

# The Oligometastatic State and the Evolving Paradigms



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**PGY-3**

Ok, so maybe the title was a little  
ambitious

# Outline

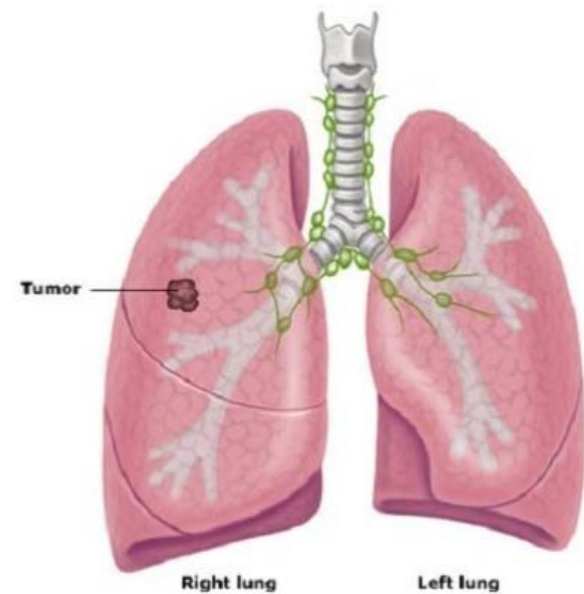
- General approach to cancer treatment
- Oligometastatic state
- Novel treatment approaches in oligometastases
- Future directions

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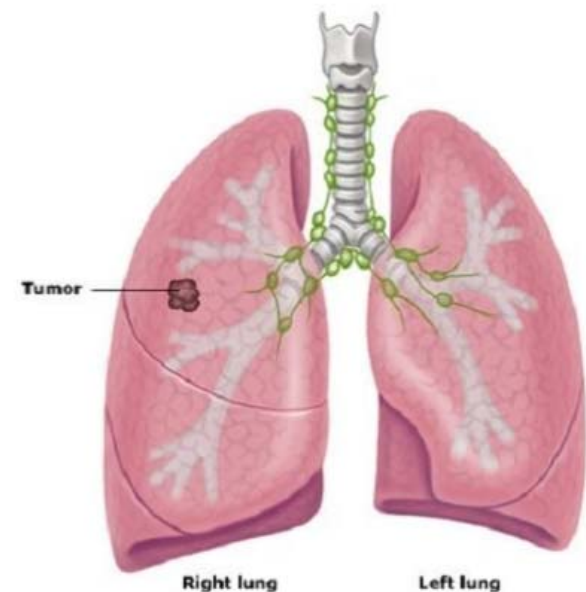
# General approach to solid tumors

- Local/Locoregional disease-> surgery and/or radiation $\pm$ chemotherapy
- Curative intent
- Best chance of local control
- Short and possibly long term morbidity



# General approach to solid tumors

- Stage IV – metastatic (systemic) disease, uncurable
- Rely on systemic treatments (chemotherapy)



+ disease in bones

# Metastatic disease

- Gross disseminated disease accompanied by more subclinical
- Local treatments add morbidity
- Systemic treatments control, don't cure



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Are all metastatic patients equal?

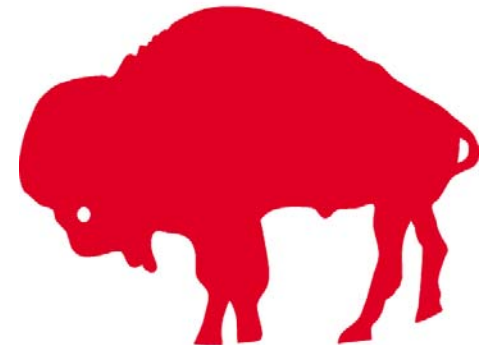
# Oligometastatic State

- First described by Hellman and Weichselbaum in 1995
- Definitions can vary
- May represent a more favorable biology
- Patients may benefit from aggressive local therapies

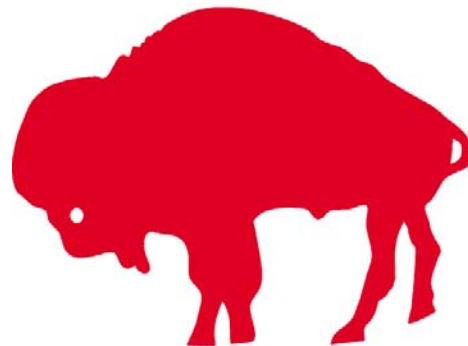
Metastatic-*ish*

# Biology

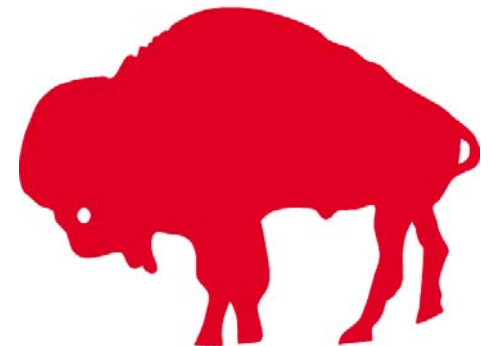
- Tumor type and natural history



- Clinical aggressiveness

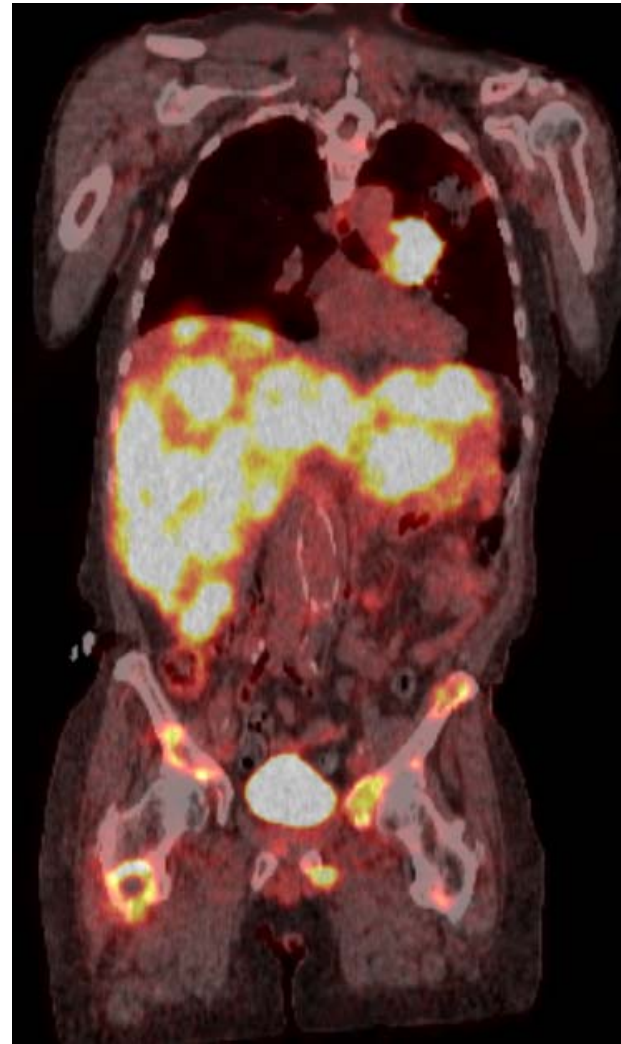


**1990**



**2001**

# Disease Burden



# Response to treatment

- Response of known disease predicts response of unknown disease
- Longer duration of disease control
- Progression is not favorable

# Patient Selection!





**BUT THEY NEVER ASK**

**HOW'S THE GOOD BOY**



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# Changing landscapes

- Systemic therapy is improving
- Failure is common at known sites of disease
- Benefit to local therapy in this setting?

# Local treatments in metastatic disease

- Local treatment to lower volume metastatic disease is not new



# Stereotactic body radiation therapy (SBRT)

- High doses of radiation therapy
- Five or less fractions
- Highly conformal
- Very precise

# Stereotactic body radiation therapy (SBRT)

- Requires resources (SBRT bags, fiducials)
- Time consuming
- Expensive
- Possibly higher rates of complications

# Recent trials

- Often NSCLC
- At least stable disease after chemotherapy
- 3-5 sites of disease
- RT to primary and sites of metastatic disease
- Various dosing regimens used

# Doses

- Often hypofractionated regimens ( e.g. 15fx) for primary tumor or mediastinum
- SBRT doses included 20-24Gy/1-3fx, 30-33Gy/3-5fx
- Other trials did 30-60Gy in 3-8fx or 16-24Gy in a single fraction (Brain or spine)

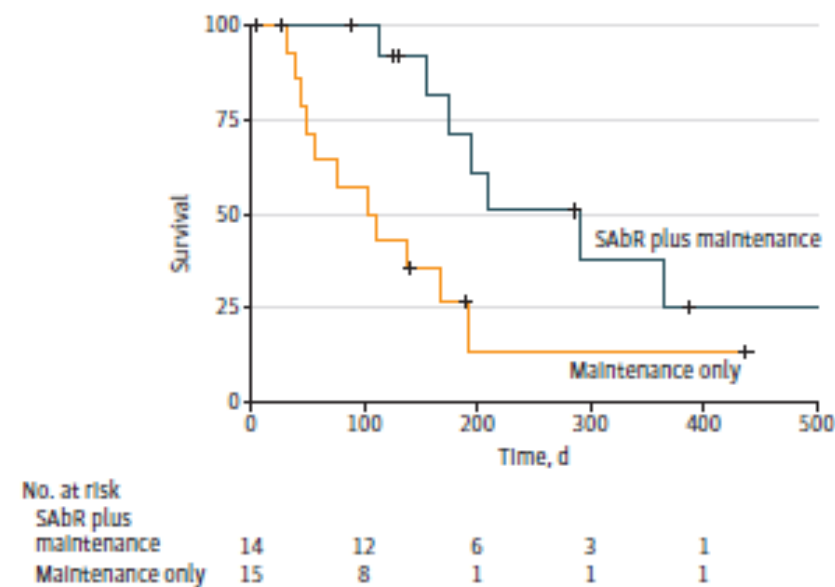
JAMA Oncology | Original Investigation

# Consolidative Radiotherapy for Limited Metastatic Non-Small-Cell Lung Cancer

## A Phase 2 Randomized Clinical Trial

Puneeth Iyengar, MD, PhD; Zabi Wardak, MD; David E. Gerber, MD; Vasu Tumati, MD; Chul Ahn, PhD;  
Randall S. Hughes, MD; Jonathan E. Dowell, MD; Naga Cheedella, MD; Lucien Nedzi, MD;  
Kenneth D. Westover, MD, PhD; Suprabha Pulipparacharuvil, PhD; Hak Choy, MD; Robert D. Timmerman, MD

Figure 2. Analysis of Progression-Free Survival



Log-rank testing reveals a statistically significant benefit in progression-free survival for SABR-plus-maintenance chemotherapy (hazard ratio, 0.304; 95% CI, 0.113-0.815;  $P = .01$ ). SABR indicates stereotactic ablative radiotherapy.

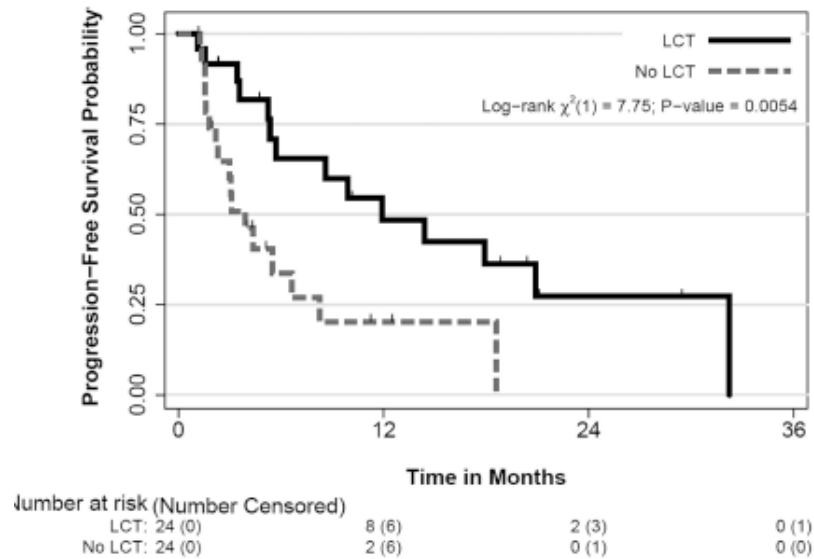
Median PFS:  
3.5 mo vs 9.7mo

Median OS  
1yr vs NYR

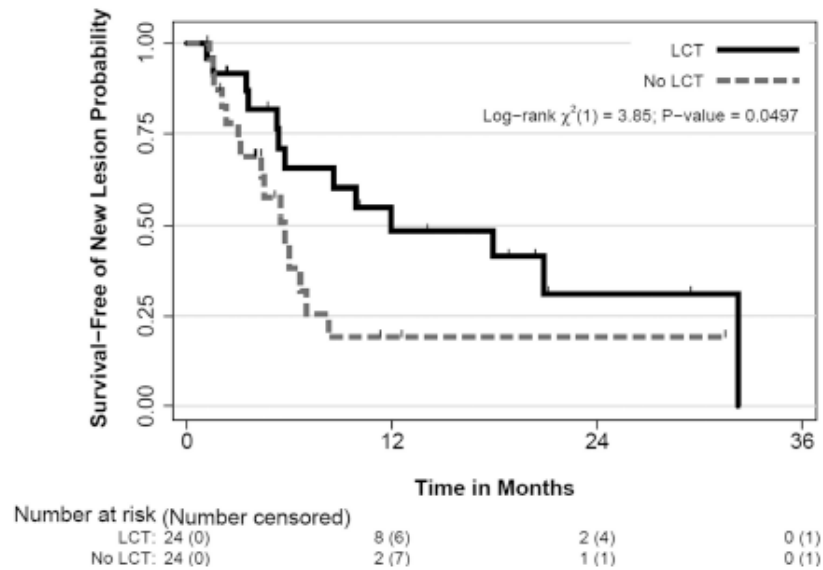


# **Local Consolidative Therapy versus Maintenance Therapy/ Observation for Patients with Oligometastatic Non-Small Cell Lung Cancer without Progression after Front-Line Systemic Therapy: Results of a Multi-Institutional Phase II Randomized Study**

Daniel R. Gomez, M.D.<sup>1</sup>, George R. Blumenschein, M.D.<sup>2,†</sup>, J. Jack Lee, Ph.D.<sup>3</sup>, Mike Hernandez, M.S.<sup>3</sup>, Rong Ye, M.S.<sup>3</sup>, D. Ross Camidge, M.D.<sup>4,†</sup>, Robert C. Doebele, M.D.<sup>4</sup>, Ferdinandos Skoulidis, M.D.<sup>2</sup>, Laurie E. Gaspar, M.D.<sup>5,†</sup>, Don L. Gibbons, M.D.<sup>2</sup>, Jose A. Karam, M.D.<sup>6</sup>, Brian D. Kavanagh, M.D.<sup>5,†</sup>, Chad Tang, M.D.<sup>1</sup>, Ritsuko Komaki, M.D.<sup>1,†</sup>, Alexander V. Louie, M.D.<sup>7</sup>, David A. Palma, M.D.<sup>8</sup>, Anne S. Tsao, M.D.<sup>2</sup>, Boris Sepesi, M.D.<sup>9</sup>, William N. William, M.D.<sup>2</sup>, Jianjun Zhang<sup>2</sup>, Qiuling Shi, Ph.D.<sup>10</sup>, Xin Shelley Wang, M.D.<sup>10</sup>, Stephen G. Swisher, M.D.<sup>9,\*†</sup>, and John V. Heymach, M.D.<sup>2,\*†</sup>



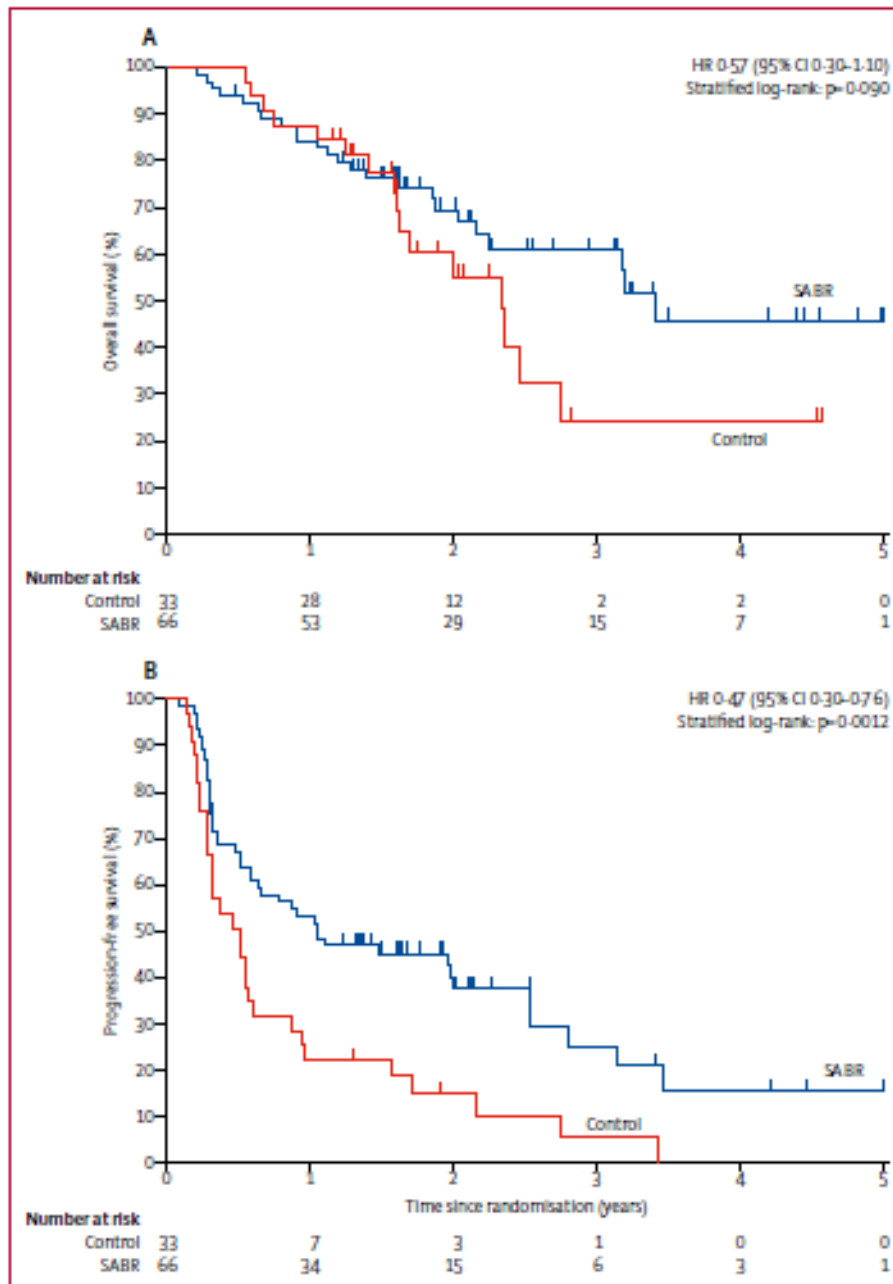
PFS:  
3.9 mo vs 11.9 mo



OS:  
17 mo vs 41 mo

# Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial

*David A Palma, Robert Olson, Stephen Harrow, Stewart Gaede, Alexander V Louie, Cornelis Haasbeek, Liam Mulroy, Michael Lock, George B Rodrigues, Brian P Yaremko, Devin Schellenberg, Belal Ahmad, Gwendolyn Griffioen, Sashendra Senthil, Anand Swaminath, Neil Kopeck, Mitchell Liu, Karen Moore, Suzanne Currie, Glenn S Bauman, Andrew Warner, Suresh Senan*



**Median OS  
28 mo vs 41 mo**

**Grade 2 toxicity  
61% w/ SBRT**

**3 out 66 had  
treatment  
related deaths**

# Overall findings

- Consolidative local therapy significantly improves disease-free survival
- Overall survival was improved in NSCLC patients and likely with many other cancers
- SBRT is associated with improved OS over standard palliative regimens
- SBRT is not necessarily benign

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# Ongoing work

- Multiple Phase II in specific disease sites
- SABR-COMET 10
- BR-002
- LONESTAR Trial (Phase III)

# ASTEROID Trial

- Assessing Single-fraction SBRT versus STandard Palliative RadiatiOn In patients with Metastatic Disease (ASTEROID)
- SBRT vs standard for quality of life and pain relief due to metastases



# Conclusions

- Oligometastatic state is a function of tumor biology, disease burden, and treatment efficacy
- Local treatments improve outcome in oligometastatic patients
- SBRT appears superior to conventional RT

Questions?