

Managing the Evolving Landscape for NHL

Jonathon B. Cohen, MD, MS
Winship Cancer Institute of Emory University
Associate Professor, Hematology and Medical Oncology
Emory University School of Medicine

Disclosures

- Advisory Board/Consultant: Janssen, Astra Zeneca, BeiGene, Loxo/Lilly, Kite/Gilead, HUTCHMED, Aptitude Health, Adaptive
- Research Funding: Takeda, Novartis, Loxo/Lilly, Genentech, BMS/Celgene, AstraZeneca

This Is Not a Review of All New Therapies

- Many lymphoma subtypes (and “sub” subtypes)
- Many new therapy classes and agents:
 - Oral therapies
 - Cellular therapies
 - Antibodies and bispecifics
 - Biosimilars
 - Supportive therapies
 - Etc, etc
- You are younger and smarter than me and can rattle off these data
- Today’s goal – provide context and strategies for career development in a constantly changing landscape

Case 1 – MCL Circa 2011-2012

- 67-year-old male with mantle cell lymphoma
- Treated with R-CHOP in 2008, presenting with progression in 2011
- Otherwise healthy
- Treatment options?
 - Bortezomib
 - Chemotherapy
 - ± Lenalidomide
 - Allo transplant? Auto Transplant?

Case 1 – MCL Circa 2011-2012

- Poor response to bortezomib
- Enrolled in phase 2 study of PCI-32765
- Fantastic response x 1-2 years, then progressed and died of disease

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

ESTABLISHED IN 1812

AUGUST 8, 2013

VOL. 369 NO. 6

Targeting BTK with Ibrutinib in Relapsed or Refractory Mantle-Cell Lymphoma

Michael L. Wang, M.D., Simon Rule, M.D., Peter Martin, M.D., Andre Goy, M.D., Rebecca Auer, M.D., Ph.D., Brad S. Kahl, M.D., Wojciech Jurczak, M.D., Ph.D., Ranjana H. Advani, M.D., Jorge E. Romaguera, M.D., Michael E. Williams, M.D., Jacqueline C. Barrientos, M.D., Ewa Chmielewska, M.D., John Radford, M.D., Stephan Stilgenbauer, M.D., Martin Dreyling, M.D., Wieslaw Wiktor Jedrzejczak, M.D., Peter Johnson, M.D., Stephen E. Spurgeon, M.D., Lei Li, Ph.D., Liang Zhang, M.D., Ph.D., Kate Newberry, Ph.D., Zhishuo Ou, M.D., Nancy Cheng, M.S., Bingliang Fang, Ph.D., Jesse McGreivy, M.D., Fong Clow, Sc.D., Joseph J. Buggy, Ph.D., Betty Y. Chang, Ph.D., Darrin M. Beaupre, M.D., Ph.D., Lori A. Kunkel, M.D., and Kristie A. Blum, M.D.

Case 2 – Refractory DLBCL

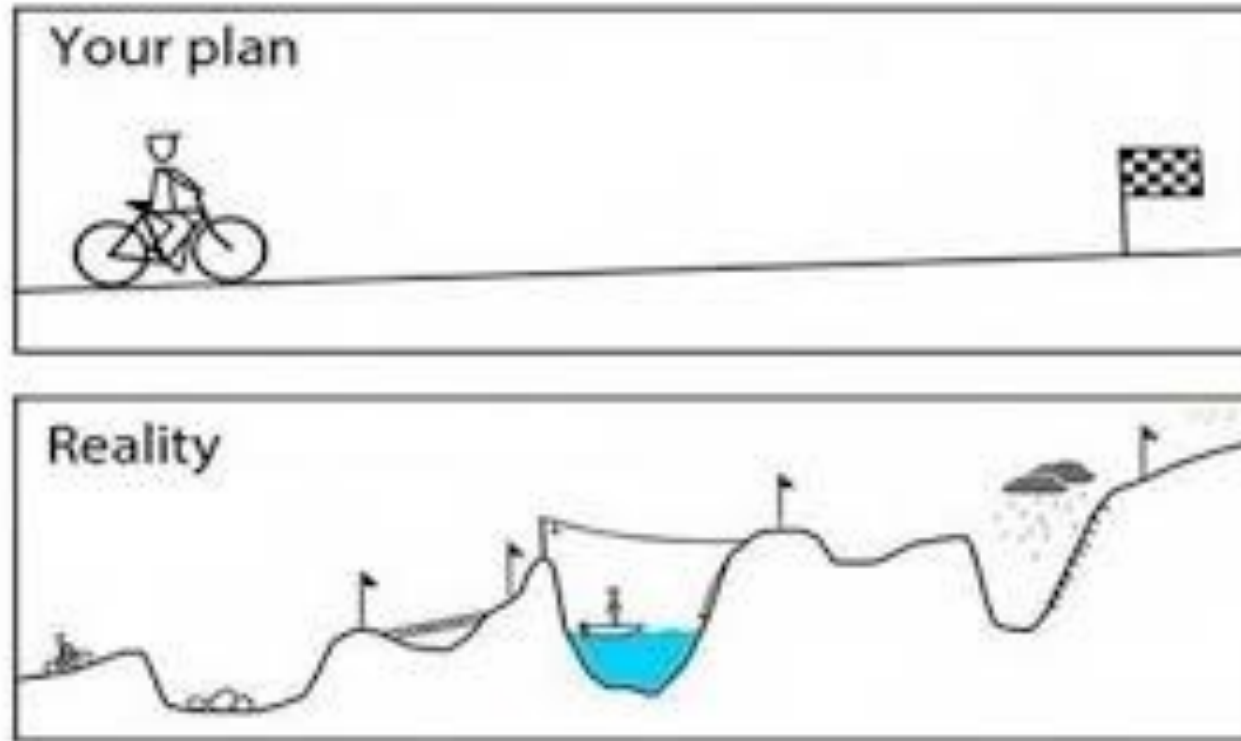
- 53-year-old male with refractory DLBCL
- Initially treated with R-CHOP with early relapse
- Received R-ICE with questionable chemosensitivity, proceeded to auto
- Early relapse post-auto
- Started on additional salvage chemotherapy combinations
- Referred for allogeneic but with poor disease control unable to proceed

BRIEF REPORT

Chimeric Antigen Receptor–Modified T Cells in Chronic Lymphoid Leukemia

David L. Porter, M.D., Bruce L. Levine, Ph.D., Michael Kalos, Ph.D.,
Adam Bagg, M.D., and Carl H. June, M.D. Aug 2011

Progress in NHL Comes Fast and Slow



Strikeouts, Groundouts, and Singles

- Proteasome inhibitors
- Ofatumumab
- R-EPOCH
- Daratumumab
- PI3K Inhibitors
- Selinexor
- Fimepinostat
- Tazemetostat
- Etc, etc

Biomarkers

- Cell of origin
- MYC/BCL2 IHC expression
- Molecular subtyping?
- Minimal residual disease?

Extra Bases & Home Runs

- BTK inhibitors
- CAR-T
- Bispecifics
- Checkpoint inhibitors
- Venetoclax (for CLL)
- Brentuximab vedotin

Questions for the Next 10 Years

(That we need you to help answer)

- Will anyone still require cellular therapies?
- Can we cure aggressive NHL without chemotherapy? Does it matter?
- Can we cure indolent NHL or mantle cell lymphoma? Does it matter?
- Can we truly achieve a personalized approach based on molecular assessments for most patients?
- Is MRD important and can we use it to manage patients?



Questions for the Next 10 Years

(That we need you to help answer)

My Thoughts

- Will anyone still require cellular therapies? **Yes, with fewer transplants**
- Can we cure aggressive NHL without chemotherapy? Does it matter?
- Can we cure indolent NHL or mantle cell lymphoma? Does it matter?
- Can we truly achieve a personalized approach based on molecular assessments for most patients?
- Is MRD important and can we use it to manage patients?

Questions for the Next 10 Years

(That we need you to help answer)

My Thoughts

- Will anyone still require cellular therapies? **Yes, with fewer transplants**
- Can we cure aggressive NHL without chemotherapy? **Yes** Does it matter? **For some patients, yes**
- Can we cure indolent NHL or mantle cell lymphoma? Does it matter?
- Will we offer a personalized approach based on molecular assessments for most patients?
- Is MRD important and can we use it to manage patients?

Questions for the Next 10 Years

(That we need you to help answer)

My Thoughts

- Will anyone still require cellular therapies? **Yes, with fewer transplants**
- Can we cure aggressive NHL without chemotherapy? **Yes** Does it matter? **For some patients, yes**
- Can we cure indolent NHL or mantle cell lymphoma? **Yes** Does it matter? **Probably not for *most* patients with iNHL**
- Will we offer a personalized approach based on molecular assessments for most patients?
- Is MRD important and can we use it to manage patients?

Questions for the Next 10 Years

(That we need you to help answer)

My Thoughts

- Will anyone still require cellular therapies? **Yes, with fewer transplants**
- Can we cure aggressive NHL without chemotherapy? **Yes** Does it matter? **For some patients, yes**
- Can we cure indolent NHL or mantle cell lymphoma? **Yes** Does it matter? **Probably not for *most* patients with iNHL**
- Will we offer a personalized approach based on molecular assessments for most patients? **No**
- Is MRD important and can we use it to manage patients?

Questions for the Next 10 Years

(That we need you to help answer)

My Thoughts

- Will anyone still require cellular therapies? **Yes, with fewer transplants**
- Can we cure aggressive NHL without chemotherapy? **Yes** Does it matter? **For some patients, yes**
- Can we cure indolent NHL or mantle cell lymphoma? **Yes** Does it matter? **Probably not for *most* patients with iNHL**
- Will we offer a personalized approach based on molecular assessments for most patients? **No**
- Is MRD important and can we use it to manage patients? **Yes**

Keys to Future Success in NHL

- Keep an open mind and take chances
- Be prepared for disappointing results
- Be prepared for good results but disappointing decisions
- Recognize unmet needs and unanswered questions
- Identify the clinical challenges you encounter with your patients
- Great new therapies have limited benefit if they can't be implemented widely

Final Thoughts

- Clinical trials, real-world evidence, and clinical experience all important
- Expect both rapid and slow progress
- Be persistent but know when to move on
- Be honest, but respectful
- Follow the data, but chart your own course
- Be humble and realize that the patient doesn't always read the textbook

THANK YOU!

