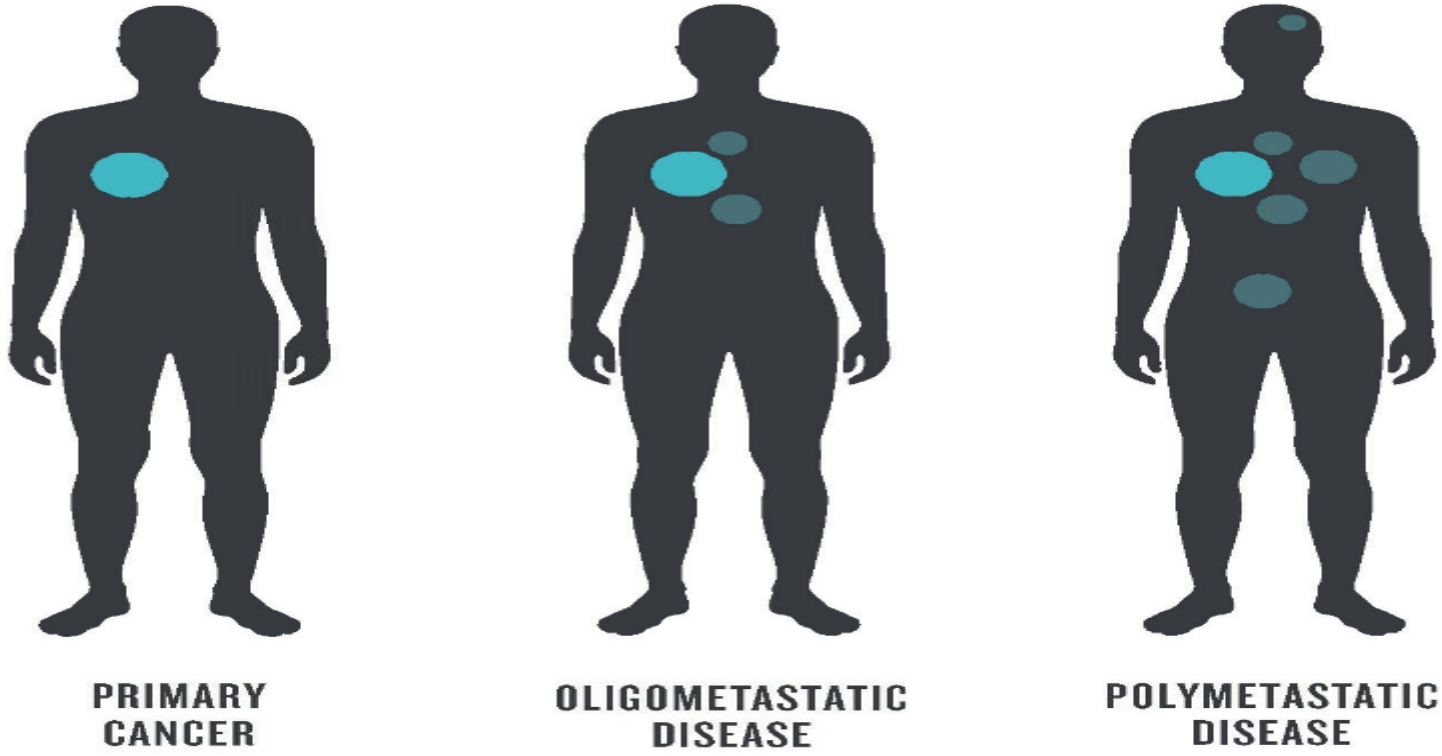

Oligometastatic HNSCC: Where are we now?

Lauren Mayo, MD

Associate Professor, MD Anderson Cancer Center

Ochsner Multidisciplinary Cancer Update, October 10, 2025

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No Disclosures

Background & Rationale For Treating Oligo Disease

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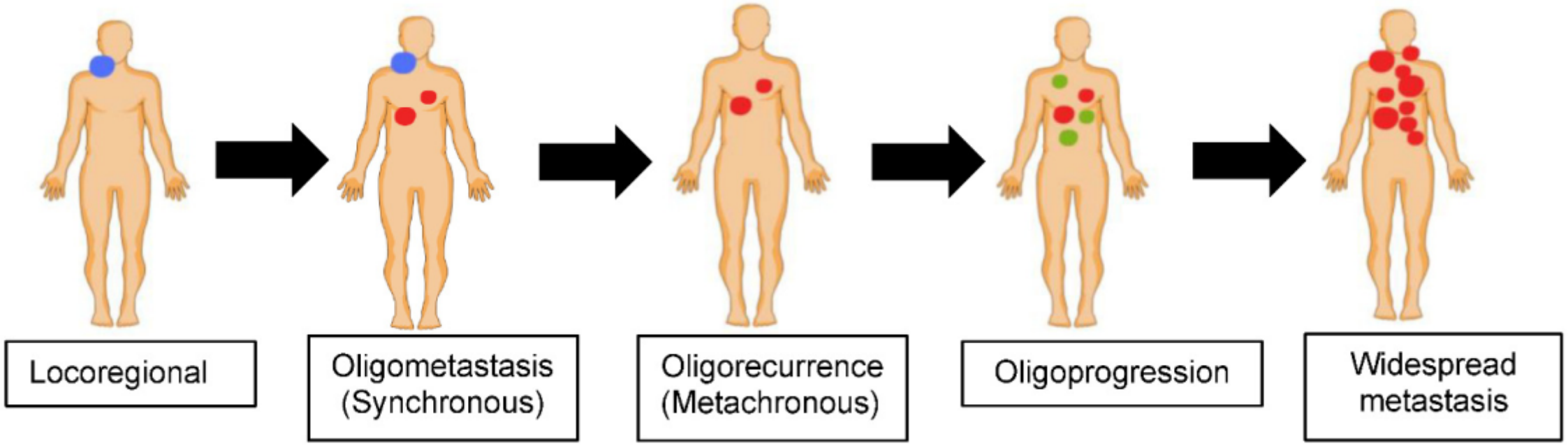
Definitions:

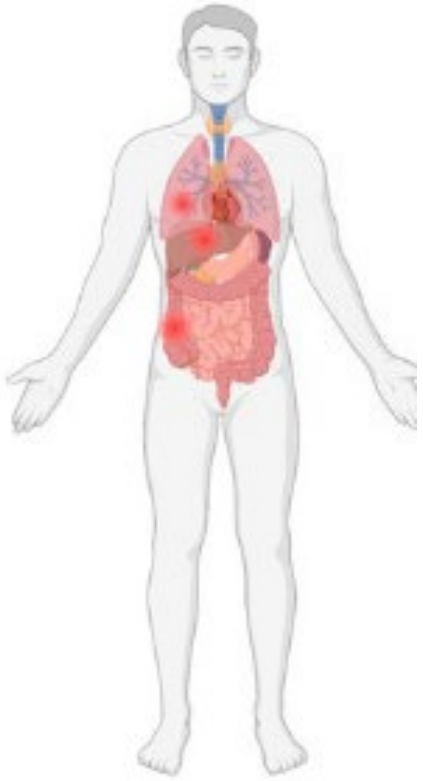


Bahig, Huang, O'Sullivan. Cancers 2022

Definitions

Definition of Oligometastatic:

- ESMO: up to 3 metastases
- NCCN: 3-5 metastases
- EORTC: up to 5 metastases in up to 3 organs[a]

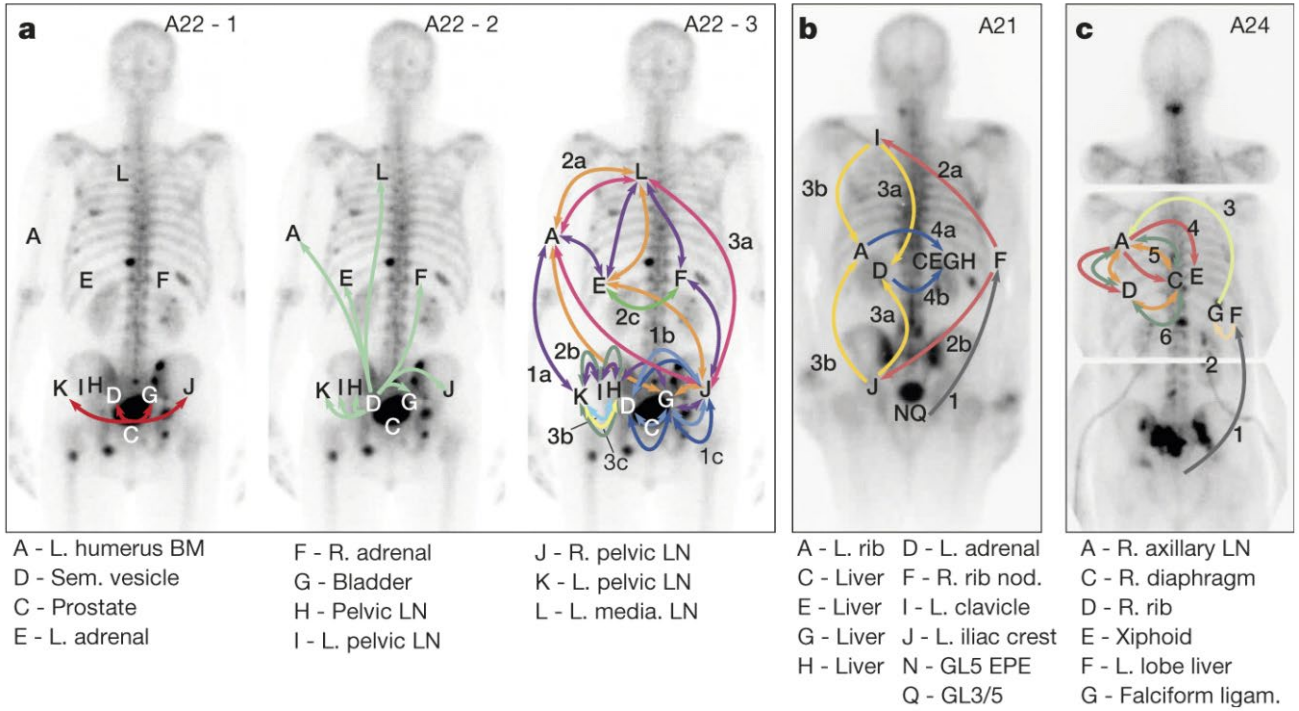


SABR= Stereotactic Ablative Radiation Therapy

SBRT= Stereotactic Body Radiation Therapy

MDT= Metastasis Directed Therapy

Metastasis-to-metastasis seeding occurs either by a linear or by a branching pattern of spread.



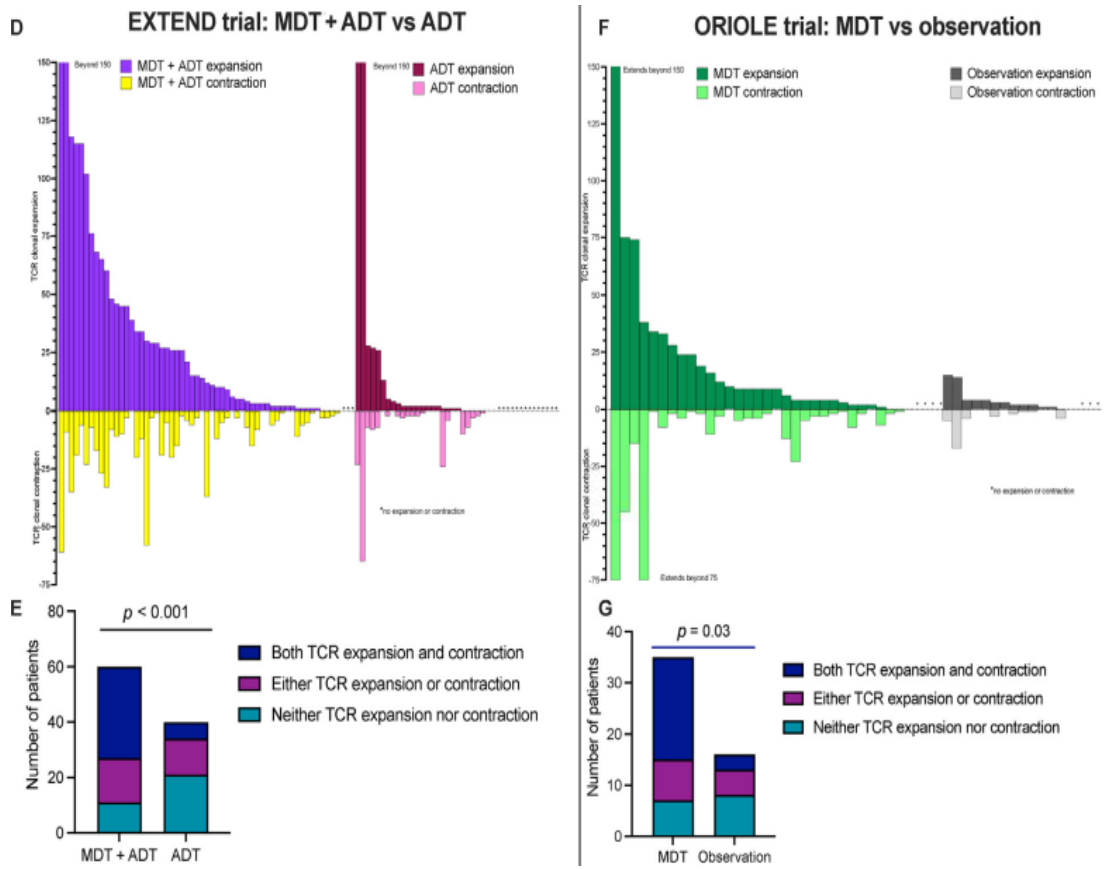
G Gundem *et al. Nature* **000**, E1-E5 (2015) doi:10.1038/nature14347

nature

- Identified metastasis can be seeded by:
  - Subclones from primary tumor
  - Subclones from other metastatic sites
  - Polyclonal seeding (multiple subclones) seed distant sites. Not just single cell seeding.
  - Linear from metastasis to metastasis
  - Branched from 1 metastasis seeding 2 or more sites

SABR effects on immunity?

- **Priming effect**
  - Focused high dose RT causes immunogenic tumor cell death by activating cross-presenting DCs and priming CD8 T cells
- **Better Tumor visibility to T Cells**
  - RT increases MHC-I expression and reshapes the peptide repertoire on tumor cells, making them easier targets for cytotoxic T cells.
- **Fractionation matters**
  - Very large single fractions can induce TREX1, which chews up the cytosolic DNA signal and blunts STING/type-I IFN. Repeated moderate fractions (e.g., ~8 Gy × 3) stay below that TREX1 threshold and are more immunogenic.
- **Fixing adaptive resistance**
  - RT + anti-CTLA-4 can induce PD-L1–mediated T-cell exhaustion; adding PD-1/PD-L1 blockade restores responses—i.e., RT creates targets and checkpoint blockade keeps T cells active.



AD Sherry et al. Eur Urol 2025

SABR-COMET Palma et al. Lancet 2019

- A randomized, open-label, phase II screening trial conducted across 10 centers in Canada, Netherlands, Scotland, and Australia.
- Included adult patients (≥18 years) with a controlled primary tumor and 1 to 5 metastatic lesions, good performance status (ECOG 0–1), and life expectancy ≥6 months.
- Randomization was in a 1:2 ratio: standard palliative systemic alone (control) versus standard of care plus SABR (stereotactic ablative radiotherapy) to all metastases
- N=99 included breast, prostate, colorectal, lung and HN (<10%)
- Median FU 51 months

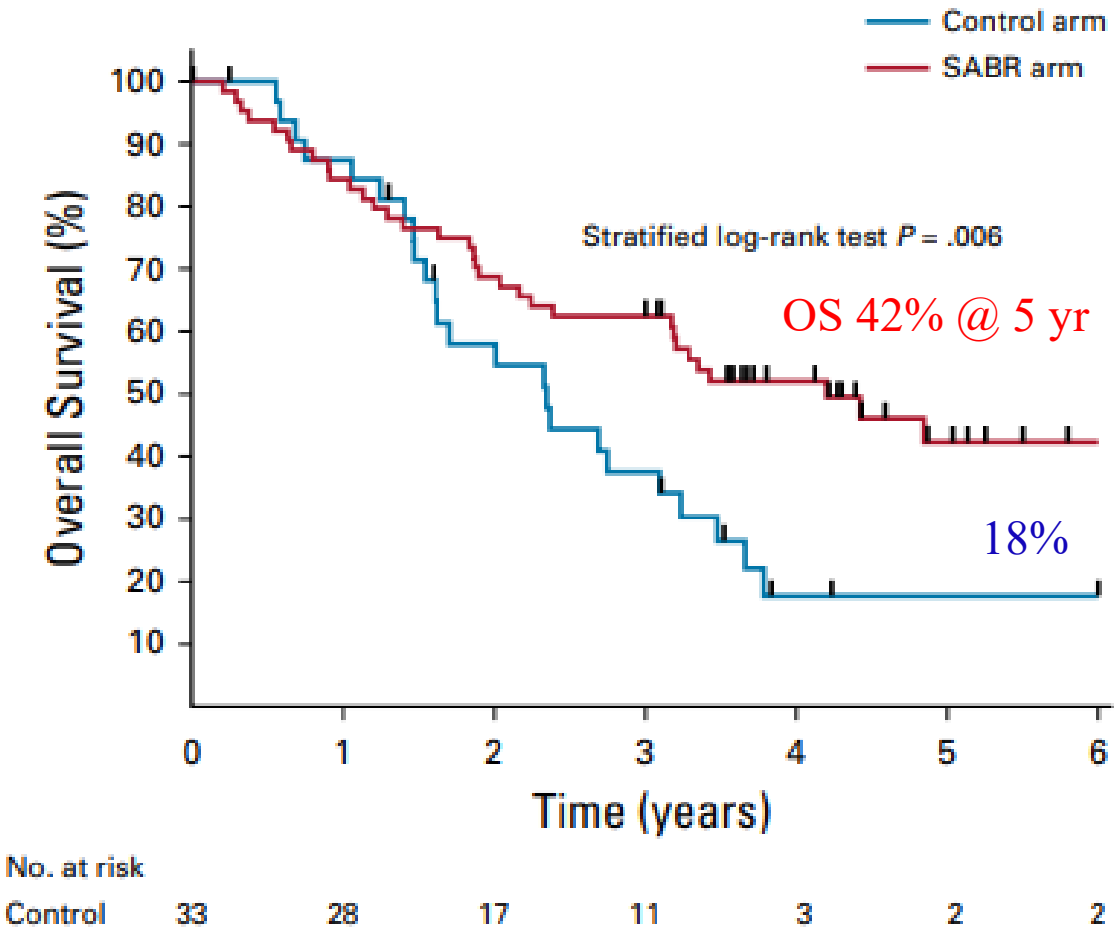
	Control group (n=33)	SABR group (n=66)
Age	69 (64-75)	67 (59-74)
Sex		
Men	19 (58%)	40 (61%)
Women	14 (42%)	26 (39%)
Site of original primary tumour		
Breast	5 (15%)	13 (20%)
Colorectal	9 (27%)	9 (14%)
Lung	6 (18%)	12 (18%)
Prostate	2 (6 %)	14 (21%)
Other	11 (33%)	18 (27%)
Time from diagnosis of primary tumour to randomisation (years)	2·3 (1·3-4·5)	2·4 (1·6-5·3)
Number of metastases		
1	12 (36 %)	30 (46%)
2	13 (40%)	19 (29%)
3	6 (18%)	12 (18%)
4	2 (6%)	2 (3%)
5	0 (0%)	3 (5%)
Location of metastases		
Adrenal	2/64 (3%)	7/127 (6%)
Bone	20/64 (31%)	45/127 (35%)
Liver	3/64 (5%)	16/127 (13%)
Lung	34/64 (53%)	55/127 (43%)
Other*	5/64 (8%)	4/127 (3%)

Data are n (%), n/N (%), or median (IQR). SABR=stereotactic ablative radiotherapy. *Other comprises brain (n=3 lesions in control group; n=1 lesion in SABR group), lymph nodes (n=1 lesion in control group; n=3 lesions in SABR group), and para-renal (n=1 lesion in control group).

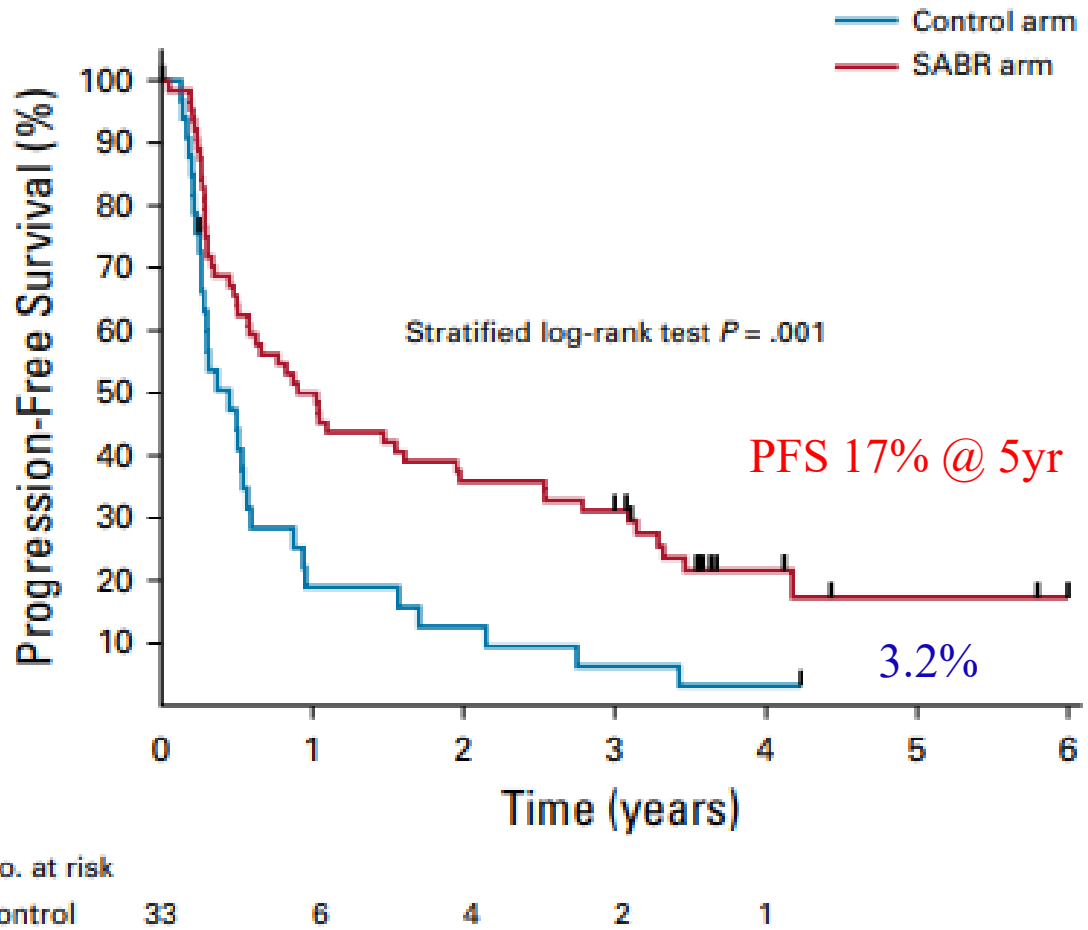
***Table 1:* Baseline characteristics**

SABR-COMET Palma et al. JCO 2020

Median OS 41 vs. 28 mo



PFS 12 vs. 6 mo



Local Consolidation vs. Maintenance in NSCLC DR Gomez. JCO 2019

- Phase II, Randomized, Median FU 39 mo
- Population: Patients with stage IV NSCLC, three or fewer metastases, and no progression after ≥3 months of first-line systemic therapy (e.g., platinum doublets or EGFR/ALK inhibitors)
- Randomization (1:1):LCT arm: Local consolidative therapy (radiotherapy or surgery to all active sites) ± maintenance therapy/observation.MT/O arm: Maintenance therapy or simple observation
- Primary endpoint: Progression-free survival (PFS).
- Secondary endpoints: Overall survival (OS), toxicity, and emergence of new lesions
- The trial enrolled 49 patients and was closed early because of a pronounced PFS benefit in the LCT arm

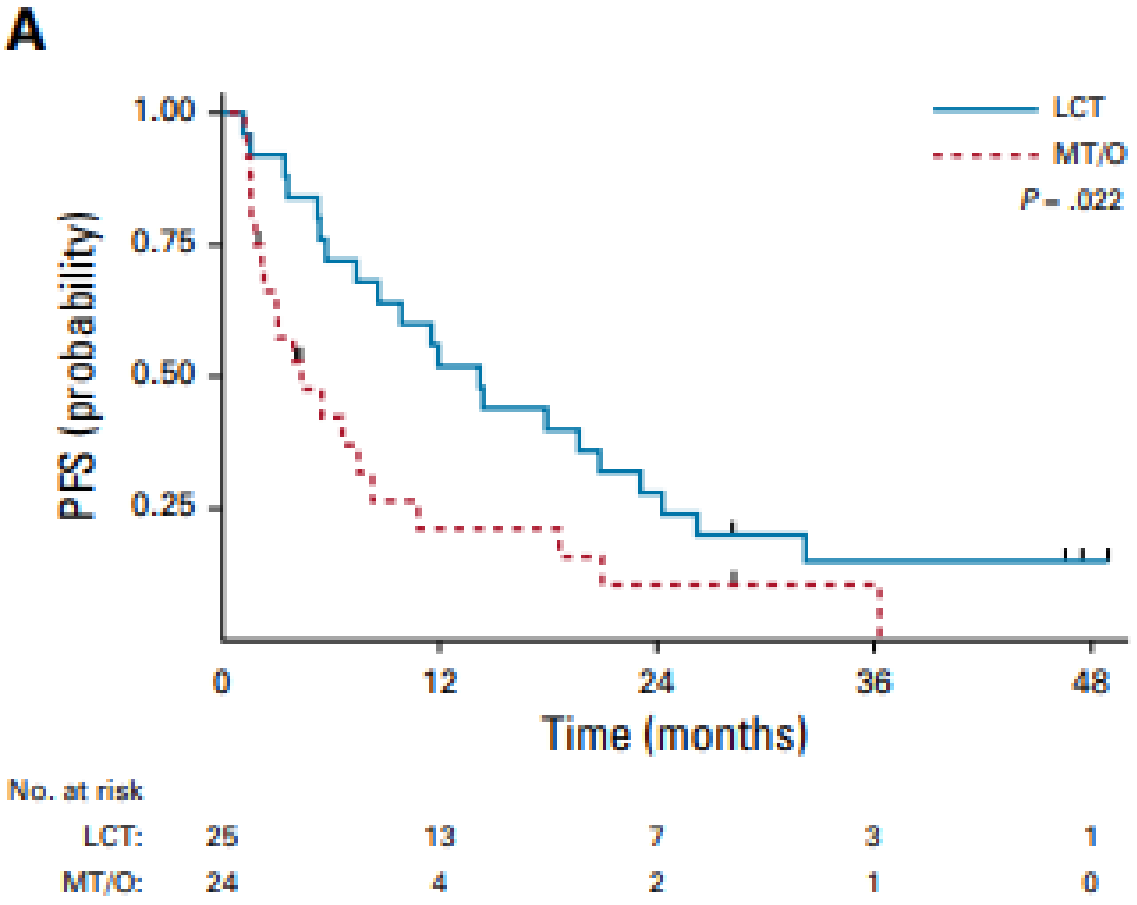
TABLE 1. Patient Characteristics

Characteristic	No. (%) of Patients		
	LCT (n = 25)	No LCT (n = 24)	Total (N = 49)
Age, years			
Mean ± standard deviation	64 ± 10	63 ± 10	63 ± 10
Median (range)	63 (43-83)	61 (43-80)	61 (43-83)
Sex			
Male	12 (48)	10 (42)	22 (45)
Female	13 (52)	14 (58)	27 (55)
Ethnicity			
White	20 (80)	18 (75)	38 (78)
Black	2 (8)	3 (12)	5 (10)
Hispanic	2 (8)	0 (0)	2 (4)
Asian	1 (4)	3 (12)	4 (8)
Tumor histology			
Adenocarcinoma	21 (84)	18 (75)	39 (80)
Adenosquamous	0 (0)	1 (4)	1 (2)
NSCLC, NOS	1 (4)	0 (0)	1 (2)
Poorly differentiated NSCLC, NOS	2 (8)	0 (0)	2 (4)
SCC	1 (4)	4 (17)	5 (10)
Sarcomatoid carcinoma	0 (0)	1 (4)	1 (2)
Timing of metastatic disease			
Metachronous	1 (4)	2 (8)	3 (6)
Synchronous	24 (96)	22 (92)	46 (94)
No. of nonregional metastases after initial systemic therapy			
0-1	17 (68)	15 (62)	32 (65)
2-3	8 (32)	9 (38)	17 (35)
Response to first-line chemotherapy			
PR/CR	9 (36)	9 (38)	18 (37)
SD	16 (64)	15 (62)	31 (63)
CNS metastases			
No	18 (72)	18 (75)	36 (73)
Yes	7 (28)	6 (25)	13 (27)
Nodal status			
N0/N1	12 (48)	11 (46)	23 (47)
N2/N3	13 (52)	13 (54)	26 (53)
Mutation type			
None	20 (80)	21 (88)	41 (84)
EGFR	3 (12)	3 (12)	6 (12)
EML4ALK	2 (8)	0 (0)	2 (4)

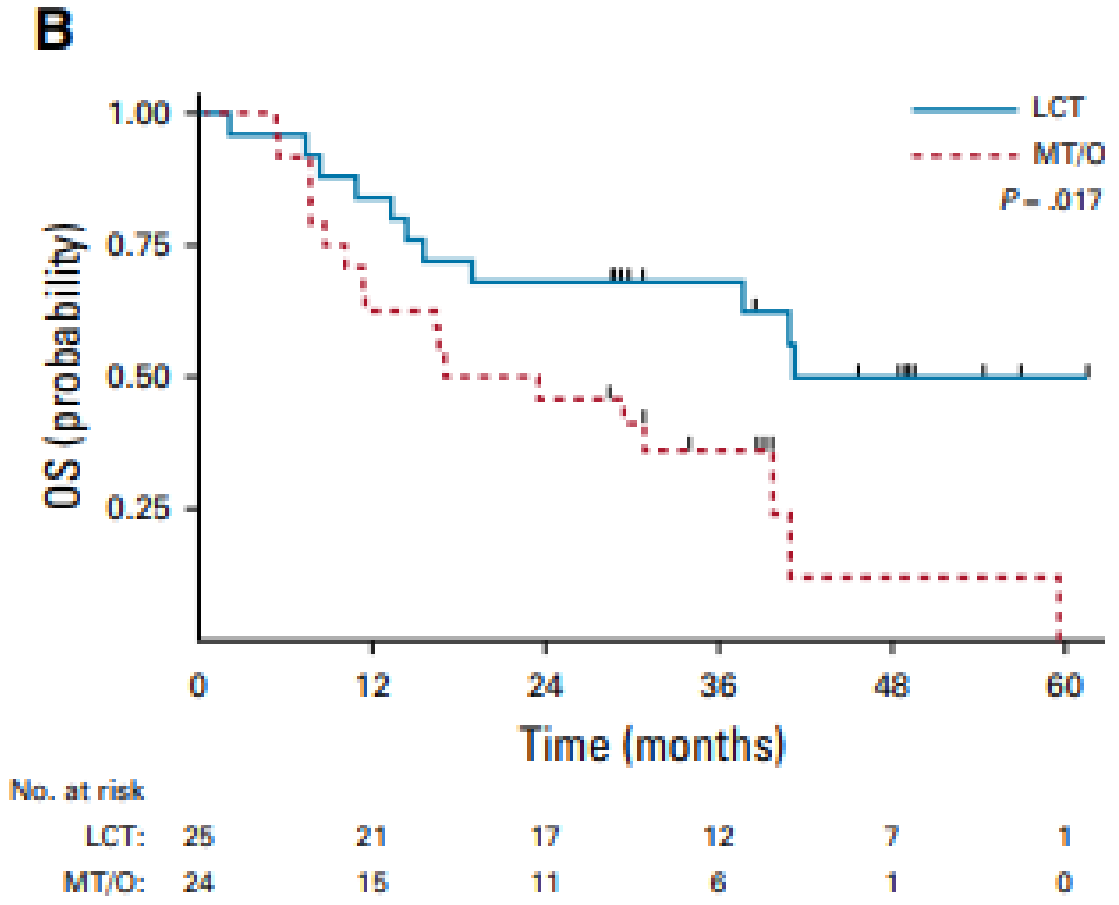
Abbreviations: LCT, local consolidative therapy; NSCLC, non–small-cell lung cancer; NOS, not otherwise specified; SCC, squamous cell carcinoma; PR, partial response; CR, complete response; SD, stable disease.

Local Consolidation vs. Maintenance in NSCLC DR Gomez. JCO 2019

Median PFS 14.2 vs. 4.4 mo

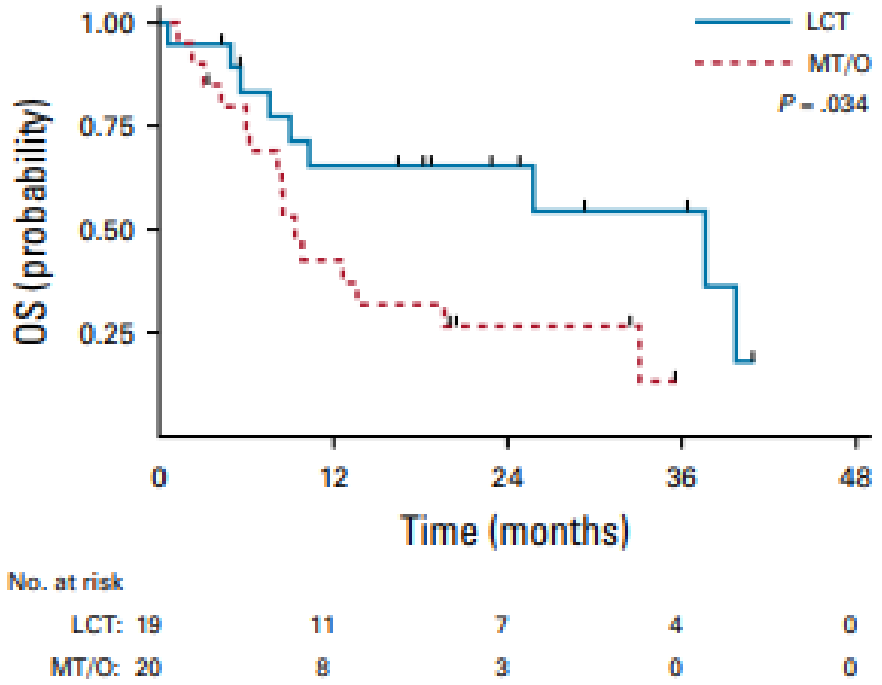


Median OS 41.2 vs. 17.0 mo

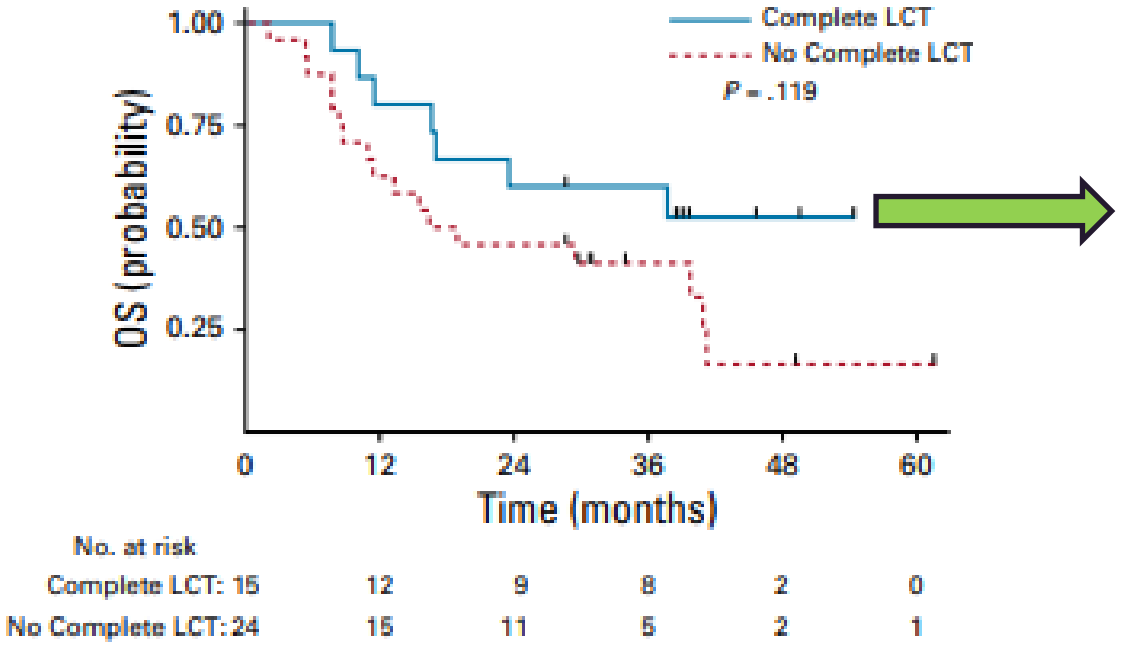


Local Consolidation vs. Maintenance in NSCLC DR Gomez. JCO 2019

Median Post Progression survival 37.6 mo vs. 9.4 mo



Overall survival (OS) after disease progression among patients originally assigned to local consolidative therapy (LCT) or maintenance therapy or observation (MT/O).



Overall survival (OS) from time of progression, for patients who did or did not receive late local consolidation therapy (LCT) for that progression. “Complete” LCT designates radiation therapy or surgery to all active sites of disease at the time of progression.

CORE Preliminary Data ESTRO 2023 and Radio & Onc 2023

- **Ph2 Randomized with ≤ 3 mets metachronous, systemic therapy naïve, FU 42.5 mo**
- **Breast, Prostate, NSCLC**
- **SOC+SABR vs. SOC**

- **1° end pt:**
  - PFS ITT HR 0.79 (95% CI 0.57-1.09), p=0.16
  - PFS per protocol HR 0.73 (95% CI 0.5-1.06), p=0.1
  - Median PFS 25.2 vs 19.9mo
  - Ph II objectives met with PFS signal favoring SABR supporting need for Ph III

Controlling the Primary

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Controlling the Primary in NON-Oligo met HNSCC

- **You et al., JAMA Oncology 2020**
  - Randomized phase III (dmNPC): adding locoregional RT to the primary/neck after chemo response improved OS vs chemo alone (HR≈0.42; 24-mo OS 76% vs 55%). Practice-changing for NPC and the clearest proof that treating the primary can matter.
- **Zumsteg et al., Cancer 2017**
  - High-intensity local therapy to the primary (≥60 Gy or oncologic resection) + systemic therapy was associated with better survival than systemic therapy alone (PS-matched 2-yr OS 34% vs 21%). Benefit concentrated when given within 6 months.
- **Kabarriti et al., Head & Neck 2019**
  - In newly diagnosed metastatic HNSCC receiving upfront chemo, adding head/neck RT correlated with longer OS of 2.5 mo. Also showed 6 mo improved OS for BED of $72Gy_{10}$ (60Gy/30fx)
- **Nguy et al., Laryngoscope 2021**
  - In de novo metastatic OPSCC on systemic therapy, head/neck RT was associated with improved 1-yr OS (67% vs 58%; adj HR 0.78).
- **Rambeau et al., Oral Oncology 2019**
  - Locoregional irradiation linked to better OS (median 16.1 vs 7.5 mo); signal strongest when used as consolidation after non-progression to first-line chemo.
- **Borson et al., Laryngoscope Investigative Otolaryngology 2022**
  - **Definitive surgery/chemoradiation to the primary in synchronous mHNSCC showed encouraging OS, especially with induction and/or anti-PD-1, young age, and number of mets (median OS ~42 mo in IO-treated subset).**
- **Kharouta et al., Cancers (MDPI) 2024**
  - **Primary-site RT improved OS regardless of HPV status (HPV+ median 24.9 vs 17.1 mo; HPV− 12.9 vs 8.4 mo).**
- **Petrelli et al., Oral Oncology 2025 (Meta-analysis)**
  - **Pooled data suggest treating the primary tumor in metastatic HNSCC associates with improved OS and PFS; greatest benefit in NPC and Asian population.**

Controlling the Primary in Oligo met HNSCC

Weissmann et al., Radiation Oncology 2021

- **Single institution, Retrospective, Mets 1-7 (median 1), all sites could be safely ablated, radical treatment to primary and all met sites**
- **N=40, median age 60.5, lung most common, 30% had active LR disease, 33% synchronous, 67% metachronous oligorecurrence, median FU 65 mo**
- **Systemic therapy: platinum doublets, Cetux, rare IO.**
- **UVA: Similar as MVA with addition of pulmonary site, higher RT dose**
- **MVA: ECOG, no bone/brain, lower total tumor volume.**
- **# of mets or # involved organs were not significant**

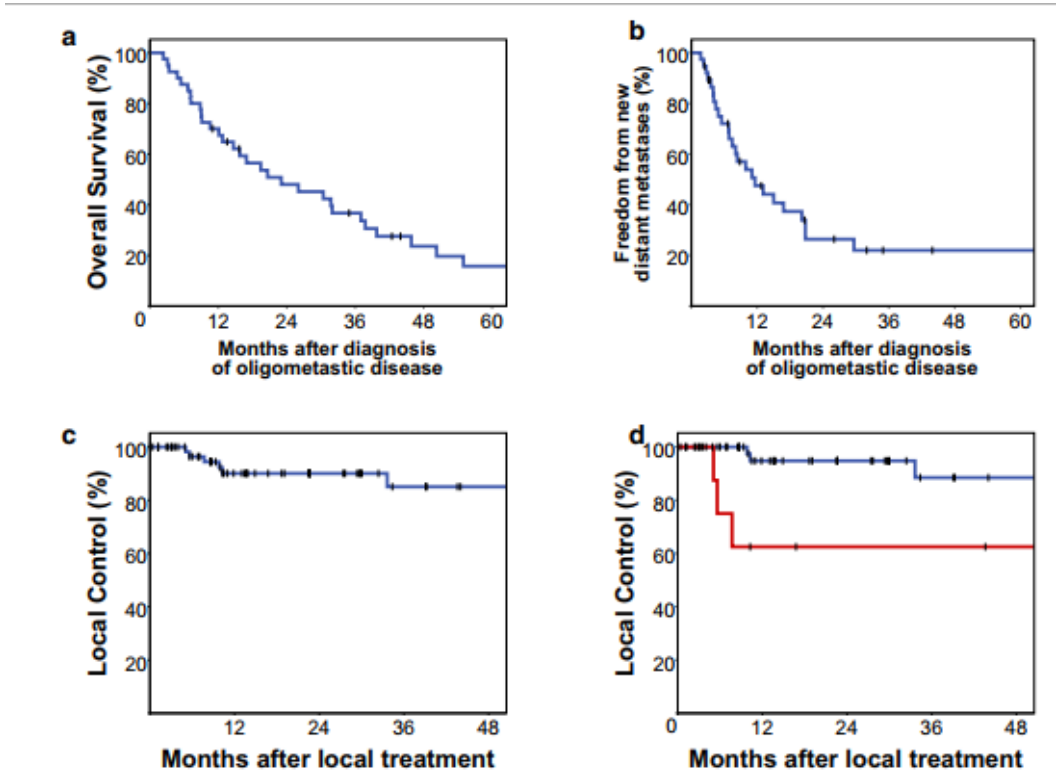
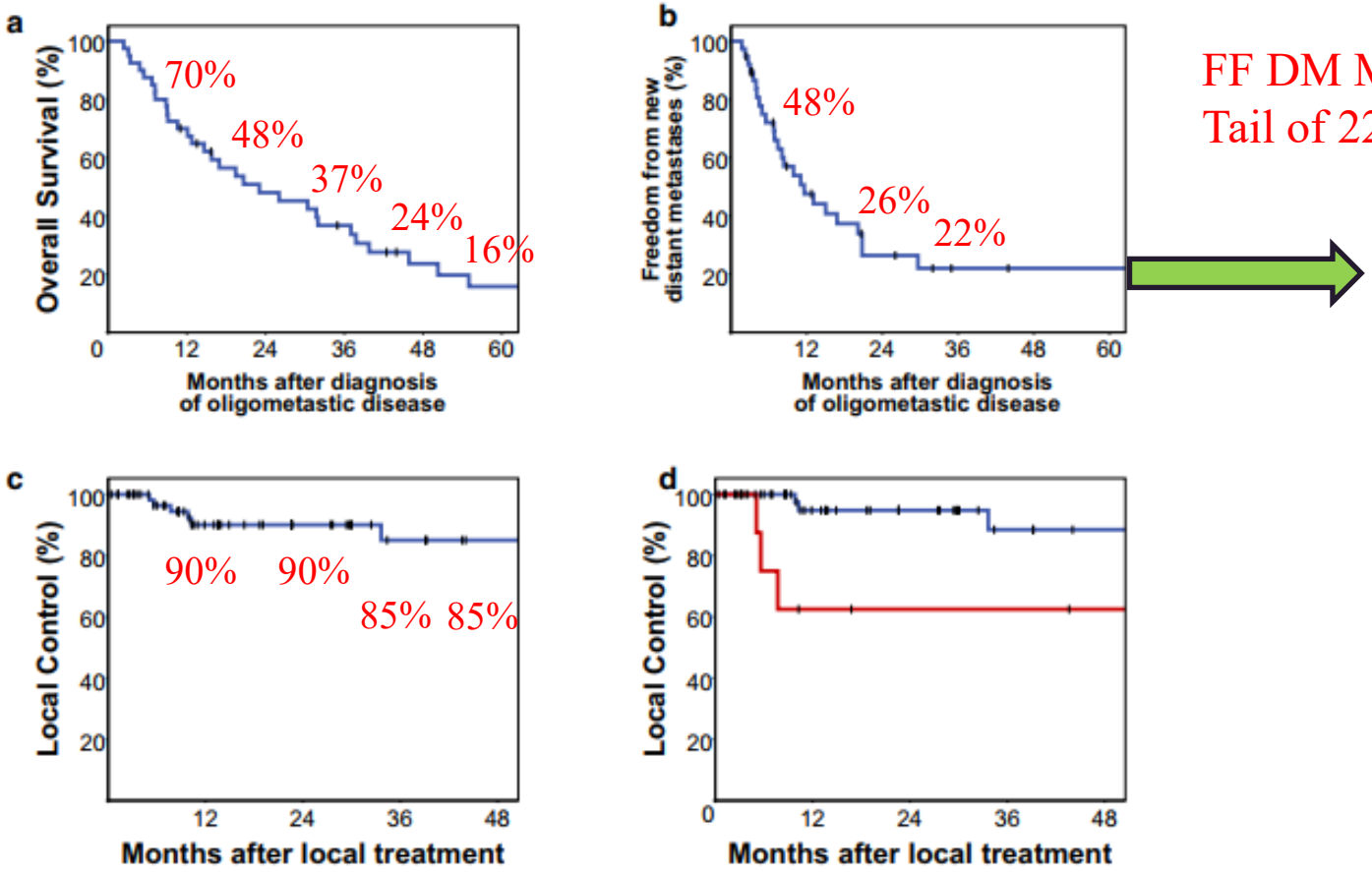


Fig. 2 **a** Kaplan–Meier plot showing overall survival since first diagnosis of oligometastatic disease and **b** freedom from new distant metastases in all 40 patients. **c** Local control in all of the 75 treated tumour sites and **d** local control for locoregional tumour manifestations versus distant metastases

Controlling the Primary in Oligo met HNSCC

Weissmann et al., Radiation Oncology 2021

Median OS 23.0 mo



FF DM Median 11.6 mo
Tail of 22% at 3 yr

Fig. 2 **a** Kaplan–Meier plot showing overall survival since first diagnosis of oligometastatic disease and **b** freedom from new distant metastases in all 40 patients. **c** Local control in all of the 75 treated tumour sites and **d** local control for locoregional tumour manifestations versus distant metastases

Controlling the Primary in Oligo met HNSCC

Weissmann et al., Radiation Oncology 2021

- **Consider aggressive consolidation:**
  - Good ECOG
  - Lung only metastasis
  - No Brain or bone metastasis
  - Low total tumor volume

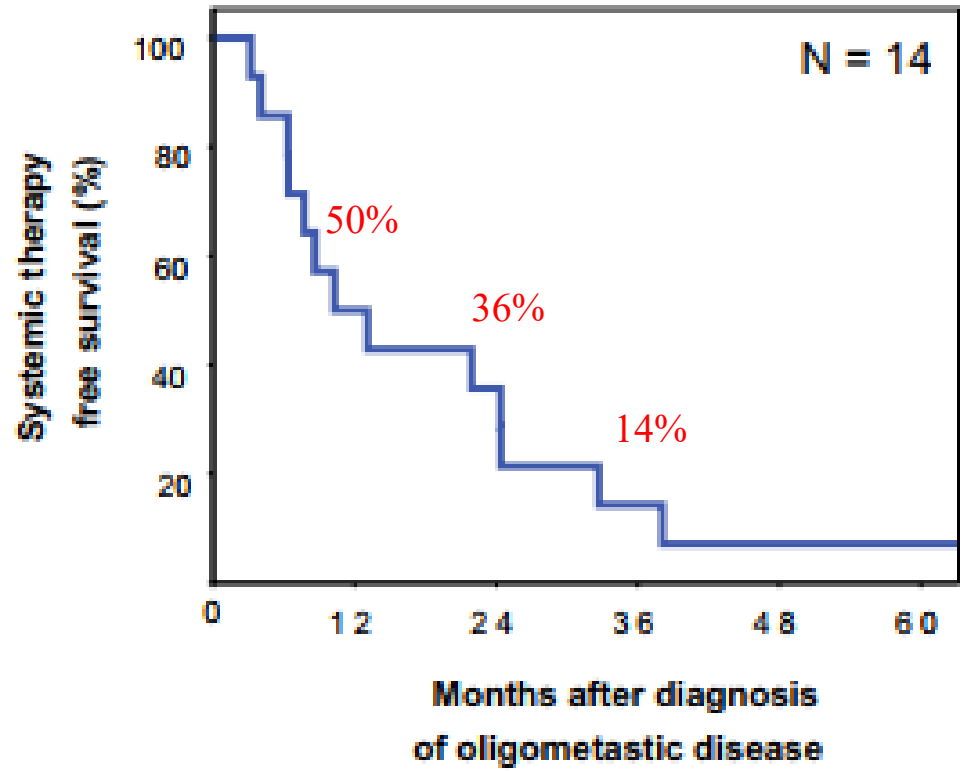


Fig. 3 Systemic therapy-free survival in the subgroup of patients, in which systemic therapy was deferred after local treatment of metastases (N = 14)

Controlling Distant Mets in Oligo HNSCC

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Decreasing Benefit of SABR # Lesions

Fleming et al. Oral Oncol. 2020

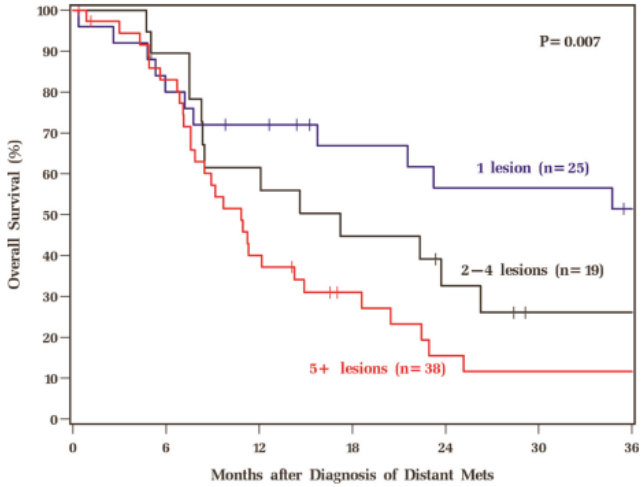


Fig. 3. Overall survival after distant metastasis, stratified by lesion number.

McBride Oral Onc. 2014

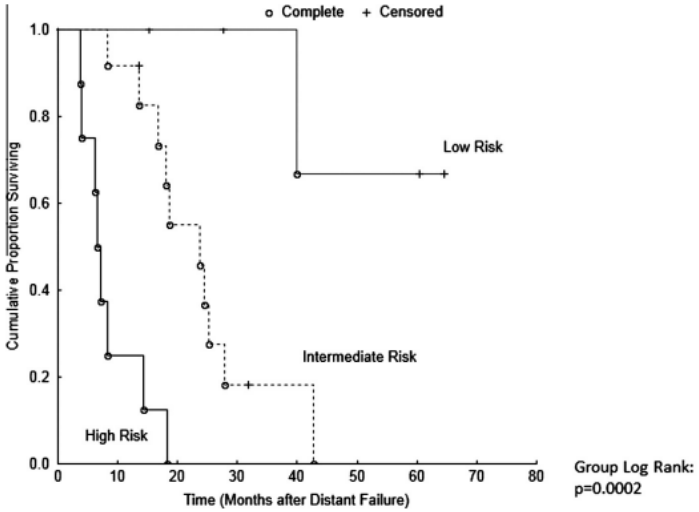
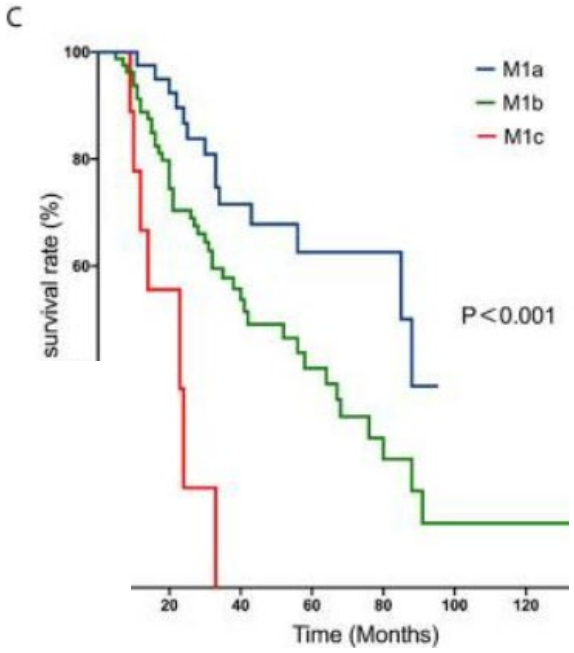
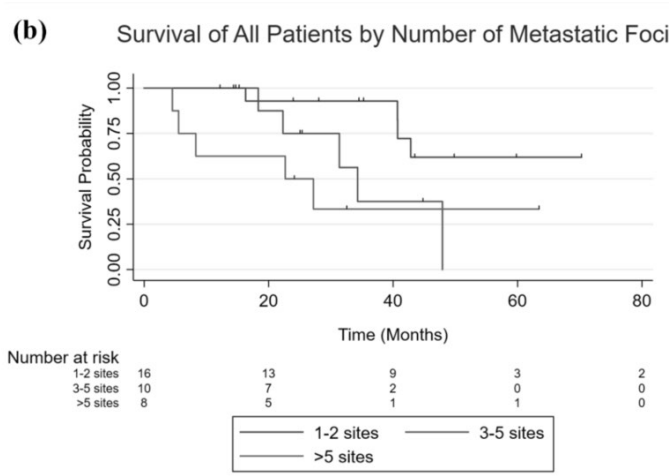


Figure. 1. Kaplan–Meier estimates of overall survival after distant metastasis by risk group.

Ni et al. Front. Oncol. 2021

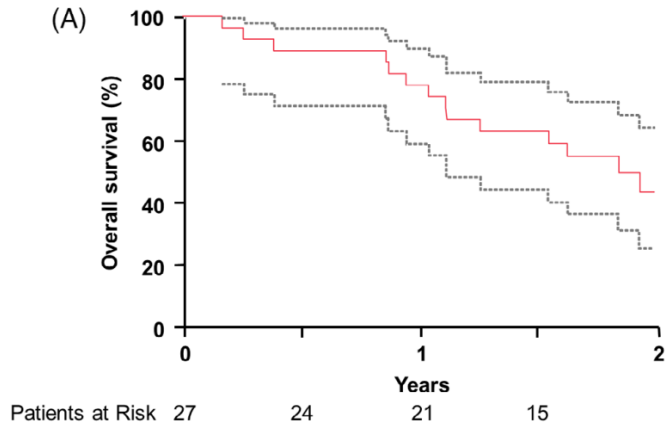


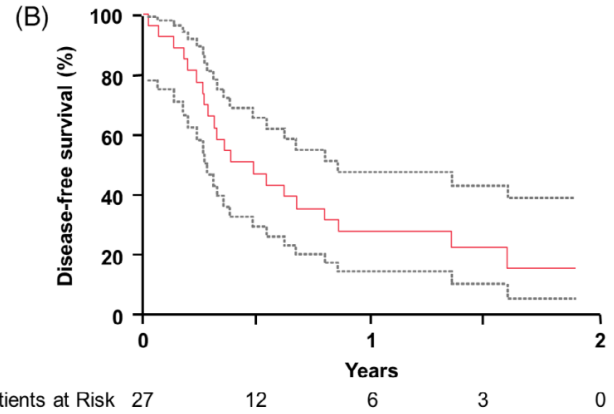
Wright Oral Onc. 2021

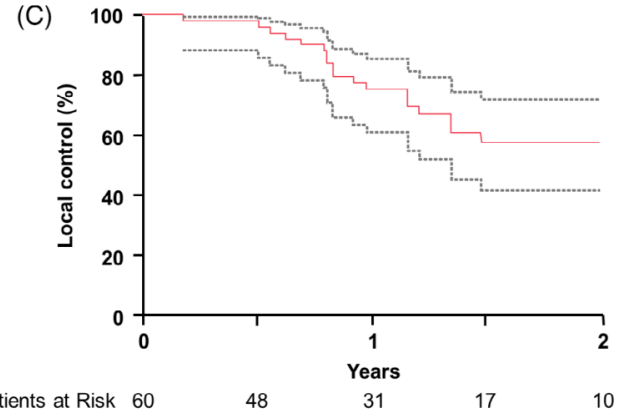


SABR Oligometastatic HNSCC Bates et al. Head Neck 2019

- Retro, ≤5 lesions, 27 pts, FU 18 mo, no systemic therapy
- MS 23 mo, 1 yr 78%, 2 yr 43%
- LC 1 yr 75%, 2 yr 57%
- TTP 6 mo
- SBRT can provide good LC and good OS, but systemic progression remains the primary failure

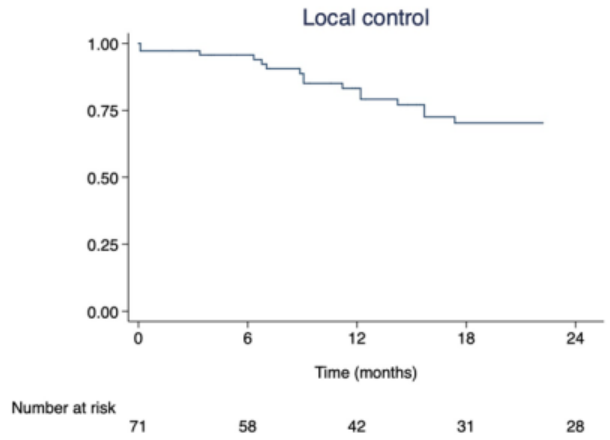


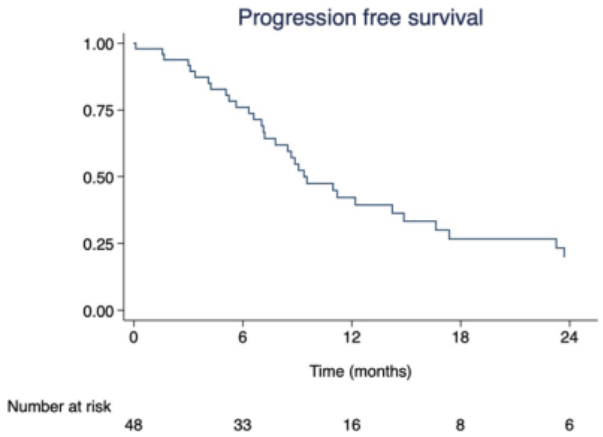


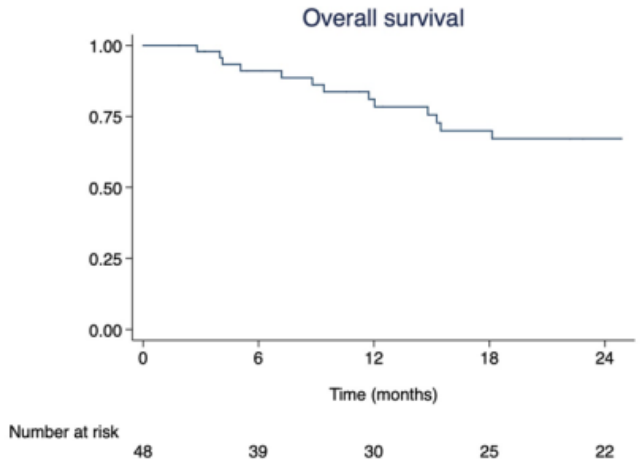


Metastasis directed SABR Franzese et al. J Cancer Res. Clin. Oncol 2021

- **Retro, 48 pts, ≤5 lesions in ≤ 2 organs, SABR, systemic allowed, FU 20.2 mo**
- **LC: 1 yr 83%, 2 yr 70%**
- **PFS: 1 yr 42%, 2 yr 20%**
- **OS 1 yr 81%, 2 yr 67%**
- **Worse LC:** Prior local therapy, Oligoprogression vs. oligometastasis, Untreated additional mets
- **Worse PFS:** older age, non-ACC, non-lung mets
- **Worse OS:** Poor PS, non-salivary primary, non-lung mets







SABR Lung Only Oligometastasis Bonomo et al. Oral Oncology 2019

- **Can SABR defer systemic therapy in lung only ≤5 oligomet?**
- **Retro, 27 pts, 22 mo FU**
  - most HPV- & de novo metastatic
- **Median time to progression 10 mo**
- **1 yr TTP 56%**
- **2 yr TTP 35%**
- **MVA worse outcomes with T3/4**
- **In well selected patients, lung only oligomet, SABR can provide high response rates and months of systemic therapy deferral**

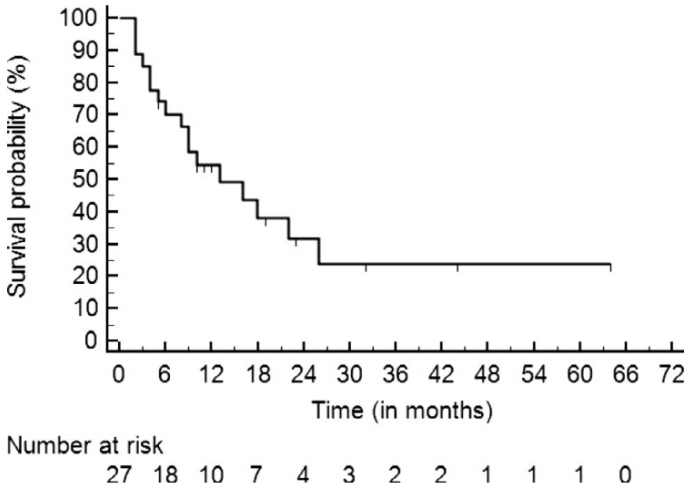


Fig. 3. Time to progression.

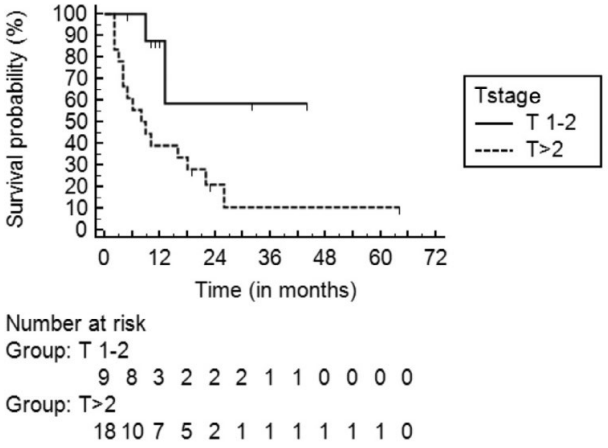
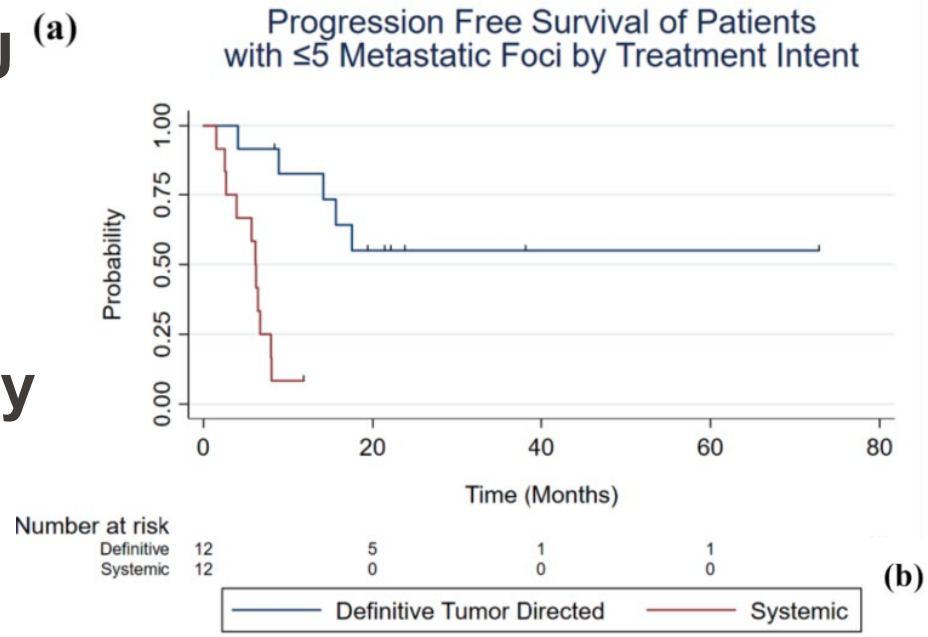
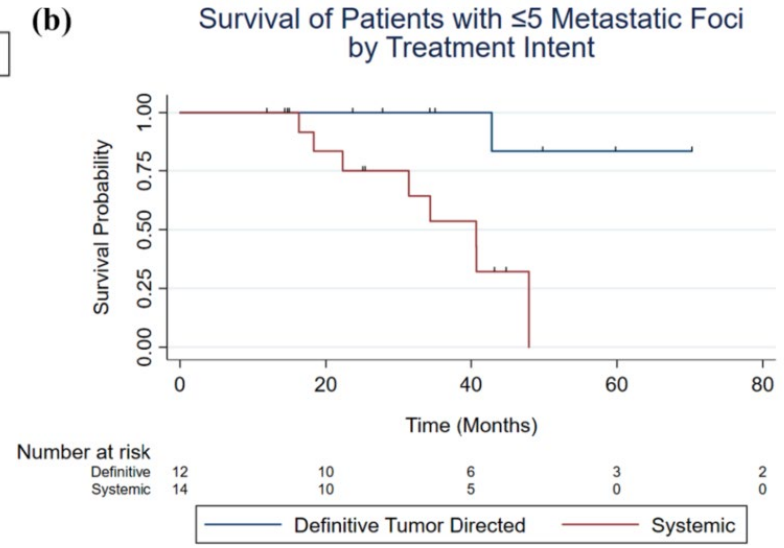


Fig. 4. Impact of T stage on time to progression.

HPV+ Metachronous Oligometastatic Wright et al. Oral Oncol. 2021

- **Retrospective, 34 pts, FU 30mo, Prior TORS/LND**
- **Oligo ≤5 lesions**
- **Compared upfront MDT alone to systemic therapy**
- **PFS: p 0.001**
  - MDT: Not Reached
  - Systemic: 6.13 mo
- **OS: p 0.004**
  - MDT: Not reached
  - Systemic: 40.7 mo
- **Future studies to compare MDT +/- systemic therapy**





Nivolumab +/- SABR for Abscopal McBride JCO 2021

- **Ph II, Nivo +/- SABR to only 1 lesion, 62 pts, FU 20.2 mo, nonoligo**
- **1°: ORR in non-irradiated lesions**
  - ORR Nivo 34.5% vs. Nivo+SABR 29.0%, p=0.86
  - PFS 1.9 mo vs. 2.6 mo (p=0.79)
  - OS 14.2 mo vs. 13.9 mo (p=0.75
- **SABR does not induce abscopal effect with Nivolumab**
- **Only 1 lesion treated, not all ablated, polymetastatic**

TABLE 3. Overall Response Rate of Eligible Patients (n = 60)

Treatment Arm	PR or CR, No. (%)	SD or PD, No. (%)	*P*
Nivolumab (n = 29)	10 (34.5)	19 (65.5)	.86
Nivolumab + SBRT (n = 31)	9 (29.0)	22 (71.0)	

Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SBRT, stereotactic body radiotherapy; SD, stable disease.

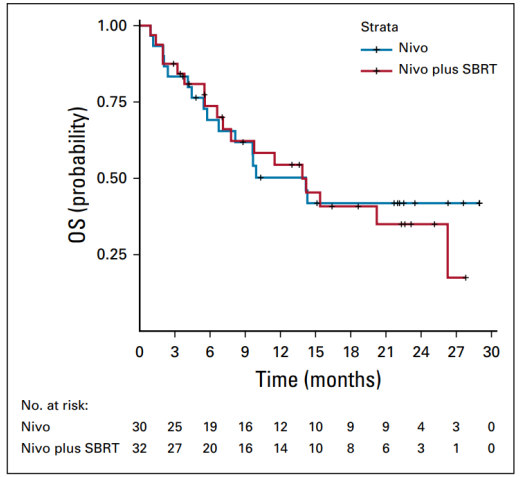


FIG 2. Overall survival (OS) in the intention-to-treat population (n = 62). Nivo, nivolumab; SBRT, stereotactic body radiotherapy.

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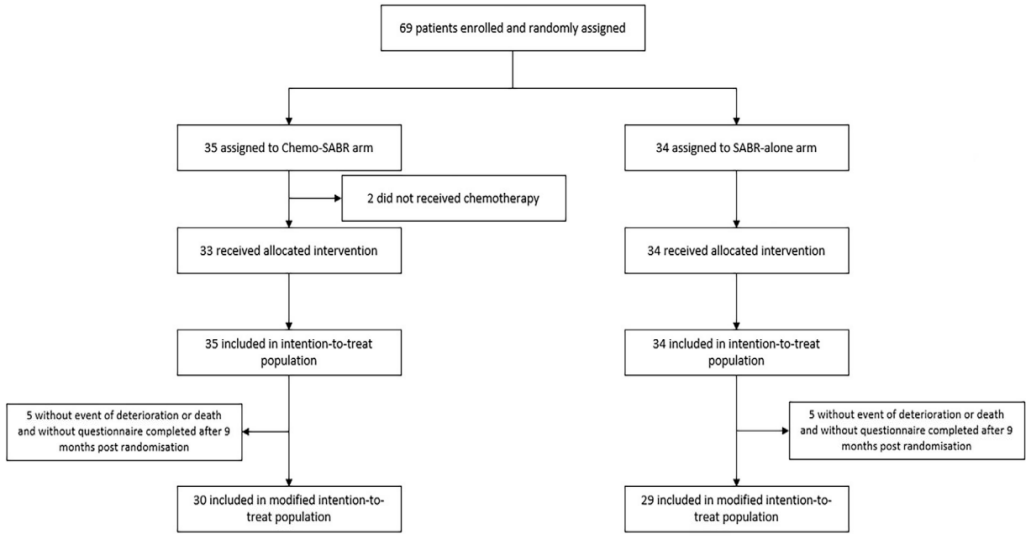
- **Multicenter, Randomized Ph II Trial**
- **HNSCC with 1-3 oligomet, 2015-2022**
- **ECOG 0-2**
- **1:1 SABR alone vs. Chemo+SABR tx all sites**
  - Prior cohort showed 35.5% had ≤ 3 mets
  - High % ≥ Gr 3 toxicity: Chemo 80%, IO 55%, Chemo/IO 80%
  - Designed after SABR-COMET so chemo alone not deemed ethical
- **N = 69, Median FU 55 mo**
- **83% had Lung only mets, 58% Solitary met**
- **Chemo: EXTREME**
  - Cetuximab+platinum+5FU up to 6 cycles
  - Maintenance Cetuximab allowed/rec for stable disease
  - No Immunotherapy
- **New sites allowed repeat SABR**

- **Primary: Survival without definitive QOL deterioration at 1 year**
- **Secondary: OS, PFS, Toxicity, time until definitive deterioration (TUDD), cost of omitting chemo**



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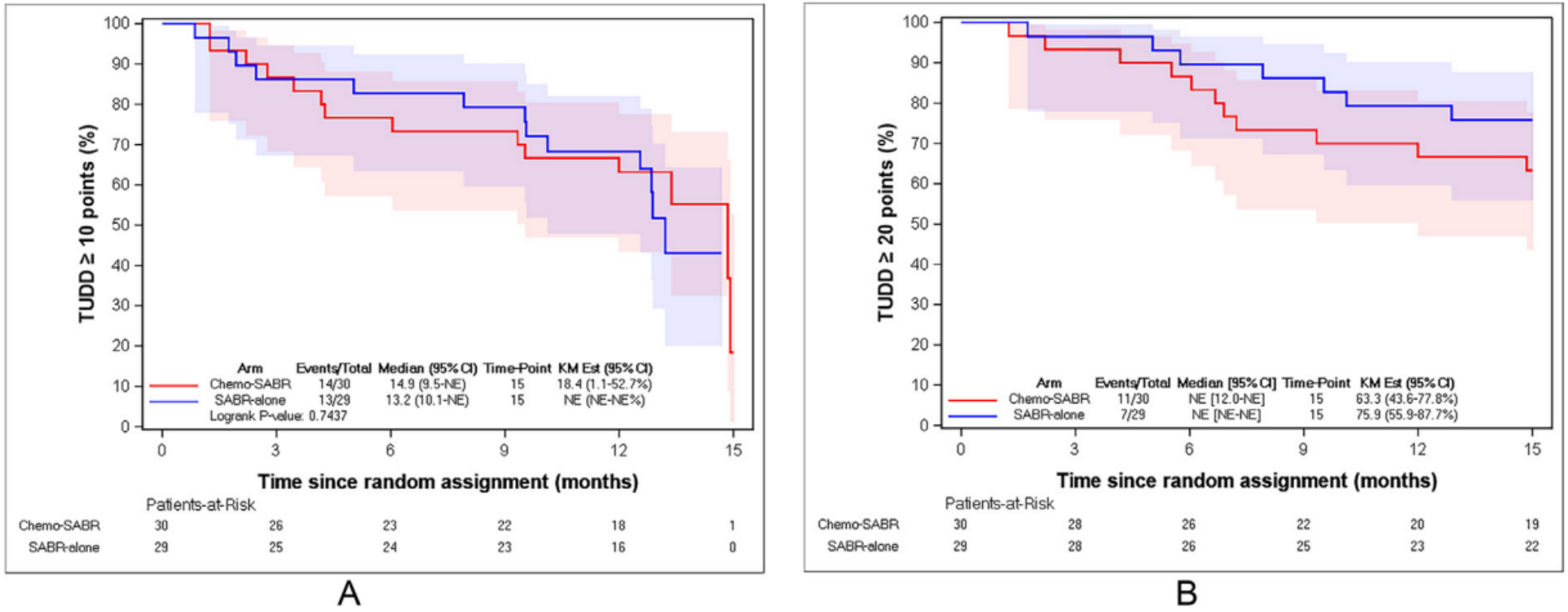

Fig. 2. Kaplan-Meier (KM) estimates of time until definitive deterioration for global QoL score (mITT population) with a minimal important difference (MID) at 10 points (A) and with a MID at 20 points (B). *Abbreviations:* mITT = modified intent-to-treat; QoL = quality of life; SABR = stereotactic ablative radiation therapy; TUDD = time until definitive deterioration.

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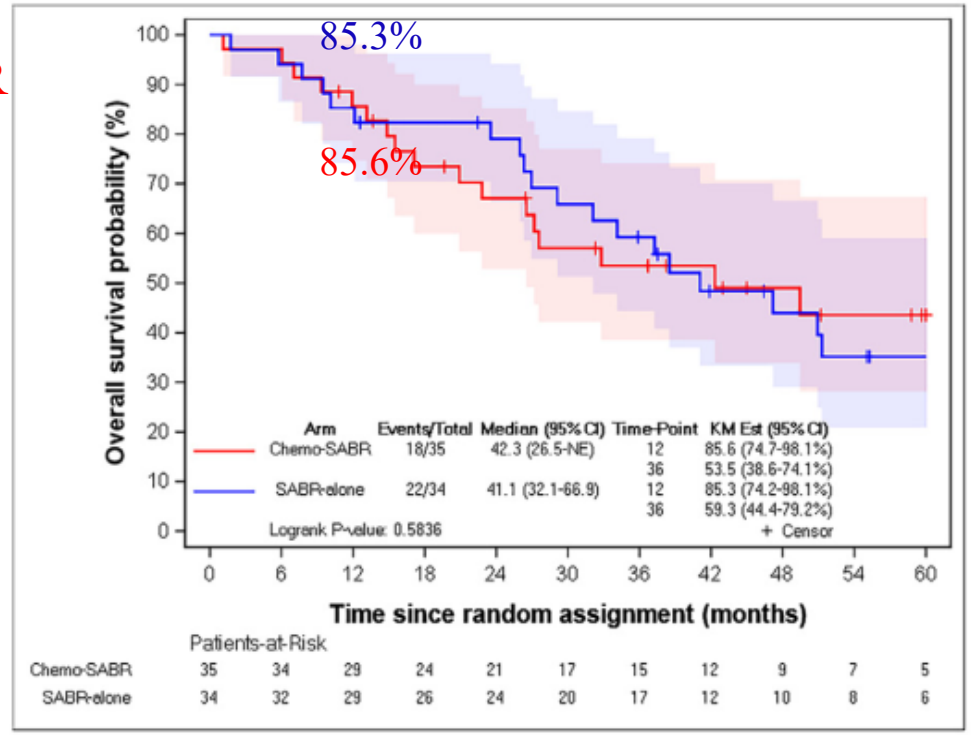
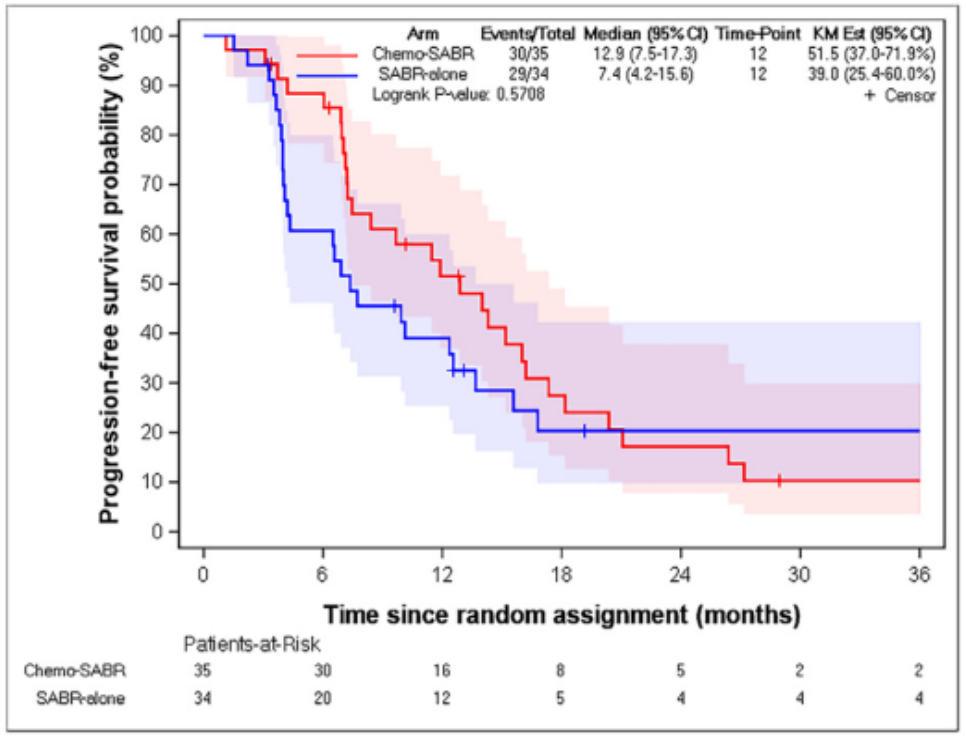
Median OS:
Chemo-SABR
42.3 mo

SABR Alone
41.1 mo



A



B

Median PFS:
Chemo-SABR
12.9 mo

SABR Alone
7.4 mo

Fig. 3. Kaplan-Meier (KM) estimates of overall survival (A) and progression-free survival (B) of patients. *Abbreviations:* SABR = stereotactic ablative radiation therapy.

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Table 2 Univariable and multivariable Cox model analysis on overall survival

	Univariable analysis					Multivariable analysis				
Variable	**N**	**events**	**HR**	**95% CI**	***P* value**	**N**	**events**	**HR**	**95% CI**	***P* value**
Age at inclusion (y)						66	40			
Continuous	69	40	0.985	0.950-1.021	.411					
≤65	39	24	1							
>65	30	16	0.709	0.371-1.354	.298					
Gender										
Female	13	5	1					1		
Male	56	35	2.305	0.893-5.945	.084			3.125	1.068-9.141	.038
Primary tumor site					.024					
Oropharynx	30	14	1					1		
Oral cavity	13	8	2.147	0.862-5.352	.101			2.010	0.786-5.142	.145
Larynx	12	7	2.947	1.201-7.231	.018			3.364	1.351-8.376	.009
Hypopharynx	11	9	3.687	1.492-9.110	.005			2.860	1.137-7.191	.026
Cervical node of UK primary	3	0	-	-	-					
T category										
T1-T2	21	13	1							
T3-T4	45	27	0.962	0.494-1.873	.910					
N category										
N0-N1	27	14	1							
N2-N3	41	26	1.461	0.754-2.828	.261					
Primary tumor resection										
No	40	21	1							
Yes	29	19	1.140	0.610-2.127	.682					
Systemic treatment										
No	21	13	1							
Yes	48	27	0.823	0.420-1.614	.572					
Number of metastatic sites										
1	40	20	1					1		
2-3	29	20	1.731	0.898-3.336	.101			1.688	0.853-3.344	.133
Metastatic site										
Pulmonary only	57	32	1							
Others	12	8	1.451	0.661-3.184	.353					
Performance status at inclusion										
0	31	18	1							
1-2	34	19	1.125	0.589-2.147	.722					
Quality of life at inclusion										
0-66	24	12	1							
66-100	45	28	1.352	0.687-2.663	.383					
Arm										
Chemo-SABR	35	18	1							
SABR-only	34	22	1.194	0.633-2.250	.584					

Abbreviations: CI = confidence interval; HR = hazard ratio; N = lymph node; SABR = stereotactic ablative radiation therapy; T = the size and extent of the main tumor (the primary tumor); UK = United Kingdom.

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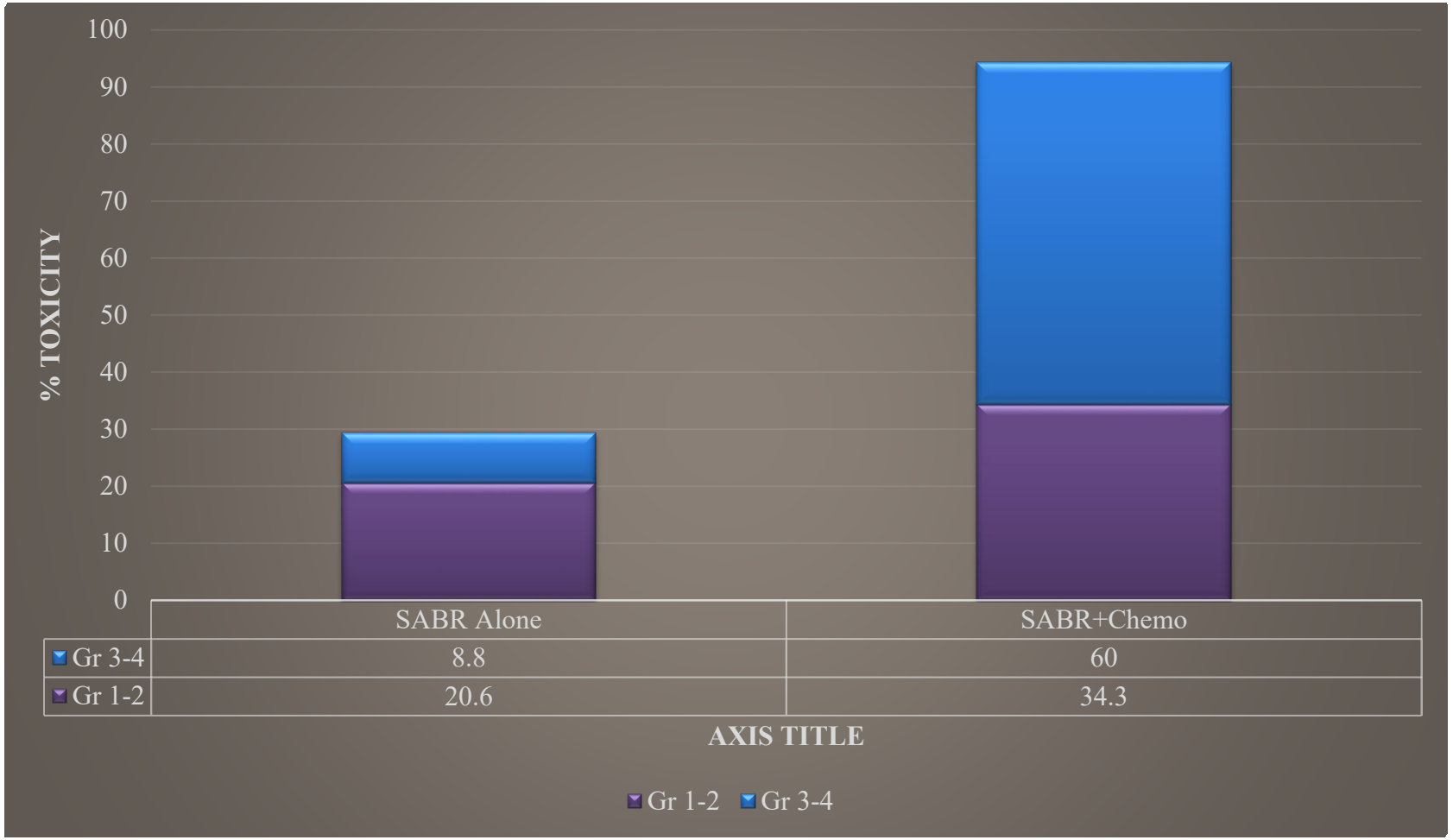

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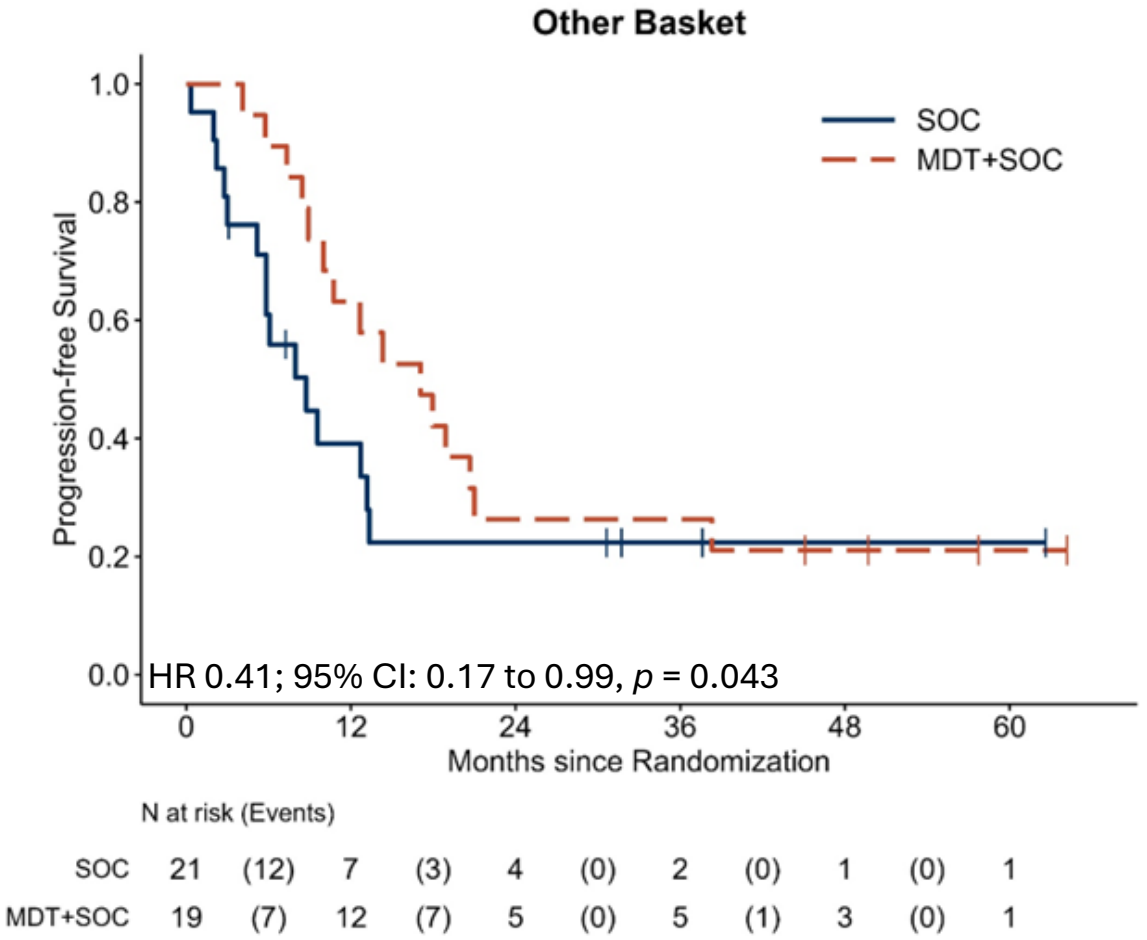
Conclusions:

- **Best data to date for oligo mets 1-3**
- **Supports evidence to delay systemic therapy to avoid deterioration of QOL & toxicities**
- **SABR in both arms likely contributes to the high median OS exceeding 40 mo**
  - Chemo alone ~ 10-14 mo
  - Keynote 048 (Keytruda/Chemo) ~ 14.9 mo
  - CheckMate 141 (Nivolumab) ~ 8 mo
- **Trial deviations associated with worse OS**
- **SABR alone 5x lower cost while maintaining similar OS**
- **Limitations:**
  - Strategic trial design instead of comparative
  - Slow accrual
    - Rare histology
    - Competing trials
    - IO publications/SOC
    - SABR off trial
    - COVID
  - Early termination
  - Powered for phase II

Other: PFS is improved with MDT+SOC



Median PFS

SOC 8.7 mo

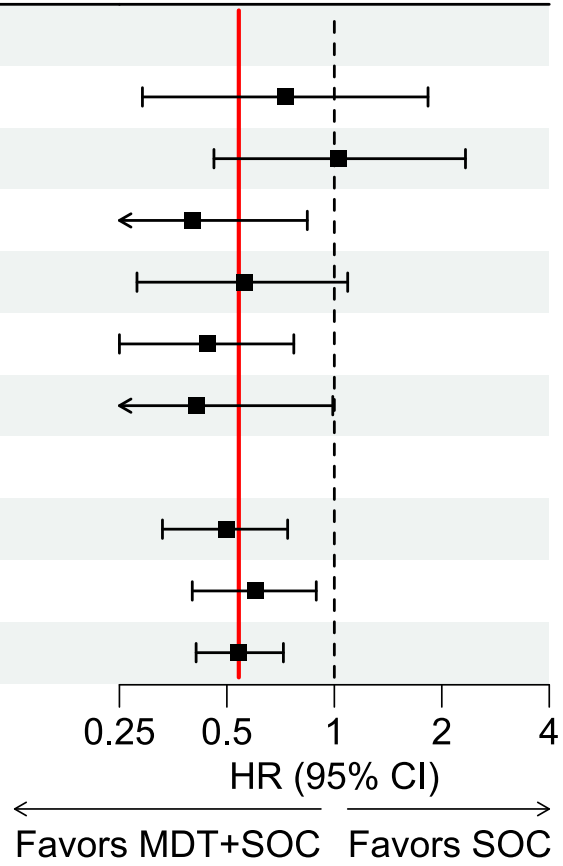
SOC+SABR 17.1 mo

Median follow-up: 50 months

Primary endpoint for all baskets

HOT OFF THE PRESS

Subgroup	Event/N	HR (95% CI)
Individual baskets		
Breast	23/40	0.73 (0.29 to 1.83)
Kidney	34/40	1.03 (0.46 to 2.33)
Pancreas	35/40	0.40 (0.19 to 0.84)
Prostate continuous ADT	48/87	0.56 (0.28 to 1.09)
Prostate intermittent ADT	69/87	0.44 (0.25 to 0.77)
Other	30/40	0.41 (0.17 to 0.99)
Aggregated baskets		
Prostate baskets aggregated	117/174	0.50 (0.33 to 0.74)
All baskets aggregated without prostate	122/160	0.60 (0.40 to 0.89)
All baskets aggregated	239/334	0.54 (0.41 to 0.72)



* Updated follow-up for breast, pancreas, and prostate baskets

EXTEND Toxicity

Grade	MDT+SOC n (%)	SOC n (%)
2	21 (13)	6 (4)
3	9 (5)	4 (2)
4	0	0 (0)
5	1 (1)	0 (0)

There was no significant difference in the rate of grade 3 or greater toxicity between groups ($P = 0.11$ by Fisher's exact test).

Summary

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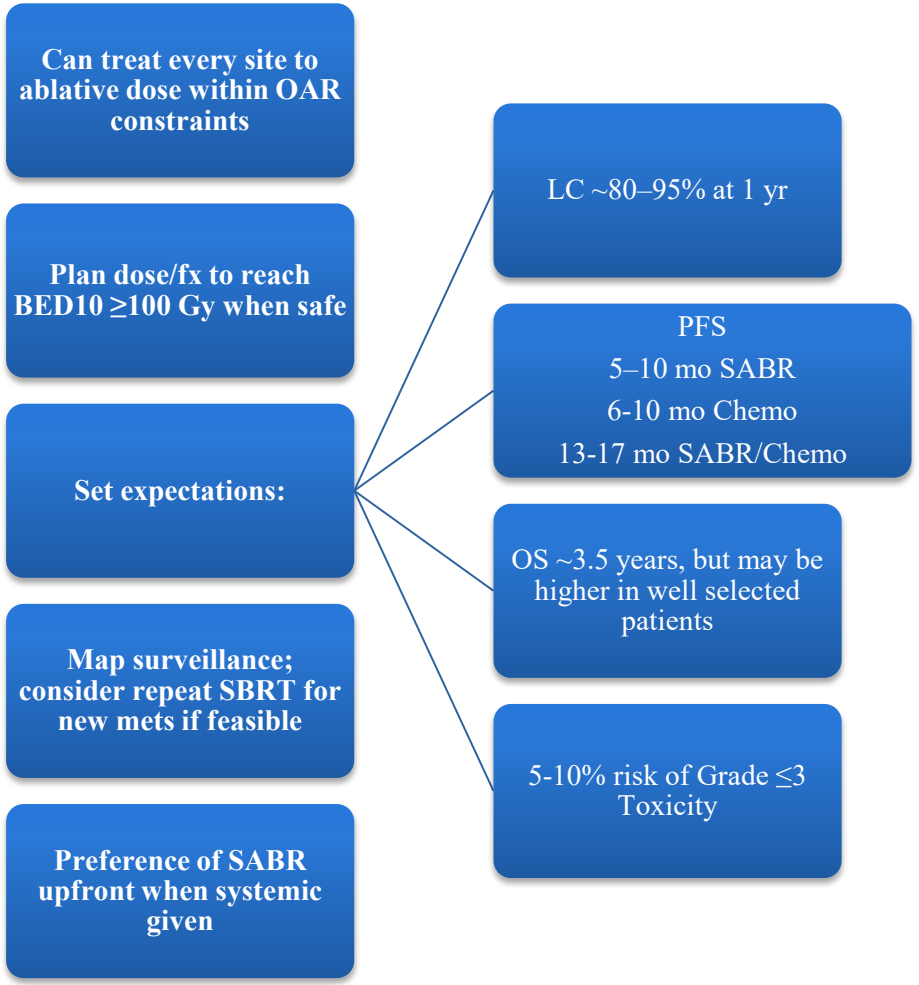
When SABR Alone is Reasonable

- ECOG 0–1
- All disease sites can be safely ablated (typically ≤3–5 lesions)
- Low total metastatic volume (more important than raw lesion count)
- Favorable sites: lung-only; avoid brain/bone if possible
- Indolent oligorecurrence or oligoprogression
- HPV/EBV+
- Good control of locoregional disease
- Able to deliver definitive doses (target BED10 ≥100 Gy)
- Patient prioritizes QoL / toxicity minimization without sacrificing OS

When to Avoid SABR alone

- Rapidly progressive or polymetastatic disease / high burden
- Symptomatic systemic disease needing quick cytoreduction
- Unfavorable sites (brain/bone)
- Multi organ involvement
- Poor ECOG
- Large cumulative volume → OAR limits
- Clear indication for immediate IO/targeted therapy in aggressive R/M disease

Go/No Go


Can treat every site to ablative dose within OAR constraints
Plan dose/fx to reach BED10 ≥100 Gy when safe
Set expectations:
Map surveillance; consider repeat SBRT for new mets if feasible
Preference of SABR upfront when systemic given
LC ~80–95% at 1 yr
PFS
5–10 mo SABR
6-10 mo Chemo
13-17 mo SABR/Chemo
OS ~3.5 years, but may be higher in well selected patients
5-10% risk of Grade ≤3 Toxicity

National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2025
Very Advanced Head and Neck Cancer

NCCN Guidelines Index
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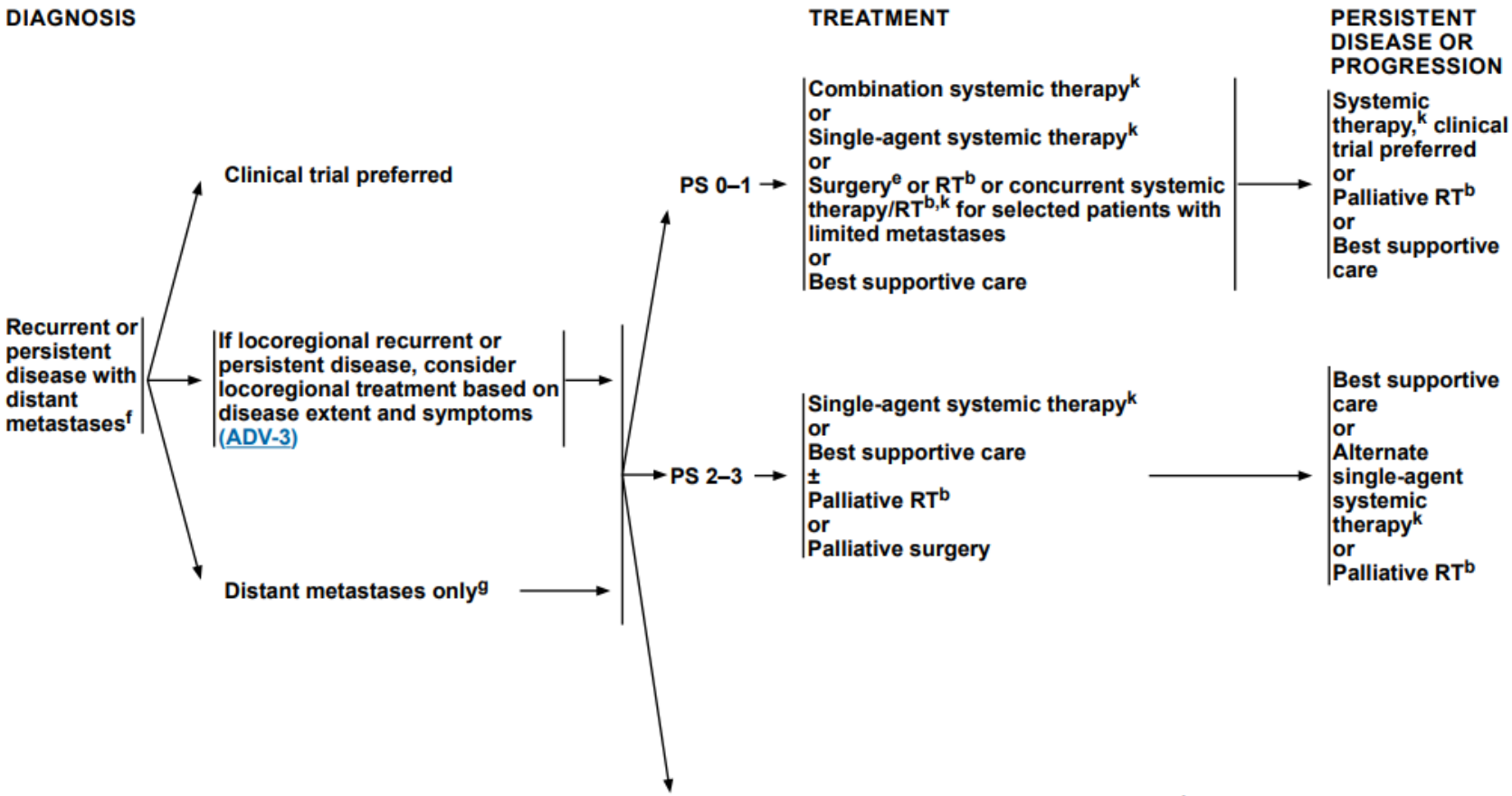


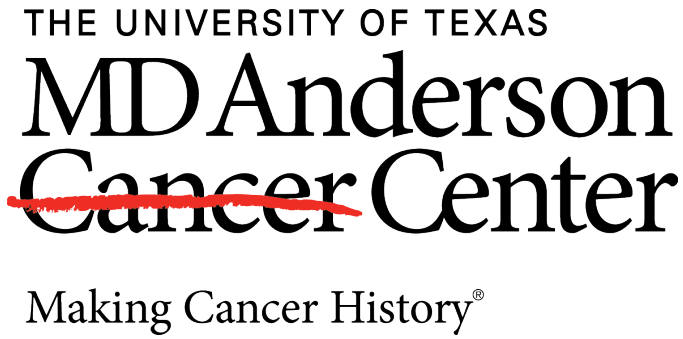
[b] Principles of Radiation Therapy (ADV-A).
[e] Principles of Surgery (SURG-A).
[f] Consider NGS genomic profiling for biomarker identification.
[g] Consider palliative RT as clinically indicated (eg, bone metastases) (RAD-A).
[k] See Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A) or Systemic Therapy for Nasopharyngeal Cancers (NASO-B).

Note: All recommendations are category 2A unless otherwise indicated.

Ongoing Trials/Future Directions

- **IMPORTANCE – Ph II Randomized, Pembro +/- SABR 36Gy/3fx to 1-3 mets. Still recruiting. 1° Best Response.**
- **ARREST-2– Ph II/III, randomize SOC+/- SABR for Poly-metastatic disease > 10 mets w/ no systemic planned. Still recruiting. 1° OS**
- **SABR-COMET-3—Ph III, randomize SOC+/-SABR for 1-3 mets, all disease sites, stratified by disease sites and DFS. Completed accrual. Not reported. 1° OS**
- **SABR-COMET-10 –Ph III, randomize pts with 4-10 mets to SOC+/-SABR. Stratified by disease site and planned systemic therapy. Completed accrual 12/2023. Not reported. 1° OS**
- **SUPPRESS/HNC—PhII, randomize pts with1-5 oligoprogressive mets to SOC+/-SABR. Still recruiting. 1° PFS.**
- **LM-HNSCC—Ph II, single arm, pts with 1-10 mets to sintilimab/chemo/SABR. Not Reported. 1° PFS.**

- **ctDNA**
- **Radionuclides/ radiopharmaceuticals to differentiate cold vs. hot tumors**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Pembro +/- SABR for Met NSCLC Theelan. Lancet Respir Med 2020

NRG_LU002 (IO+/-SABR) vs. CURB Trial (Oligoprogression)

HPV mediated oligometastatic Fleming et al. Oral Oncol. 2020