



Penn Medicine
Abramson Cancer Center

Late Effects of Cancer and Cancer Treatment: How little we know.....

Lawrence N Shulman, MD, MACP, FASCO
Deputy Director for Clinical Services
Abramson Cancer Center
University of Pennsylvania

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Disclosures

- ▶ Research Grants
 - Breast Cancer Research Foundation
 - Bristol Myers Squibb

Neither relevant to this talk

Long-term survival....some examples

- ▶ Hodgkin lymphoma
 - ▶ Acute lymphoblastic leukemia
 - ▶ Testicular Cancer
 - ▶ Early stage breast cancer
-
- ▶ *All require systemic therapy +/- radiation*
 - ▶ *All with long-term survival in excess of 85%*
 - ▶ *All can occur in young people with long potential life expectancy*

What do we know.....

- ▶ Children's Oncology Group (COG)
 - Very good data on long-term effects for childhood cancers
- ▶ For Adults.....
 - No systematic way to accrue data
 - We know only patchwork data

Hodgkin Lymphoma as a paradigm

- Median age at presentation = 26 years
- Generally treated with chemotherapy (anthracycline based) +/- radiation
- Long-term remission > 85%

Hodgkin Lymphoma – Case Study

- ▶ 1983, age 21, Hodgkin Lymphoma, Stage IIA, splenectomy, MOPP x 6, mantle and para-aortic radiation
- ▶ 1987, age 25 – thyroid failure, and oral replacement – *4 years after diagnosis*
- ▶ 1994, age 32 – breast ca – T1c, N0, bilateral mastectomies, CMF chemotherapy - *11 years after diagnosis*
- ▶ 2006, age 44 – fibroblastic proliferation left posterior back (in radiation field), most consistent with extra-abdominal desmoid tumor – resected with poorly healing wound - *23 years after diagnosis*
- ▶ 2009, age 47 - > 40 colon sessile serrated polyps - *26 years after diagnosis*
- ▶ 2010, age 48 – Barrett's esophagus – *27 years after diagnosis*
- ▶ 2012, age 50 – coronary artery disease, tachy-arrhythmias, intermittent complete heart block, permanent pacemaker placement, continued exertional dyspnea, aortic valve replacement - *29 years after diagnosis*
- ▶ 2015, age 53 – total colectomy due to increased pre-malignant polyps - *32 years after diagnosis*
- ▶ 2017. age 55 – neck muscle weakness, cervical/thoracic kyphosis - *34 years after diagnosis*

Hodgkin Lymphoma – Case Study – 34 years of follow-up

► In 1983.....

- We didn't know about the risk of second cancers, including breast ca (except acute leukemia)
- We didn't know about the cardiac complications of radiation
 - Coronary artery disease
 - Valvular disease
 - Conduction defects
 - Autonomic dysfunction
- We didn't know about neck and spine effects

But we are much smarter now!!

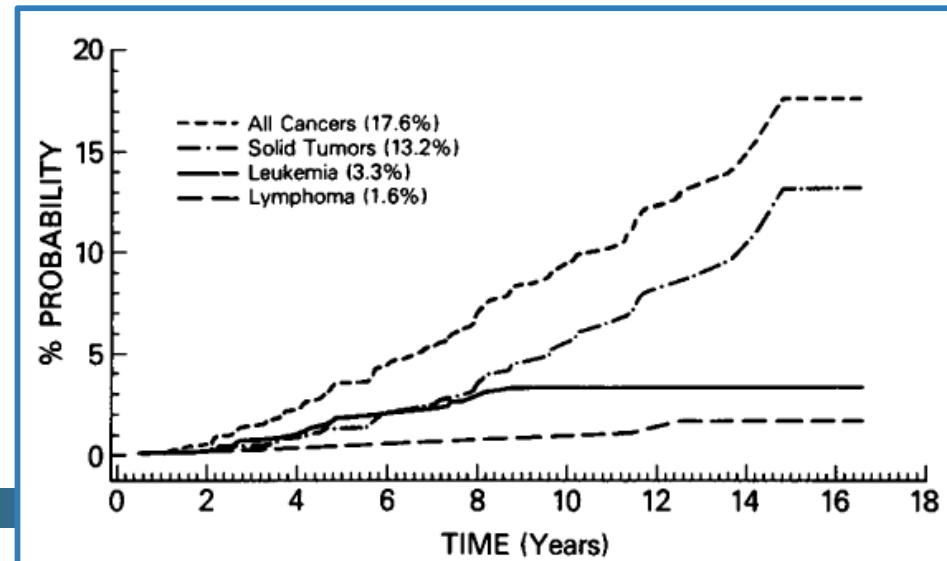
- Are we? Probably not.
- What are the long-term effects of check point inhibitors?

RISK OF SECOND CANCERS AFTER TREATMENT FOR HODGKIN'S DISEASE

M.A. TUCKER, M.D., C.N. COLEMAN, M.D., R.S. COX, PH.D.,
A. VARGHESE, AND S.A. ROSENBERG, M.D.

Abstract We estimated the risk of second cancers among 1507 patients with Hodgkin's disease treated at Stanford University Medical Center since 1968. Eighty-three second cancers occurred more than one year after diagnosis, as compared with 15.9 expected on the basis of rates in the general population (relative risk, 5.2; 95 percent confidence interval, 4.2 to 6.5). The mean (\pm SE) 15-year actuarial risk of all second cancers was 17.6 ± 3.1 percent, of which 13.2 ± 3.1 percent was due to solid tumors. The risk of leukemia appeared to reach a plateau level of 3.3 ± 0.6 percent at 10 years, whereas non-Hodgkin's lymphoma continued to increase, to 1.6 ± 0.7 percent by the end of the follow-up period. The

risk of solid tumors did not vary significantly according to treatment category, with the array of neoplasms resembling that previously observed in populations exposed to radiation and in immunosuppressed groups. The risk of leukemia, although elevated after radiation therapy alone (relative risk, 11; 95 percent confidence interval, 1.2 to 38), was much higher after either adjuvant chemotherapy (relative risk, 117; 95 percent confidence interval, 69 to 185) or chemotherapy alone (relative risk, 130; 95 percent confidence interval, 26 to 380). These data suggest that the risk of solid tumors after therapy for Hodgkin's disease continues to increase with time. (N Engl J Med 1988; 318:76-81.)



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Second Cancer Risk Up to 40 Years after Treatment for Hodgkin's Lymphoma

Michael Schaapveld, Ph.D., Berthe M.P. Aleman, M.D., Ph.D., Anna M. van Eggermond, M.Sc., Cécile P.M. Janus, M.D., Augustinus D.G. Krol, M.D., Ph.D., Richard W.M. van der Maazen, M.D., Ph.D., Judith Roesink, M.D., Ph.D., John M.M. Raemaekers, M.D., Ph.D., Jan Paul de Boer, M.D., Ph.D., Josée M. Zijlstra, M.D., Ph.D., Gustaaf W. van Imhoff, M.D., Ph.D., Eefke J. Petersen, M.D., Ph.D., Philip M.P. Poortmans, M.D., Ph.D., Max Beijert, M.D., Marnix L. Lybeert, M.D., Ina Mulder, Ph.D., Otto Visser, Ph.D., Marieke W.J. Louwman, Ph.D., Inge M. Krul, M.Sc., Pieterella J. Lugtenburg, M.D., Ph.D., and Flora E. van Leeuwen, Ph.D.

ABSTRACT

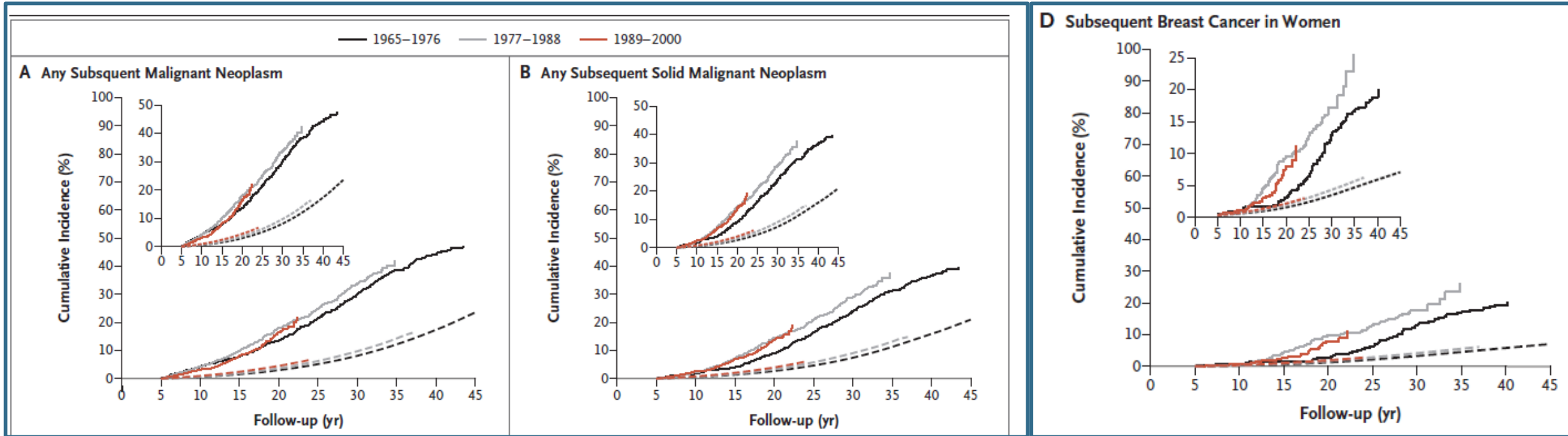
BACKGROUND

Survivors of Hodgkin's lymphoma are at increased risk for treatment-related subsequent malignant neoplasms. The effect of less toxic treatments, introduced in the late 1980s, on the long-term risk of a second cancer remains unknown.

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. van Leeuwen at the Department of Epidemiology, Netherlands Cancer Insti-



Second Malignancies after Hodgkin treatment – things are NOT getting better



Schaapveld, The Netherlands, NEJM 2015

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ABVD Alone versus Radiation-Based Therapy in Limited-Stage Hodgkin's Lymphoma

Ralph M. Meyer, M.D., Mary K. Gospodarowicz, M.D., Joseph M. Connors, M.D., Robert G. Pearcey, M.D., Woodrow A. Wells, M.D., Jane N. Winter, M.D., Sandra J. Horning, M.D., A. Rashid Dar, M.D., Chaim Shustik, M.D., Douglas A. Stewart, M.D., Michael Crump, M.D., Marina S. Djurfeldt, M.Sc., Bingshu E. Chen, Ph.D., and Lois E. Shepherd, M.D., for the NCIC Clinical Trials Group and the Eastern Cooperative Oncology Group

ABSTRACT

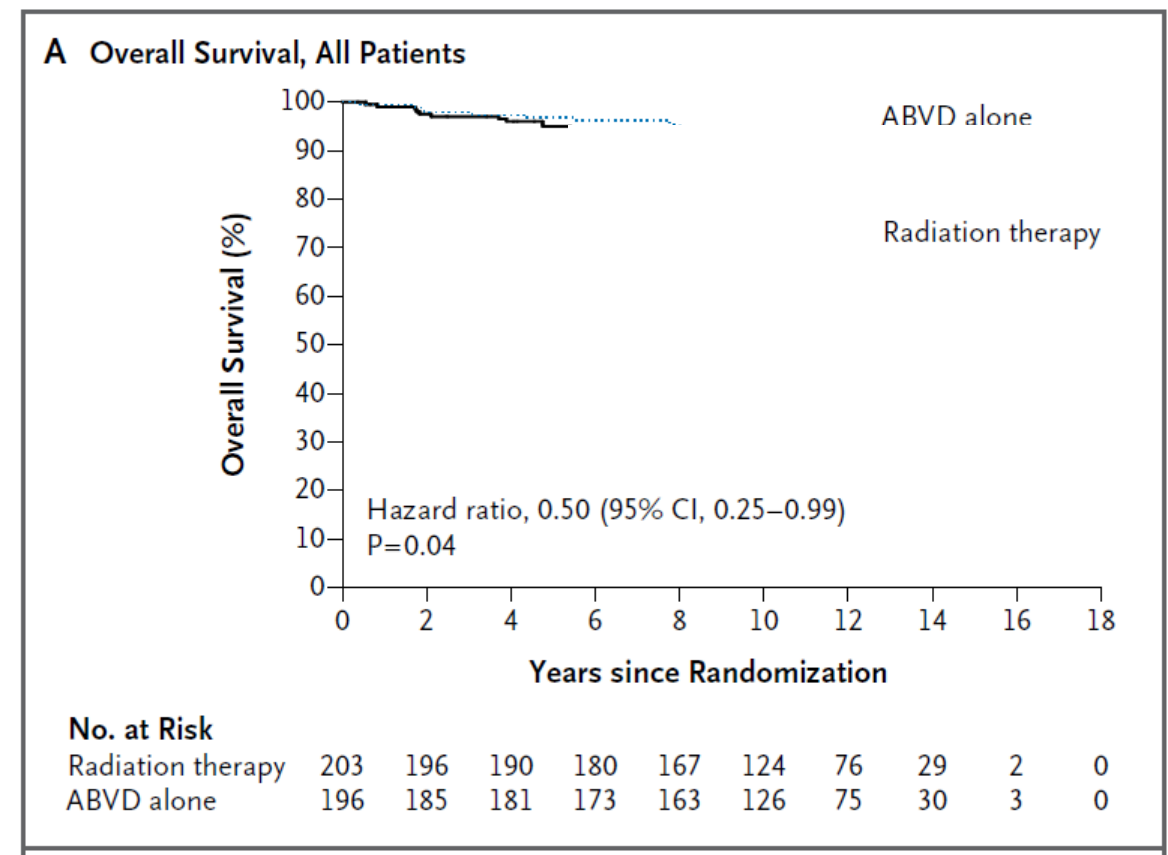
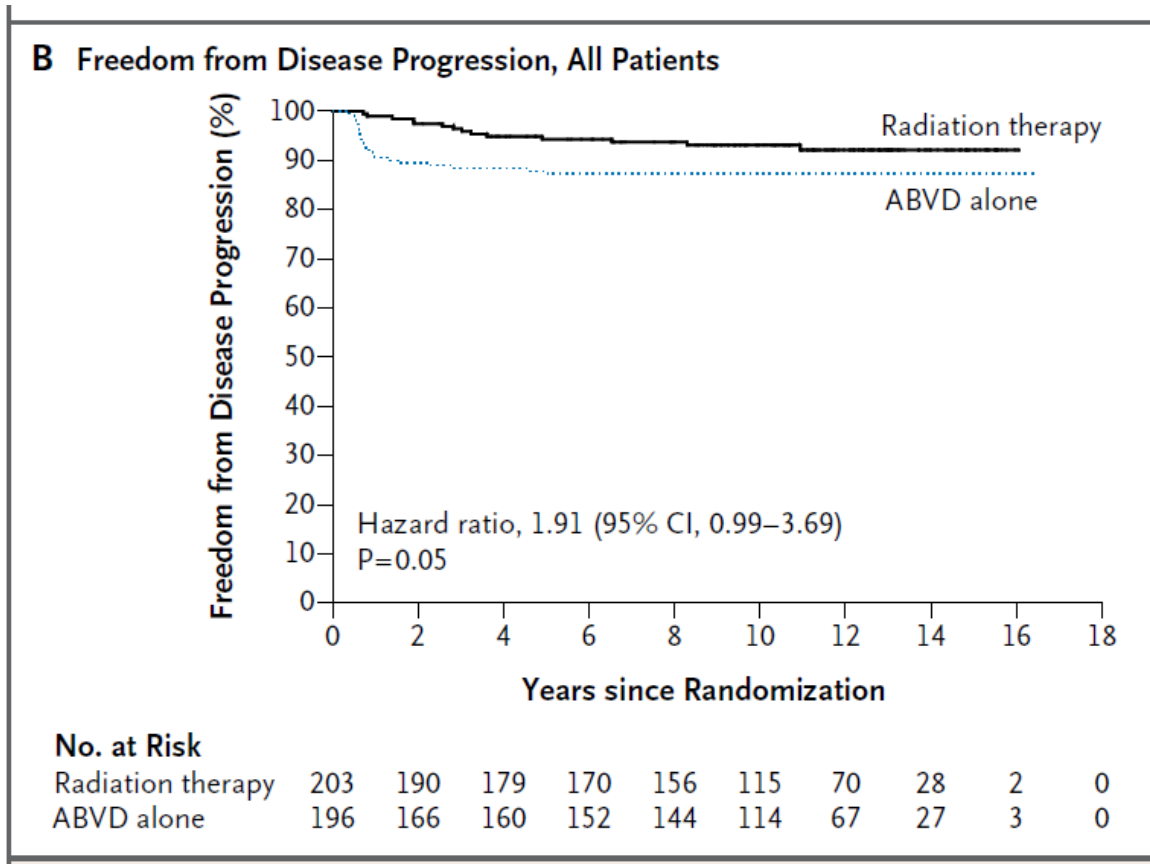
BACKGROUND

Chemotherapy plus radiation treatment is effective in controlling stage IA or IIA nonbulky Hodgkin's lymphoma in 90% of patients but is associated with late treatment-related deaths. Chemotherapy alone may improve survival because it is associated with fewer late deaths.

From the NCIC Clinical Trials Group and Queen's University, Kingston, ON (R.M.M., M.S.D., B.E.C., L.E.S.); the University of Toronto, Toronto (M.K.G., W.A.W., M.C.); the British Columbia Cancer Agency Centre for Lymphoid Cancer



Hodgkin Lymphoma – Disease Control vs Survival



Meyer, NCIC, NEJM 2012

What are our data gaps.....

original report

Health-Related Quality of Life in Patients With Hodgkin Lymphoma: A Longitudinal Analysis of the German Hodgkin Study Group

Stefanie Kreissl, MD¹; Horst Müller, PhD¹; Helen Goergen, Dipl Math¹; Julia Meissner, MD²; Max Topp, MD³; Martin Sökler, MD⁴; Jana Markova, MD⁵; Jürg Bernhard, PhD^{6,11}; Richard Greil, MD⁷; Bastian von Tresckow, MD¹; Karolin Behringer, MD¹;

RESULTS We analyzed 4,215 patients with any HRQoL assessment within 5 years after treatment. Higher tumor burden at diagnosis was associated with impaired baseline scores in many HRQoL domains. During survivorship, cognitive, emotional, role, and social functioning and fatigue, dyspnea, sleep, and financial problems were severely and persistently affected. From year 2 on, mean deviations from reference values ranged between

analyzed a systematically assessed, comprehensive range of HRQoL domains in patients with HL of all stages from diagnosis up to 5 years of survivorship.

editorials

Longitudinal Assessment of Health-Related Quality of Life Among Survivors of Hodgkin Lymphoma: It Is About Time!

Susan K. Parsons, MD, MRP¹



Why do we need to do better at data acquisition??.....

- ▶ How will we be able to learn more quickly about short and long-term toxicities and co-morbidities - particularly new therapies?
- ▶ How will we be able to tell patients what to expect?
- ▶ How will we be able to compare treatments on what really matters?
- ▶ How will we be able to evaluate new therapies and interventions designed to improve patient outcomes?



What do we need to accomplish this??.....

- ▶ PROs linked to EHR and registry data
 - Survival without QoL only half the story
- ▶ Way to better capture toxicities and co-morbidities as structured EHR data
- ▶ Way to follow patients over years and across sites of care
 - Including patients enrolled on clinical trials
- ▶ Need databases combining data from multiple sources –
 - EHRs (RWE), registries, clinical trials, genomics, claims, etc

How can Amazon know more about us than we know about our cancer patients?

