APCCC
ADVANCED PROSTATE CANCER CONSENSUS CONFERENCE

OLIGORECURRENT PROSTATE CANCER

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DISCLOSURES

Type of affiliation / financial interest	Name of commercial company
Institutional receipt of grants/research supports:	Merck, Bayer, Ferring,
Receipt of honoraria or consultation fees (institution):	Astellas, Bayer, Ferring, Janssen, Sanofi
Participation in a company sponsored speaker's bureau:	None
Stock shareholder:	None
Spouse/partner:	None
Other support (please specify):	None

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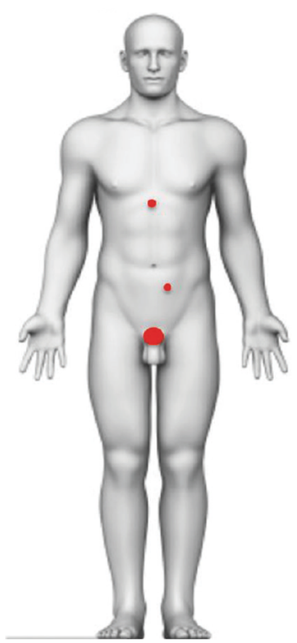
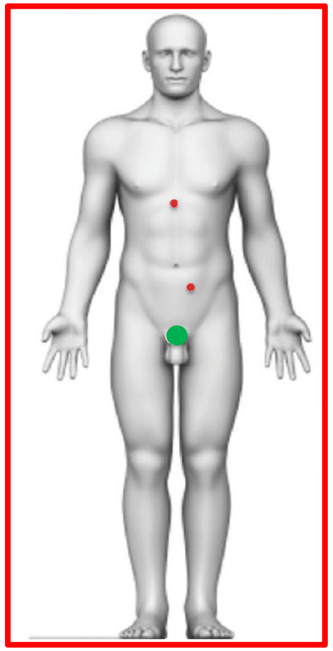
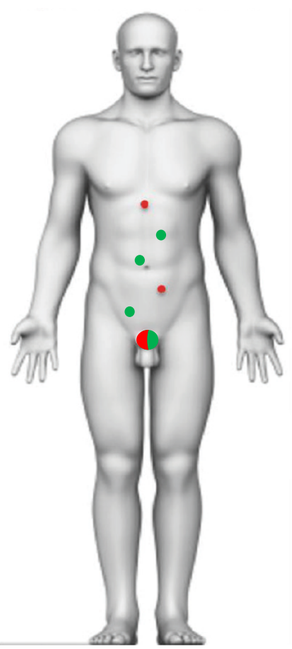
OLIGOMETASTATIC RECURRENCE

- Uncontrolled lesion
- Controlled lesion







Category name	De novo oligometastases (synchronous oligometastases)	Oligometastatic recurrence (metachronous oligometastases)	Oligometastatic progression (induced oligometastases)
Primary tumor status	Not controlled	Controlled	Controlled/ucontrolled
Systemic treatment	Naive	Naive	Resistant
Location of metastases	N1 or M1	N1 or M1	N1 or M1

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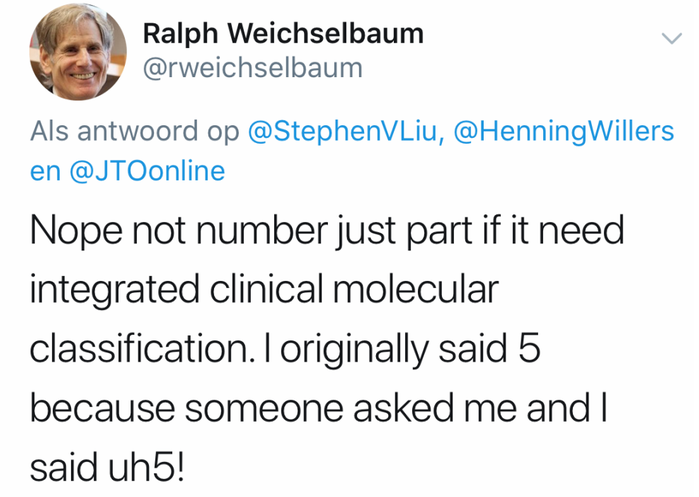
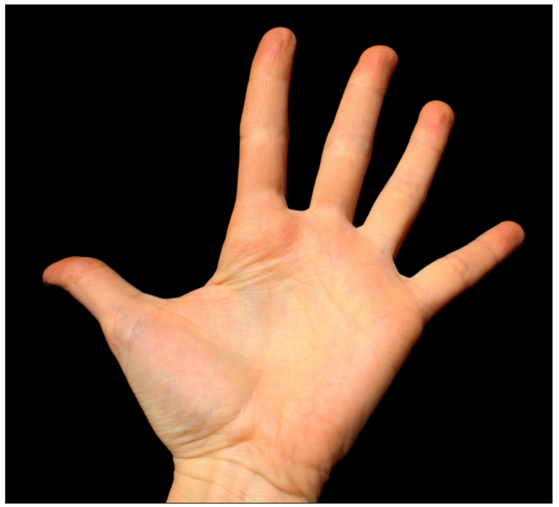
NO CONSENSUS DEFINITION OF OLIGOMETASTATSES





- Different terminologies used and lesion cut-offs used.
- EORTC-ESTRO is working on a consensus wording definition to be used in papers.
- Future: molecular definition (GAP6 Movember initiative)

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WHAT DO THE GUIDELINES SAY ON RE-STAGING?

Prostate-specific antigen (PSA) recurrence after radical prostatectomy	**LE**	**Strength rating**
Perform prostate-specific membrane antigen (PSMA) positron emission tomography (PET) computed tomography (CT) if the PSA level is > 0.2 ng/mL and if the results will influence subsequent treatment decisions.	2b	Weak
In case PSMA PET/CT is not available, and the PSA level is ≥ 1 ng/mL, perform fluciclovine PET/CT or choline PET/CT imaging if the results will influence subsequent treatment decisions.		Weak
PSA recurrence after radiotherapy		
Perform prostate multiparametric magnetic resonance imaging to localise abnormal areas and guide biopsies in patients fit for local salvage therapy.	3	Strong
Perform PSMA PET/CT (if available) or fluciclovine PET/CT or choline PET/CT in patients fit for curative salvage treatment.	2b	Strong

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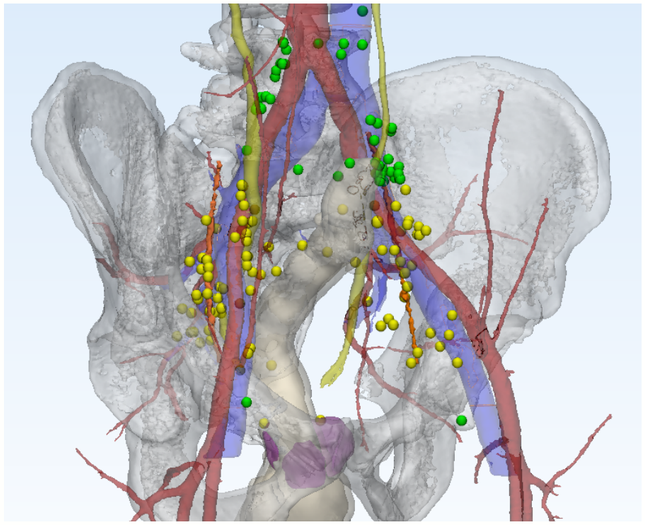
Increase in low volume recurrences expected!

WHERE DO YOU EXPECT RECURRENCES IN GENERAL?



Choline

Site of recurrence	
A. Prostate (bed)	22% (34)
B. Lymph nodes	
B1. Pelvic	51% (78)
B2. Extrapelvic	29% (44)
C. Bone lesions	
C1. Axial	16% (24)
C2. Appendicular	10% (15)
D. Visceral lesions	3% (5)

Median PSA: 3 ng/ml

PSMA

	Total population *n* = 78
A. Local (prostate bed)	**16 (20.5%)**
Lymph node recurrence	**55 (70.5%)**
B. Distal to common iliac bifurcation	41 (52.6%)
C. Common iliac and presacral	12 (15.4%)
D. Retroperitoneal	15 (19.2%)
E. Perirectal	4 (5.1%)
F. Inguinal	2 (2.6%)
G. Thorax and mediastinal	1 (1.3%)
H. Supraclavicular	2 (2.6%)
Bone	**14 (17.9%)**
I. Axial	12 (15.4%)
J. Appendicular	3 (3.8%)
K. Visceral	**0**

Median PSA: 2,6 ng/ml

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De Bruycker et al. BJUI 2017, and Eur Urol 2019
Devos et al. Eur Urol 2019

METASTASIS-DIRECTED THERAPY FOR OLIGOMETASTASES

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BIOLOGICAL RATIONALE FOR METASTASIS-DIRECTED THERAPY

If **metastases are able to metastasize** and systemic therapy induces more resistant and lethal clones, the addition of **local therapy** directed at metastases might **delay lethal disease progression**…

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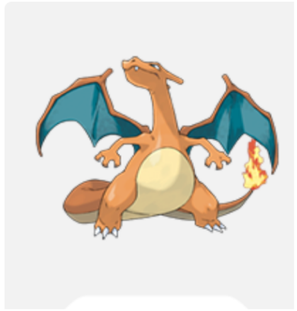
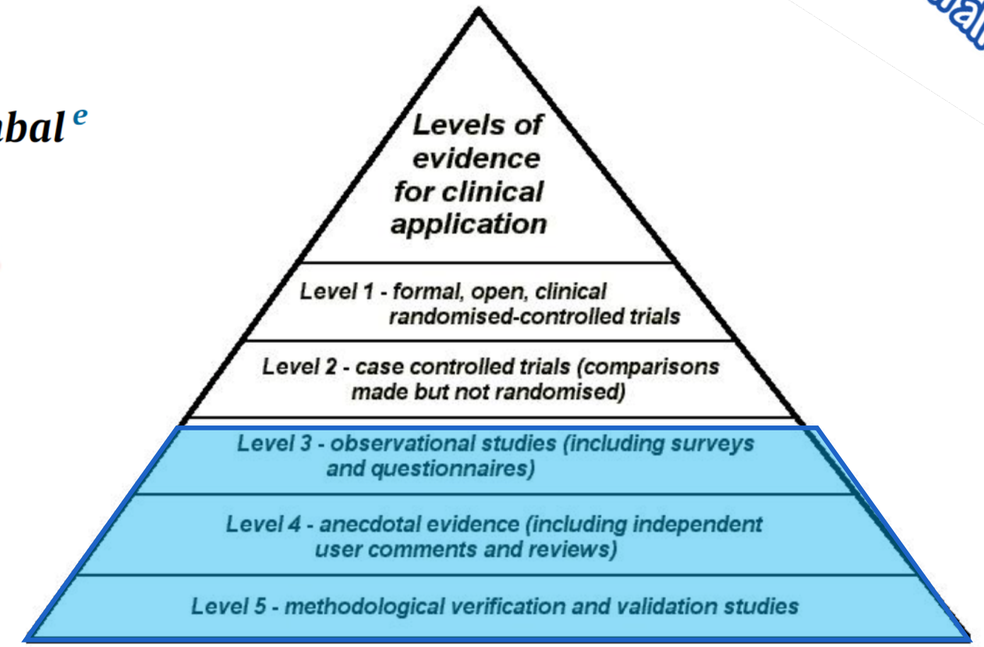
2 YEARS AGO…

Platinum Opinion

“Gotta Catch ’em All”, or Do We? *Pokemet* Approach to Metastatic Prostate Cancer

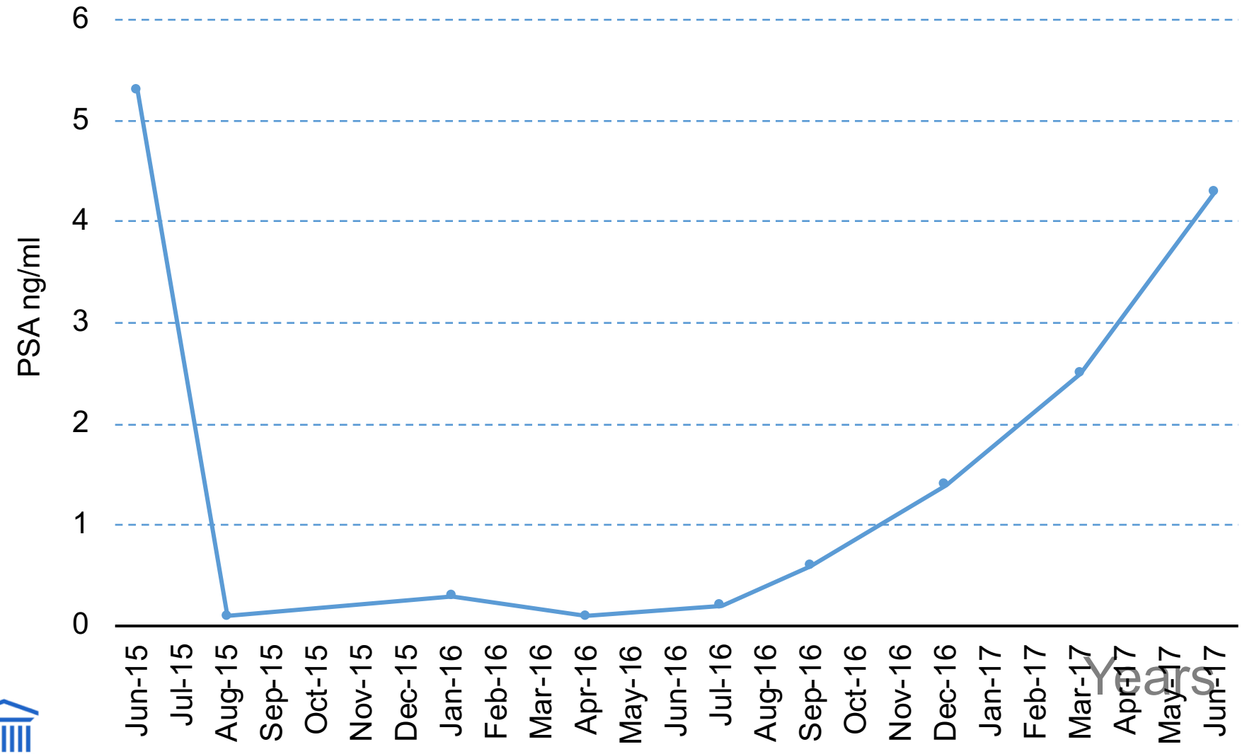
Declan G. Murphy [a,b,c,*], *Christopher J. Sweeney* [d], *Bertrand Tombal* [e]

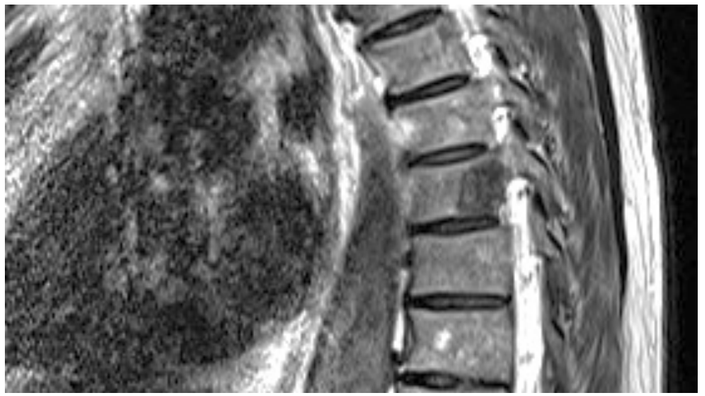


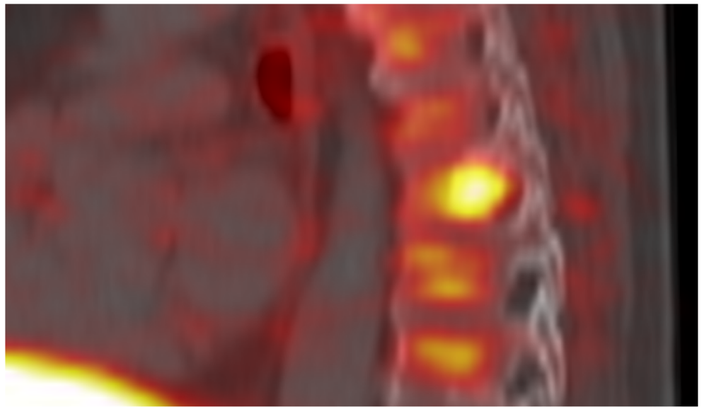


A FAMILIAR TALE

- 61 year old male; PSA 5.3ng/ml
- MRI and biopsy: Gleason 3+4=7 in 6/21 cores
- RARP: pT3a 4+3=7; N0; pos margin
- Salvage radiotherapy







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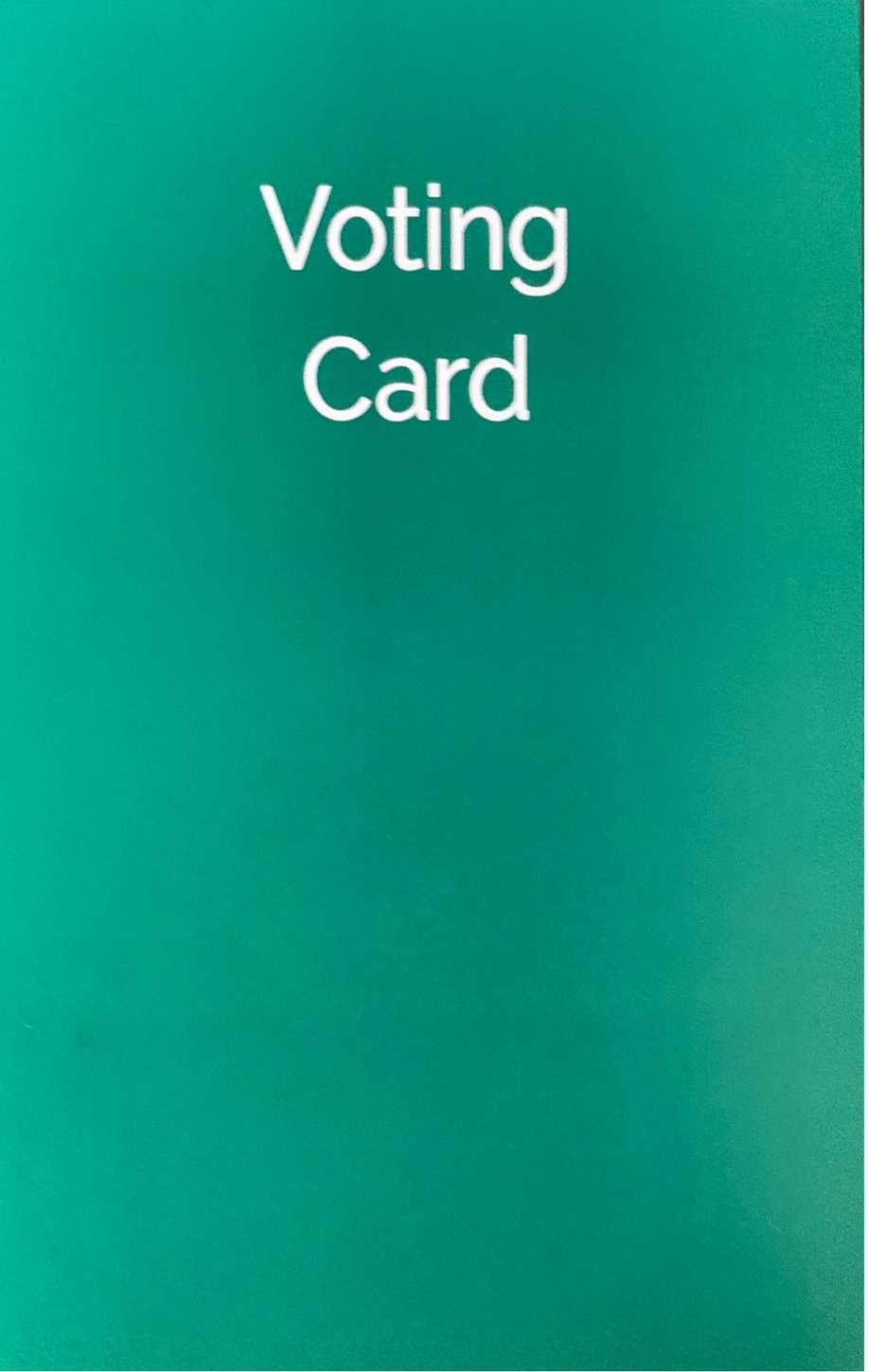
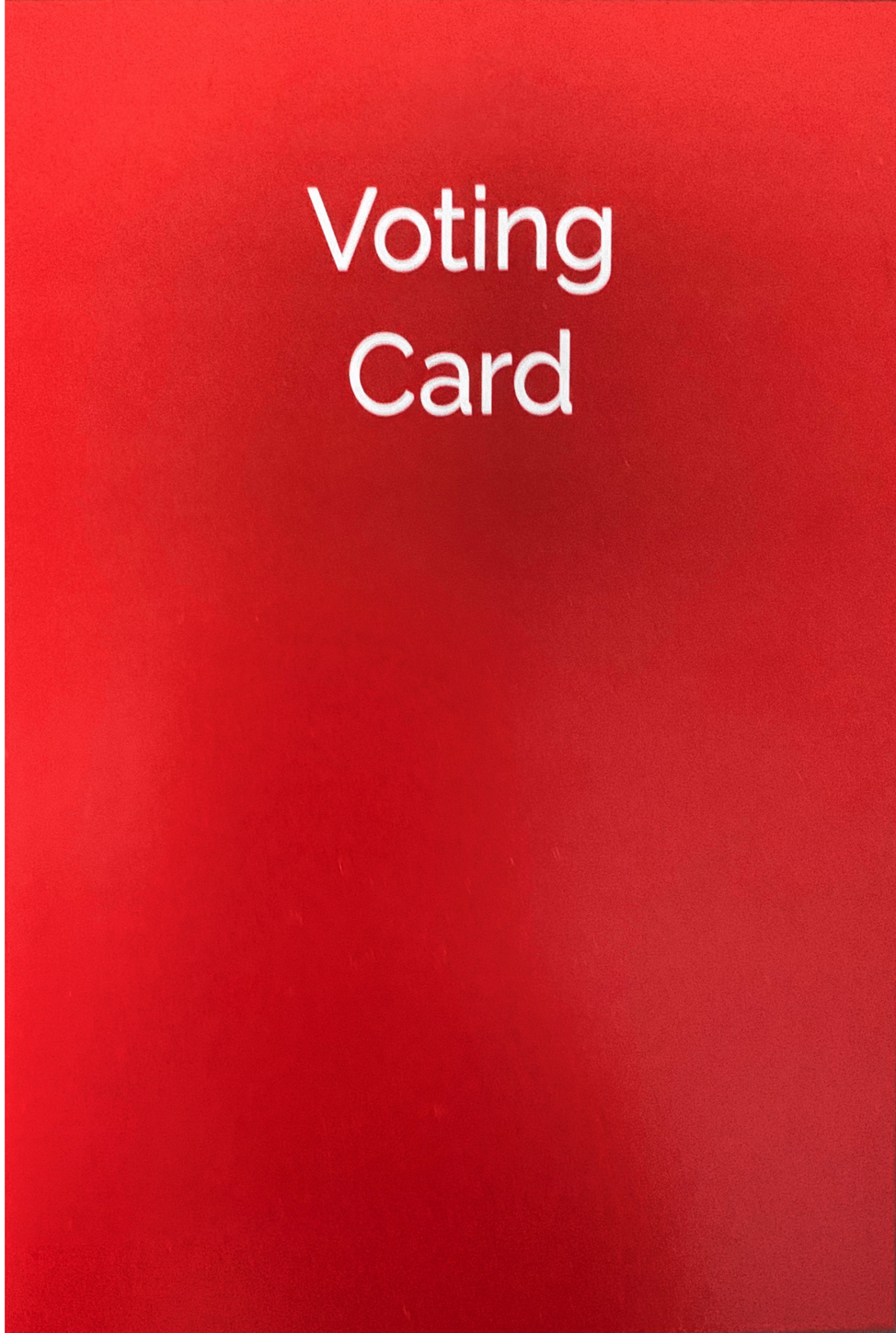
PSA DT calculated on
https://www.mskcc.org/nomograms/prostate/psa_doubling_time

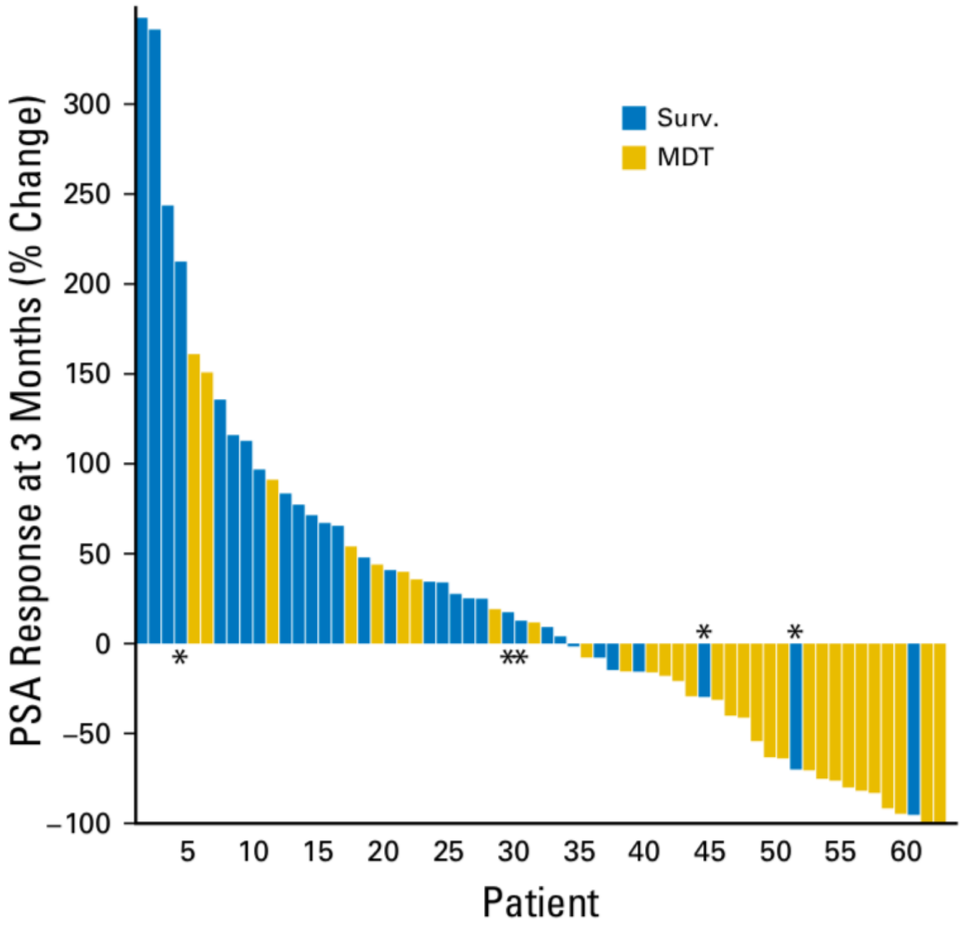


SBRT?

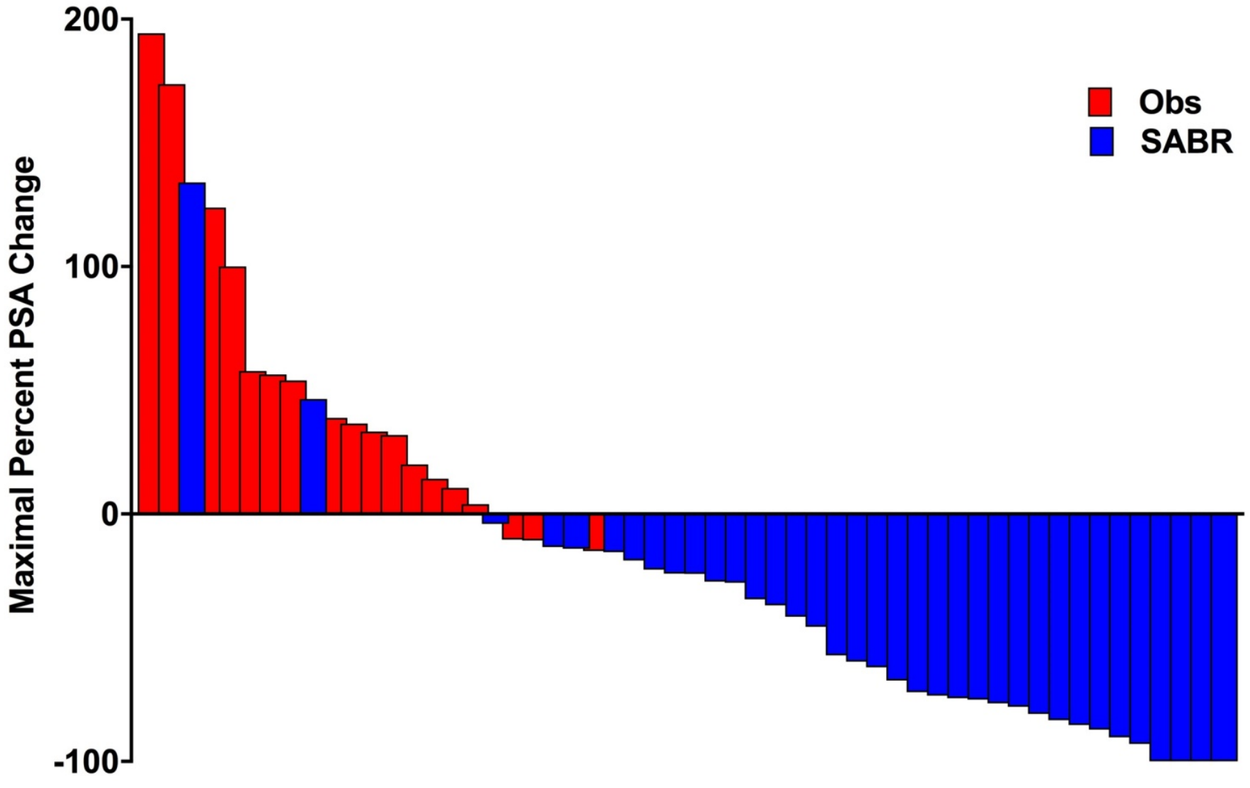



Voting
Card
68%
SBRT?
Voting
Card
32%

2 PHASE II TRIALS: MDT VS OBSERVATION



STOMP

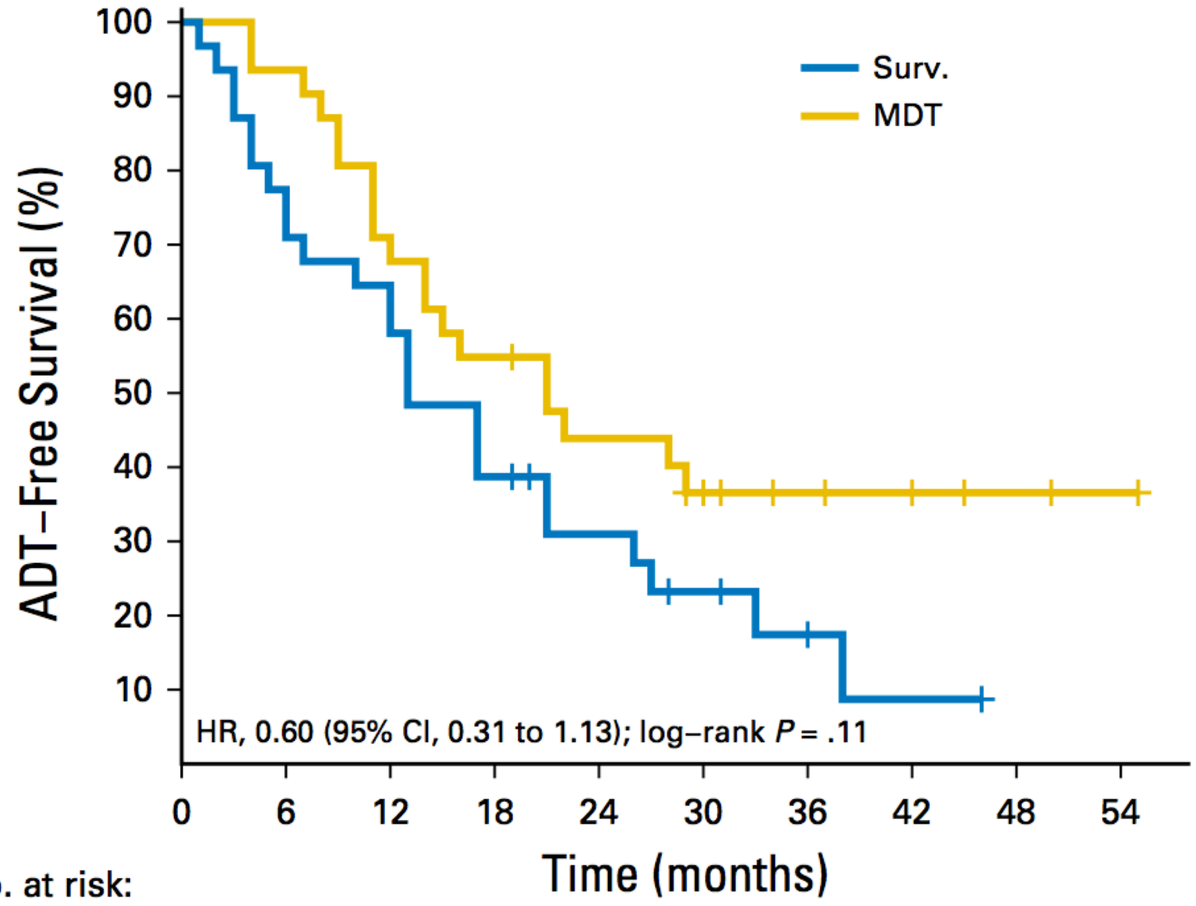


ORIOLE

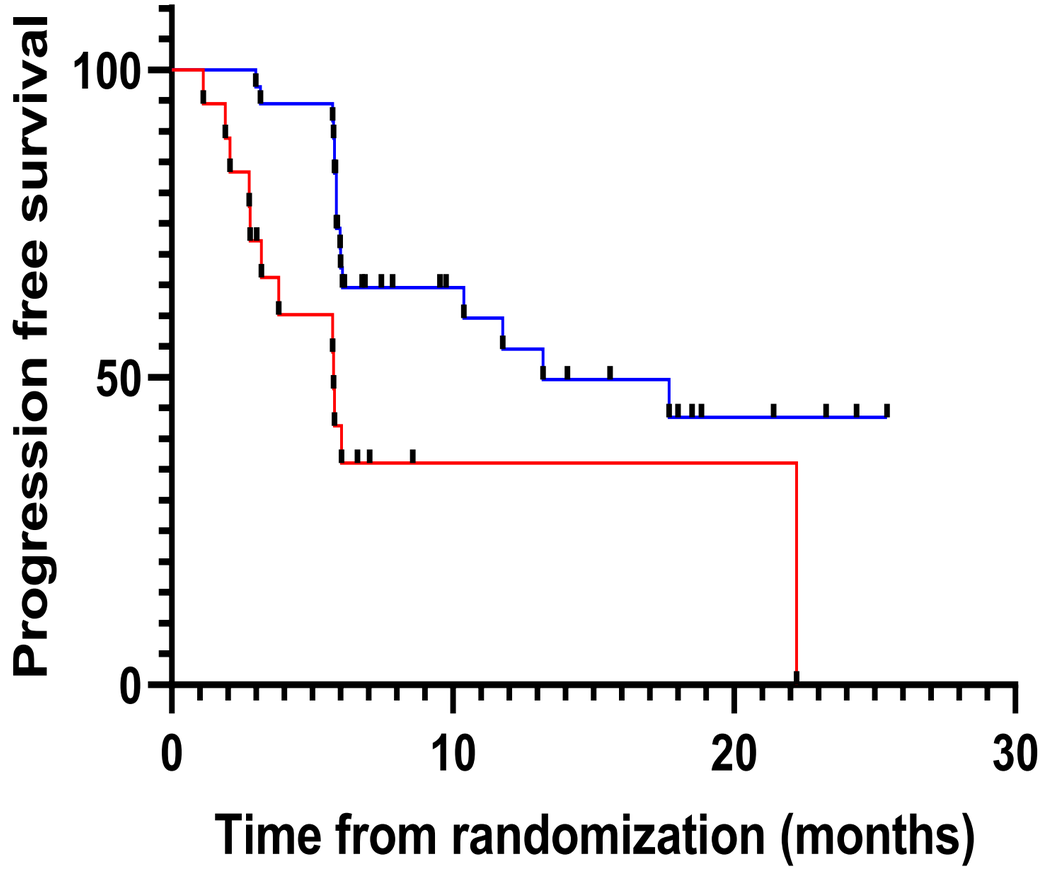
Ost et al. JCO 2018

Tran et al. ASTRO 2018

PROGRESSION-FREE SURVIVAL



No. at risk:



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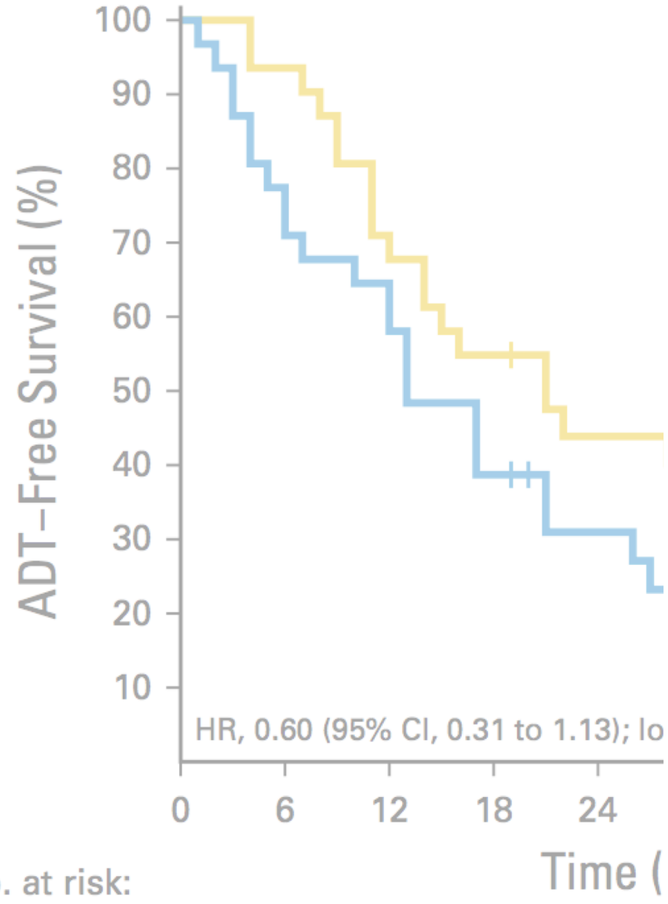
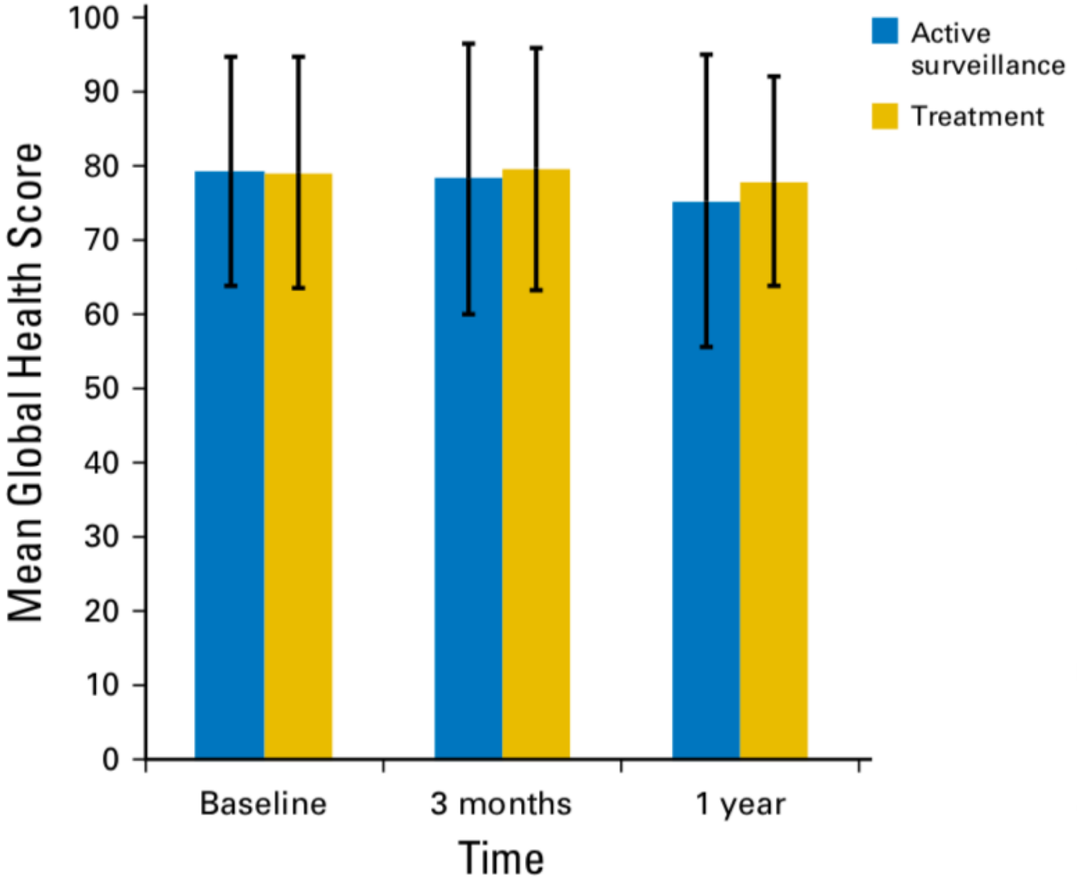
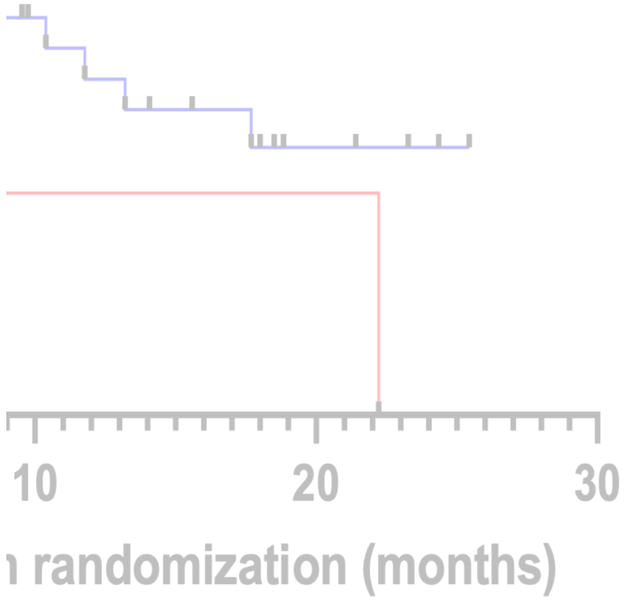
Ost et al. JCO 2018

Tran et al. ASTRO 2018

PROGRESSION-FREE SURVIVAL







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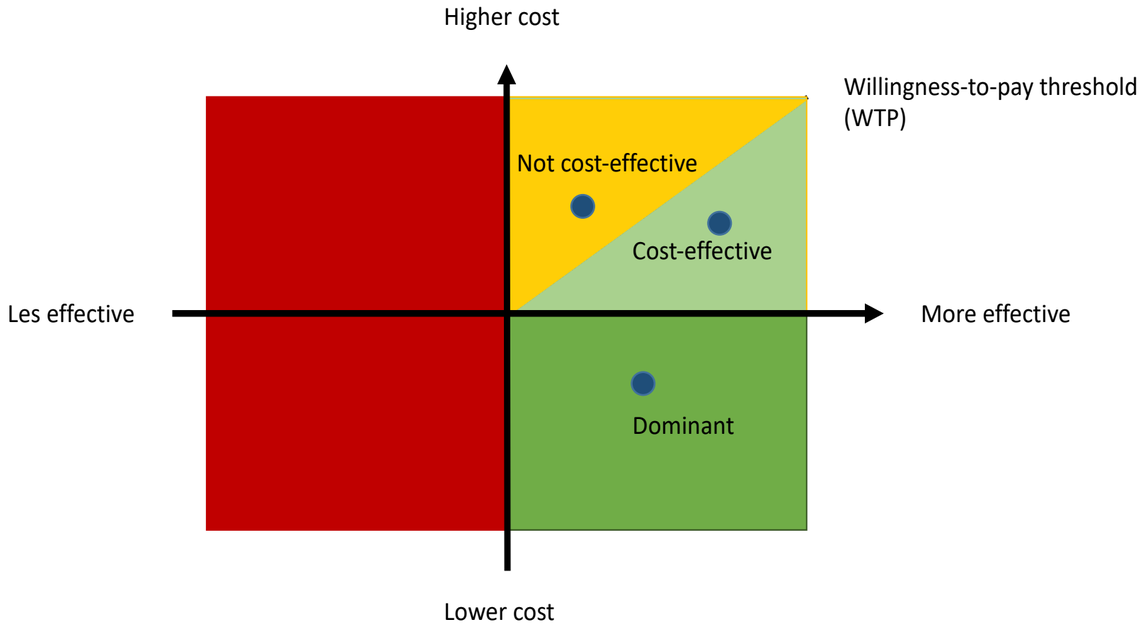
Ost et al. JCO 2018

Tran et al. ASTRO 2018

WHAT ABOUT THE COSTS OF MDT?



ICER: incremental cost-effectiveness ratio?

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De Bleser et al. submitted

Markov Model characteristics

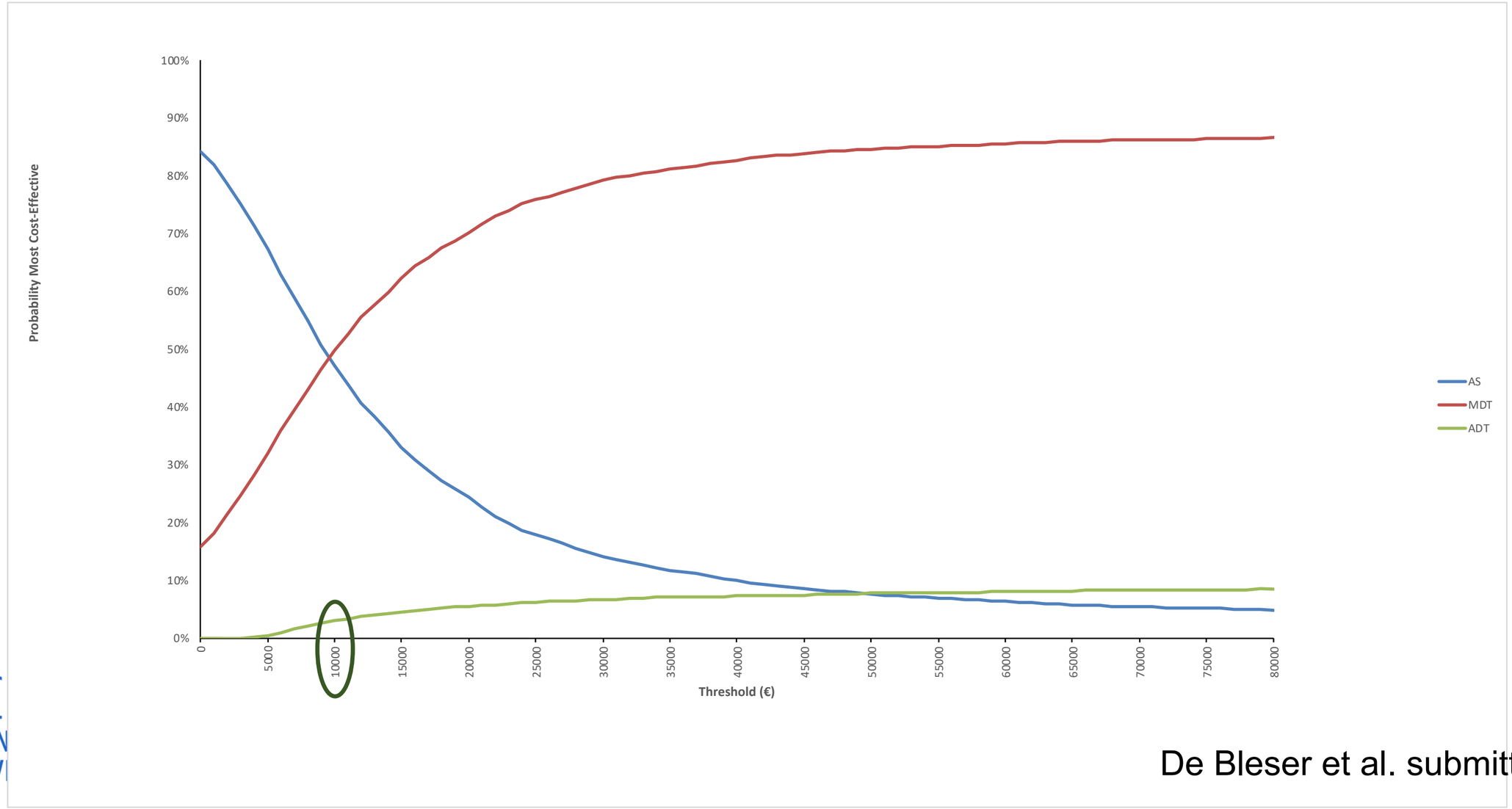
- **Perspective:** healthcare payer
- **Costs:** diagnostics, intervention (with possibility of multiple rounds of SBRT), FU & side-effects
- **Effects:** Quality-adjusted life years (QALY)
- **Time horizon:** 5 years (one-month cycle)
- **Discount rate**: 3% costs & 1.5% effects
- **Handling uncertainty:** one-way sensitivity analysis, probabilistic sensitivity analysis & scenario analysis
- **WTP threshold:** € 40.000 per QALY

Model inputs (data source)

- **Health state transition probabilities**
  - STOMP trial (Ost et al., 2018)
  - Expect for ADT-state to CRPC-state (De Bruycker et al., 2017)
- **Death**
  - Other causes (Belgian age-specific life tables, 2017)
  - Risk of dying in CRPC state (De Bruycker et al., 2017)
- **Toxicity per treatment**
  - Literature & expert opinion (Walker et al., 2013; Ploussard et al., 2018; Decastecker et al., 2014)
  - No toxicity cost of next line systemic drugs in CRPC setting
- **Utilities per health state**
  - Literature & expert opinion (Stewart et al., 2005; Tengs et al., 2000; Cooperberg et al., 2013; Heijnsdijk et al., 2016)
  - 80/20 ratio SBRT/surgery was taken in account
- **Costs (€)**
  - Belgium National Institute for health and disability insurance and cross-checked with hospital invoices.

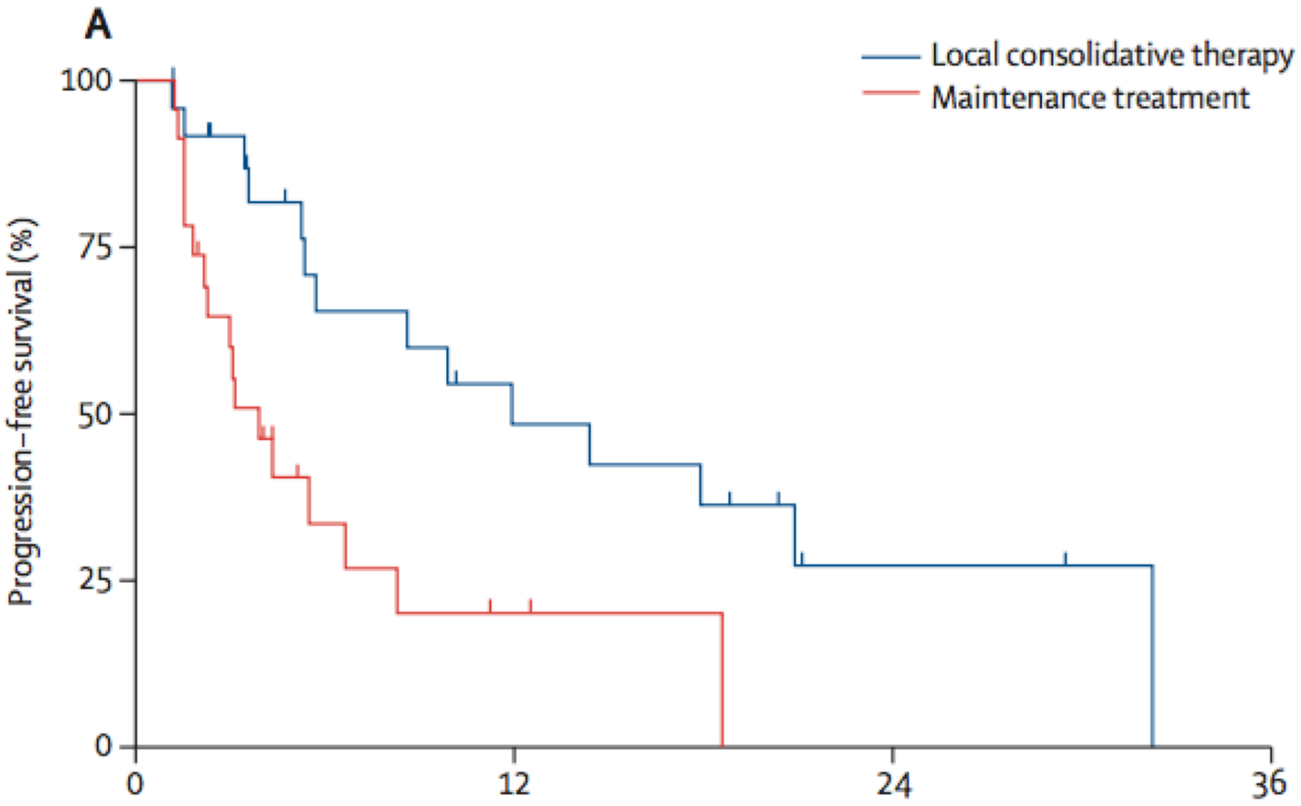
MOST COST-EFFECTIVE TREATMENT AT VARYING THRESHOLDS:

– the cost-effectiveness acceptability curve (CEAC)

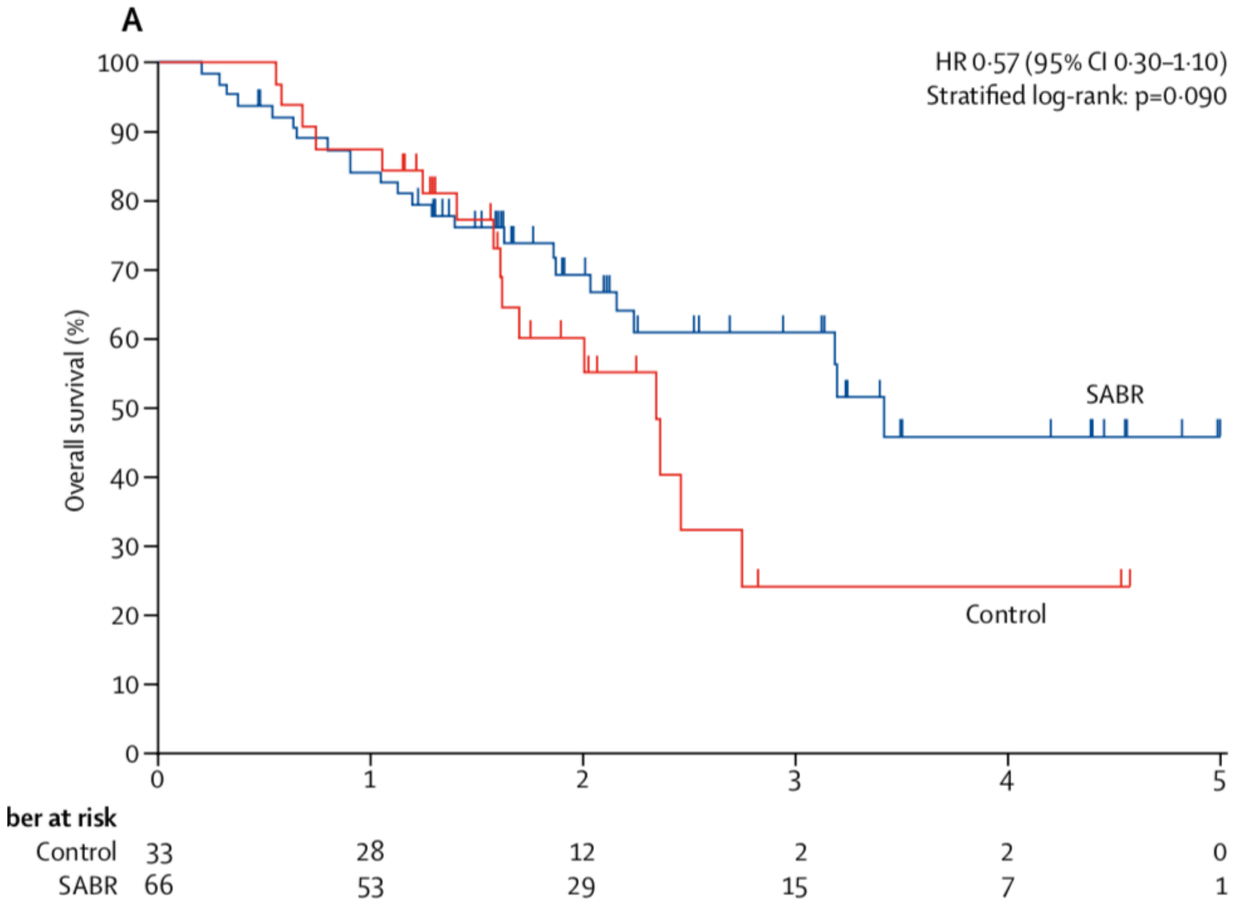


De Bleser et al. submitted

OTHER TUMOR TYPES?



Lung cancer



Mixed tumor types
(16% prostate cancer)

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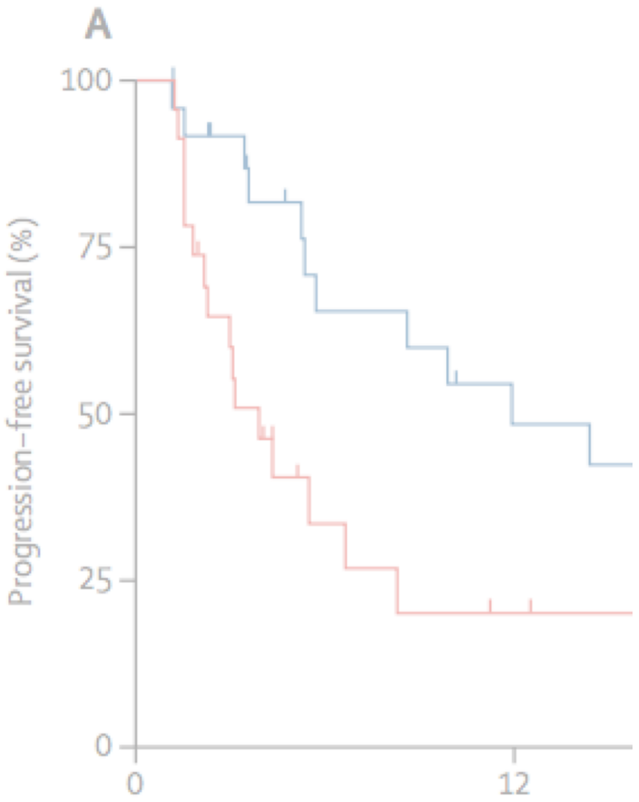
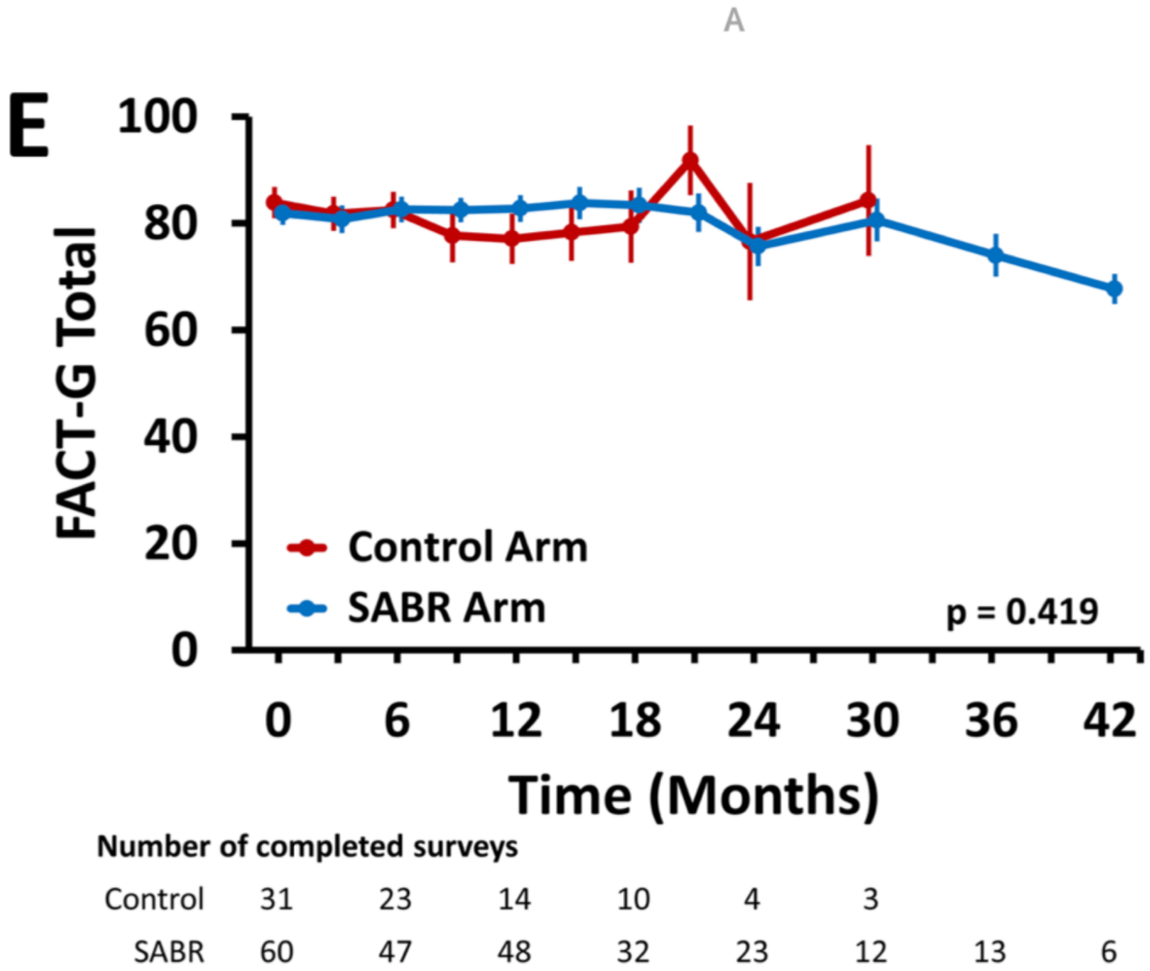
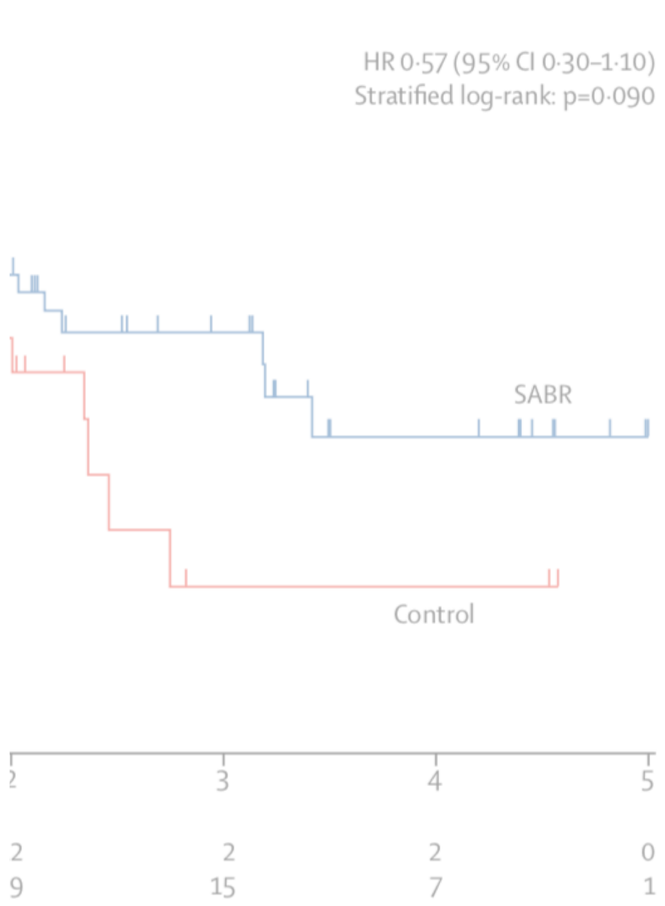
Gomez et al. Lancet Oncol 2016
Palma et al. Lancet 2019

OTHER TUMOR TYPES?







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Gomez et al. Lancet Oncol 2016
Palma et al. Lancet 2019
Olson et al. Red Journal 2019

CONCLUSION

- Phase II trials indicate that MDT is **feasible, well tolerated** and **improve biochemical response and PFS** as compared to observation

- MDT in other tumor types: improvement in OS
- MDT should **not be considered SOC** based on phase II trials!
- Phase III trial underway

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