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# What Does “Cure” Mean And How Do We Find Treatments To Accomplish It?

# The History Of Curing Cancer:

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## Therapies Used to Treat Cancers:

- **Surgery**
- **Radiotherapy**
- **Chemotherapy**
  - **Traditional cytotoxic drugs**
  - **Small molecule inhibitors**
  - **antibodies**
- **Immunotherapy**

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# Miraculous Responses

# “Alternative” Cancer Therapies

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- Proponents argue these are suppressed by the cancer establishment for financial reasons
- Frequently said to work for all cancers
- Usually said to be nontoxic
- Paid for out of pocket
- Sometimes requires travel to another country

# Examples of Alternative Cancer Therapies

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- Unusual diets
- Shark cartilage (myth that sharks don't get cancer)
- \*laetrile (B17) from apricot pits
- Essiac tea
- Bioresonance therapy
- Orgone accumulators (harness "lifeforce")
- Psychic surgery
- Germanic new medicine (treating emotional trauma)
- Ozone therapy

# How Are New, More Effective Therapies Developed (e.g. CAR T Cell Therapy)?

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## Clinical Trials:

- **Phase 1**                      **Safety and Activity**
- **Phase 2**                      **Efficacy**
- **Phase 3**                      **Compare to previous treatments**

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# Pitfalls In Finding The “Best” Therapy

# Natural History of New Chemotherapy Regimens

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- More intensive (more toxic?)
- Only given to younger, healthier patients
- Excellent results
- Unfair to withhold from poor-risk-patients
- Poorer results

# The Will Rogers Phenomenon

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**Group 1**

Highest  
Scores

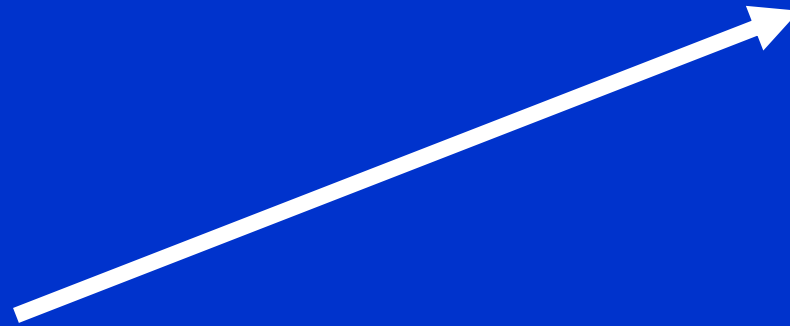
Middle  
Scores

Average Improves

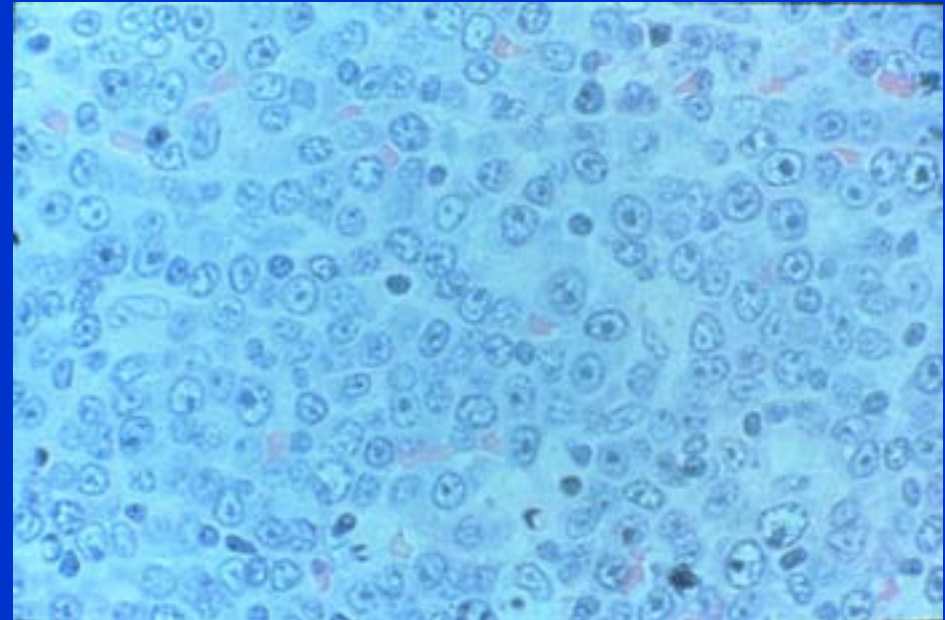
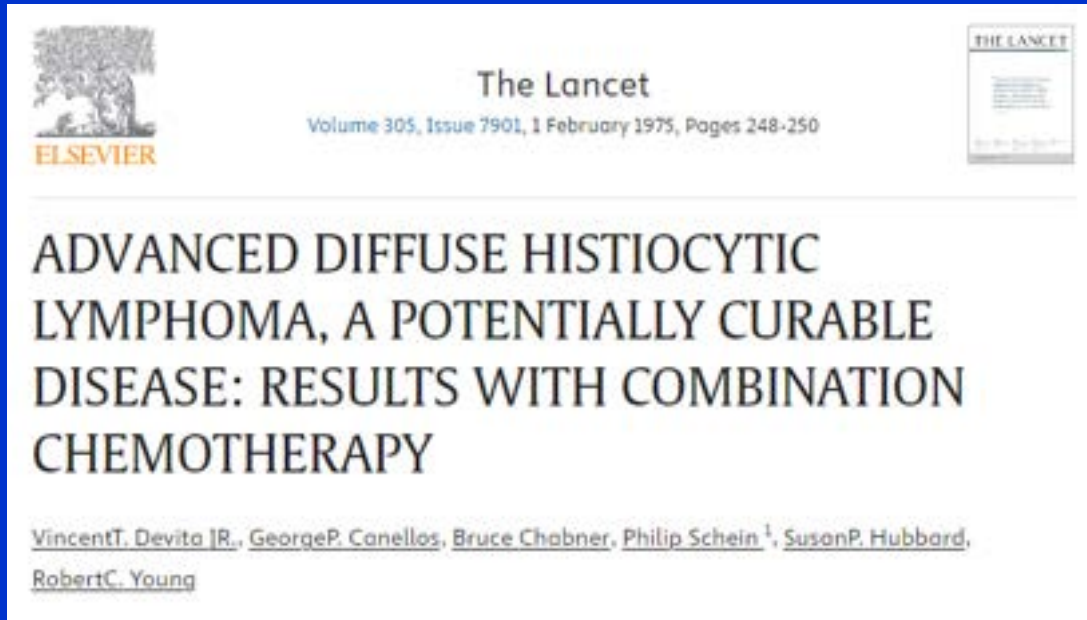
**Group 2**

Lowest  
Scores

Average Improves



# Diffuse Large B-Cell Lymphoma

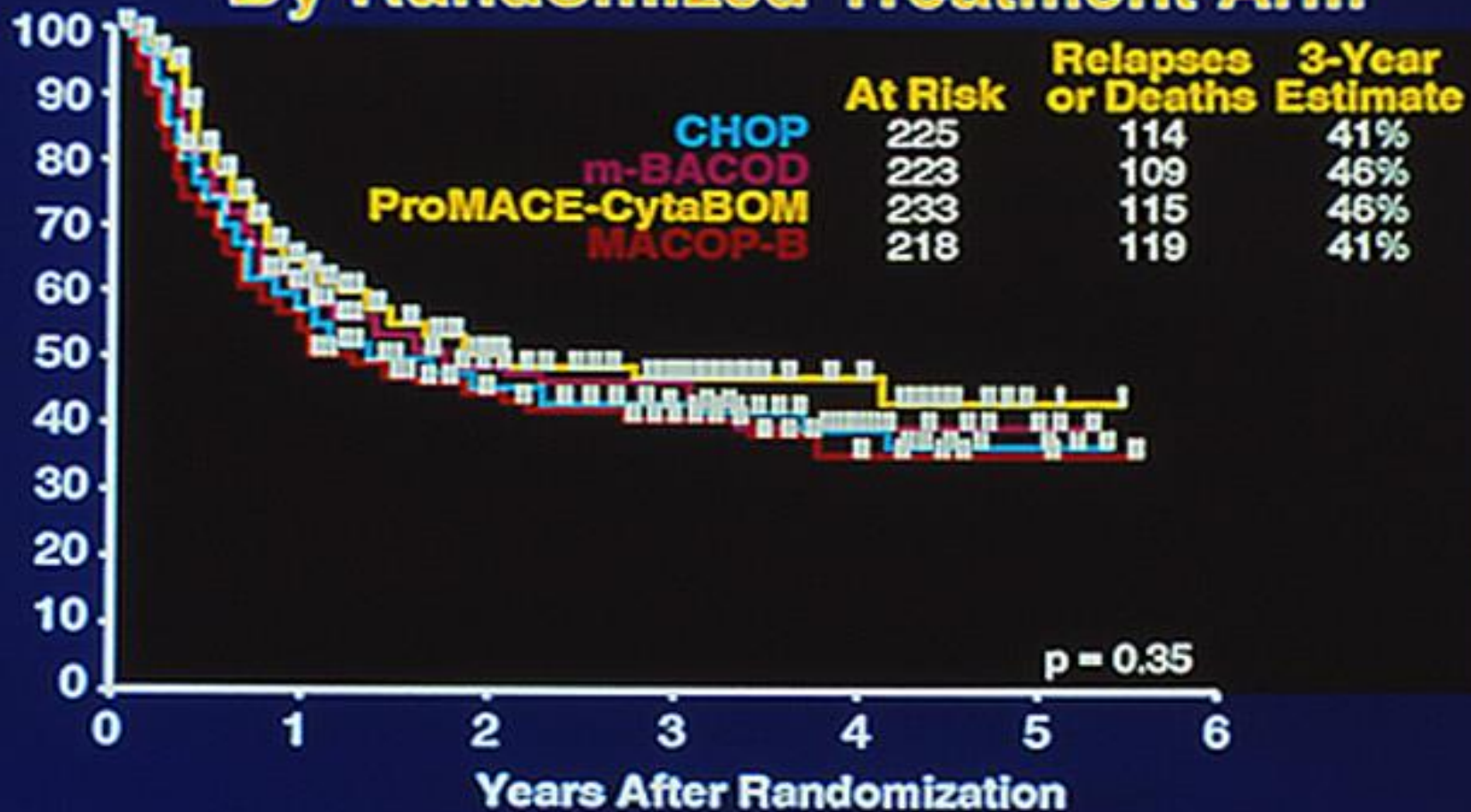


# Popular Regimens In The 1980's and 1990's

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- CHOP
- ProMACE/CytaBOM
- M-BACOD
- MACOP-B

## Time to Treatment Failure By Randomized Treatment Arm

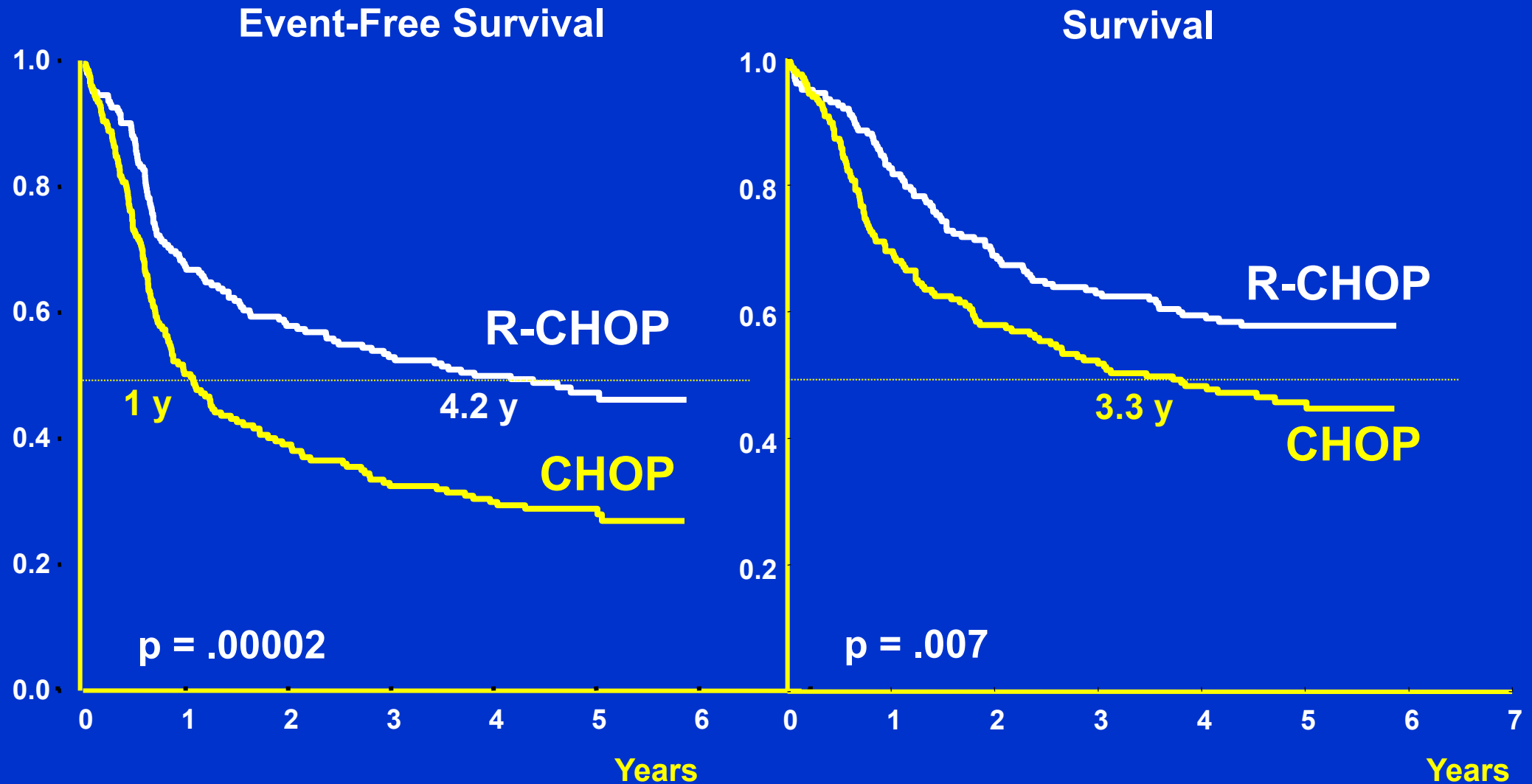


# Rituximab in NHL

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- 50% response rate in relapsed follicular NHL
- 12 mo median response duration
- ~35% response rate in DLBC lymphoma

# GELA study – Median follow-up 5 y

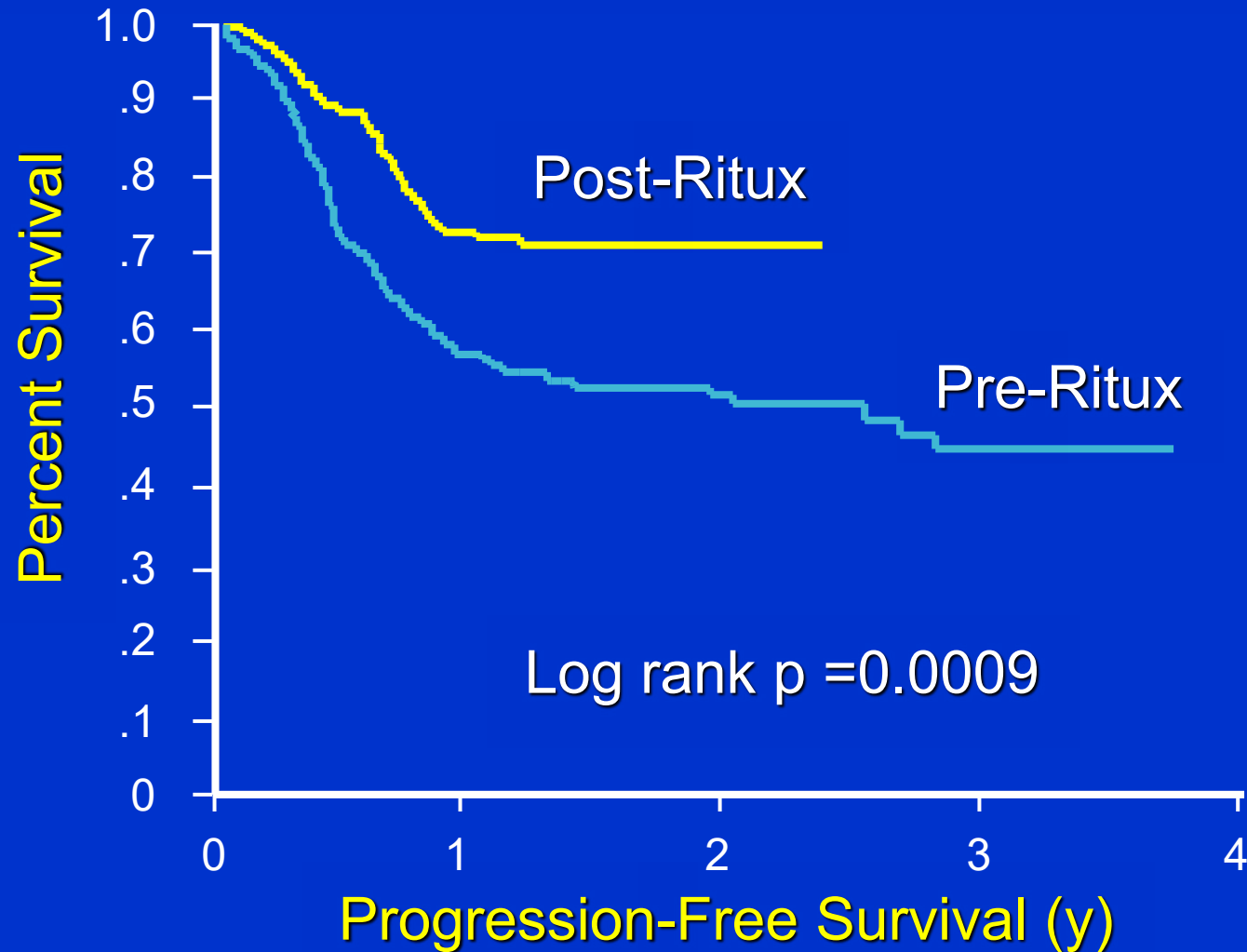


# Population-Based Effect of Rituximab in British Columbia

- Analysis of survival 18 months after (152 pts) and before (142 pts) this recommendation
- No difference in age, IPI score, LDH or bulky disease

	n	CHOP	R-CHOP
Before March 2001	142	91%	9%
After March 2001	152	15%	85%

# The Impact of Adding Rituximab To CHOP in British Columbia



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**Sometimes Effective New  
Treatments Only Benefit A  
Subset Of Patients With A  
Disease**

# Substituting Polatuzumab Vedotin For Vincristine In CHOP-R For Primary Therapy Of Patients With DLBCL (NEJM 2022; 356:351-62)

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- 879 patients
- Overall PFS was 77% (Pola-R-CHP) and 70% (CHOP-R)
- Benefit was primarily in patients > 60 years of age, those with ABC subtype, and those with higher IPI scores

# Outcome By Subgroups (2 year PFS)

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<u>Group</u>	<u>Pola-R-CHP</u>	<u>R-CHOP</u>
age > 60	78%	70%
Male	76%	66%
IPI 3-5	75%	65%
ABC genetic subtype	84%	59%

# Which Factors Determine Widespread Acceptance And Application?

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- Efficacy
- Guidelines
- Ease of use/convenience
- Side effects/safety
- Habits/previous standard
- Cost
- Profitability
- Insurance coverage/national approval
- Peer pressure/ethics

# What Is A “Cure”?

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1) No cancer cells left

2) No relapse

# Even in Curable Cancers, Late Relapses Sometimes Occur

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Long-term follow-up of 368 patients with aggressive lymphoma who achieved a complete remission:

30 patients (8%) relapsed more than 5 years after therapy. The latest relapse was at 14 years post-therapy.

If these patients who were destined to have a late relapse died of another cause before they relapsed, they would have considered themselves cured of lymphoma.

# How Can We Tell Which Patients Are Likely To Be Cured?

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## Before Treatment:

Stage

Prognostic Factors

Molecular features of cancer

## During Therapy:

Rapid Response

## After Therapy:

Complete Remission

ctDNA

# What I Tell Patients:

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1. If surviving without relapse is what defines cure, we cure most patients with many cancers, and some patients with all types of cancer
2. In explaining their prognosis, be honest but hopeful (e.g. we don't do immortality but if we have a good chance to keep you from dying of this cancer)
3. Don't underestimate the anxiety patients feel in remission