BIOLOGIA E TRATTAMENTO RADIANTE CURATIVO DELLA **MALATTIA OLIGOMETASTATICA**

VIRTUAL
26 MARZO 2021

Final remarks

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Summary: evidences for MDT in OMD: RCT, all positive findings!!

Study	# patients	Tumor site	Study Design	HR PFS	HR OS
Iyengar *JAMA Oncol 2018*	N = 29	NSCLC	Phase 2 RCT, single institution; 1:1 maintenance chemotherapy vs SABR to all disease sites, followed by maintenance chemotherapy	0.30	-
Gomez *JCO 2019*	N = 49	NSCLC	Phase 2 RCT, multi-institutional; 1:1 maintenance systemic therapy or observation vs local consolidative therapy to all disease sites	PFS 14.2 vs 4.4 mo (p = .02)	0.41
Wang *ASCO 2020*	N = 133	EGFR + NSCLC	Phase 3 trial	0.62	0.68
Ruers *JNCI 2017*	N = 119	Colorectal liver mts	RFA-liver	0.57	0.58
Ost *JCO 2018*	N = 62	Prostate	Phase 2 RCT, multi-institutional; 1:1 ADT vs SBRT to all metastatic disease sites	ADT-free survival 0.60	
Phillips *JAMA Oncol 2020*	N = 54	Prostate		0.30	-
Palma *JCO 2019*	N = 99	Miscellaneous (Breast cancer, colorectal cancer, prostate cancer)	Phase 2 RCT, multi-institutional; 1:2 standard of care vs standard of care plus SABR to all sites of disease	0.48	0.47

Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation

Matthias Guckenberger, Yolande Lievens, Angelique B Bouma, Laurence Collette, Andre Dekker, Nandita M deSouza, Anne-Marie C Dingemans, Beatrice Fournier, Coen Hurkmans, Frédéric E Lecouvet, Icro Meattini, Alejandra Méndez Romero, Umberto Ricardi, Nicola S Russell, Daniel H Schanne, Marta Scorsetti, Bertrand Tombal, Dirk Verellen, Christine Verfaillie, Piet Ost

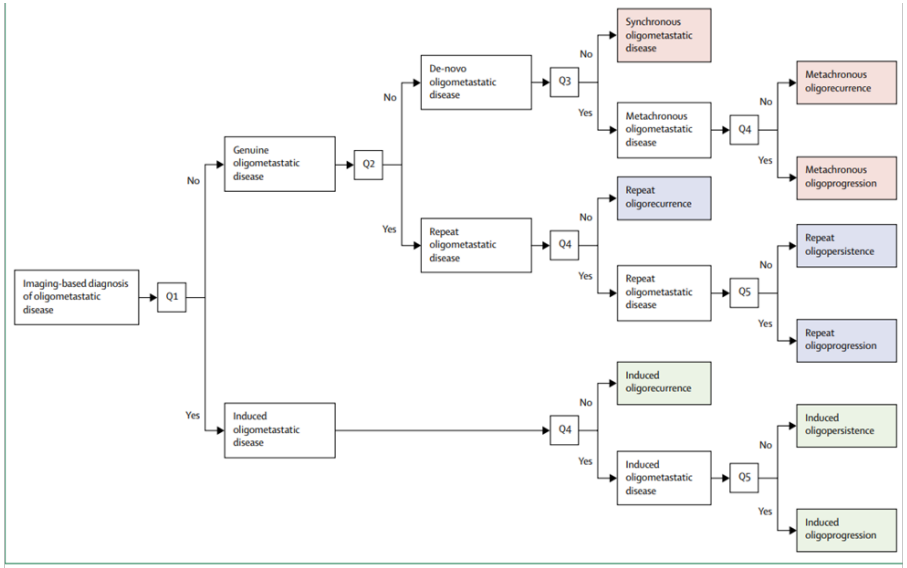
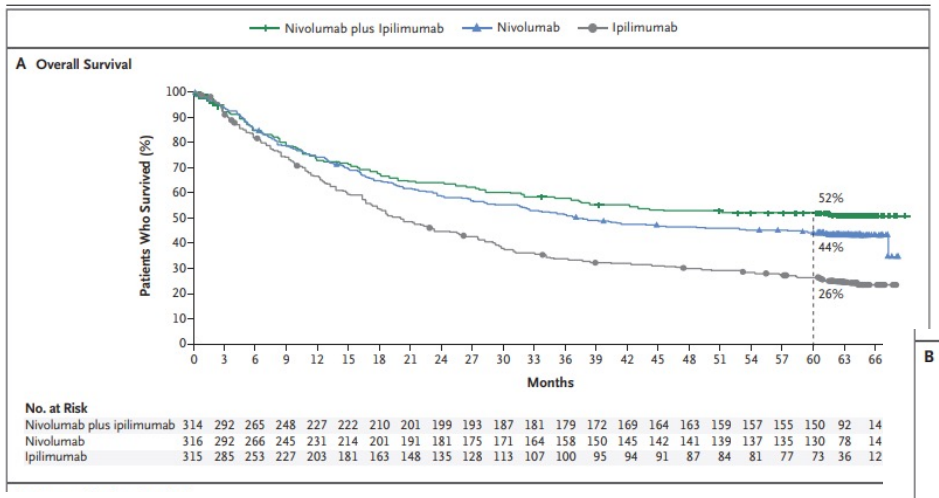
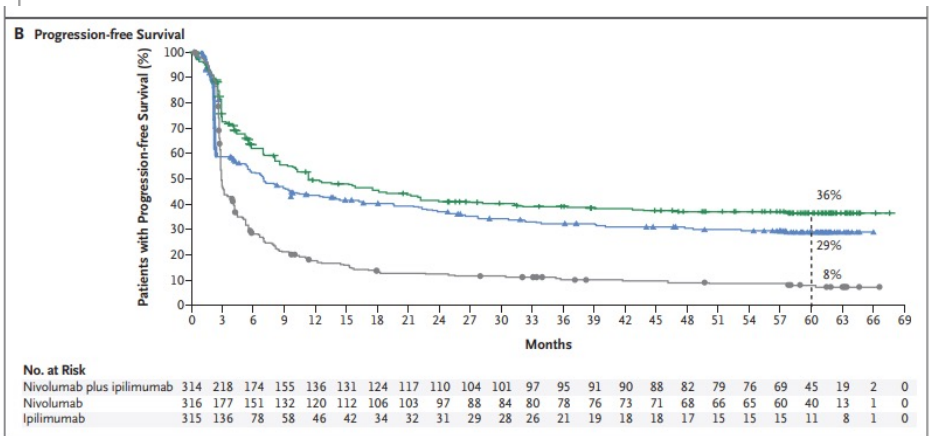


Figure 3: **Decision tree for classification of oligometastatic disease**
The decision tree starts with oligometastatic disease as umbrella term. Questions 1 and 2 differentiate between the upper-level oligometastatic states of de-novo (red), repeat (blue) and induced oligometastatic disease (green). Question 3 differentiates de-novo oligometastatic disease into synchronous and metachronous oligometastatic disease. Questions 4 and 5 subclassify into oligorecurrence, oligoprogression, and oligopersistence. Q1: Does the patient have a history of polymetastatic disease before current diagnosis of oligometastatic disease? Q2: Does the patient have a history of oligometastatic disease before current diagnosis of oligometastatic disease? Q3: Has oligometastatic disease been first diagnosed more than 6 months after the primary cancer diagnosis? Q4: Is the patient under active systemic therapy at the time of oligometastatic disease diagnosis? Q5: Are any oligometastatic lesions progressive on current imaging?

Lancet Oncology 2020 Jan;21(1):e18-e28

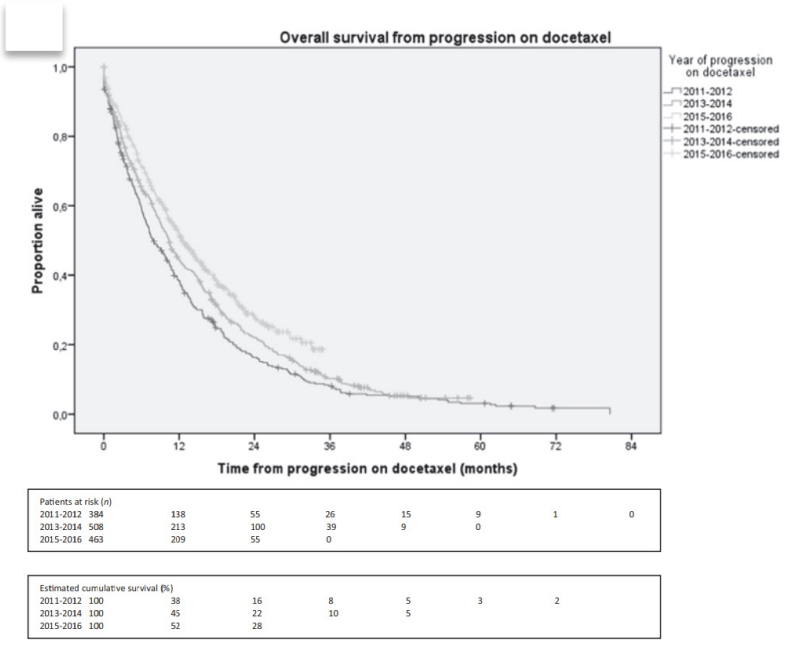
5-Year Survival: > 50% surviving after 5-years in advanced metastatic disease

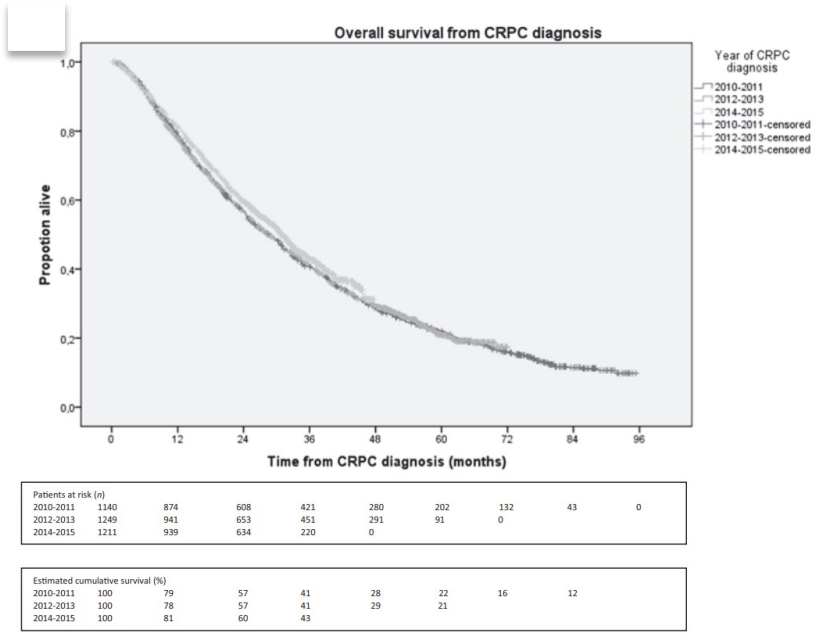




Randomized Controlled Trial > N Engl J Med. 2019 Oct 17;381(16):1535-1546.
doi: 10.1056/NEJMoa1910836. Epub 2019 Sep 28.

The effects of new life-prolonging drugs for metastatic castration-resistant prostate cancer (mCRPC).

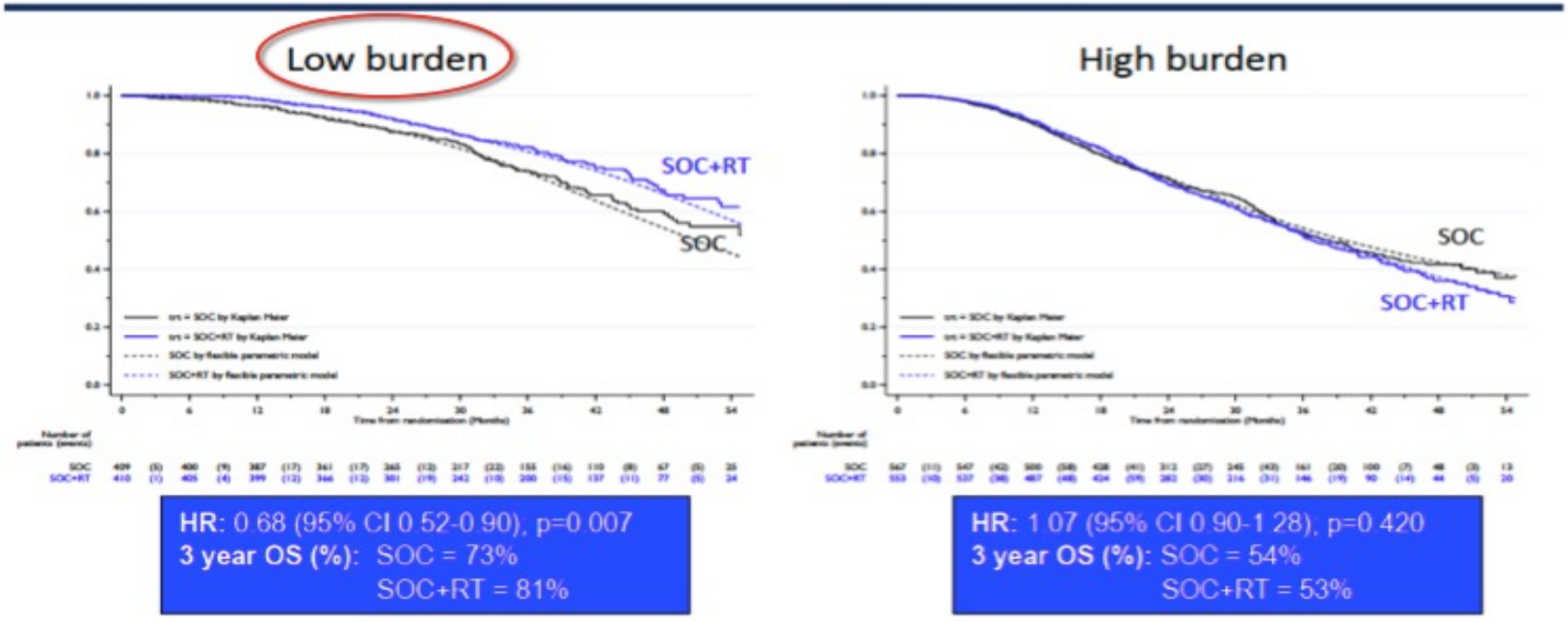




H M Westgeest Prostate Cancer Prostatic Dis. 2021 Mar 21

Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

Overall survival: metastatic burden subgroup analysis



HR: 0.68 (95% CI 0.52-0.90), p=0.007
3 year OS (%): SOC = 73%
SOC+RT = 81%

HR: 1.07 (95% CI 0.90-1.28), p=0.420
3 year OS (%): SOC = 54%
SOC+RT = 53%

ESMO

Annals of Oncology 30: 1813–1820, 2019
doi:10.1093/annonc/mdz397
Published online 27 September 2019

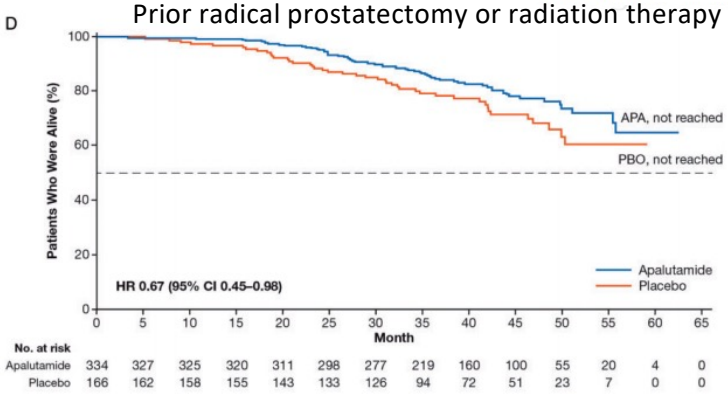
ORIGINAL ARTICLE

Apalutamide and overall survival in non-metastatic castration-resistant prostate cancer

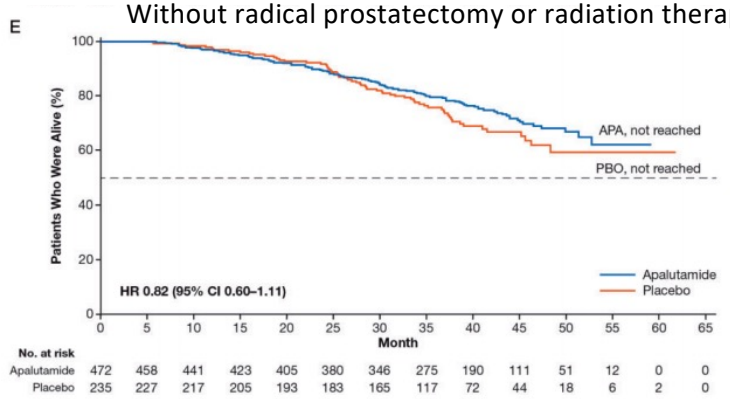
E. J. Small[1*], F. Saad[2], S. Chowdhury[3,4], S. Oudard[5], B. A. Hadaschik[6,7], J. N. Graff[8,9], D. Olmos[10,11], P. N. Mainwaring[12], J. Y. Lee[13], H. Uemura[14], P. De Porre[15], A. A. Smith[16], K. Zhang[17], A. Lopez-Gitlitz[18] & M. R. Smith[19,20]

[1]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA; [2]Centre Hospitalier de l'Université de Montréal, Université de Montréal, Montréal, QC, Canada; [3]Guy's, King's and St. Thomas' Hospitals, London; [4]Sarah Cannon Research Institute, London, UK; [5]Georges Pompidou Hospital, University René Descartes, Paris, France; [6]University of Duisburg-Essen, Essen; [7]Ruprecht-Karls University Heidelberg, Heidelberg, Germany; [8]VA Portland Health Care System, Portland; [9]Knight Cancer Institute, Oregon Health & Science University, Portland, OR, USA; [10]Spanish National Cancer Research Centre (CNIO), Madrid; [11]Hospitales Universitarios Virgen de la Victoria y Regional, Institute of Biomedical Research in Málaga (IBIMA), Málaga, Spain; [12]Centre for Personalized Nanomedicine, University of Queensland, Brisbane, Australia; [13]St. Mary's Hospital of Catholic University, Seoul, South Korea; [14]Yokohama City University Medical Center, Yokohama, Japan; [15]Janssen Research & Development, Beerse, Belgium; [16]Janssen Research & Development, Spring House, PA; [17]Janssen Research & Development, San Diego, CA; [18]Janssen Research & Development, Los Angeles, CA; [19]Massachusetts General Hospital Cancer Center, Boston, MA; [20]Harvard Medical School, Boston, MA, USA

Prior radical prostatectomy or radiation therapy

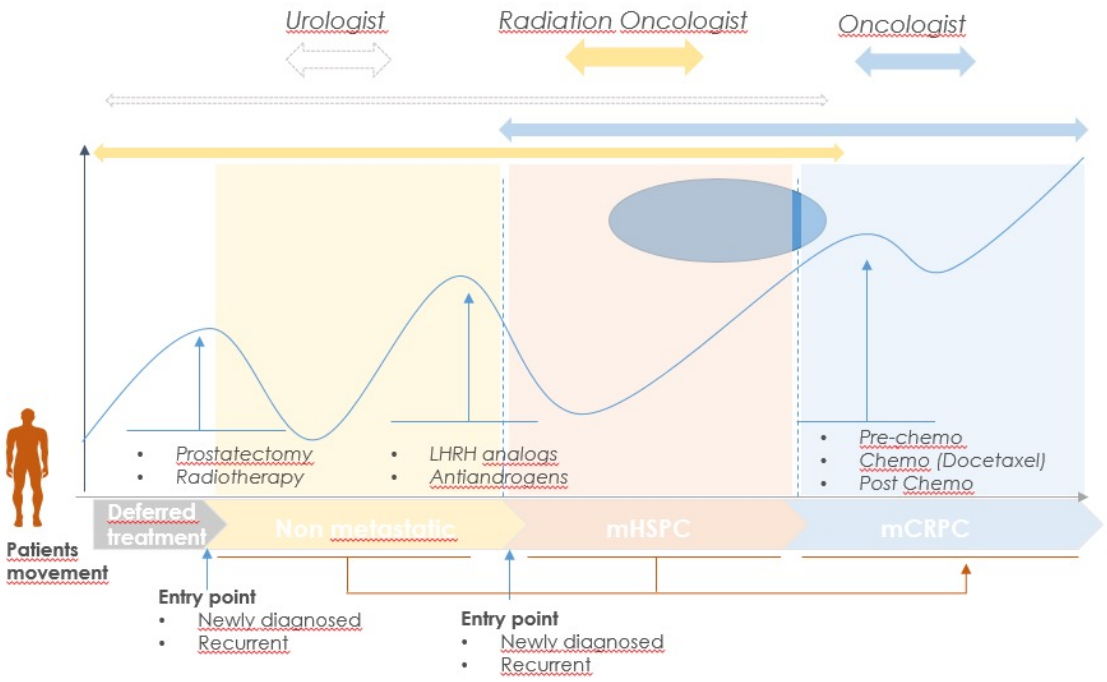


Without radical prostatectomy or radiation therapy



In the patients who had undergone **prior definitive local therapy, the HR for OS favored apalutamide** (HR 0.67; 95% CI 0.45–0.98), and there was a clear, early, and consistent separation of the Kaplan–Meier survival curves **between apalutamide and placebo groups beginning at 15 months**

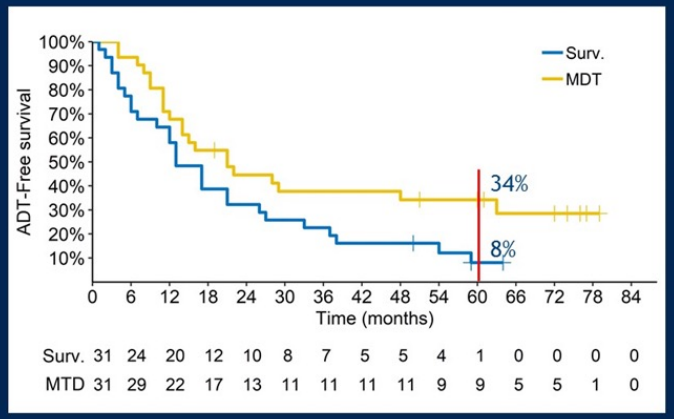
nmCRPC may be diagnosed by Urologist, Radiation Oncologist and Oncologist



Lo studio STOMP

ADT-free survival

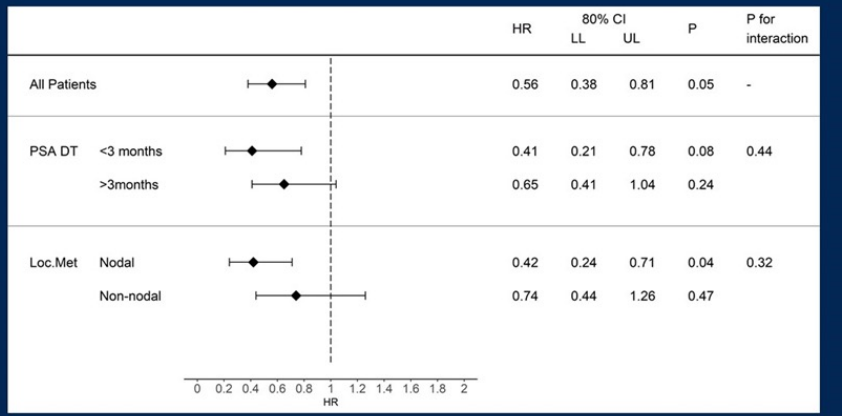
ITT



HR 0.57 (80% CI: 0.38−0.84); p=0.06

Per protocol HR 0.53 (80% CI: 0.35−0.79); p=0.04

Subgroup analysis: interaction test



A significant improvement in median ADT-free survival was seen in the MDT group (13 vs 21 months p=0.11), acknowledging that the p-value threshold for significance was set at 0.20 for this phase II trial.

PRESENTED AT: Genitourinary Cancers Symposium #GU20

PRESENTED BY: Piet Ost

Lo studio STOMP: CRPC free-survival

Difference in 5-year castrate-resistant prostate cancer free survival rate of 54% vs 76% (hazard ratio 0.62 [80% CI: 0.35−1.09]; p = 0.27).

Although it did not reach statistical significance, even by the looser 0.20 cutoff set by the study group, it does numerically favor MDT in this much more meaningful clinical endpoint.

This, along with the very low toxicity of MDT (0 grade 2-5 events) and the overall good prognosis of this population in general (median survival 5.3 years IQR 4.3-6.3), does lend further evidence MDT is worth further study in the population.

Lo studio STOMP

Questions/issues

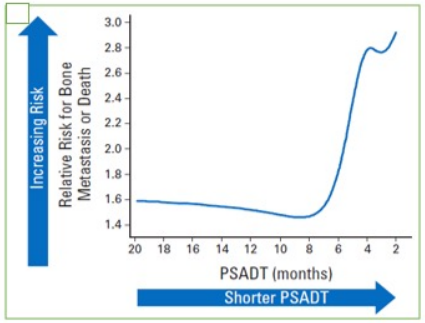
- PET-CT tracers evolve quickly: impact on results?
- What is the correct SOC for PET-detected metachronous oligorecurrent prostate cancer?
- What endpoint is ideal?
- SBRT + temporary systemic therapy?

Chi è il paziente non metastatico resistente alla castrazione (nmCRPC) ad alto rischio?

M0 CRPC : Biochemical progression while on ADT + Serum testosterone levels below 50 ng/dL + No evidence of metastasis with CT/bone scan

Alto rischio
Di sviluppare metastasi

PSA DT ≤ 10 mesi



Despite the risk of poor outcomes, the previous Standard of Care for high risk nmCRPC patients was continuous ADT until they develop detectable metastatic disease

Smith MR, et al. J Clin Oncol. 2013;31:3800-6.

PSA value	PSMA results
0.2-0.49 ng/mL	30% Positive/70% Negative
0.5-0.99 ng/mL	60% Positive/40% Negative
1.0-3.9 ng/mL	80% Positive/20% Negative
> 4 ng/mL	90% Positive/10% Negative

Courtesy Dr. K. Pienta

Precision Medicine and Imaging

Clinical Cancer Research

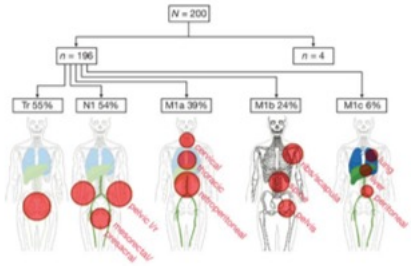
Prostate-Specific Membrane Antigen Ligand Positron Emission Tomography in Men with Nonmetastatic Castration-Resistant Prostate Cancer

Wolfgang P. Fendler[1,2], Manuel Weber[1], Amir Iravani[3], Michael S. Hofman[3], Jérémie Calais[2], Johannes Czernin[2], Harun Ilhan[4], Fred Saad[5], Eric J. Small[6], Matthew R. Smith[7], Paola M. Perez[6], Thomas A. Hope[6], Isabel Rauscher[8], Anil Londhe[9], Angela Lopez-Gitlitz[10], Shinta Cheng[11], Tobias Maurer[8,12], Ken Herrmann[1], Matthias Eiber[8], and Boris Hadaschik[1]

- PSMA-PET imaging was positive in 98% of patients, with similar detection rates in patients with PSADT of 10 months (97%) and those with a Gleason score of 8 (100%)
- ***After PSMA-PET,*** *a significant proportion of patients had stage migration: 24% of patients had disease confined to the prostate bed, 44% had disease limited to the pelvis,* ***and 55% had M1 disease.***

Fendler, et al. Clin Cancer Res. 2019 Dec 15;25(24):7448-7454

A



B

Variable	Median (months) Placebo	Apalutamide	Hazard ratio (95% CI)	Events/N Placebo	Apalutamide
All patients	16.2	40.5	0.30 (0.24–0.36)	194/401	184/806
Age, years					
<65	7.3	NE	0.14 (0.08–0.27)	25/43	19/106
≥65	18	40.5	0.33 (0.26–0.40)	169/358	165/700
Baseline ECOG					
0	15.7	40.5	0.27 (0.21–0.34)	150/311	133/623
1	18.4	27.8	0.40 (0.27–0.60)	44/89	51/183
Gleason score					
<8	21.2	40.5	0.36 (0.27–0.47)	95/218	98/443
≥8	11.1	NE	0.22 (0.16–0.30)	93/169	79/341
Baseline PSA					
<5.5	18.5	NE	0.25 (0.17–0.38)	60/148	40/298
≥5.5	14.5	40.5	0.30 (0.24–0.38)	134/253	144/508
PSA doubling time, months					
≤6	14.6	40.5	0.29 (0.23–0.36)	149/284	147/576
>6	22.8	NE	0.30 (0.20–0.47)	45/117	37/230
Locoregional disease					
N0	18.3	40.5	0.33 (0.26–0.41)	155/336	153/673
N1	10.8	NE	0.15 (0.09–0.25)	39/65	31/133
Prestudy local therapy					

Overview of prostate cancer lesion location depicted on PSMA-PET and subgroup analysis of SPARTAN patients. **A,** Three subregions with highest disease prevalence (red circles) are given for each miT/N/M stage. Circle area is proportional to prostate cancer lesion prevalence in the respective subregion. PSMA-PET PROMISE criteria allow patients to be counted under multiple categories. **B,** Metastasis-free survival in SPARTAN patients by subgroups including those stratified by risk factors of M1 disease by PSMA-PET. Baseline Eastern Cooperative Oncology Group (ECOG) performance status and variables associated with M1 disease in the PSMA-PET dataset were included. NE, not estimable; PRT, primary radiotherapy; RPE, radical prostatectomy; SRT, salvage radiotherapy.

Combination with MDT?

Il trattamento con Apalutamide riduce il rischio di metastasi

Alla comparsa, la maggior parte delle metastasi erano localizzate nell'osso ed in un unico sito (oligoprogressione)

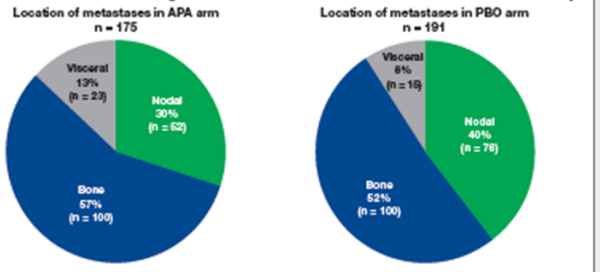
RESULTS (continued)

Table 1. Summary of Metastasis Sites in Patients With nmCRPC From the SPARTAN Study

	APA (N = 806)	PBO (N = 401)
Total patients with metastases, n (%)	175 (22)	191 (48)
	APA (n = 175)	**PBO (n = 191)**
Type of metastasis[a], n (%)		
Bone	100 (57)	100 (52)
Nodal	52 (30)	76 (40)
Any visceral	23 (13)	15 (8)
Number of sites[b], n (%)		
Single	161 (92)	165 (86)
Multiple	14 (8)	26 (14)

[a]Bone (bone ± M1 nodes), nodal (M1 nodes + soft tissue), and visceral (visceral, regardless of other sites). [b]Single, metastases occurring in a single type (bone, nodal, or visceral); multiple, metastases occurring in more than 1 type.

Figure 1. Site of Metastasis at Progression in Patients With nmCRPC From the SPARTAN Study[a]



[a]Only patients with confirmed baseline observations are included in this analysis.

Smith M.R, et al. Poster presented at ASCO 2018, Abstract 5033.

SACRO CUORE DON CALABRIA I R C C S
ARO ADVANCED RADIATION ONCOLOGY DEPARTMENT

Combination with MDT?

PSA DT > 10 mesi

Basso rischio
di sviluppare (poly) metastasi?

PSA DT ≤ 10 mesi

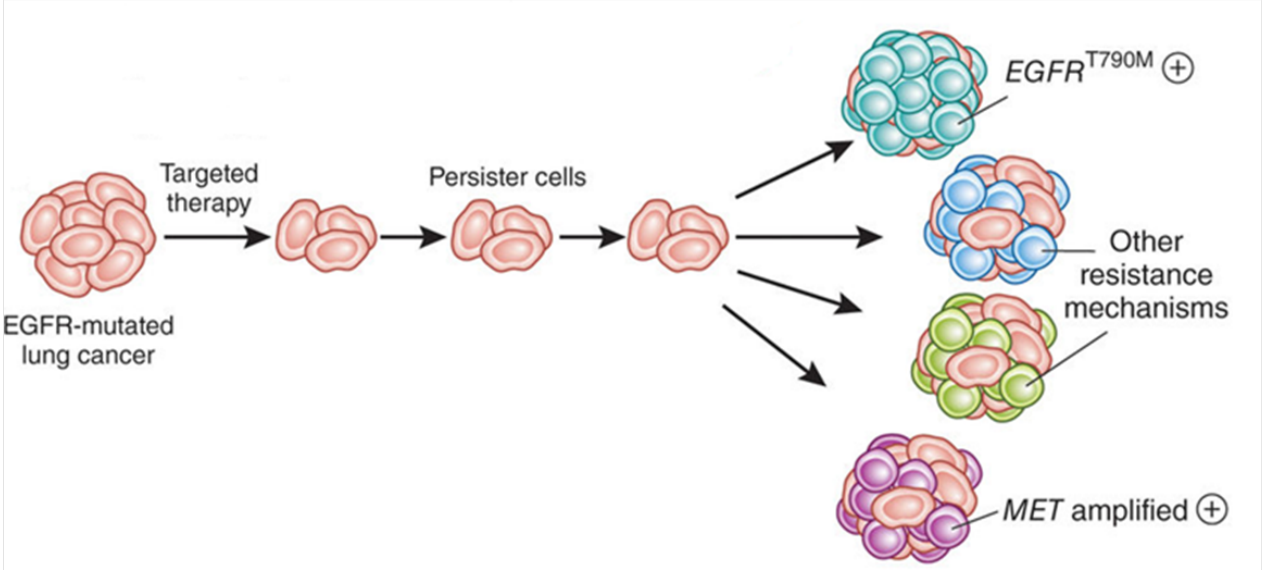
Alto rischio
Di sviluppare metastasi

NSCLC e colorectal oligometastases

Local ablative therapy in oligoprogressive disease: ***THE NSCLC MODEL***

- Oncogene-addicted disease (10-15%)
- Median disease-free survival in metastatic NSCLC treated with target therapy range between 8 and 13 months, but some patients present only with an oligo-progression
- **Clonal selection during target therapies - Clonal progressive disease?**
- Combining with Immunotherapy in order to increase the likelihood of abscopal effect

Local ablative therapy of oligoprogressive disease prolongs disease control by tyrosine kinase inhibitors in oncogene-addicted non-small-cell lung cancer



J Thorac Oncol. 2012 Dec;7(12):1807-14

THE NSCLC MODEL

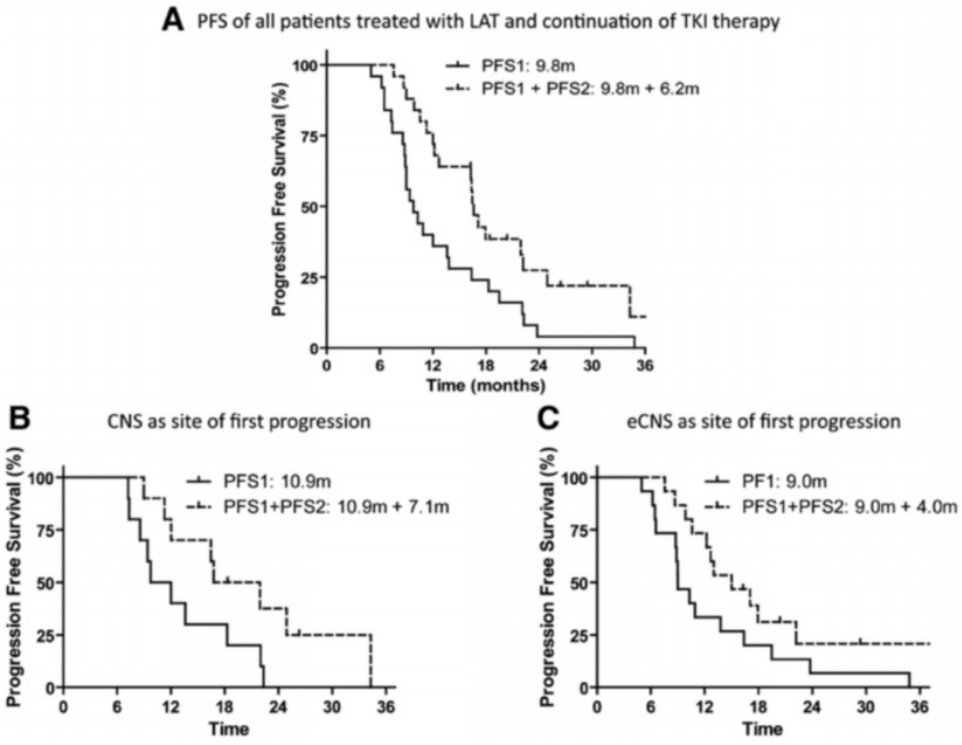


FIGURE 1. *A*, PFS1 and PFS1+PFS2 survival curves of all 25 patients treated with LAT. *B*, Ten patients treated with LAT who first progressed only in the CNS. *C*, Fifteen patients treated with LAT who first progressed in extra-CNS locations, including three patients with simultaneous CNS and eCNS progression. PFS1, median progression-free survival; PFS2, progression-free survival from the time of first progression; LAT, local ablative therapy; CNS, central nervous system; eCNS, extra-CNS.

Weickhardt et al. *Journal of Thoracic Oncology* • Volume 7, Number 12, December 2012

THE NSCLC MODEL

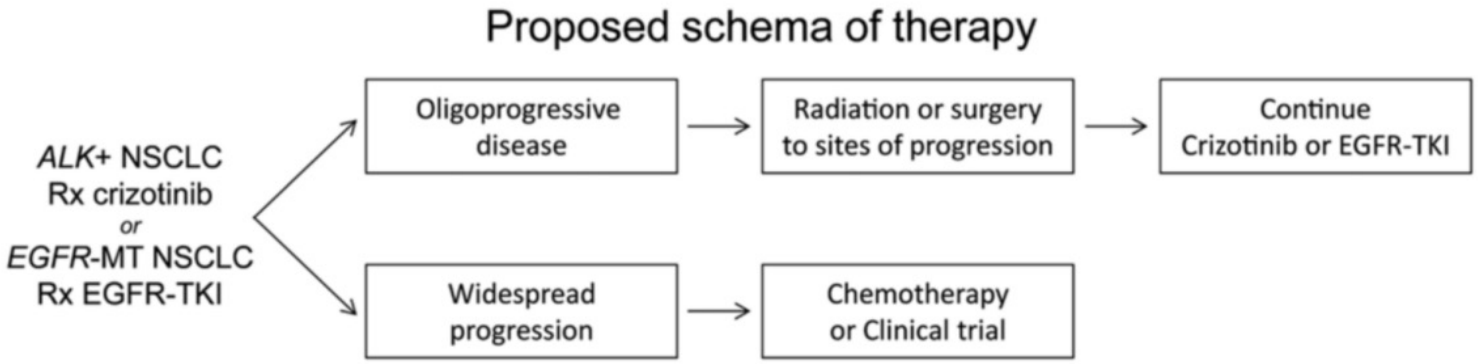


FIGURE 2. Proposed schema for incorporating local ablative therapy into therapy at time of first progression with *ALK*+ or *EGFR*-MT NSCLC patients treated with TKI therapy. *ALK*+, anaplastic lymphoma kinase gene rearrangement; *EGFR*-MT NSCLC, epidermal growth factor receptor-mutant non–small-cell lung cancer; TKI, tyrosine kinase inhibitors.

THE NSCLC MODEL

Table 2 Clinical outcomes by the selected studies

Authors (year of publication)	Local Control	Distant progression free survival	Overall Survival	Toxicity
Theelen et al. (2019) [17]	NS	6.6 months	15.9 months	12 > G3
Lesueur et al. (2018) [20]	64,4% 2 yr	2,7 months	11,1 months	14,4% > G3
Chen et al. (2018) [15]	88% 1 yr	2.3 months	24,7 months	16% > G3
Schapira et al. (2017) [21]	100% 1 yr	N.S.	17.6 months	0 ≥ G4
Bauml et al. (2019) [19]	N.S.	19.1 months	41.6 months	5 > G3
Hubbeling et al. (2018) [22]	N.S.	N.S.	N.S.	9 > G3
Verma et al. (2018) [16]	N.S.	N.S.	N.S.	25 > G3

PEMBRO-RT TRIAL enrolled NSCLC patients with at least 2 metastases (upper limit was not specified).

- Patients were randomized to receive Pembrolizumab or Pembrolizumab + SBRT to a single metastatic site, in order to increase the likelihood of abscopal effect.
- Objective response rate at 12 weeks was doubled (36% vs 18%)
- Median PFS and OS were also improved (6.6 months and 15.9 months respectively)
- Addition of SBRT to Pembrolizumab did not increase toxicity *JAMA Oncol. 2019 Jul 11;5(9):1276-82*

SACRO CUORE DON CALABRIA I R C C S
ARO ADVANCED RADIATION ONCOLOGY DEPARTMENT

Liver colorectal oligomts

Surgical Treatment of Hepatic Metastases From Colorectal Cancers

Stephen M. Wilson, MD, Martin A. Adson, MD

• Follow-up data covering periods of two to 23 years have been collected on 60 patients who had resection of hepatic metastases for colorectal cancer. Multiple lesions were removed from 20 patients, and solitary lesions were excised from the other 40 patients.

Only one patient died during hospital convalescence. No patient who had multiple lesions excised lived for five years. In contrast, 15 of the 36 patients eligible for five-year survival study who had resection of apparent solitary lesions lived for five years or more, and eight patients were alive without evidence of recurrence ten years or more after operation.

These surprisingly favorable results of surgical treatment were analyzed in relation to results in patients who had biopsy specimens taken of lesions of comparable size and number, but no removal at the time of colonic resection. No patient in this control group lived for five years. Aggressive surgical treatment of apparent solitary hepatic metastatic lesions from colorectal cancer seems to be justified by the survival rate of surgically treated patients.

(*Arch Surg* 111:330-334, 1976)

Nearly 15 years ago, Waugh[1] reported his personal experience in our clinic with resection of various tumors that had metastasized to the liver. He found that 20% of patients survived five years or more after resection, without evidence of recurrence. Operative mortality was 4%.

Accepted for publication Dec 4, 1975.

From the departments of surgery, Mayo Clinic and Mayo Foundation (Dr Adson) and the Mayo Graduate School of Medicine, University of Minnesota (Dr Wilson), Rochester.

Read before the 83rd annual meeting of the Western Surgical Association, Colorado Springs, Colo, Nov 20, 1975.

Some surgeons accepted this report as justification for an aggressive approach to hepatic metastases. However, even within our clinic, various attitudes regarding the management of such lesions are evident. Surgical decisions seem to reflect personal philosophies more than a uniform plan of treatment, and a consistent policy of surgical consultation for patients who have hepatic metastases has not been adopted by our colleagues in medical gastroenterology.

The reasons for divergent views are many. Pessimism is fostered by the frequent occurrence of multiple, obviously unresectable lesions, and the apparently solitary metastatic lesion is suspect relative to problems in detecting other foci of disseminated cancer. Also, the results of treatment are difficult to assess in relation to great variations in the natural history of some metastatic lesions,[2,3] and in some collective reviews, the reported operative risk of surgical treatment is distressingly similar to the chance for significant palliation or cure.[4-6]

Recognizing the need for reasonable guidelines for the management of hepatic metastases, we have reassessed the results of surgical treatment and made a comparative analysis with a control group of patients. This review is limited to patients who had primary tumors in the colon and rectum.

SUBJECTS AND METHODS

Sixty patients with colorectal cancer underwent resection of hepatic metastases during the years 1949 through 1972. The records were analyzed with reference to the location, histologic

"For liver-only resectable metastases, surgery is recommended, representing the first therapeutic aim, in association or not with perioperative chemotherapy"

Lì, 1975

From 1975 to 2021….

There are no randomized trials between radiotherapy and other local modalities or surgery

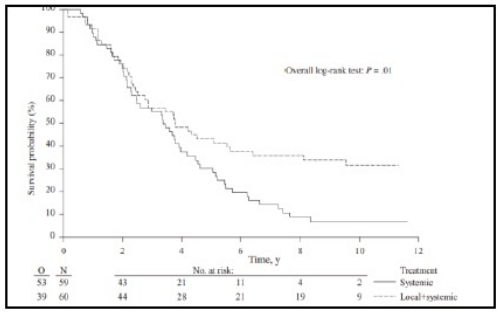
Unresectable colorectal liver metastases: the importance of patient selection…..

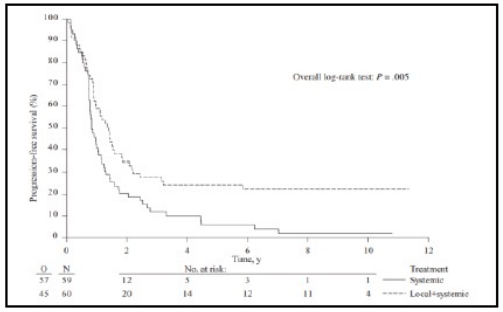
EORTC 4004

ARTICLE

Local Treatment of Unresectable Colorectal Liver Metastases: Results of a Randomized Phase II Trial

Theo Ruers, Frits Van Coevorden, Cornelis J. A. Punt, Jean-Pierre E. N. Pierie, Inne Borel-Rinkes, Jonathan A. Ledermann, Graeme Poston, Wolf Bechstein, Marie-Ange Lentz, Murielle Mauer, Gunnar Folprecht, Eric Van Cutsem, Michel Ducreux, Bernard Nordlinger; for the European Organisation for Research and Treatment of Cancer (EORTC) Gastro-Intestinal Tract Cancer Group, Arbeitsgruppe Lebermetastasen und tumoren in der Chirurgischen Arbeitsgemeinschaft Onkologie (ALM-CAO), and the National Cancer Research Institute Colorectal Clinical Study Group (NCRI CCSG)





Improved OS for pts with up to 9 mets receiving RFA + systemic therapy vs systemic therapy alone (Combined modality treatment arm: 5-year OS: 43.1%; 8-year OS: 35-9%). Median OS: 45-6 moths

‘Ideal colorectal liver metastasis,’ **that is, surgically unresectable**, solitary tumor up to 3 cm, that can be completely destructed percutaneously, and, in selected cases, 5-year overall survival (OS) up to 70% have been reported

Visc Med 2017; 33:62–68.

SACRO CUORE DON CALABRIA I R C C S

ARO ADVANCED RADIATION ONCOLOGY DEPARTMENT

Evidences for isolated colorectal pulmonary metastases?

- About 5% of the patients with CRC will develop isolated pulmonary metastases
- Randomized clinical trials are not available
- Highly selected patients (disease free interval >36 months, number of metastases < 3 mo. normal CEA and absence of hilar or mediastinal nodes) can benefit from a resection, leading to 5-year OS ranging from 45 to 65%

Page`s PB, Rev Mal Respir 2016; 33:838–852

Colorectal oligomts

Clinical Oncology 28 (2016) 505–512

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Original Article

Exploratory Analysis on Overall Survival after Either Surgery or Stereotactic Radiotherapy for Lung Oligometastases from Colorectal Cancer

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Received 13 May 2015; received in revised form 13 January 2016; accepted 14 January 2016

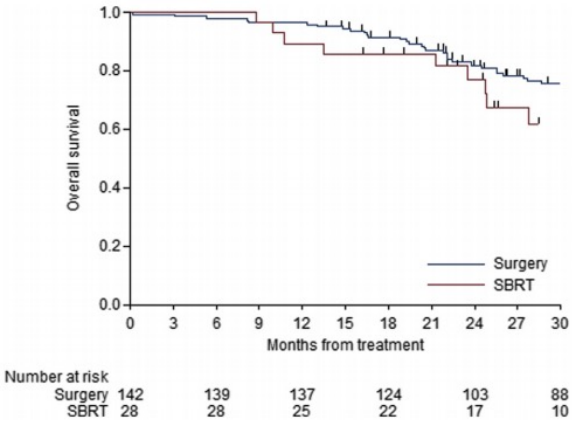

Fig 1. Overall survival according to the treatment received.

Propensity score analysis - at 2 years, overall survival estimates were comparable -

82% for surgery (95% CI 0.74-0.87) **77% for SBRT** (95% CI 0.56-0.89)

Beyond 24 months, any reliable evaluation is impaired by the limited follow-up time of the SBRT cohort (median 27 months).

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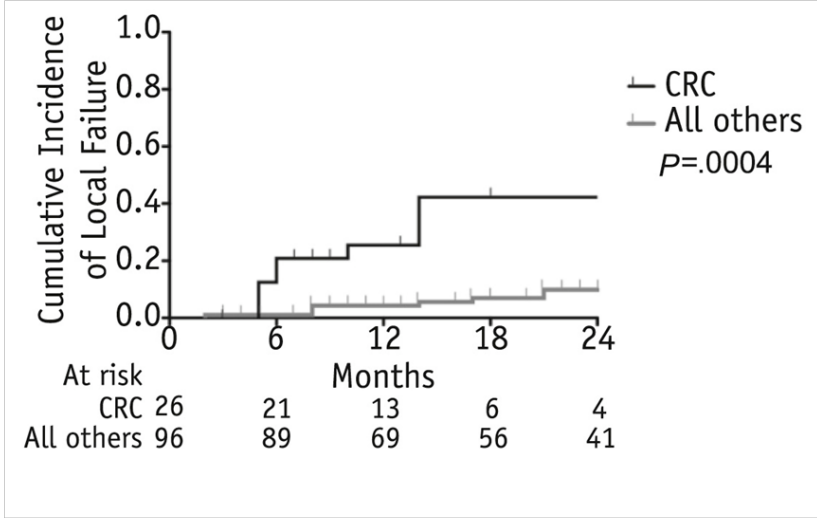
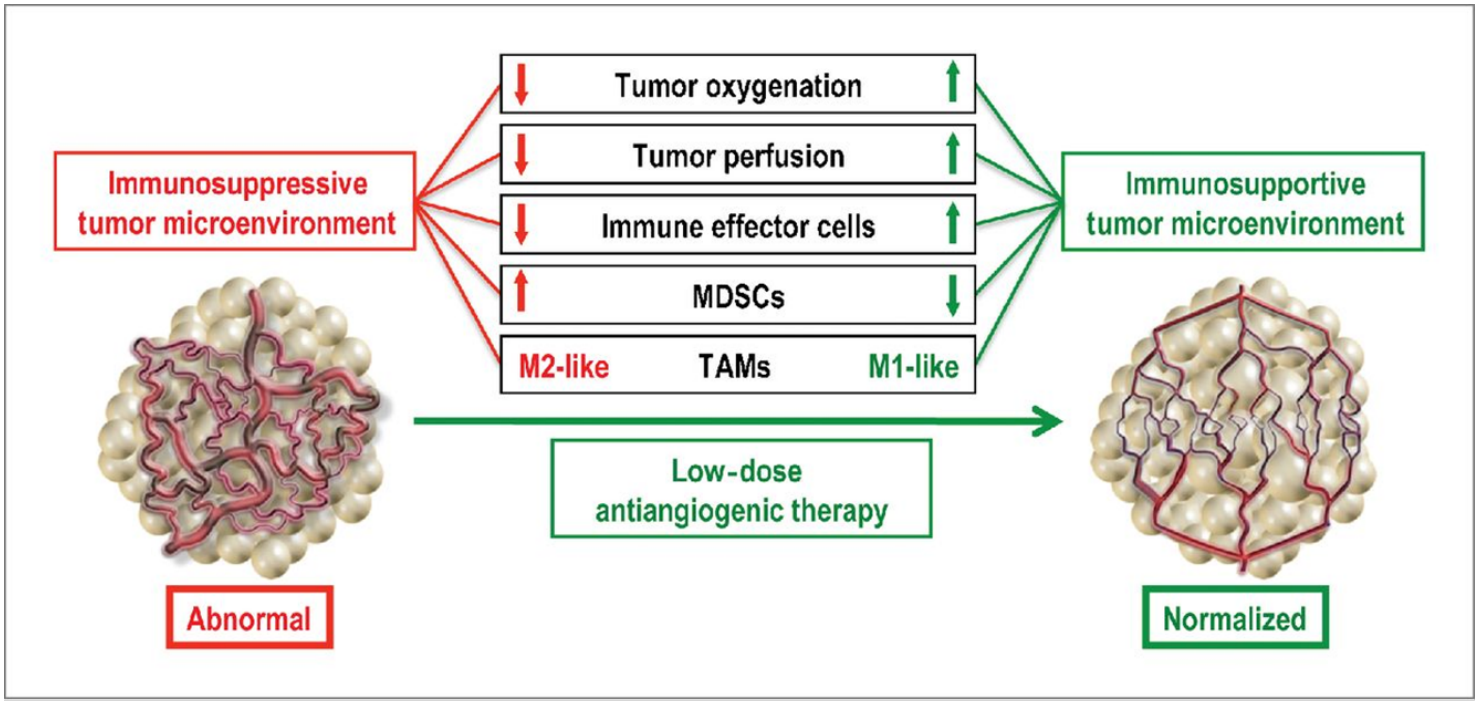
ARO ADVANCED RADIATION ONCOLOGY DEPARTMENT

Colorectal Histology Is Associated With an Increased Risk of Local Failure in Lung Metastases Treated With Stereotactic Ablative Radiation Therapy

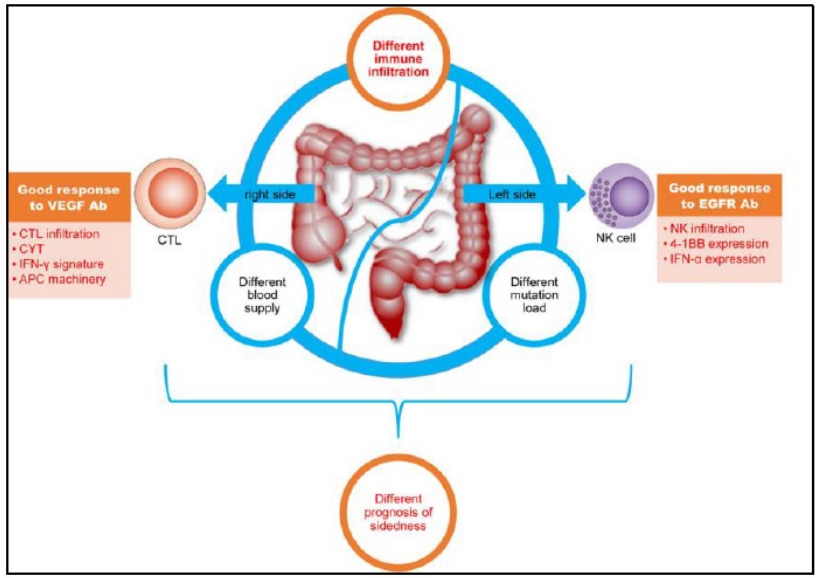
International Journal of Radiation Oncology biology • physics
www.redjournal.org

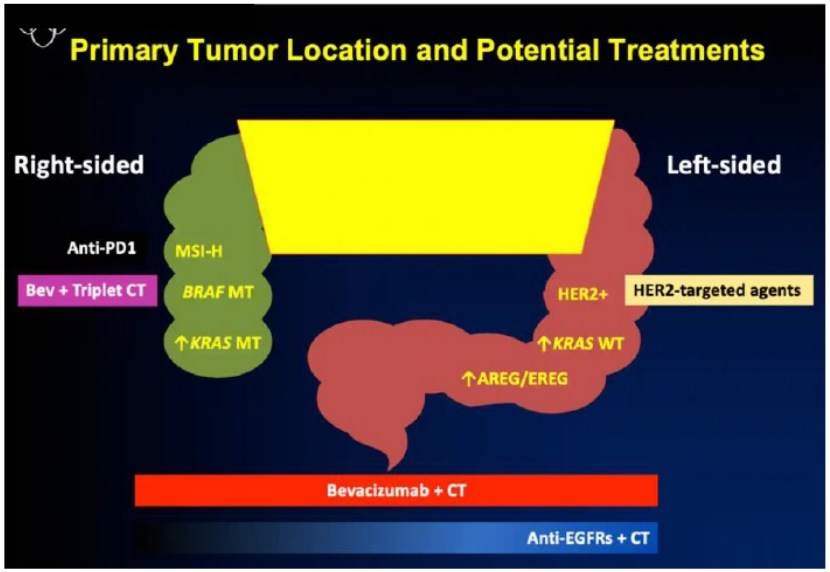


Binkley et al. IJROBP, 2015



Huang Y, Cancer Res 2013


Different immune infiltration
Good response to VEGF Ab
• CTL infiltration
• CYT
• IFN-γ signature
• APC machinery
CTL
right side
Left side
NK cell
Good response to EGFR Ab
• NK infiltration
• 4-1BB expression
• IFN-α expression
Different blood supply
Different mutation load
Different prognosis of sidedness


Primary Tumor Location and Potential Treatments
Right-sided
Left-sided
Anti-PD1
MSI-H
Bev + Triplet CT
BRAF MT
↑KRAS MT
HER2+
HER2-targeted agents
↑KRAS WT
↑AREG/EREG
Bevacizumab + CT
Anti-EGFRs + CT

the LaIT-SABR study

Patients affected by lung oligometastases from colorectal cancer treated with SABR

Primary end-point:

- Identification of biological and dosimetrical parameters predictive for local control (EGFR, KRAS, NRAS, BRAF, MSI, dose, fractionation, volume)

Secondary end-point:

- Time to polymetastatic conversion (tPMC)

Large Retrospective Database
1023 lung metastases in 622 colorectal cancer patients

SACRO CUORE DON CALABRIA I R C C S
ARO ADVANCED RADIATION ONCOLOGY DEPARTMENT

Stereotactic ablative body radiotherapy in patients with oligometastatic cancers: a prospective, registry-based, single-arm, observational, evaluation study

Anastasia Chalkidou, Thomas Macmillan, Mariusz T Grzeda, Janet Peacock, Jennifer Summers, Saskia Eddy, Bola Coker, Hannah Patrick, Helen Powell, Lee Berry, Gareth Webster, Peter Ostler, Peter D Dickinson, Matthew Q Hatton, Ann Henry, Stephen Keevil, Maria A Hawkins, Nick Slevin, Nicholas van As

Findings Between June 15, 2015, and Jan 30, 2019, 1422 patients were recruited from 17 hospitals in England. The median age of the patients was 69 years (IQR 62–76), and the most common primary tumour was prostate cancer (406 [28·6%] patients). Median follow-up was 13 months (IQR 6–23). Overall survival was 92·3% (95% CI 90·5–93·9) at 1 year and 79·2% (76·0–82·1) at 2 years. The most common grade 3 adverse event was fatigue (28 [2·0%] of 1422 patients) and the most common serious (grade 4) event was increased liver enzymes (nine [0·6%]). No treatment-related deaths were reported.

Interpretation In patients with extracranial oligometastatic cancer, use of SABR was associated with high overall survival and low toxicity. 'The study findings complement existing evidence from a randomised, phase 2 trial, and represent high-level, real-world evidence supporting the use of SABR in this patient cohort, with a phase 3 randomised, controlled trial to confirm these findings underway. Based on the selection criteria in this study, SABR was commissioned by NHS England in March, 2020, as a treatment option for patients with oligometastatic disease.

Funding NHS England Commissioning through Evaluation scheme.

SACRO CUORE DON CALABRIA I R C C S

ARO ADVANCED RADIATION ONCOLOGY DEPARTMENT

Stereotactic ablative body radiotherapy in patients with oligometastatic cancers: a prospective, registry-based, single-arm, observational, evaluation study

Anastasia Chalkidou, Thomas Macmillan, Mariusz T Grzeda, Janet Peacock, Jennifer Summers, Saskia Eddy, Bola Coker, Hannah Patrick, Helen Powell, Lee Berry, Gareth Webster, Peter Ostler, Peter D Dickinson, Matthew Q Hatton, Ann Henry, Stephen Keevil, Maria A Hawkins, Nick Slevin, Nicholas van As

Primary tumour diagnosis	
Prostate cancer	406 (28·6%)
Colorectal cancer	397 (27·9%)
Renal cancer	143 (10·1%)
Breast cancer	78 (5·5%)
Lung cancer	64 (4·5%)
Melanoma	58 (4·1%)
Other†	
Known site	
Yes	
Missing	
Site of first	
Lung	
Spine	
Bone	
Adrenal	
Liver	135 (9·6%)
Lymph nodes	439 (31·3%)
Other‡	77 (5·5%)
Known number of metastases	
Yes	1421 (99·9%)
Missing*	1 (0·1%)
Number of metastases (n=1421)	
1	1074 (75·6%)
2	279 (19·6%)
3	68 (4·8%)

(Table 1 continues in next column)

Interpretation In patients with extracranial oligometastatic cancer, use of SABR was associated with high overall survival and low toxicity. 'The study findings complement existing evidence from a randomised, phase 2 trial, and represent high-level, real-world evidence supporting the use of SABR in this patient cohort, with a phase 3 randomised, controlled trial to confirm these findings underway. Based on the selection criteria in this study, SABR was commissioned by NHS England in March, 2020, as a treatment option for patients with oligometastatic disease.

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	Overall survival (95% CI)
Prostate cancer (n=406)	
1 year	NA*
2 year	94·6% (90·4–97·0)
Colon cancer (n=233)	
1 year	92·0% (86·6–95·3)
2 year	80·3% (71·8–86·5)
2 year	83·2% (69·5–91·2)
Lung cancer (n=64)	
1 year	80·2% (67·1–88·6)
2 year	65·4% (50·6–76·7)
Melanoma (n=58)	
1 year	NA*
2 year	60·5% (38·0–77·0)

NA=not available. *Survival estimates only obtained by Kaplan-Meier analysis when more than five events (deaths) occurred.

Table 2: **Overall survival estimates at 1 year and 2 years after the start of stereotactic ablative body radiotherapy by primary tumour histology**

Lancet Oncol 2021; 22: 98–106

Summary: what have we learned?

- Some patients with oligometastases can be cured
- Promising Phase II randomized data about the role of ablative treatments in patients with oligometastases
- We are entering in the era of phase III trials… the future will be exciting! (Or not!)