22nd

INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

APRIL 4 - 5, 2025

WESTIN CHICAGO RIVER NORTH

#IUCLS2025

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22nd INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

Prioritizing Clinical Research in a Clinical Practice

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Disclosures (none relevant to this presentation)

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- **Membership on a Board or Advisory Committee:** Pfizer/SeaGen, Roche/Genentech, Genmab/Abbvie, KITE/Gilead

Rise up by Andra Day

Selected Lyrics

“When the silence isn't quiet
And it feels like it's getting hard to breathe
And I know you feel like dying
But I promise **we'll take the world to its feet**
And move mountains”

“I'll rise up. **I'll rise unafraid**. I'll rise up
And I'll do it a thousand times again”

“All we need, **all we need is hope**
And for that we have each other”

“And we'll rise up. High like the waves
We'll rise up. In spite of the ache. **We'll rise up.**
And we'll do it a thousand times again”

Andra Day

Statement from the Cooperative Group Chairs: Feb 20, 2025

Dear Colleagues and Friends,

The Cooperative Groups that come together in the National Clinical Trials Network (NCTN) are responsible for a number of significant advances in cancer treatment arising over the past 40 years. In that time, as published by Unger et al (J Clin Oncol, 2023), this research has led to an estimated 14 million life-years saved for patients with cancer, in an incredibly cost-effective manner ($326 per life-year saved). In communities and cancer centers across the land, Cooperative Group trials are continually changing standards of care and providing much needed treatment options for patients. As Chairs of the US Cooperative Groups, we are grateful for NIH and NCI funding that has made this lifesaving work possible and concerned about the impact of the proposed changes in their budgets. We encourage you to emphasize and promote the significance of our collective work in public discourse.

Policymakers should be aware of the contributions of our research to local economies. A guide to this is provided by NIH: In fiscal year 2023, every $1 of NIH funding generated approximately $2.46 of economic activity. The multiplier is well-recognized, creates employment, and is a key factor behind the extensive availability of cutting-edge, practice-changing trials. It is important to emphasize that our work has a patient-centered focus. We rely on patients to help set research priorities, as part of our commitment to reducing the side effects of treatment and improving the patients' quality of life.

The American Association for Cancer Research (AACR) this week issued a statement of concern, as well as a call to action. We are providing a link to the full statement here to invite our members to engage in informing legislators about the critical importance of NIH and NCI's mission, and that progress against cancer is being made in nearly every congressional district. It is essential that we advocate for widespread support of the Cooperative Groups' efforts in providing treatment options to patients with cancer throughout the US. Please follow this link to the AACR statement, which includes a button to allow you to send comments to your representative.

On behalf of:
Alliance for Cancer Trials in Oncology: Eva Galanis, MD
Children's Oncology Group: Douglas Hawkins, MD
ECOG-ACRIN Cancer Research Group: Peter O'Dwyer, MD and Mitch Schnall, MD, PhD
NRG Oncology Group: Quynh-Thu Le, MD, Robert Mannel, MD, and Norman Wolmark, MD
SWOG Cancer Research Network: Charles Blanke, MD

https://ecog-acrin.org/a-statement-from-the-cooperative-groups/

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Introduction

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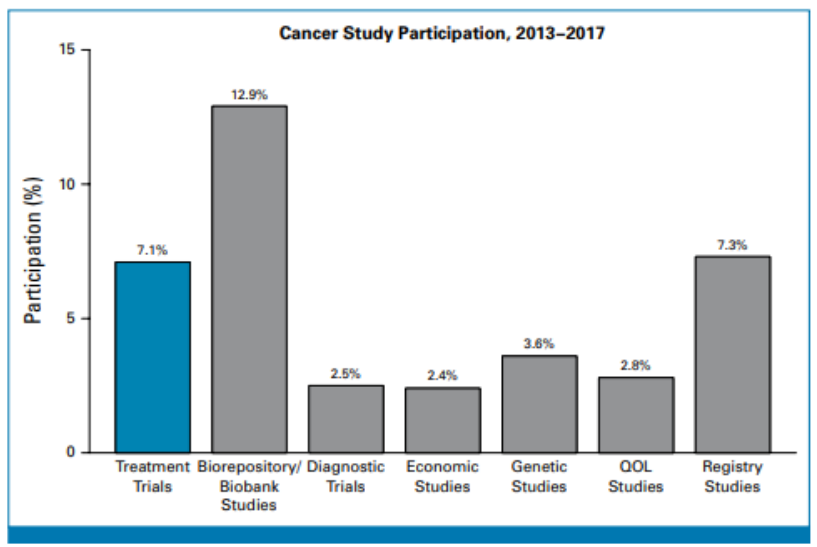
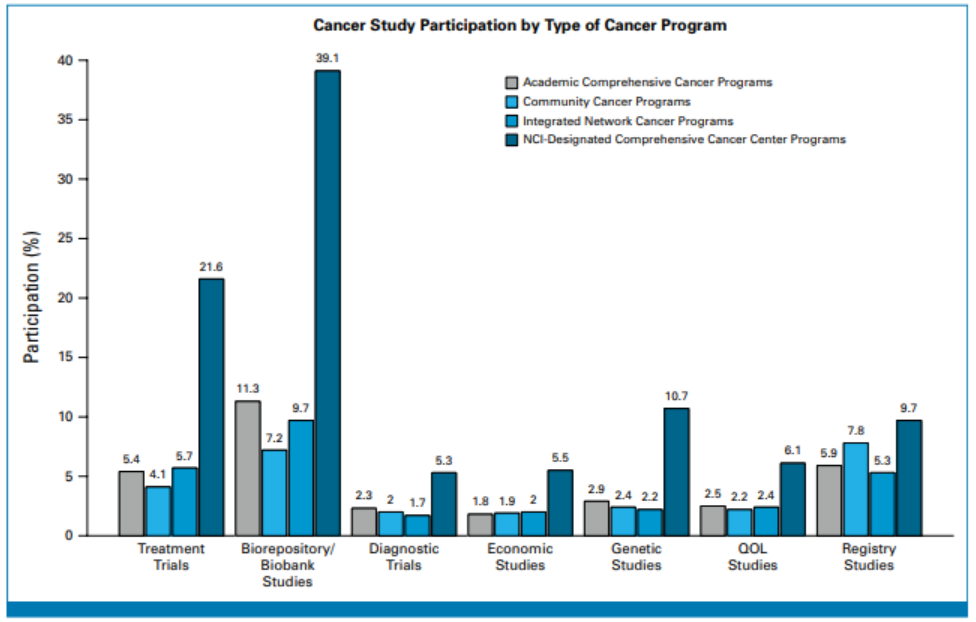
Clinical Trial Participation for Adults with Cancer in the US: 2013-2017

- 1990s data estimated 2%-3% of adult cancer pts participated in clinical trials
  - Only govt sponsored studies
  - Only treatment trials

- Data from Commission on Cancer Accreditation Repository
  - Includes 70% of all cases of cancer dx in US
  - Clinical trial enrollment data required

- Overall 7.1% of pts participated in treatment trials
  - 21. 6% at NCI designated comprehensive cancer centers
  - 5.4% at academic comprehensive cancer centers
  - 5.7% at integrated network cancer programs
  - 4.1% at community cancer programs



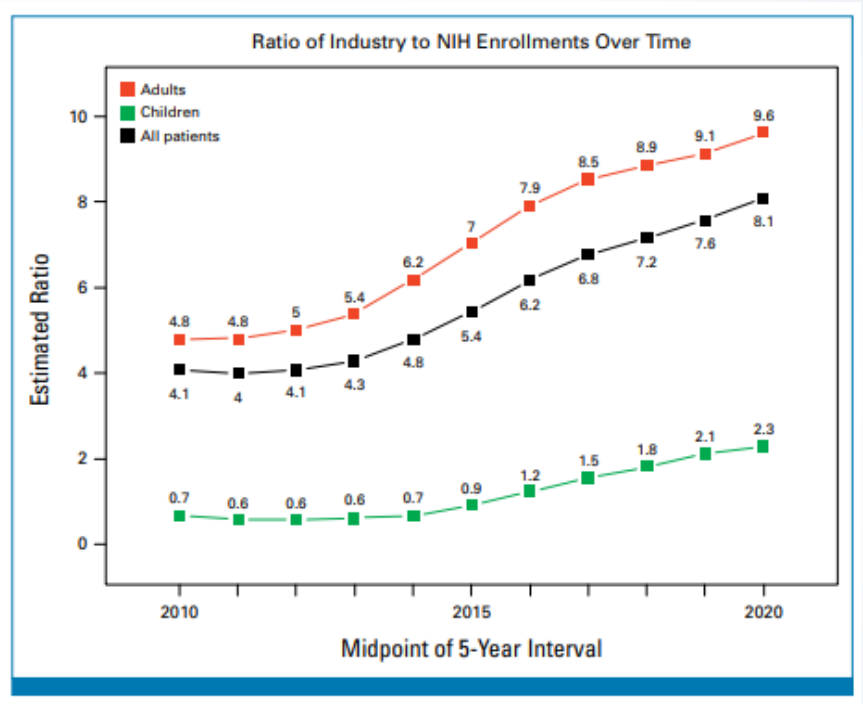


Unger JM et al. J Clin Oncol 2024;42:2139-2148

Enrollment to Industry-Sponsored vs Federally-Funded Cancer Clinical Trials

- Data from ClinicalTrials.gov
  - Enrollment 2008-2022
  - 26,080 studies examined

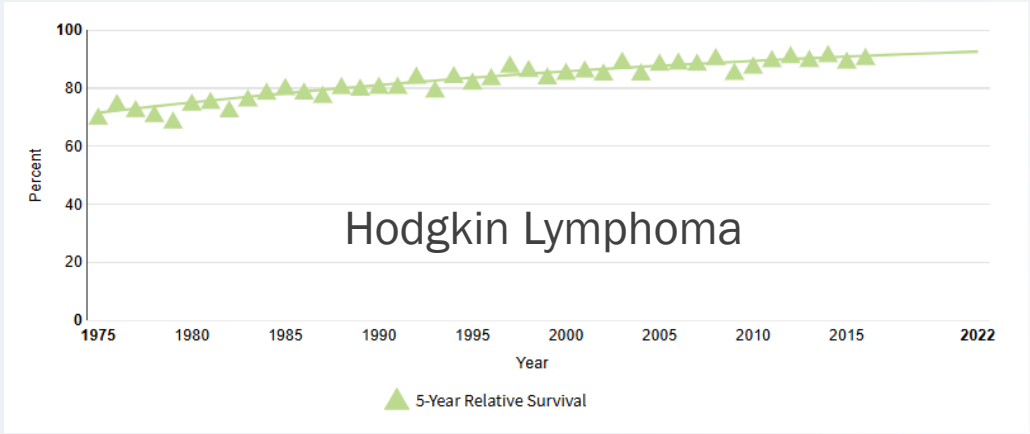
- Results
  - Enrollment ratio of industry sponsored vs federally funded
    - Adults 2008–2012 4.8 → 2018–2022 9.6
    - Children 2008–2012 0.7 → 2018–2022 2.3
  - Enrollment to federally-sponsored research flat 2008-2022

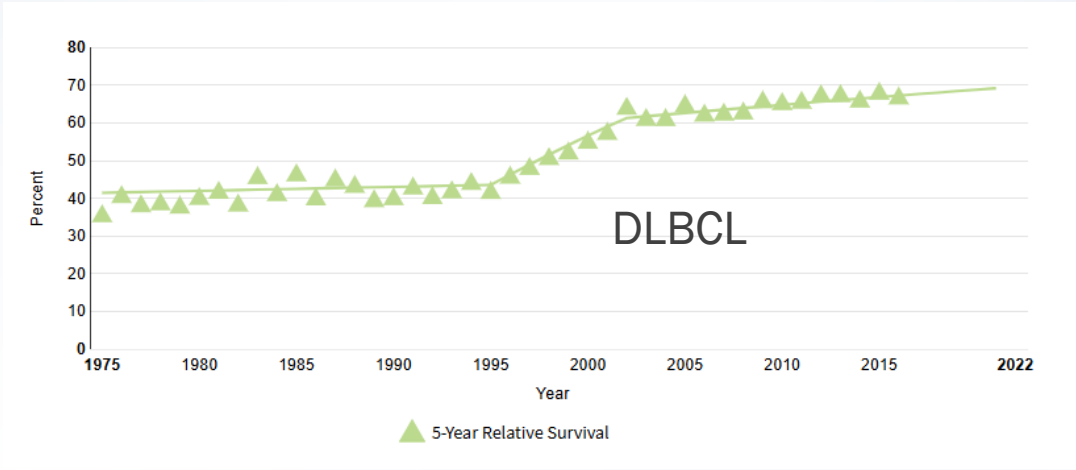


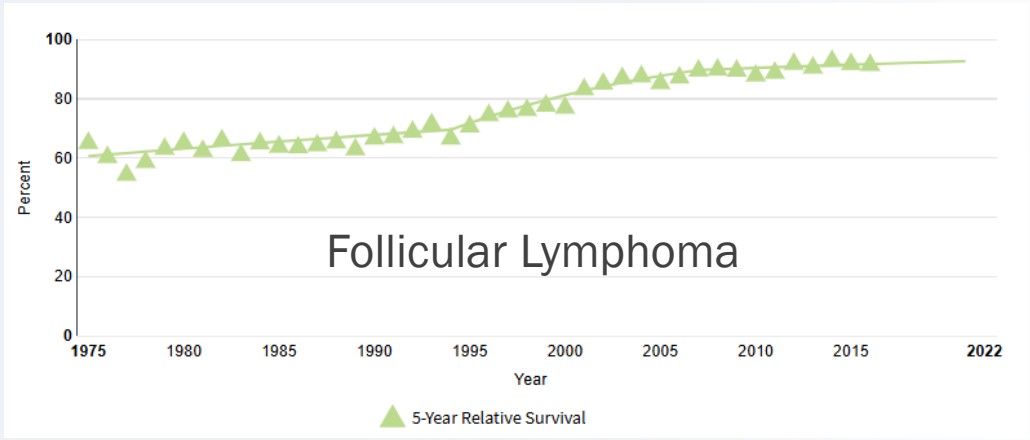
- Authors Conclusions: Growing reliance on industry to conduct cancer clinical research comes at a cost for pts and researchers with lost opportunities for scientific, clinical, and population advances

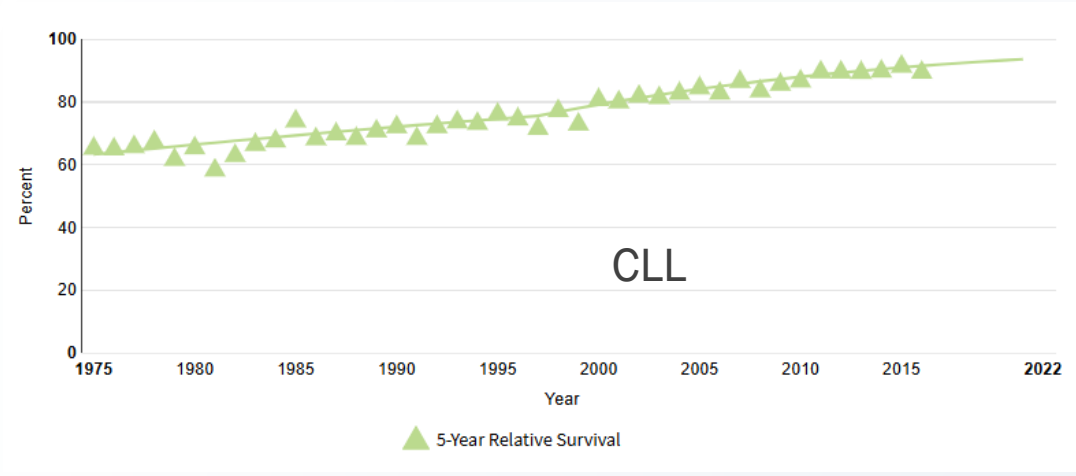
Unger JM et al. J Clin Oncol 2024;42:3917-3925

Change in 5-year Relative Survival over last 40 Years









Pancreatic cancer 5-yr survival 2% to 12% over 40 yrs

SEER database, 2025; https://seer.cancer.gov/statfacts/

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#1. Believe in the Mission

Prioritizing Clinical Research in a Clinical Practice

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Mission Statements: NCTN Cooperative Groups

- ALLIANCE
  - *Reduce the impact of cancer* by uniting a broad community of scientists and clinicians who are committed to the prevention and treatment of cancer
- SWOG
  - *Significantly improve lives* through cancer clinical trials and translational research
- ECOG-ACRIN
  - *Reduce the burden of cancer and improve the quality of life and survival* of adult patients with cancer
- COG
  - *Cure and prevent childhood and adolescent cancer* through scientific discovery and compassionate care

Mission of Pharmaceutical and Investigator Initiated/Sponsored Trials

- Pharma
  - Marketing approval of new agents that have a commercial value

- IIT/IST
  - Address scientific questions usually with insufficient commercial implications
    - Rare disease (e.g. PTLD)
    - Combinations that might have rationale based on local preclinical studies
    - Correlative studies of interest to site with available funding
  - Opportunities for young investigators to “get their feet wet”
    - Trial design and conduct
    - Data analysis in collaboration with statisticians
    - Manuscript preparation

My Journey to being “all in” with the clinical trials mission……

- Residency
  - Journal club presentation: NEJM article, adjuvant Tamoxifen for node negative breast cancer
  - Senior Resident Grand Rounds on Prostate Cancer (pre-PSA days)
    - Fascination with concept of “watchful waiting”
    - Importance of proving a therapy was “better than nothing” in older men with incidental finding of prostate ca

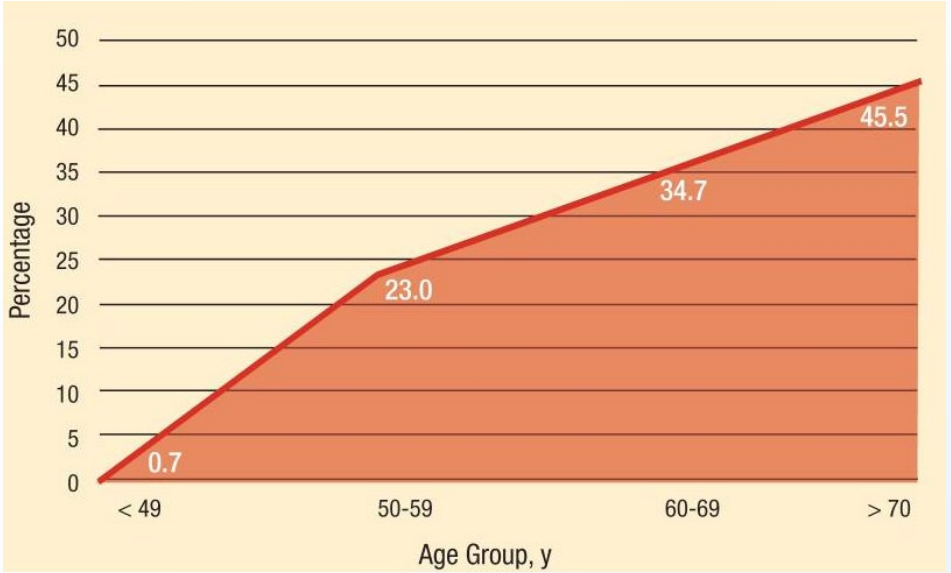
A RANDOMIZED CLINICAL TRIAL EVALUATING TAMOXIFEN IN THE TREATMENT OF PATIENTS WITH NODE-NEGATIVE BREAST CANCER WHO HAVE ESTROGEN-RECEPTOR–POSITIVE TUMORS

Bernard Fisher, M.D., Joseph Costantino, Dr.P.H., Carol Redmond, Sc.D., Roger Poisson, M.D., David Bowman, M.D., Jean Couture, M.D., Nikolay V. Dimitrov, M.D., Norman Wolmark, M.D., D. Lawrence Wickerham, M.D., Edwin R. Fisher, M.D., Richard Margolese, M.D., Andre Robidoux, M.D., Henry Shibata, M.D., Jose Terz, M.D., A.H.G. Paterson, M.D., Merrill I. Feldman, M.D., William Farrar, M.D., James Evans, M.D., H. Lavina Lickley, M.D., Mary Ketner, R.N., and Others*

Abstract We conducted a randomized, double-blind, placebo-controlled trial of postoperative therapy with tamoxifen (10 mg twice a day) in 2644 patients with breast cancer, histologically negative axillary nodes, and estrogen-receptor–positive (≥10 fmol) tumors.

No survival advantage was observed during four years of follow-up (92 percent for placebo vs. 93 percent for tamoxifen; P = 0.3). There was a significant prolongation of disease-free survival among women treated with tamoxifen, as compared with those receiving placebo (83 percent vs. 77 percent; P<0.00001). This advantage was observed in both the patients ≤49 years old (P = 0.0005) and those ≥50 (P = 0.0008), particularly in the former, among whom the rate of treatment failure was reduced by 44 percent. Multivariate analysis indicated that all subgroups of patients benefited. Tamoxifen significantly reduced the rate of treatment failure at local and distant sites, tumors in the opposite breast, and the incidence of tumor recurrence after lumpectomy and breast irradiation. The benefit was attained with a low incidence of clinically appreciable toxic effects.

The magnitude of the improvement obtained does not preclude the need for future trials in which patients given tamoxifen could serve as the control group in an evaluation of potentially better therapies. Tamoxifen treatment is justified in patients who meet the eligibility criteria of the present study and who refuse to participate in those trials. Since patients with tumors too small for conventional analysis of estrogen-receptor and progesterone-receptor concentrations were not eligible for this study, no information is available to indicate that such patients should receive tamoxifen. (N Engl J Med 1989; 320:479-84.)



Prevalence of Incidental Prostate Ca (autopsy series)

Chin HS et al. 2015;32 (Suppl 4):41S–44S.

My Journey to being “all in” with the clinical trials mission (cont).....

- Oncology Fellowship
  - Outstanding role models for prioritizing clinical research:
    - Senior fellows (Andy Zelenetz, David Maloney, Ned Waller)
    - Faculty: Sandra Horning, Saul Rosenberg, Ron Levy, Tom Davis (ECOG PI at Stanford)
  - Palo Alto VA rotation as first year fellow (ECOG solid tumor trials)
    - Accrued 2-3 pts a week to ECOG trials during my 2 mo rotation
    - **First experience seeing how excited pts were to participate** (different generation)
  - Examples of *lymphoma clinical trials* ongoing at Stanford during my fellowship
    - IITs: Stanford V, single agent Rituximab in FL, idiotype vaccine for FL
    - Pharma: Phase 2 of neupogen with CHOP-14 in DLBCL
    - Cooperative group - none
  - Recruiting pts to clinical trials highly gratifying...interesting, challenging, finding better treatments.....

My Journey to being “all in” with the clinical trials mission (cont).....

- Joined the faculty at Wash U in 1994 → culture shock
  - Much more diverse population especially older age
- 5 clinical oncology faculty (breast, H&N, lung, GI, gyn), 3 BMT faculty
- No lymphoma trials or MDs
- Got back on track by
  - Joining CALGB lymphoma committee (interloper for few years before granted official membership)
    - 30+ years of opportunities/collaborations within committee
    - Found my lymphoma community
  - Becoming PI of CALGB program at Wash U (3rd yr on faculty)
    - Total immersion in setting up cooperative group clinical trials program at Wash U across all disease sites
  - Small multi-center trials with Stanford/OSU

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#2. Developing Your Trial Portfolio

No Perfect Trial!

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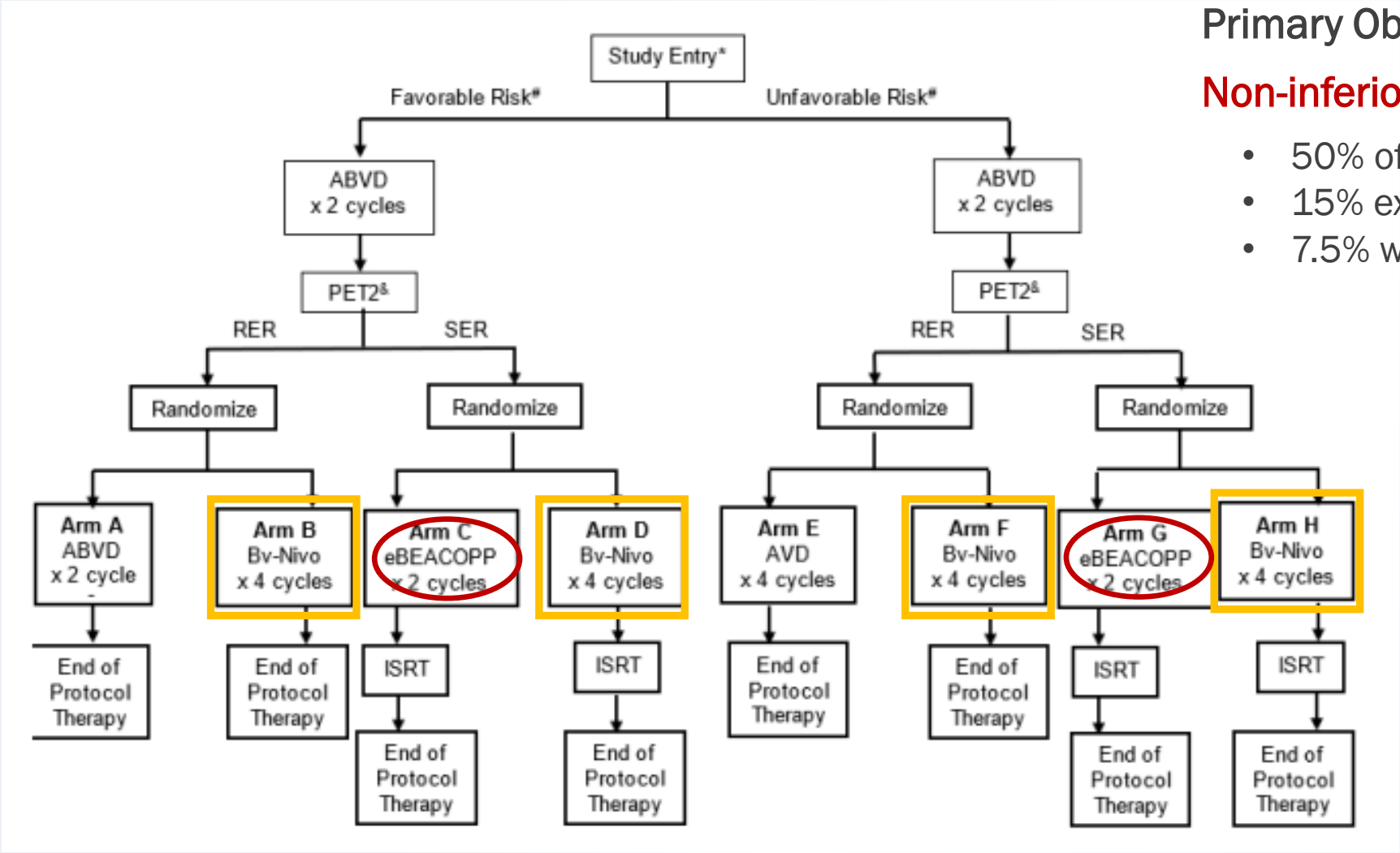
Compromise critical to trial design and accrual

- Most cooperative group and pharma trials have been vetted at multiple levels
  - Trust this expertise

- Common frustrations/complaints
  - Not novel or “exciting” (NCTN trials)
    - DA-EPOCH-R vs R-CHOP in DLBCL
  - Too complex (usually pharma, PKs, extra visits)
  - Straw man control arm… decide whether worth it to potentially make this drug available…
    - Phase 3 confirmatory trial: Ibrutinib (67% ORR) vs ofatumumab (4% ORR) in R/R CLL

- Can you support the trial despite a few less than perfect aspects?

Current NCTN early stage HL trial: AHOD2131



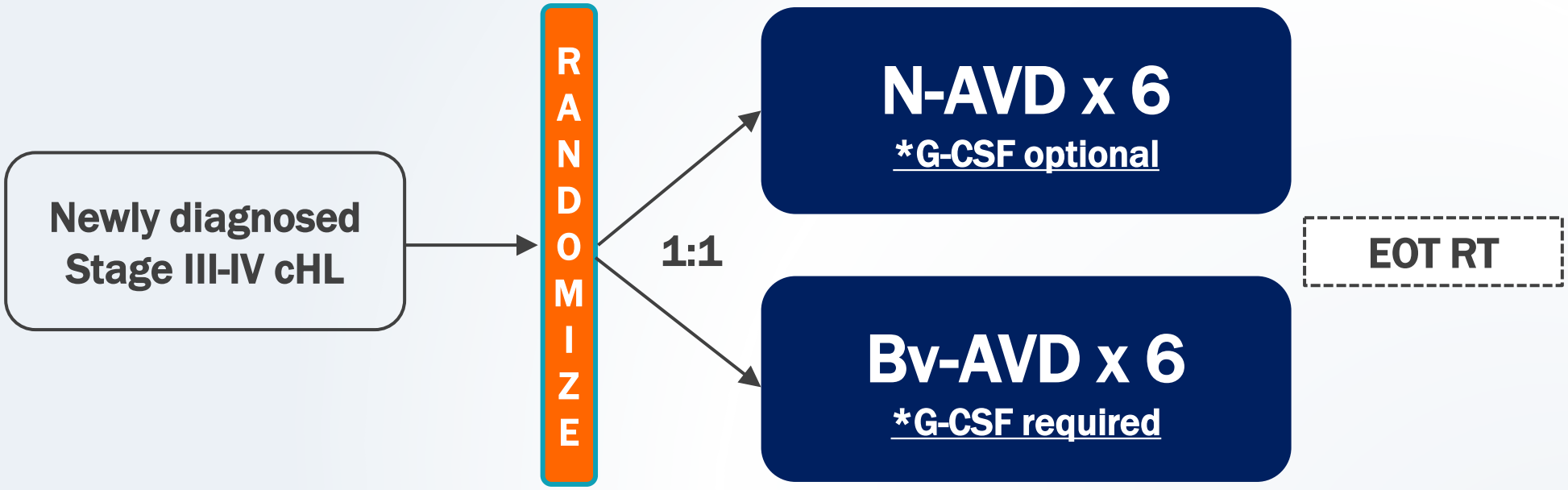
Primary Objective:

Non-inferior PFS in Bv-Nivo arms

- 50% of pts will get Bv-Nivo
- 15% expected to need RT
- 7.5% will get BEACOPP/BrECADD

NCTN S1826 trial for advanced stage HL

Maybe a perfect trial.....



- All risk groups included
- No interim monitoring
- Samples collected for ctDNA that will be used to inform the next trial

Accrued 970 eligible pts in 3 yrs
1 yr ahead of schedule

Trial Portfolio: Will differ according to type of clinical practice

- Which trials to open?
  - Engage all stakeholders
    - All potential treating physicians. Will they accrue pts to study?
    - Research staff re complexity. Rarely a deal breaker in academic setting
    - Finance team re “how much $$ you will lose” (NCTN, IST, multi-center)
  - My primary decision criteria
    - Asking “decent” question? Encouraging Phase I/II or pre-clinical data? Most will not be practice changing.
    - Competing trial?
      Yes → How long will it be open? Is it accruing well? Can you support a second study in space?
      No → Do you have enough pts to support opening? (my bar is minimum 6 to open study)
    - Anything else on the horizon that looks “better”?
    - For pharma studies
      How many total sites? International sites?
      Already open at other sites?
      Total expected accrual?
      Limit on individual site accrual?
      Registration study? (I like these!)

Trial Portfolio continued…..

- Core group of trials essential (“backbone”)
  - Cover most common diseases
  - Straightforward design and objectives
  - Phase 3 or large Phase 2 (Pharma, NCTN)
  - Robust accrual expected at site
  - *These trials keep everyone’s spirits up*!
- Multi-center trials run by another center
  - Usually painfully slow contracting process
  - Cannot start contract, IRB submission, orders, etc until OPEN at lead site
  - Usually small studies
  - “Good citizen”
- Academic centers need to have some ≥ 3rd line trials open

Trial Portfolio continued….

- Investigator Sponsored Trials
  - Should be part of portfolio for young investigators
  - Often have to make compromises in design if requesting support/drug from pharma
    - They may have an agenda for their ISTs.

- Cancer Control studies (usually important part of NCORPs portfolio)

- Registry studies
  - Can be data source for young investigators
  - Not sure it is worth it unless your site will be able to query the registry
  - Can potentially be done with minimal physician involvement if have adequate site staff
  - Should never be a money loser!

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#3. Engagement and Logistics

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Engaging the research team

- Physician enthusiasm for the studies is the key

- When hiring your “clinical team” (NPs, PAs, nurse coordinators, treatment room nurses) be clear about the high priority of clinical research in your practice.
  - Will add a layer of complexity to caring for these pts. Must be onboard.
  - We do have not a “separate team” for study pts.

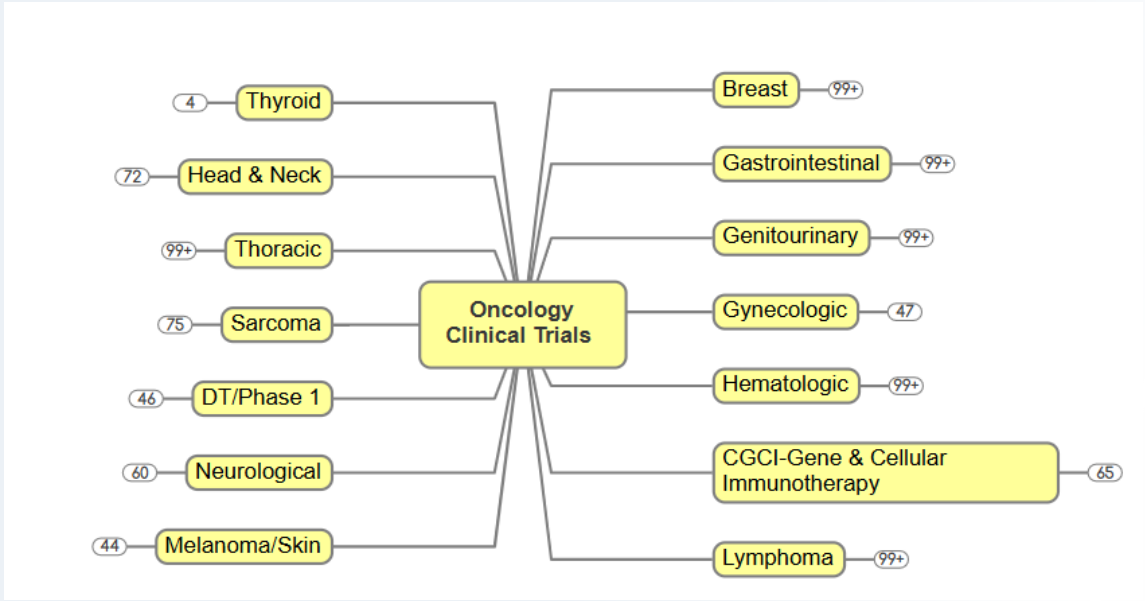
- CRAs/Research nurses
  - Education, education, education
  - Background and objectives of trials – not just the logistics
  - Share results – abstracts, manuscripts
  - Observing new pt appts where trial being discussed!

- Fellows in your clinic must be on board

Successful Patient Recruitment (many others more adept)

- Prepare, prepare, prepare
- Physician review of new patients and progressing pts in advance → notify CRA if trial option
  - Some practices have CRAs screen first (simpler trials, research nurse)
- CRA "initial review" of physician identified pts before patient visit
  - Looking for labs (CrCl ☺), PMH that would make them ineligible
  - What other testing would be required?
- Physician should be primary player in discussing all aspects of trial with pt
  - Objectives, trial treatment, side effects, alternative treatment options, extras visits, etc.
  - First 1-2 pts on trial always uncomfortably "clunky" in my experience
- Consider seeing new pts at end of day – maybe less rushed

Wash U Online Protocol Tree



Minimizing “glitches” while caring for pts on trials during a busy clinic……

- Advance preparation
  - Practitioner: Review interim labs, phone calls, events since last visit
  - CRA/nurse: Confirm all required tests for visit ordered
  - CRA: visit instruction sheet for the following visit: required tests, schedule, etc.
- Expect will take “a little longer” than non-trial visit re potential side effects and pt questions
- CRA on deck to do any reconsenting, QOLs, answer schedule or logistics questions
- Unexpected labs or side effects at visit (ensure have immediate access to protocol)
  - Is dose modification or treatment hold needed? (physician to double check CRA recommendation)
- Deviations (“stuff happens”…)
  - If intentional (best interest of the pt), document reasoning (they will still “ding you”)
  - If unintentional, try and figure out how to prevent it with future pts/cycles.
  - Don’t beat yourself up – especially when the monitor lists the dozens of “minor” (and often meaningless) deviations “Let it Go” (Elsa from Frozen)….

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Second Song

For the residents, fellows, early career faculty….

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#4. Lighting the Fire in Trainees

"Education is not the filling of a pail, but the lighting of a fire"*

*Yeats vs Plutarch

Encouraging trainees to prioritize clinical trials in clinical practice

- Critical to keep the pipeline stoked
- Trainees often yearn for didactics (filling the pail)
- My opinion: a clinical practice with a heavy dose of clinical trials is where you light the fire
- Model for them…
  - How to screen for trials (our trial tree)
  - How to discuss trials with pts
  - How to consent
  - How fun and occasionally frustrating the whole process is
- Wonderful opportunity to learn more about
  - standard of care (background section of trials required reading),
  - new agents under study
  - toxicities
  - evaluating response

Encouraging trainees to prioritize clinical trials in clinical practice

- Emphasize collaboration
  - Timely accrual is the most critical component to trial success
  - Understand the importance of this contribution to “the mission”

- Do not create “publication as end game” culture
  - Every middle author critical to trial completion
  - Every pt recruited is a contribution

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#5. Financial Aspects

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Finances: The least satisfying and often most frustrating part….

- Academic centers
  - Beg for support from division, dept, cancer center, medical school, hospital
    - It is in their best interest!
    - Brings in patients and more patients means more money
  - Can use some pharma studies to offset portion of losses from NCTN, ISTs
- Community centers
  - Beg hospital and “practice” for support

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#6. What would make it easier to prioritize clinical research in a clinical practice

Prioritizing Clinical Research in a Clinical Practice

Wish List (excluding better reimbursement of NCTN trials)

- Simple, broad eligibility
  - Proper histology
  - Proper stage
  - Initial treatment vs relapsed/refractory
  - Have not been treated with the study drug previously
  - PS 0-2 (3 allowed if disease related)
  - Any counts if disease related, CrCl >30
  - Generic statement about physician confirming PMH does not put pt at undue risk
- Maximum consent length 10 pages
- Minimize: extra visits, unnecessary tests (triplicate ECGs, many labs, PET AND diagnostic CT)
- Liberalize all visit/test windows to reflect “real life”

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#7. The Ultimate Motivation

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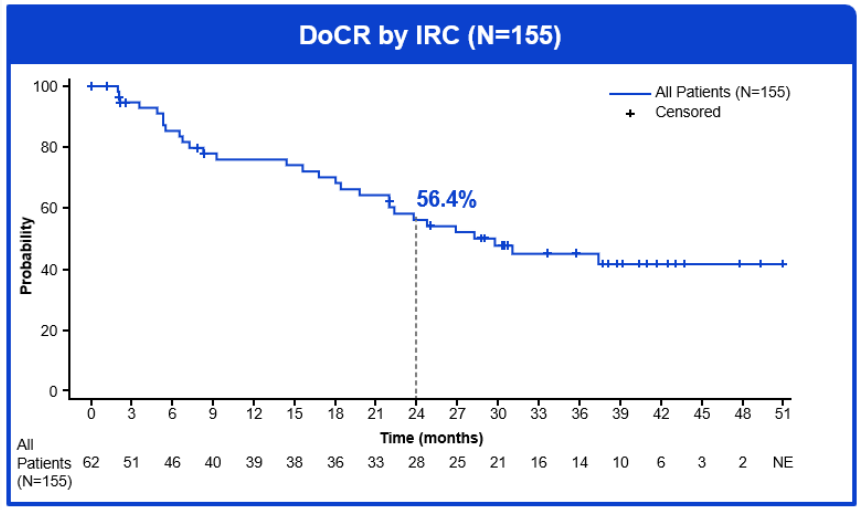
Patient Presentation 1

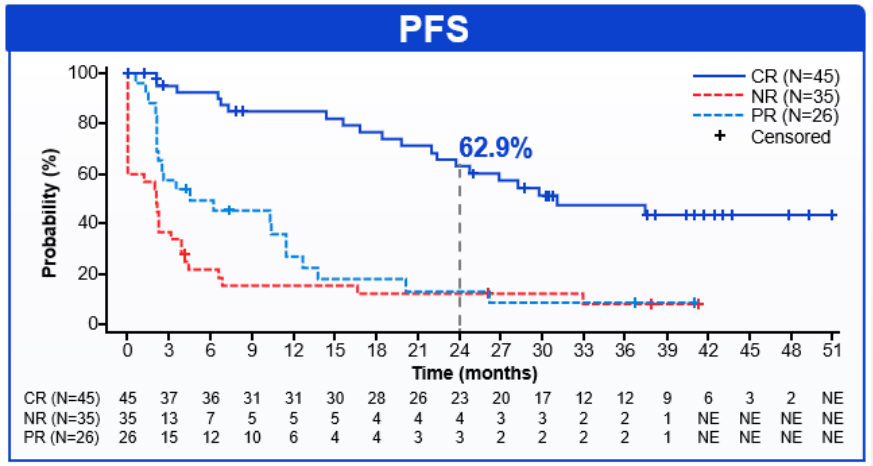
- 26 yo man dx *2001* - **stage IVB Hodgkin lymphoma**
  - 1st line: **Stanford V + IFRT (mantle field)**
- Relapse *2002*
  - **DHAP x 2** with CR
  - Ph1/2 **ASCT trial (gem, navelbine, BCNU, etop, cytoxan)**
- Relapse *2015*, stage IVA (multiple extranodal sites),
  - **ICE x 2** with CR, **BEAM ASCT**, **maintenance Bv x 11**

- Dx **DLBCL, GCB in 2020 at age 45, Stage IVA, IPI 3**
  - **R-CHOP x 2** → bad "PR" (5PS 5)
  - **R-DHAX x 2** → PD
  - Clinical trial of **dual CAR T (CD19/CD22)** → PD
  - Phase 2 registration trial **Glofit x 12 →**
    - **PR post-C2, 5, 8, CR post C12; remains in CR 4 years post EOT**

Glofit: Duration of CR



Landmark Analysis by Response at C3



Dickinson et al, ASH, 2024

Patient Presentation 1 Follow-up.

- Currently an Endowed Professor at Olin School of Business at Wash U
  - 04/03/2025 Delivered Keynote at Chancellor's Symposium on "Business of Healthcare"
- Recruited him to start sharing his story at local LLS Fundraising Events in 2024
  - "I feel like the crazy luck of surviving has given me an obligation to help."

Patient permission to share photos and social history

Patient Presentation 2

- 1999: 20 old woman dx with bulky mediastinal HL
- **ABVD x 6 → IFRT cervical nodes and mediastinum**
- 2003: Relapsed, **ESHAP x3**, MR → **BEAM ASCT**
- 2007: progressive disease
- CALGB 50502, **GVD ± anti-CD30 mAb x 5** → SD (**placebo**)
- IST trial **Len x 20**, initially SD → PD
- **Everolimus x 5**, initially PR → PD
- 2011: **Brentuximab vedotin x 16 (compassionate use trial before approval). Remains in remission 14 yrs post-tx**
- **2017: Baby Jack (donor eggs)**

"Feel free to use my history and the attached photo in your slide. It includes my guys and my gray hairs, all of which I'm so grateful for."


SITEMAN
Thank you
SITEMAN
CANCER CENTER
Washington
University in St. Louis
SCHOOL OF MEDICINE
BJC HealthCare
siteman.wustl.edu • info@siteman.wustl.edu • 800.600.3606