were included.

The primary endpoint was the proportion of treated lesions free from progression at 12 months. Secondary endpoints were disease- free survival (DFS), overall survival (OS), and toxicity.

| LMs | No. (%) 71 (100) |
|---|---|
| LMs treated for patients, No. | |
| 1 | 25 (56.8) |
| 2 | 13 (29.6) |
| 3 | 4 (9.1) |
| 4 | 2 (4.5) |
| Maximum diameter, median (range), cm | 2 (0.9-5) |
| Volume, median (range), $cm^3$ | 3.96 (0.36-62) |
| Site | |
| Right upper lobe | 15 (21.1) |
| Middle lobe | 7 (18.9) |
| Right lower lobe | 14 (19.7) |
| Left upper lobe | 14 (19.7) |
| Lingula | 2 (2.8) |
| Left lower lobe | 17 (23.9) |
| Peripheral | 64 (90.1) |
| Central | 7 (9.9) |
| Total dose/fractions | |
| 48 Gy/4 fractions | 61 (85.9) |
| 60 Gy/3 fractions | 3 (4.2) |
| 60 Gy/8 fractions | 7 (9.9) |

*Abbreviations:* Gy = Gray; LM = lung metastasis; SBRT = stereotactic body radiation therapy.

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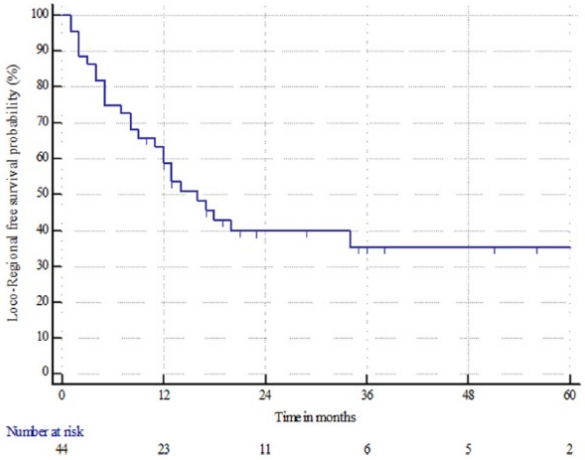


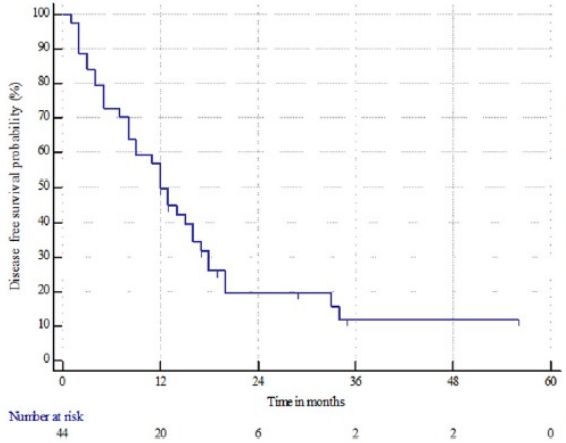


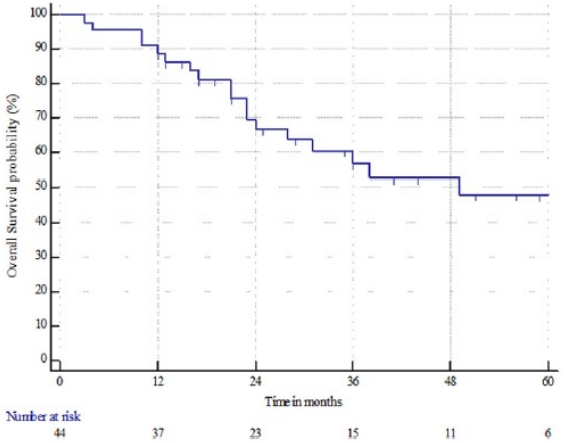


Twelve-month **local control** was **98.5%**

Median DFS time was 12 months

1-, 2- and 5-year PFS rates were 50%, 19.5%, 11.7%, respectively

Median OS time was 49 months

1-, 2-, and 5-year OS rates were 88.6%, 66.7%, 48.2%, respectively

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# AGENDA

- Where do we stand
- Large database
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- Prospective trials (histology driven)
- More than the big killers
- Predictive models

# Oligoscore: a clinical score to predict overall survival in patients with oligometastatic disease treated with stereotactic body radiotherapy

Davide Franceschini, Vanessa Polenghi, Ciro Franzese, Tiziana Comito, Pierina Navarria, Giuseppe R. D'Agostino, Francesca Ieva & Marta Scorsetti

997 pts

Table 2. Score associated with statistically significant variables for Overall Survival (OS).

| Covariate [type] | | Score | Hazard ratio | 95% CI HR |
|---|---|---|---|---|
| Location of the primary tumor [categorical] (baseline = colorectal) | Lung | 412 | 1.510 | (1.157; 1.971) |
| | Pancreas | 517 | 1.677 | (1.134; 2.481) |
| | Prostate | −2240 | 0.106 | (0.033; 0.342) |
| Performance status [categorical] (baseline = 0) | 1 | 341 | 1.406 | (1.140; 1.734) |
| | 2 | 634 | 1.885 | (1.348; 2.636) |
| Location of irradiated lesions [categorical] (baseline = lung) | Liver | 583 | 1.792 | (1.357; 2.366) |
| Extra target [binary] (baseline = no) | Yes | 620 | 1.859 | (1.463; 2.364) |
| BED [continuous] | | −3 | 0.997 | (0.994; 0.999) |

Table 3. Class summaries.

| Risk class | Number of patients | Median survival (years) | 1 year OS (%) | 3 year OS (%) |
|---|---|---|---|---|
| Low risk | 336 | 5.67 | 93 | 64 |
| Medium risk | 329 | 2.47 | 88 | 42 |
| High risk | 332 | 1.82 | 76 | 24 |

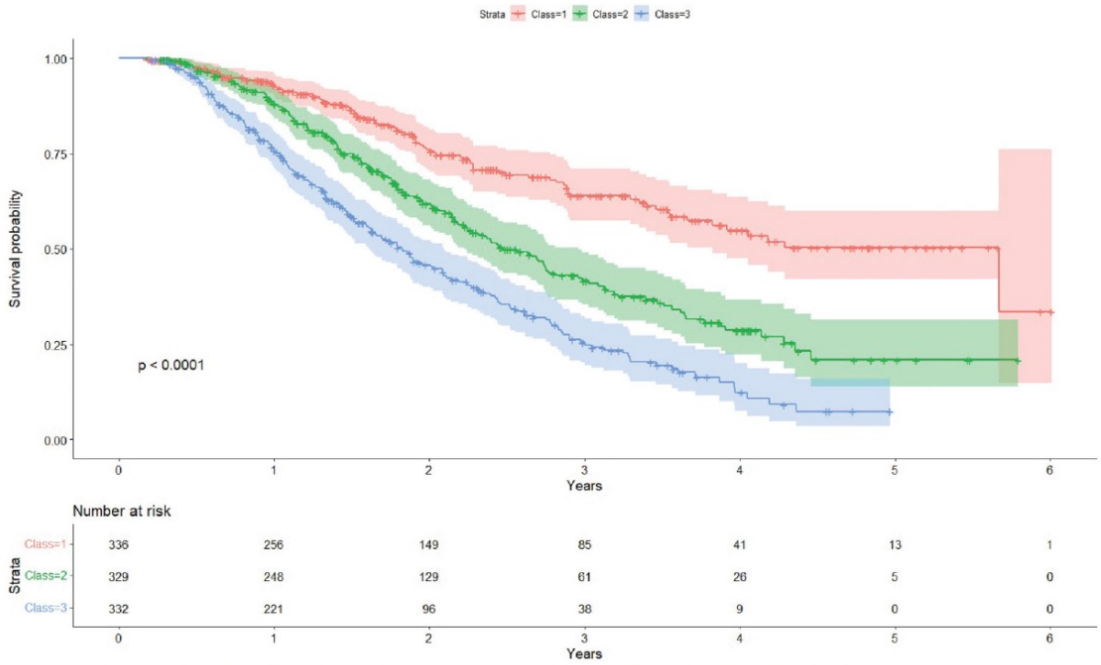


Figure 1. Kaplan Meier estimator divided by risk class. Class 1 represents low risk, Class 2 medium risk and Class 3 high risk.

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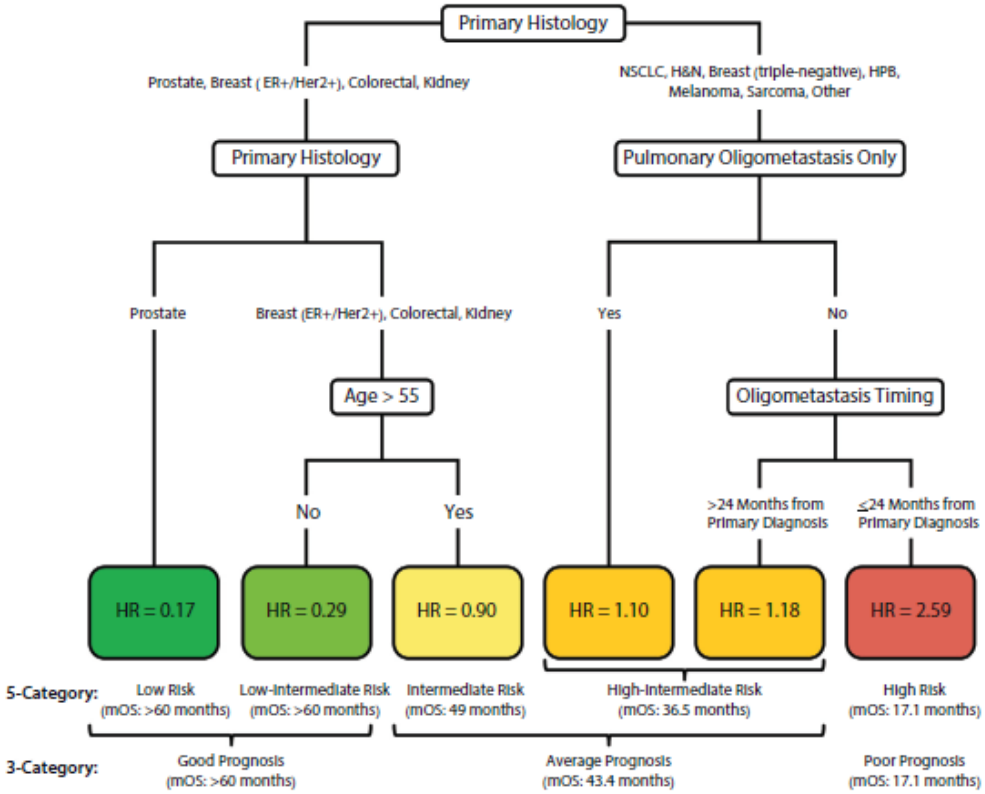
Acta Oncologica 2022

## Development of a Prognostic Model for Overall Survival in Patients With Extracranial Oligometastatic Disease Treated With Stereotactic Body Radiation Therapy

Hanbo Chen, MD, MPH,* Ian Poon, MD,* Eshetu G. Atenafu, MSc,† Serena Badellino, MD,‡ Tithi Biswas, MD,§ Roi Dagan, MD,|| Darby Erler, MRT(T),* Matthew Foote, MD,¶ Kristin J. Redmond, MD,# Umberto Ricardi, MD,‡ Arjun Sahgal, MD,* and Alexander V. Louie, MD, MSc, PhD*

1033 patients

primary histology, lung-only OMD on presentation, the timing of OMD presentation, and age at the start of SBRT

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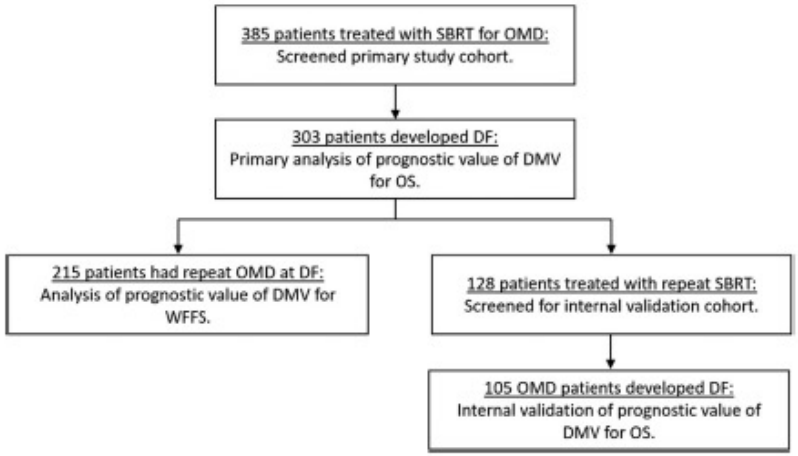
**Distant Metastasis Velocity as a Novel Prognostic Score for Overall Survival After Disease Progression Following Stereotactic Body Radiation Therapy for Oligometastatic Disease**

Jonas Willmann, MD, Eugenia Vlaskou Badra, MD, Selma Adilovic, Sebastian M. Christ, MD, PhD, Maiwand Ahmadsei, MD, Michael Mayinger, MD, Stephanie Tanadini-Lang, PhD, Matthias Guckenberger, MD, and Nicolaus Andratschke, MD

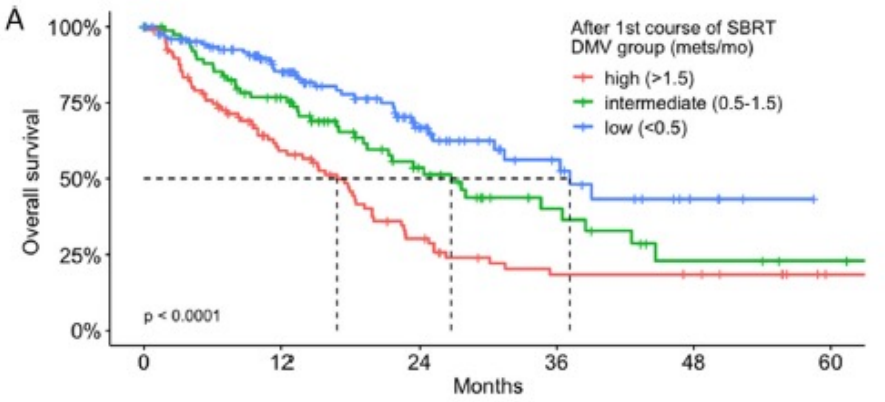


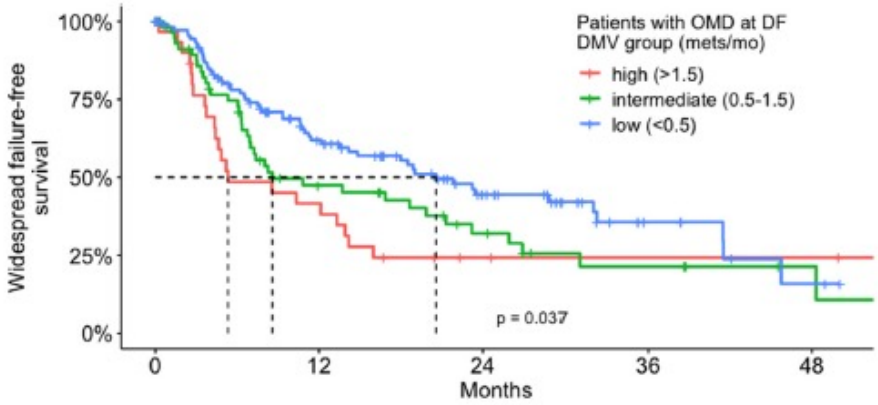

Patients with **≤5 metastases from solid organ malignancies** treated with SBRT

**Distant Metastasis Velocity (DMV)**

$$DMV = \frac{Number\ of\ new\ metastases\ at\ distant\ failure}{Time\ (months)\ from\ end\ of\ SBRT\ to\ distant\ failure}$$

Low, intermediate, and high DMV groups, corresponding to <0.5, 0.5 to 1.5, and >1.5 metastases per month (mets/mo)




On multivariable analysis, **DMV** was a strong independent **predictor of OS**, with a hazard ratio of 0.31 for low (P < .001) compared with high DMV.

Lower DMV was significantly associated with longer WFFS (P = .04).

# The oligometastatic spectrum in the era of improved detection and modern systemic therapy

Rohan R. Katipally, Sean P. Pitroda, Aditya Juloori, Steven J. Chmura and Ralph R. Weichselbaum

**Box 1 | Recommendations for future trials of metastasis-directed local therapy**

- Delivery of local therapies (such as radiotherapy, surgery and radiofrequency ablation) to multiple tumour sites is likely to be more effective than treatment of a single lesion.
- If feasible and safe, local therapy should be delivered to all known sites of disease.
- Improved methods of cancer detection (for example, circulating tumour DNA assays and novel imaging techniques) might help select the patients most likely to benefit from local therapies, and could potentially identify patients for whom systemic therapy could be de-escalated or even omitted.
- Multifaceted risk stratification (leveraging standard clinical factors, as well as biomarkers of tumour and host biology) will also help select patients who are most likely to benefit from local therapies.
- If stereotactic body radiotherapy is utilized, ablative dose regimens should be used.



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# Thanks for your attention

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