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A Comprehensive Cancer Center Designated by the National Cancer Institute

# Recent advances in Radiation Oncology

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University of North Carolina Chapel Hill

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## Disclosure Information



**I have the following financial relationships to disclose:**

**Stockholder/Co-founder in: Capiro Biosciences and Archimmune therapeutics**

**Research funding from Capiro Biosciences**

*- and -*

**I will not discuss off label use and/or investigational use in my presentation.**

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## Radiation Oncology

- A key component of cancer treatment
- 60% of cancer patients receive radiotherapy sometime during their illness
- Together with surgery and chemotherapy, radiation is part of the trimodality regimen that treats and cures cancer



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## UNC Radiation Oncology

- **8 Sites** including main campus (UNC Chapel Hill)
- **Faculty:**
  - 21 physicians
  - 15 physicists
- **Capabilities:**
  - 12 LINAC machines
  - Cyberknife Radiosurgery
  - Tomotherapy machines
  - HDR brachytherapy
  - LDR brachytherapy
  - Intraoperative Radiation



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**UNC Health Care System  
Rad Onc Facilities**

**Smith McMichael Cancer Center  
UNC Rockingham Health Care**  
336-623-9713  
• Mohit Kasibhatia, MD

**NC Cancer Hospital, UNC Medical Center**  
984-974-8415 (Clinic)  
984-974-8452 (CyberKnife)  
• Ron Chen, MD  
• Bhisam Chera, MD  
• Gaorav Gupta, MD, PhD  
• Ellen Jones, MD, PhD  
• Lawrence Marks, MD  
• Colette Shen, MD, PhD  
• Joel Tepper, MD  
• Andrew Wang, MD  
• Ashley Weiner, MD, PhD

**Wakefield (UNC/Rex)**  
919-570-7550  
• Roger Anderson, MD  
• Justin Wu, MD

**McCreary Cancer Center,  
Caldwell Memorial Hospital  
in Lenoir, NC**  
828-759-4960  
• Roger Holland, MD

**UNC/Rex Cancer Care  
in Raleigh, NC**  
919-784-3018  
• Courtney Bui, MD  
• John Fakiris, MD  
• Byron Huff, MD  
• Nathan Sheets, MD  
• Justin Wu, MD

**Hayworth Cancer Center  
High Point Regional Hospital**  
336-878-6036  
• Heather Pacholke, MD

**East Raleigh (UNC/Rex)**  
919-334-3900  
• John Reilly, MD

**Smithfield (UNC/Rex)**  
919-209-3555  
• Debra Harr, MD  
• Daniel Oh, MD


**Clayton (UNC/Rex)**  
919-585-8550  
• Debra Harr, MD  
• John Reilly, MD

Updated: April 17, 2018


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**Radiation technologies**

**LINAC**

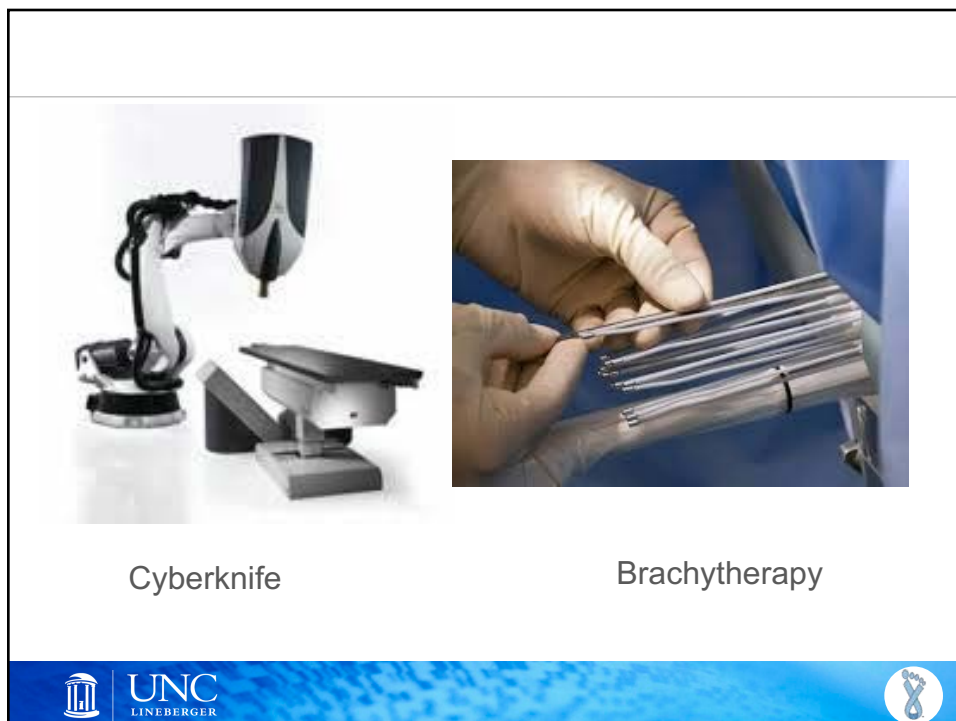


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## Oligometastasis

- A condition with a few metastases arising from tumors that have not acquired a potential for widespread metastases
- Potentially curable disease and treatment can bring survival benefit
- Long history of oligometastasis treatment—liver metastasis from colorectal cancer, brain mets from lung cancer
- Challenge: adequate treatment of the oligometastasis
- Solution: stereotactic ablative body radiotherapy

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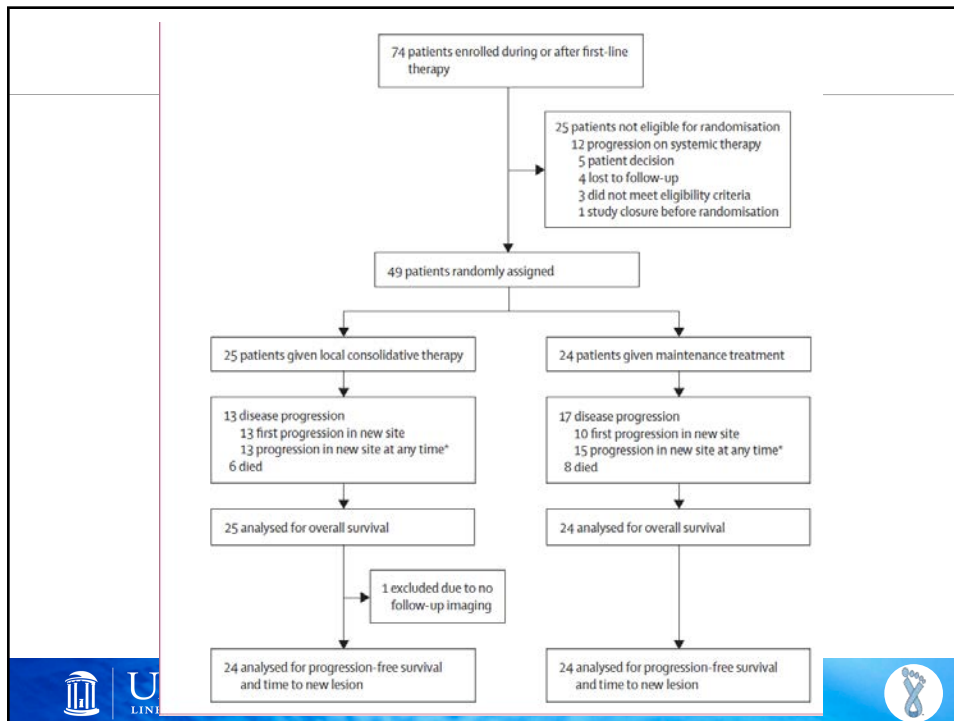
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### Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study

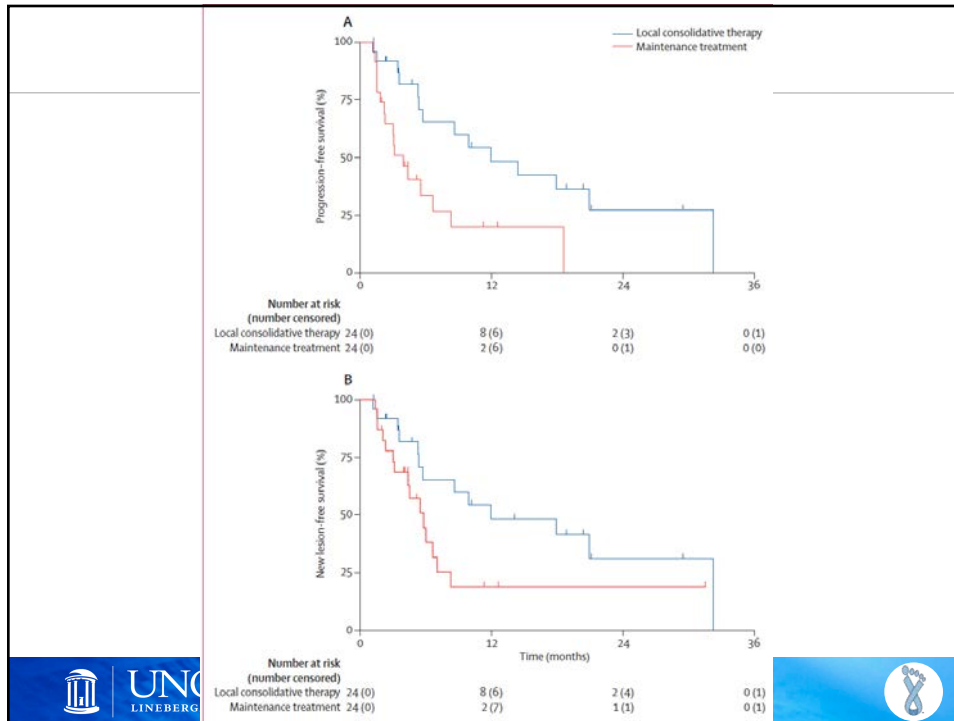
Daniel R Gomez, George R Blumenschein Jr, Jack Lee, Mike Hernandez, Rong Ye, D Ross Camidge, Robert C Doebele, Ferdinando Skoulidis, Laurie E Gaspar, Don L Gibbons, Jose A Karam, Brian D Kavanagh, Chad Tang, Ritsuko Komaki, Alexander V Louie, David A Palma, Anne S Tsao, Boris Sepesi, William N Williams, Jianjun Zhang, Qiuling Shi, Xin Shelley Wang, Stephen G Swisher\*, John V Heymach\*

- Randomized phase II
- Three or fewer metastases, not including the primary tumour (nodes are counted collectively)
- Randomly assigned (1:1) to either local consolidative therapy (radiotherapy or surgery) with or without maintenance treatment or to maintenance treatment alone

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JAMA Oncology | Original Investigation

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

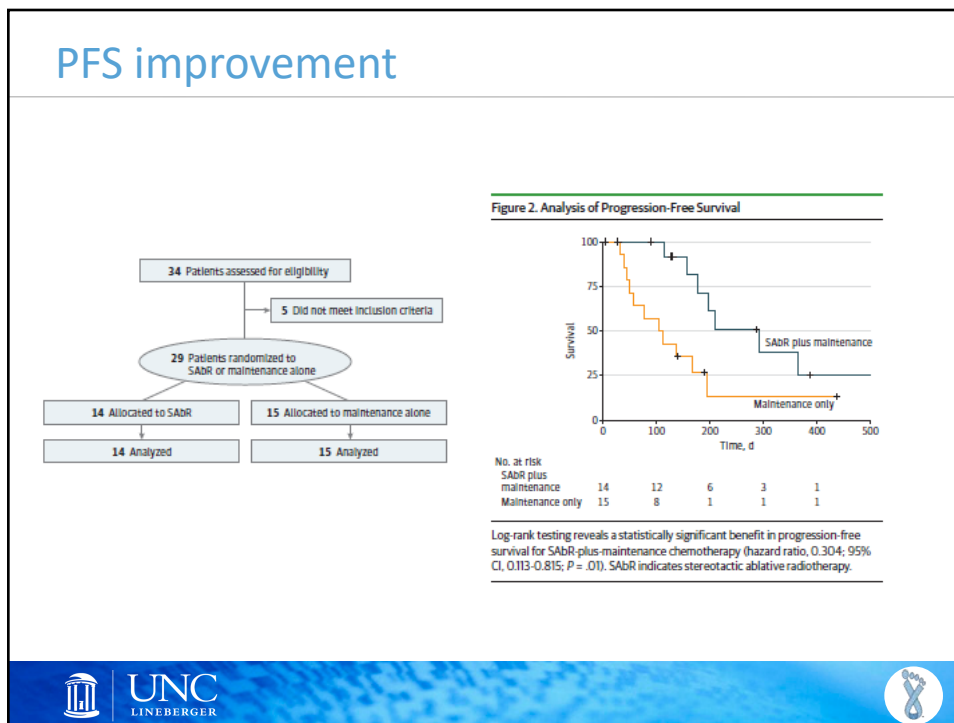
#### A Phase 2 Randomized Clinical Trial

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

- Single institution randomized phase II
- Maintenance chemotherapy alone vs SABR followed by maintenance chemotherapy
- Primary plus up to 5 metastatic sites

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## Summary

- SABR treatment of oligometastatic disease in NSCLC appears to improve survival
- Similar data in other cancers such as prostate cancer
- SABR is easy to do with limited toxicities
- Cyberknife is an excellent tool for SABR treatment
- Patients with oligometastatic disease should be considered for SABR
  - Less than 5 metastases
- Indication for oligo-progressive disease is emerging
  - Doing well on systemic therapy with 1 or small number of lesions progressing only

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## Local radiation for low-volume metastatic prostate cancer

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



Christopher C Parker, Nicholas D James, Christopher D Brawley, Noel W Clarke, Alex P Hoyle, Adnan Ali, Alastair W S Ritchie, Gerhardt Attard, Simon Chowdhury, William Cross, David P Dearnaley, Silke Gillessen, Clare Gilson, Robert J Jones, Ruth E Langley, Zafar I Malik, Malcolm D Mason, David Matheson, Robin Millman, J Martin Russell, George N Thalmann, Claire L Amos, Roberto Alonzi, Amit Bahl, Alison Birtle, Omar Din, Hassan Douis, Chinnamani Eswar, Joanna Gale, Melissa R Gannon, Sai Jonnada, Sara Khaksar, Jason F Lester, Joe M O'Sullivan, Omi A Pankh, Ian D Pedley, Debra M Pudney, Denise J Sheehan, Narayanan Nair Srihari, Anna T H Tran, Mahesh K B Parmar\*, Matthew R Sydes\*, on behalf of the Systemic Therapy for Advanced or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators†



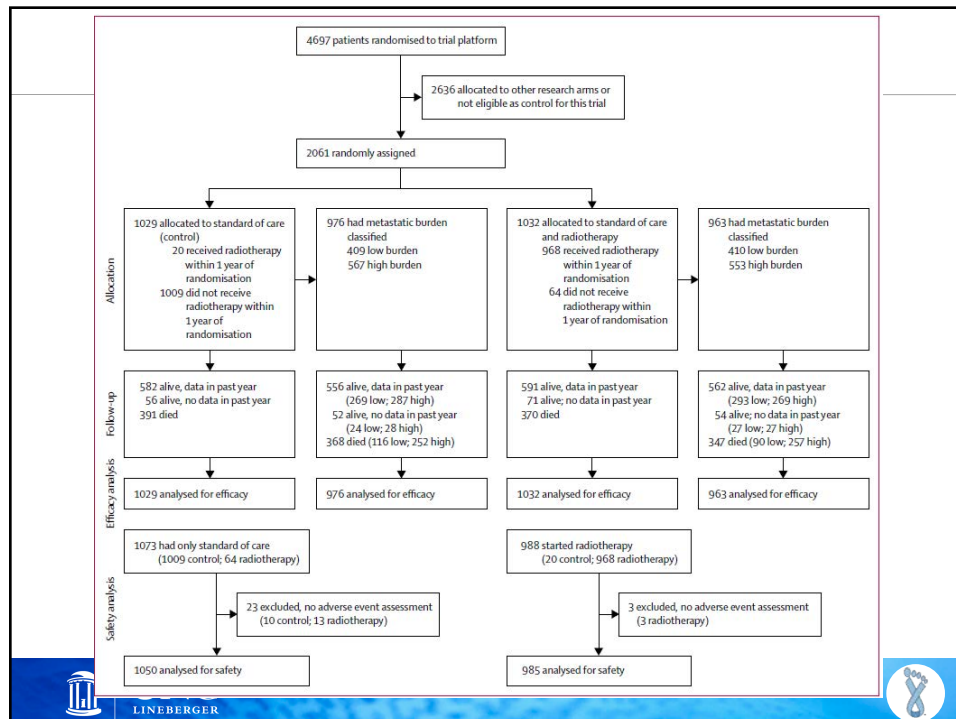
- Randomized phase III at 117 hospitals in Switzerland and UK
- Newly diagnosed metastatic prostate cancer
- 1:1 randomization to standard of care vs. standard of care+local XRT



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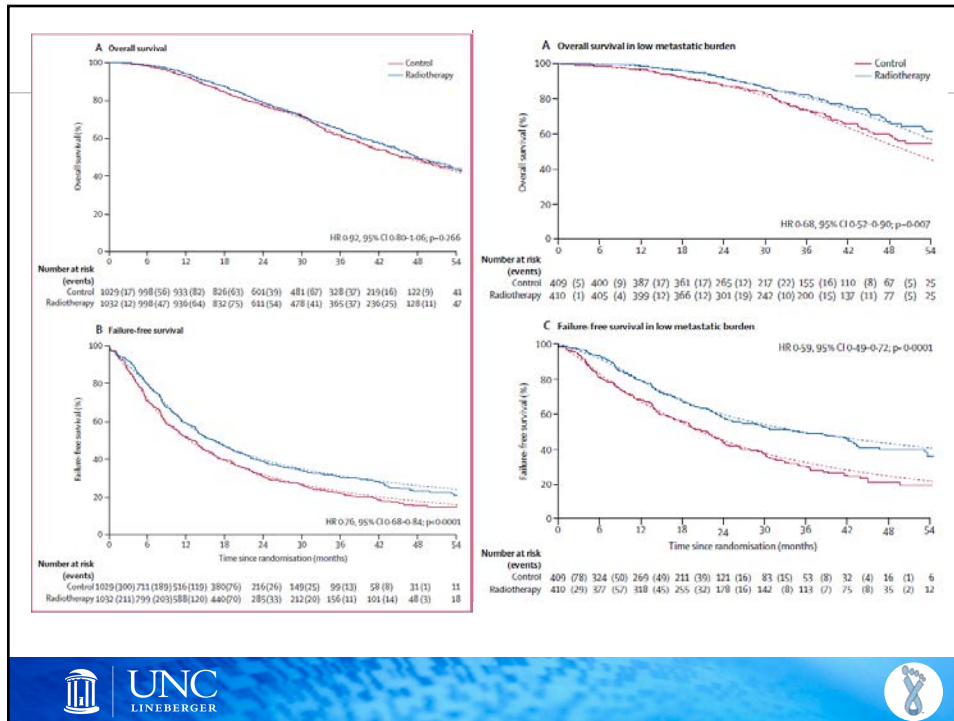


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## Summary

- Four or more bone sites outside the vertebrae and pelvis, and/or visceral metastases was considered a high metastatic burden and all other assessed patients classified as low
- Low metastatic burden PCa patients should be considered for local XRT
- Patients with locally obstructive symptoms should also be considered for XRT

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## ASCEND-RT for high risk prostate cancer

### Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (th ASCENDE-RT Trial): An Analysis of Survival Endpoints for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost to a Dose-Escalated External Beam Boost for High- and Intermediate-risk Prostate Cancer

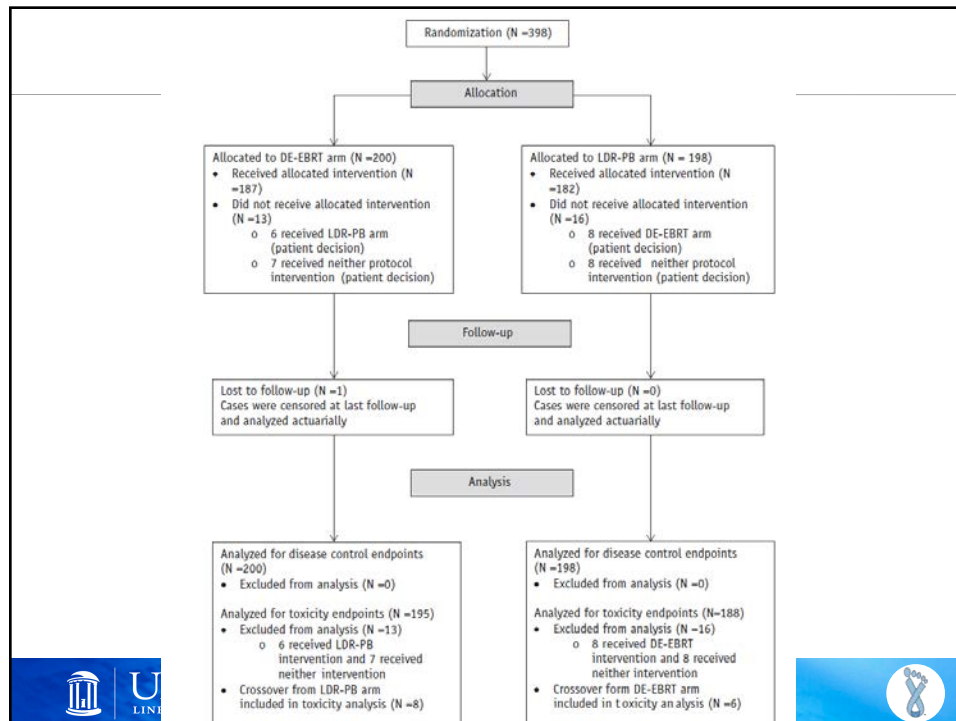
W. James Morris, MD, FRCPC,<sup>\*,†</sup> Scott Tyldesley, MD, FRCPC,<sup>\*,†</sup>  
 Sree Rodda, MBBS, MRCP, FRCR,<sup>\*</sup> Ross Halperin, MD, FRCPC,<sup>\*,‡</sup>  
 Howard Pai, MD, FRCPC,<sup>\*,§</sup> Michael McKenzie, MD, FRCPC,<sup>\*,†</sup>  
 Graeme Duncan, MB, ChB, FRCPC,<sup>\*,†</sup>  
 Gerard Morton, MB, MRCPI, FRCPC, FFRRCSI,<sup>||</sup> Jeremy Hamm, MSC,<sup>¶</sup>  
 and Nevin Murray, MD, FRCPC<sup>‡,#</sup>



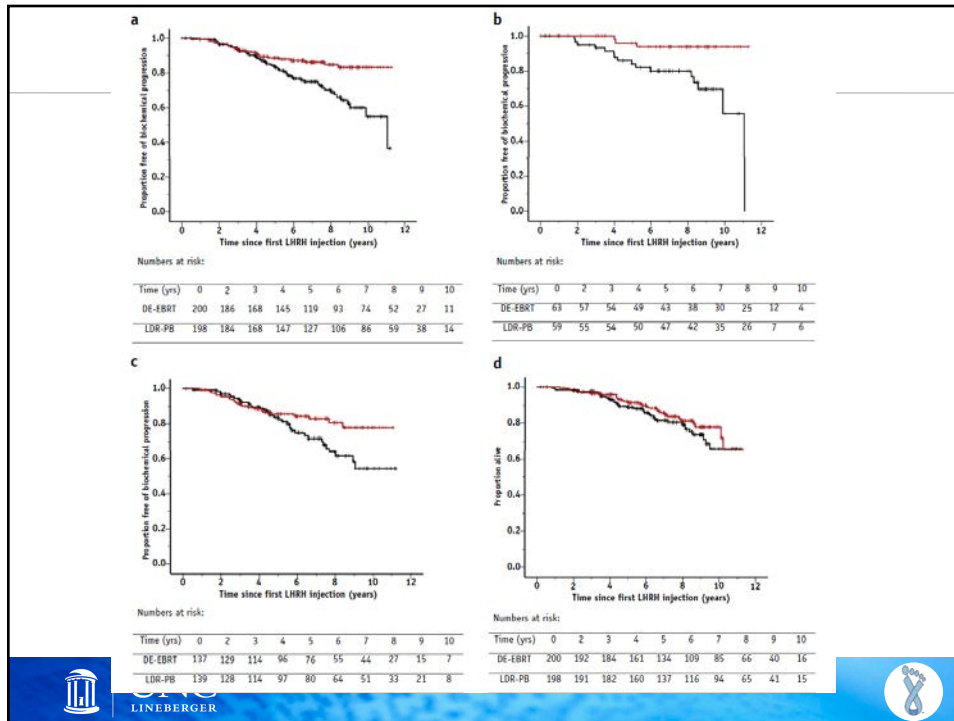
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## Summary

- Patients with high risk or high intermediate risk PCa should be considered for the ASCEND-RT regimen
- Brachytherapy should be done at a high volume place as quality of brachytherapy is associated with volume

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## Early salvage radiotherapy for prostate cancer

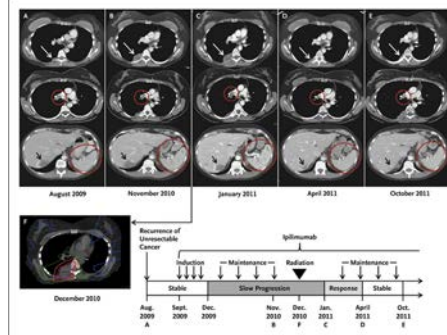
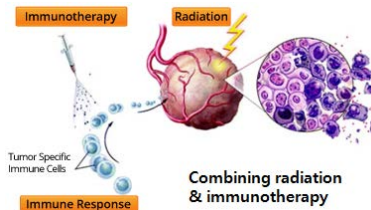
- RADICALS trials
- Adjuvant vs early salvage RT
- Reported at ESMO—no benefit to adjuvant
- Await publication
- Important: early salvage means PSA >0.1 would trigger treatment



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## Radiation and cancer immunotherapy

Clinical strategy: Radiation +  
checkpoint inhibitors  
Abscopal effect  
Improved antigen exposure  
No improvement in antigen  
presentation



Postow MA et al. N Engl J Med 2012;366:925-931.

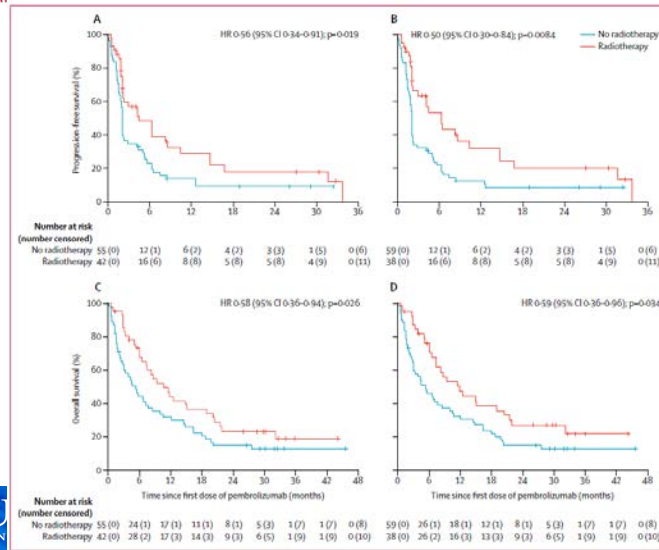
[http://www.gnsbio.co.kr/?page\\_id=217&lang=en](http://www.gnsbio.co.kr/?page_id=217&lang=en)



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## Previous radiotherapy and the clinical activity and toxicity of pembrolizumab in the treatment of non-small-cell lung cancer: a secondary analysis of the KEYNOTE-001 phase 1 trial

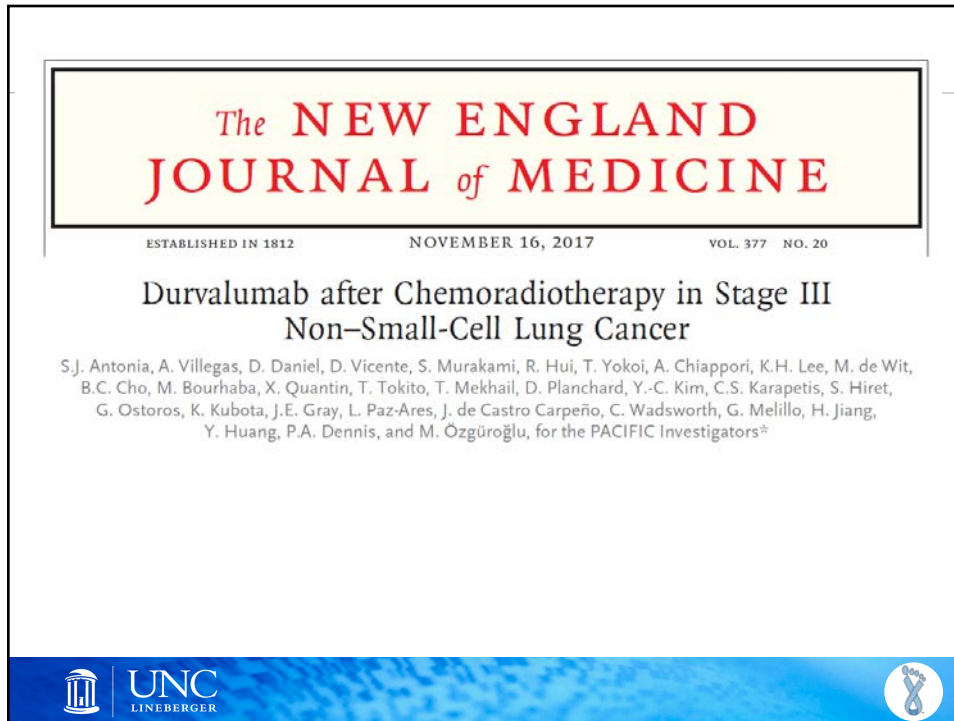
Narek Shajerdian\* Aaron El Ichern\* Vrlior Bannazian Darlene Morrittina Jonathan W Goldman Silvia C Enemanti Edward R Grant\* Percy Lee†



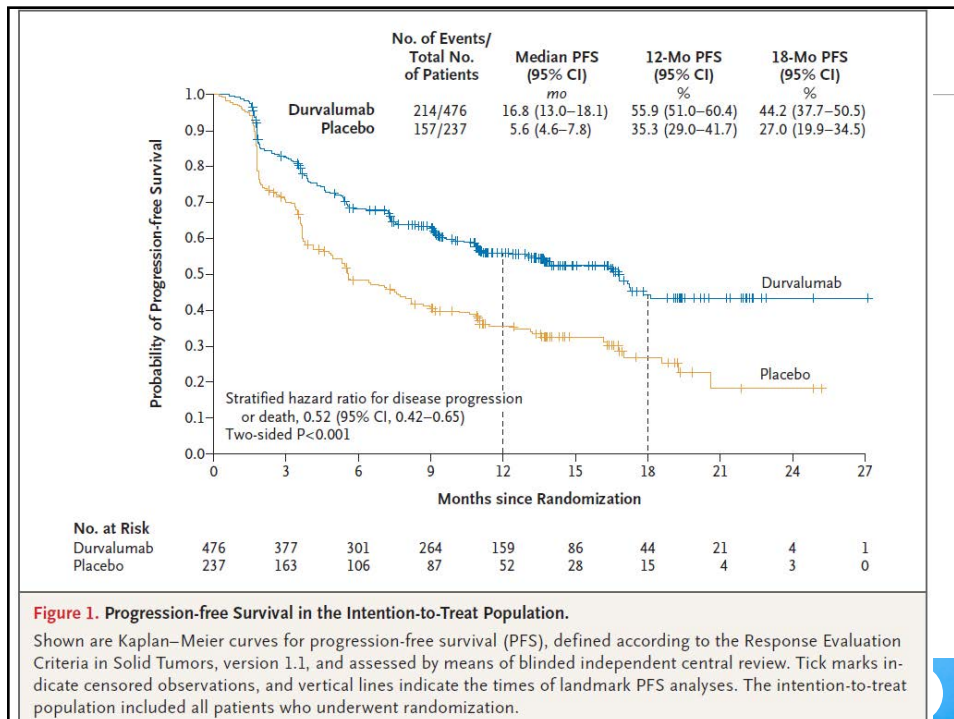
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	No previous thoracic radiotherapy (n=73)	Previous thoracic radiotherapy (n=24)	p value
<b>All recorded pulmonary toxicities*</b>			
Any pulmonary toxicity	29 (40%)	15 (63%)	0.052
<b>Specific pulmonary toxicities</b>			
Dyspnoea	15 (21%)	6 (25%)	0.64
Cough	16 (22%)	7 (29%)	0.46
Wheezing	3 (4%)	1 (4%)	0.99
Pneumonitis	1 (1%)	2 (8%)	0.15
Respiratory failure†	4 (6%)	3 (13%)	0.25
Grade ≥3 pulmonary toxicity	9 (12%)	4 (17%)	0.58
Dyspnoea	6 (8%)	0	..
Pneumonitis	1 (1%)	1 (4%)	..
Respiratory failure	2 (3%)	3 (13%)	..
<b>Treatment-related pulmonary toxicities‡</b>			
Any pulmonary toxicity	1 (1%)	3 (13%)	0.046
<b>Specific pulmonary toxicities</b>			
Dyspnoea	0	2 (8%)	0.059
Pneumonitis	1 (1%)	2 (8%)	0.15
Grade ≥3 pulmonary toxicity (pneumonitis)	1 (1%)	1 (4%)	0.44

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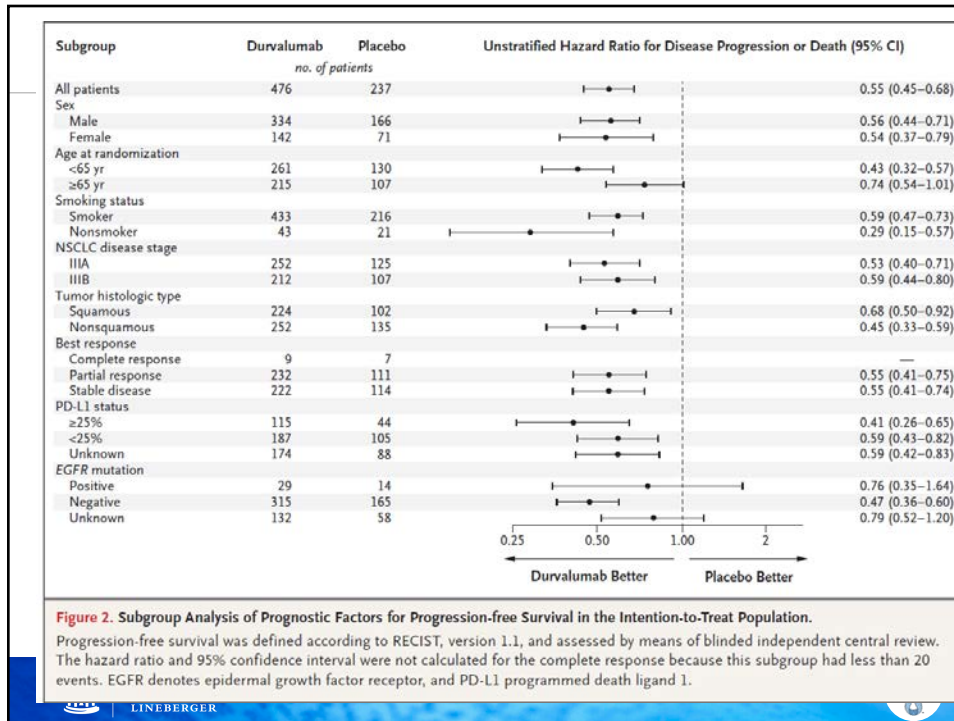


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## Summary

- Radiotherapy is synergistic with cancer immunotherapy
- Growing data on how to apply radiotherapy to improve cancer immunotherapy
- Though higher side effects, patients can remain on immunotherapy while receiving radiation

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## SBRT for pancreatic cancer

“SBRT” vs. Conventional radiation: What’s the difference?

1. Precision (Higher)
2. Dose (Higher dose per fraction)
3. Volume (Lower)
4. Time (Fewer fractions, more convenient)

How do these factors translate into cancer control and toxicity?

- Potentially better control for smaller tumors
- Risk of severe toxicity if dose or volume are too high

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Summary of SBRT evidence – Learning curve

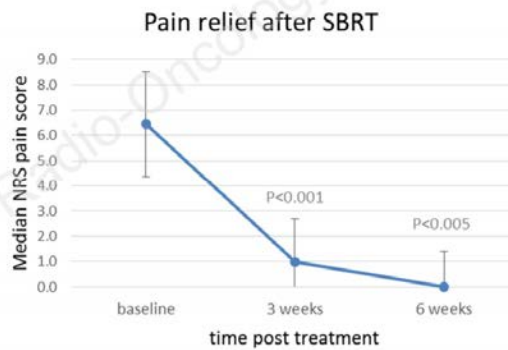
Study	Pts	Tx	Med. f/u	Outcomes
Chang 2009 Stanford	77 LAPC	25 Gy / 1 fx	12M	1-yr LC: 84% 9% G3 tox (3 ulcers, 3 stricture, 1 perf)
Pollom 2014 Stanford	167 LAPC	25 Gy / 1 fx 25-45 Gy / 5 fx	8M	1-yr LC: 90% 26% G2 tox with 1 fx 8% G2 tox with 5 fx
Comito 2016 Milan, Italy	45 LAPC	45 Gy / 6 fx	24M	2-yr LC: 87% No G3 toxicity
Herman 2016 Hopkins	49 LAPC	33 Gy / 5 fx	14M	1-yr LC: 78% 6% G3 tox (1 fistula, 2 bleed)
Rwigema 2011 Pitt	71 LAPC	18-25 Gy / 1 fx	13M	1-yr LC: 47% No late toxicity
Mahadevan 2011 Harvard	39 LAPC	24-36 Gy / 3 fx	21M	2-yr LC: 85% 9% G3 tox (bleed, bowel obs)
Mellon 2015 Moffitt	110 BRPC 49 LAPC	30 Gy / 5 fx	14M	BRPC: 49% R0 resection 7% G3 tox (bleed)

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Celiac plexus SBRT – preliminary results in 21 patients

### Results – Primary endpoint

- All patients reported decrease in celiac pain after three weeks
- One third of patients reported pain eliminated entirely by six weeks



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### Overall summary

- Radiation oncology is an integral part of cancer treatment
- Indications for radiation continue to evolve
- More patients can benefit from radiation treatment with recent updates



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