TG Therapeutics

# Introduction

**Michael S. Weiss**
Executive Chairman & CEO

UNITY CLL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PHASE 3 TRIAL IN CLL

UNITY NHL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PREVIOUSLY TREATED NHL PATIENTS

# Forward Looking Safe Harbor Statement

*This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are often, but not always, made through the use of words or phrases such as "anticipates", "expects", "plans", "believes", "intends", and similar words or phrases. Such statements involve risks and uncertainties that could cause TG Therapeutics' actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in clinical trials, drug development, and commercialization. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and TG Therapeutics undertakes no obligation to update these statements, except as required by law.*

# AGENDA

| Topic | Presenter |
|---|---|
| Welcome / Introductions | Michael Weiss,<br>CEO TG Therapeutics |
| TGR-1202 Differentiation | Owen O'Connor, MD, PhD |
| Integrated Analysis Safety<br>Current Treatment & Future Plans in the Treatment of Front-line & Rel/Ref CLL | Kathryn Kolibaba, MD |
| Current Treatment Landscape Rel/Ref FL/MZL/DLBCL<br>Current Use & Future Plans for Novel Agents<br>How does Umbra fit in? | Bruce Cheson, MD |
| Treatment Challenges and<br>Personal Experience with U2 | Kathy Cutter |
| Questions & Answer Session | |
| Closing Remarks | Michael Weiss |

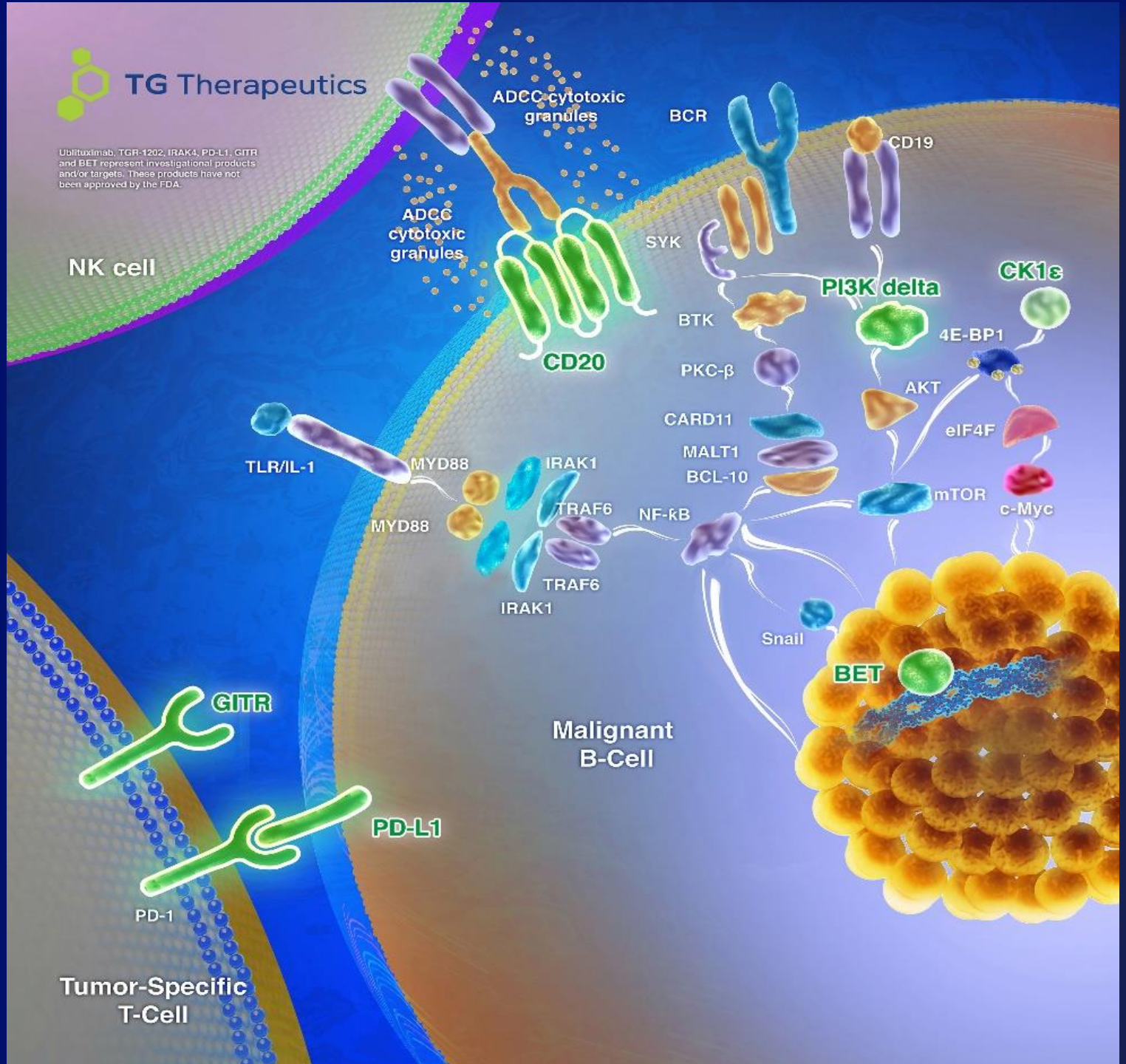
# TG Therapeutics, Inc.

- Biopharmaceutical company focused on B-cell cancers (CLL and NHL) & autoimmune-related diseases (MS, RA, Lupus)
- **Headquarters:** New York, NY
- **NASDAQ:** TGTX

- Developing portfolio of B-cell targeted agents

- **TG-1101 – (ublituximab) Novel Glycoengineered, Anti-CD20 monoclonal antibody**
  - Enhanced ADCC profile for increased potency, similar to Gazyva® (GA101)
  - Robust activity demonstrated in CLL and NHL
  - **GENUINE Phase 3 Registration Trial in CLL positive results announced!**
  - **ULTIMATE I & II Phase 3 Trials Ongoing in Multiple Sclerosis under SPA**

- **TGR-1202 – (umbralisib) – Novel PI3Kδ inhibitor**
  - Highly active and well tolerated as monotherapy and in combination treatment
  - Demonstrated best-in-class attributes
  - **UNITY- CLL Phase 3 trial under FDA-Special Protocol Assessment (SPA)**
    - **Full Enrollment reached- October 2017**


TG Therapeutics
Ublituximab, TGR-1202, IRAK4, PD-L1, GITR and BET represent investigational products and/or targets. These products have not been approved by the FDA.
ADCC cytotoxic granules
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NK cell
BCR
CD19
SYK
PI3K delta
CK1ε
BTK
4E-BP1
CD20
PKC-β
AKT
CARD11
eIF4F
MALT1
BCL-10
TLR/IL-1
MYD88
IRAK1
mTOR
c-Myc
TRAF6
NF-κB
MYD88
TRAF6
IRAK1
Snail
BET
GITR
PD-L1
Malignant B-Cell
PD-1
Tumor-Specific T-Cell

TG Therapeutics

# TGR-1202 Preclinical Differentiation

Owen O'Connor, MD

UNITY CLL
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PHASE 3 TRIAL IN CLL

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GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PREVIOUSLY TREATED NHL PATIENTS

# Deciphering the Mechanistic Similarities and Differences Among the PI3 Kinase Inhibitors

Owen A. O'Connor, M.D., Ph.D.
Founding Director, Center for Lymphoid Malignancies
Professor of Medicine and Developmental Therapeutics
The New York Presbyterian Hospital
Columbia University College of Physicians and Surgeons
New York, N.Y.

**American Society of Hematology 2017**
**Atlanta, GA**

Columbia University Medical Center

NCI CCC A Comprehensive Cancer Center Designated by the National Cancer Institute

NewYork-Presbyterian The University Hospital of Columbia and Cornell

# Deciphering the Mechanistic Similarities and Differences Among the PI3 Kinase Inhibitors

## Observations and Questions

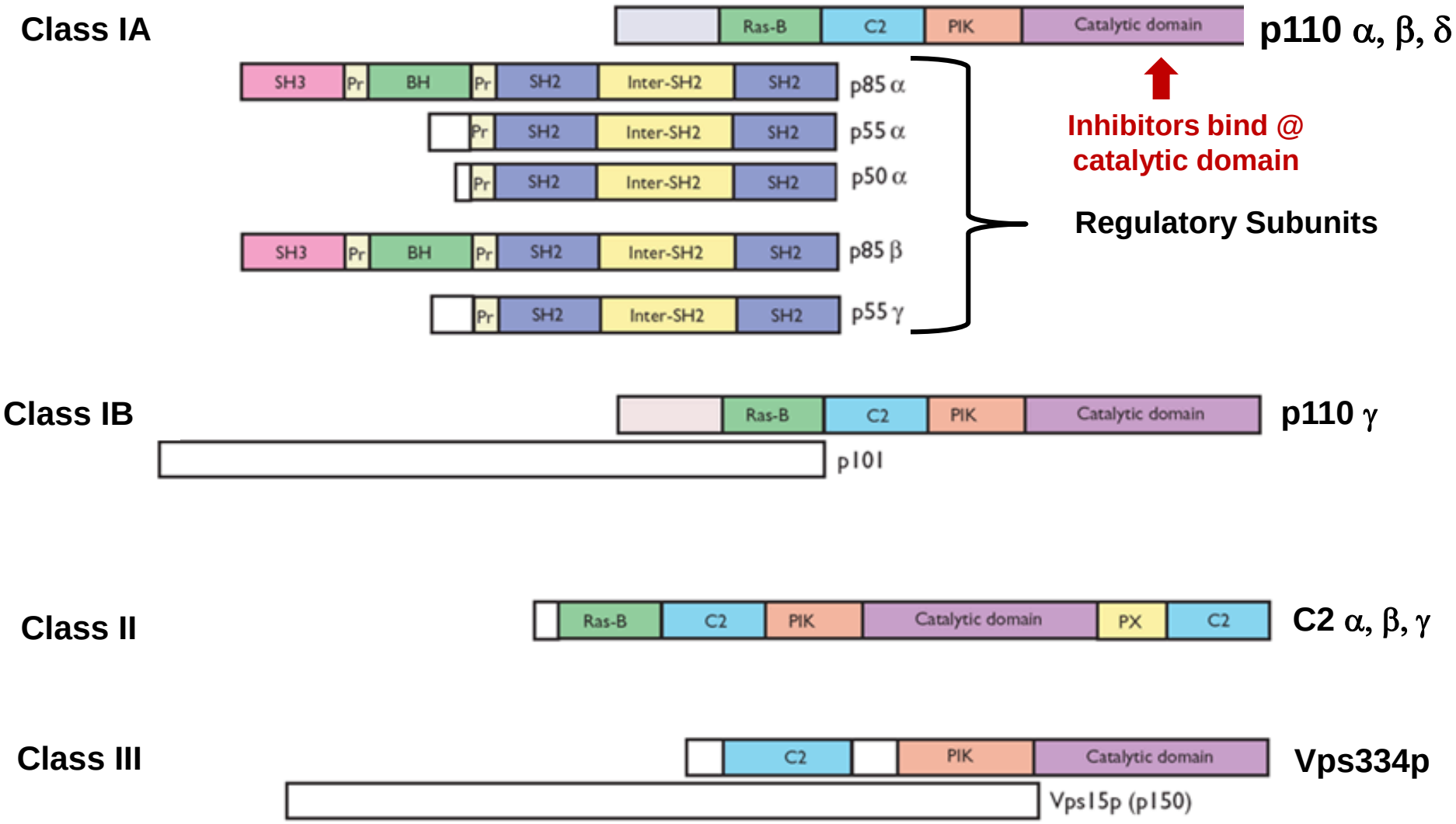
**OBSERVATIONS**

- **The PI3K pathway is undisputedly one of the most important 'driver' pathways across all of cancer – regulating major oncogenes like c-myc, bcl-2 and cyclin D1, among others**
- **The target in not a simple single protein/gene target. Like the proteasome and HDAC there is enormous family diversity**
- **Inhibitors of the pathway have important clinical activity in lymphoid malignancies, but that activity is not uniform across all subtypes.**
- **Some inhibitors have demonstrated unusual adverse events manifest as GVHD-like toxicity and increased infections.**

**QUESTIONS**

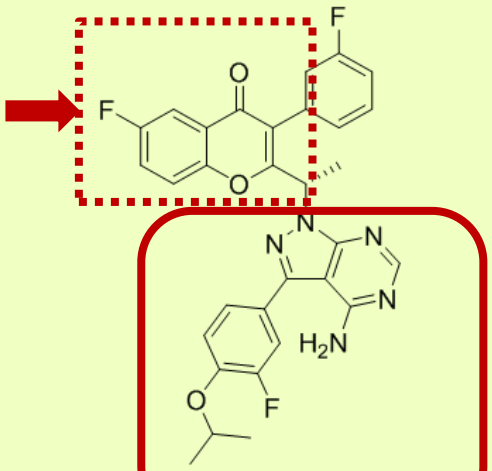
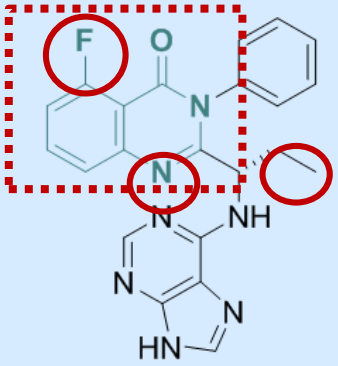
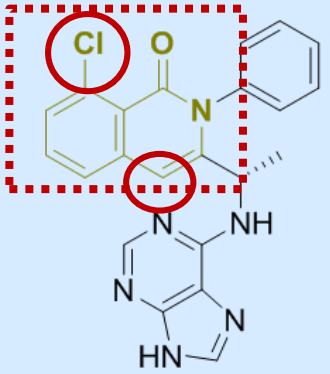
- **Are there differences in the on- or off-target affects that might account for differences in toxicity and/or clinical activity? How do we interpret the balance between potency and selectivity?**
- **Are all agents in the class 'equivalent' with regard to toxicity, efficacy and drug:drug interactions? How might differences in molecular pharmacology provide clues into the deciphering those differences?**
- **How do we deconvolute the immunologic influences among the compounds? Are they even different?**

# THE PI3 KINASES EXIST AS COMPLEX HETERODIMERS




Koyasu Nature Immunology 2003

# The PI3 Kinase Inhibitors Share Similarities & Differences

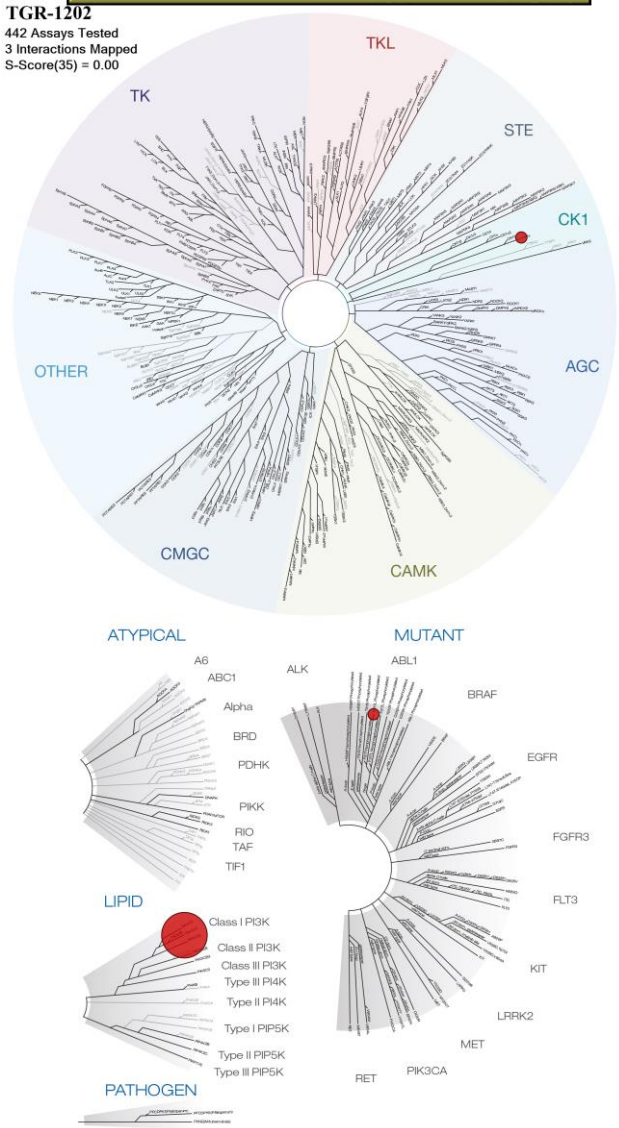
| TGR-1202 | Idelalisib (GS-1101) | Duvelisib (IPI-145) |
|---|---|---|
|  |  |  |
| Delta | Delta | Delta/Gamma |
| QD | BID | BID |

- Similarities in the upper structural motif – differences in the lower structural motif
- Subtle pharmacologic and target difference

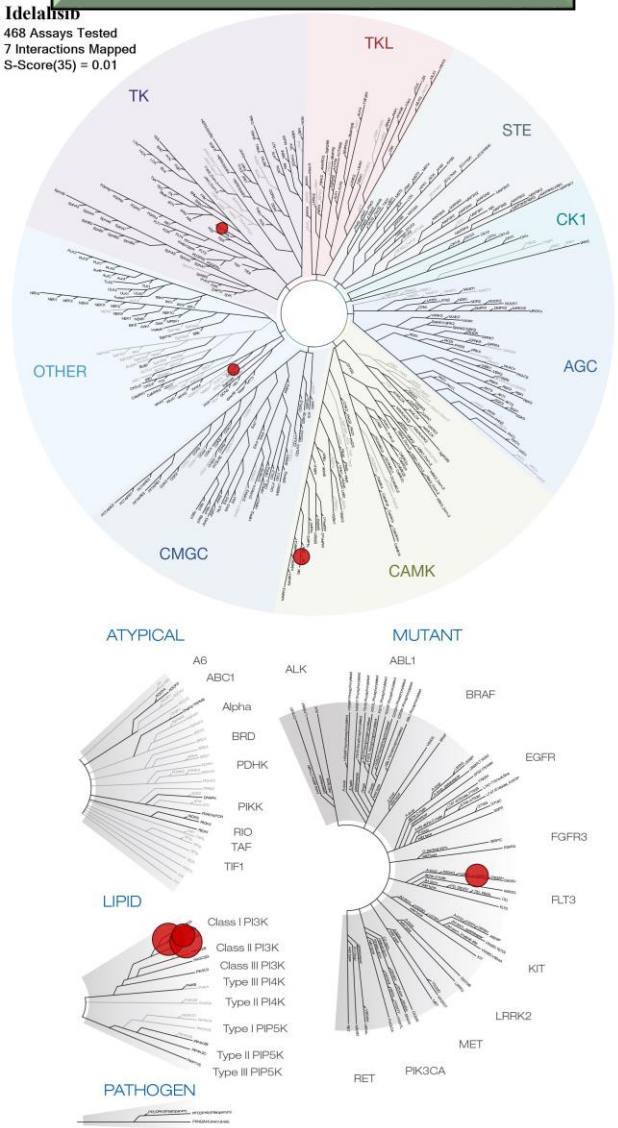
[1]O'Connor et al, ASCO 2015, Abstract # 7069

# KINOME SCAN SPECIFICITY OF 3 PI3K

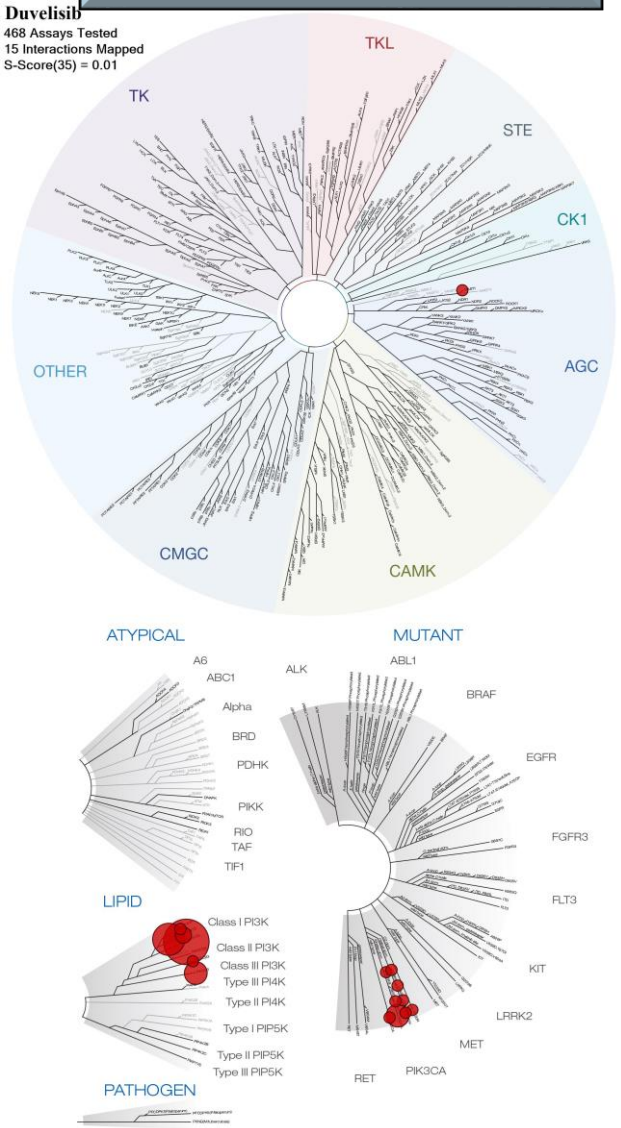
**Umbralisib (TGR-1202)**




**Idelalisib**



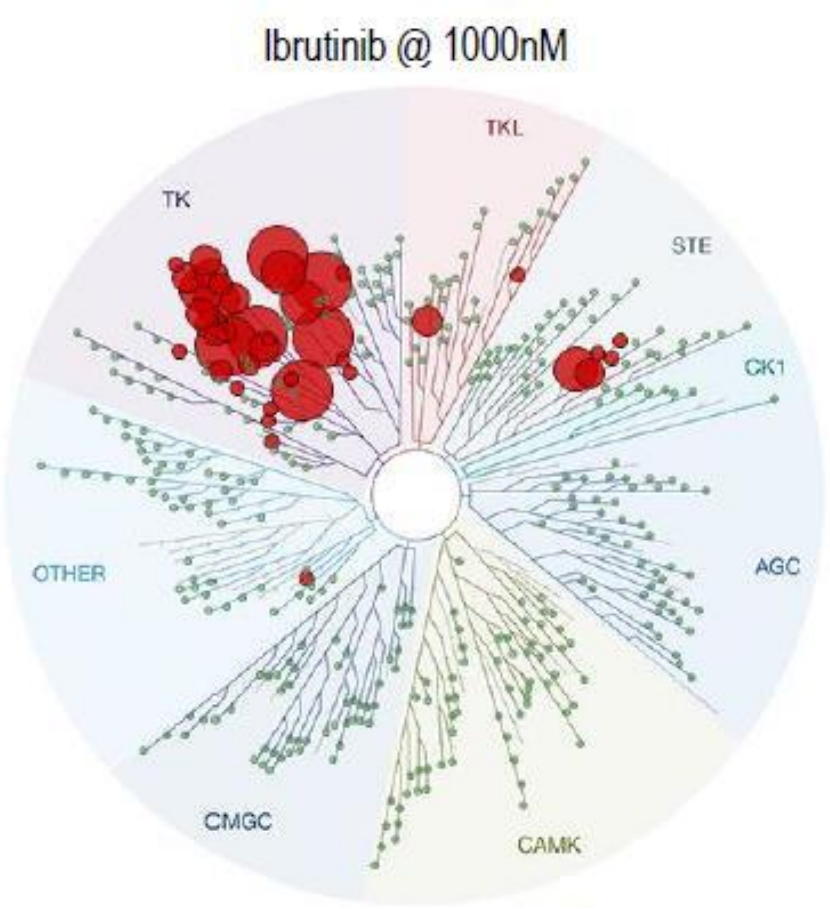

**Duvalisib**

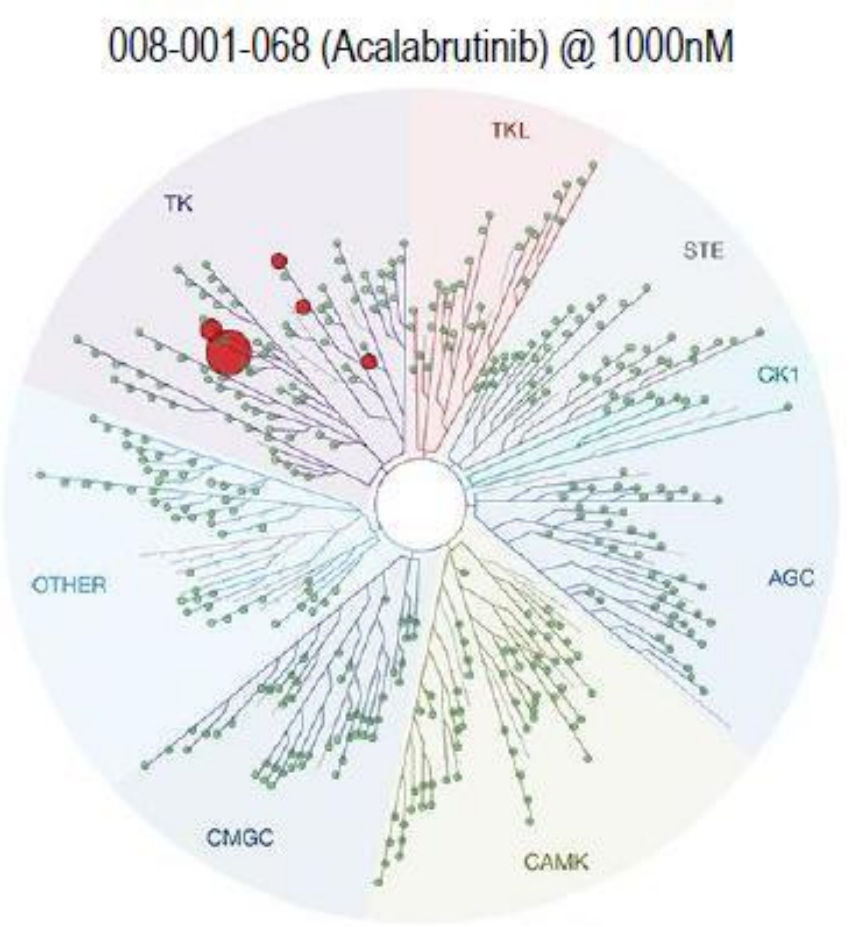



***DiscoverRx Kinome Scan against a panel of 442 kinases***

# By Comparison, BTK Inhibitors Have Substantially Different Levels of **Selectivity**

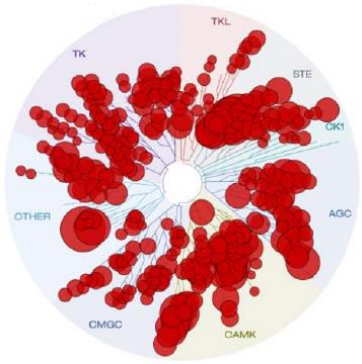
Does Anyone Doubt the More Selective Features of Acalabrutinib Don't Account for the Clinical Differences Between These Drugs?



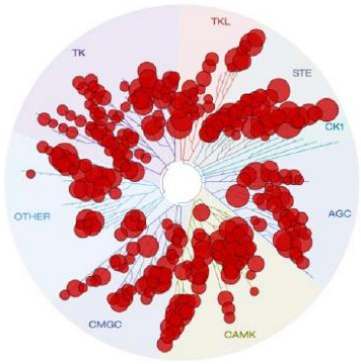



# KINOME PROFILES OF FLT3 INHIBITORS:

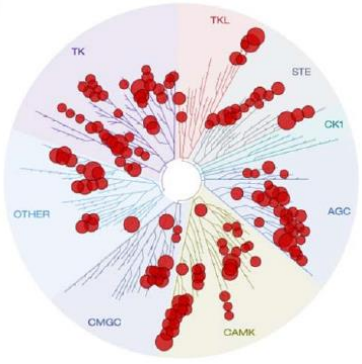
## SELECTIVITY EVOLUTION – DOES IT TRACK WITH IMPROVED CLINICAL APPLICATION?



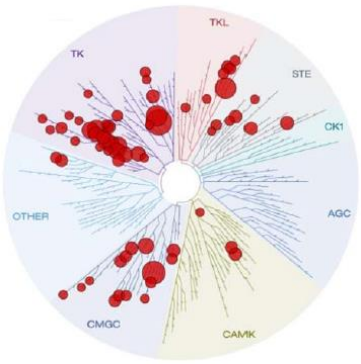

Staurosporine



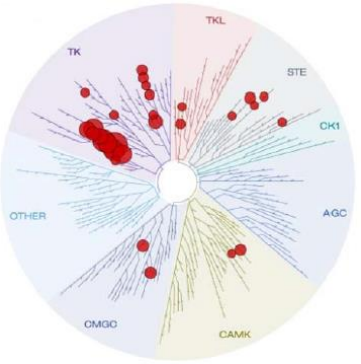

Lestaurtinib




Midostaurin




Sorafenib




Quizartinib

FDA Approved April 2006

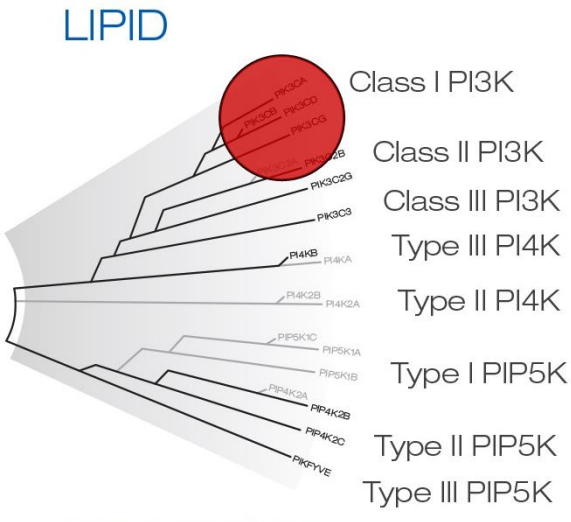
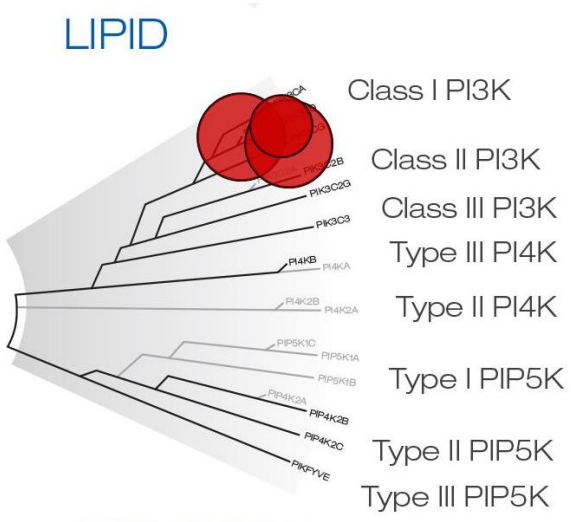
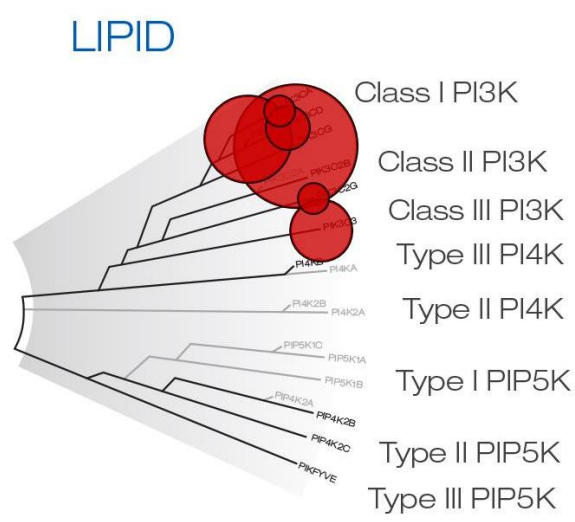
FDA Approved April 2017

Registration Studies underway 2016

Adapted from Davis et al; *Nat Biotechnology* 2011; 29(11):1046-1051

Courtesy Mark Levin, MD, PHD - Hopkins

# KINOME SCAN FOCUS ON PI3K ONLY – DIRECT COMPARISON OF SPECIFICITY

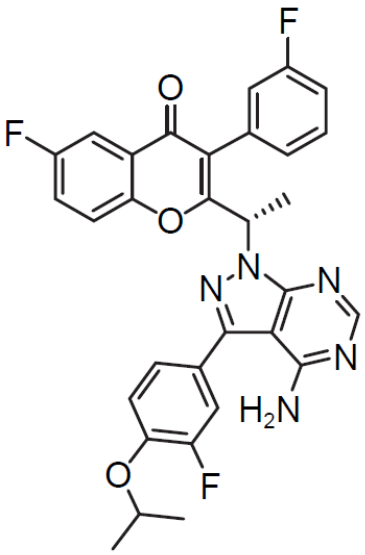
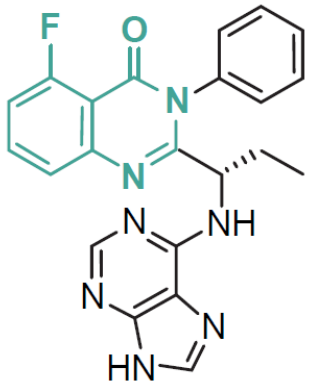
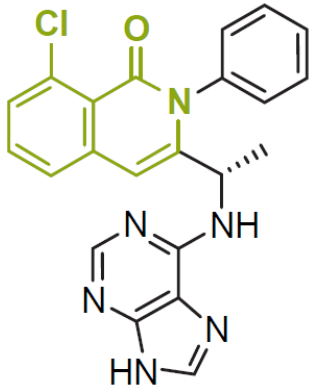
| Umbralisib | Idelalisib | Duvelisib |
|---|---|---|
|  |  |  |



Is it possible these subtle differences explain some of the clinical observations?

*DiscoverRx Kinome Scan*

# Structures and Dissociation Constants (Kd) Against Class I PI3K Isoforms of Umbralisib (TGR-1202), Idelalisib, and Duvelisib

| | TGR-1202 | Idelalisib | Duvelisib |
|---|---|---|---|
| |  |  |  |
| **Isoform** | **$K_d$ (nM)** | | |
| **PI3Kα** | >10,000 | 600 | 40 |
| **PI3Kβ** | >10,000 | 19 | 0.89 |
| **PI3Kγ** | 1400 | 9.1 | 0.21 |
| **PI3Kδ** | 6.2 | 1.2 | 0.047 |

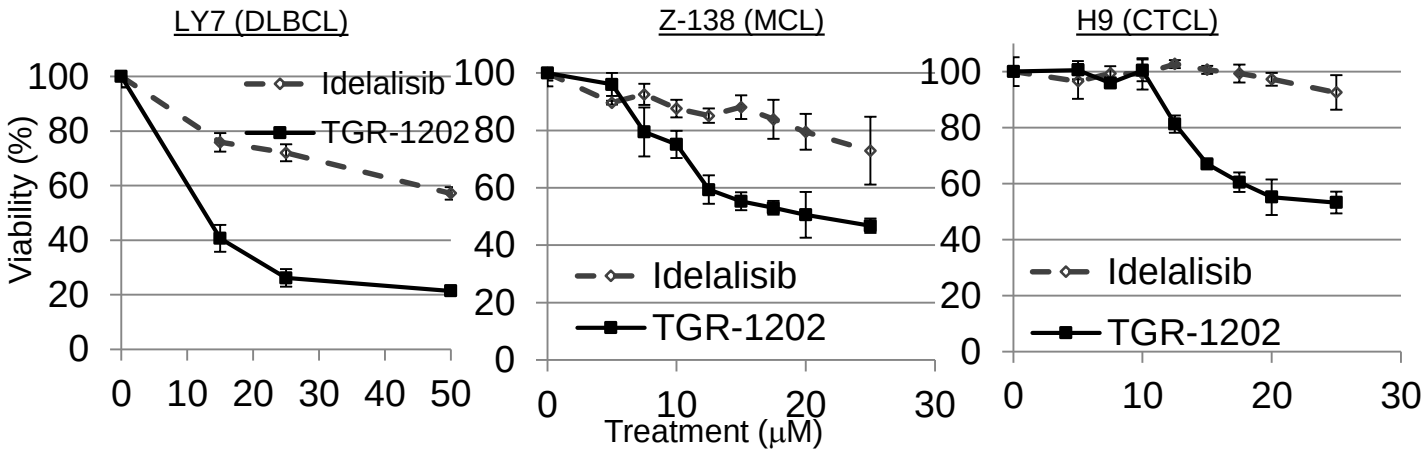
# Comparison of Pharmacologic and Pharmacodynamic Features Across the PI3K Inhibitors

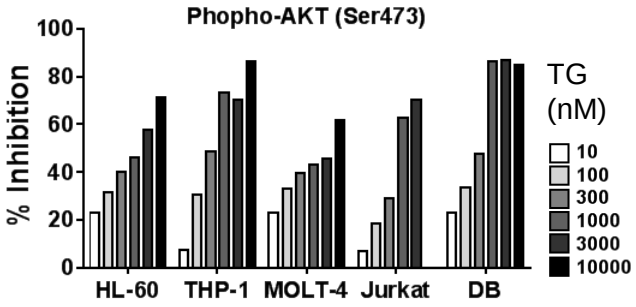
| | Umbralisib | Idelalisib | Duvelisib |
|---|---|---|---|
| **Kd PI3K-delta (nM)** | 6.2 nM | 1.2 nM | 0.047 nM |
| **Enzyme $IC_{50}$ for PI3k-δ (nM)** | 22.23[1] nM | 8 nM | 2.5[2] nM |
| **Whole Blood Assay $IC_{50}$ (nM) FcεR1 induced CD63 expresssion** | 67 | 65 | 78 |
| **Reported Cmax** | ~9 μM | ~6.5 μM | ~3.5 μM |
| **Reported AUC (ng*h/mL)** | 91,000 | 13,800 | 8,129 |

A 3-log fold difference between the IC50 and plasma concentrations

***Massive Excess of Drug Concentration Likely Make Differences in Potency Insignificant***

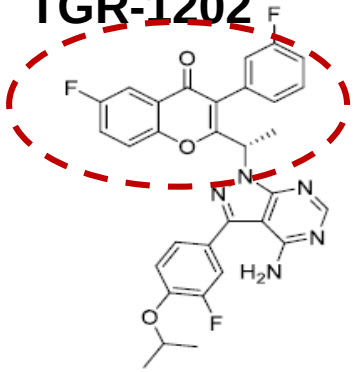
# While Idelalisib, Duvelisib & TGR-1202 Are Comparable Across Many Cell Lines – TGR-1202 Is Superior in a Few ……Why?



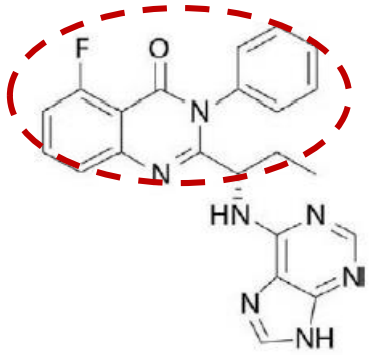




**Phospho-AKT Inhibition a Relative Constant Across All Cell Lines Studied**

**TGR-1202**

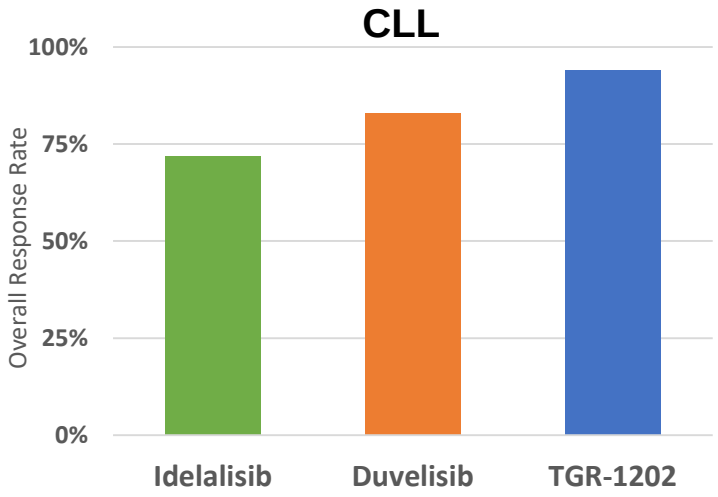


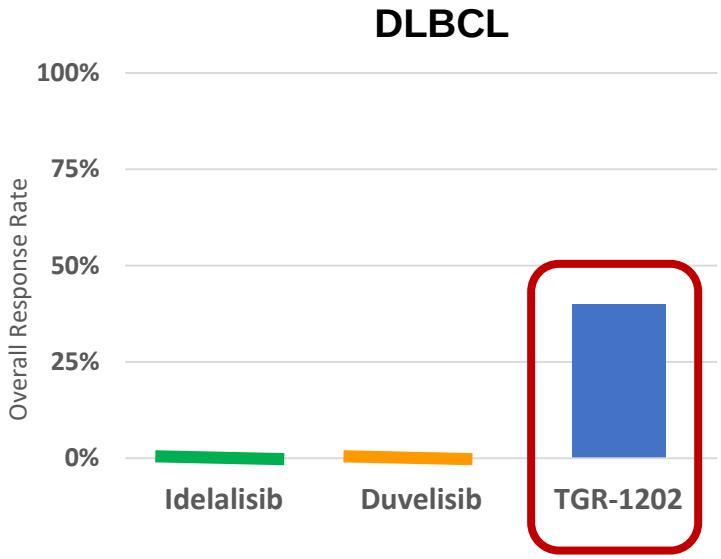
**Idelalisib**

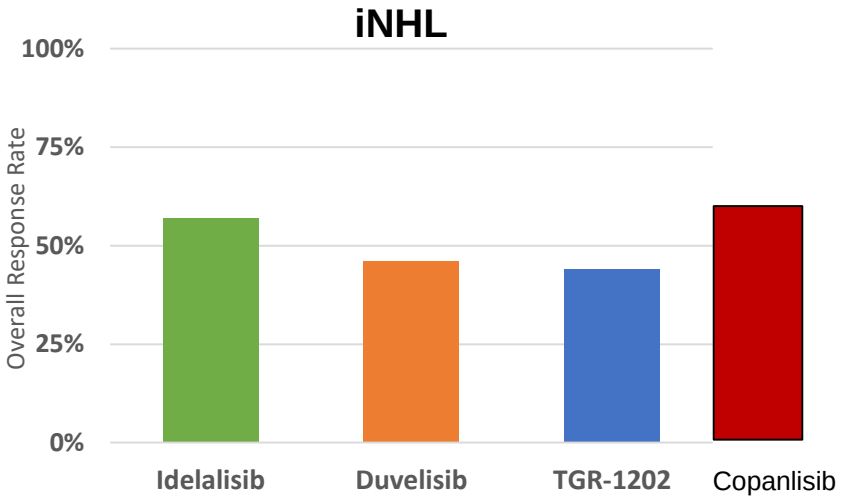


Deng et al., BLOOD, 2016

# Clinically the PI3K Inhibitors Appear to Have Comparable Activity Across CLL and iNHL



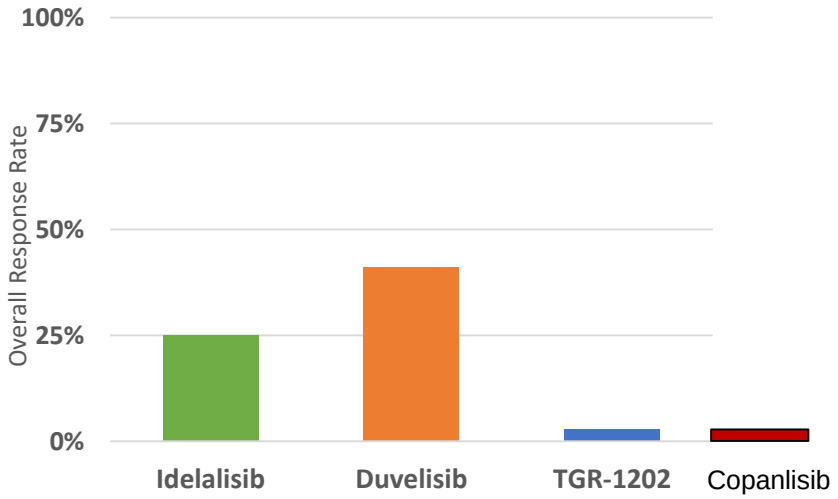




- Comparable activity across CLL and iNHL
- More activity seen in DLBCL with Umbralisib
- Small numbers across multiple studies so lots of population variability.

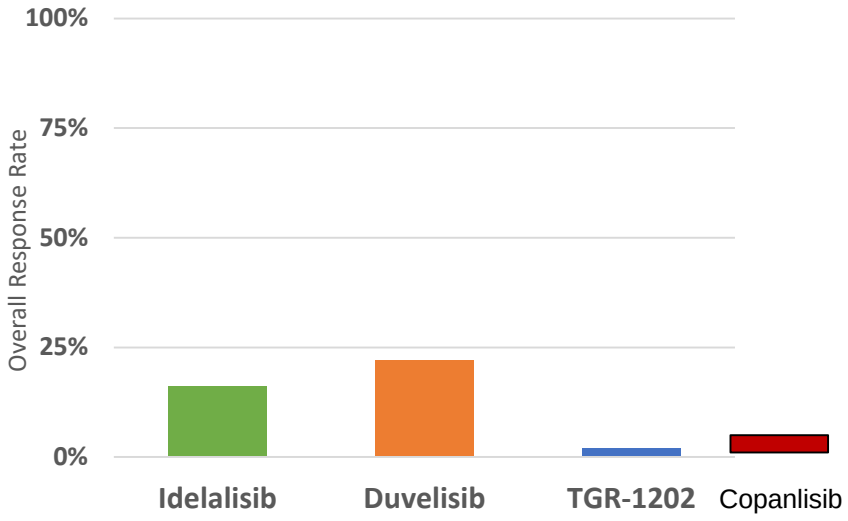

Brown et al, iwCLL 2013
O'Brien et al, ASH 2014
O'Connor et al, ASH 2015
Gopal et al, NEJM 2014
Infinity PR, 2016
O'Connor et al, EHA 2016
Westin et al, 2014
O'Connor et al, EHA 2016

# …..Though There are Substantial Differences in Tolerability Across the PI3K Inhibitors

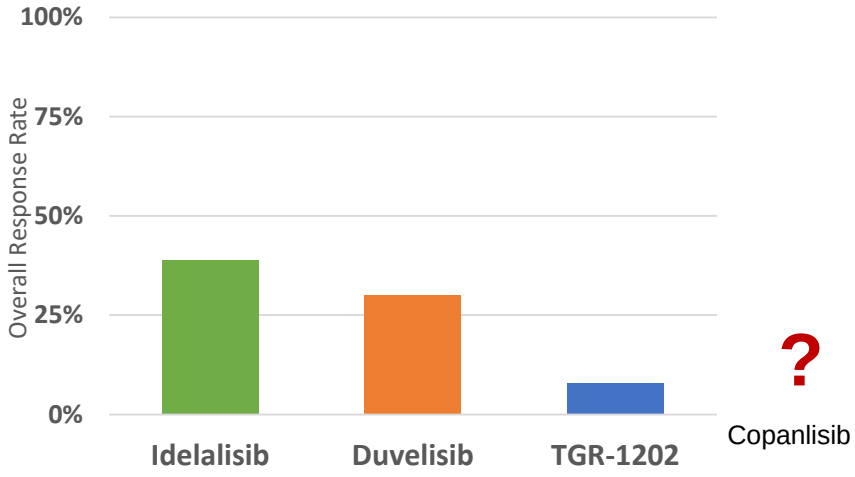
## Grade 3 and 4 Hepatotoxicity (LFT elevations)




## Grade 3 or 4 Diarrhea & Colitis




## Discontinuations Secondary to AE




- Reduced incidence of hepatic toxicity with TGR1202 & copanlisib
- Reduced gastrointestinal toxicity with TGR1202 & copanlisib
- Fewer discontinuations due to AE with TGR1202

Brown et al, iwCLL 2013; O'Brien et al, ASH 2014; O'Connor et al, ASH 2015; Gopal et al, NEJM 2014; Infinity PR, 2016; O'Connor et al, EHA 2016; Jones et al, ASCO 2016; Coutre et al, 2015; Flinn et al, Blood 2014;

| Adverse Reaction | Copanlisib (N= 168*) | | |
|---|---|---|---|
| | All Grades | Grade 3 N (%) | Grade 4 N (%) |
| **Hypergylcemia** | 90 (54%) | 56 (33%) | 10 (6%) |
| **Leukopenia** | 61 (36) | 20 (10%) | 26 (15%) |
| **Neutropenia** | 53 (32%) | 16 (10%) | 26 (15%) |
| **Thrombocytopenia** | 37 (22%) | 12 (7%) | 2 (1%) |
| **Reduced strength** | 61 (36%) | 6 (4%) | 0 |
| **Diarrhea** | 60 (36) | 8 (5%) | 0 |
| **Nausea** | 43 (26%) | 1 (<1%) | 0 |
| **Stomatitis** | 24 (14%) | 3 (2%) | 0 |
| **Vomiting** | 21 (13%) | 0 | 0 |
| **Hypertension** | 59 (35%) | 46 (27%) | 0 |
| **Lower respiratory tract infections** | 35 (21%) | 20 (12%) | 3 (2%) |
| **Rash** | 26 (15%) | 2 (1%) | 1 (<1%) |

**Occurring in > 10% of patients**

# Copanlisib Laboratory Abnormalities (20% of patients)

| Laboratory Parameter | Copanlisib Monotherapy (N = 168) | | |
|---|---|---|---|
| | Any Grade N (%) | Grade 3 N (%) | Grade 4 N (%) |
| **Anemia** | 130 (78%) | 7 (4%) | 0 |
| **Lymphopenia** | 126 (78%) | 43 (27%) | 4 (2%) |
| **Leukopenia** | 118 (71%) | 30 (18%) | 3 (2%) |
| **Thrombocytopenia** | 109 (65%) | 11 (7%) | 3 (2%) |
| **Neutropenia** | 104 (63%) | 20 (12%) | 25 (15%) |
| **Hyperglycemia** | 160 (95%) | 72 (43%) | 9 (5%) |
| **Hypertriglyceridemia** | 74 (58%) | 6 (5%) | 0 |
| **Hypophosphatemia** | 72 (44%) | 24 (15%) | 0 |
| **Hyperuricemia** | 42 (25%) | 40 (24%) | 2 (1%) |
| **Serum lipase increase** | 34 (21%) | 11 (7%) | 2 (1%) |

# Umbralisib Adverse Events Occurring >10% of Patients: Single Agent Phase 1

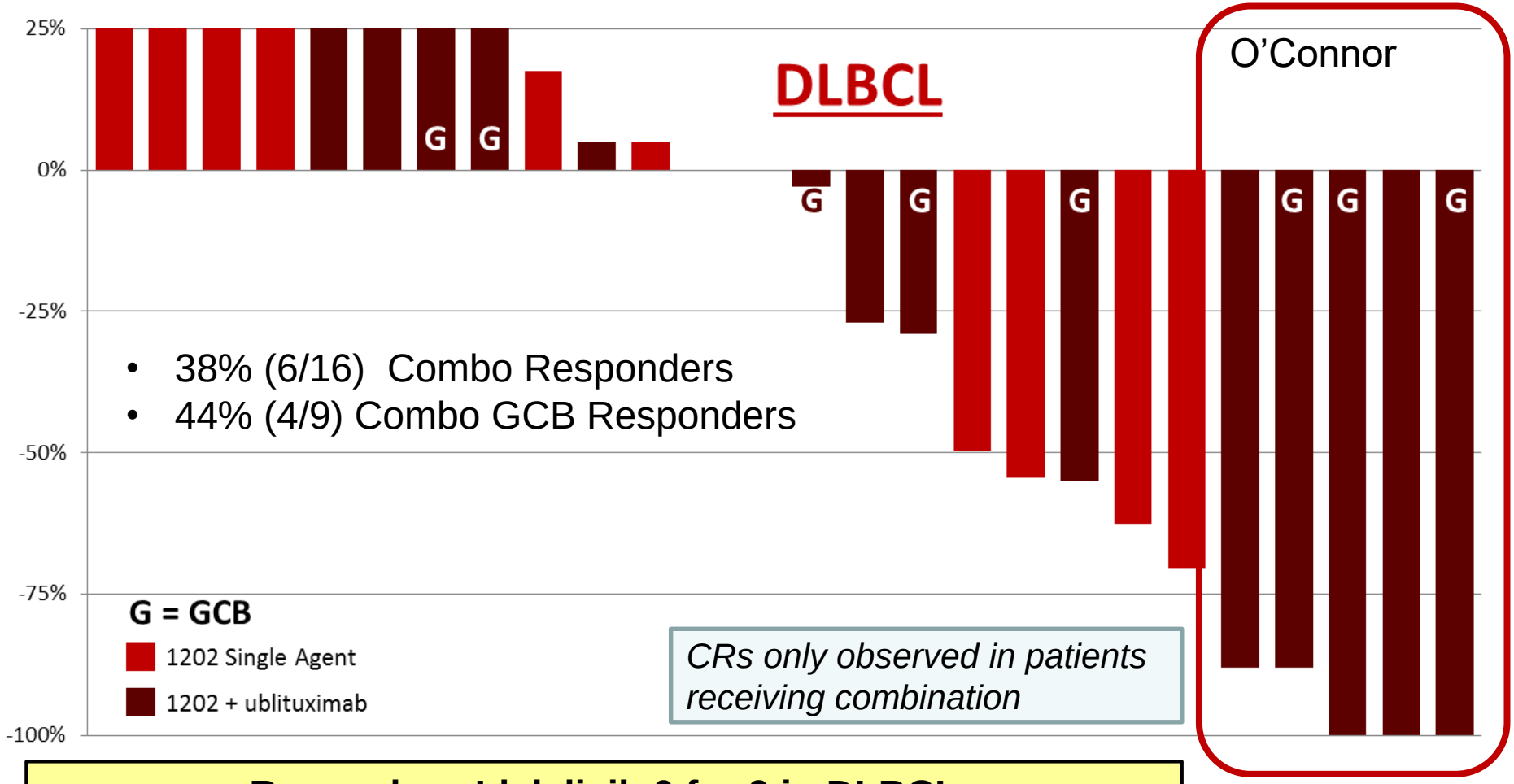
| Adverse event, n (%) | All grades | | Grades 3 or 4 | |
|---|---|---|---|---|
| **Diarrhea** | 39 | 43% | 3 | 3% |
| **Nausea** | 38 | 42% | 1 | 1% |
| **Fatigue** | 28 | 31% | 3 | 3% |
| **Vomiting** | 25 | 28% | - | - |
| **Cough** | 19 | 21% | - | - |
| **Headaches** | 19 | 21% | 2 | 2% |
| **Rash** | 17 | 19% | 4 | 4% |
| **Constipation** | 14 | 16% | 1 | 1% |
| **Decreased Appetite** | 14 | 16% | - | - |
| **Hypokalemia** | 14 | 16% | 4 | 4% |
| **Anemia** | 13 | 14% | 8 | 9% |
| **Neutropenia** | 13 | 14% | 12 | 13% |
| **Arthralgia** | 12 | 13% | - | - |
| **Dyspnea** | 12 | 13% | 4 | 4% |
| **Pyrexia** | 12 | 13% | - | - |
| **Upper Respiratory Tract Infection** | 12 | 13% | - | - |
| **Abdominal Pain** | 12 | 13% | - | - |
| **Dizziness** | 11 | 12% | - | - |
| **Insomnia** | 11 | 12% | - | - |
| **Thrombocytopenia** | 10 | 11% | 6 | 7% |
| **Abdominal Distension** | 10 | 11% | - | - |

- Grade 3 or 4 diarrhea 3%
- Essentially no cases of colitis
- No cases of pneumonitis
- No cases of Grade 5 toxicity
- Infections rare
- Median time on treatment now about 6 months

Burris et al. 2017. *Submitted*

# Integrated Analysis TGR-1202 Monotherapy & TGR-1202 + Ublituximab: DLBCL Efficacy

Patients Treated at "Higher Doses" of TGR-1202
Best Percent Change from Baseline in Disease Burden

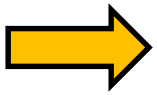


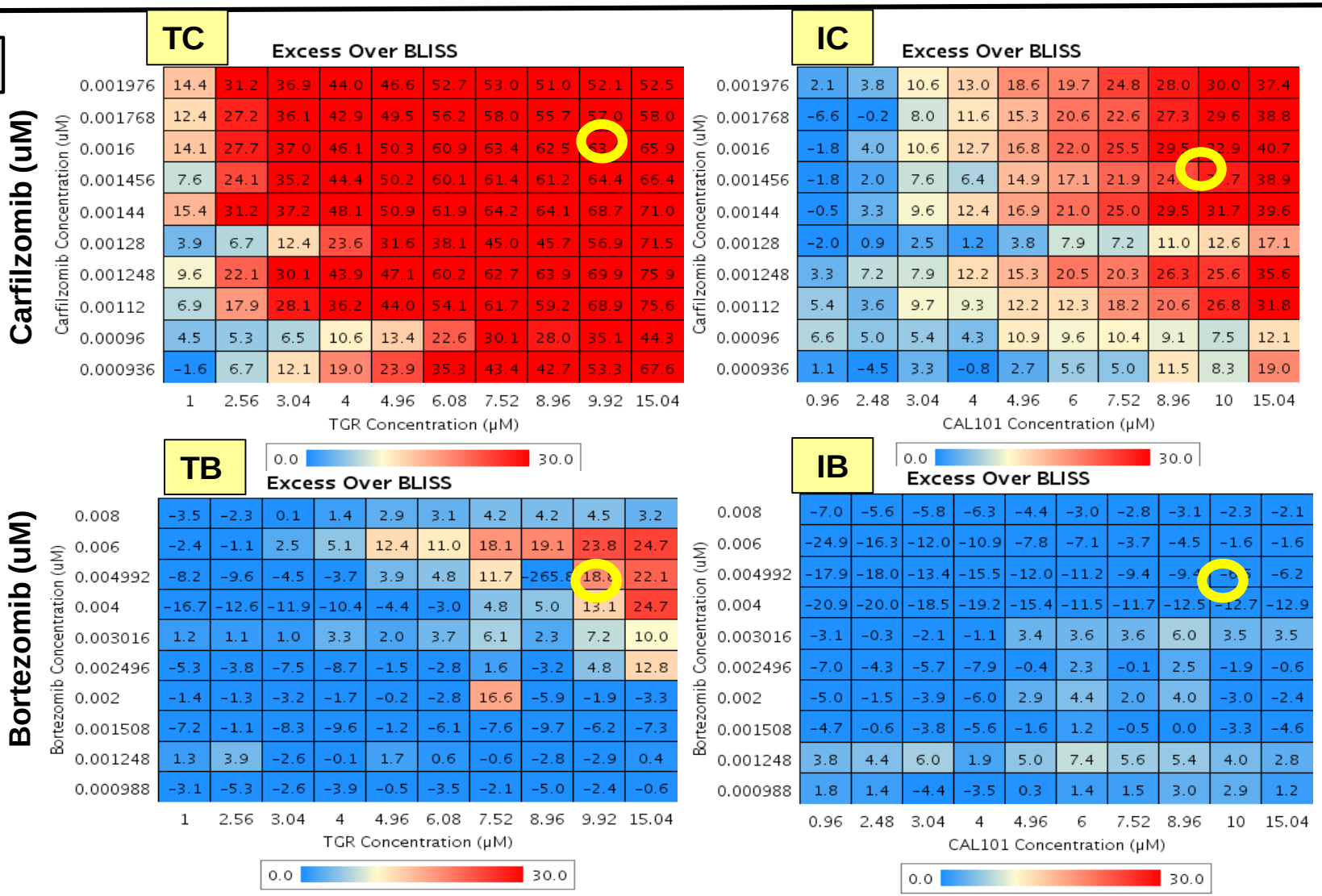

**Remember: Idelalisib 0 for 9 in DLBCL**

O'Connor et al, ASH 2015

# HTS of PI3K Inhibitors PLUS Reveal **Highly Synergistic Interactions** Unique to the TGR-1202 - Carfilzomib (TC) Combination

**LY-10**

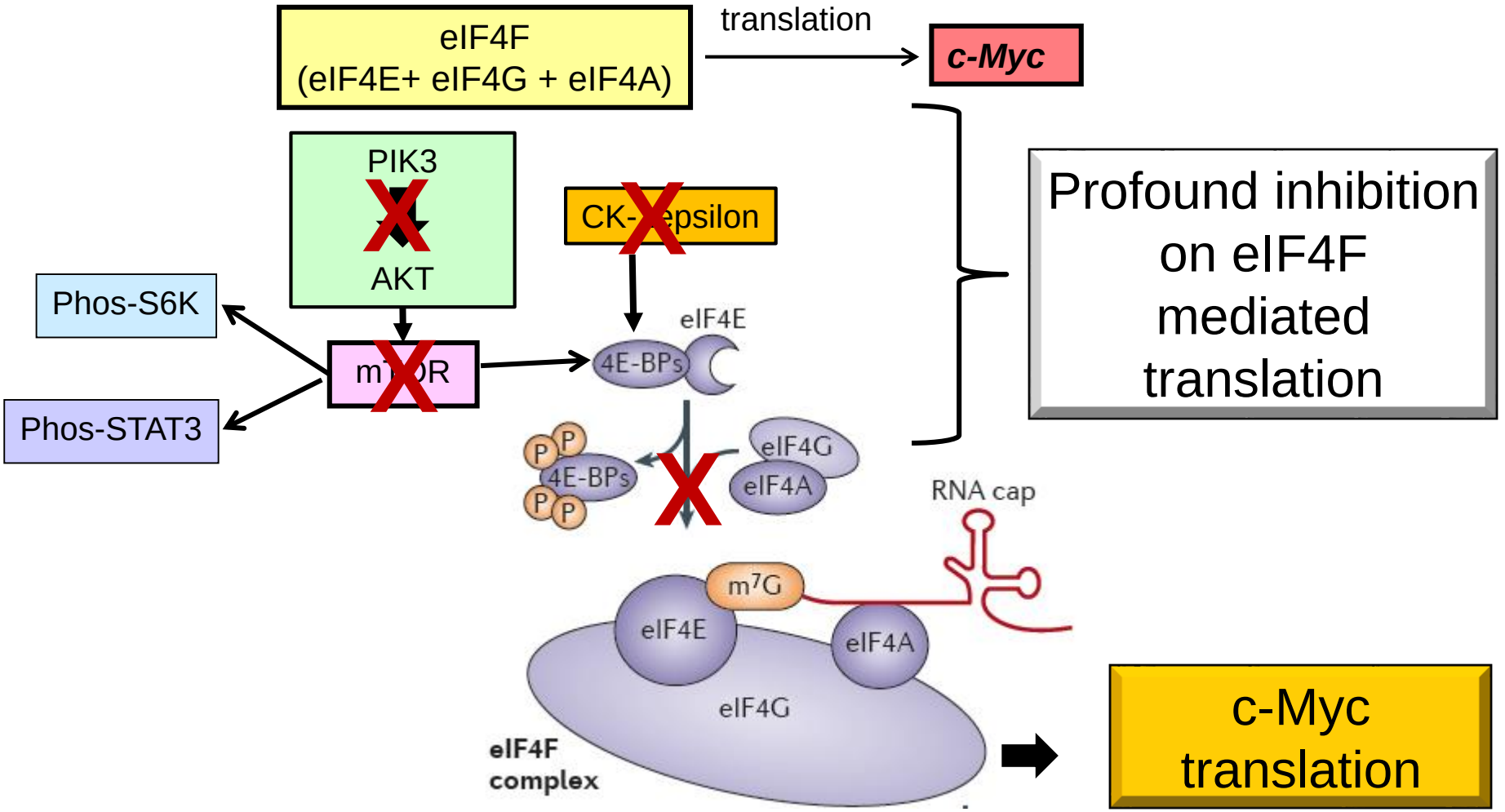





**TGR-1202 (uM)** **CAL-101 (uM)**

Similar Patterns Across Every Cell Line Evaluated [>10])

# Could the Complementary Effects on eIF4F Translation be Mediated Simultaneous CK-1 epsilon Inhibition?

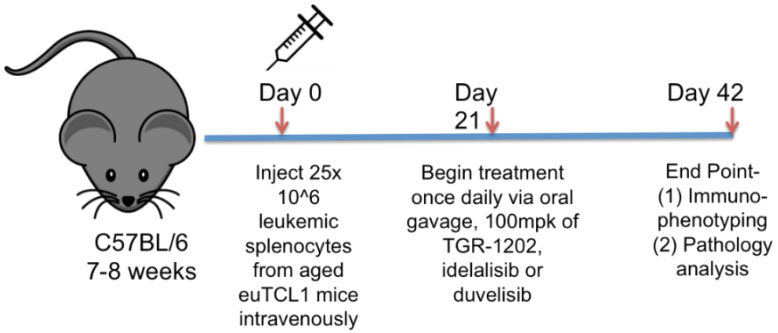


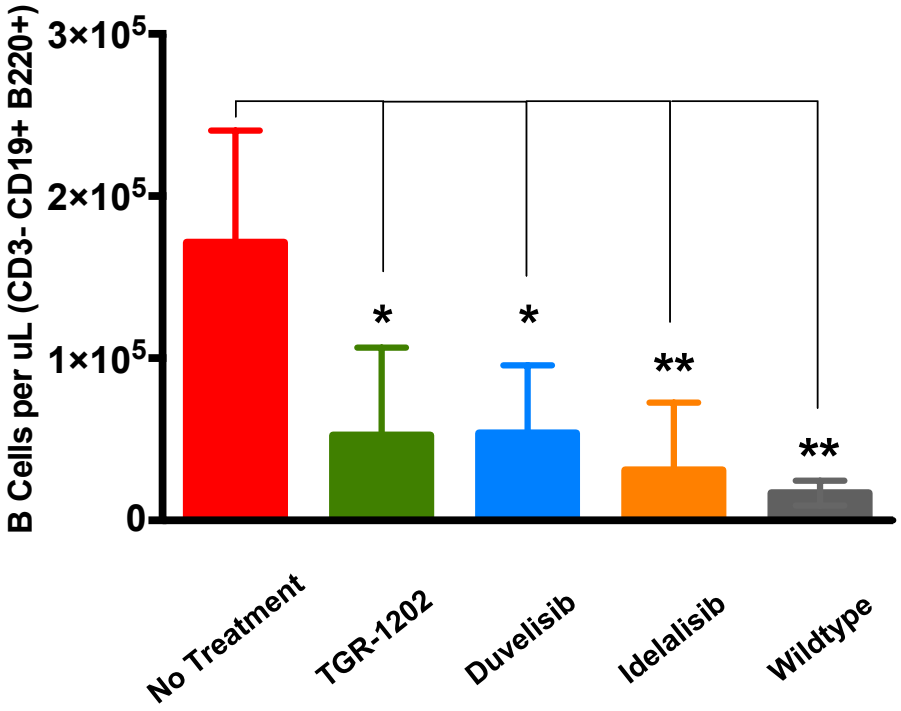

Pourdehnad PNAS 2013; Zhang Nature 2014; Hutter Leukemia 2012; Quy JBC 2013; Tang PLOS One 2014; Bhat et al., Nat Rev Drug Disc 2015

# What Do All The GEM Tell Us?

| Author | Model | Relevant Findings |
|---|---|---|
| Okkenhaug, et. al Science 2002 | KI Delta model | All other organs appeared to be normal, except mice developed a **mild inflammatory bowel disease** |
| Jou et. al. Molecular and Cell Biology 2002 | KO Delta model | **Did not observe** an inflammatory bowel disease in mice |
| Uno, et. al. Gastroenterology November 2010 | Double KI Delta – KO IL10 | A mild spontaneous colitis was demonstrated in Delta KI mouse. **Double** KI-KO mice developed **severe colitis** |
| Kaneda et. al Nature November 2016 | Role of Gamma | Macrophages lacking **PI3Kγ activity induced pro-inflammatory cytokines such as IL12 with a concomitant reduction in IL10** |
| Okkenhaug, et. al Blood 2007 | Double KI/KO Delta –Gamma | Mice lacking **PI3Kγ and PI3Kδ** function developed eosinophilic **inflammation in multiple mucosal organs** |

# Differential Regulation by PI3KΔI on T regs
## No Real Difference on Efficacy

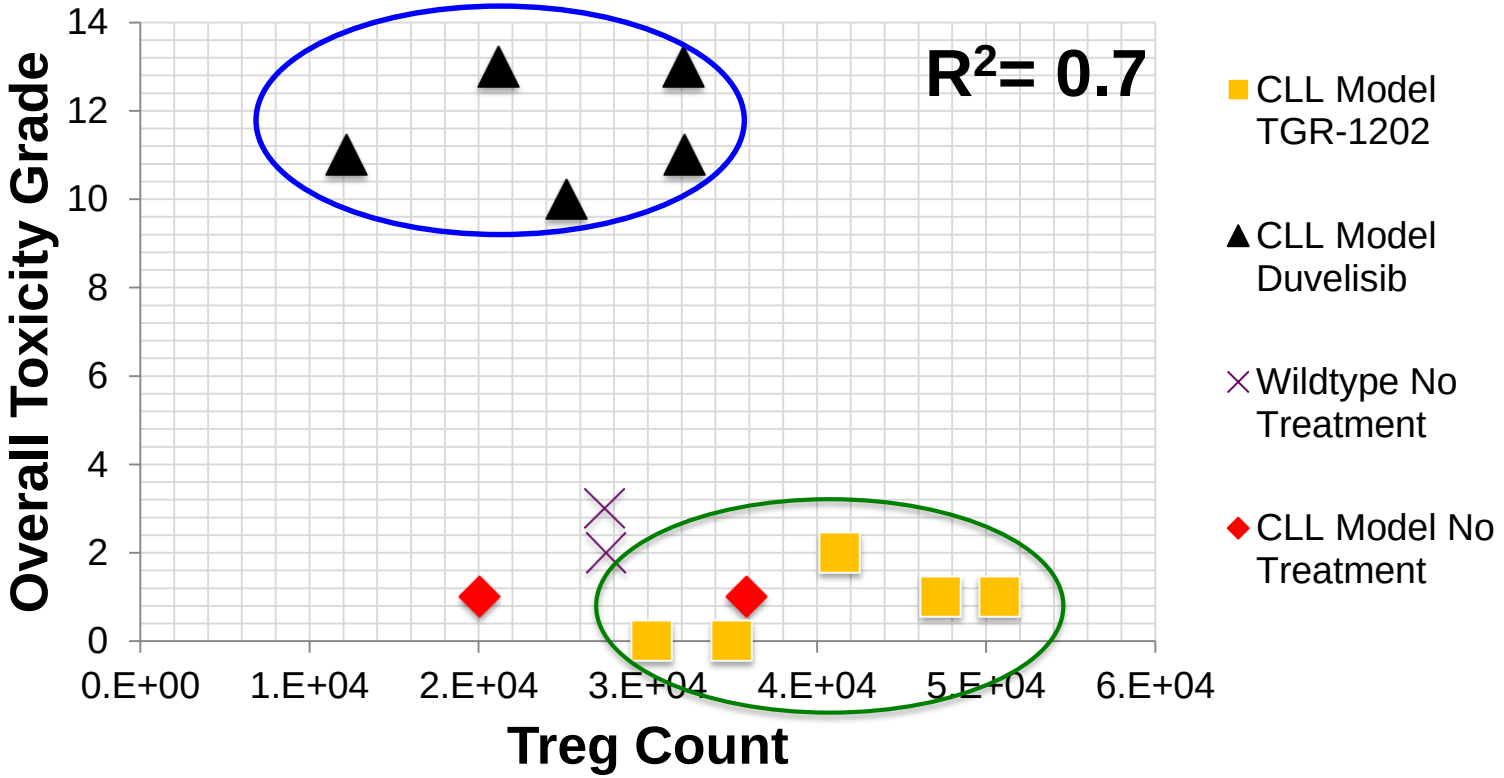



*In vivo* efficacy equivalent among cohorts treated with TGR-1202, duvelisib and idelalisib

Maharaj, Pinilla et al iwCLL 2017

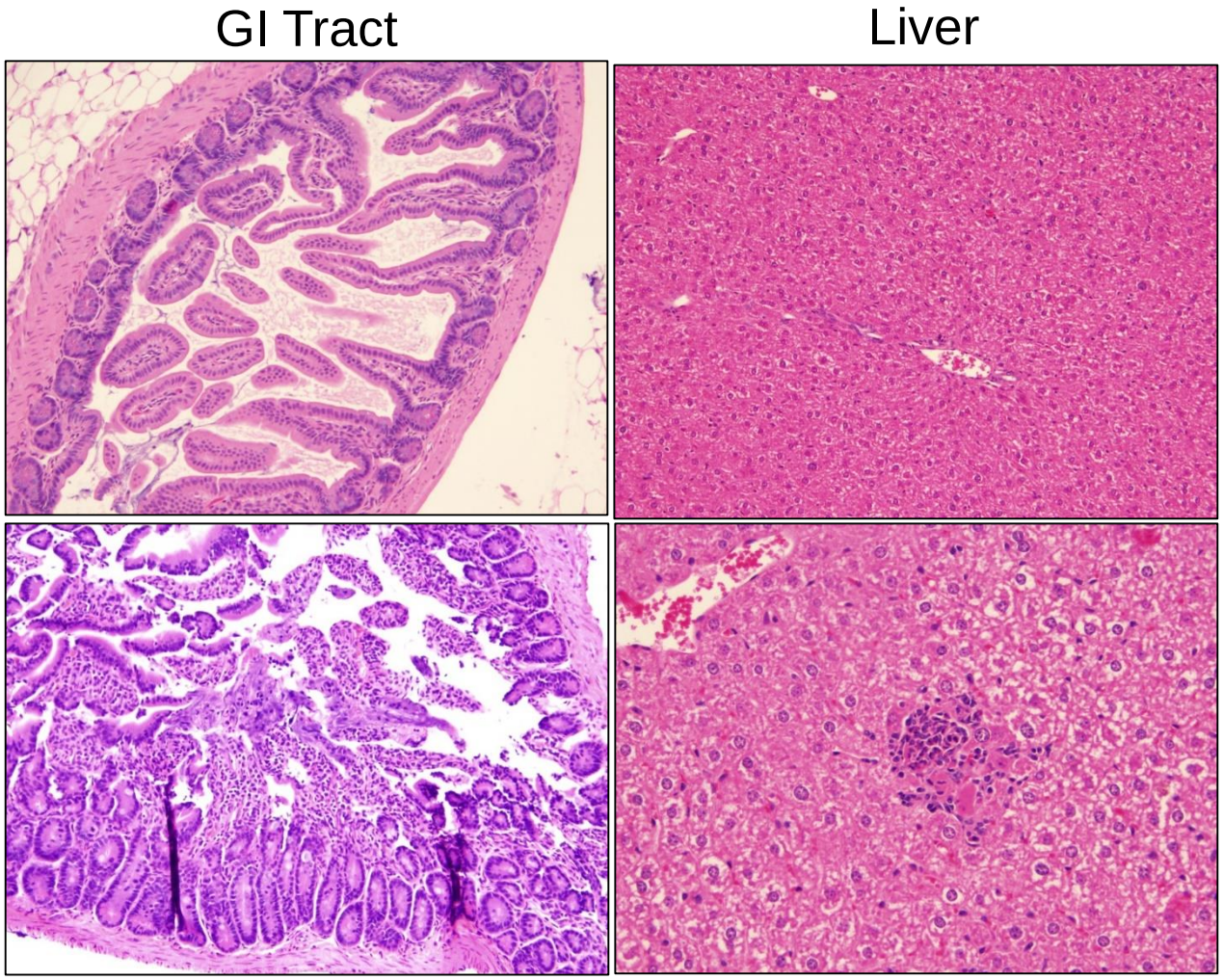
# DIFFERENTIAL REGULATION BY PI3KΔI ON T REGS




Correlation analysis – overall toxicity grade was determined after H&E stain using blinded histological analysis of liver and GI tract using known indicators of immune-mediated adverse events.

Maharaj, Pinilla et al
iwCLL 2017

# Differential Regulation by PI3KΔI on T regs




**Representative histologic findings.**

**Top Left**: bowel section from TGR-1202 treated mouse with normal appearance.

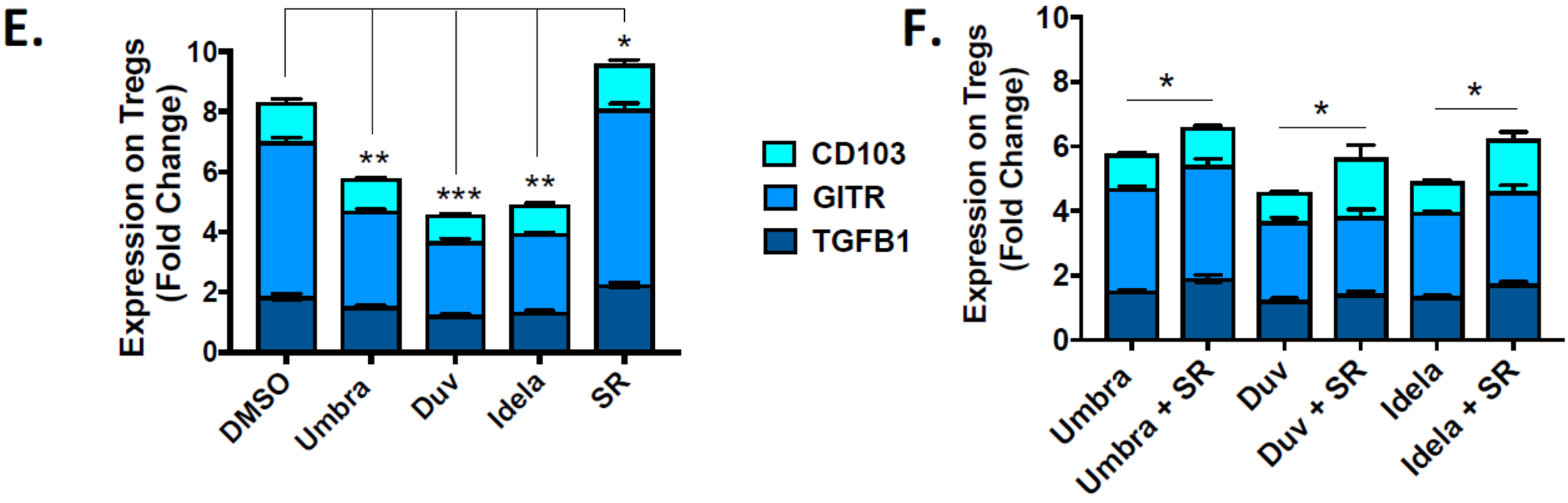
**Top Right**: liver section from TGR-1202 treated mouse with normal appearance.

**Lower Left**: Bowel section from duvelisib treated mouse with inflammation and denuded mucosa indicating GI tract toxicity.

**Lower right**: Liver section from duvelisib treated mouse with inflammation indicating immune-mediated hepatotoxicity

Maharaj, Pinilla et al
iwCLL 2017

# Effect of CK1e inhibition on murine CLL T cells




- Umbralisib uniquely inhibited CK1e in euTCL1 T cells dose-dependently
- CK1e inhibi1on by umbralisib may offer an explanation for less anti-Treg effects.

Maharaj, Pinilla et al ASH 2017

# CONCLUSIONS

- While generally selective, there are differences in the relative selectivity of agents in the class. The marked differences among the agents in the clinic are unlikely explained by differences in potency – **all are highly selective potent low nanomolar inhibitors of PI3K δ (+/– γ)**

- Is it possible other off-target (**PI3K +/– γ**) effects contribute to produce some of the GVHD like toxicities?

- **Complementary - synergistic - inhibition of other kinases (ex CK-1) may help explain some of the differences in toxicity and efficacy.**

- Drug : drug interactions (ex: with proteasome inhibitors), albeit limited, appear **markedly different** and requires further work to understand all contributing factors

- Clinically, there are differences in toxicity - in the preclinical setting there are marked differences on T-regs and cytokine effects

- A significant investment in appreciating differences at the SCIENTIFIC level is required in order to leverage the advantages of the available agents

# THANK YOU!


COLUMBIA UNIVERSITY MEDICAL CENTER

NCI CCC
A Comprehensive Cancer Center Designated by the National Cancer Institute

NewYork-Presbyterian
The University Hospital of Columbia and Cornell

TG Therapeutics

# TGR-1202 Clinical Safety & CLL Landscape Discussion

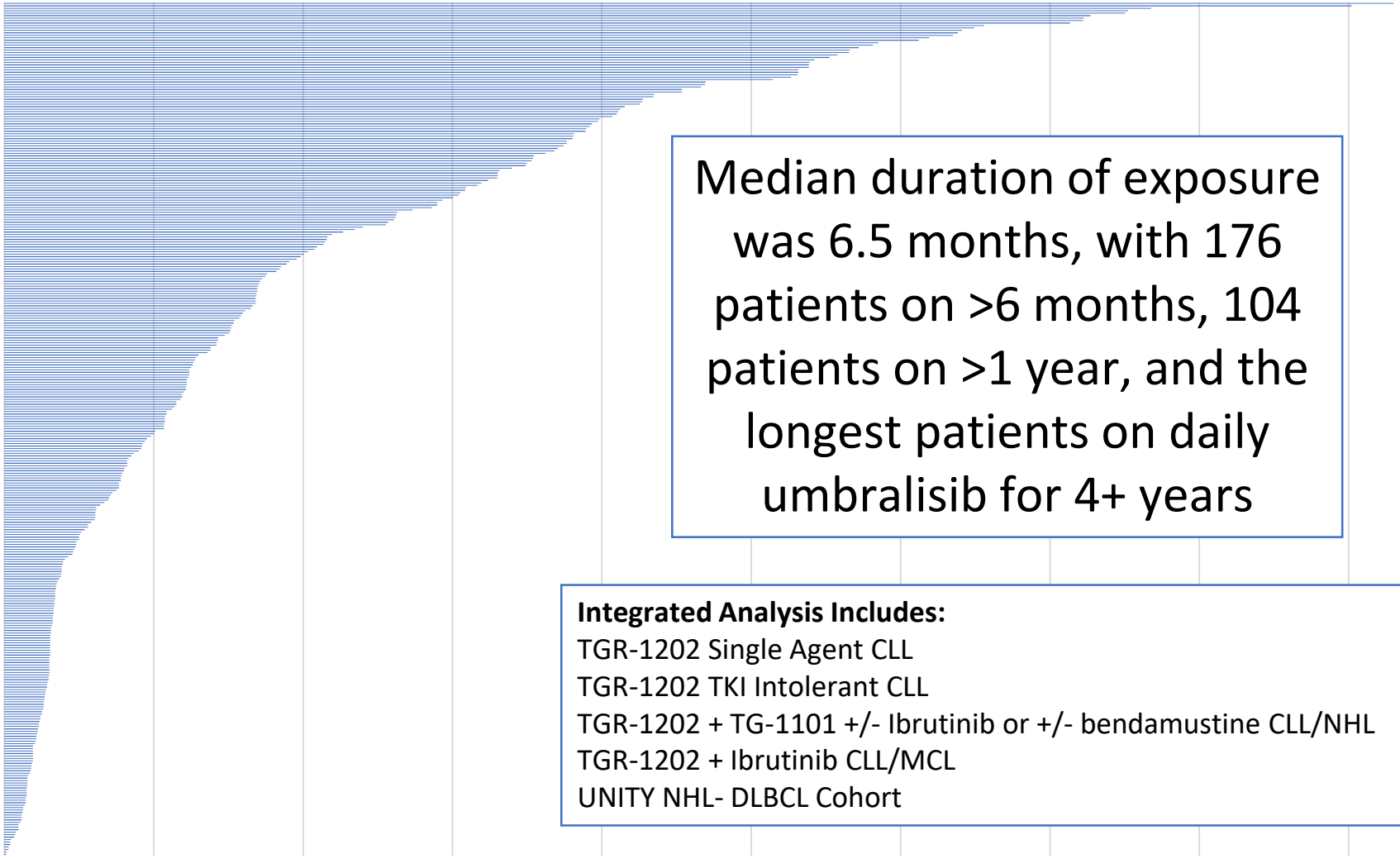

## Kathryn Kolibaba, MD
## Northwest Cancer Specialists/ US Oncology


UNITY CLL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PHASE 3 TRIAL IN CLL

UNITY NHL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PREVIOUSLY TREATED NHL PATIENTS

# TGR-1202 Integrated Analysis

## Duration on Therapy




Median duration of exposure was 6.5 months, with 176 patients on >6 months, 104 patients on >1 year, and the longest patients on daily umbralisib for 4+ years

**Integrated Analysis Includes:**
TGR-1202 Single Agent CLL
TGR-1202 TKI Intolerant CLL
TGR-1202 + TG-1101 +/- Ibrutinib or +/- bendamustine CLL/NHL
TGR-1202 + Ibrutinib CLL/MCL
UNITY NHL- DLBCL Cohort

Davids et al, ASH 2017

# Results

## Safety

### Grade 3/4, All Causality, Adverse Events Occurring in >2% of Patients

| | Study 101 Umbra Alone N=90 | Study 201 Umbra Alone N=33 | Study 105 Umbra + Ibrutinib N=32 | Study 103 Umbra + Ubli (U2) N=75 | Study 103 U2 + Ibrutinib N=38 | Study 103 U2 + Benda N=33 | Study 205 U2 or Umbra N=46 | TOTAL N=347 |
|---|---|---|---|---|---|---|---|---|
| Neutropenia | 11% | 18% | 13% | 28% | 18% | 24% | 2% | **16%** |
| Anemia | 8% | 3% | 9% | 4% | 3% | 6% | 4% | **5%** |
| Thrombocytopenia | 6% | 6% | 9% | 5% | 8% | 6% | 0% | **5%** |
| Diarrhea | 2% | 9% | 3% | 8% | 3% | 9% | 0% | **4%** |
| Pneumonia | 4% | 0% | 0% | 8% | 11% | 0% | 2% | **4%** |
| Dyspnea | 4% | 0% | 0% | 3% | 3% | 3% | 4% | **3%** |
| Hypokalemia | 4% | 3% | 3% | 3% | 0% | 9% | 0% | **3%** |
| Febrile Neutropenia | 3% | 9% | 0% | 4% | 3% | 0% | 2% | **3%** |

Davids et al, ASH 2017

# Results

## Safety

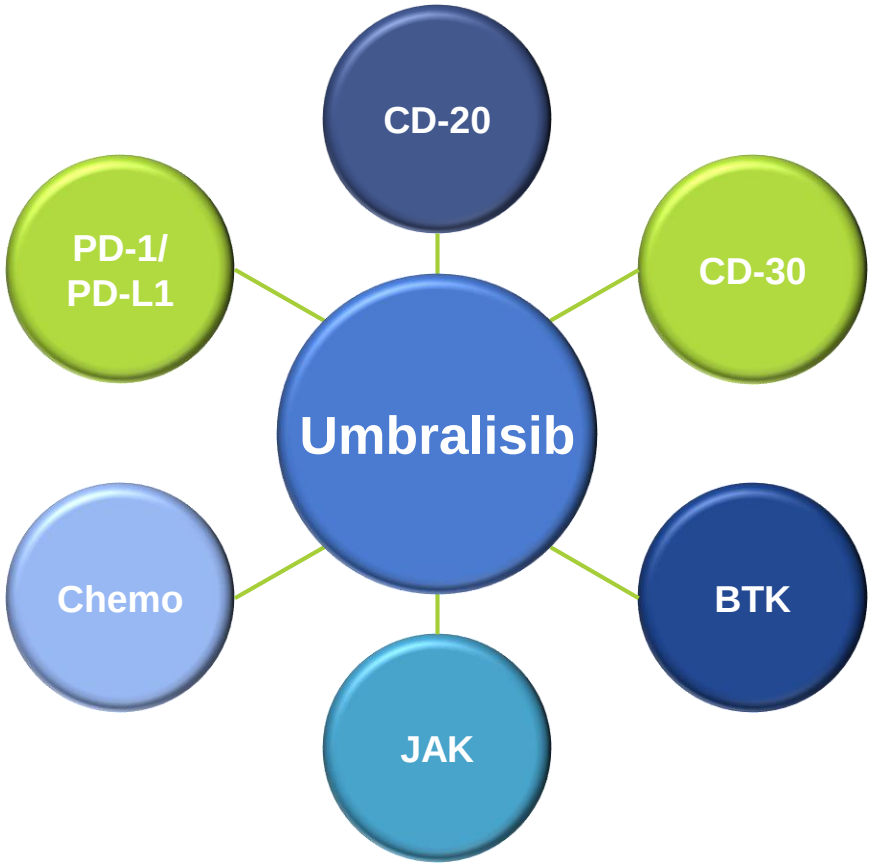
**Immune-mediated adverse events were infrequent:**

- transaminitis (9%; Gr.3/4 2%);
- colitis (<1.5%; Gr.3/4 <1%);
- pneumonitis (<1.5%; Gr.3/4 <0.5%)

Davids et al, ASH 2017

# Umbralisib = Unique
# Uniquely combinable PI3K delta inhibitor

- Limited CYP450 inhibition and overall tolerability profile allows for highly active combination regimens for a variety of indications in CLL and beyond




| Completed & Ongoing Combination Studies |
|---|
| ***Doublets*** |
| **TGR-1202 + ublituximab** |
| **TGR-1202 + ibrutinib** |
| **TGR-1202 + brentuximab vedotin** |
| **TGR-1202 + ruxolitinib** |
| ***Triplets*** |
| **TGR-1202 + TG-1101 + ibrutinib** |
| **TGR-1202 + obinutuzumab + Clb** |
| **TGR-1202 + TG-1101 + pembrolizumab** |
| **TGR-1202 + TG-1101 + bendamustine** |

# Oncology Treatment Pathways

Most centers have electronic decision tools/ treatment pathways to help recommend treatment options for patients

- **GOALS:** improve quality of care, and reduce cost of care
  - Adherence to pathways is a mark of high quality care monitored by payors and practices
- **PATIENT DATA ENTRY:** Diagnosis, biomarkers, stage of disease, number of previous treatments
- **DECISION TOOL:** provides recommended treatment options based on patient characteristics
  - NCCN guidelines for approved drugs
  - Ongoing clinical trials

# CLL Landscape

| | CLL PROJECTED TREATMENT LANDSCAPE | | | | | |
|---|---|---|---|---|---|---|
| **Front-Line** | FCR/ BR | TG-1101 + TGR-1202 *(UNITY-CLL)* | Ibrutinib or Ibrutinib +Gazyva | Acala + Gazyva | Venetoclax + Gazyva | Gazyva + CHL |
| **Relapsed/ Refractory** | BR<br><br>BR + Idela<br><br>R + Idela | TG-1101 + TGR-1202 *(UNITY-CLL)* | Ibrutinib or Ibrutinib +Gazyva | Ibrutinib + TG-1101 *(GENUINE)* | Venetoclax or Venetoclax + Rituxan | |

*FCR: Fludarabine Cyclophosphamide Rituxan; BR: Bendamustine Rituxan; Idela: Idelalisib; R:Rituxan; CHL: Chlorambucil*

# Ibrutinib Discontinuation

| Reason for ibrutinib 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** | **50.0** | **77.7** | **52.5** | **38.7** |
| CLL progression | 10.0 | 22.2 | 19.0 | 35.5 |
| Other/unrelated death | 10.0 | 0.0 | 12.0 | 12.9 |
| Physician or patient preference | 20.0 | 0.0 | 6.0 | 9.7 |
| RT DLBCL | 0.0 | 0.0 | 4.5 | 0.0 |
| Stem cell transplantation/ CAR T-cell | 0.0 | 0.0 | 3.5 | 3.2 |
| Financial concerns | 0.0 | 0.0 | 1.0 | 0.0 |
| Secondary malignancy | 10 | 0.0 | 1.0 | 0.0 |
| RT Hodgkin lymphoma | 0.0 | 0.0 | 0.5 | 0.0 |



**Mato et al, ASH 2016**

# Most Common Ibrutinib Related Toxicity

| Most common ibrutinib related toxicities as reasons for discontinuation | |
|---|---|
| **Relapsed CLL (%)** | **Front-line CLL (%)** |
| Atrial fibrillation (12.3) | |
| Infection (10.7) | Arthralgia (41.6) |
| Pneumonitis (9.9) | Atrial fibrillation (25) |
| Bleeding (9) | Rash (16) |
| Diarrhea (6.6) | |

| Median times to ibrutinib discontinuation stratified by toxicity | |
|---|---|
| Bleeding | 8 months |
| Diarrhea | 7.5 months |
| Atrial fibrillation | 7 months |
| Infection | 6 months |
| Arthralgia | 5 months |
| Pneumonitis | 4.5 months |
| Rash | 3.5 months |

- In the largest reported series on ibrutinb treated CLL patients, 40% of patients have discontinued ibrutinib during this observation period.
- Ibrutinib intolerance was the most common reason for discontinuation in all settings.

Mato et al, ASH 2016

# CLL Landscape

| | CLL PROJECTED TREATMENT LANDSCAPE | | | | | |
|---|---|---|---|---|---|---|
| **Front-Line** | FCR/ BR | TG-1101 + TGR-1202 *(UNITY-CLL)* | Ibrutinib or Ibrutinib +Gazyva | Acala + Gazyva | Venetoclax + Gazyva | Gazyva + CHL |
| **Relapsed/ Refractory** | BR<br><br>BR + Idela<br><br>R + Idela | TG-1101 + TGR-1202 *(UNITY-CLL)* | Ibrutinib or Ibrutinib +Gazyva | Ibrutinib + TG-1101 *(GENUINE)* | Venetoclax or Venetoclax + Rituxan | |

*FCR: Fludarabine Cyclophosphamide Rituxan; BR: Bendamustine Rituxan; Idela: Idelalisib; R:Rituxan; CHL: Chlorambucil*

TG Therapeutics

# FL, MZL & DLBCLCurrent Treatment Landscape & Future Plans for Novel Agents

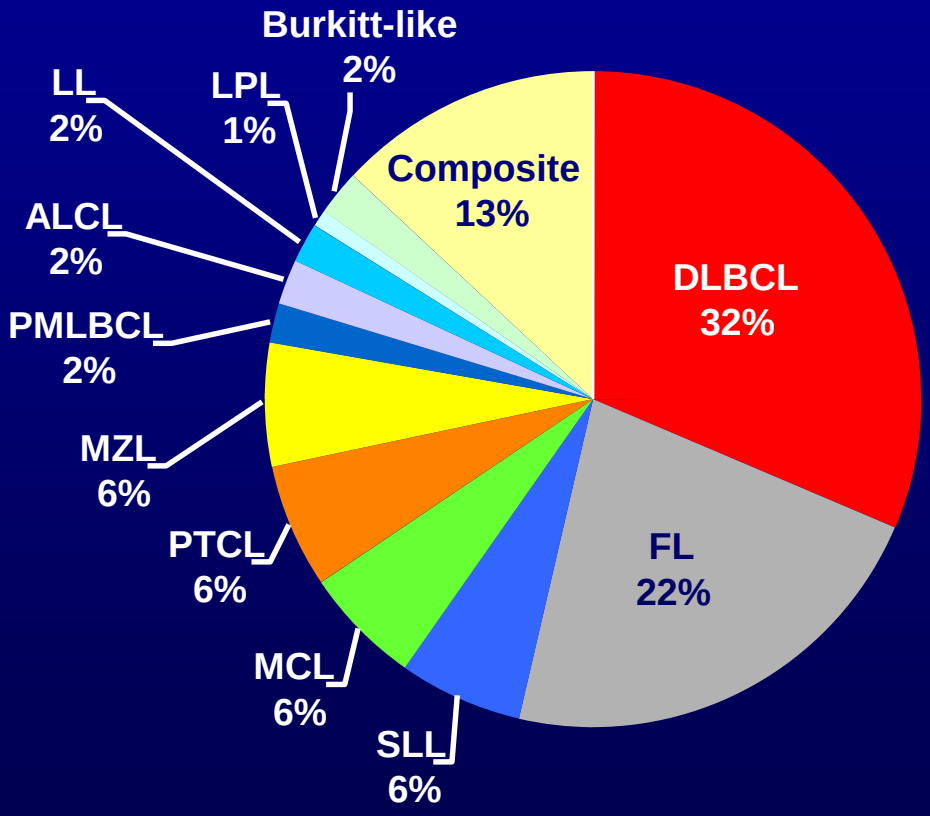

**Bruce D. Cheson, MD**
**Georgetown University Hospital**
**Lombardi Comprehensive Cancer Center**


UNITY CLL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PHASE 3 TRIAL IN CLL

UNITY NHL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PREVIOUSLY TREATED NHL PATIENTS

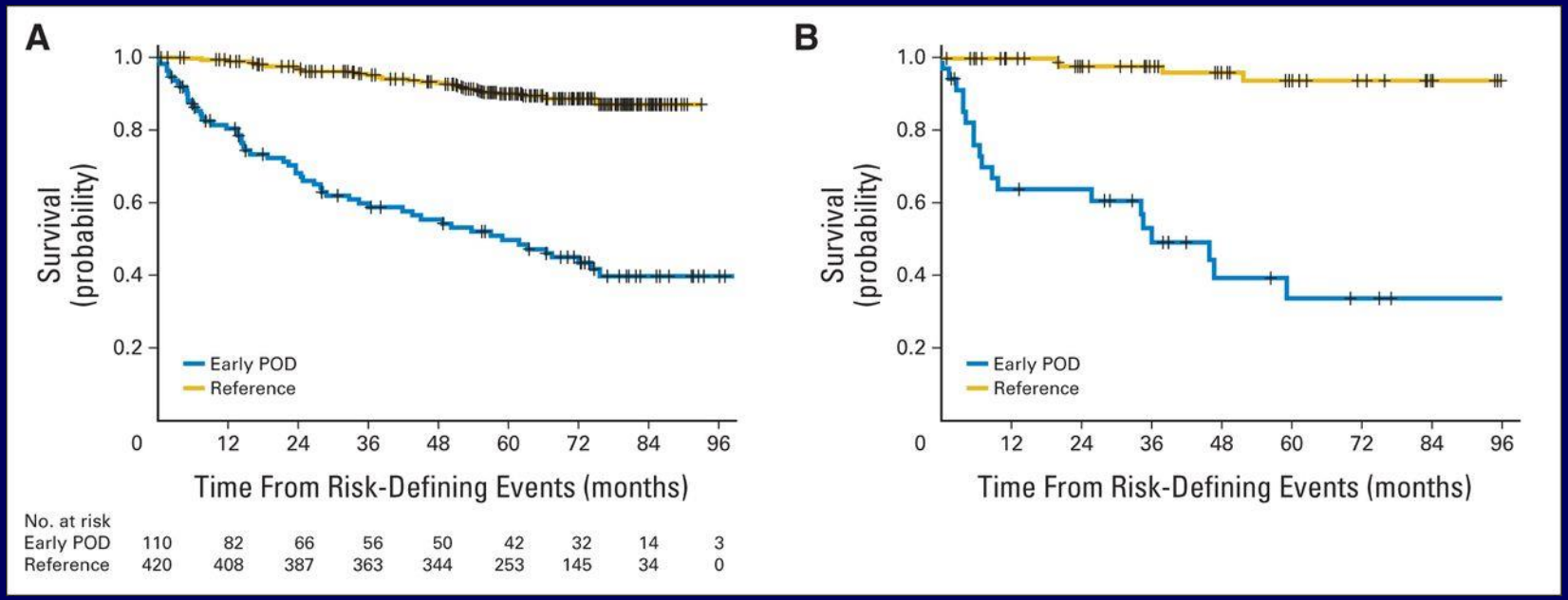
# Relative Incidence of NHL Subtypes

>72,000 cases in US in 2017




Armitage and Weisenburger. *J Clin Oncol.* 1998;16:2780.
Adapted from Seigel et al. 2017:76:7

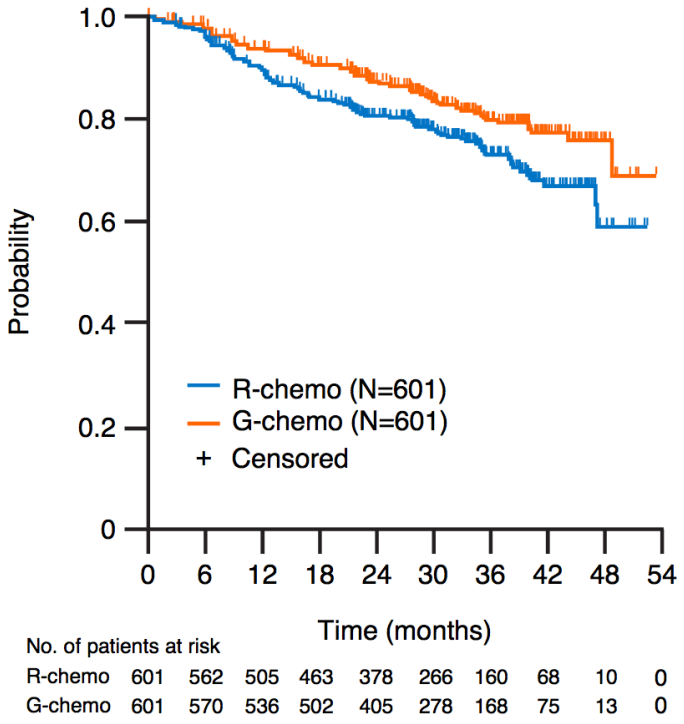
# OS from a risk-defining event after diagnosis in FL patients who received R-CHOP chemotherapy in the National LymphoCare Study group.




Carla Casulo et al. JCO 2015;33:2516-2522

# GALLIUM PFS

## INV-assessed PFS (FL; primary endpoint)



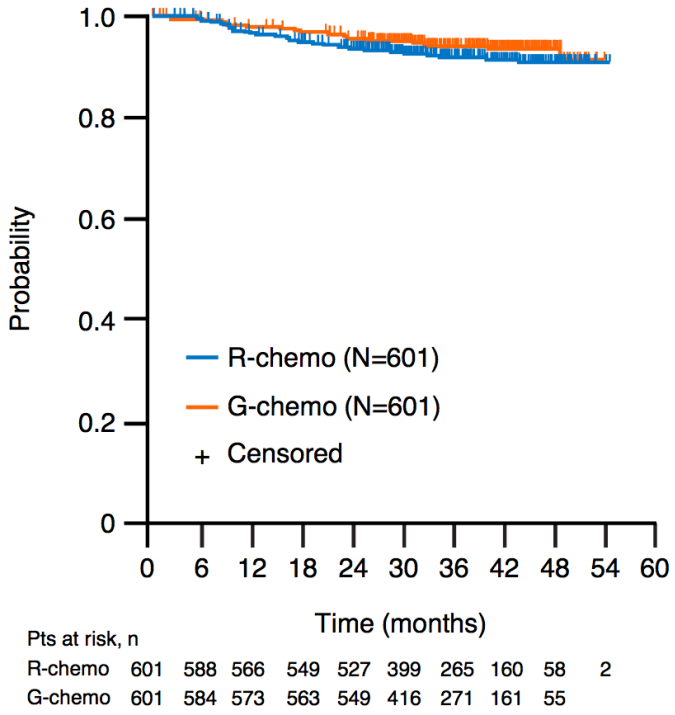

| | *R-chemo, n=601* | *G-chemo, n=601* |
|---|---|---|
| Pts with event, n (%) | 144 (24.0) | 101 (16.8) |
| 3-yr PFS, % (95% CI) | 73.3 (68.8, 77.2) | 80.0 (75.9, 83.6) |
| HR (95% CI), p-value* | 0.66 (0.51, 0.85), p=0.0012 | |

*Median follow-up: 34.5 months*

*Stratified analysis; stratification factors: chemotherapy regimen, FLIPI risk group, geographic region

# GALLIUM OS

## OS (FL)




| | *R-chemo, n=601* | *G-chemo, n=601* |
|---|---|---|
| Pts with event, n (%) | 46 (7.7) | 35 (5.8) |
| 3-yr OS, % (95% CI) | 92.1 (89.5, 94.1) | 94.0 (91.6, 95.7) |
| HR (95% CI), p-value* | 0.75 (0.49, 1.17), p=0.21 | |

*Median follow-up: 34.5 months*

*Stratified analysis; stratification factors: chemotherapy regimen, FLIPI risk group, geographic region

# Approved Treatment Options for R/R FL in the US

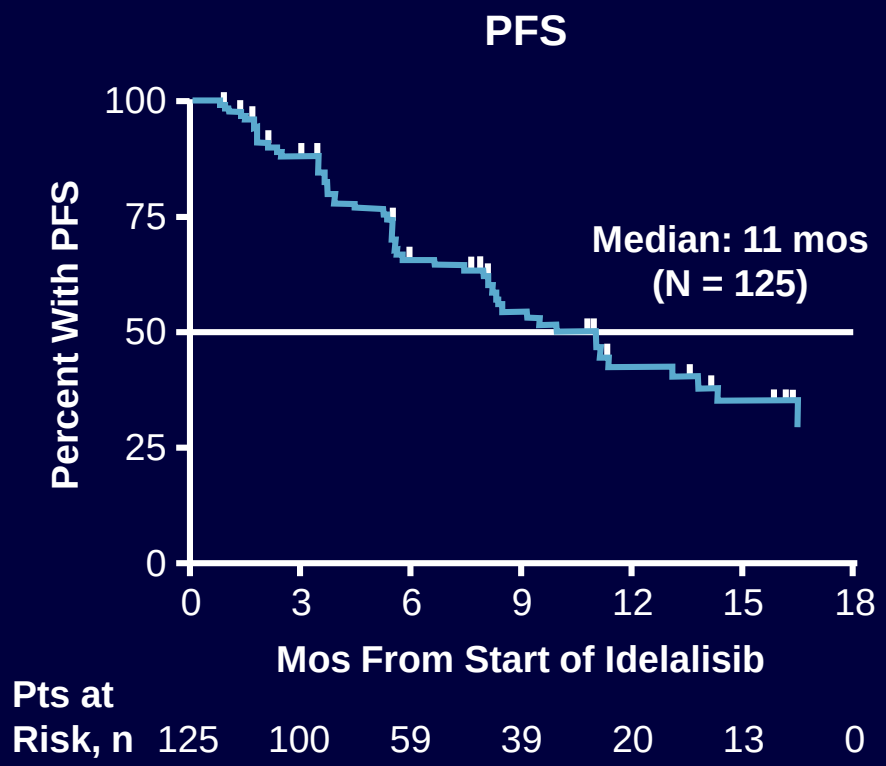
| Agent | Issues |
|---|---|
| $Y^{90}$-ibritumomab tiuxetan (Zevalin) | Eligibility critieria, MDS/AML; no survival benefit |
| Bendamustine; B-G | BR used upfront |
| Idelalisib | Toxicities |
| Copanlisib | Route/schedule |
| $R^2$ | Relapsed, not refractory; RELEVANCE |
| Allo BMT | Age of pts, toxicity, reimbursement |

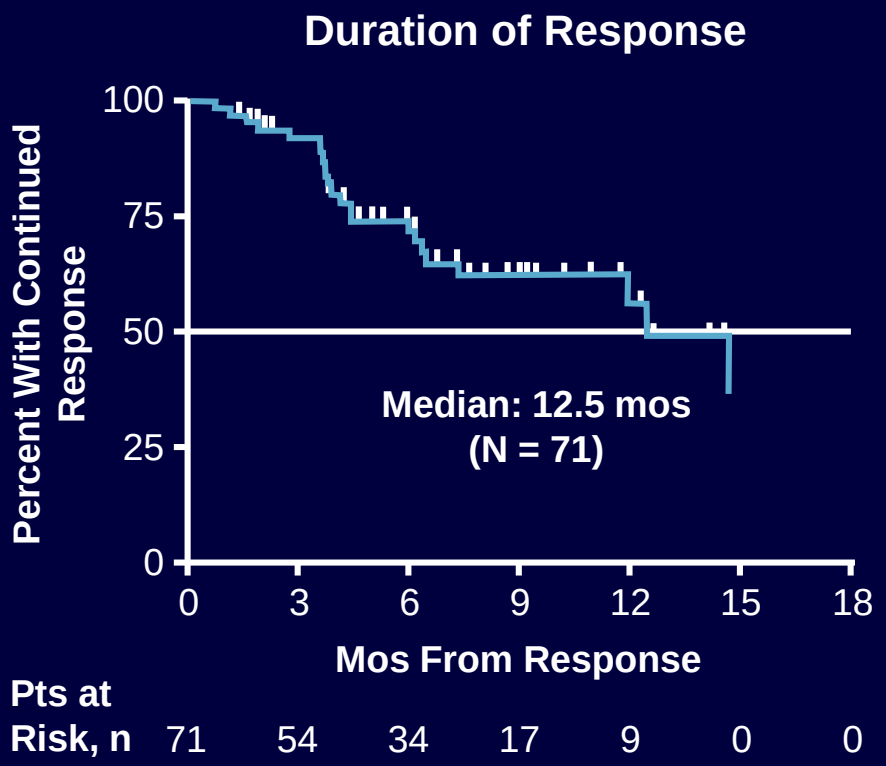
# Idelalisib Monotherapy in Refractory iNHL (Phase II): Responses

| Characteristic | Patients, n (%) (N = 125) |
|---|---|
| ORR, n (%) | 71 (57) |
| CR | 7 (6) |
| PR | 63 (50) |
| Minor response* | 1 (1) |
| SD | 42 (34) |
| PD | 10 (8) |
| Not evaluated | 2 (2) |
| Time to response, mos (n = 71) | |
| Median (interquartile range) | 1.9 (1.8-3.7) |

Gopal A, et al. N Engl J Med. 2014;370:1008-1018.

# Phase II Study of Idelalisib Monotherapy in Refractory iNHL: PFS and DOR




Gopal A, et al. N Engl J Med. 2014;370:1008-1018.

# Idelalisib Monotherapy in Refractory iNHL (Phase II): Adverse Events

| AE, n (%) | Any Grade | Grade ≥3 |
|---|---|---|
| Diarrhea | 54 (43) | 16 (13) |
| Fatigue | 37 (30) | 2 (2) |
| Nausea | 37 (30) | 2 (2) |

| Transaminases, n (%) | Any Grade | Grade 3/4 |
|---|---|---|
| ALT elevated | 59 (47%) | 16 (13%) |
| AST elevated | 44 (35%) | 10 (8%) |

Gopal A, et al. N Engl J Med. 2014;370:1008-1018.

BloombergBusiness | News | Markets | Insights | Video

# Gilead Cancer Drug Reviewed After Deaths in Combo Trials

by Doni Bloomfield
DoniBloomfield

March 11, 2016 – 6:39 PM CET *Updated on* March 11, 2016 – 11:50 PM CET

- FDA, European drug regulators are reviewing Gilead treatments
- Deaths, side effects reported after drug used in combination

U.S. and European regulators are reviewing Gilead Sciences Inc.'s cancer drug Zydelig after some patients died or suffered other side effects while taking it with other drugs in

# Gilead Sciences Halts Drug Studies Over Side Effects, Death

By THE ASSOCIATED PRESS •
FOSTER CITY, Calif. — Mar 15, 2016, 5:37 PM ET

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3
SHARES

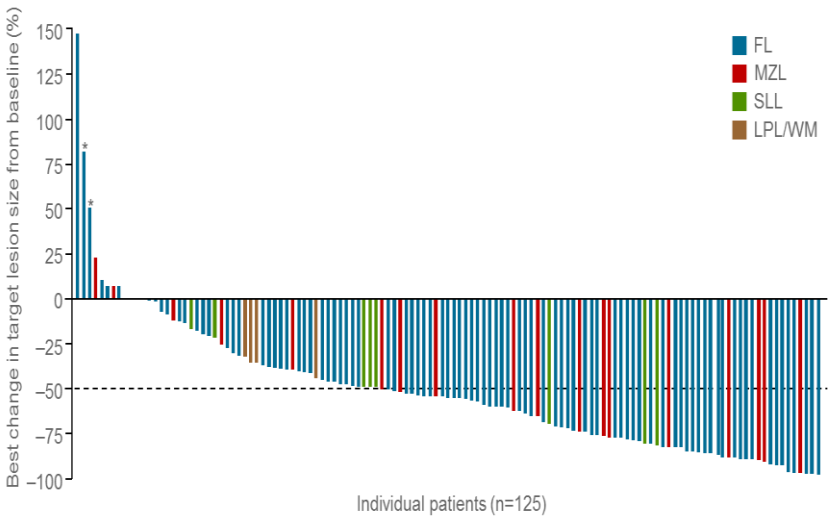
Biologic drugmaker Gilead Sciences Inc. has halted several patient studies of its cancer drug, Zydelig, because of increased risk of death and serious side effects.

The company told The Associated Press the "adverse events" were spotted during an ongoing review of late-stage testing in patients with chronic lymphocytic leukemia, a blood cancer, and patients with relapsed non-Hodgkin's lymphoma, a cancer of the infection-fighting lymphatic system.

Nathan Kaiser, a spokesman for the Foster City, California, company, wouldn't disclose details, including how many patients died or suffered serious side effects.

"We are conducting a comprehensive review of all ongoing studies and are consulting with regulatory authorities," Kaiser wrote in an email Tuesday.

# Copanlisib Demonstrated Anti-Tumor Efficacy in Patients with Relapsed or Refractory iNHL

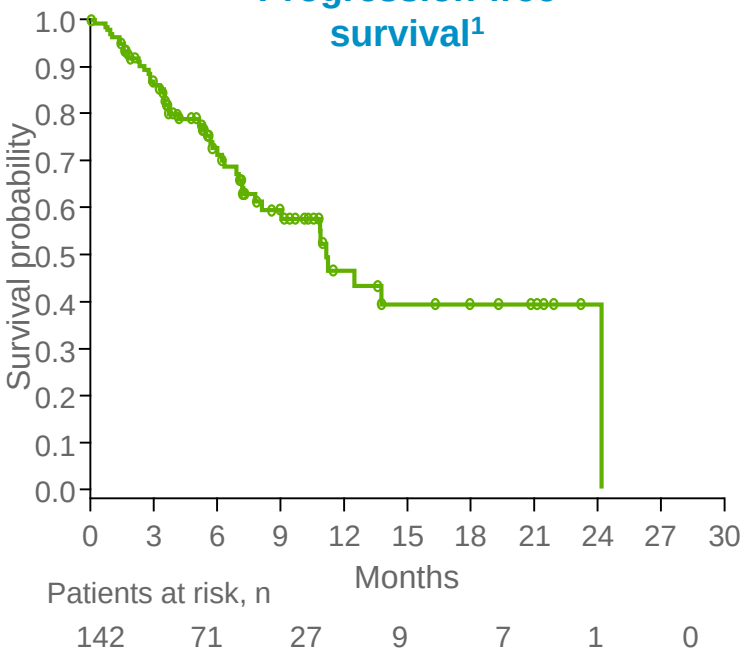



| | FL (n=104) | MZL (n=23) | SLL (n=8) | LPL/WM (n=6) | Total[a] (N=142) |
|---|---|---|---|---|---|
| **Best response, n (%)** | | | | | |
| Complete response | 15 (14%) | 2 (9%) | 0 | 0 | 17 (12%) |
| Partial response | 46 (44%) | 14 (61%) | 6 (75%) | 1 (17%) | 67 (47%) |
| Stable disease | 35 (34%) | 4 (17%) | 1 (13%) | 3 (50%) | 42 (30%) |
| Progressive disease | 2 (2%) | 0 | 1 (13%) | 0 | 3 (2%) |
| NE/NA | 6 (6%) | 3 (13%) | 0 | 2 (33%) | 12 (9%) |
| **ORR, n (%)** | 61 (59%) | 16 (70%) | 6 (75%) | 1 (17%) | 84 (59%) |
| 95% CI | 49–68 | 47–87 | 35–97 | 0.4–64 | 51–67 |

*Patient was assessed by independent review as having stable disease.
[a]One patient with follicular lymphoma who received treatment was later confirmed by the local investigator to have diffuse large B-cell lymphoma.
**CI**, confidence interval; **NA**, not available; **NE**, not evaluable; **ORR**, objective response rate.
Dreyling M *et al. J Clin Oncol* 2017; doi: 10.1200/JCO.2017.75.4648.

# Copanlisib Demonstrated Durable Responses in Patients with Relapsed or Refractory iNHL

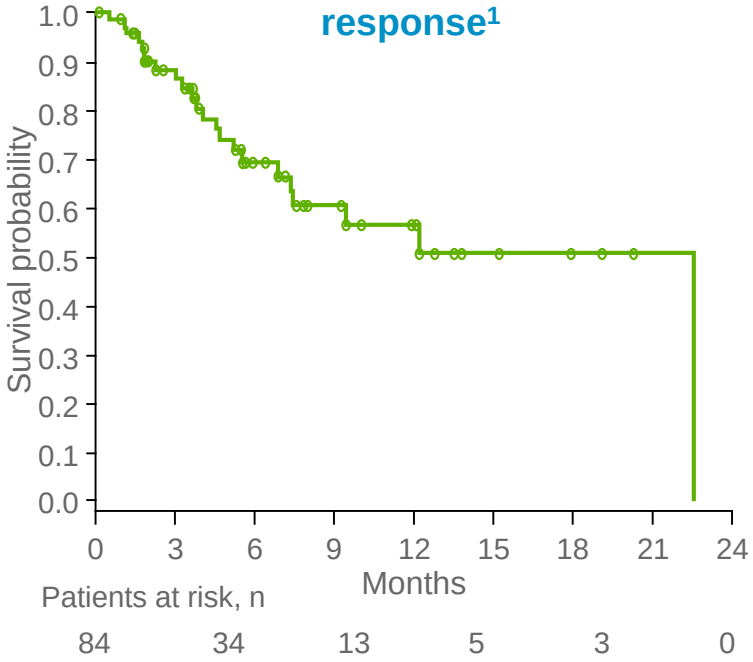
**Progression-free survival[1]**




**Median progression-free survival:**

- **Overall:** 11.2 months (95% CI: 8.1–24.0)[1]
- **FL:** 11.2 months (95% CI: 7.8–24.2)[2]

**Duration of response[1]**




**Median duration of response:**

- **Overall:** 22.6 months (range 0–22.6; 95% CI: 7.4–22.6)[1]
- **Refractory patients:** 12.2 months (range 0–22.6; 95% CI: 7.4–22.6)[2]
- **FL:** 12.2 months (range 0–22.6; 95% CI: 6.9–22.6)[2]

**1**. Dreyling M *et al. J Clin Oncol* 2017; doi: 10.1200/JCO.2017.75.4648. **2.** Dreyling M *et al.* Presented at: International Conference on Malignant Lymphoma; June 14–17, 2017; Lugano, Switzerland.

# Most Common Treatment-Emergent AEs Reported in CHRONOS-1

| Treatment-emergent AEs, n (%) | Total (N=142) | | | |
|---|---|---|---|---|
| **Grade** | **All** | **3** | **4** | **5** |
| Any treatment-emergent AE | 140 (99%) | 75 (53%) | 38 (27%) | 6 (4%) |
| Hyperglycemia | 71 (50%) | 48 (34%) | 10 (7%) | 0 |
| Diarrhea | 48 (34%) | 7 (5%) | 0 | 0 |
| Fatigue | 43 (30%) | 3 (2%) | 0 | 0 |
| Hypertension | 43 (30%) | 34 (24%) | 0 | 0 |
| Neutrophil count decreased | 42 (30%) | 11 (8%) | 23 (16%) | 0 |
| Fever | 36 (25%) | 6 (4%) | 0 | 0 |
| Nausea | 33 (23%) | 1 (1%) | 0 | 0 |
| Lung infection | 30 (21%) | 18 (13%) | 3 (2%) | 2 (1%) |
| Platelet count decreased | 29 (20%) | 9 (6%) | 1 (1%) | 0 |
| Oral mucositis | 28 (20%) | 4 (3%) | 0 | 0 |
| Laboratory toxicities | | | | |
| Aspartate aminotransferase increased | 39 (28%) | 1 (1%) | 1 (1%) | 0 |
| Alanine aminotransferase increased | 32 (23%) | 1 (1%) | 1 (1%) | 0 |
| AEs of special interest | | | | |
| Pneumonitis (non-infectious) | 11 (8%) | 2 (1%) | 0 | 0 |
| Colitis[a] | 1 (1%) | 0 | 1 (1%) | 0 |

- Two patients (1%) had Grade 3 pneumonitis and 1 patient had Grade 4 colitis[a] (1%)
- Three deaths (2%) were considered drug-related: lung infection, respiratory failure, and a cerebral thromboembolic event (1% each)

[a]Patient had medical history of diverticulosis; **AE**, adverse event.

Dreyling M *et al. J Clin Oncol* 2017; doi: 10.1200/JCO.2017.75.4648.

# DAWN Study: Primary End Point: IRC-Assessed Clinical Response With Single-Agent Ibrutinib

| | All Treated Patients (N = 110) | |
|---|---|---|
| Clinical response, n (%) | | 95% CI |
| Overall response rate (ORR) | **23 (20.9)** | 13.7-29.7 |
| Complete response (CR) | 12 (10.9) | 5.8-18.3 |
| Partial response (PR) | 11 (10.0) | 5.1-17.2 |
| Stable disease (SD) | 34 (30.9) | 22.5-40.4 |
| Progressive disease (PD) | 47 (42.7) | 33.3-52.5 |
| Not evaluable/unknown | 6 (5.5) | 2.0-11.5 |

- Disease control rate (ORR + SD for ≥ 6 months) was 33.6% (37/110)

CI, confidence interval.

58th ASH Annual Meeting 2016, DAWN Study, Gopal A, et al.

# New Targeted Agents

| Agent | Target |
|---|---|
| Obinutuzumab/Ublituximab | CD20 |
| Polatuzumab vedotin<br>Blinatumomab | CD79b<br>CD3/CD19 |
| MOR-208 | CD19 |
| Ibrutinib | Btk |
| Acalabrutinib (ACP-196) | Btk |
| Idelalisib, | PI3-K |
| Umbralisib, Copanlisib | PI3-K |
| Venetoclax (ABT-199)<br>Tazemetostat | Bcl-2<br>EZH2 |
| Selinexor | XP01 (Nuclear transport) |
| Lenalidomide | Multiple |
| Nivolumab/Pembrolizumab | PD-1 |
| Atezolizumab | PDL-1 |

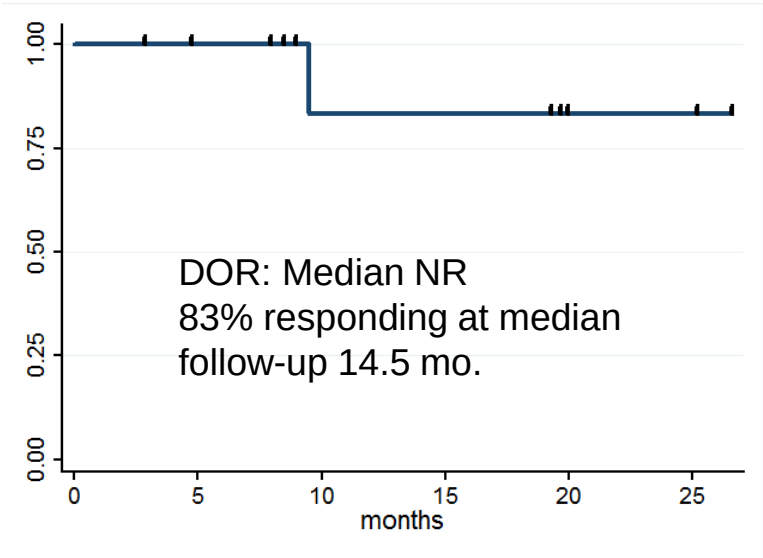
# Ongoing “Non-chemo” Combination Trials in FL

| Drugs | Sponsor |
|---|---|
| Obinutuzumab-B/CHOP+Atezolizumab | Genentech |
| Obinutuzumab+Polatuzumab | Genentech |
| Obinutuzumab+Atezolizumab+lenalidomide | Genentech |
| Obinutuzumab+Polatuzumab+lenalidomide | Genentech |
| Obinutuzumab+Polatuzumab+venetoclax | Genentech |
| GO29687 (Thiomab)+rituximab | Genentech |
| Acalabrutinib (ACP-196)+pembrolizumab | Acerta |
| Acalabrutinib+ACP-319 | Acerta |
| Acalabrutinib+rituximab | Acerta |
| Ono/GS-4059+idelalisib | Gilead |
| Ibrutinib+Venetoclax | Georgetown |
| Ublituximab+ibrutinib | TG Therapeutics |
| Ublituximab+TGR-1202 | TG Therapeutics |
| Ublituxumab+TGR-1202+ibrutinib | TG Therapeutics |
| Rituximab +/- copanlisib | Bayer |

# CAR T-cell Efficacy in Follicular Lymphoma (CTL019)

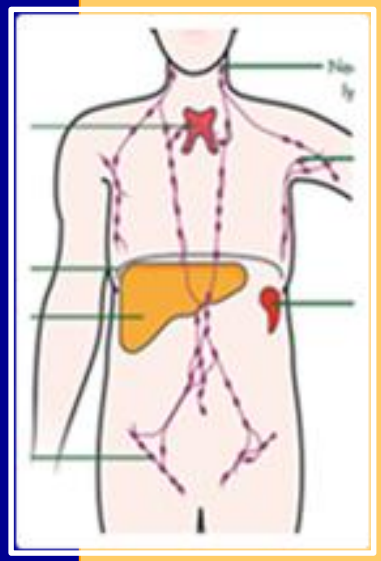
| Response at 3 mo. (N = 14) | Best Response (N = 14) |
|---|---|
| ORR: 79% | ORR: 79% |
| CR: 7 (50%) | CR: 10 (71%) |
| PR: 4 | PR: 1 |
| PD: 4 | PD: 3 |

**Duration of Response (n = 11; CR + PR)**




Chong EA, et al. *Blood*. 2016;128: abstract 1100.

# Marginal Zone Treatment

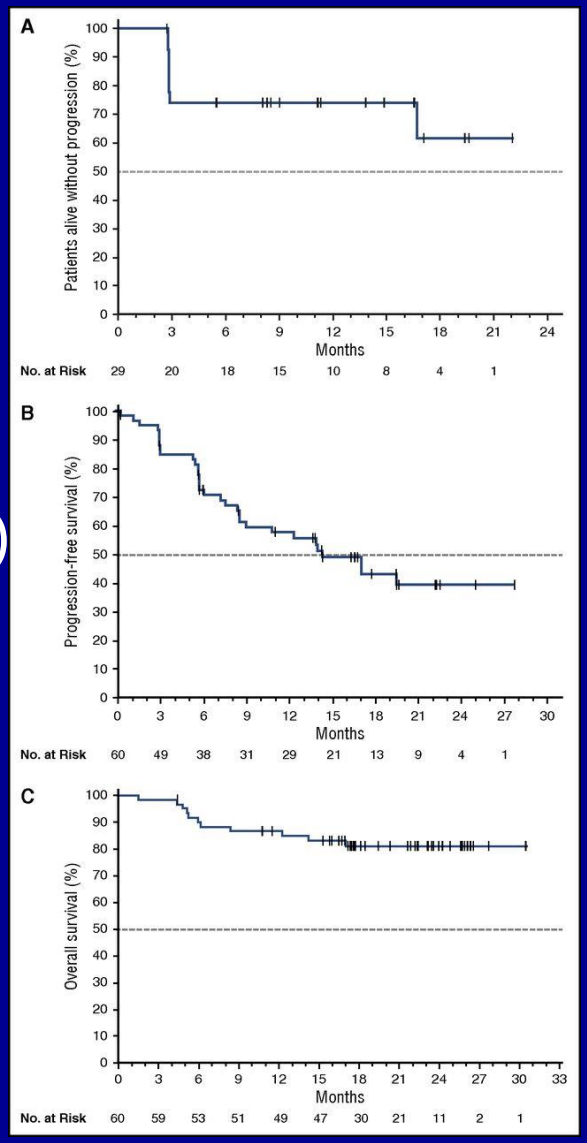


## Nodal

- Rituximab + Chemo
  - Bendamustine
  - CHOP
  - Fludarabine
- Ibrutinib

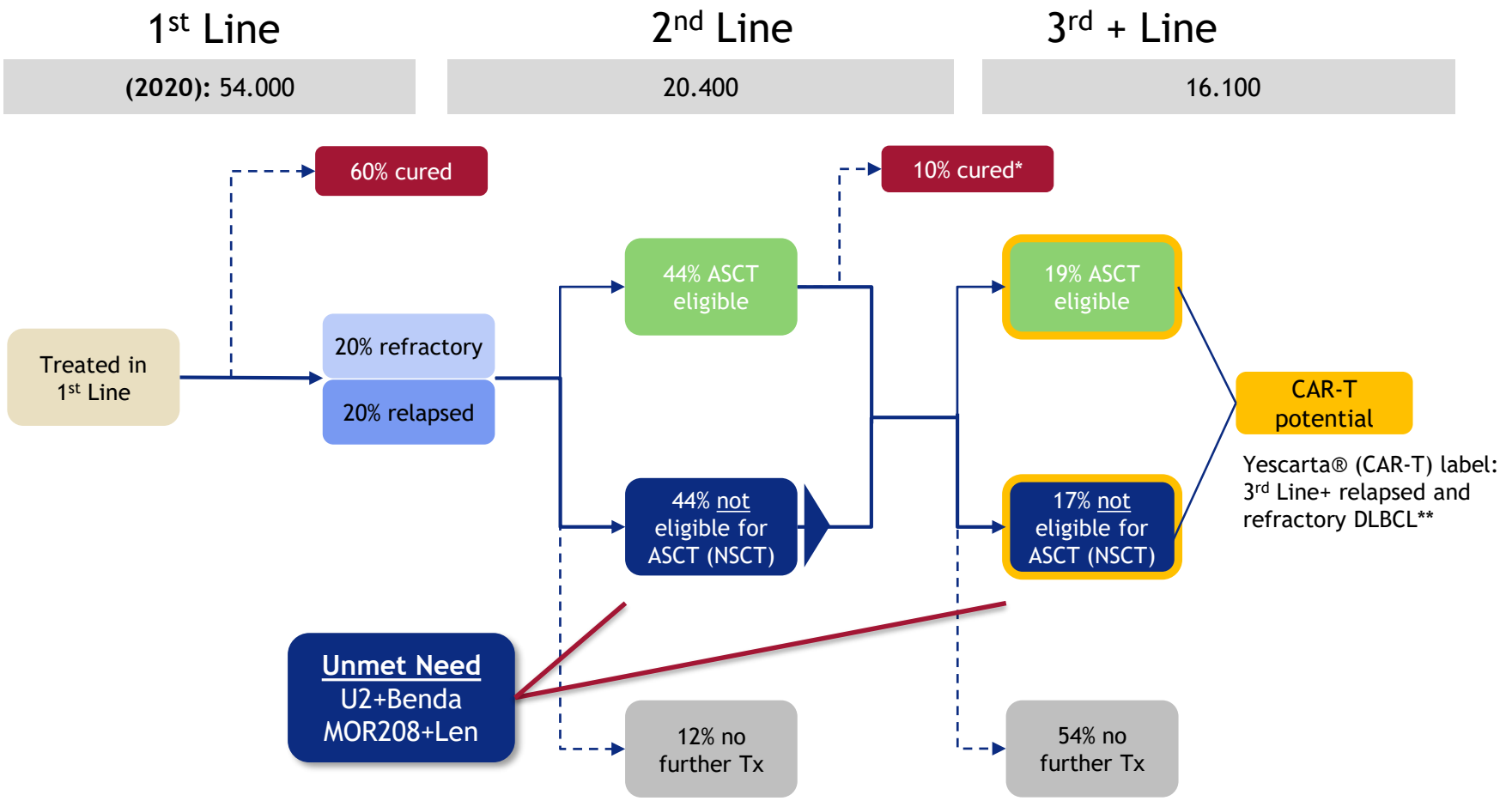
# DOR, PFS, and OS with ibrutinib in R/R MZL

N=63
ORR 48% (3%CR)




Noy et al. Blood 2017;129:2224-2232

# Algorithm for DLBCL




Source: Market Research AplusA, *Friedberg et al., 2011; and **Yescarta® SmPC Oct 2017

# CAR T-cell therapies in DLBCL

## *UPENN Single Institution Study*

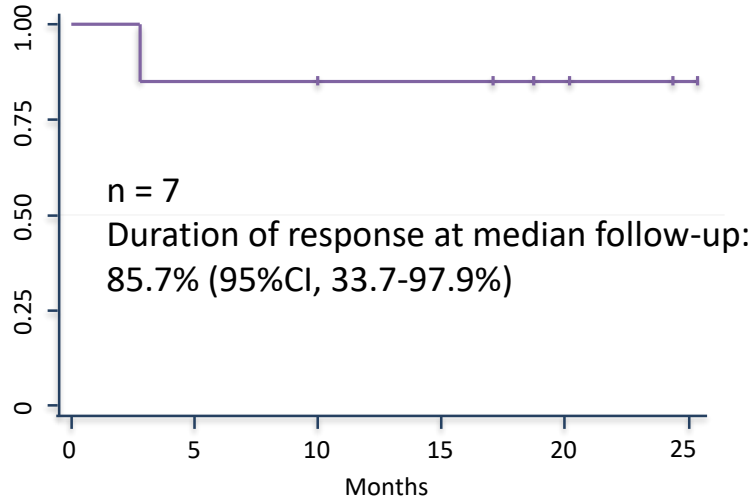
- Results from a single-center, phase 2 study at the University of Pennsylvania showed durable remissions with a single infusion of CTL019 in r/r DLBCL (Cohort A)[1,2]
  - No patient in CR at 6 months has relapsed (median follow-up, 23.3 months)

**Response Rates (N = 15)**

| | Month 3 | Month 6 |
|---|---|---|
| ORR | 7 (47%) | 7 (47%) |
| CR | 3 (20%) | 6 (40%) |
| PR | 4 (27%) | 1 (7%) |

CR, complete response; DLBCL, diffuse large B-cell lymphoma; ORR, overall response rate; PR, partial response.

**Duration of Response (n = 7; CR + PR)**





1. Schuster SJ, et al. *Blood*. 2015;126(23):[abstract 183].
2. Schuster SJ, et al. *Blood*. 2016;128(22):[abstract 3026].

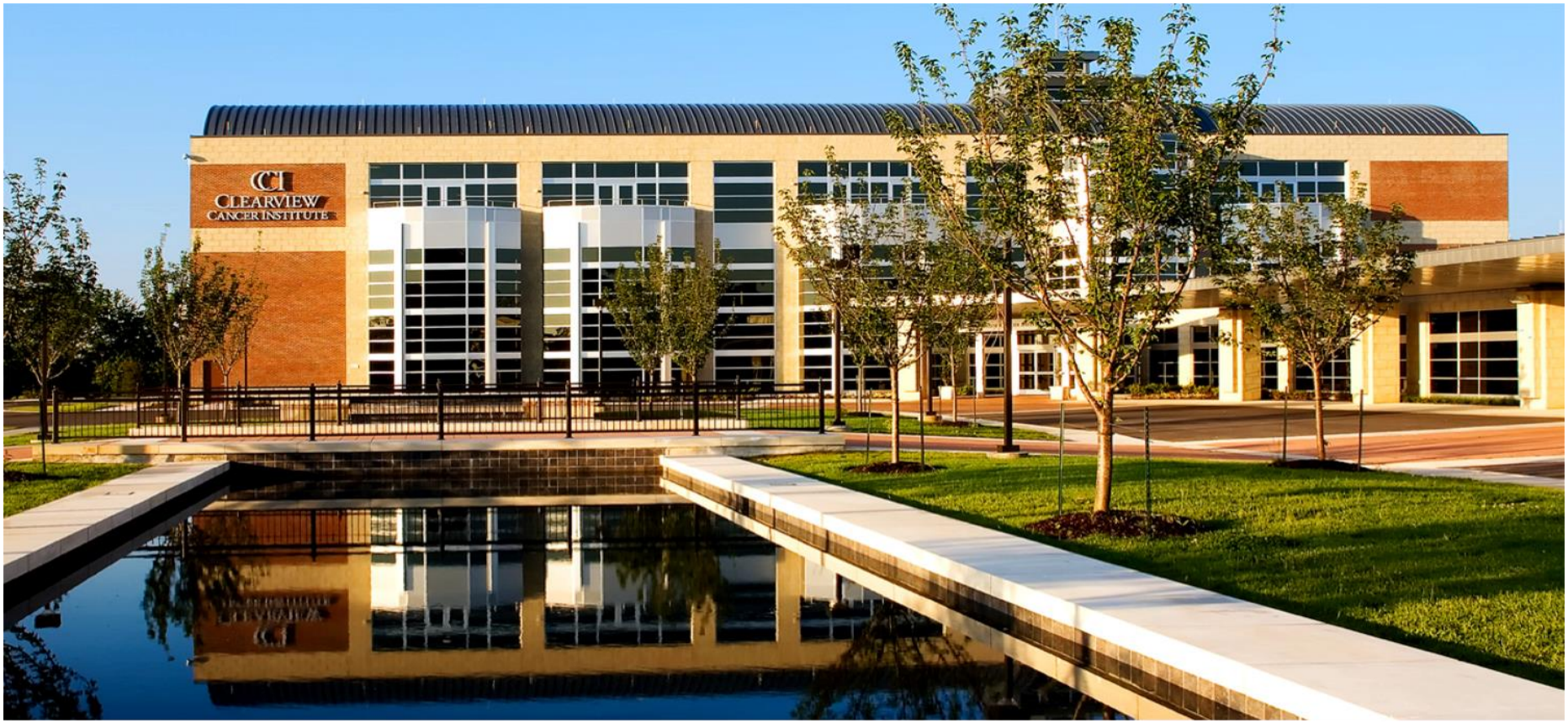
TG Therapeutics

# Personal Experience


## Kathy Cutter, RN, BSN
## Clearview Cancer Institute
## Huntsville, AL


UNITY CLL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PHASE 3 TRIAL IN CLL

UNITY NHL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
PREVIOUSLY TREATED NHL PATIENTS


CI
CLEARVIEW
CANCER INSTITUTE

# Experience with Ublituximab and Umbralisib

In the past 4 years at the Clearview Cancer Institute, we have treated over 80 patients on TG protocols:

| TG Therapeutics Protocol | Patient Population | Patients Treated |
|---|---|---|
| Umbralisib + Ublituximab (+/- ibrutinib or bendamustine) | R/R CLL, iNHL, DLBCL | 45 |
| Umbralisib + Gazyva + Chlorambucil | Front line CLL | 10 |
| Ublituximab + Lenalidomide | R/R NHL | 7 |
| UNITY-CLL | CLL | 7 |
| Ublituximab + Ibrutinib | R/R CLL, MCL | 5 |
| Ublituximab Single Agent | R/R NHL & CLL | 4 |
| GENUINE | CLL | 4 |
| UNITY-NHL | iNHL, DLBCL | 2 |
| **TOTAL** | | **84** |

# Experience with Idelalisib and Obinutuzumab at Clearview Cancer Institute

**Idelalisib Experience:**

- Idelalisib: Phase 1 single agent extension trial
- Idelalisib: Phase 1 in combination with Rituxan / Bendamustine or Ofatumumab
- Idelalisib:  Five Phase 3 randomized trials for CLL and NHL

**Gazyva (Obinutuzumab) Experience:**

- Phase 1 Gazyva/Bendamustine
- Expanded access Gazyva/Chlorambucil
- Phase 2 Gazyva/Bendamustine

# Differences in Ublituximab and Obinutuzumab in Infusion Times and AE's

**Ublituximab** – Month 1 infusions 3-4 hours
All subsequent infusions administered in **90 minutes**

**Obinutuzimab-** C1D1 and C1D2 infusion over **4 hours**.
All subsequent infusions administered over **3.25 hours**.

| Grade 3/4 Event | Ublituximab* | Obinutuzumab/ Chlorambucil** |
|---|---|---|
| Infusion Reactions | ~5% | 20% |
| Neutropenia | 28% | 46% |
| Thrombocytopenia | 5% | 13% |
| Bleeding | 0% | 5% |

*Combination with umbralisib

**Prescribing Information

# It’s all About the Quality of Life

# Comparison of Common AE's between Umbralisib and Idelalisib

| Grade 3/4 Event | Umbralisib* | Idelalisib** |
|---|---|---|
| Diarrhea | 4% | 14% |
| Neutropenia | 16% | 25% |
| Anemia | 5% | 2% |
| Thrombocytopenia | 5% | 6% |
| Elevated LFT's | 2% | 18% |
| Colitis | <1% | 14% |
| Nausea | <2% | 1% |
| Fatigue | <2% | 1% |
| Rash | <2% | 4% |

*Integrated Analysis Poster ASH 2017

**Prescribing Information

# Ublituximab + Umbralisib Case Study: CLL

**Relapsed CLL Patient (Initials JSM)**

- History – 53 year old male
- Disease information – Original diagnosis September 1992 requiring treatment.

**Prior treatments (n=8)**

- #1 – Chlorambucil + Prednisone (x 2)
- #3 – Fludarabine
- #4 – Rituxan (x 2)
- #6 – CVP + Rituxan Maintenance
- #7 – R-CVP
- #8 – Bendamustine Rituxan + Rituxan Maintenance

# Case Study CLL (continued)

- Treatment start date - Ublituximab + Umbralisib - 9/3/14; ECOG 1

**RESULTS**

- First Response assessment at 8 weeks = Partial Response
- Last Response assessment as of Oct 2017 = Partial Response
- AE's: 1 Drug Interruption for Grade 3 neutropenia and Grade 2 Influenza (not related) both occurring at the same time from Dec 24 – Dec 30, 2014
  - No events of diarrhea or elevated LFTs observed
- Per Protocol Design in 2014/2015, patients could remain on ublituximab for 1 year and continue umbralisib indefinitely
- As of Dec 2017, patient remains on umbralisib single agent now 3+ years

# Ublituximab + Umbralisib Case Study 1

## Transformed DLBCL Patient

- History – 63 year old Caucasian male; career military. Sniper in the army. Hx of multiple gunshot wounds; PTSD; Stroke in 2010 which left him temporarily aphasic.
- Disease information – Original diagnosis 11/19/2001- Follicular lymphoma stage 2. Transformed to DLBCL in 2013; site nasopharyngeal mass.

## Prior treatments (n=7)

- #1 – R-CHOP - 12/2001-06/2002 – 8 cycles
- #2 – Rituxan - 8/2003 - 10/2003 8 weekly tx
- #3 – Rituxan - 6/2005 - 2 treatments
- #4 – Treanda – 02/2009 – 05/2009 – 6 cycles

# Case Study #1 (continued)

- #5 – Radiation - L inguinal 30 GY - 2011
- #6 – Treanda – 4/2012 - 7/2012 – 6 cycles
- #7 – ICE - 01/2014 – 2/24/14 – 3 cycles – no response
- The patient was screened 3/24/14
- Treatment start date - Ublituximab + Umbralisib - 4/14/14

**RESULTS**

- Original naso-pharangeal mass was 5.7 cm x 3.2 cm. Patient achieved a Complete Response during cycle 5 (8/25/14) and has been in CR since that time (3.5+ years).
- AE's: Gr. 2 IRR, nausea gr 2; neutropenia gr 3; dehydration gr 2; diarrhea gr 2/3; fatigue – gr 1

# Ublituximab + Umbralisib + Benda Case Study 2

## Refractory DLBCL Patient

- History – 60 year old female
- History/Disease information – 60 yo female, Original diagnosis 11/2010 – Aggressive Stage 3 DLBC:

## Prior treatments (n=7)

- #1 – R-CVAD – Remission for 3 years
- #2 – R-ICE followed by PBSCT
- #3 – Beam Condition to Transplant - 3/2015
- Patient Relapses from March 2015 Transplant in October 2015
- Patient starts Ublituximab + TGR-1202 + Benda October 29, 2015
- Baseline Tumor Mass:  3 Target Lesions = 27.68 cm in SPD
- ECOG of 1

# Case Study #2 (continued)

**RESULTS**

- Partial Response (92% reduction) at week 8
- Complete Response by week 20 and continued with CR until October 2016 (12 months later) which 12 month CT showed a new lesion present (progression)
- AE's:  Gr. 3/4 neutropenia and thrombocytopenia; Gr. 3 anemia, Gr. 1 rash

**As a research nurse, there is nothing more rewarding than to have a patient receive treatment with Ublituximab and Umbralisib, leave your clinic, fly directly to Florida, where he boards his yacht and captain's his boat to the Bahamas!**

**The good life!**

TG Therapeutics

# Questions & Answer Session

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PREVIOUSLY TREATED NHL PATIENTS

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# Concluding Remarks

**Michael S. Weiss**
Executive Chairman & CEO

UNITY CLL
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202
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