Verastem Oncology

Duvelisib: Harnessing the Power of Dual PI3K Inhibition

Omni Berkshire Place, New York City
May 2, 2018

Forward Looking Statements

This presentation includes forward-looking statements about Verastem's strategy, future plans and prospects, including statements regarding the development and activity of Verastem's investigational product candidates, including duvelisib and defactinib, and Verastem's PI3K and FAK programs generally, the structure of our planned and pending clinical trials, Verastem's potential collaboration opportunities and the timeline and indications for clinical development and regulatory submissions. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks that approval of the NDA will not occur on the expected timeframes or at all, including by the FDA's target action date; that a filing of a European Marketing Application may not be achieved before the end of the year, if at all; that even if data from clinical trials is positive, regulatory authorities may require additional studies for approval and the product may not prove to be safe and effective; that the preclinical testing of Verastem's product candidates and preliminary or interim data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials; that the full data from the DUO study will not be consistent with the previously presented results of the study; that data may not be available when expected, including for the Phase 3 DUO™ study; that the degree of market acceptance of product candidates, if approved, may be lower than expected; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that our product candidates will cause unexpected safety events or result in an unmanageable safety profile as compared to their level of efficacy; that duvelisib will be ineffective at treating patients with lymphoid malignancies; that Verastem will be unable to successfully initiate or complete the clinical development of its product candidates; that the development of Verastem's product candidates will take longer or cost more than planned; that Verastem may not have sufficient cash to fund its contemplated operations; that Verastem or Infinity Pharmaceuticals, Inc. (Infinity) will fail to fully perform under the duvelisib license agreement; that Verastem may be unable to make additional draws under its debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that Verastem will not pursue or submit regulatory filings for its product candidates, including for duvelisib in patients with CLL/SLL or iNHL; and that Verastem's product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients. Other risks and uncertainties include those identified under the heading "Risk Factors" in Verastem's Annual Report on Form 10-K for the year ended December 31, 2017 and in any subsequent filings with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Verastem's views as of the date of this release, and Verastem does not undertake and specifically disclaims any obligation to update any forward-looking statements.

Verastem

Oncology

AGENDA

CEO Welcome

Robert Forrester, *President & Chief Executive Officer, Verastem Oncology*

The CLL Patient Journey

Brian Koffman, MDCM, DCFP, FCFP, DABFP, MSEd, *Physician, Medical Director of the Chronic Lymphocytic Leukemia (CLL) Society and CLL Patient*

The Evolution of Blood Cancer Treatments

Lori Kunkel, MD, *Former Chief Medical Officer, Pharmacyclics*

Unmet Needs and the Role of PI3K Inhibitors

Jennifer Brown, MD, PhD, *Associate Professor of Medicine, Harvard Medical School; Director, CLL Center of the Division of Hematologic Malignancies, Dana-Farber Cancer Institute*

Duvelisib for the Treatment of CLL/SLL and FL

Ian Flinn, MD, PhD, *Director, Blood Cancer Research Program at Sarah Cannon Research Institute, and Lead Investigator of the DUO and DYNAMO Studies*

Duvelisib for the treatment of T-cell lymphomas

Steven Horwitz, MD, *Medical Oncologist, Memorial Sloan Kettering Cancer Center and NYC Health + Hospitals/Bellevue*

Unlocking the potential of duvelisib: Path to commercial launch

Joseph Lobacki, *Chief Commercial Officer, Verastem Oncology*

Question & Answer Session with Full Panel

Verastem Oncology

The CLL Patient Journey

Brian Koffman, MDCM, DCFP, FCFP, DABFP, MSEd

Brian Koffman

MDCM, FCFP, DABFP, MS Ed

Disclosure

- I am alive and here today because I started on a Phase 1 clinical trial of new oral drug, PCI-32765 now known as ibrutinib or IMBRUVICA
- I am planning to be around much longer due to my very recent CAR-T trial
- I have a bias towards expert care, novel therapies, and keeping options open

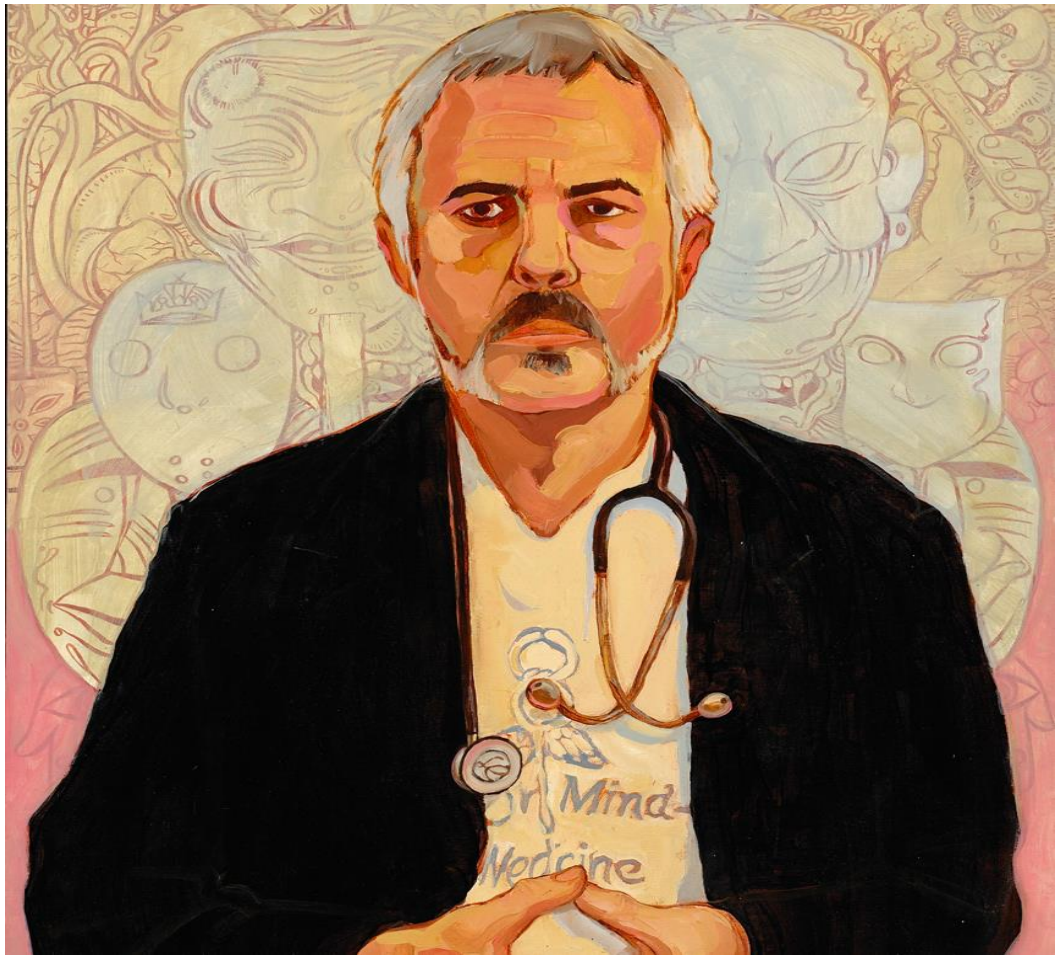
Disclosure

- I am a physician, patient, advocate, retired professor, teacher, writer, blogger http://bkoffman.blogspot.com,
- Founder and Medical director of nonprofit CLL Society Inc. http://cllsociety.org
- Cancer survivor

Learning Objectives

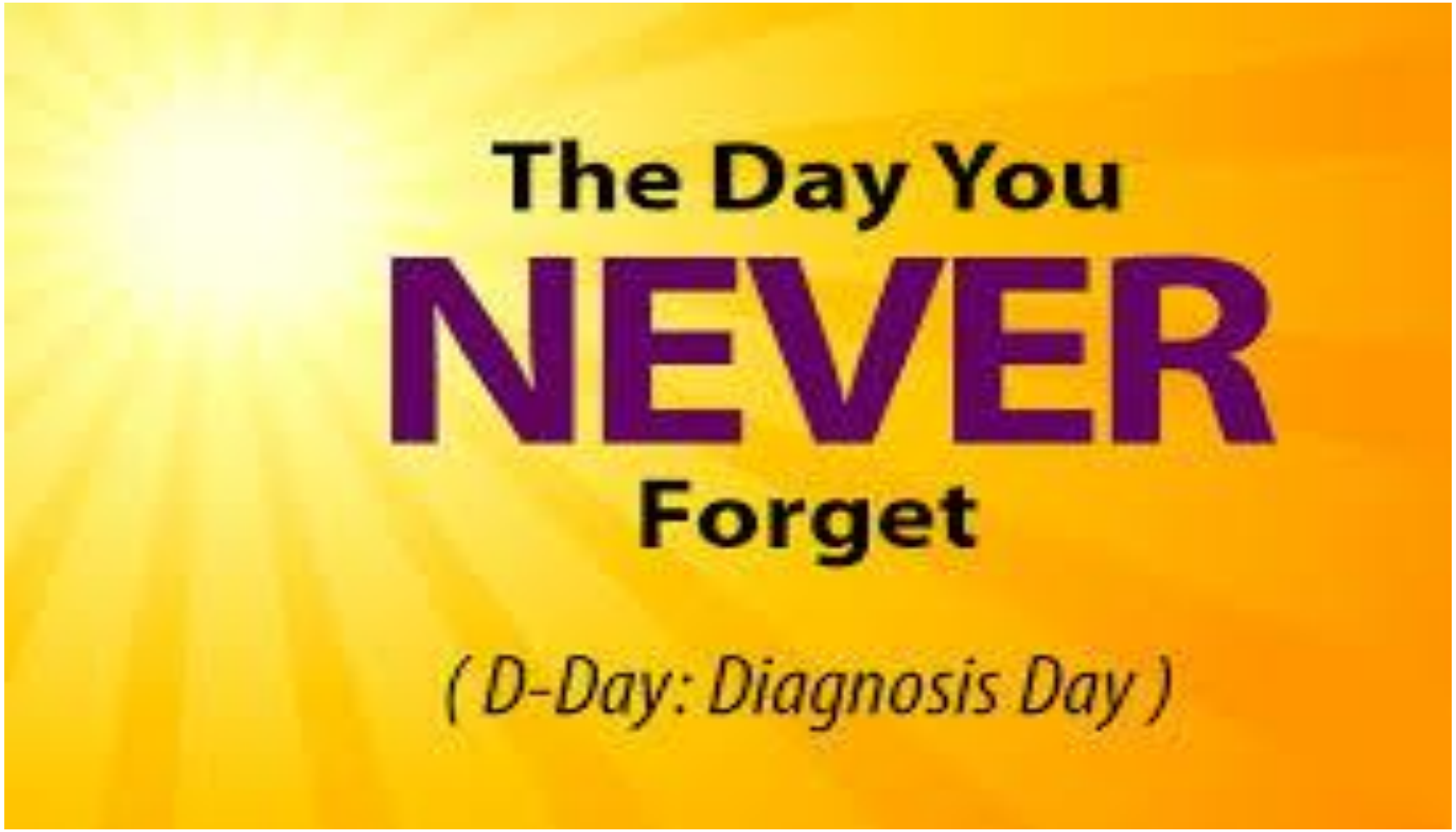
- Use one case history (mine) and a recent online survey to illustrate how we patients make decisions and get our information.
- Recognize what patients want and don’t want out of their therapy as options change.
- Weigh patient’s view of the risks and benefits of novel therapies inside and out of clinical trials.

How I have Survived



- What I Have Done to Beat those Odds despite very High Risk Disease
  - Refusing some treatments and choosing others
  - Hiring and firing HCPs
  - Getting expert on my team
  - Becoming an “expert” patient
  - Enrolling in clinical trials
  - Insuring “next” options
  - Getting Insurance to pay
  - Joining a Support group

Diagnosed when 54 years old in 2005



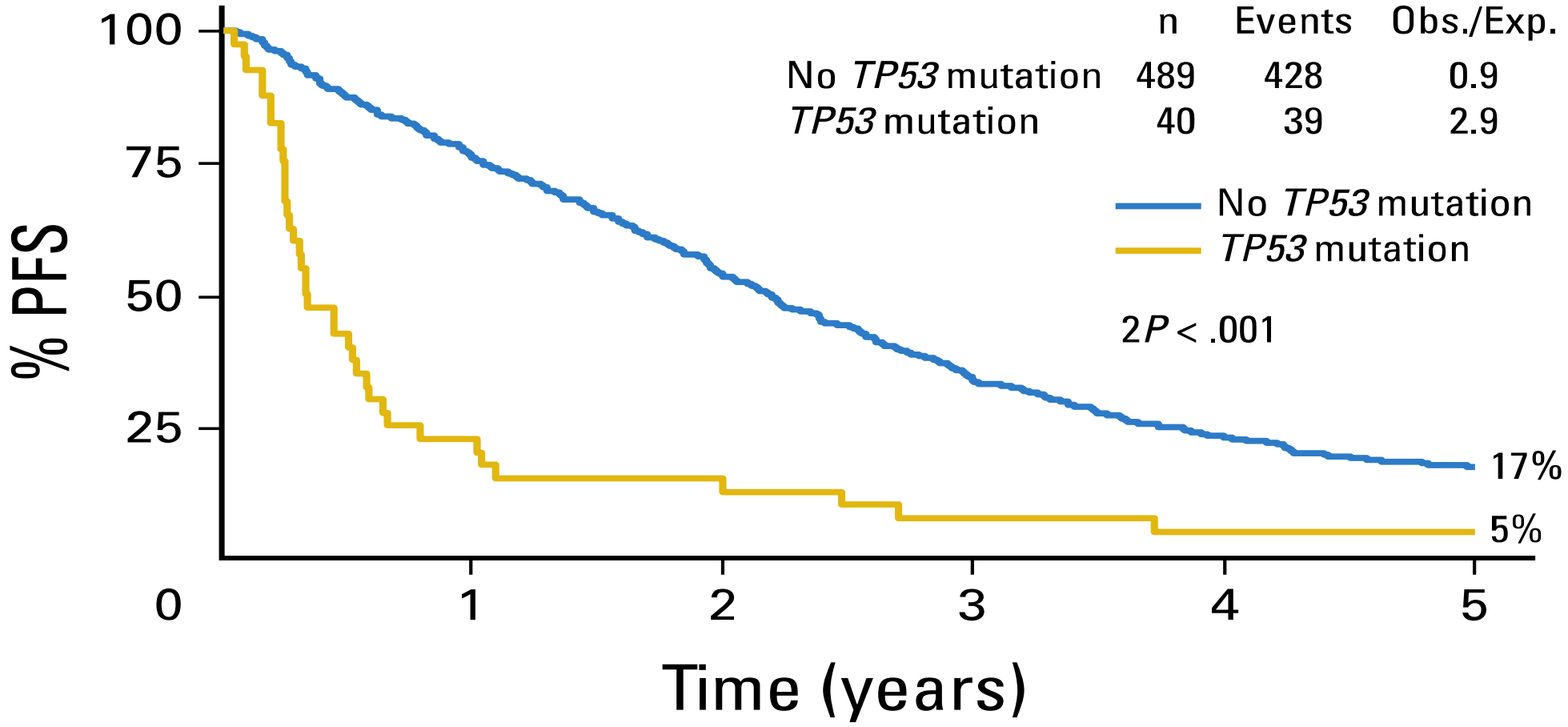
"I'm afraid you've had a paradigm shift."

I'm afraid you've had a paradigm shift

Prognosis

11q deletion (later 17p deletion), complex karyotype, CD38+, unmutated, ZAP70 +,
(now loss of Notch 1, CDKN2A, Dnmt3a, XOP1)

Kaplan Meir Curve
(or my 1 in 20 chance of living >5 years)



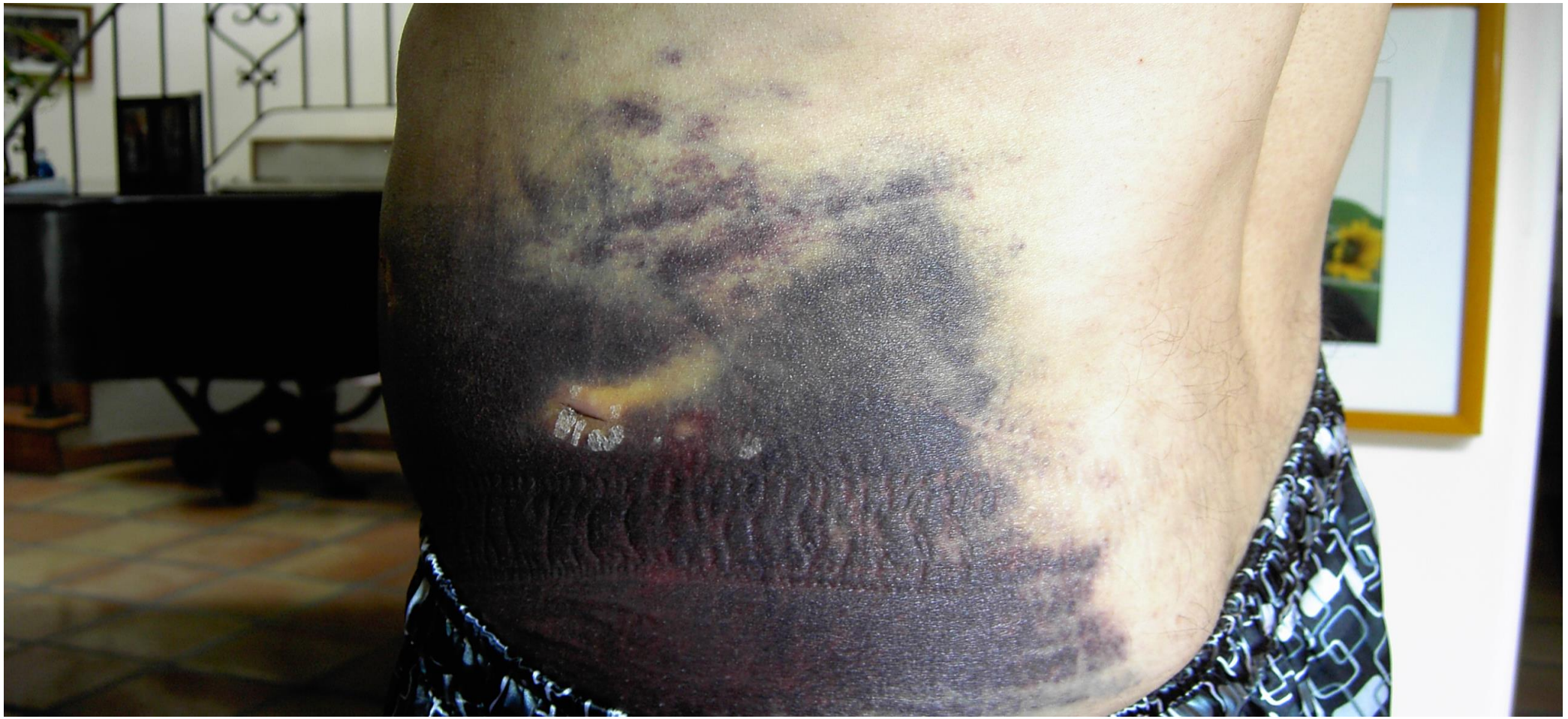
April 11, 2011 as 10.1200/JCO.2010.32.0838

Big Bearded Mountain Man Look To Hide my Lymph Nodes

Complication (ITP) and Its Treatment

- Single digit platelets with spontaneous petechiae and bruising
- **Failed**
  - Steroids
  - IVIG
  - Rituximab
  - Cyclosporin
  - Emergency Laparoscopic Splenectomy
    - HCT dropped from 14 to 7 post-op

Bleeding after Splenectomy



Surprise Remission → Aggressive Therapy Decision

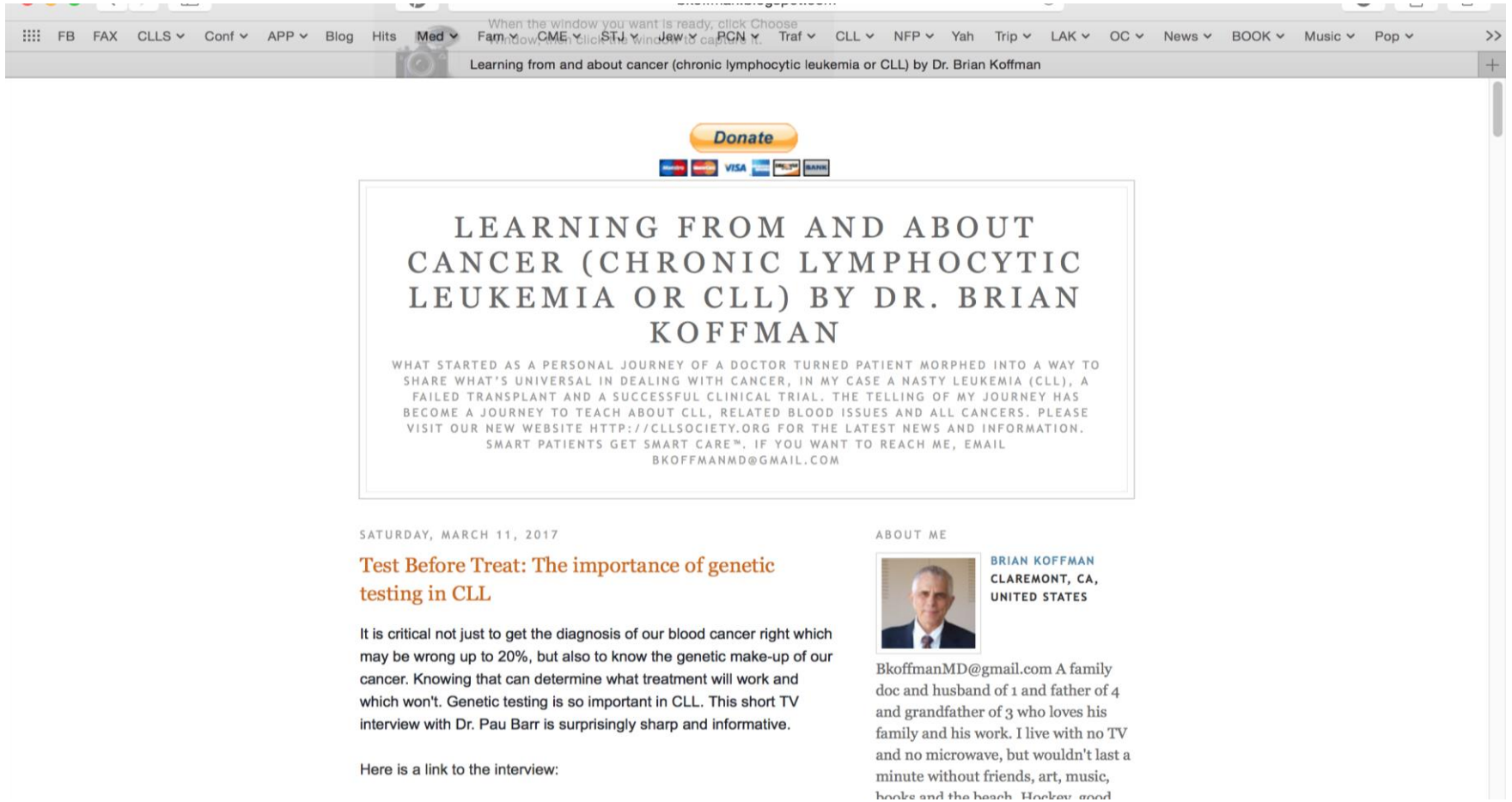
- Combination of Rituximab and cyclosporin (with no chemotherapy) not only controlled ITP but remitted the CLL
  - 90% bone marrow involvement → 6%
  - Normal CBC and no palpable nodes but enlarged nodes on CT scan
- **NO TWO PATIENTS ARE ALIKE**

Treatment (2007)

First Remission Allogeneic Stem Cell Transplant

- 12 out of 12 matched unrelated young male donor
- FRC conditioning, no ATG

How to Tell my Story?



http://bkoffman.blogspot.com > 1.3 million page views since established

TRANSPLANT DAY JULY 1/2008 drawing by Will Koffman

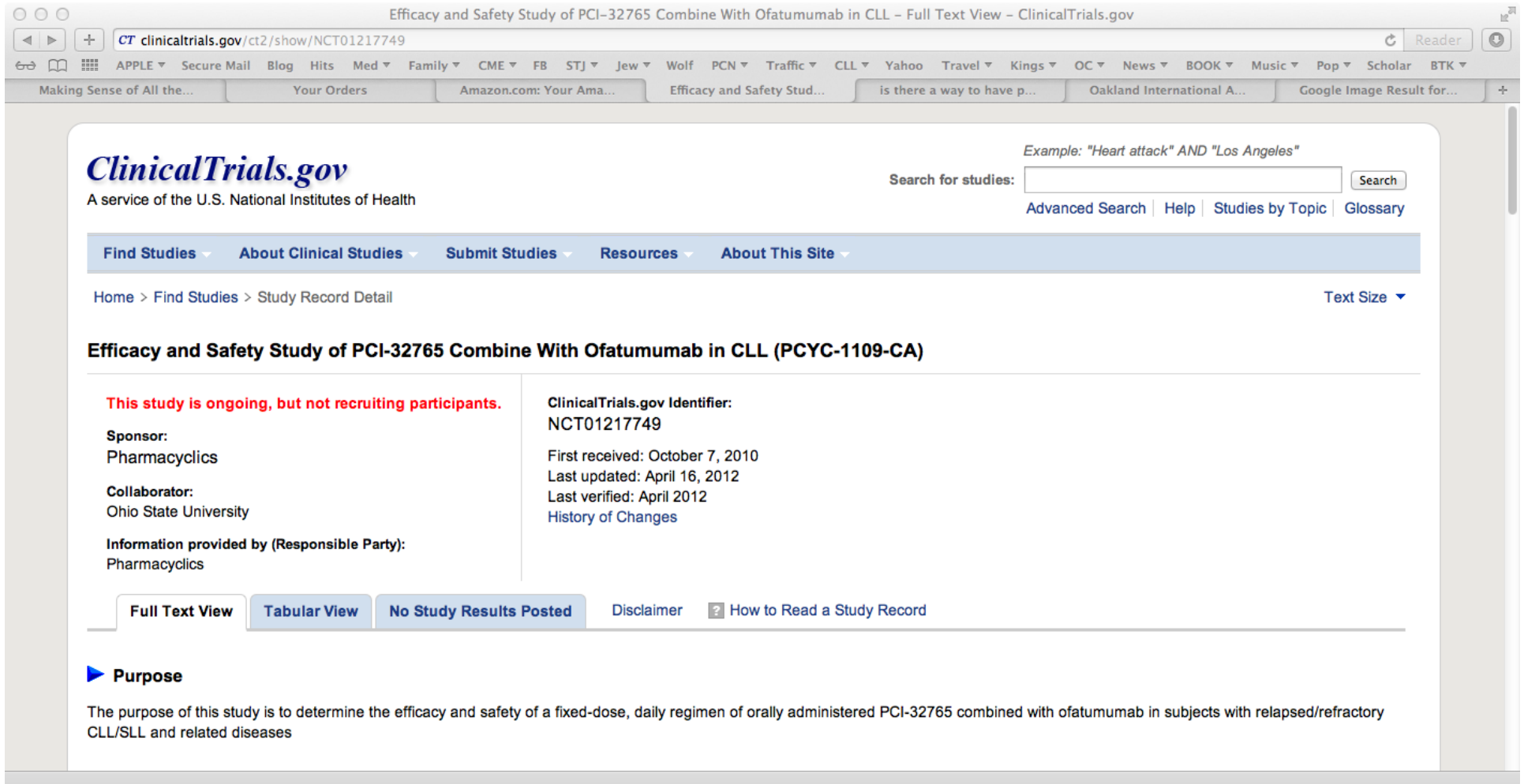
Quick Relapse

Rejected graft, relapsed CLL and ITP

ASH 2011: The Early Buzz about PCI-32765 (ibrutinib) & CAL -101 (idelasib)

- Cracked the biology of CLL
- Optimism about a new oral BTK and PI3K inhibitors in trials
- Broad agreement this was something very different

Paradigm Shift


Efficacy and Safety Study of PCI-32765 Combine With Ofatumumab in CLL – Full Text View – ClinicalTrials.gov
clinicaltrials.gov/ct2/show/NCT01217749
Reader
APPLE Secure Mail Blog Hits Med Family CME FB STJ Jew Wolf PCN Traffic CLL Yahoo Travel Kings OC News BOOK Music Pop Scholar BTK
Making Sense of All the...
Your Orders
Amazon.com: Your Ama...
Efficacy and Safety Stud...
is there a way to have p...
Oakland International A...
Google Image Result for...
ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Example: "Heart attack" AND "Los Angeles"
Search for studies:
Search
Advanced Search | Help | Studies by Topic | Glossary
Find Studies
About Clinical Studies
Submit Studies
Resources
About This Site
Home > Find Studies > Study Record Detail
Text Size
Efficacy and Safety Study of PCI-32765 Combine With Ofatumumab in CLL (PCYC-1109-CA)
This study is ongoing, but not recruiting participants.
Sponsor:
Pharmacyclics
Collaborator:
Ohio State University
Information provided by (Responsible Party):
Pharmacyclics
ClinicalTrials.gov Identifier:
NCT01217749
First received: October 7, 2010
Last updated: April 16, 2012
Last verified: April 2012
History of Changes
Full Text View
Tabular View
No Study Results Posted
Disclaimer
How to Read a Study Record
Purpose
The purpose of this study is to determine the efficacy and safety of a fixed-dose, daily regimen of orally administered PCI-32765 combined with ofatumumab in subjects with relapsed/refractory CLL/SLL and related diseases

Ask your doctor if taking a pill to solve all your problems is right for you

Deep and Durable Partial Remission

- Now 71 months on ibrutinib (IMBRUVICA)
- Markedly improved QOL
  - Improved energy with traveling around the world
- Bruising and brittle nails most persists AE
- Slow relapse at a genetic level x 18 months, then clinically picking up pace in last few months
- Left trial at OSU Feb. 19, 2018
- Started CAR-T trial at SCCA/Hutch Feb. 28, 2018

Laboratory Treated T Cells in Treating Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia, Non-Hodgkin Lymphoma, or Acute Lymphoblastic Leukemia

ClinicalTrials.gov Identifier: NCT01865617

Recruitment Status ! : Recruiting
First Posted ! : May 31, 2013
Last Update Posted ! : October 26, 2017

See **Contacts and Locations**

Sponsor:
Fred Hutchinson Cancer Research Center

Collaborator:
National Cancer Institute (NCI)

Information provided by (Responsible Party):
Fred Hutchinson Cancer Research Center

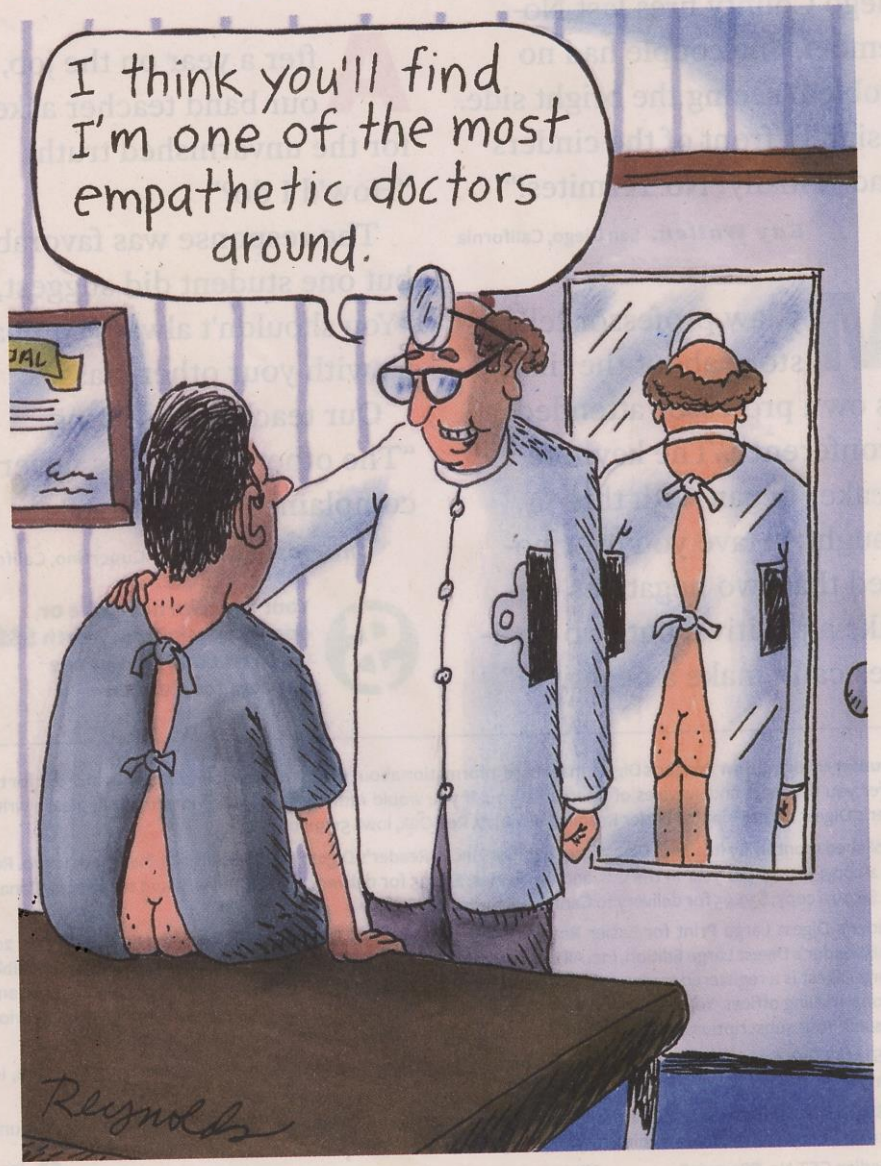
CAR-T Trial

- Chosen due my aggressive and mutagenic disease
- Kept my options open for a novel agent if CAR-T fails
- DOWNSIDE:
  - CAR-T science and art is still in the early learning phase
  - CAR-T is usually quite toxic
- 2 months in Seattle
  - 2 admissions including one with severe inflammation where I was unable to move for days
  - Developed blood clot from immobility
  - Anemia and persistent inflammation
- **Day 28+: No CLL detectable in blood, marrow and nodes**

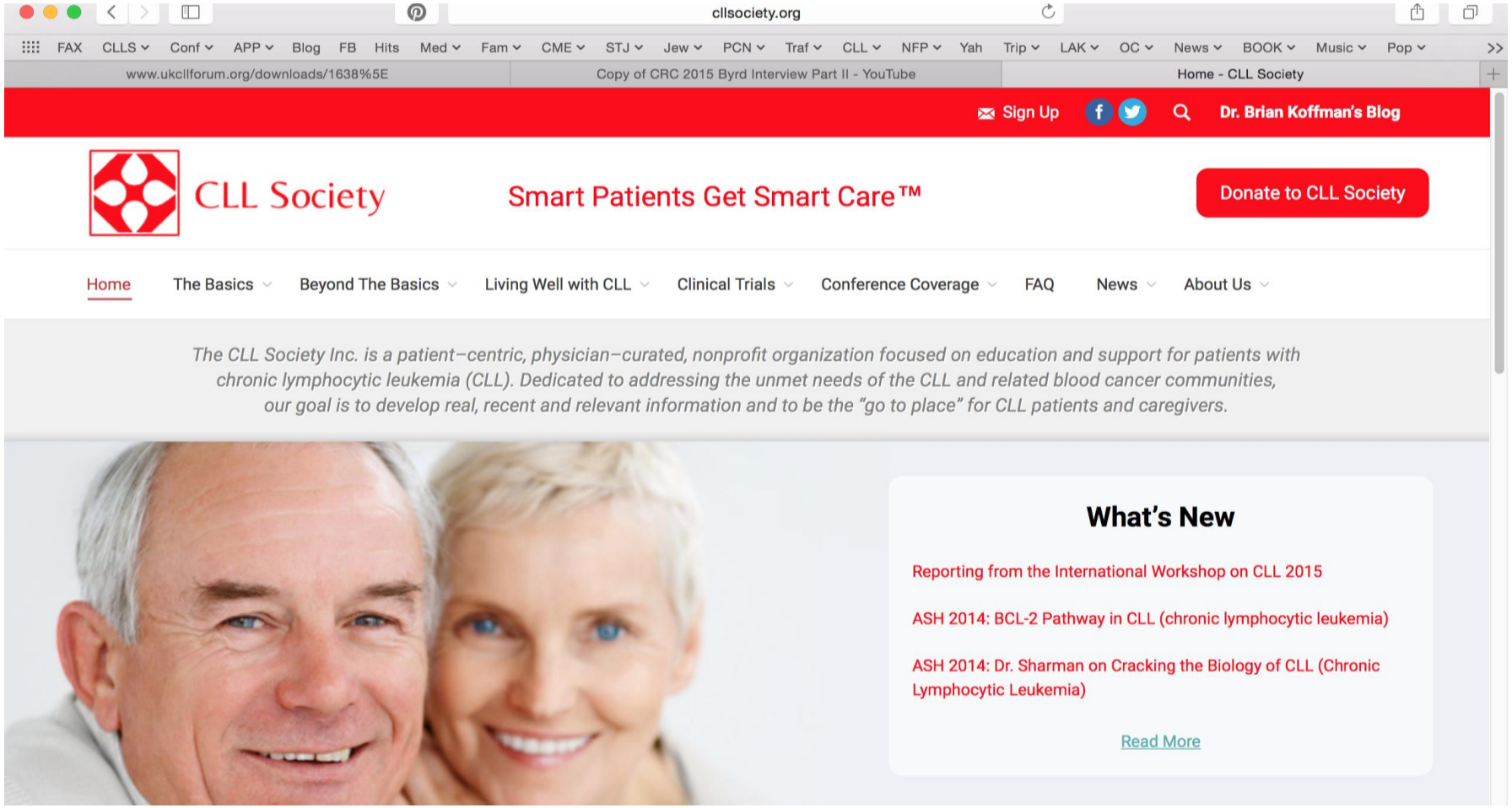
Giving Forward

- Speaking from the patients perspective to 1000s of hematologists at iwCLL, EHA and ESH
- Non-profit: **THE CLL SOCIETY** http://cllsociety.org
  - 65,000 page views a month
  - Established 24 Peer to Peer Support Groups
  - Free Access to Expert Opinions
  - Dozens of Patient and Caregiver Educational Forums at major universities (Dana- Farber, NIH, U. Penn, etc)
  - Research presented at ASH, ASCO and EHA

Last Laugh


I think you'll find I'm one of the most empathetic doctors around.
Reynolds

http://cllsociety.org



Factors That Influence Patient Treatment Decision Making in the Era of Novel Agents: An Internet-Based Survey of 281 Patients with Chronic Lymphocytic Leukemia (CLL)

Brian Koffman, MDCM, DCFP, DABFM, MS Ed[1], Betsy Dennison, RN, MS[2], Kaitlin H Kennard, BSN[3], Chadi Nabhan, MD, MBA, FACP[4], John C. Byrd, MD[5] and Anthony R. Mato, MD, MSCE[3]

[1]CLL Society Inc, Claremont, CA; [2]CLL Society Inc, Pompton Lakes, NJ; [3]Center for CLL, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; [4]Cardinal Health, Dublin, OH, [5]Division of Hematology, Department of Internal Medicine, The Ohio State University, Columbus, OH

BACKGROUND ABOUT CLL IN 2016

Chronic Lymphocytic Leukemia (CLL) may be the most common blood cancer in adults in the Western world (37%)[1], but it is still a relatively rare malignancy. Its treatment is further complicated by the wide heterogeneity of its clinical course with some patients never needing treatment and having similar life expectancies as those without CLL and others having rapidly progressive disease.

The recent approval of five novel agents with more in late stage clinical trials, as well as better prognostication of CLL have transformed the therapeutic landscape.

These realities have pushed some patients to become more expert in their disease and more involved in their care and treatment decisions.

OBJECTIVES

- To identify the clinical factors that drive patient's decision-making in treatment selection
- To understand the role of the patient, physician and others in making treatment decisions.
- To identify where patients gather information to inform their decisions

METHODS

Study Design

- This was an online survey of patients with CLL over a 4 week period from Mar 30-Apr 27, 2016.

Patients

- Patients were registered to receive the CLL Society newsletter, *The CLL Tribune*, or registered with the online CLL-specific patient forums hosted by ACOR (Association of Cancer Online Resources) and groups.IO. Only the subset of 281 patients residing in the USA were included in this analysis.

Questionnaire

- A survey containing 11 multi-part questions consisting of demographics, treatment status, factors that drive treatment decision-making, and sources of information.

Statistical Analysis:

- Data were analyzed using descriptive methods. Chi-square was used to evaluate statistical significance.
- Analyses and comparisons were made between the following subgroups:
  - Low-risk or unknown risk versus high-risk
  - Untreated versus treated patients
  - Untreated patients versus those who have received 1 treatment versus received 2 or more treatments
  - Male versus female
  - ≥65 year old treated patients versus <65 year old treated patients
  - Unless mentioned, subgroup analyses were not statistically significant.

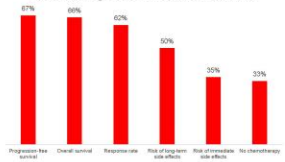
RESULTS

Table 1. Patient Characteristics

Median age, years (range)	64 (38-84)
Males, %	46
Median time from diagnosis, years (range)	7 (0-27)
Self-identified Risk Level, %	
High-risk (del 17p, p53 mutated, del 11q, or IGVH unmutated)	40
Unaware of risk level	13
Treatment status, %	
Watch & Wait	31
Considering or receiving 1st treatment	37
Males (51%); ≥65 years old (52%)	
Considering or receiving 2nd or later treatment	32
Males (49%); ≥65 years old (48%)	

RESULTS (continued)

Figure 1. Most Important Criteria When Considering Treatment (% rated 1, 2 or 3)



Important Criteria for Treatment Selection

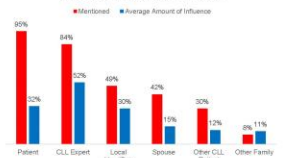
Respondents were asked to rate treatment-related criteria from 1-10, with 1=most important and 10=least important. [Figure 1]

Cost (30%), ability to take treatment orally (23%), participation in a clinical trial (20%), location of treatment administration (19%) and ability to stop treatment after a defined period of time (16%) were of lower importance to patients.

Role of the Patient, Physician and Others in Making Treatment Decisions

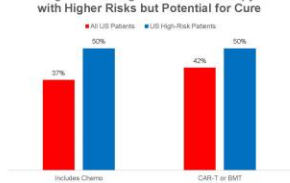
- 14% allow the physician to make the treatment decision without patient input.
  - Reasons included trust in their doctor or lack of understanding enough to contribute their opinion
- 44% listen to the options their doctor presents, but primarily make their own decision
- 43% proactively research treatment options and the currently available clinical trials and also suggest treatments to their physician

Figure 2. Influence on Decisions Related to Treatment for CLL



Survey respondents that were actively involved in the decision-making process were asked to indicate who influenced their decisions related to treatment, as well as the percentage of influence provided towards that decision. 95% of respondents stated their own involvement in the treatment decision: 84% involved a CLL expert and 49%, a local hematologist. The average amount of influence for each was 32%, 52% and 30%, respectively. [Figure 2]

Figure 3. Willingness to Take Therapy with Higher Risks but Potential for Cure

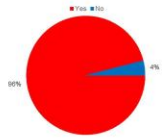


Only 37% of respondents would be willing to take a treatment that included chemotherapy despite higher risks, but a potential for cure.

Similarly, 42% would be willing to consider "CAR-T" or "bone marrow transplant" if it offered a chance of cure. [Figure 3]. Differences between treated patients that were ≥65 and <65 were statistically significant (34%/55%, P=.003), but may represent knowledge that BMT may not be offered to patients ≥65. Future surveys would separate these treatment options.

96% of respondents would be willing to take life-long therapy. [Figure 4].

Figure 4. Willingness to Take Life-long Therapy for Long-term Control Without Potential for Cure



Main Sources of Information About CLL

CLL websites were listed most often (87%) as a source of information about CLL, followed by healthcare providers (HCP) (74%), web-based blogs (72%), patient forums (68%) and webcasts (47%). HCPs and webcasts were less frequently mentioned by untreated patients and may reflect the less frequent contact with HCPs and less interest in webcasts. The difference between responses of treated and untreated patients was statistically significant for mentioning HCPs (P=.001) and webcasts (P=.032) as a source of information about CLL.

CONCLUSIONS

In the era of modern therapies, these data provide insight as to what criteria are important to patients when making treatment decisions, who influences patients in their CLL treatment decision-making process and what resources patients use to gain information about CLL.

In summary:

- 87% of patients reported that they are actively involved in treatment decision-making.
- PFS and OS were mentioned as the most important factors driving their treatment choices.
- Patients rely on multiple sources of information beyond their physician, with online sources mentioned more frequently, perhaps related to the constant availability of the internet compared to infrequent doctor visits.
- There is broad patient acceptance of long-term non-curative treatment.
- There is significant patient hesitancy for chemotherapy, CAR-T therapy and stem cell transplantation despite the possibility of cure.

Recommendations

- All medical decisions should be shared between the patient and the doctor.
- Educated patients are more likely to participate in shared decision-making.
- Encourage and accept patient involvement in their care.
- Be prepared for second opinions – and they may not be from a colleague.
- Don't assume patients are unwilling to consider long-term non-curative but lower-risk therapies.

Limitations

- Our patient respondents were younger (median age 64 years old) compared to the median age of 71 in SEER data[2]. There were also more females (54%) than generally reported (43%)[1]. This likely reflects a selection bias of those completing the survey. Information provided were based on patients' answers and could not be independently verified.
- The survey was only available online, hence the results are obviously influenced by the self-selection of those who use the Internet and access the sources mentioned above and may reflect a group of patients who may be more sophisticated and involved in their care.

Response to Limitations

While we recognize the limits imposed by a survey that was only available online, we believe these data are a true reflection of a growing number of CLL patients who are web savvy and knowledgeable about their disease.

We hope to offer a paper version of a similar survey in 2017 in order to address these concerns.

About The CLL Society Inc.

The CLL Society Inc. is a 501(c)3 nonprofit that focuses on patient education and patient support to address the unmet needs of the CLL community.

- The CLL Society website http://cllsociety.org which contains the most up-to-date, accurate and patient-friendly information on CLL.
- *The CLL Tribune*, a quarterly online newsletter with both patient and physician authors
- CLL-specific patient support groups and educational forums
- CLL Patient peer to peer counseling efforts

The CLL Society wishes to thank the patients who participated in this important research.

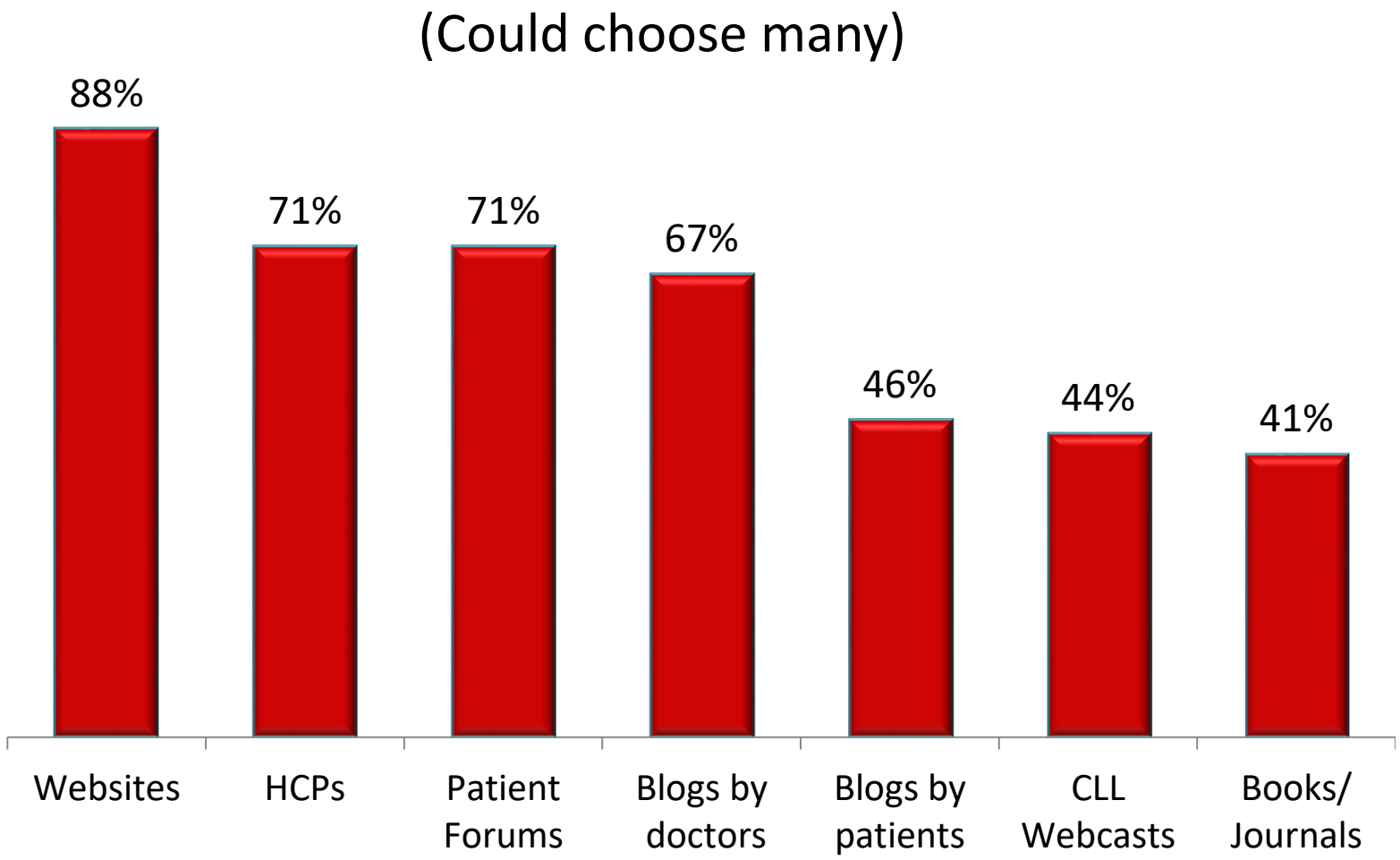
REFERENCES

1. Cancer Facts & Figures 2016 http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-047079.pdf Accessed 11/2/2016
2. SEER Cancer Statistics Factsheets: Chronic Lymphocytic Leukemia. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/clyl.html. Accessed 11/2/2016

The authors (Koffman, Dennison, Kennard, Nabhan, Byrd, Mato) have no relevant financial relationships to disclose.

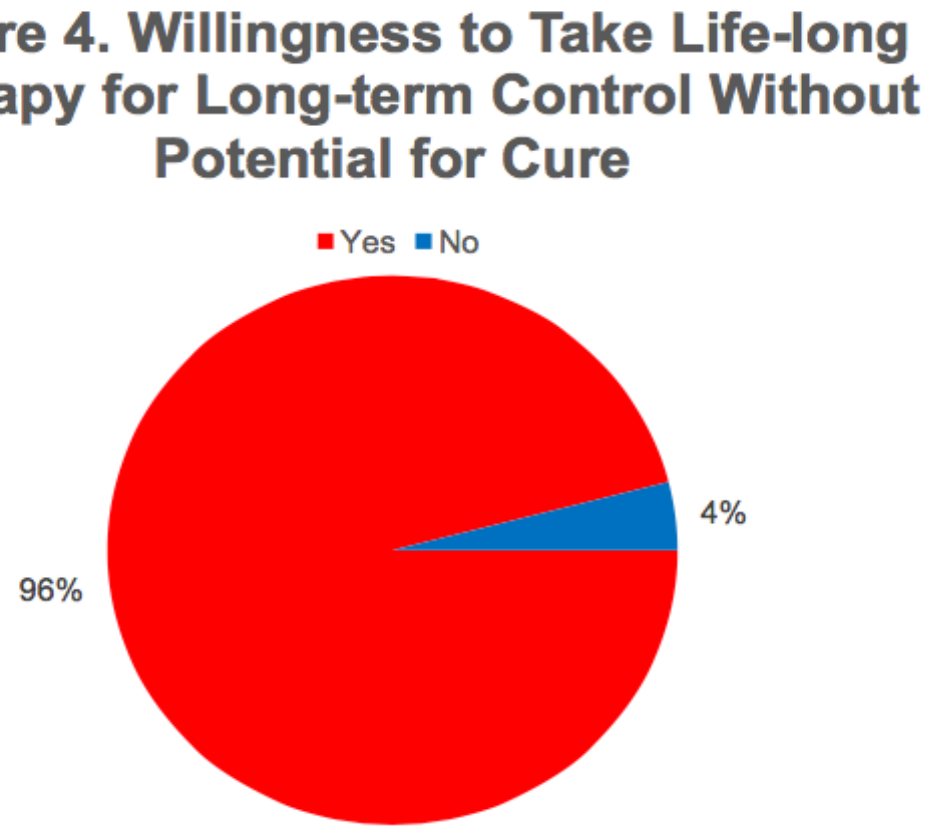
Presented at the 58th Meeting of the American Society of Hematology, San Diego, CA, USA, December 3-6, 2016.

Patient Sources of Information about CLL



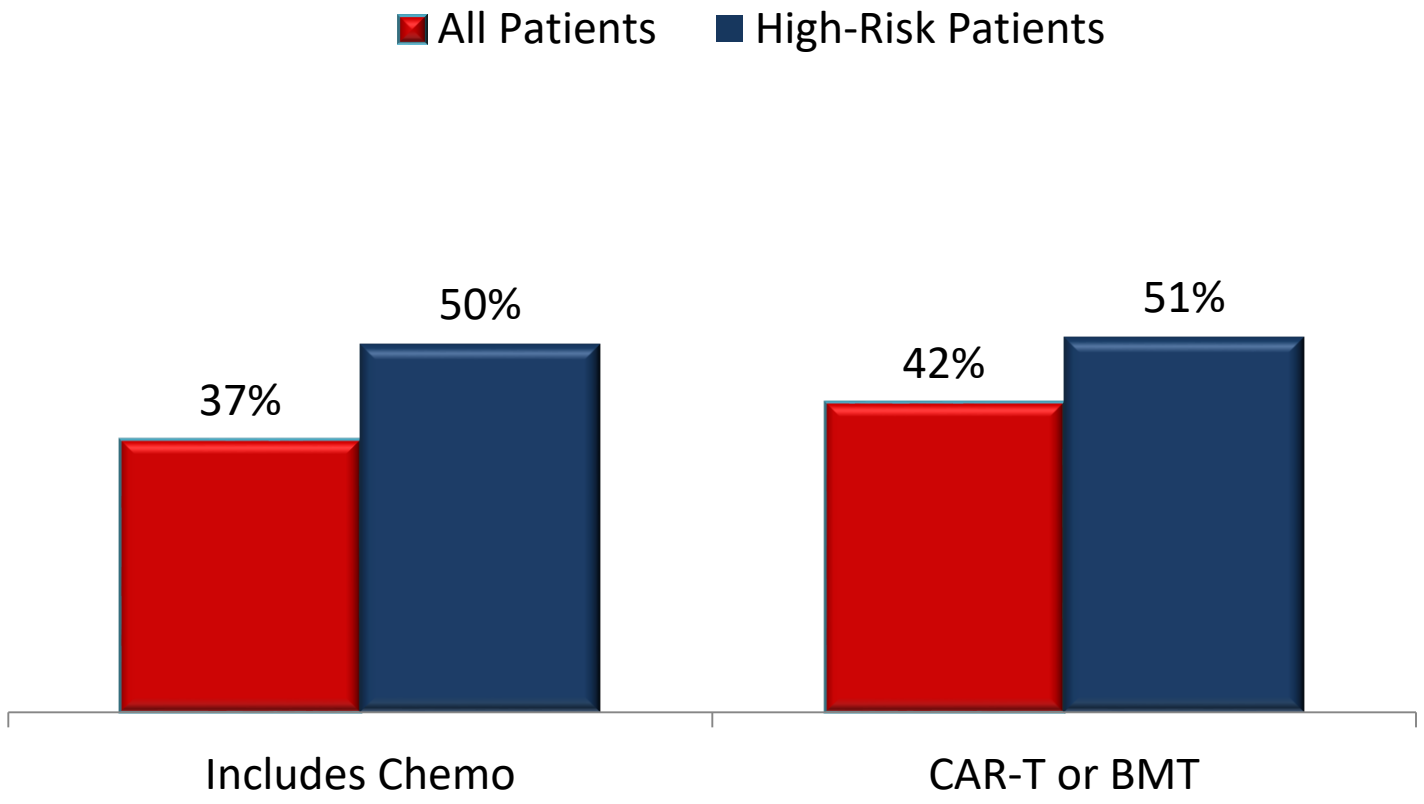
Source: CLL Society Reader Poll from *The CLL Tribune* Q1 2016

Patient Sources of Information about CLL



Source: CLL Society Reader Poll from *The CLL Tribune* Q1 2016

Willingness to Take Therapy with Higher Risks but with Potential for Cure



CLL Society Reader Poll from *The CLL Tribune* Q1 2016

What Patients Aren't Worried About

- **OUR MINOR CONCERN are short term:**
  - **Infusion reactions**
  - **Tumor lysis syndrome**
  - **Cytokine release syndrome**
  - **Acute infections**
  - **Acute GI, CNS Neuro, Derm**

We trust our doctors to save us

What Patients Are Worried About

- **OUR MAJOR CONCERN are long term:**
  - **Damage to our bone marrow**
  - **DNA mutation**
  - **Selection of more aggressive clones**
  - **Immune damage → late serious infections**
  - **Late complications including CVS and neurological**
  - **Refractory disease when we relapse**
  - **Secondary cancers (including MDS)**

BECAUSE:

- **Infections are the leading cause of death in CLL**
- **50% risk of secondary cancers**

So What Patients Do Want?

We want more targeted, less toxic therapies:

Because Today:

- Targeted therapies are preferred frontline for all high risk and most other patients and should be the only choice in nearly all relapsed patients.
- More targeted options needed for relapses and to match different patients' profiles and preferences
- CIT should be reserved for the few healthy young patients where it is potentially curative.

Because in the Future:

- Curative therapies are possible: either cellular or combinations novel agents or both used in combination.

Learning Objectives

- Use one case history (mine) and a recent online survey to illustrate how we patients make decisions and get our information.
- Recognize what patients want and don’t want out of their therapy as options change.
- Weigh patient’s view of the risks and benefits of novel therapies inside and out of clinical trials.

Brian Koffman

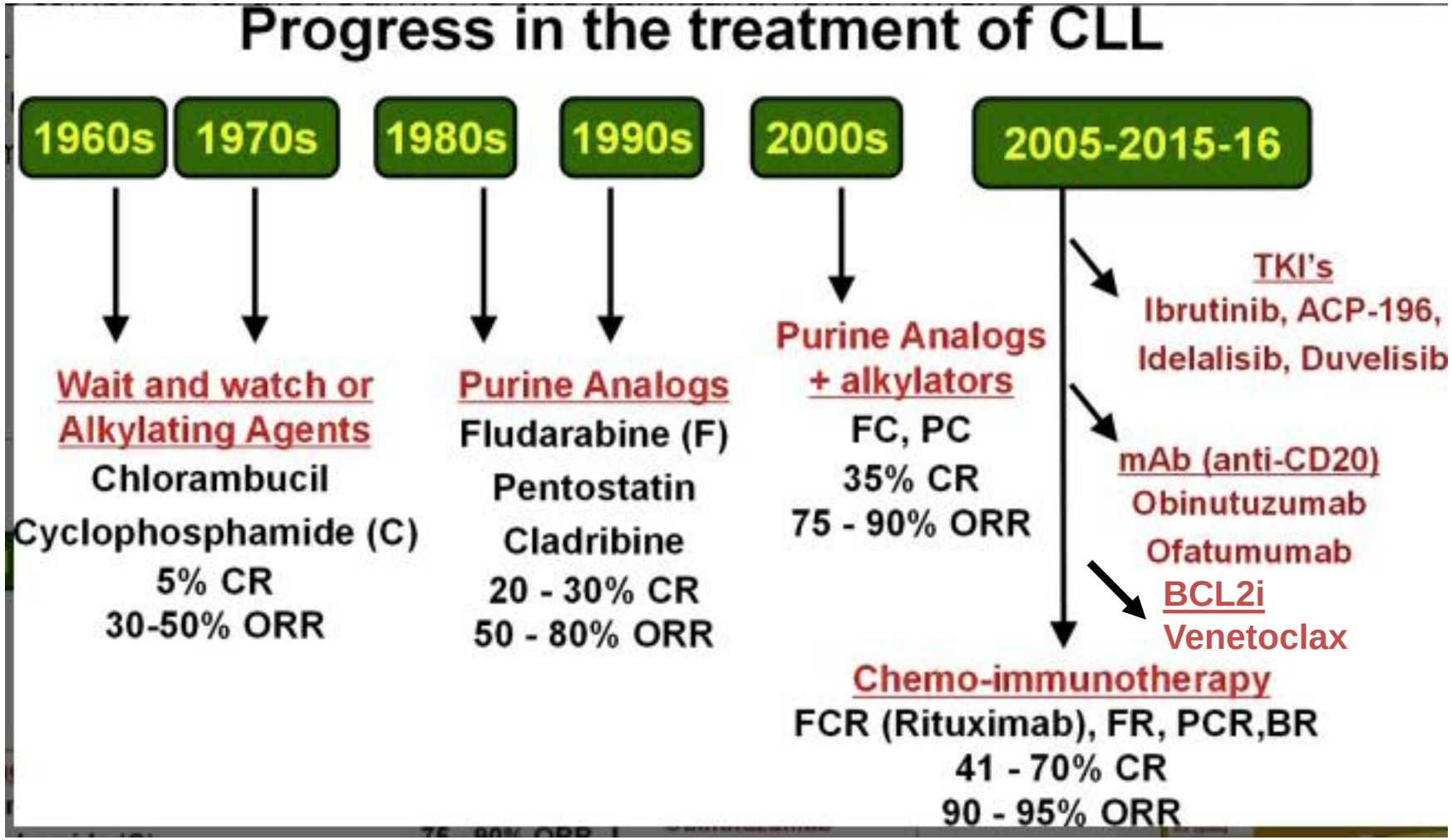
MDCM, FCFP, DABFP, MS Ed

Thank You

Verastem Oncology

The Evolution of Blood Cancer Treatments

Lori Kunkel, MD



DNA Damaging Agents→Non selective

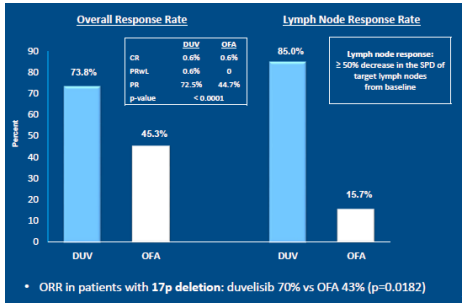
CD20 B cell specific mAb

B Cell receptor signaling

BCL2i

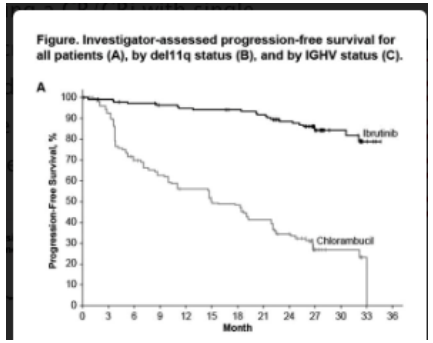
Adapted: Rai Am J Hem 2016

The big breakthroughs and take home



Most patients respond to targeted agents

Durability can be years



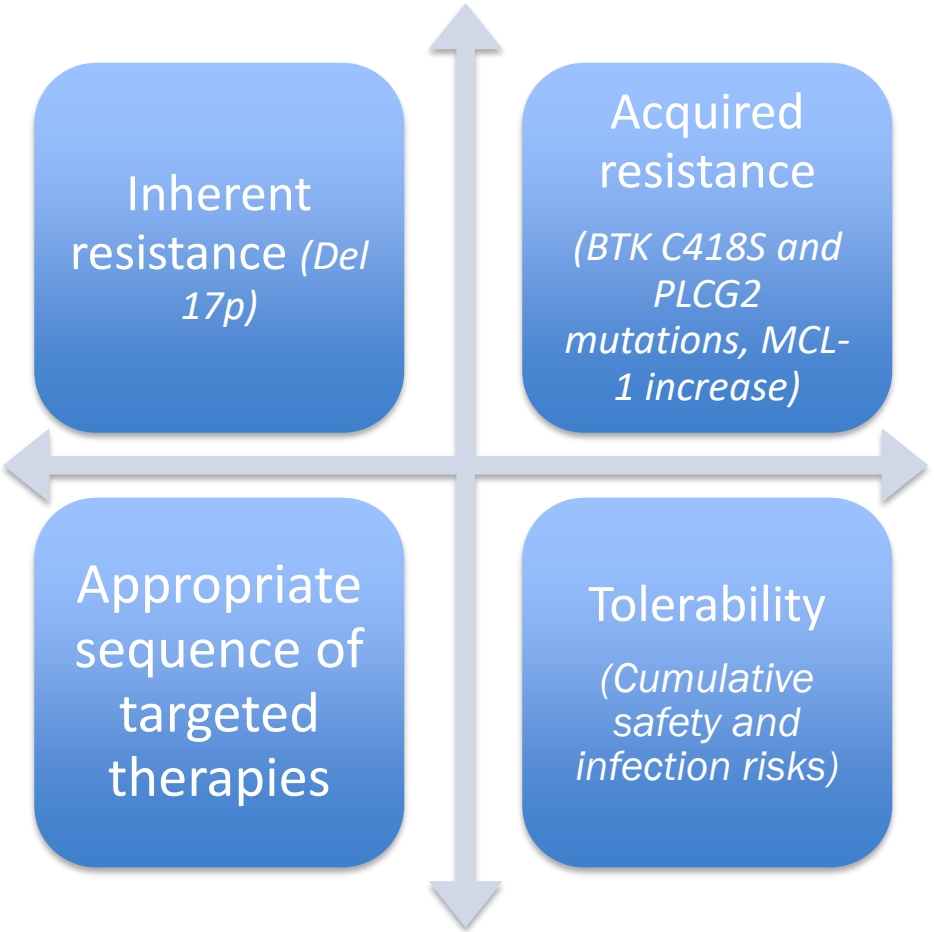
Each agent has “unique” safety issues

Resistance will occur

BTKi:BLEEDING/Afib
BCL-2:TLS
Pi3K:Colitis/Pneumonitis

Alternative pathways
Mutations

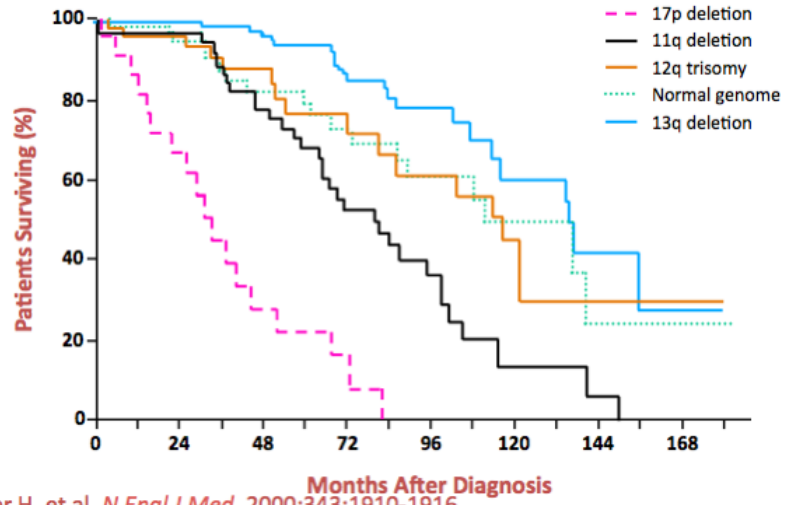
The evolving unmet medical needs in CLL



Inherent resistance Del17p (p53)

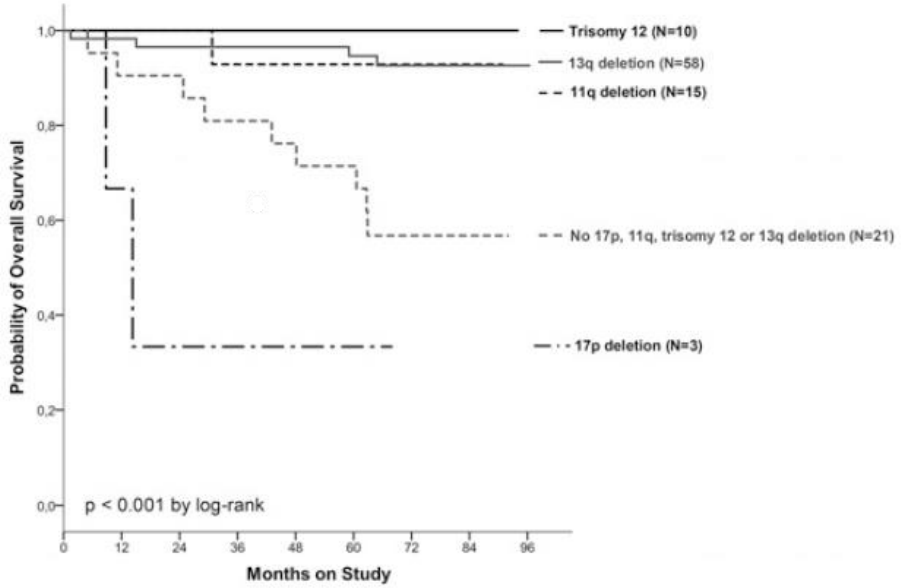
Genetic Abnormalities May Influence Survival in CLL

Effects of genetic abnormalities on survival in patients with CLL (N=325)



Döhner H, et al. *N Engl J Med*. 2000;343:1910-1916.

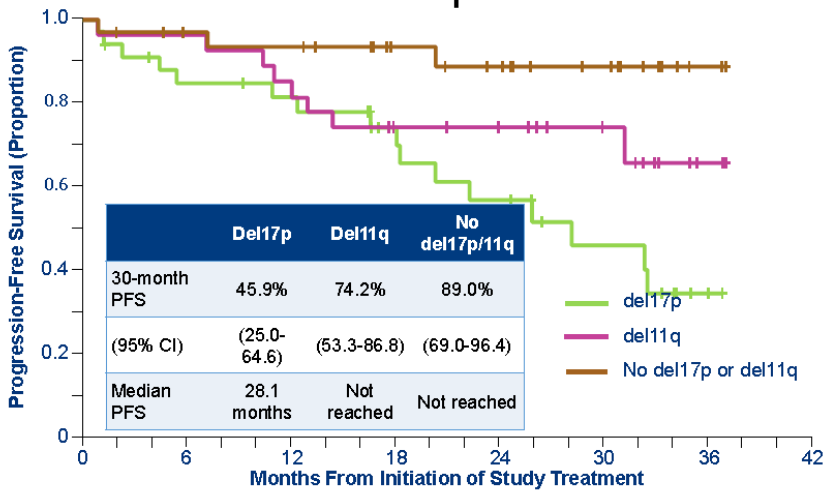
Genetic Abnormalities and inherent chemoresistance to FCR



Fisher Blood 2016

BTKi, BCL2i and PI3Ki overcome inherent resistance → PFS inferior to non-Del17p

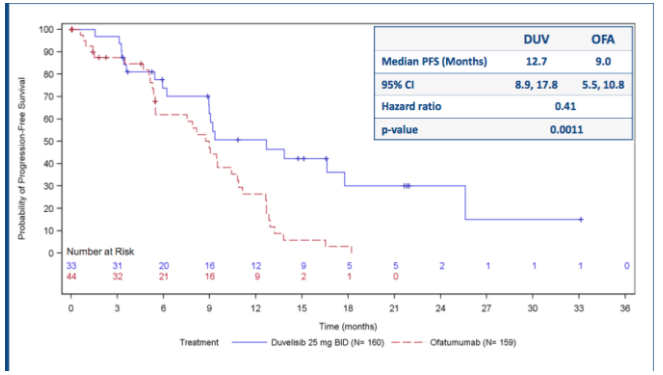
Ibrutinib-del 17p



	Del17p	Del11q	No del17p/11q
30-month PFS	45.9%	74.2%	89.0%
(95% CI)	(25.0-64.6)	(53.3-86.8)	(69.0-96.4)
Median PFS	28.1 months	Not reached	Not reached

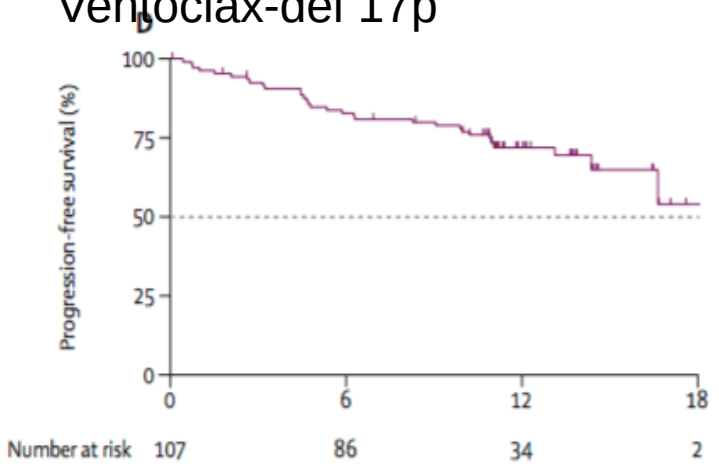
O'brien ASCO 2014

Duvelisib-del 17p



Flinn, ASH 2017

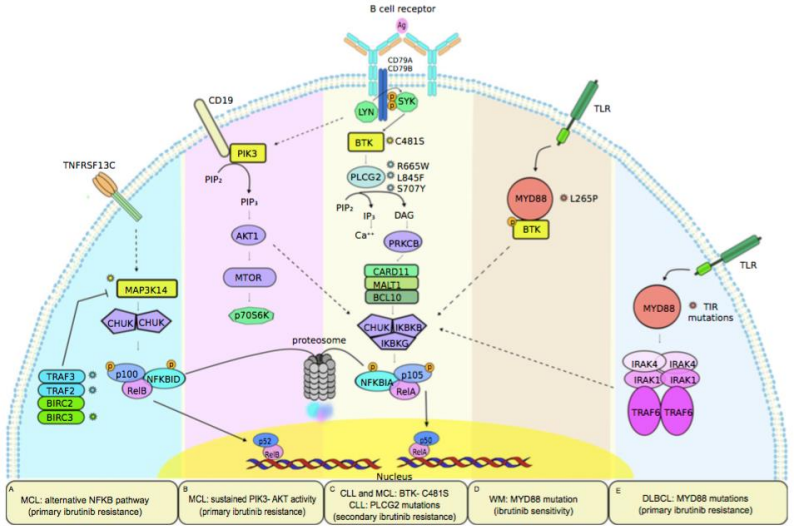
Ventoclax-del 17p



Stilgenbauer, Lancet 2014

Acquired resistance mechanisms

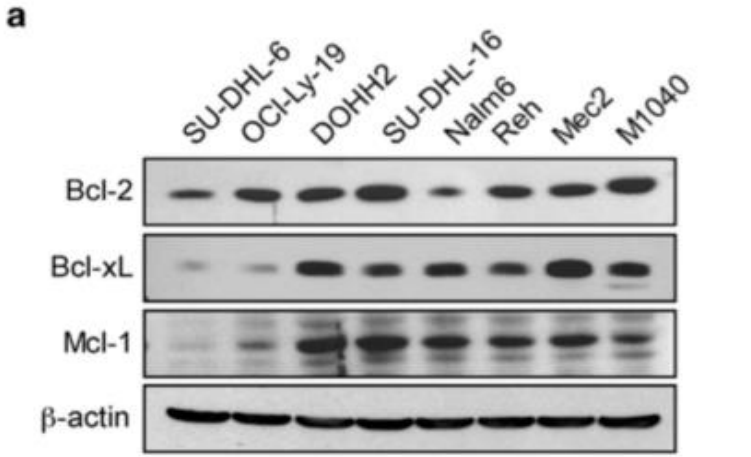
Ibrutinib



Zhang Br J Hem 2017

- Alternative pathways→NFKB, PIK3-ALT
- BTK C418S mutation
- PLCG2 mutations

Venetoclax



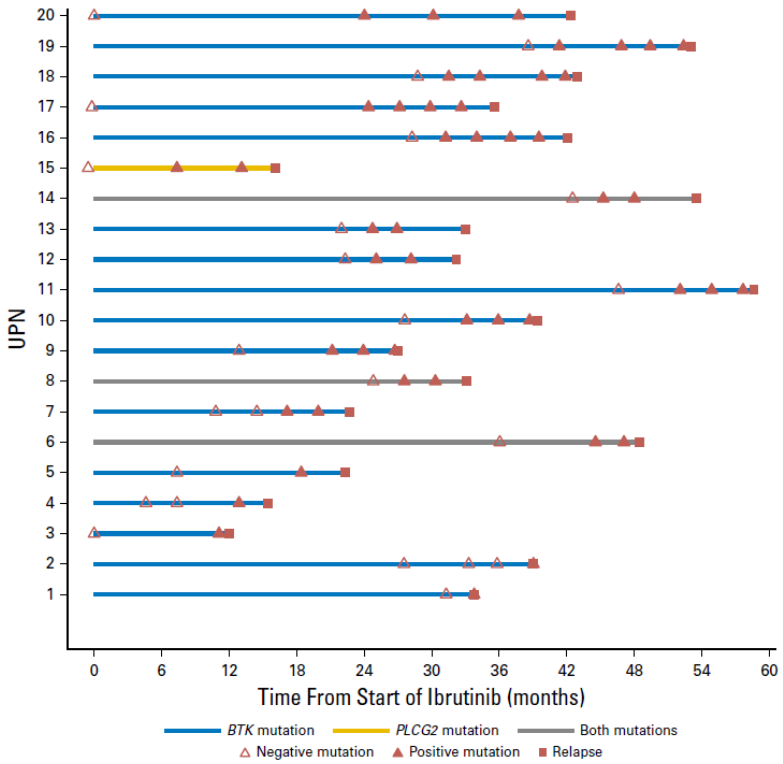
Choudary Cell Death and disease 2015

- ↟ **Mcl-1**
- ↟ **Bcl-xL**

Real world experience:

Ibrutinib resistance stems from resistance mutations, which are detectable before clinical relapse

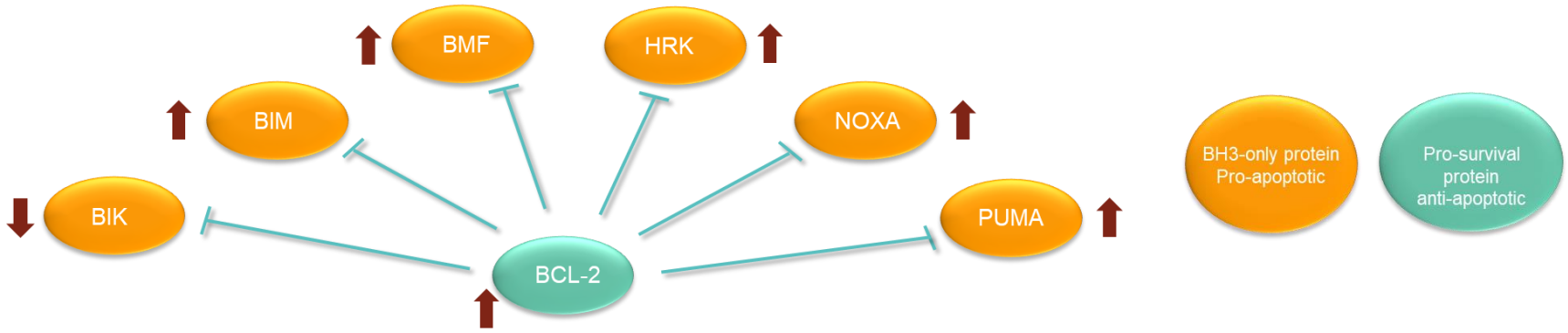
Woyach et al., JCO 2017



- Mutations in BTK or PLCG2 are the predominant mechanism by which CLL becomes resistant to ibrutinib
- Clinical resistance is preceded by a prolonged period of asymptomatic clonal expansion
- Initial clone could be detected at an estimated median of 9.3 months before relapse

Addressing inherent and acquired resistance

- Pre-emptively target with alternative therapies before the patient becomes acutely ill with refractory disease
- Treatment earlier in disease with targeted agents
  - C418S does not appear at same rate in frontline patients
  - Less mutated or natural history of DNA damage
- Combinations of novel:novel agents

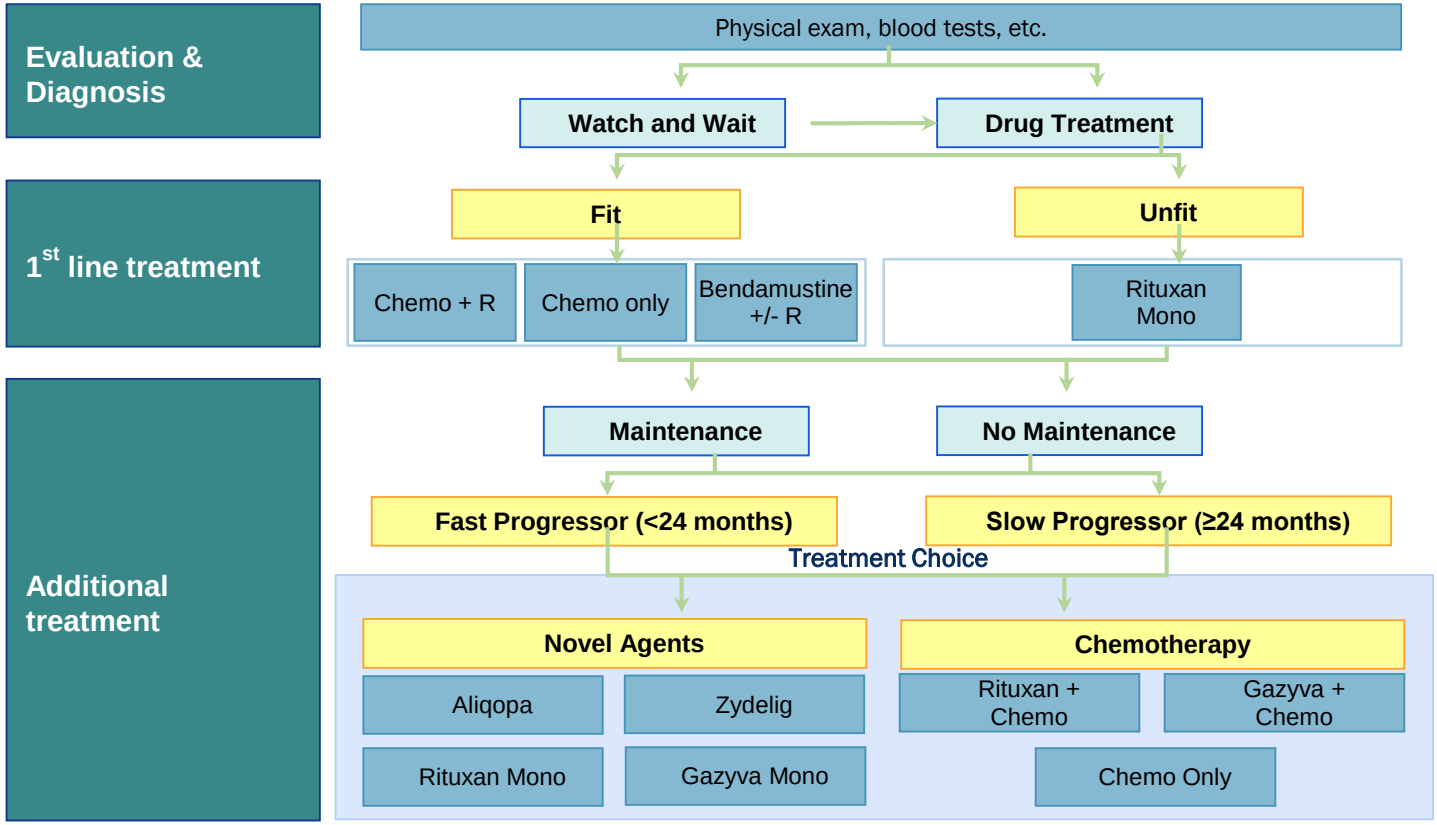


CLL cells from duvelisib-treated patients are primed for apoptosis from sequential BCL-2 inhibition

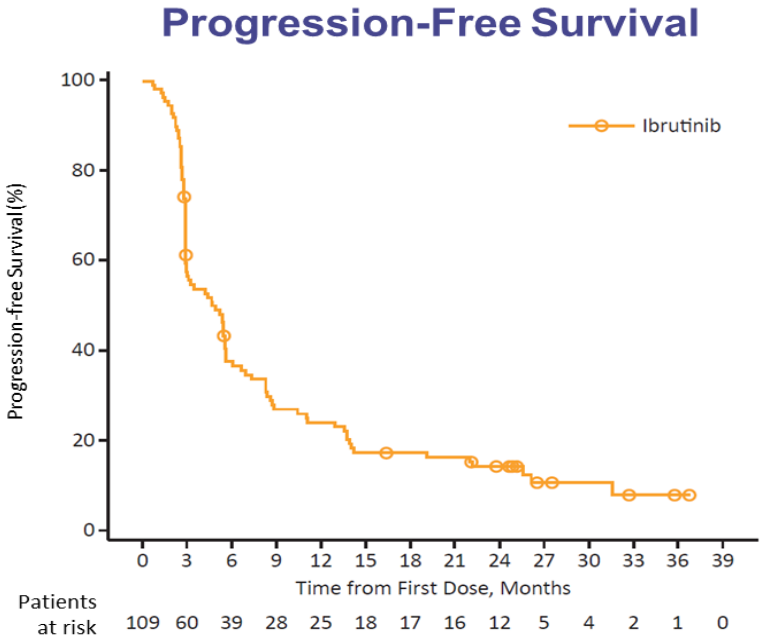
Side effect mitigation and therapy sequencing

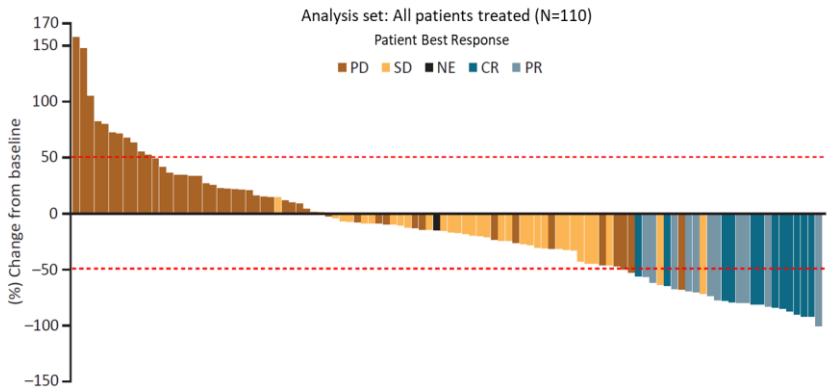
- Pre-existing co-morbidities and emergent side effects are a consideration with all therapies
  - Age of patients necessitates a consideration of co-morbidities
    - atrial fibrillation, bleeding risks, use of anti-clotting factors, renal insufficiency
  - Infections are a risk and prophylaxis can play a major part in reducing the threat
  - Immune-related side effects are becoming better characterized and managed
- Sequence of therapy is an important determinant while data from combination treatments is being gathered
  - Each patient is different
    - Pre-existing conditions or other medical considerations
    - Adherence to therapeutic regimen
    - Convenience of in-patient treatments
  - Recognition of patient goals – disease maintenance or curative intent?

The revolution from R-Chemo to targeted therapies in FL is behind what we've seen in CLL



Ibrutinib has limited effect in CIT-resistant patients with follicular lymphoma (DAWN study)





- Only 20% of patients with chemoimmunotherapy-resistant follicular lymphoma respond to ibrutinib monotherapy
- Median PFS in the ITT of 4.6 months

Advent of targeted agents in the treatment of FL

- The average age of patients in the US is 67 years old
- Primary treatment options still consist of R-based chemotherapy
- BTK and BCL-2 inhibition appears to be inferior to PI3K
- Establishment of treatment modalities for chemo-refractory patients is evolving
- Combination therapies with PI3K may hold particular promise for future treatment

Summary: CLL and follicular NHL chronic disease

- Little evidence that they will be curable
- Infections and cumulative side effects remain an issue
  - Rapid evolution of the field and new management techniques are evolving
- Most patients will not achieve a CR
- Patient goals are paramount
  - Identifying the proper sequence of medications for disease maintenance based on patient-specific characteristics
  - Progression of combination therapies with potential of curative intent
- Goal→ Maintain disease control as we evolve to a safe and tolerable combination regimen earlier in the disease course

Investor conference Galapagos 2014

Verastem Oncology

Unmet Needs and the Role of PI3K Inhibitors

Jennifer Brown, MD, PhD

DANA-FARBER CANCER INSTITUTE

BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

Where Does PI3K Inhibition Fit?

Jennifer R Brown, MD PhD
Director, CLL Center
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
May 2, 2018

Moving Toward a Chemo-Free Future in CLL

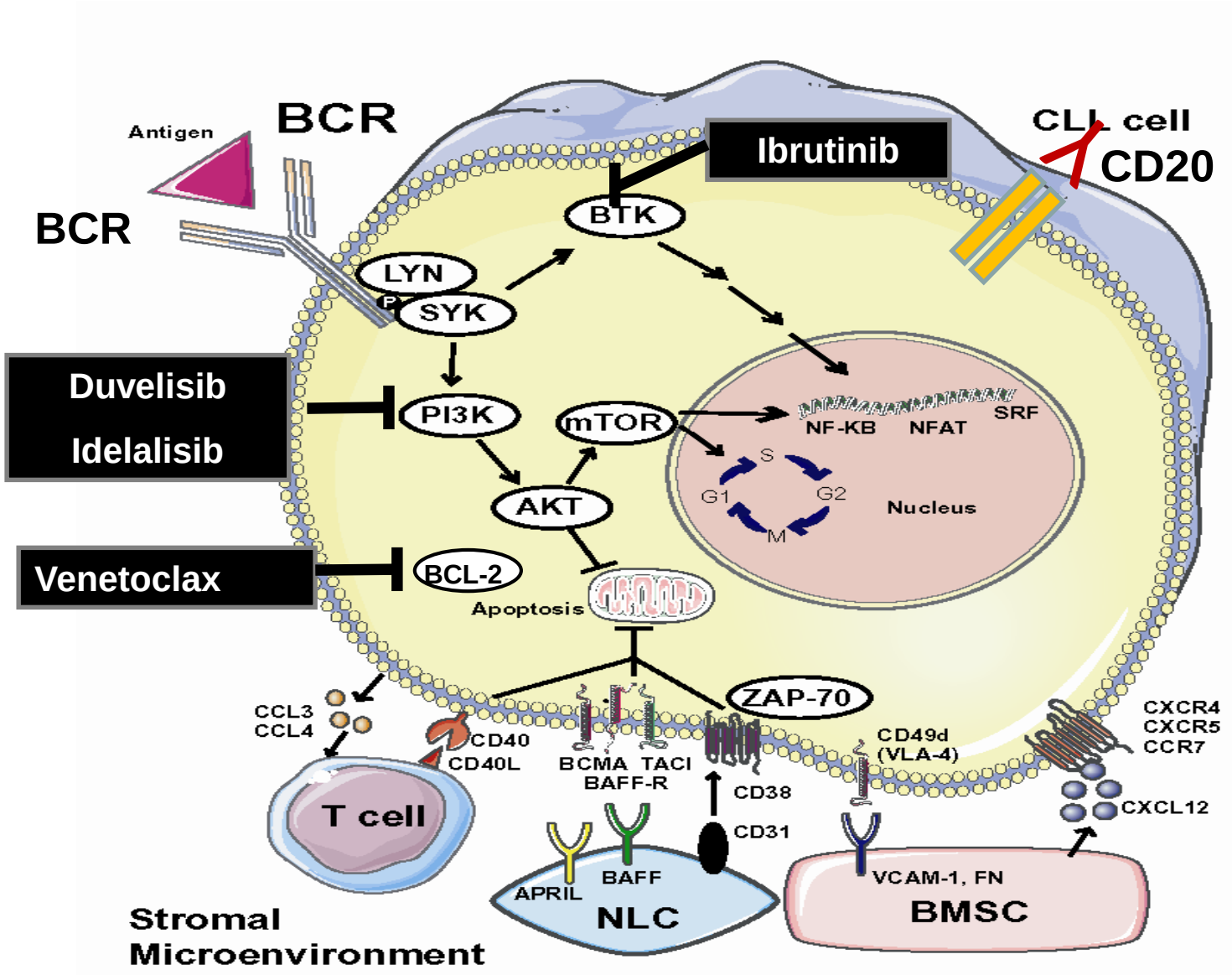
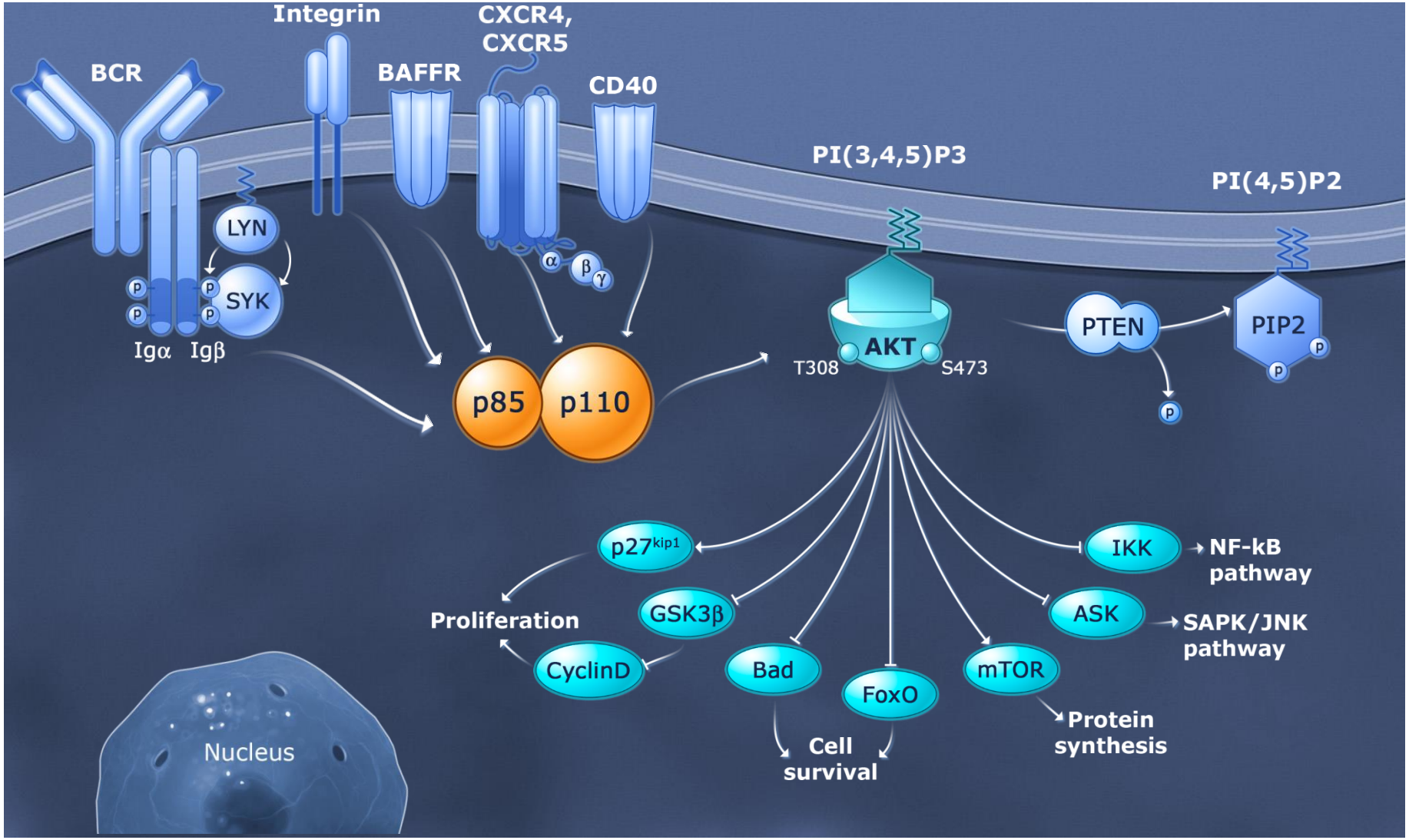
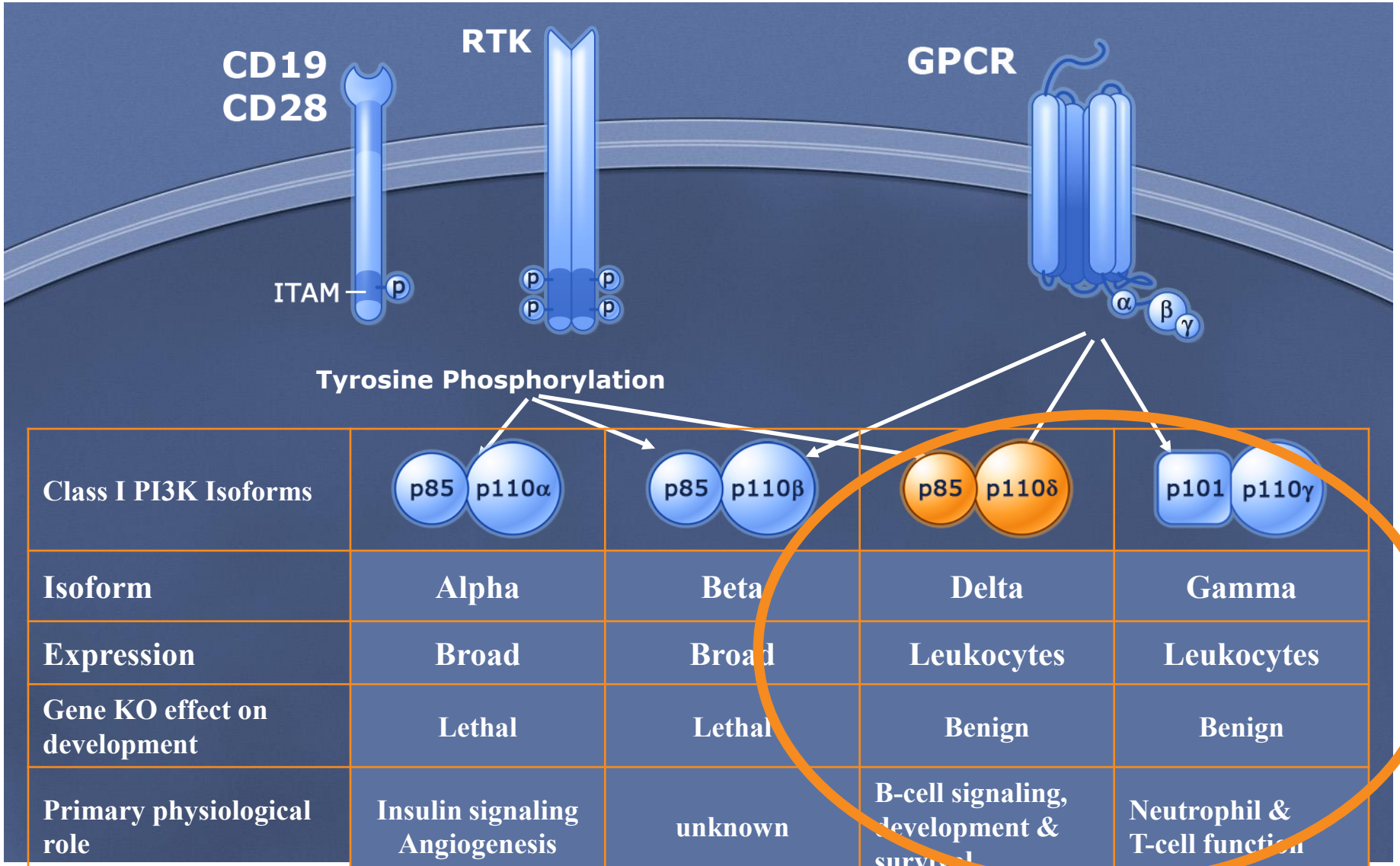


Figure was produced using Servier Medical Art, http://www.servier.com/Smart/ImageBank.aspx?id=729

PI3K Signaling Pathway as a Target in B Cells



PI3K Delta: Target for B Cell Diseases

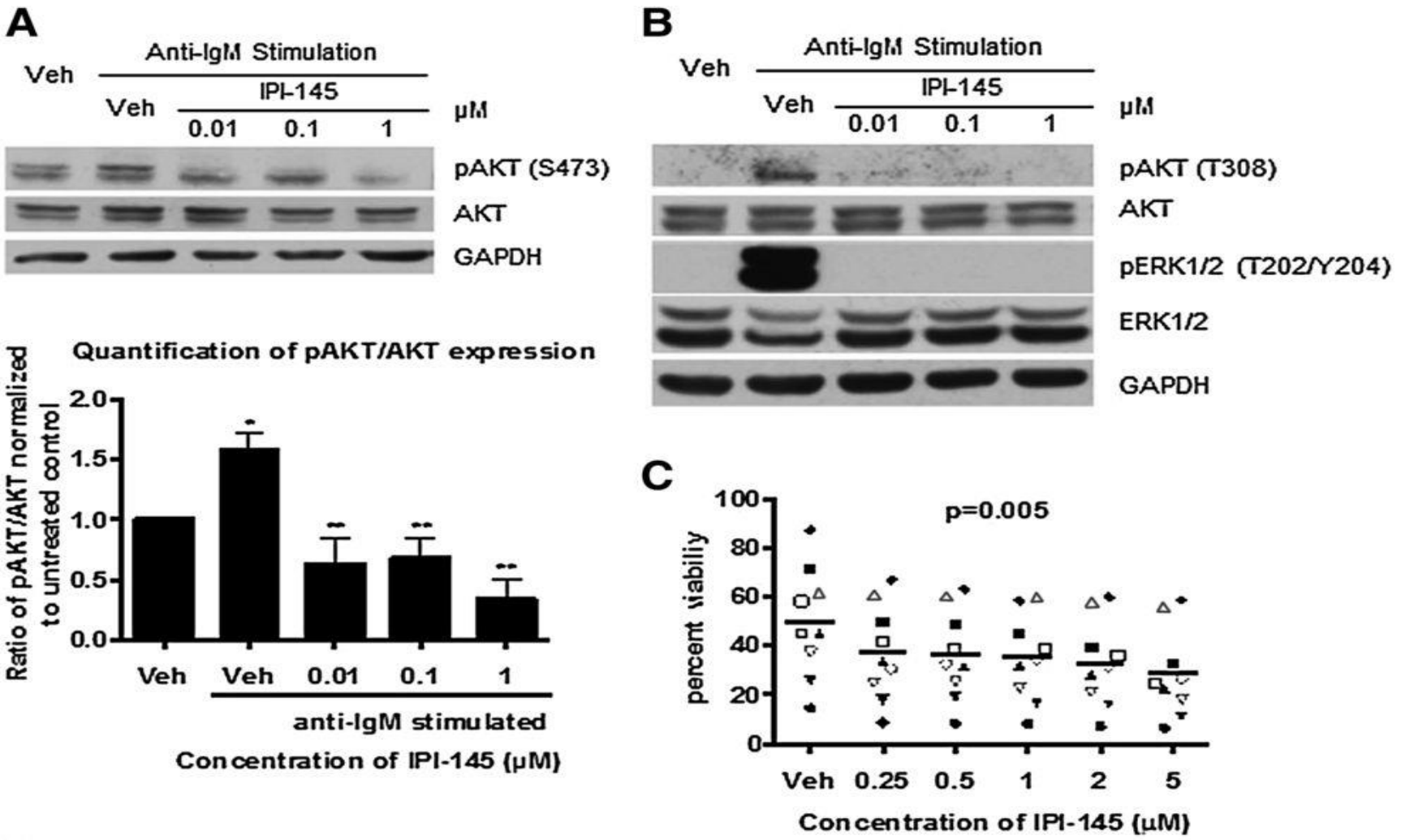


Class I PI3K Isoforms	p85 p110α	p85 p110β	p85 p110δ	p101 p110γ
Isoform	Alpha	Beta	Delta	Gamma
Expression	Broad	Broad	Leukocytes	Leukocytes
Gene KO effect on development	Lethal	Lethal	Benign	Benign
Primary physiological role	Insulin signaling Angiogenesis	unknown	B-cell signaling, development & survival	Neutrophil & T-cell function

Role of PI3Kδ in B Lymphocytes from Knockout or Kinase Dead Mice

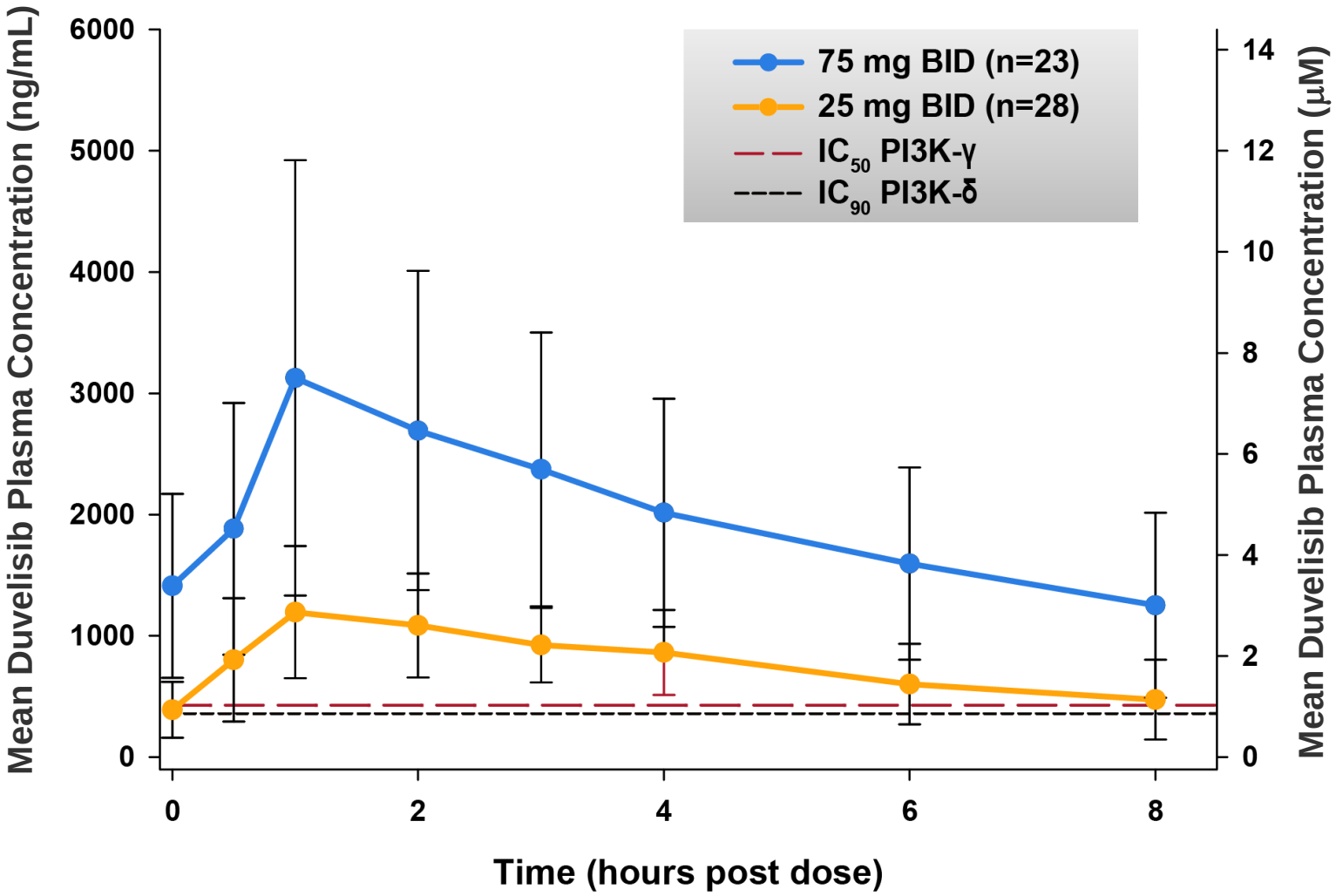
- Signaling downstream of BCR, cytokine/chemokine receptors and RTKs in B cells is deficient
- Reduced mature B cells: follicular (B2), marginal zone, peritoneal (B1)
  - Lack of germinal centers in spleen, lymph nodes or Peyer's patches
  - Reduced immunoglobulins and humoral response to antigen
- Deletion of p110α, β, and γ has no overt effect on B cell number or function

Duvelisib Inhibits PI3K Signaling and Induces Selective Killing of CLL Cells



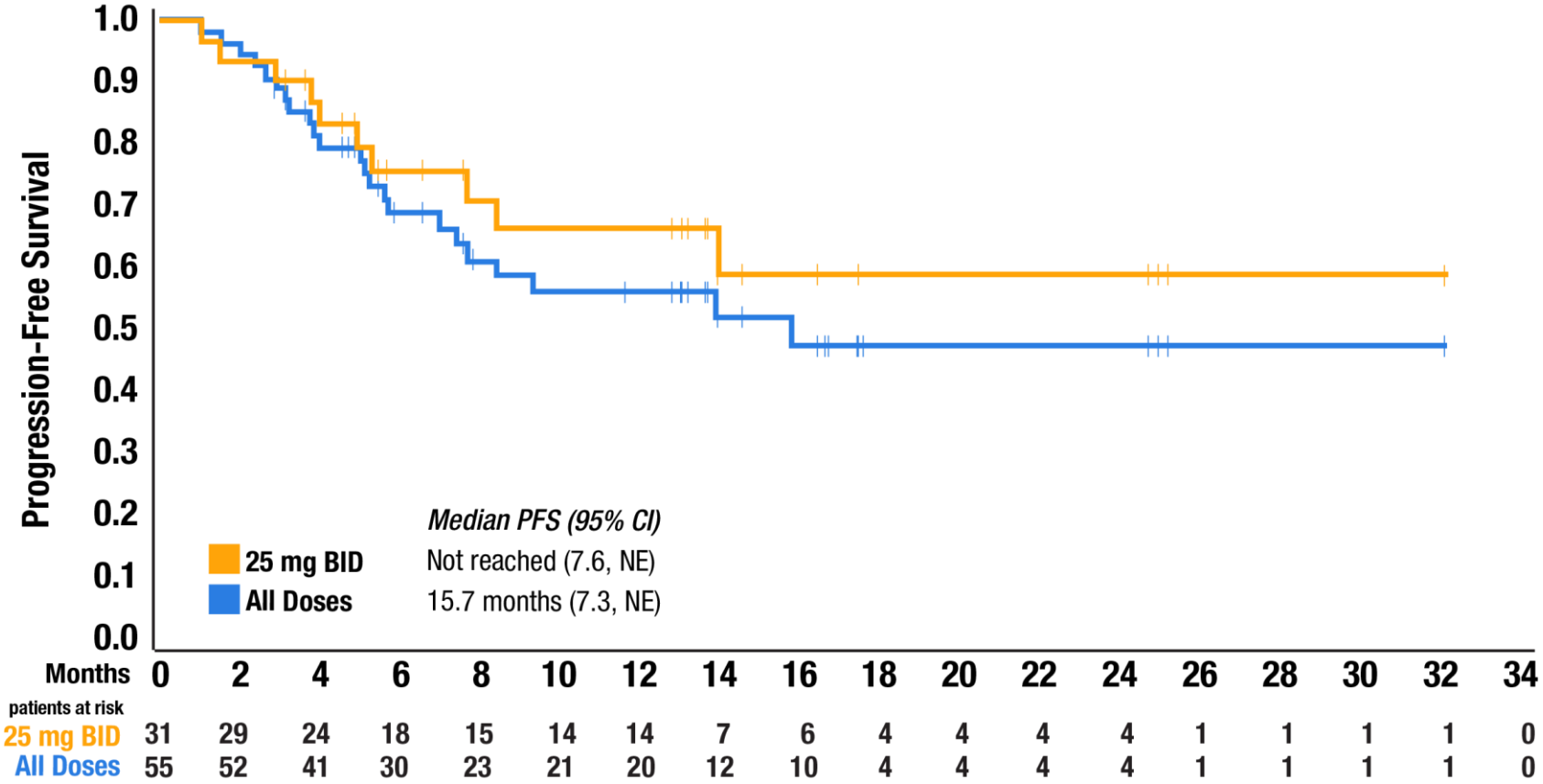
Shuai Dong et al. Blood 2014;124:3583-3586

Study IPI-145-02 (Phase I): Duvelisib PK



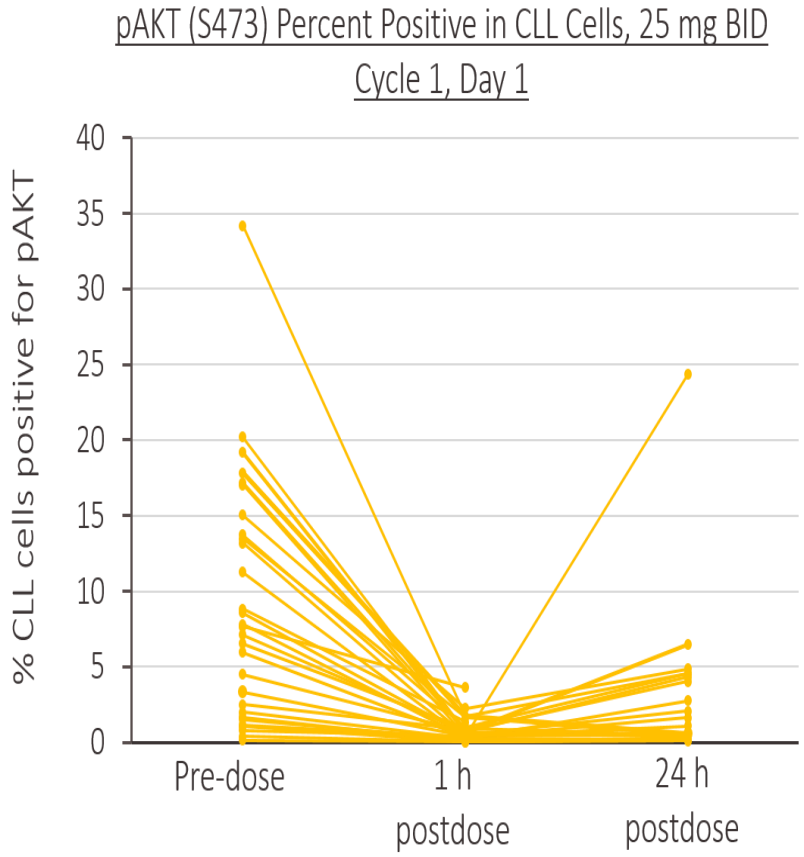
Patel et al. ASCO 2013

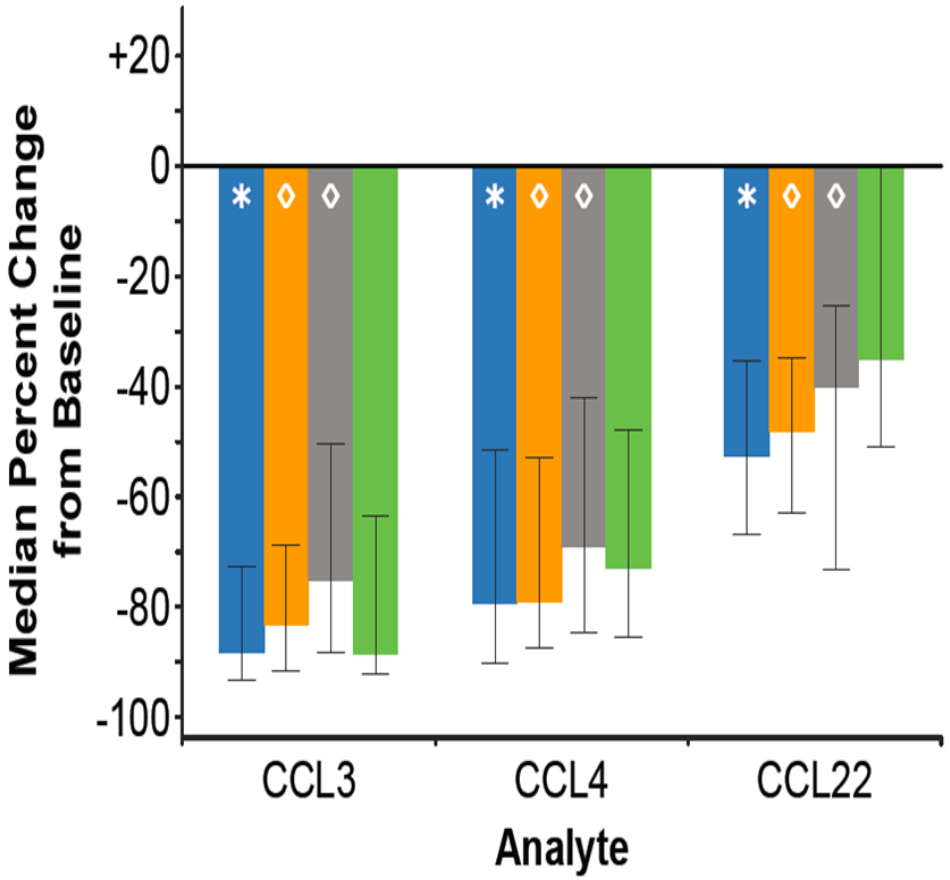
Study 145-02 R/R CLL
PFS, All Doses and 25 mg BID



- Median PFS at 25 mg BID not reached
  - 66% progression-free at 12 months
  - 59% progression-free at 24 months

Duvelisib Inhibits PI3K Signaling and Reduces Serum Factors Made By CLL Cells in Patients





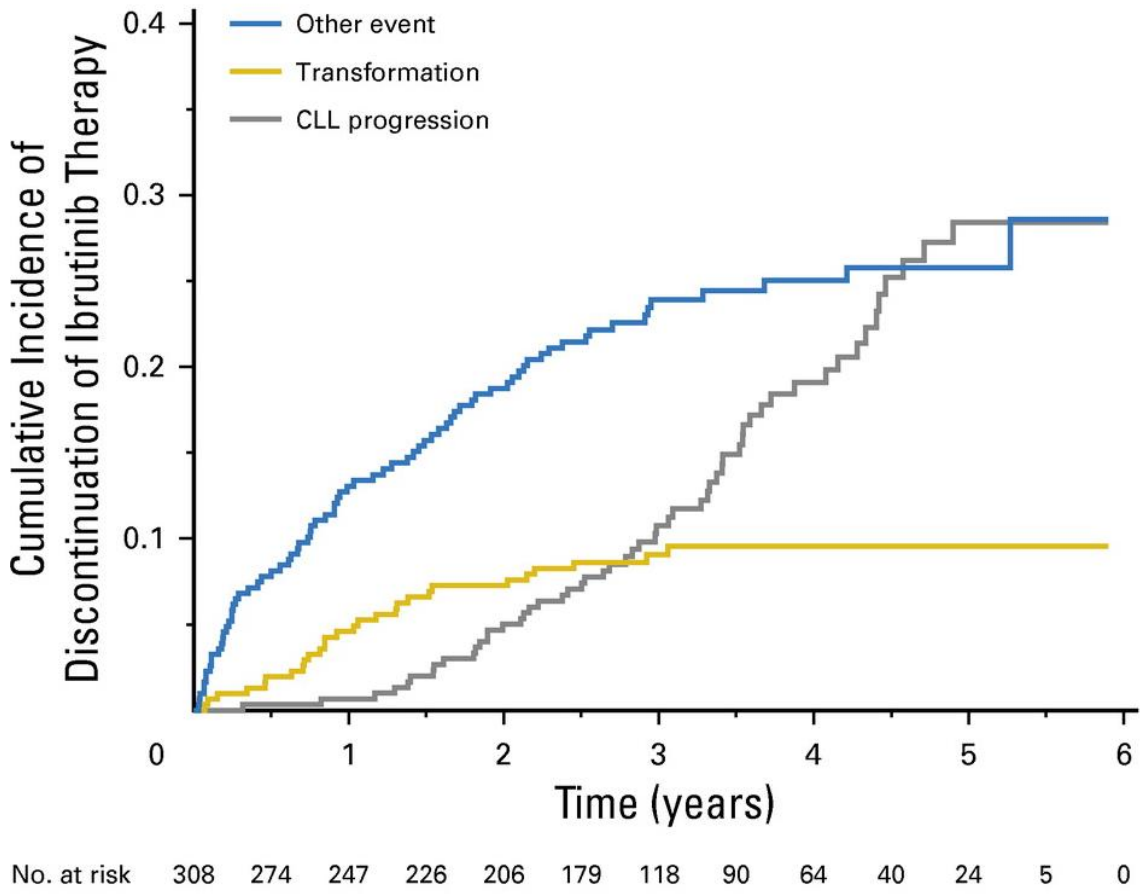
N = 29 patients with at least pre-dose and 1h postdose evaluable samples, 25 mg BID dose level
Source: IPI-145-02 CSR

Different Patient Populations for Different Inhibitors?

- **Problems for BTK inhibitors:**
  - **Cardiac comorbidity, older age**
  - **Bleeding risk / anticoagulation**

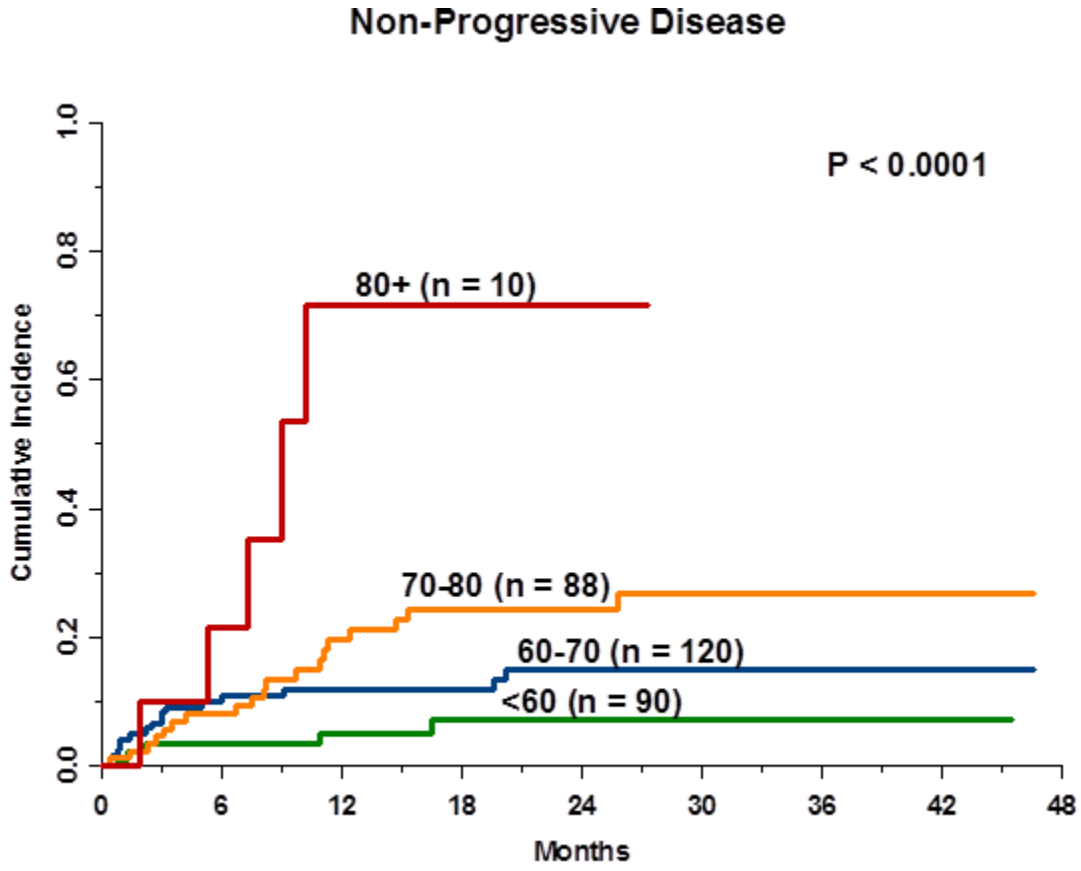
- **Problems for BCL-2 Inhibitors:**
  - **Renal failure a contra-indication**
  - **Frequent clinic or even hospital monitoring for more than a month**

OSU Experience: Long-Term Ibrutinib



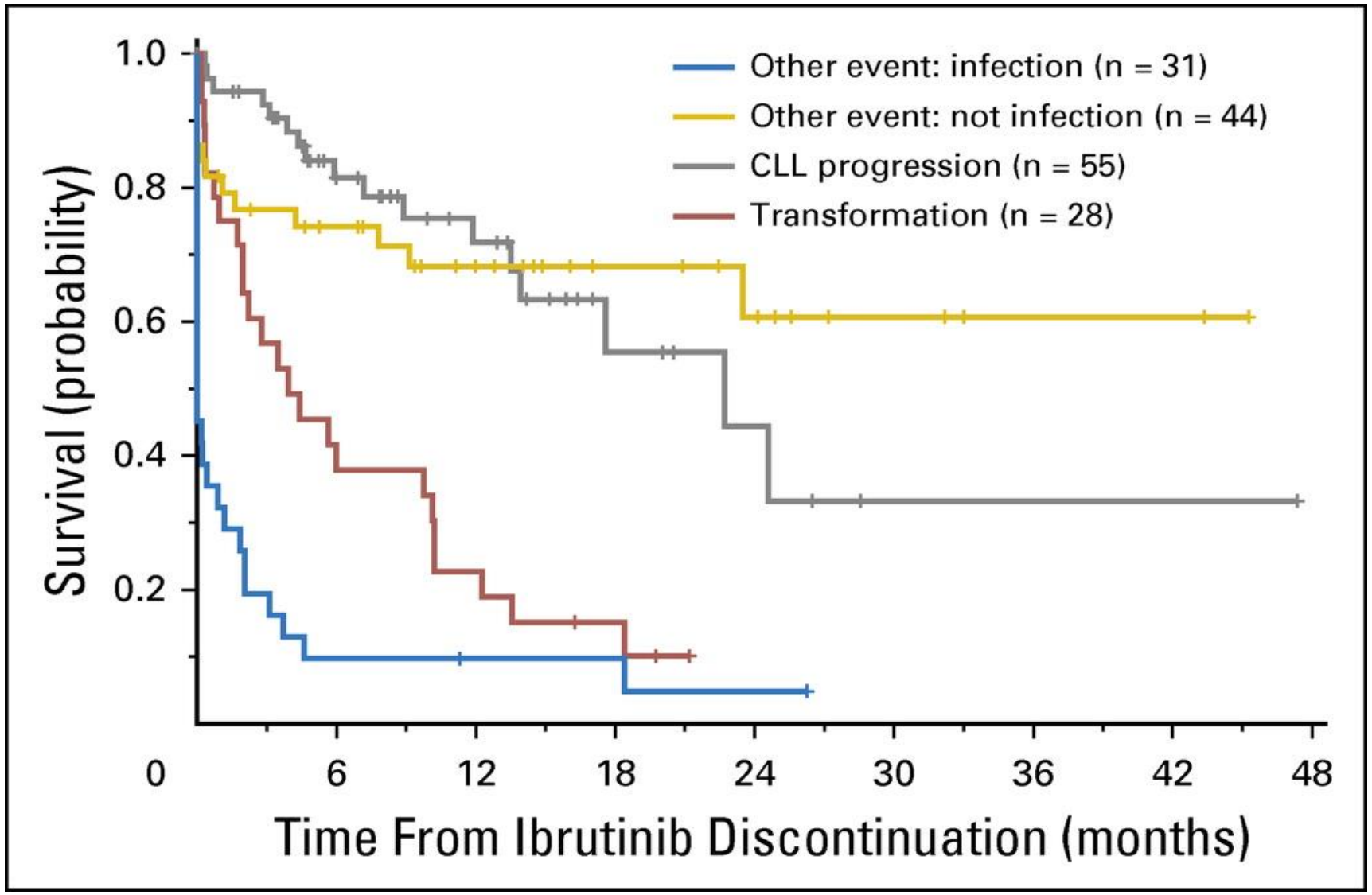
Cumulative Incidence Estimates	At 2 Years	At 3 Years	At 4 Years
CLL progression	5.0%	10.8%	19.1%
Transformation	7.3%	9.1%	9.6%
Other event	18.7%	23.9%	25.0%

OSU: Ibrutinib Discontinuation for Non-PD by Age



Maddocks *et al. JAMA Oncology* (2015)

OSU Experience: Survival After Ibrutinib Discontinuation



Retrospective Analysis of Toxicities and Outcomes for Ibrutinib-Treated Patients: Discontinuations

- **With a median follow-up of 17 months, estimated discontinuation rate was 42%**
  - **Median time to discontinuation of 6 months**

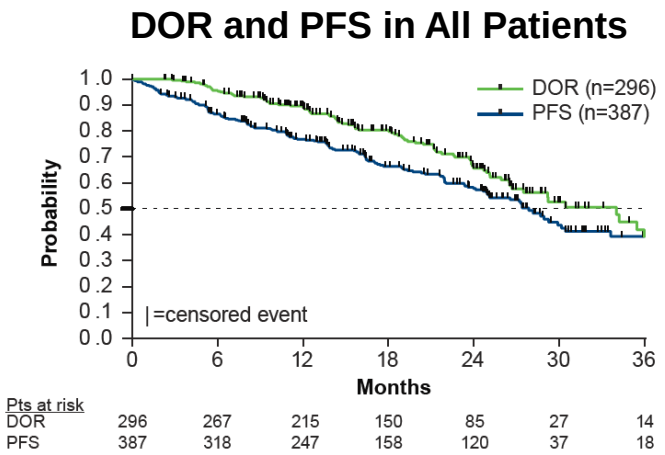
Reasons for Discontinuation, %	Ibrutinib in Front Line		Ibrutinib in Relapse	
	Commercial use (n=10)	Clinical Trial (n=9)	Commercial Use (n=200)	Clinical Trial (n=31)
Toxicity	50	78	53	39
CLL progression	10	22	19	36
Other/unrelated death	10	0	12	13
Physician or patient preference	20	0	6	10
RT DLBCL	0	0	5	0
SCT/CAR-T cells	0	0	4	3
Financial concerns	0	0	1	0
Secondary malignancy	10	0	1	0
RT Hodgkin lymphoma	0	0	1	0

Mato et al, Blood 2016.

Pooled Multi-Trial Analysis of Venetoclax Efficacy in R/R CLL

Patient Disposition	N=387
Venetoclax 400 mg/day*, n	305
Median duration of venetoclax, months (range)	16.3 (0.03-54)
Discontinuation, % Due to PD Due to AEs Due to stem cell transplant Withdrew consent	 50 34 10 3 3

- **ORR 76%** for all patients and in patients receiving the 400 mg RP2D of venetoclax
- Estimated PFS in all 387 patients was **76.8% at 12 mos** (95% CI 72.1-80.8) and **57.8 at 24 mos** (95% CI 51.8-63.4)



Role for Duvelisib in CLL

- **Unmet need patient populations:**
  - **(Large and growing) population intolerant of BTK inhibitors, particularly older patients**
    - **PI3K immune related toxicity is significantly more common in younger patients**
  - **Steadily increasing population progressing on BTK inhibitors**
  - **Venetoclax very challenging to give in a community setting and not widely adopted**
  - **Duvelisib: effective, novel mechanism, easily given, no infusions required**

Verastem Oncology

Duvelisib for the Treatment of CLL/SLL and FL

Ian Flinn, MD, PhD

SARAH CANNON
Research Institute

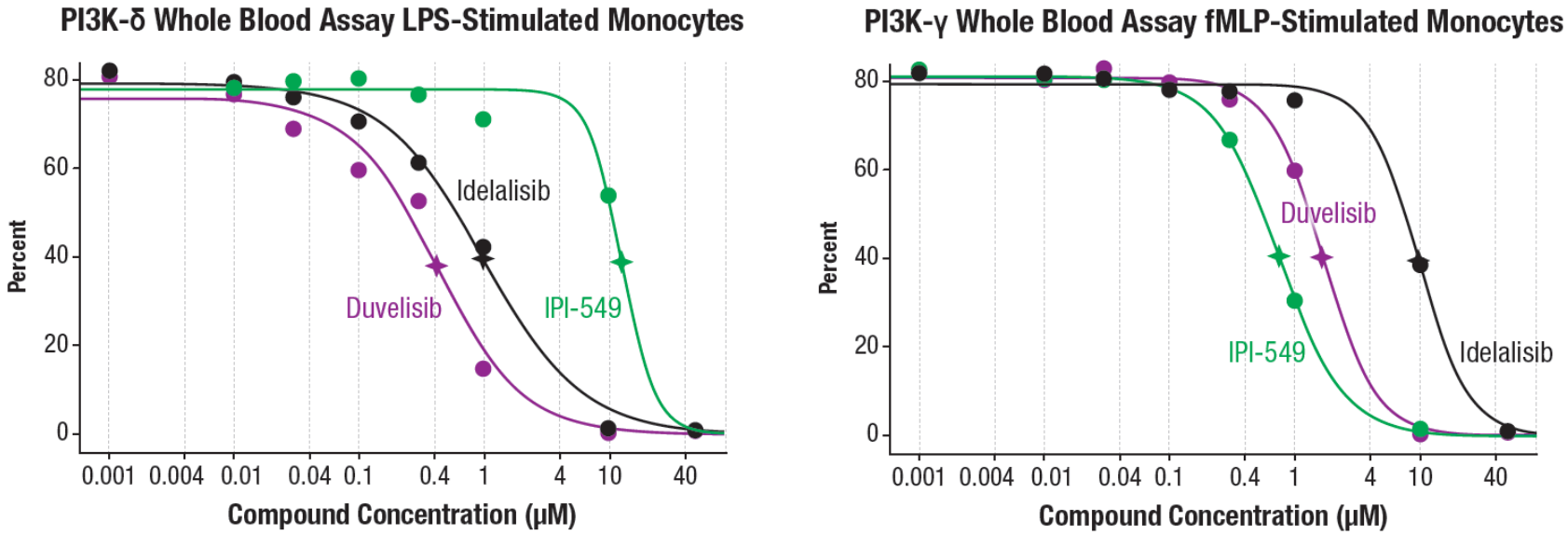
DUVELISIB REGISTRATION STUDIES

Ian Flinn, MD, PhD

Director, Blood Cancer Research Program at Sarah Cannon Research Institute

May 2, 2018

Duvelisib is a dual inhibitor of PI3K-δ & PI3K-γ at clinical exposures

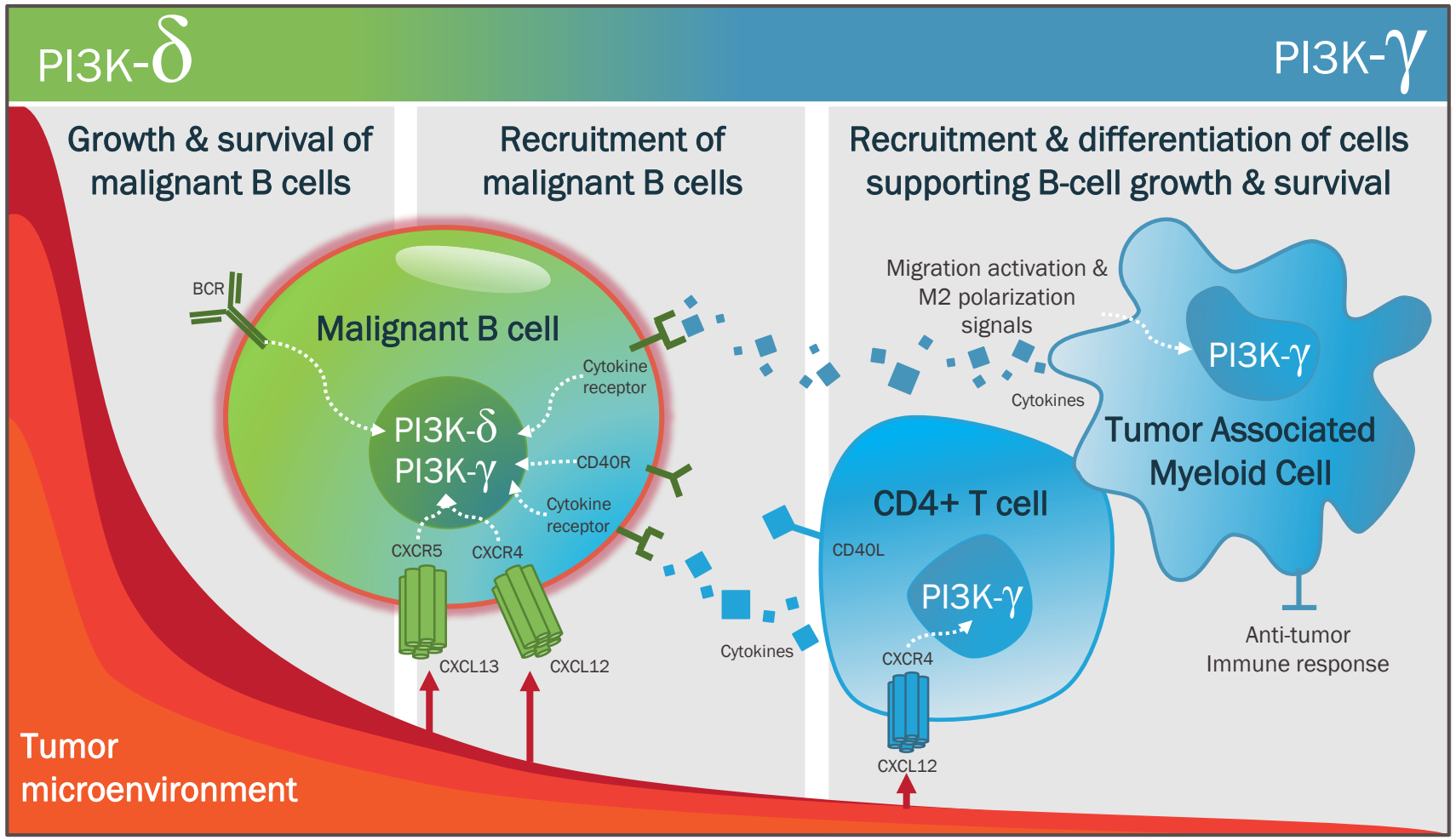


Drug	Mechanism of Action	PI3K-δ IC_{50} (μM)	PI3K-γ IC_{50} (μM)	C_{max} (ss) (μM)
Duvelisib	Dual PI3K-δ/PI3K-γ Inhibitor	0.4 ± 0.1	1.6 ± 0.2	2.5
Idelalisib	PI3K-δ Inhibitor	1.0 ± 0.2	9.4 ± 2.3	4.8
IPI-549	PI3K-γ Inhibitor	12 ± 0.5	0.5 ± 0.2	9.1

Inhibition of LPS-stimulated monocytes and fMLP-stimulated monocytes were used to measure whole blood potencies of PI3K inhibitors against PI3K-δ & PI3K-γ, respectively. The graphs show dose responses with monocytes from human donors. Whole blood assay IC_{50} values, which encompass enzyme inhibition, cell penetration and protein binding of inhibitors, are related to reported clinical plasma exposures of each agent at RP2D.

- Duvelisib human PK. C_{max} @ 25 mg BID (RP2D) = 1062 ng/ml; MW = 417 g/mol
- Idelalisib human PK from Webb, ASH 2010. C_{max} @ 150 mg BID (RP2D) = 2000 ng/ml; MW = 415 g/mol
- IPI-549 human PK from Hong, SITC 2017. $C_{max\text{-}ss}$ @ 60 mg QD (RP2D) = 4800 ng/ml, MW = 529 g/mol

Duvelisib's dual PI3K inhibition targets both malignant B cells (-δ) and the supportive tumor microenvironment (-γ)



Source: Lannutti BJ, et al. *Blood.* 2011;117(2):591-594.; Hoellenriegel J, et al. *Blood.* 2011;118(13):3603-3612.; Balakrishnan, et al. *ASH 2013* (Infinity).; Chen, et al. *ASH 2015* (Infinity).; Okkenhaug and Burger. *Curr Top Microbiol Immunol.* 2016; 393:123-142.; Kaneda, et al. *Nature.* 2016; 539:437–442.; Davis, et al. *Cancer Res.* March 31 2017.; De Henau, et al. *Nature*. 2016; 539:443–447.

DYNAMO:
A PHASE 2 STUDY DEMONSTRATING THE CLINICAL ACTIVITY OF DUVELISIB IN PATIENTS WITH DOUBLE-REFRACTORY INDOLENT NON-HODGKIN LYMPHOMA

Presented at 14-ICML, 14 June 2017, Lugano Switzerland by Pier Luigi Zinzani, MD, PhD. University of Bologna, IT

DYNAMO™ STUDY OVERVIEW

Single arm
n=129

Duvelisib 25 mg BID
Continuously

Treatment until progression or unacceptable toxicity

- **Accrual complete**
- **Final Analysis: April 2016**
- **Mature Follow-up: March 2017**

Response Assessments
• Baseline, Cycles 3, 5, 7, 10, every 4 cycles thereafter • Cycle = 28 days
Criteria
IWG (Cheson 2007), as assessed by independent review committee (IRC)

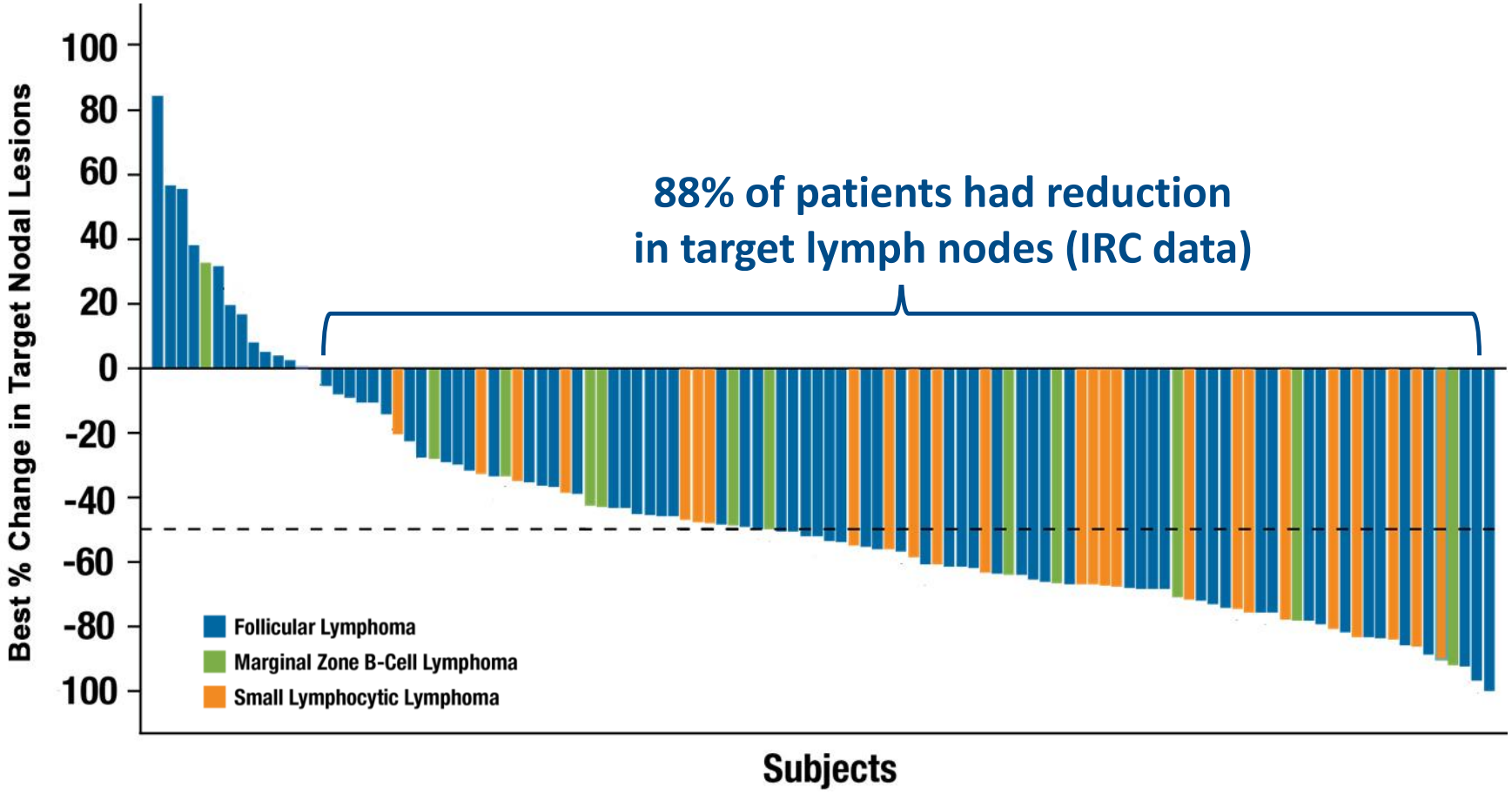
Primary Endpoint
ORR = best response of CR or PR per IRC
Key Secondary Endpoints
• Duration of response (DOR) • Progression-free survival (PFS) • Overall survival (OS) • Safety

OVERALL RESPONSE RATE

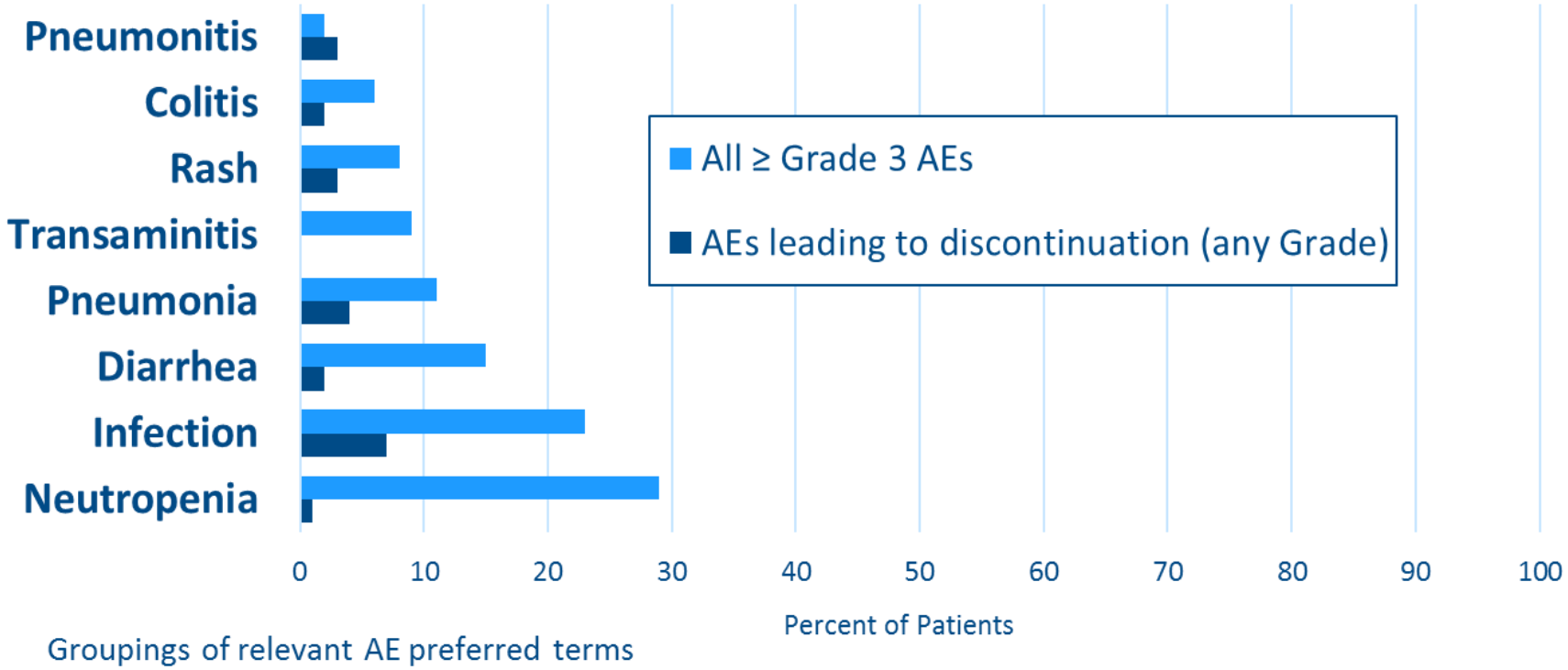
	OVERALL N = 129	FL N = 83	SLL N = 28	MZL N = 18
ORR per IRC	**47%**	**43%**	**68%**	**33%**
P-value	*p = 0.0001*	--	--	--
95% CI	*(38-56)*	--	--	--
Complete Response	*1%*	*1%*	*0*	*0*
Partial Response	*47%*	*42%*	*68%*	*33%*
ORR per Investigator	**60%**	**53%**	**86%**	**50%**
Complete Response	*3%*	*2%*	*4%*	*6%*
Partial Response	*57%*	*51%*	*82%*	*44%*

- **Rapid time to response: median 2 months (range: 1.4 – 12)**
- **Primary endpoint met at final analysis**
- **Median time on duvelisib: 7 months (range: 0.4-35)**

PERCENT CHANGE IN NODAL TARGET LESIONS



ADVERSE EVENTS OF INTEREST



- **Few discontinuations due to severe AEs of interest**
- **Serious opportunistic infections < 4%**: PCP *(unconfirmed)* (n=1); CMV (n=2); fungal pneumonia (n=2)
- **Deaths attributed to treatment (n=6)***

*colitis (n=1); toxic epidermal necrolysis/sepsis syndrome (n=1); drug reaction/eosinophilia/systemic symptoms (n=1); pneumonitis/pneumonia (n=1); viral infection (n=1); septic shock (n=1)

DYNAMO STUDY CONCLUSIONS

- Duvelisib monotherapy is clinically active in double-refractory iNHL
  - ORR of 47% per IRC; ORR of 60% per Investigator
  - 88% of patients had tumor reduction
  - Responses were durable (median 10 months)
- Duvelisib has a manageable safety profile
- In long-term follow-up (median 18 months), duvelisib remains well tolerated
- Duvelisib showed favorable risk-benefit in double-refractory iNHL, and may represent an important treatment option for these patients

There is a significant unmet need in the treatment of Follicular Lymphoma (FL)

- The initial treatment of FL is primarily anti-CD20 based chemotherapy regimens (CIT)
  - R-CHOP / BR / R-CVP
- Following failure to CIT, there are limited treatment options. CIT re-challenge (or switch), anti-CD20 monotherapy and PI3Ki-based treatments
- BTK and BCL-2 inhibitors have demonstrated only limited efficacy for the treatment of R/R FL to date
- Additional agents and clinical studies are necessary to improve the available treatment options
- The transition to oral, targeted therapies, as seen in CLL has been slower in FL due to a lack of efficacious agents

Results from the Phase 3 DUO™ Study of Duvelisib vs Ofatumumab in Relapsed/Refractory CLL/SLL

Ian Flinn[1], Peter Hillmen[2], Marco Montillo[3], Zsolt Nagy[4], Árpád Illés[5], Gabriel Etienne[6], Julio Delgado[7],Bryone Jean Kuss[8], Constantine Tam[9], Zoltán Gasztonyi[10], Fritz Offner[11], Scott Lunin[12], Francesco Bosch[13],Matthew Davids[14], Nicole Lamanna[15], Ulrich Jaeger[16], Paolo Ghia[17], Florence Cymbalista[18], Craig Portell[19], Alan Skarbnik[20], Amanda Cashen[21], Virginia Kelly[22], Barry Turnbull[22], Stephan Stilgenbauer[23]

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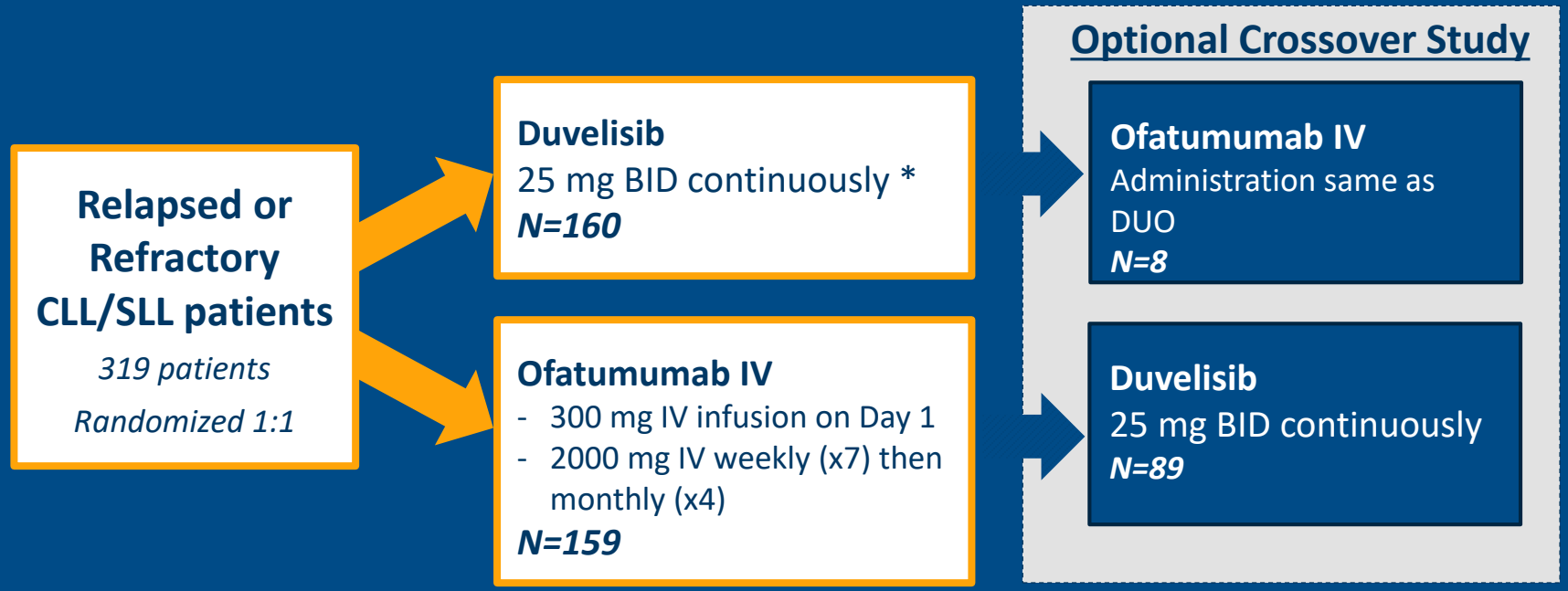
DUO: A Phase 3 Randomized Study in Relapsed/Refractory CLL/SLL



Response per modified iwCLL/IWG Criteria **

- Assessed by independent review committee (IRC)
- Cycle 3 (C3), C5, C7, C11, C15, C19, every 6 months thereafter
- CT scan, CBC , disease related symptoms, BM biopsy ***
- Survival assessment every 6 months

Endpoints

- PFS (primary)
- ORR, DOR, OS (secondary)
- Safety (AEs and lab abnormalities)

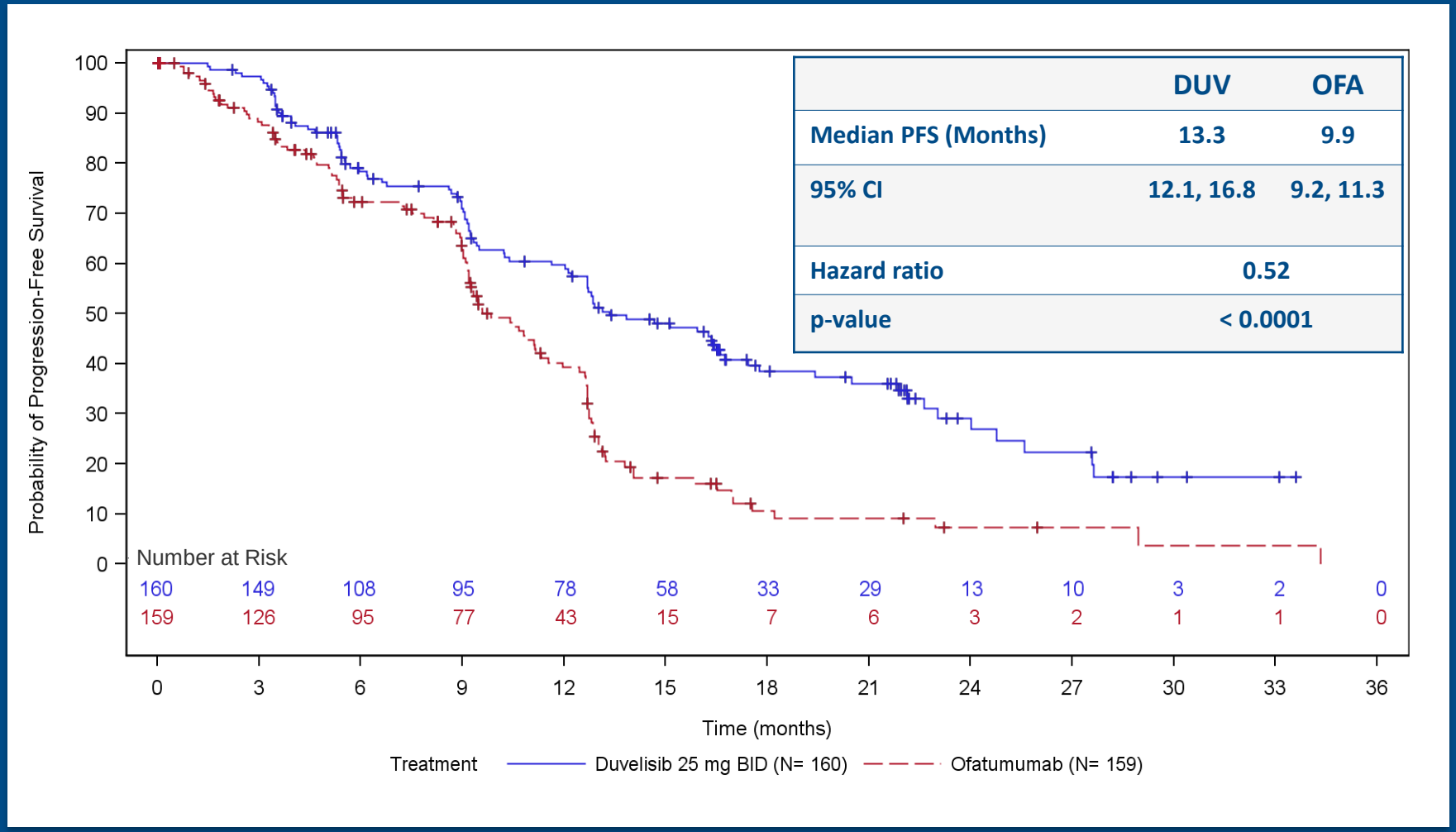
* Patients may have stopped treatment at C18 for CR/PR >3 months at discretion of Investigator

** Lymphocytosis not considered disease progression; PR = 2 Group A and 1 Group B Criteria

*** Required for confirmation of CR/CRi

Source: Flinn et al., ASH 2017

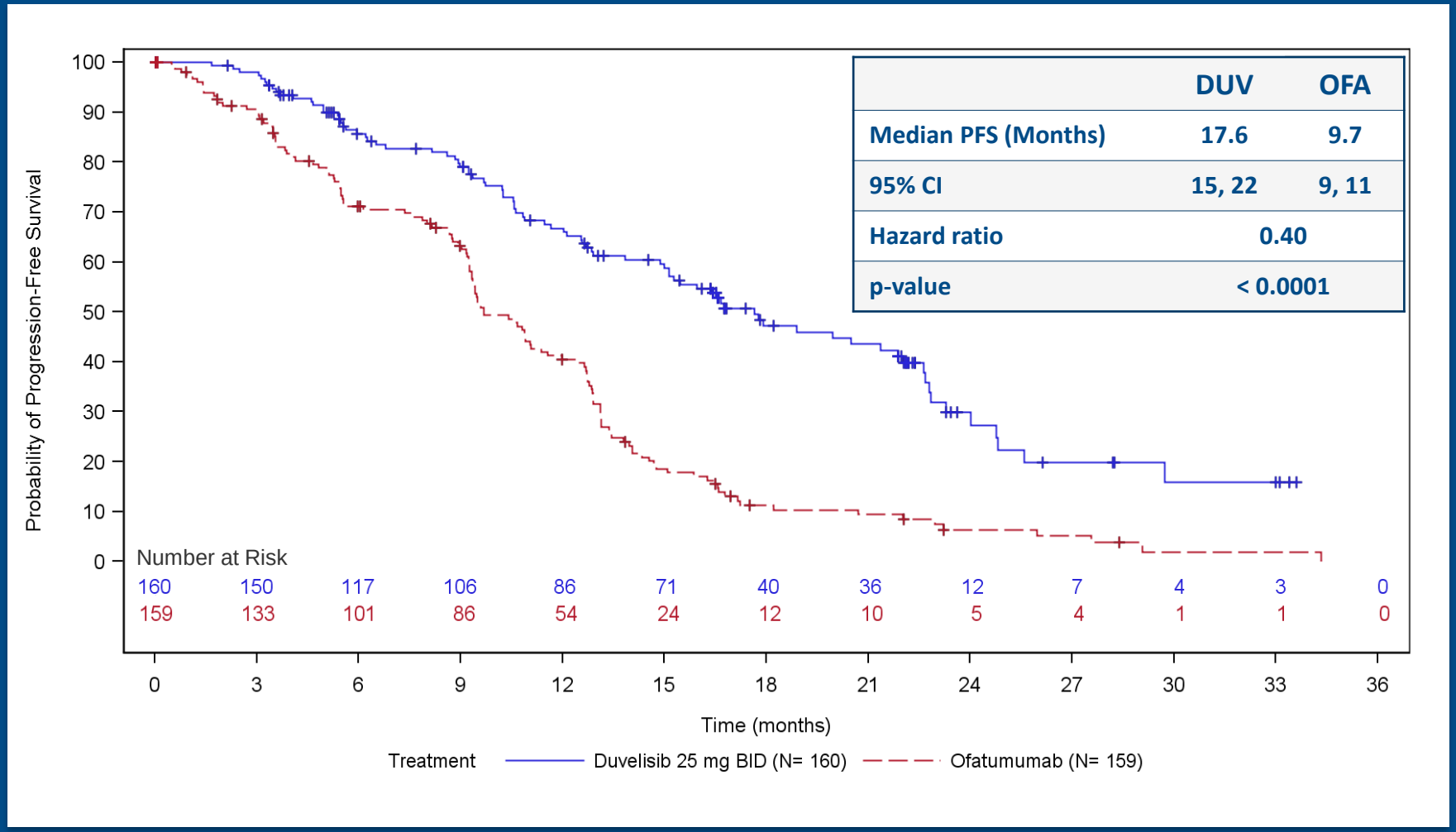
DUO Met Primary Endpoint of PFS
Significantly Longer Median PFS with Duvelisib per IRC



	DUV	OFA
Median PFS (Months)	13.3	9.9
95% CI	12.1, 16.8	9.2, 11.3
Hazard ratio	0.52	
p-value	< 0.0001	

Source: Flinn et al., ASH 2017

Significantly Longer PFS with Duvelisib per Investigator Assessment

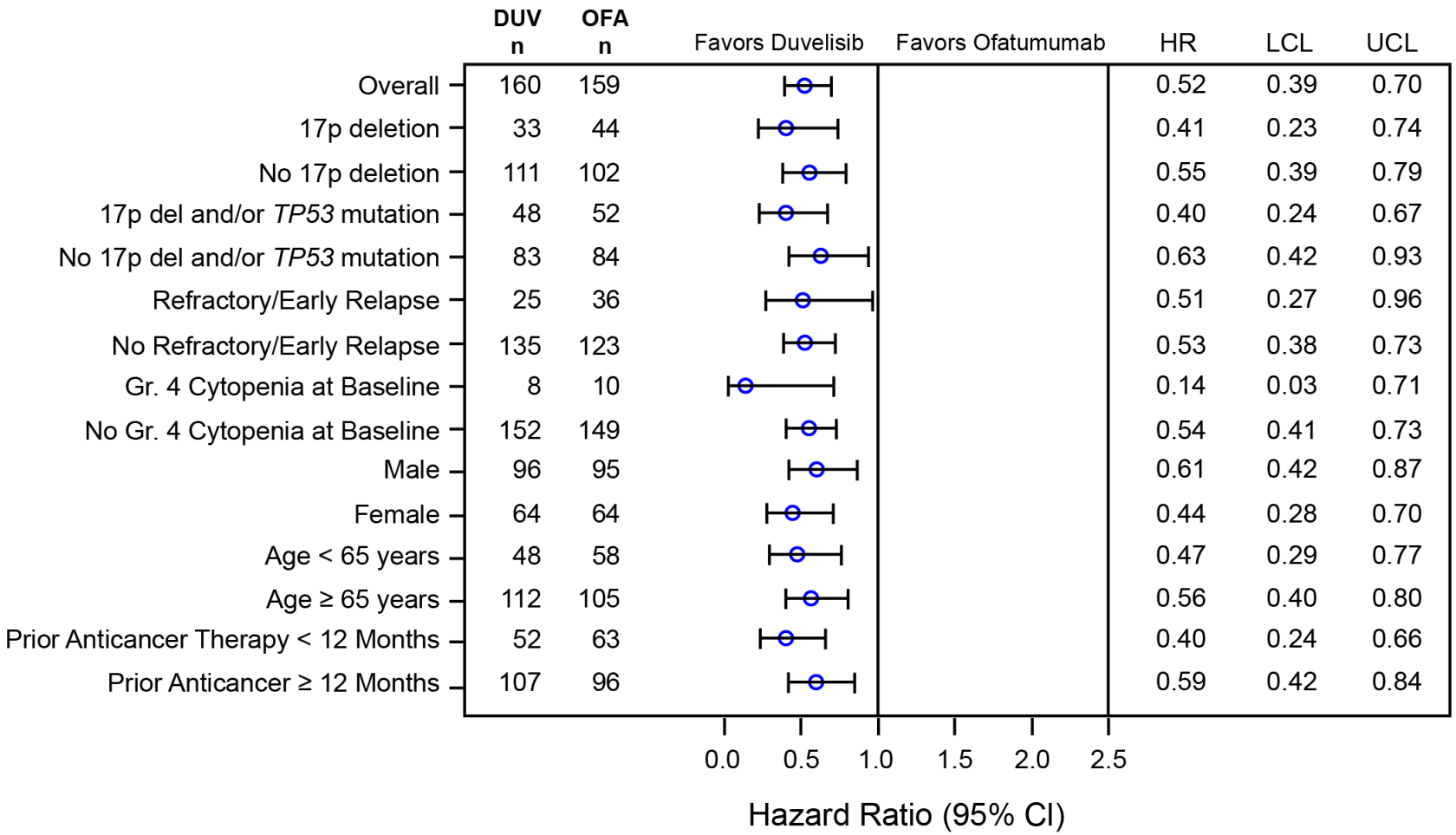


	DUV	OFA
Median PFS (Months)	17.6	9.7
95% CI	15, 22	9, 11
Hazard ratio	0.40	
p-value	< 0.0001	

- 89 patients on OFA arm received duvelisib in crossover study, achieving an ORR of 73% and a median PFS of 15 months per Investigator assessment

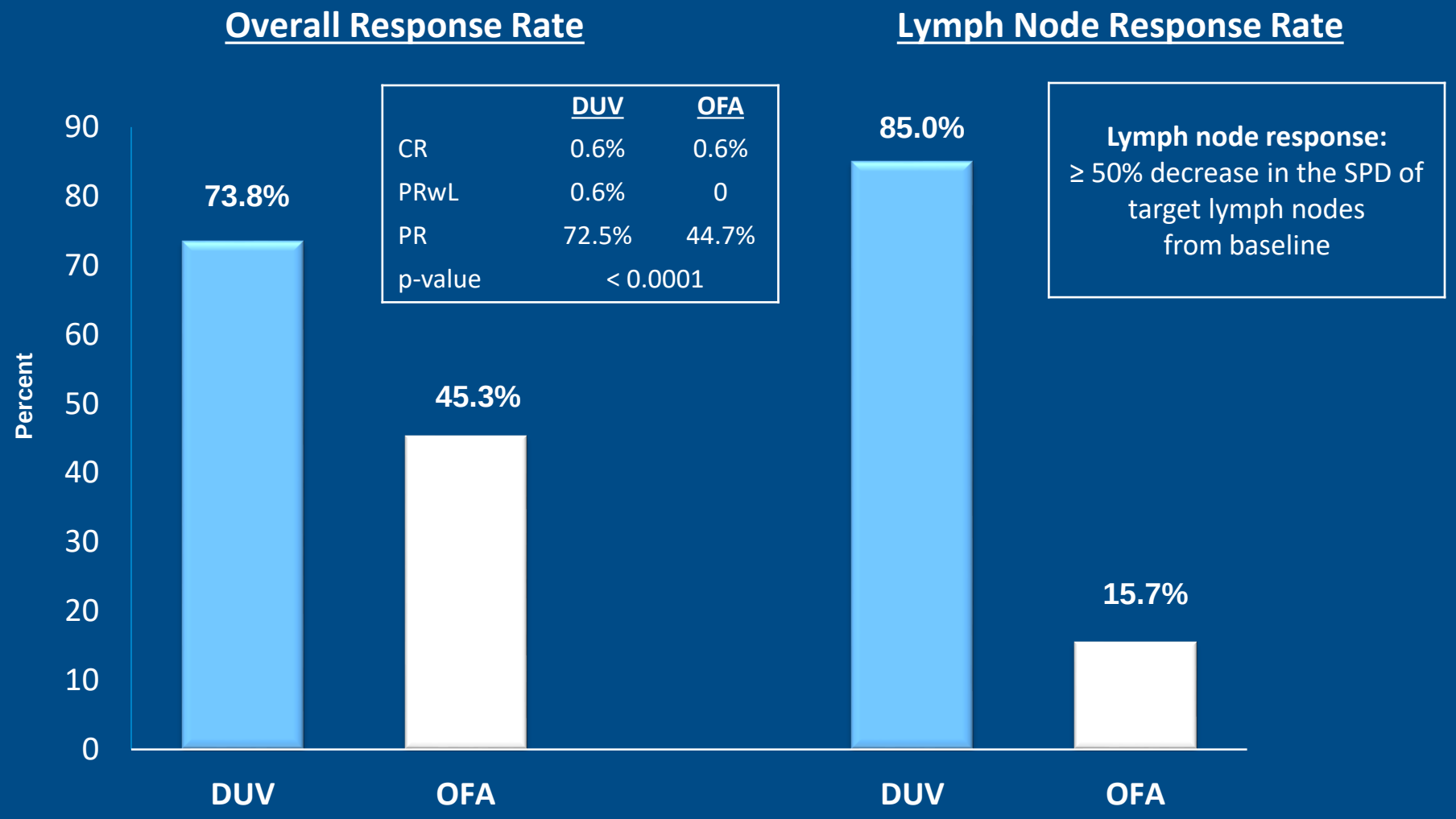
Source: Flinn et al., ASH 2017

Duvelisib Maintained PFS Advantage in All Subgroups Analyzed



Source: Flinn et al., ASH 2017

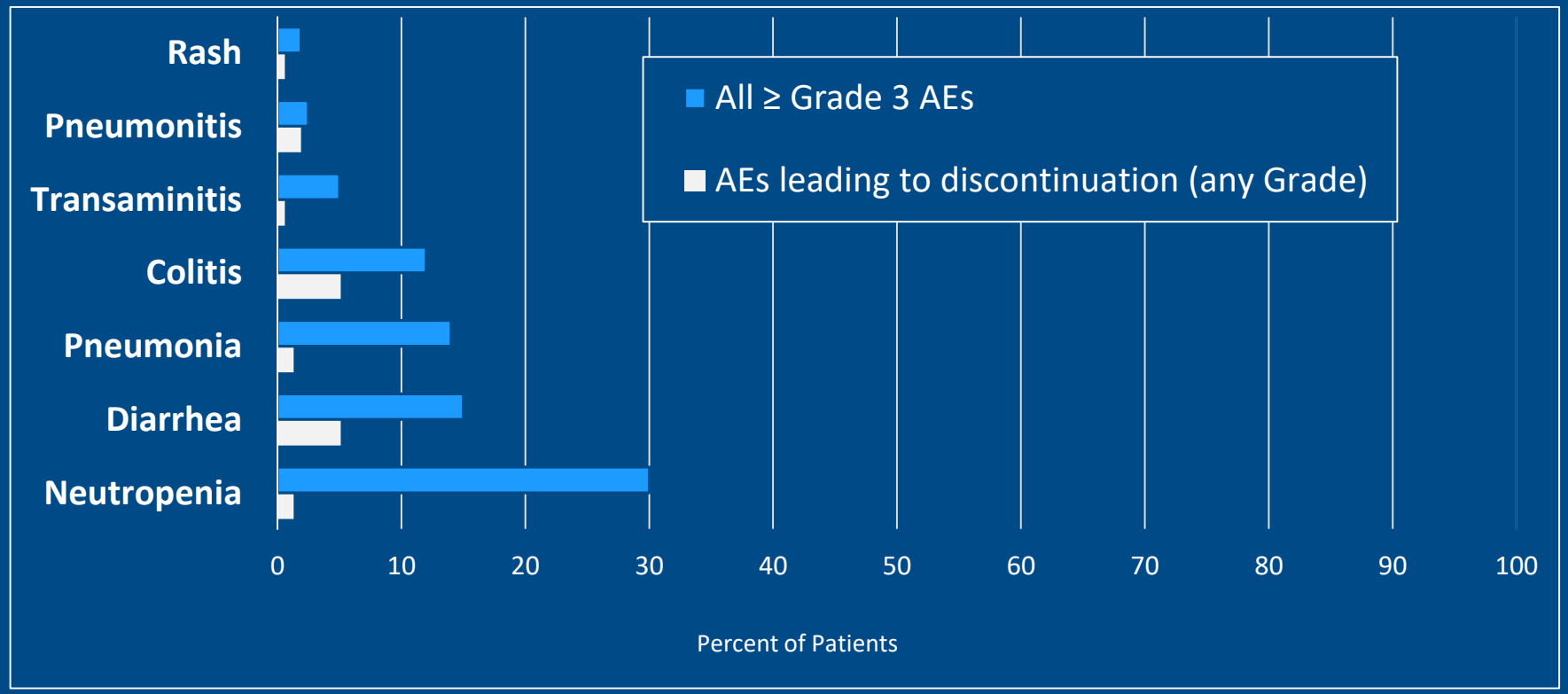
Significantly Higher ORR with Duvelisib per IRC



- ORR in patients with **17p deletion**: duvelisib 70% vs OFA 43% (p=0.0182)

Source: Flinn et al., ASH 2017

AEs of Special Interest Infrequently Led to Duvelisib Discontinuation



- **Severe opportunistic infections (6%):** bronchopulmonary aspergillosis (n=4), fungal infection (n=2), PJP (n=2)*, and cytomegalovirus colitis (n=1)
- **Treatment-related AEs leading to death** (n=4): general health deterioration (n=1); pneumonia staphylococcal (n=2); sepsis (n=1)

*** Neither patient on prophylaxis at the time of the event**

Source: Flinn et al., ASH 2017

DUO Study Conclusions

- DUO met the primary endpoint for PFS: duvelisib monotherapy achieved significant improvement in PFS vs OFA (13.3 m vs 9.9 m; HR = 0.52; $p < 0.0001$) per IRC
  - PFS per investigator response assessment significantly favored duvelisib vs OFA (17.6 m vs 9.7 m; $p < 0.0001$)
  - Similar benefit in CLL/SLL patients with 17p deletion
  - Duvelisib achieved significant improvement in ORR vs OFA (74% vs 45%; $p < 0.0001$) per iwCLL/IWG
  - Duvelisib significantly reduced lymph node burden > 50% in most patients vs OFA (85% vs 16%)
- With a median exposure of 50 weeks, the AE profile of duvelisib was manageable and consistent to what has been previously observed
  - AEs of interest (neutropenia, diarrhea, pneumonia, colitis, transaminase elevations, pneumonitis, rash) infrequently led to discontinuation
- DUO results support duvelisib oral monotherapy as a potential new and convenient treatment option for previously treated CLL/SLL patients

Summary of duvelisib registration-enabling studies

- Duvelisib monotherapy demonstrates significant clinical activity
  - Positive Phase 2 in double refractory iNHL and randomized Phase 3 in CLL/SLL
  - Broad and robust activity across stratification factors and sensitivity analyses
- Well-characterized, consistent and manageable safety profile
  - AEs of Special Interest infrequently led to duvelisib discontinuation in either the DYNAMO or DUO studies
- The DYNAMO and DUO results support duvelisib oral monotherapy as a potential new and convenient treatment option for previously treated CLL/SLL or FL patients

The treatment of CLL and iNHL is evolving with the introduction of new therapies

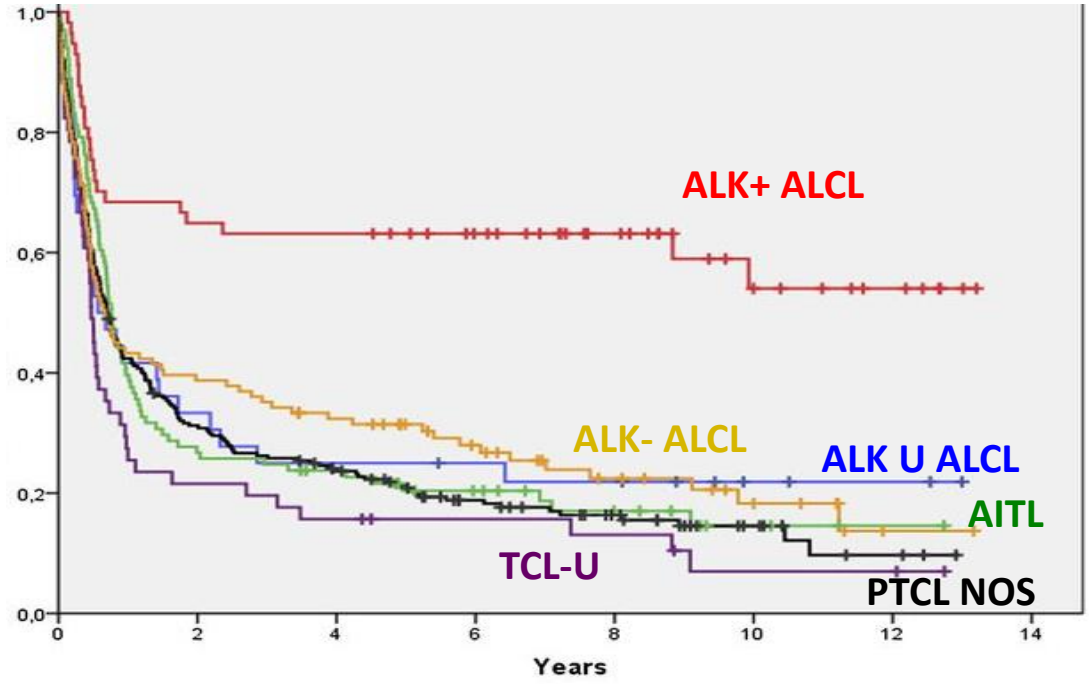
- Chemotherapy and anti-CD20 immunotherapy have a decreasing role as patients transition to oral therapies
  - Patient age and risk factors play a large part in the determination of treatment selection
- In CLL: BTK and BCL-2 inhibition have demonstrable efficacy however patient-specific considerations need to be taken into account
  - BTK: Co-morbidities, vascular risks, concomitant medications and eventual mutational progression
  - BCL-2: Diabetes, renal function, cognitive ability to adhere to protocols and proximity/access to transportation to hospital during the complexity of dosing ramp up
- In FL: PI3K inhibition has shown promising clinical activity
  - Rituximab-based chemotherapy is currently the backbone of treatment
  - BTK/BCL-2 inhibitors have demonstrated only limited efficacy for the treatment of R/R FL to date
- Additional options are needed for a physicians armamentarium in the treatment of chronic indolent lymphomas and leukemias
  - The sequential use of clinically active and manageable treatments may extend the period of disease control
  - Continued development of oral, targeted therapies, is necessary to address the unmet need

Verastem Oncology

Duvelisib for the Treatment of T-Cell Lymphomas

Steve Horwitz, MD

Unmet need for new strategies in T-cell lymphoma

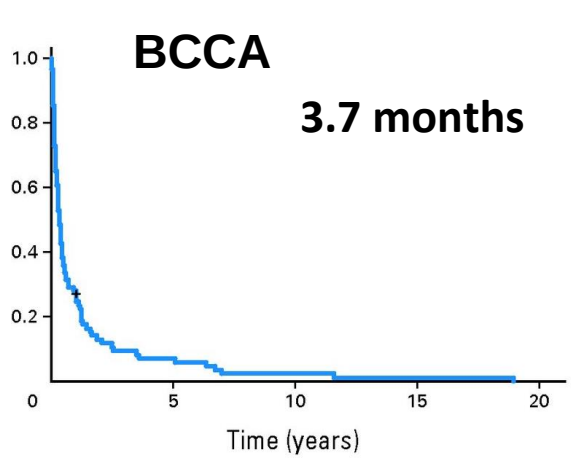


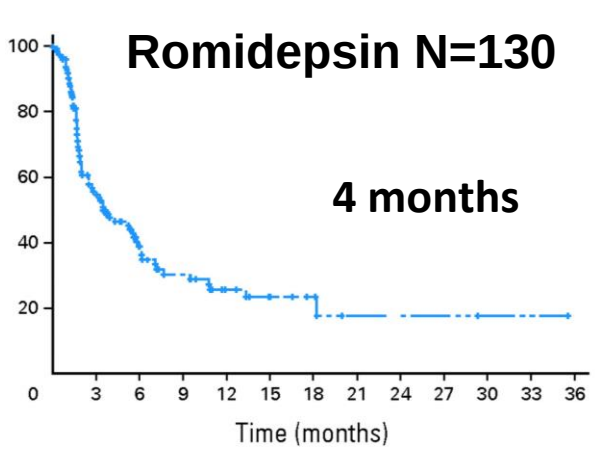
FDA approved agents for R/R TCL

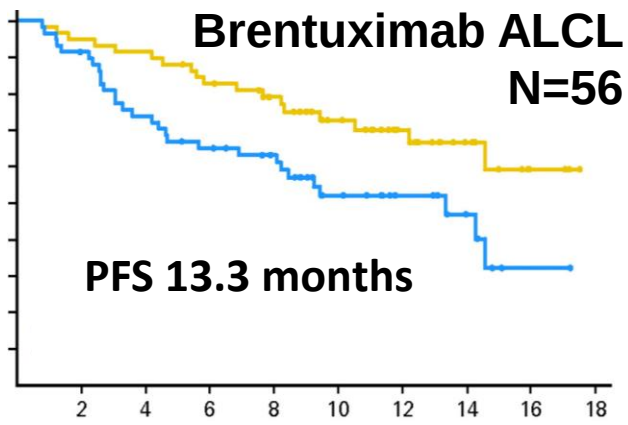
Drug	ORR
Pralatrexate	29%
Romidepsin	25%-38%
Belinostat	26%
Brentuximab vedotin	85% (ALCL)

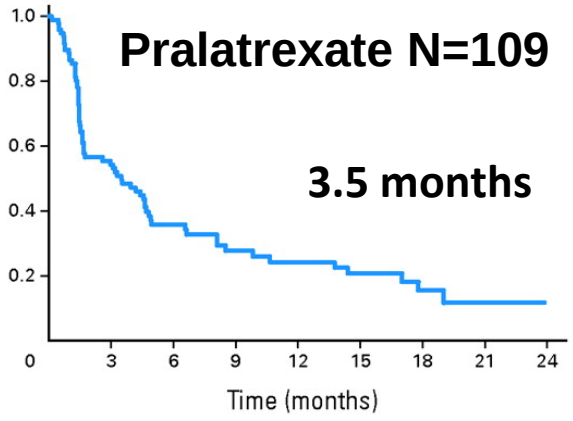
Fredrik Ellin et al. Blood 2014;124:1570-1577 O'Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189. Coiffier B, et al. *J Clin Oncol*. 2012;30:631-636. O'Connor OA, et al. *J Clin Oncol*. 2015; 33:2492-2499. Pro B, et al. *J Clin Oncol*. 2012;30:2190-2196

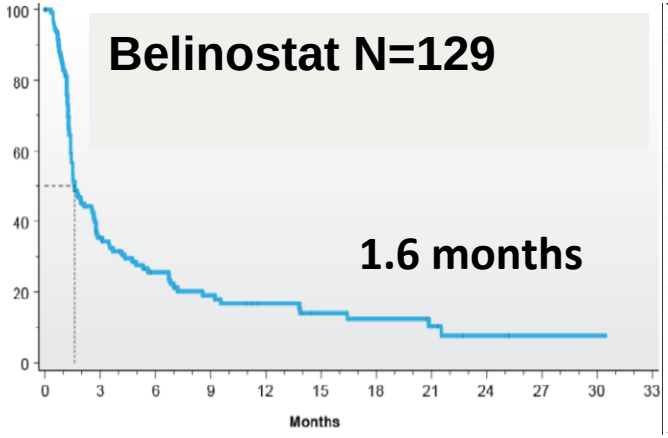
Progression Free Survival: Relapsed/Refractory PTCL

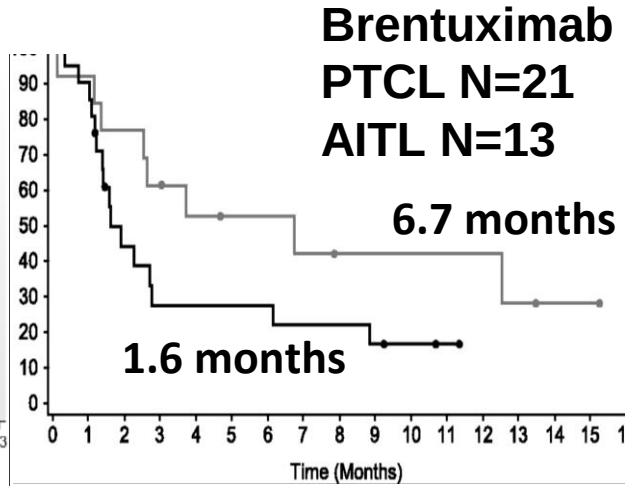






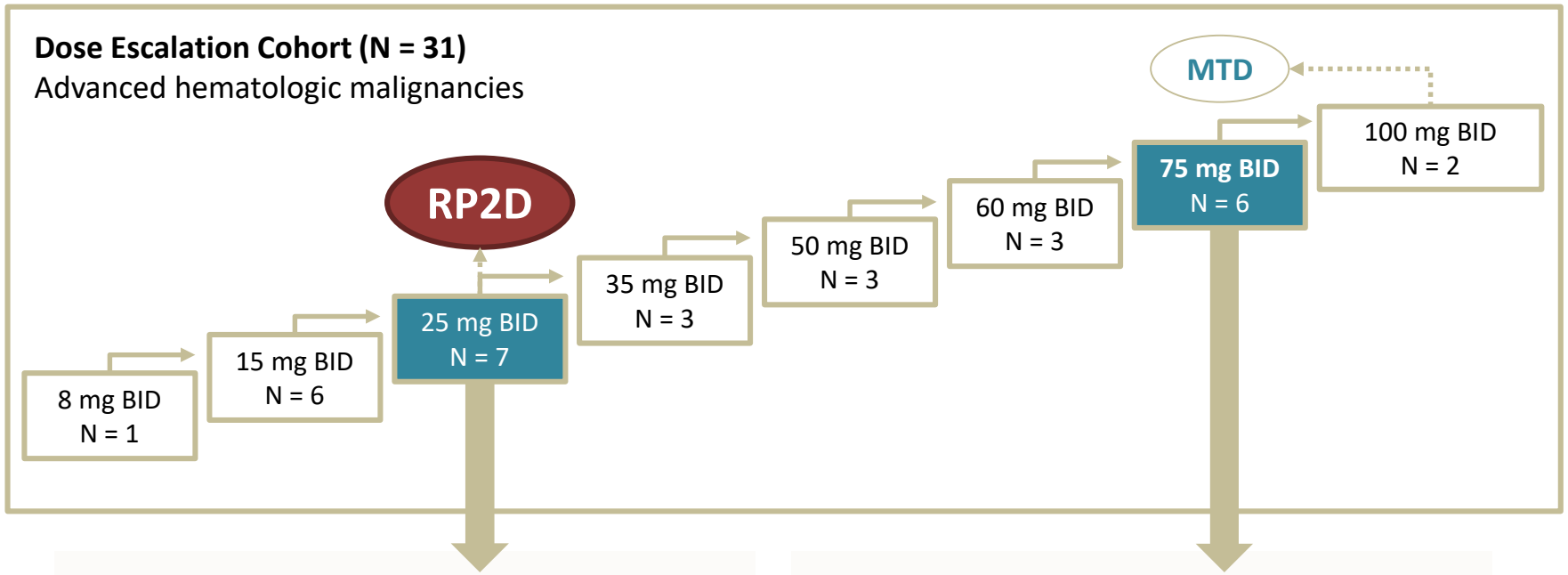






Mak V et al. JCO 2013;31:1970-1976, O'Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189,Coiffier B, et al. *J Clin Oncol*. 2012;30 :631-636, O'Connor OA et al ASCO 2013, Pro B, et al. J Clin Oncol. 2012;30:2190-2196, Horwitz S M et al. Blood 2014;123:3095-3100

Duvelisib monotherapy was studied across a wide range of B- and T-Cell malignancies



Expansion Cohorts: 25 mg BID (N = 59)

- CLL, iNHL, mantle cell lymphoma
- Treatment-naïve CLL

Expansion Cohorts: 75 mg BID (N = 118)

- CLL, iNHL, mantle cell lymphoma
- T-cell lymphomas

<u>Exploratory cohorts</u>

- Aggressive B-cell lymphomas
- Myeloid neoplasms
- T- or B-cell leukemia/lymphoma

NCT01476657

Duvelisib Clinical Activity in TCL in Phase 1

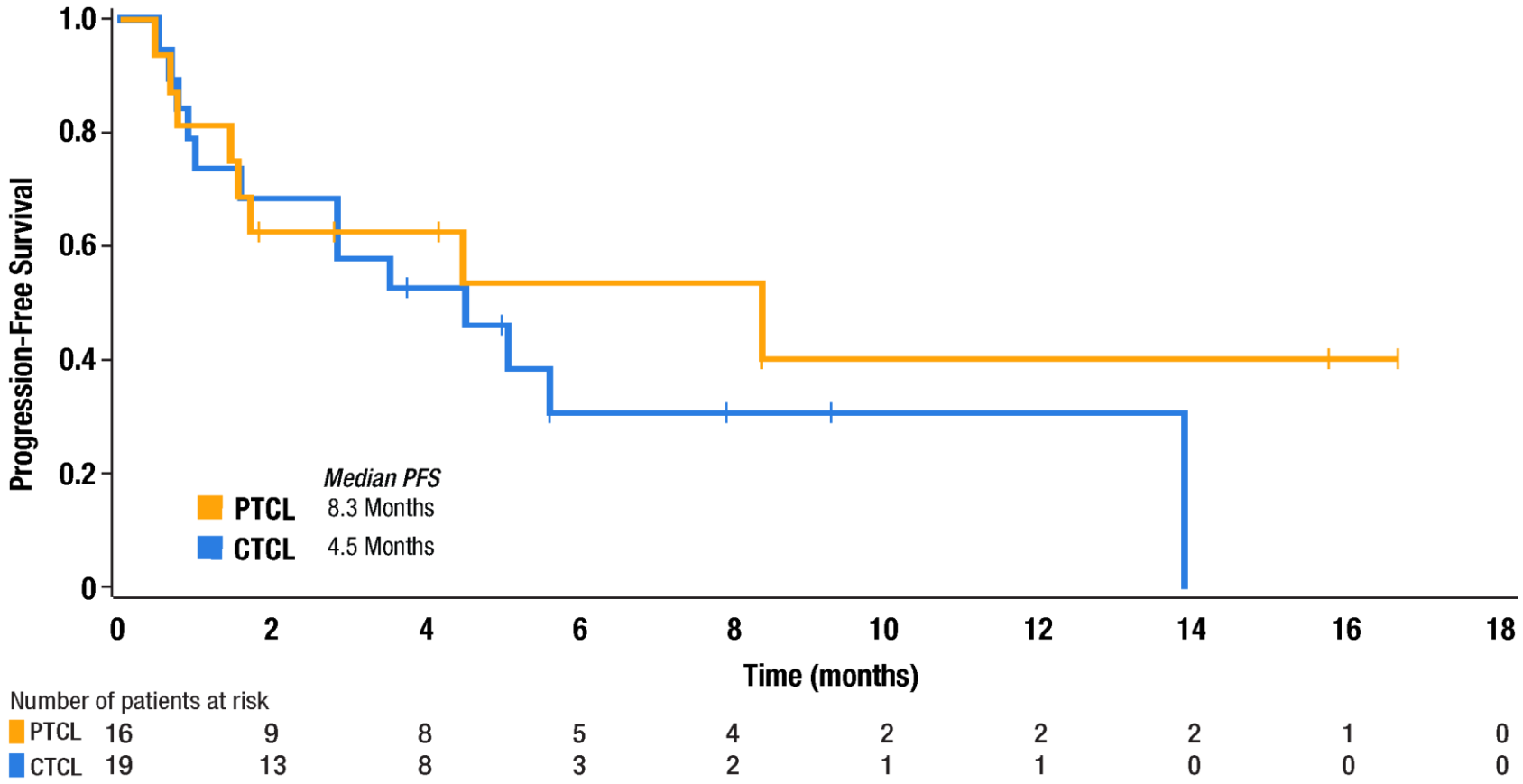
		Best Response, n (%)					Median Time to Response, months (Range)
	n	CR	PR	SD	PD	ORR	
All TCL	35	2 (6)	12 (34)	7 (20)	12 (34)	**14 (40)**	1.9 (1.5, 3.8)
CTCL	19	0	6 (31.6)	6 (31.6)	6 (33)	**6 (31.6)**	2.4 (1.6, 3.8)
PTCL	16	2 (18.8)	6 (31.3)	1 (6.3)	6 (37.5)	**8 (50)**	1.9 (1.5, 3.5)

Includes evaluable patients = at least 1 on-treatment response assessment or PD without assessment
CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease
ORR = CR + PR

- Clinical activity observed across CTCL and PTCL subtypes
  - CTCL: PRs in 4 MF, 1 Sézary syndrome, and 1 MF-LCT
  - PTCL: CRs in 1 EATCL and 1 PTCL NOS
    PRs in 2 AITCL, 2 SPTCL, 1 PTCL NOS, 1 ALCL (ALK-negative)

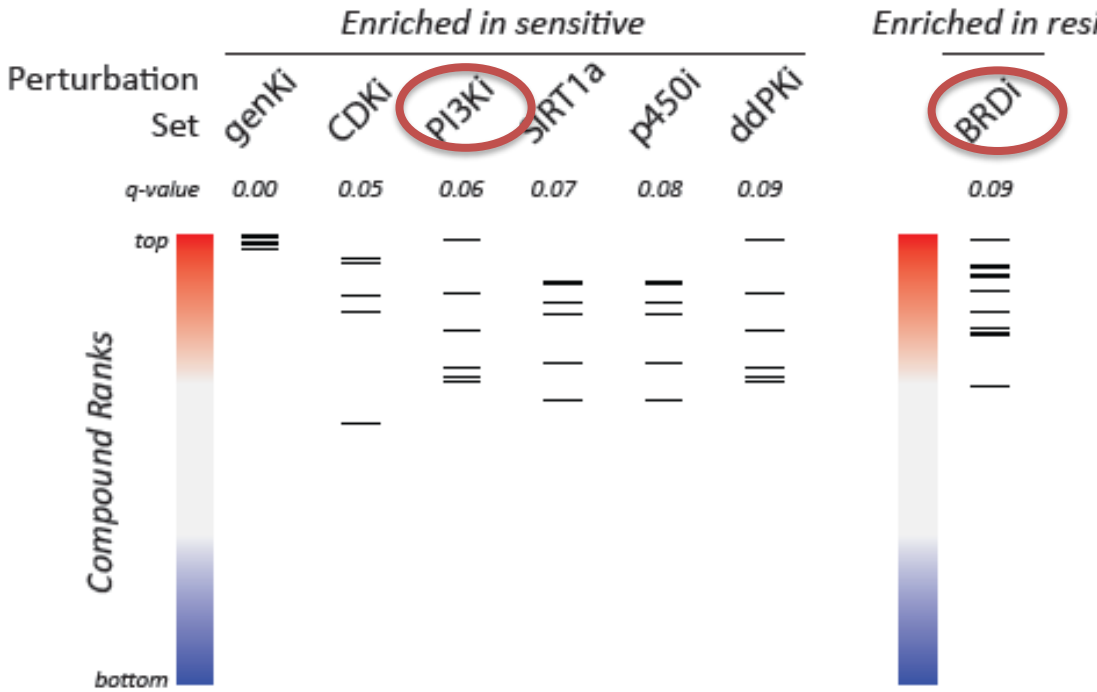
Horwitz et al, Blood 2018

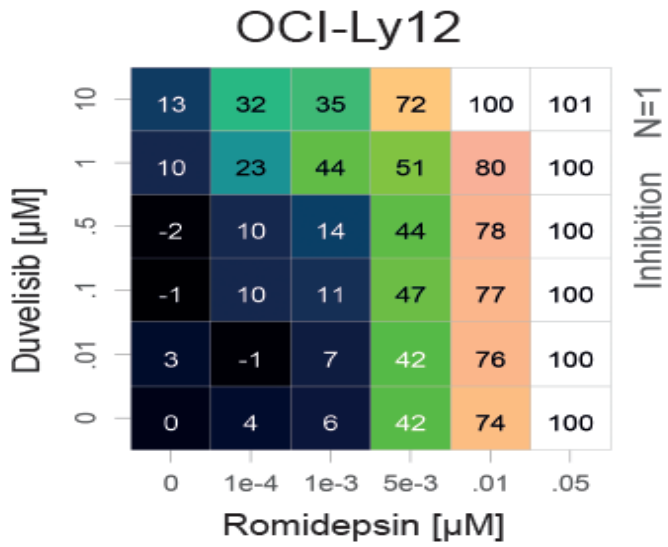
Targeting PI3K in PTCL (Duvelisib Phase 1)



Horwitz et al, Blood 2018

Phosphoproteomic profile indicates on-target effects of duvelisib and suggests mechanism of resistance

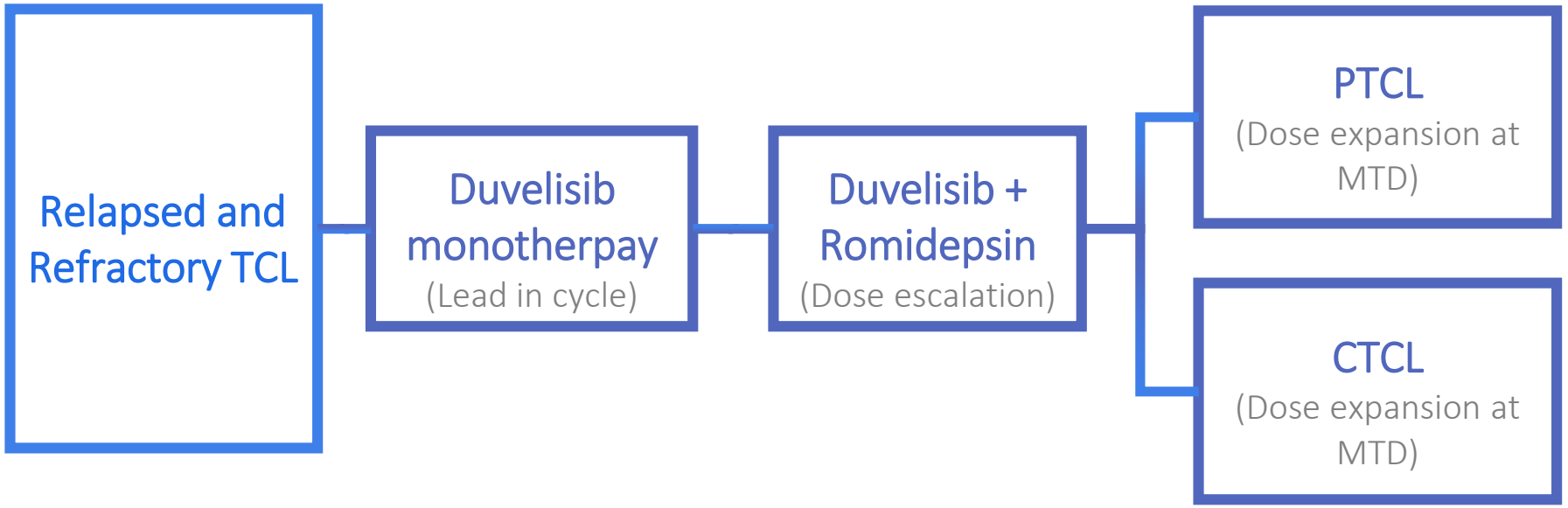




Horwitz, et al. Blood, 2018

Phase I combination study of Duvelisib plus Romidepsin

3+3 design with dose expansion at MTD



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Dose escalation and expansion

Duvelisib + Romidepsin						
Dose Level	Romidepsin days 1, 8, 15	DUV PO days 1-28	#pts enrolled	#pts evaluable for DLT	#pts with DLT	Expansion arm
1	10 mg/m^2	25mg BID	4	3	0	0
2	10 mg/m^2	50mg BID	4	3	0	0
3	10 mg/m^2	75mg BID	4	3	0	4

MTD: Dose Level 3; Romidepsin (10mg/m2 IV) + Duvelisib (75mg PO, BID)

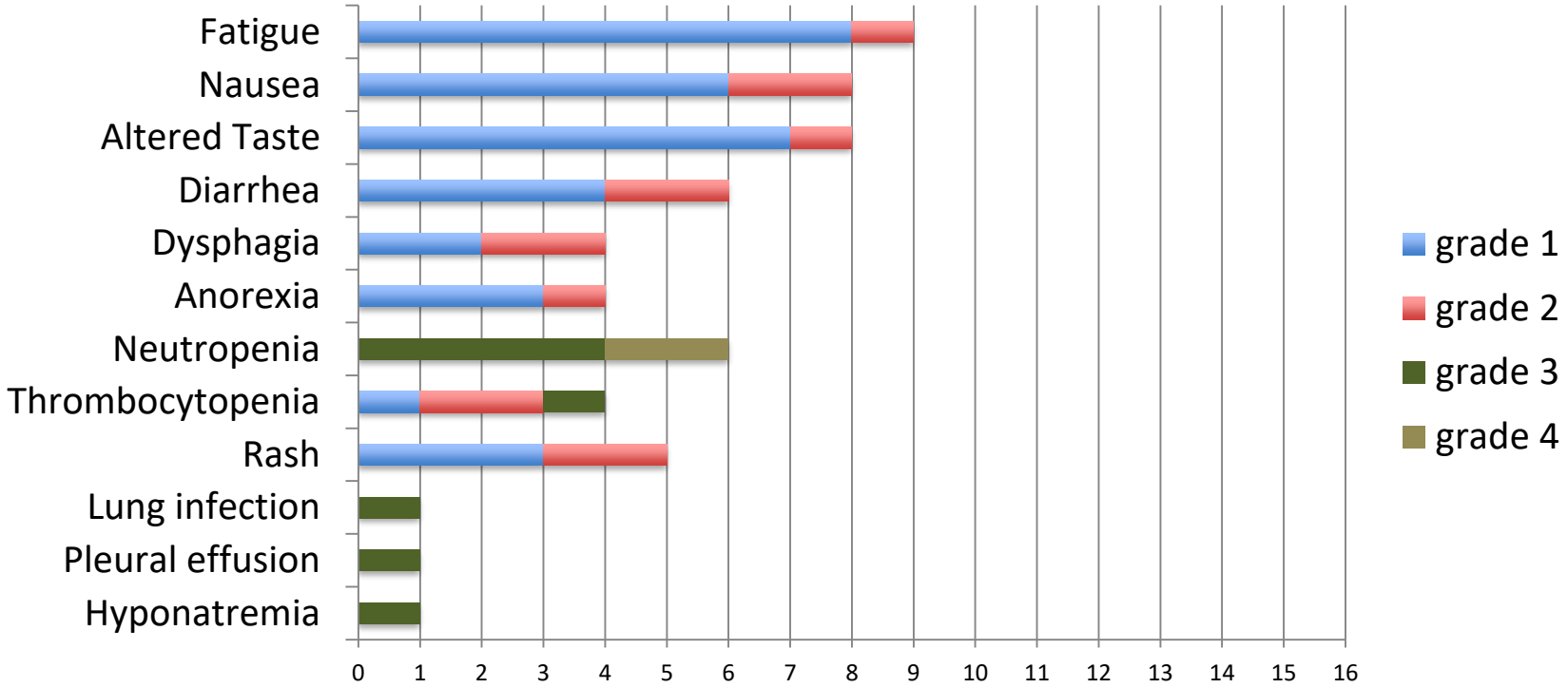
Duvelisib + Romidepsin - Response

Dose Level	# pts Evaluable for Response/Total	Overall response	Complete Response	Partial Response
1	4/4	2	0	2
2	3/4	2	1	1
3	8/8	5	3	2
TOTAL	15/16	9 (60%)	4 (27%)	5 (33%)

CTCL vs. PTCL	#pts Evaluable for Response	Overall Response Rate	Complete Response	Partial Response
CTCL	4	2 (50%)	0	2 (50%)
PTCL	11	7 (64%)	4 (36%)	3 (27%)
(AITL/Tfh)	5	3 (60%)	2 (40%)	1 (20%)
(PTCL-NOS)	4	3 (75%)	2 (50%)	1 (25%)

Duvelisib + Romidepsin adverse events

Showing events affecting ≥ 20% of patients and all grade 3 or 4 events



2 deaths unrelated to treatment:

- Diffuse alveolar hemorrhage following allogeneic stem cell transplant
- Sepsis in setting of disease progression

Conclusions

- Preclinical studies elucidated potential mechanisms of response and resistance to Duvelisib which are being further evaluated in this present phase I study

- Safety, tolerability, and responses of least 50% were observed in systemic TCL

- There were no DLTs with the combination of Duvelisib plus Romidepsin

- Expansion cohorts of patients with PTCL and CTCL are almost complete and further expansion of the Duvelisib plus Romidepsin cohort is planned to more precisely define the activity of this combination

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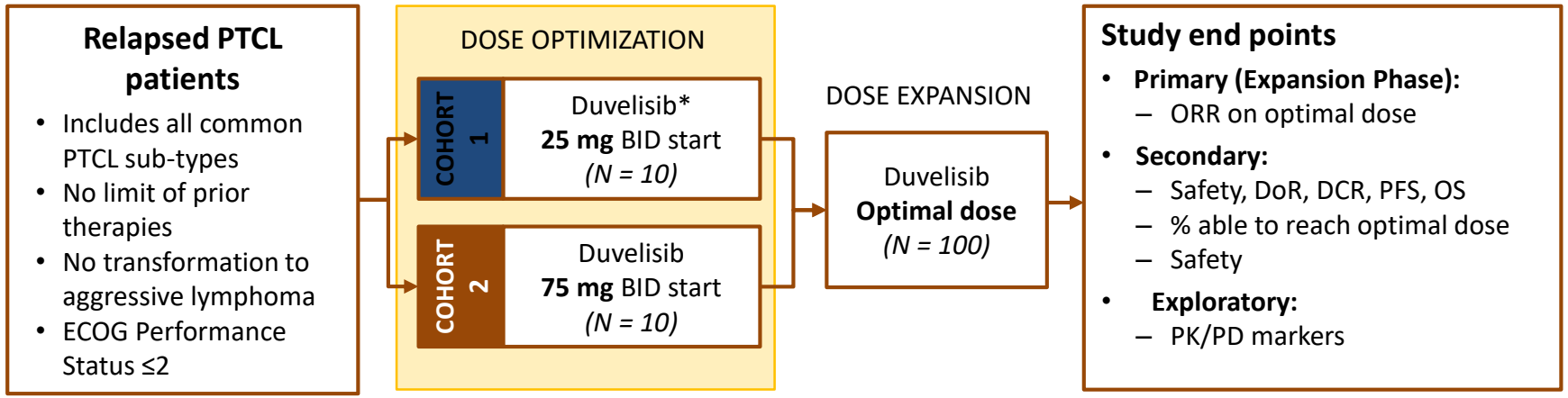
PRIMO: Confirm and extend activity of duvelisib monotherapy in relapsed/refractory PTCL



* Cohort 1: At Cycle 1, if CR/PR: maintain dose; If SD and tolerable: increase dose; if PD: discontinue if intolerable

Goal: Establish optimal dose and confirm monotherapy activity

Trial design details:

- At least one prior therapy for PTCL; for CD30+ ALCL, patients must have failed or are ineligible or intolerant to brentuximab vedotin
- Intra-patient dose escalation in Cohort 1 is allowed

The Treatment of Patients with T-Cell Lymphoma Needs Additional Therapeutic Development

- There remains a significant unmet need in the treatment options for patients with T-Cell lymphoma
  - Current NCCN guidelines recommend clinical trials over chemotherapy or agents under accelerated approval (eg. HDACi or anti-folates)
- Duvelisib represents a potential new therapy for the treatment of T-Cell lymphomas
  - Encouraging activity as a single agent in Phase 1
  - Early data from Phase 1/2 combination therapy with romidepsin indicates a synergy with a potential for increased efficacy, reduced toxicity and a longer duration of response
- Additional clinical study is warranted and ongoing
  - Single agent PRIMO study could support approval
  - Identify predictors of response and resistance
    - Better match therapy to patients
    - Identify other combination partners, move into earlier lines of therapy

Verastem Oncology

Unlocking the Potential of Duvelisib

Joe Lobacki, Chief Commercial Officer, Verastem

Unlocking the potential of duvelisib begins with **the patient**

Adapting to Chronic Disease: The Indolent Lymphoma Patient Journey

Verastem Oncology

Trends in the Chronic Indolent Lymphoma Patient Journey

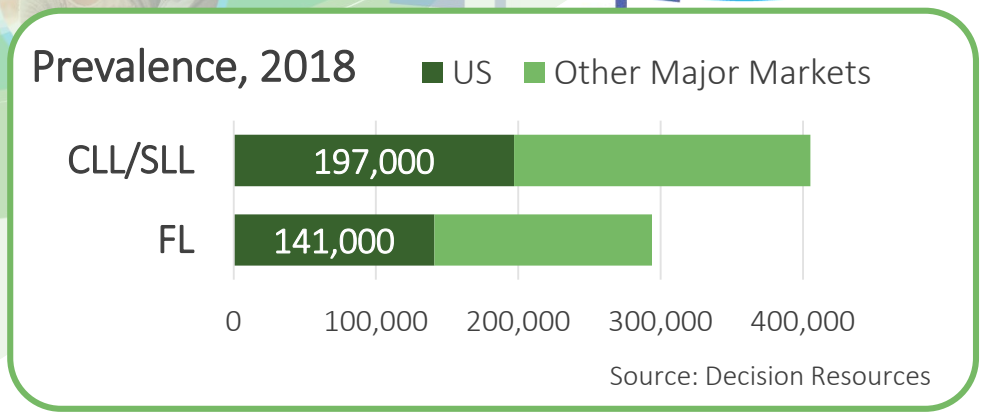
Increased Elderly Patient Population

AGING BABY BOOMER POPULATION

INCREASED DIAGNOSES

NEED FOR MORE LINES OF THERAPY

SHIFT TOWARDS TARGETED THERAPIES



Increased Treatment Options

Verastem Oncology

For the CLL/SLL and FL Patient, Current Targeted Treatment Options Remain Constrained

TODAY'S OPTIONS - choose your own sequence -

CLL/SLL

BTK inhibitor

ibrutinib 1st line

Daily oral monotherapy

PI3K inhibitor

idelalisib (δ) R/R

Daily oral therapy

\+ Given with Rituxan: Travel to infusion center required

BCL-2 inhibitor

(!) venetoclax del(17p)

Daily oral monotherapy

* Allow up to 5 weeks for dose ramp up: hospitalization may be required

FL

PI3K inhibitors

(!) idelalisib (δ) R/R

Daily oral monotherapy

(!) copanlisib (α/δ) R/R

Weekly IV infusion: Travel required

*** Please notify your doctor of your personal medical history, including any prior experience with cardiac events, bleeding, diabetes, renal insufficiency, or congestive heart failure ***

! Conditionally approved

Verastem Oncology

Duvelisib Represents a Convenient Additional Oral Treatment Option for Both CLL/SLL and FL

First in class, dual kinase inhibitor with demonstrated clinical efficacy and a well characterized and manageable safety profile

Simple, at home, oral monotherapy dosing without need for infusions

Accessible treatment in the community setting for both CLL/SLL and FL patients regardless of tumor burden or cytogenetics

Patients may consider…

NEED

What's my next step?

I'm not responding anymore…

20% of FL patients are insensitive to first line chemo and have a poor ongoing prognosis[1]

I can't continue due to AEs…

24% of CLL/SLL patients discontinue ibrutinib due to intolerance after a median of 6 months[2]

Duvelisib is a first-in-class, dual PI3K inhibitor with demonstrated clinical efficacy in relapsed lymphomas

ACCESSIBILITY

How would I get this drug?

70% of the CLL/SLL and FL patient population are treated in community settings, away from major academic centers[3]

Duvelisib requires no planned hospitalization and can be delivered to the patient's door

LIFESTYLE

Does it change my day to day?

55% of oncology patients give equal importance to QoL and survival[4]

Duvelisib is a daily oral monotherapy with no need to travel for infusions

Verastem Oncology

1. Rummel et al., The Lancet. 2013; 2. Mato et al., ASH 2017 abstract 3011; 3. ZS Associates, 2017; 4. Meropol NJ et al. Cancer 2008

Physicians may consider…

CLINICAL PROFILE

Who is this appropriate for?

Community oncologists treat a wide variety of lymphomas

74% of elderly iNHL patients experience at least one major comorbidity that may limit existing treatment options[1]

Duvelisib may offer a single CLL/SLL and FL therapy option, with a safety profile that is well characterized and manageable

UTILITY

What about subpopulations?

20% of FL patients are "fast progressors" on chemotherapy[2]

> 2/3 of CLL/SLL patients have medium to high tumor burden[3], and **>1/3** have high risk genetic alterations[4]

Duvelisib is a chemo-free option, and has demonstrated clinical efficacy regardless of tumor burden or genetic alterations

ADMINISTRATION

Will my patients be willing to take this drug?

>58% of patients feel burdened by IV hospital visits[5]

Duvelisib is a daily oral monotherapy, taken at home with no infusions and no planned hospitalizations

1. Gribben JG. Expert Rev Anticancer Ther. 2010; 2. Rummel et al., The Lancet. 2013; 3. ZS Q1 2017 ATU; 4. Mato et al., ASH abstract 3011; 5. Schott S et al., BMC Cancer.2011

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Market Expansion Comes From Availability of New Treatments

CASE STUDY

Prostate Cancer

Chronic cancer market trends:

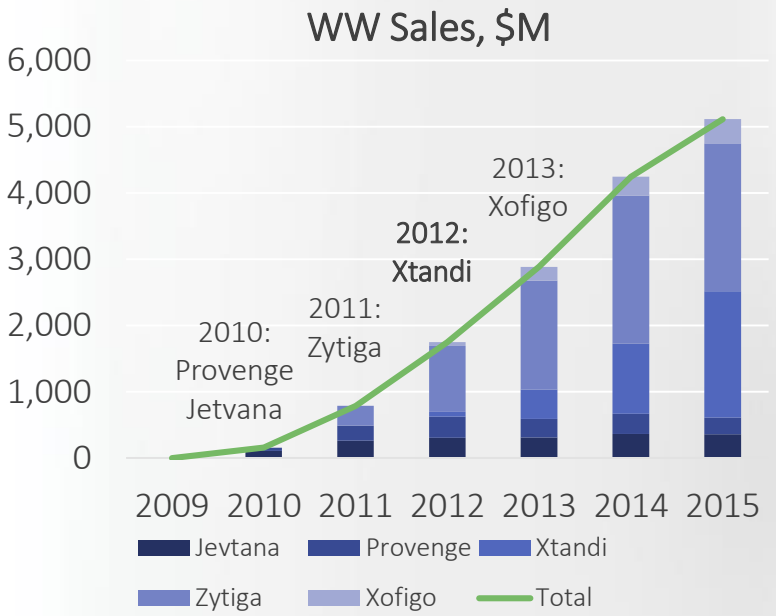
Increased Elderly Patient Population

- ✓ AGING BABY BOOMER POPULATION
- ✓ INCREASED DIAGNOSES

Increased Use of New Treatments

- ✓ INCREASE IN DRUG APPROVALS
- ✓ INCREASED LINES OF THERAPY

Resulting market expansion:



Market for new therapies alone expanded to >$5B within 5 years of first approval

Utilization of new therapies occurred across multiple lines of therapy

Source: BioMedTracker, accessed April 2018

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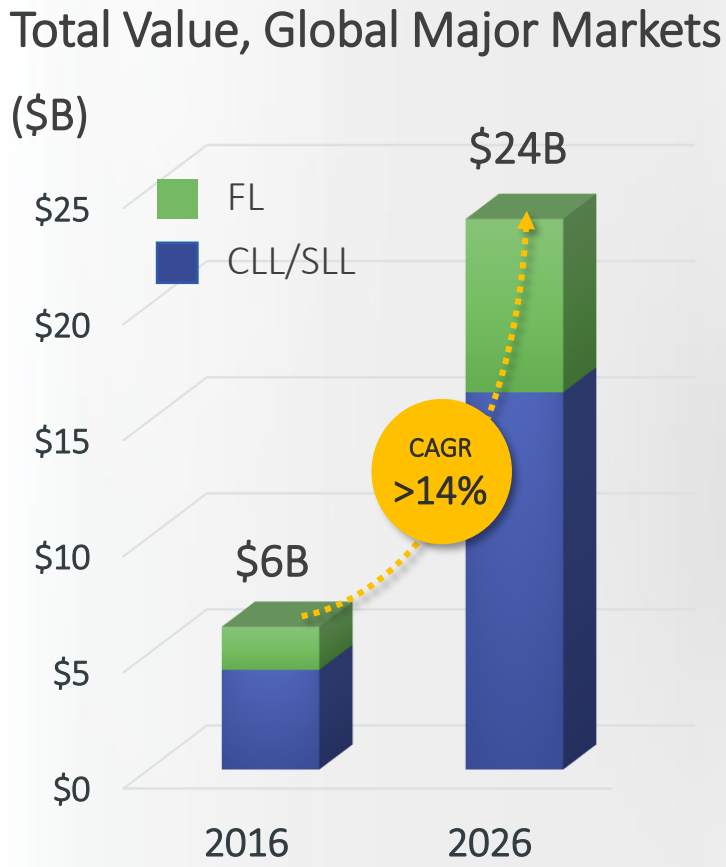
Projected Expansion of CLL/SLL and FL Markets

CLL/SLL and FL

Expectation for market growth:

Broadening care through multiple lines of therapy leads to **market expansion**



Source: Decision Resources, Projected Annual Sales in Major Markets (US, France, Germany, Italy, UK, Spain, Japan)

Unlocking the Potential of Duvelisib for CLL/SLL and FL patients

We are focused on providing an **efficacious, safe, and convenient** treatment option enhanced by a **supportive** experience to help patients **confidently** take their next step towards managing life with their chronic disease.

…because for us, and for our patients, it's **personal**

Preparing for Commercial Launch

Product: Foundation Laid to Optimize the Value of Duvelisib

LABEL

Pursuit of an Initial Registration Path

- ✓ Positive Phase 2 DYNAMO study in Relapsed FL
- ✓ Positive Phase 3 DUO study in R/R CLL/SLL
- ✓ NDA Filed: Full approval in R/R CLL and Accelerated approval in relapsed FL
- ✓ Priority Review granted for a PDUFA date of 10/5/2018

Translation of Market Insights to a Brand Plan

- ✓ Market assessment
- ✓ Account segmentation & KOL mapping
- ✓ Branding
- ✓ Message & material development and testing
- ✓ Pricing strategy
- ✓ Distribution plan

LAUNCH

Establishment of a Clinical Expansion Program

- ✓ 2 sponsored trials developed and initiated
- ✓ Active IST program
- ✓ Formation of a Verastem Steering Committee

LEVERAGE

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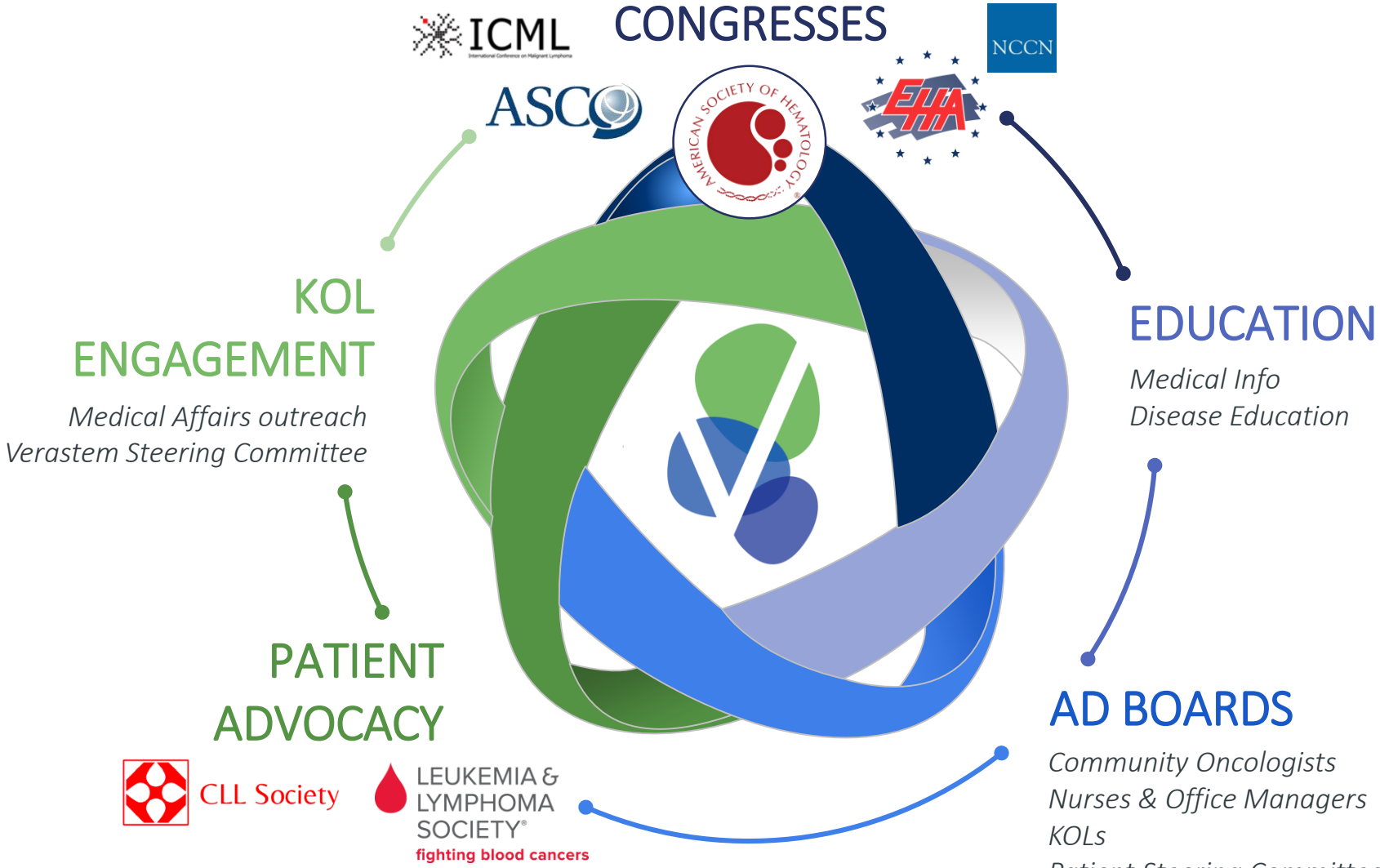
Market: Verastem Oncology Introduced to Key Stakeholders



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Market: Stakeholders Insights

"I rarely refer my patients to academic centers – if we can, we like to keep their treatment in the community"
US TDI Mar 2017

"This is a helpful addition. It's easy, oral, chemotherapy-free, and doesn't require a lot of bells and whistles, not a lot of complexity in terms or monitoring, admissions, infusion."
US TDI Mar 2017

Ad Board Apr 2017
"Both the flexibility of being able to take this with or without food and the small capsule size are a benefit, especially for older patients"

"Thank you for rescuing this drug – now let's get to work in further developing this highly clinically active class"

Community Oncologists

Ad Board 2017
"We're used to checkpoints and managing immune mediated events – this safety profile is completely manageable"

"It has a different profile – it's a dual kinase and looks like there is more sustained response"
US TDI Sep 2017

Nurses & Office Managers

Ad Board Apr 2017
"It's hard to start over on IV from an oral program. Once our patients go on Imbruvica, they don't want to go back to IV"

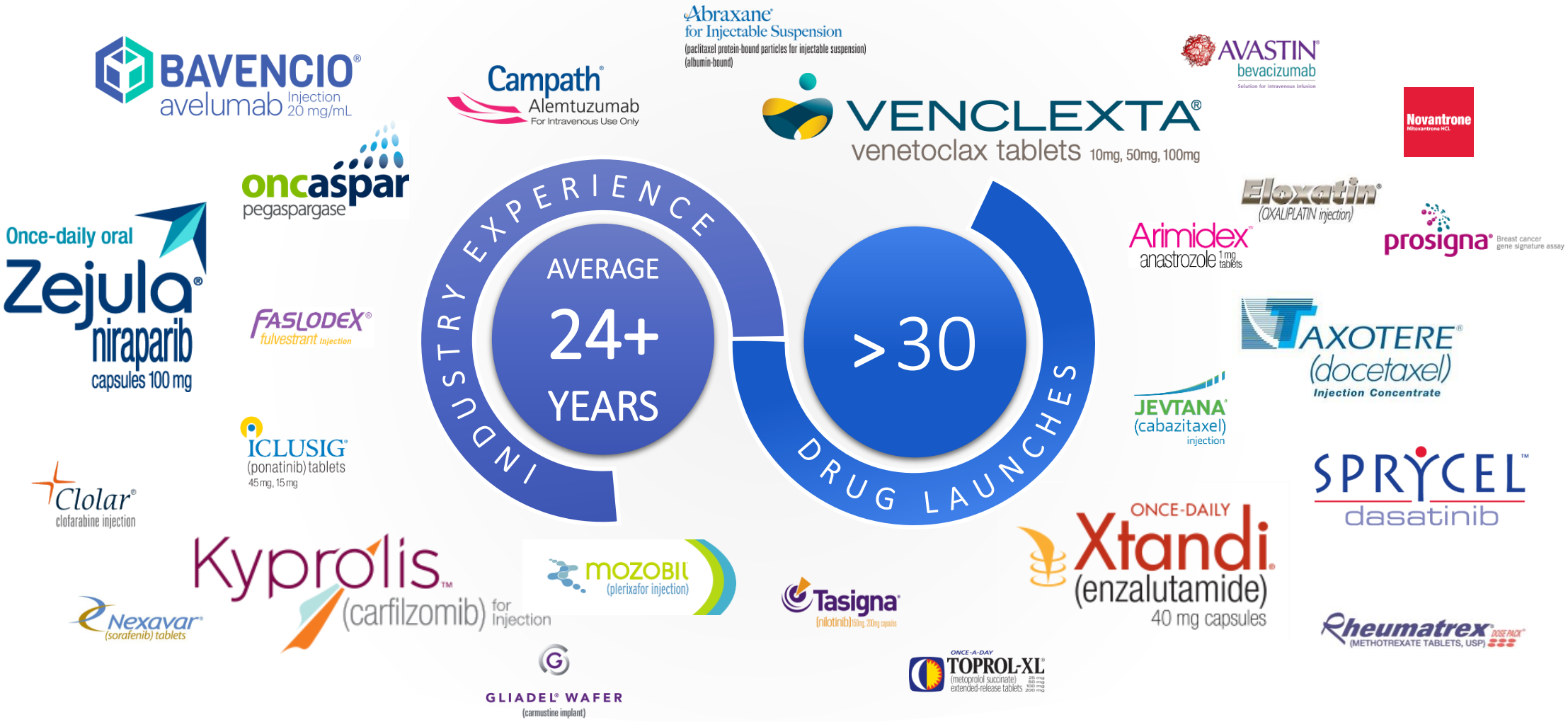
"We can manage side effects – we just want to know what we need to know and what we should be watching out for"
Ad Board Apr 2017

KOLs

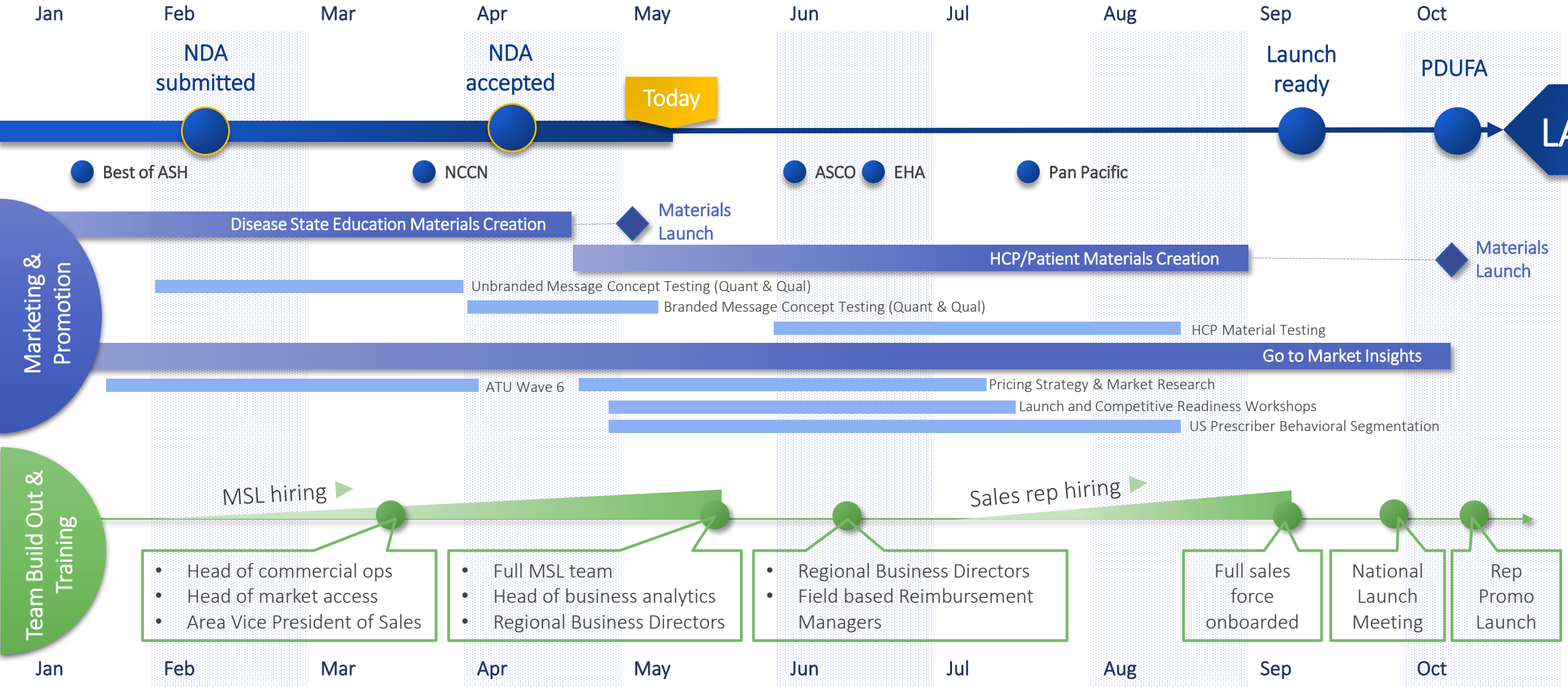
"We need additional drugs in our treatment armamentarium"

Market: Campaign Underway to Advance Understanding of PI3K

Team: Experienced Senior Leadership Assembled



Go to Market Plan



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Go to Market Plan

Targeted Field Force

*provide **One Voice** to the customer*

Broad Coverage

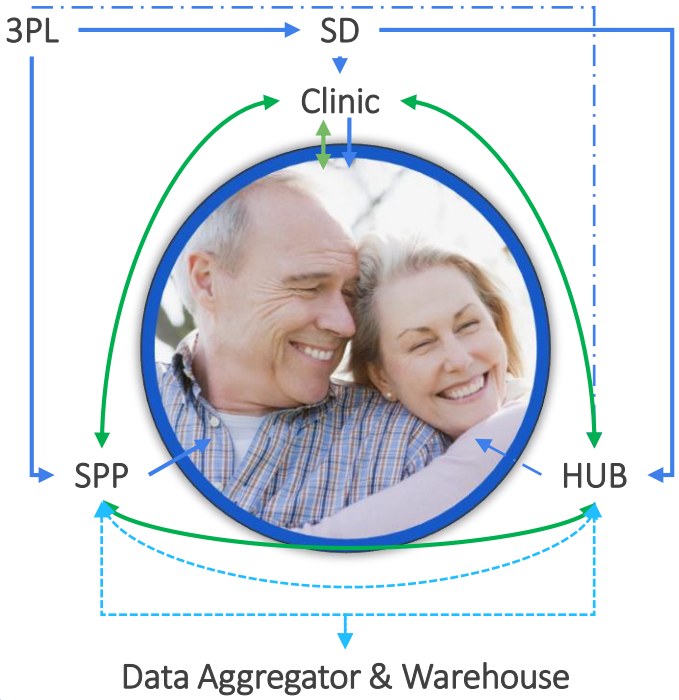
community & academic physicians reached

>95%

commercial payer & Medicare Part D patient lives reached

*enable Access & Support, **regardless of geography***

Patient-Centric Operations



*prioritize a **seamless** patient experience*

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Focused Growth of Duvelisib

TODAY:

ANCHOR

Monotherapy for R/R CLL/SLL and FL

CLL: 23,000 incidence, 197,000 prevalence[1]

FL: 13,000 incidence, 141,000 prevalence[1]

BROADEN REACH

Expand in CLL/SLL and FL

Expand into PTCL

BOLD STEPS

Combinations with I-O and SOC in aggressive NHL subtypes

DLBCL, MCL, Richter's, Transformed FL

MAXIMIZE POTENTIAL

CAR-T combinations

NHL, Myeloma, Solid Tumors

1. Decision Resources, US 2018

Focused Growth of Verastem Oncology

Build a team & organization dedicated to reaching patients

Anchor with launch of our first drug & first indications

Reach duvelisib's full potential in additional tumors

Repeat: Unlock the full potential of defactinib

Evolve to continue meeting patient needs

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Question & Answer Session

Forward Looking Statements

This presentation includes forward-looking statements about Verastem's strategy, future plans and prospects, including statements regarding the development and activity of Verastem's investigational product candidates, including duvelisib and defactinib, and Verastem's PI3K and FAK programs generally, the structure of our planned and pending clinical trials, Verastem's potential collaboration opportunities and the timeline and indications for clinical development and regulatory submissions. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks that approval of the NDA will not occur on the expected timeframes or at all, including by the FDA's target action date; that a filing of a European Marketing Application may not be achieved before the end of the year, if at all; that even if data from clinical trials is positive, regulatory authorities may require additional studies for approval and the product may not prove to be safe and effective; that the preclinical testing of Verastem's product candidates and preliminary or interim data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials; that the full data from the DUO study will not be consistent with the previously presented results of the study; that data may not be available when expected, including for the Phase 3 DUO™ study; that the degree of market acceptance of product candidates, if approved, may be lower than expected; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that our product candidates will cause unexpected safety events or result in an unmanageable safety profile as compared to their level of efficacy; that duvelisib will be ineffective at treating patients with lymphoid malignancies; that Verastem will be unable to successfully initiate or complete the clinical development of its product candidates; that the development of Verastem's product candidates will take longer or cost more than planned; that Verastem may not have sufficient cash to fund its contemplated operations; that Verastem or Infinity Pharmaceuticals, Inc. (Infinity) will fail to fully perform under the duvelisib license agreement; that Verastem may be unable to make additional draws under its debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that Verastem will not pursue or submit regulatory filings for its product candidates, including for duvelisib in patients with CLL/SLL or iNHL; and that Verastem's product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients. Other risks and uncertainties include those identified under the heading "Risk Factors" in Verastem's Annual Report on Form 10-K for the year ended December 31, 2017 and in any subsequent filings with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Verastem's views as of the date of this release, and Verastem does not undertake and specifically disclaims any obligation to update any forward-looking statements.

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Oncology