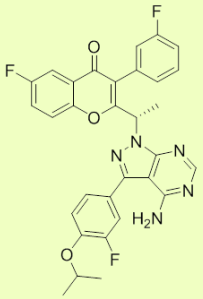
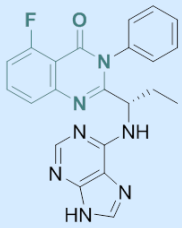
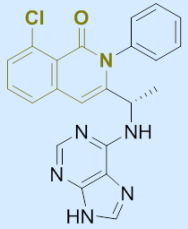
Umbralisib

Susan O'Brien, MD
UC Irvine Health

TGR-1202: Next Generation PI3Kδ (delta) Inhibitor

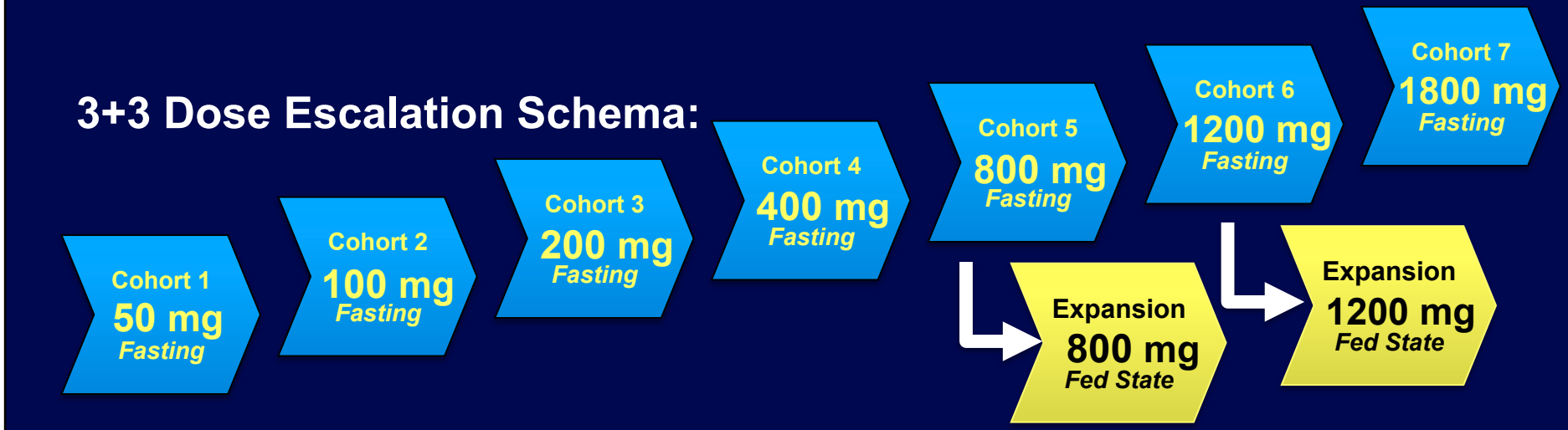
- Unique structure of TGR-1202 contributes to:
  - Favorable pharmacokinetics allowing once-daily dosing
  - Differentiated safety profile from other PI3Kδ inhibitors, notably absent of hepatic toxicity

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

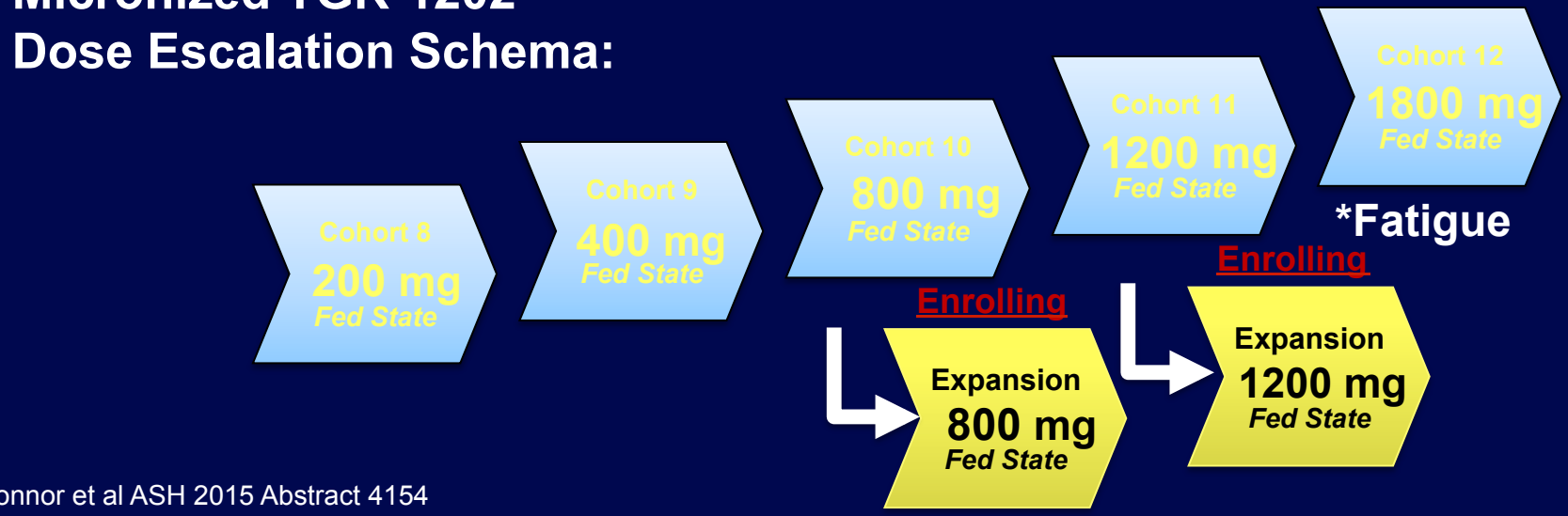
Fold-selectivity				
Isoform	PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ
TGR-1202	>10000	>50	>48	1
idelalisib[1]	>300	>200	>40	1
duvelisib[2]	>640	>34	>11	1

Burris et al, ASH 2014, [1]Flinn et al. 2009, [2]Porter et al. 2012

TGR-1202-101: Dose Escalation Schema



Fed state doubled AUC & Cmax



O'Connor et al ASH 2015 Abstract 4154

Safety of Single agent Umbralisib

All Events in >10% of Pts (N=81)				
AE	All Grades		Gr. 3/4	
	N	%	N	%
Nausea	34	42%	1	1%
Diarrhea	33	41%	2	2%
Fatigue	25	31%	3	4%
Rash	22	27%	4	5%
Headaches	20	25%	1	1%
Cough	19	23%	0	0%
Vomiting	18	22%	0	0%
Constipation	12	15%	1	1%
Decreased Appetite	12	15%	0	0%
Hypokalemia	12	15%	4	5%
Anemia	11	14%	7	9%
Dizziness	11	14%	0	0%
Dyspnea	11	14%	4	5%
Pyrexia	10	12%	0	0%
Abdominal Pain	9	11%	0	0%
Arthralgia	9	11%	0	0%
Insomnia	9	11%	0	0%

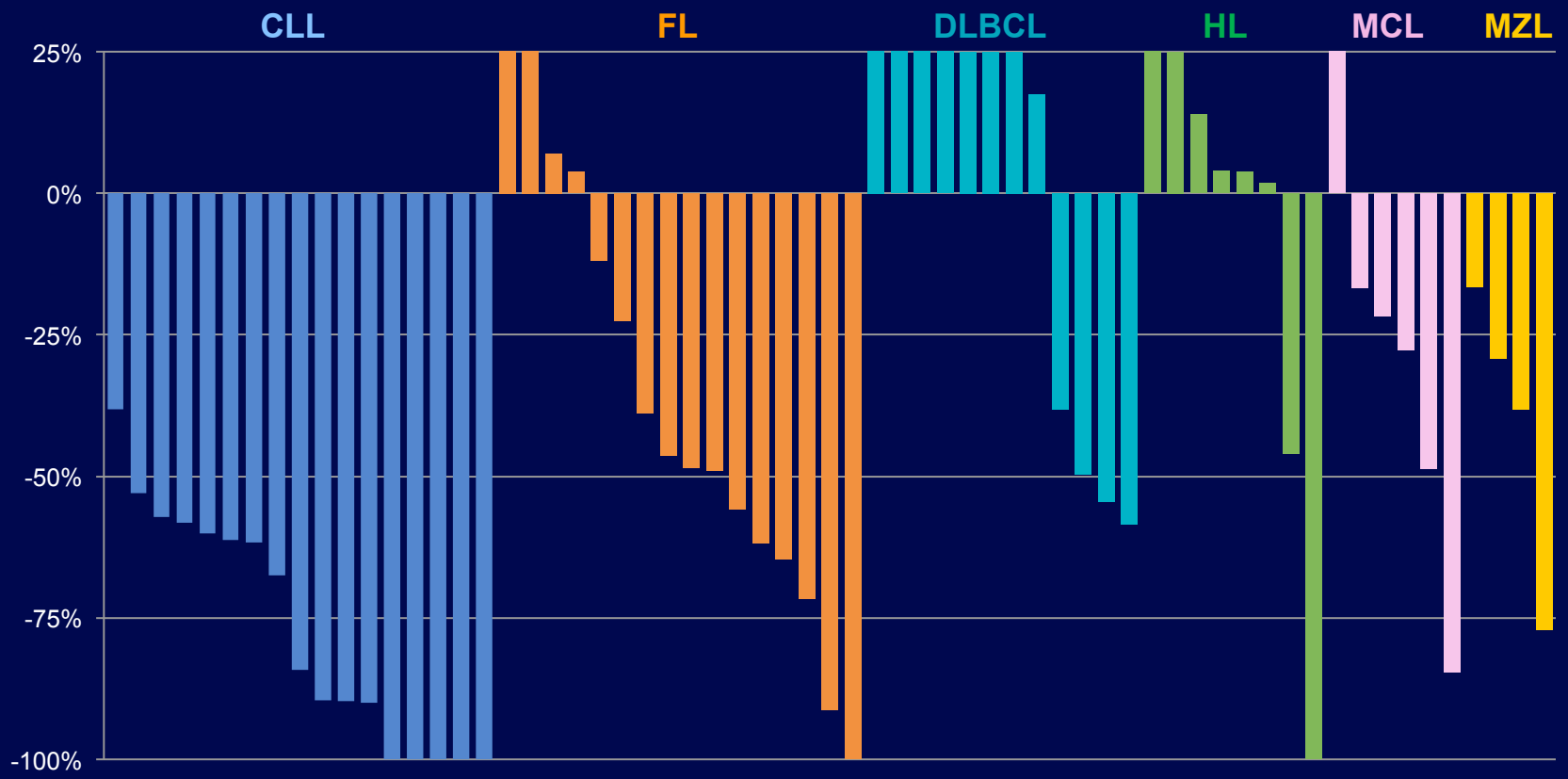
- 38 patients on study over 6 cycles, and 22 patients have been on study over 12 cycles
- TGR-1202 has been well-tolerated, with limited Gr. 3/4 events and no significant time dependent trends in AEs observed
- Grade 3/4 AST/ALT increase was 2% (4% all grades)
- 6 patients (7%) have come off study due to an adverse event
- 4 patients (5%) had Grade 3 pneumonia.

O'Connor et al, ASH 2015

TGR-1202-101: Efficacy

Best Percent Change from Baseline in Disease Burden

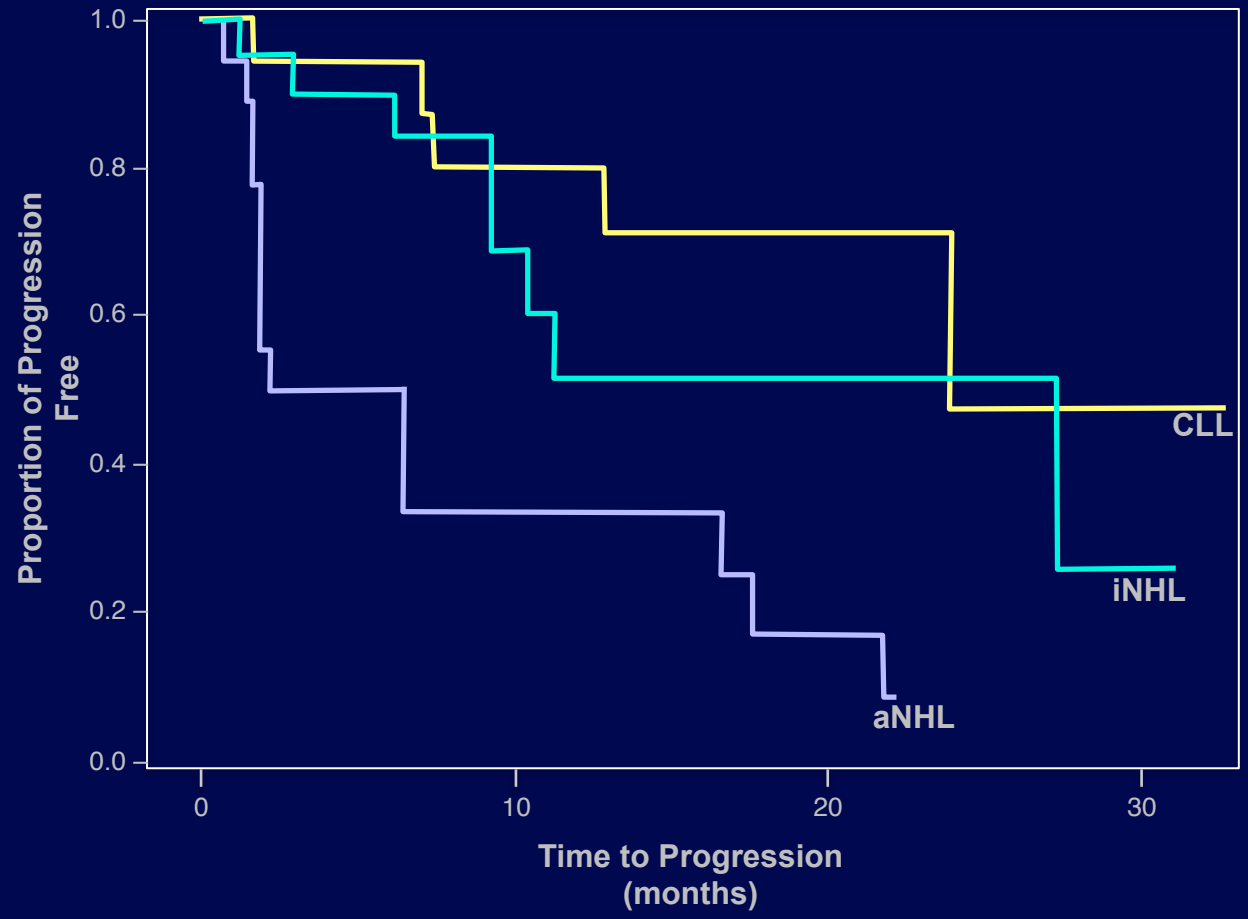
Patients Evaluable for Efficacy (n=63)



O'Connor O, et al. ASH (poster presentation) 2015. Abstract 4154.

94% CLL model PR, 59% PR

TGR-1202-101: Progression-free Survival

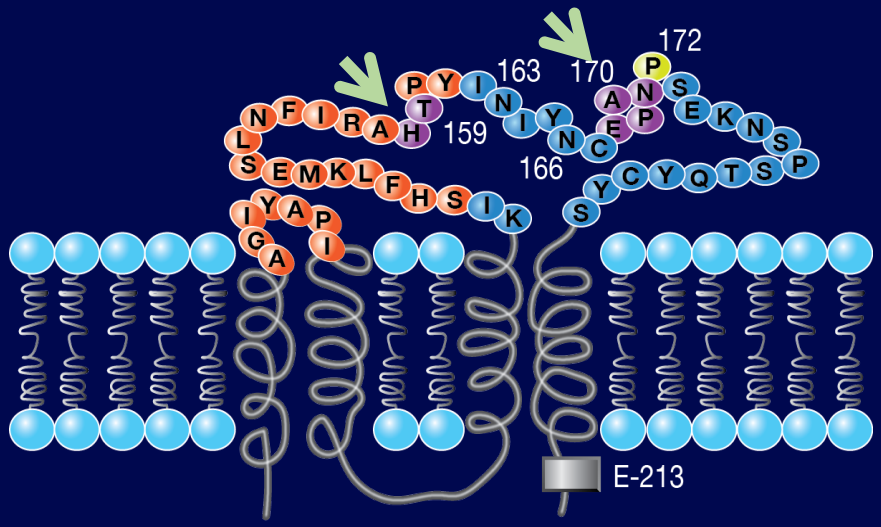


- **Median PFS:**
  - **CLL: 23.98 mos** (95% CI: 7.4, NR)
  - **iNHL (FL & MZL): 27.3 mos** (95% CI: 9.28, NR)
  - **aNHL (DLBCL & MCL): 4.33 mos (95% CI: 1.88, 16.6)**

O'Connor O, et al. ASH (poster presentation) 2015. Abstract 4154.

Ublituximab: Background

- Ublituximab (TG-1101, UTX) is a novel, chimeric monoclonal antibody that:
  - Targets a unique epitope on the CD20 antigen (green arrows); and
  - Glycoengineered to enhance affinity for all variants of FcγRIIIa receptors, thereby
  - Demonstrating greater ADCC activity than rituximab and ofatumumab
- Phase I trials of single agent ublituximab in patients with relapsed/refractory CLL and NHL reported impressive response rates with rapid and sustained lymphocyte depletion



Red: Amino acids contributing to ofatumumab binding
Yellow: Amino acids essential for rituximab, but not ofatumumab binding
Purple: Core amino acids of ublituximab epitope

ADCC, antibody-dependent cellular cytotoxicity.

Burris HA, et al. *J Clin Oncol.* 2016;34, (suppl; abstr 7512). Presented at: ASCO Annual Meeting 2016 (poster).

Mato A, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P207). Presented at: EHA Annual Meeting 2016 (poster).

O'Connor O, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P315). Presented at: EHA Annual Meeting 2016 (poster).

Study Design: TGR-1202 in Combination with Ublituximab

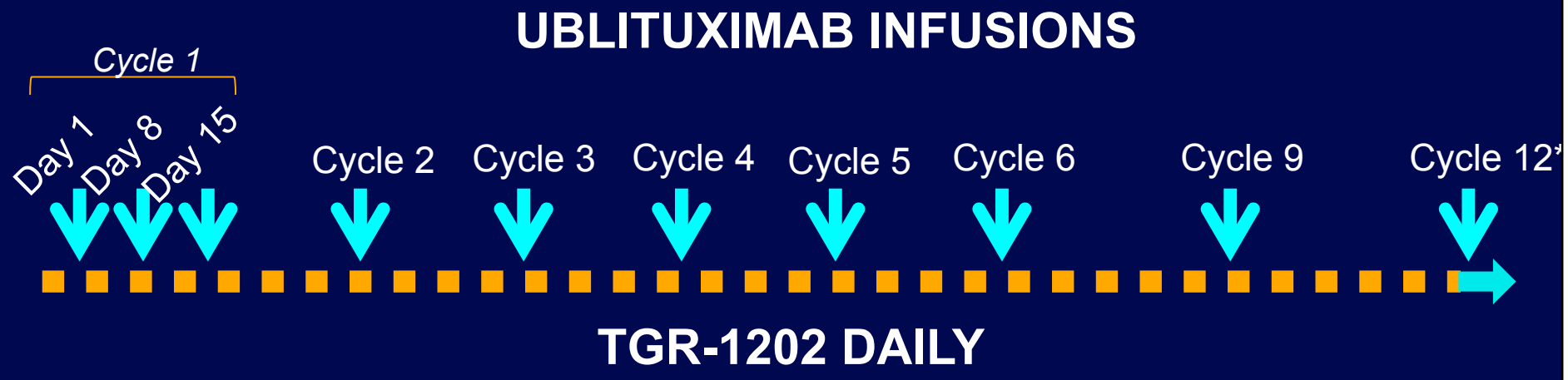
- Study UTX-TGR-103 (NCT02006485) is an ongoing Phase I/Ib trial evaluating the combination of ublituximab + TGR-1202 in patients with relapsed or refractory NHL and CLL
- The study is divided into two parts:
  - Phase I: 3+3 dose escalation evaluating Cycle 1 DLTs
  - Phase Ib: Dose expansion

Cohort	Ublituximab Dose	TGR-1202 Dose (QD)
1	900/600 mg NHL/CLL	800 mg
2	900/600 mg NHL/CLL	1200 mg
3	900 mg	400 mg (micronized)
4	900 mg	600 mg (micronized)
5	900 mg	800 mg (micronized)
6	900 mg	1000 mg (micronized)
7	900 mg	1200 mg (micronized)
Expansion	TGR-1202 at 800 mg, 1000 mg, and 1200 mg micronized	

Burris HA, et al. *J Clin Oncol.* 2016;34, (suppl; abstr 7512). Presented at: ASCO Annual Meeting 2016 (poster).
Mato A, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P207). Presented at: EHA Annual Meeting 2016 (poster).
O'Connor O, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P315). Presented at: EHA Annual Meeting 2016 (poster).

Ublituximab + TGR-1202: Treatment Schedule

- Efficacy is assessed week 8, and every 12 weeks thereafter
- Ublituximab was initially administered on Days 1, 8 and 15 of Cycles 1 and 2, and Day 1 of Cycles 4, 6, 9, and 12
- The protocol was amended to use a more convenient schedule as follows:



***After month 12, all patients remain on single-agent TGR-1202.**

Burris HA, et al. *J Clin Oncol.* 2016;34, (suppl; abstr 7512). Presented at: ASCO Annual Meeting 2016 (poster).
Mato A, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P207). Presented at: EHA Annual Meeting 2016 (poster).
O'Connor O, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P315). Presented at: EHA Annual Meeting 2016 (poster).

Results

Demographics

Evaluable for Safety (n)	55	
Evaluable for Efficacy† (n)	39	
Median Age, years (range)	64 (29 – 86)	
Male/Female	36/19	
Histology	**CLL/SLL**	15
	DLBCL	16
	FL	16
	MZL	5
	MCL	2
	Richter's	1
ECOG, 0/1/2	17/37/1	
Prior Therapies, median (range)	3 (1 – 9)	
Patients with ≥ 3 Prior Therapies (%)	60%	
Prior RTX Based Therapies, median (range)	3 (1 – 7)	
Refractory to Prior Therapy, n (%)	28 (51%)	

- Heavily pre-treated patient population with high-risk features, including ~50% refractory to last treatment with multiple previous lines of rituximab (RTX) based therapy

†16 Patients not evaluable (13 too early, 1 non-related AE, 1 removed per investigator discretion, 1 ineligible)

Results

Safety

Related AE's Occurring in ≥ 5% of Patients (n = 55)

Adverse Event	All Grades		Grade 3/4	
	N	%	N	%
Infusion Related Reaction	16	29%	1	2%
Neutropenia	15	27%	13	24%
Nausea	15	27%	-	-
Diarrhea	11	20%	1	2%
Fatigue	10	18%	-	-
Vomiting	6	11%	-	-
Abd. Pain/ Discomfort	4	7%	-	-
Muscle Cramping	4	7%	-	-
Anemia	3	5%	-	-
Bruising	3	5%	-	-
Hoarseness	3	5%	-	-
Thrombocytopenia	3	5%	-	-

- Adverse event profile has been similar across all cohorts to date
- 3 patients (~5%) have come off study due to an adverse event, including, itching (Gr. 1), pneumonitis and hypoxia
- No patients at ≥800 mg micronized TGR-1202 have discontinued due to an AE
- Neutropenia well managed through dose delays
- 1 DLT occurred—CLL Cohort 1 (Gr. 4 neutropenia in a patient with baseline Gr. 3 neutropenia), no other DLT's were observed permitting continued dose escalation

Efficacy: Response Rates in CLL/SLL, DLBCL and iNHL

Disease Type	Patients Exposed to TGR-1202 at 800 Micro					
	Pts (n)	CR (n)	PR (n)	ORR n (%)	SD (n)	PD (n)
CLL/SLL	16	2	12*	14 (88)	2	0
DLBCL	7	1	3	4 (57)	2	1
iNHL**	17	3	6	9 (53)	6	2

*CLL/SLL PR includes 1 patient with persistent lymphocytosis; **iNHL = FL and MZL.

- Higher Doses: 1200 mg of the initial formulation, or ≥600 mg of the micronized formulation
- ORR in iNHL for patients treated at *higher doses* was not only greater with the combination (55%) as opposed to monotherapy (41%), but the depth of response was significantly greater with the addition of UTX (CR rate of 5% for monotherapy vs. 30% for the combination)
- Similarly, 3 CRs observed in patients with DLBCL treated at higher doses occurred in patients receiving TGR-1202 + UTX
- An exploratory subset of patients with ibrutinib-refractory CLL were treated with TGR + UTX and analyzed separately due to the aggressive nature of their disease
- A strong dose response was observed, with patients exposed to 800 mg of the micronized formulation achieving higher rates of response

Burris HA, et al. *J Clin Oncol.* 2016;34, (suppl; abstr 7512). Presented at: ASCO Annual Meeting 2016 (poster).
Mato A, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P207). Presented at: EHA Annual Meeting 2016 (poster).
O'Connor O, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P315). Presented at: EHA Annual Meeting 2016 (poster).

Efficacy in Ibrutinib-refractory High-risk Cytogenetic Patients

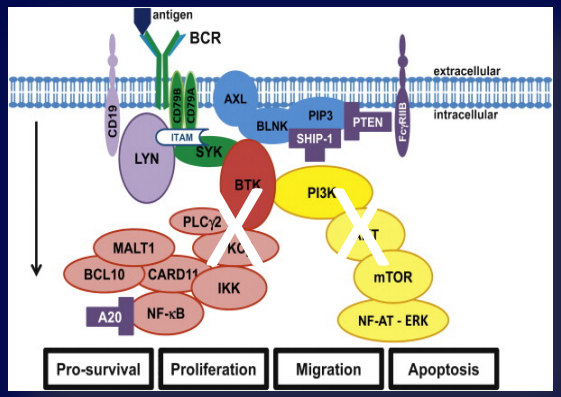
Ibrutinib Refractory Patients treated with TGR + UTX

Cyto-genetics	Number of Prior Lines	Prior Therapies		% SPD reduction	ORR	Status
11q	4	1. R-Benda 2. Ofatumumab	3. Ibrutinib 4. Ibrutinib	-100%	PR	On Study
17p	2	1. R-Fludarabine 2. Ibrutinib		-37%	SD	Off (PD)
17p, p53	2	1. Ibrutinib 2. Bendamustine and CAR T-cell		-55%	PD	Off (PD)
No del	5	1. FCR 2. R-Benda 3. FCR	4. Campath+R 5. Ibrutinib	+25%	PD	Off (PD)

- All patients were treated with 800 mg of TGR-1202 in combination with ublituximab

Burris HA, et al. *J Clin Oncol.* 2016;34, (suppl; abstr 7512). Presented at: ASCO Annual Meeting 2016 (poster).
Mato A, et al. *Haematologica.* 2016;101 (suppl 1; Abstract P207). Presented at: EHA Annual Meeting 2016 (poster).

TGR-1202 in Combination with Ibrutinib in Patients with Relapsed or Refractory CLL or MCL: Preliminary Results of a Multicenter Phase I/Ib Study



Matthew S. Davids, MD, MMSc[1], Haesook T. Kim, PhD[1], Alyssa Nicotra[1], Alexandra Savell[1], Karen Francoeur, RN[1], Jeffery M. Hellman, PA-C[1], Hari Miskin[2], Peter Sportelli[2], Asad Bashey, MD, PhD[3], Laura Stampleman, MD[4], Jens Rueter, MD[5], Adam Boruchov, MD[6], Jon E. Arnason, MD[7], Caron A. Jacobson, MD, MMSc[1], David C. Fisher, MD[1], and Jennifer R. Brown, MD, PhD[1]

[1] Dana-Farber Cancer Institute, Department of Medical Oncology, Boston, MA, USA, [2] TG Therapeutics, New York, NY, USA, [3] Bone Marrow Transplantation Group of Georgia, Atlanta, GA, USA, [4] Pacific Cancer Care, CA, USA, [5] Eastern Maine Medical Center, Bangor, ME, USA, [6] St. Francis Medical Center, Hartford, CT, USA, [7] Beth Israel Deaconess Medical Center, Department of Medical Oncology, Boston, MA, USA for the *Leukemia & Lymphoma Society Blood Cancer Research Partnership (LLS/BCRP)*

2016 ASH Annual Meeting – San Diego, California – December 5, 2016

A phase I/Ib investigator-initiated multicenter trial of TGR-1202 + ibrutinib in R/R CLL and MCL

Endpoints

Primary:

- MTD, safety, and DLTs of TGR-1202 when used in combination with ibrutinib

Secondary:

- Clinical response: ORR, CR, PR, PR-L, PFS, and remission duration
- Association of CLL prognostic factors (e.g. FISH, *IGHV*, etc.) with response

Exploratory:

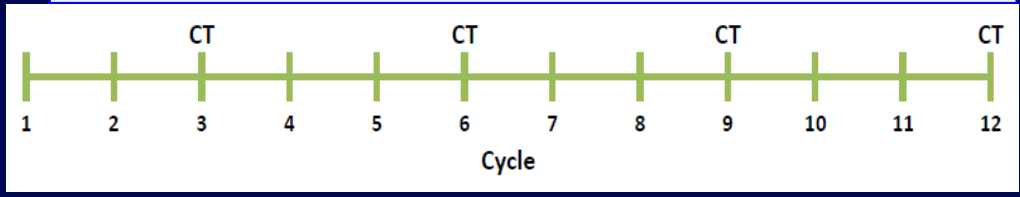
- Association of novel prognostic factors such as BH3 profiling and somatic mutations (e.g. *TP53*, *NOTCH1, SF3B1, BTK, PLCγ-2* etc.*)* with response

A 3+3 design was utilized with escalation of TGR-1202

- Parallel arms for CLL and MCL which escalated independently
- TGR-1202: oral, daily (qam) and ibrutinib: oral, 420 mg daily for CLL, 560 mg daily for MCL (qpm)
- Both agents continued until time of progression or unacceptable toxicity
- Standard toxicity assessments by CTCAE v4.03, efficacy by 2008 IW-CLL or 2014 Lugano criteria (MCL)
- Phase Ib expansion cohorts of 12 pts each in CLL and MCL

Dose escalation scheme

Dose Level	TGR-1202 Dose	Ibrutinib Dose CLL	Ibrutinib Dose MCL
1	400 mg	420 mg	560 mg
2	600 mg	420 mg	560 mg
3	800 mg	420 mg	560 mg
If > 2 DLTs in Cohort 1, 3- 6 pts will enroll in Cohort -1 as follows:			
-1	200 mg	420 mg	560 mg
If > 2 DLTs in Cohort –1, study will be terminated			



Patient Characteristics (n=31)

	All (n=31)	MCL (n=13)	CLL (n=18)
Age, median (range)	67 (48-83)	67 (50-83)	67 (48-76)
Sex, male	20 (64.5%)	10 (77%)	10 (56%)
Prior therapy, median (range)	2 (1-6)	3 (2-5)	1.5 (1-6)
Prior autoSCT	4/31 (13%)	4/13 (31%)	0
Prior ibrutinib	4/31 (13%)	2/13 (15%)	2/18 (11%)
Prior PI3K inhibitor	4/31 (13%)	0%	4/18 (22%)
WBC (K/uL), median (range)	11.2 (3.9-338)	8.1 (4-338)	16.7 (3.9-116.8)
Hgb (g/dL), median (range)	11.7 (7.7-15.9)	12.4 (7.8-15.9)	11.2 (7.7-15.1)
Platelets (K/uL), median (range)	179 (45-316)	146 (75-290)	194 (45-316)
Beta-2M (mg/L), median (range)	4.1 (2.2-19.7)	4.2 (2.6-19.7)	4.1 (2.2-9.2)
Del(17p)			4/17 (24%)
Del(11q)			7/17 (41%)
Unmutated *IGHV*			6/17 (35%)
TP53 mutation			3/18 (17%)
NOTCH1 mutation			2 pts (limited testing)

Safety Analysis

Summary of Phase I portion (n=18 patients):

- 3 CLL and 3 MCL patients each treated at TGR-1202 400 mg, 600 mg, 800 mg qd
- There were no DLTs, and an MTD was not identified
- The maximum administered dose of TGR-1202 of 800 mg daily was determined to be the RP2D for both CLL and MCL

Hematologic Toxicity(n=31)

CLL (n=18)

- Neutropenia (38%, 17% Gr 3-4)
- Thrombocytopenia (11%, all Gr 1)
- Anemia (15%, all Gr 1/2)

MCL (n=13)

- Neutropenia (38%; 7.7% Gr 3/4)
- Thrombocytopenia (38%; 7.7% Gr 3)
- Anemia (31%, 7.7% Gr 3)

Safety Analysis (cont., n=31)

Toxicities of Special Interest

- Diarrhea: 11/31 (35%) pts (29% Gr 1, 6% Gr 2, with no inflammatory colitis)

- Transaminitis: 7/31 (23%) pts, all Gr 1 and self-limited without the need for treatment interruption

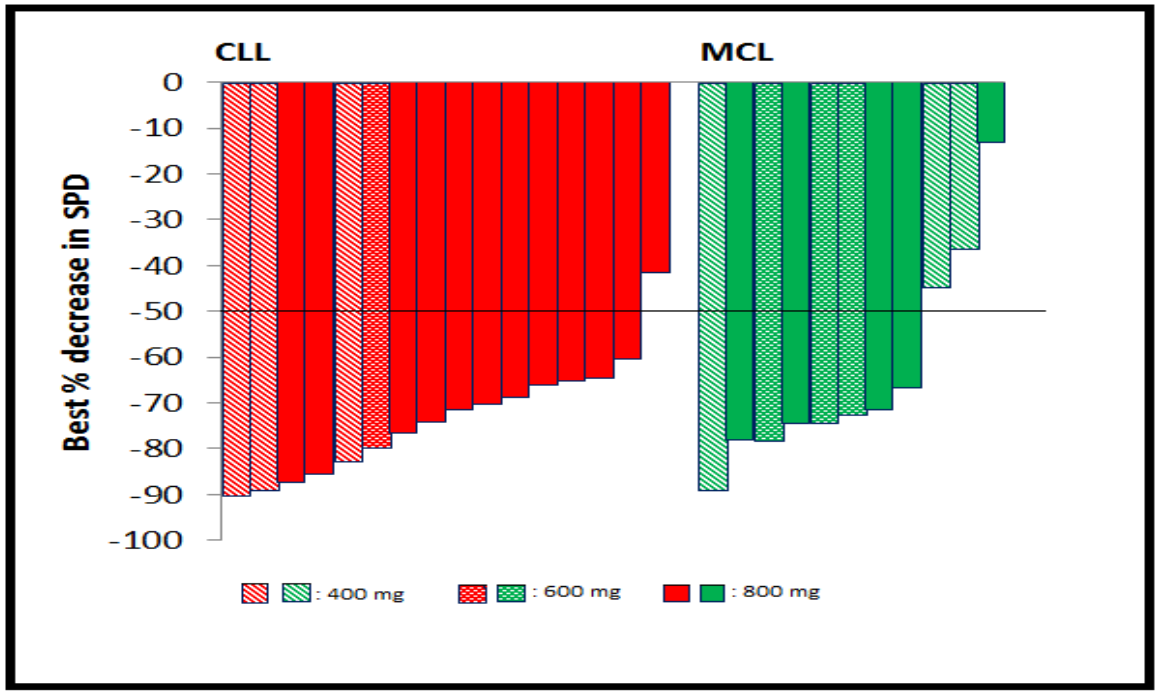
- Pneumonitis: 1/31 (3%) pts, Gr 1

- Bleeding events: Gr 1 epistaxis, hematuria, vitreous hemorrhage in 1 CLL pt each

- Atrial fibrillation: 2/31 (6%) pts (both Gr 3)

- Infection: 7/31 (23%) pts (4 Gr 1/2, 2 Gr 3 (CNS aspergillus, C. diff, 1 Gr 4 influenza)

Preliminary Efficacy Analysis (n=28)



CLL (n=17)

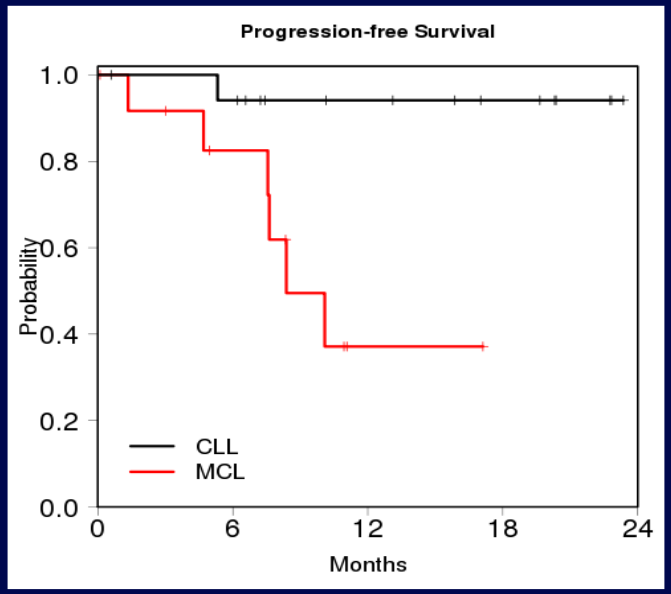
- ORR: 15/17 (88%)
  - -PR or PR-L: 14/17 (82%)
  - -CR: 1/17 (6%)
- 5 PR patients with >80% SPD decrease, nearing radiographic CR
- 3 pts with prior PI3Ki and 1 pt with prior ibrutinib responded

- ORR: 8/11 (73%), all PRs
- Clinical benefit observed in 2 additional patients

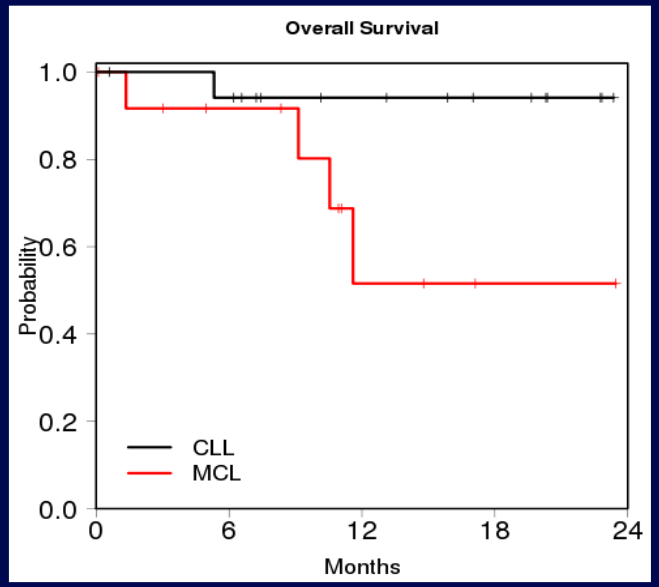
Results

Preliminary Efficacy Analysis (n=28)

PFS



OS



- Median follow-up time among survivors: 11 mo. (range 0.1-23.5)
- 1-year PFS and OS for CLL is 94% (n=17)
- 1-year PFS and OS for MCL is 37% and 52%, respectively (n=11)
- 6 MCL patients have died (5 due to PD, 1 due to toxicity from subsequent therapy)
- 1 CLL patient had sudden death deemed unlikely due to study drugs

Conclusions

- We report to our knowledge the first clinical data on a PI3K plus BTK inhibitor doublet in B cell malignancies

- TGR-1202 + ibrutinib is well-tolerated in R/R CLL and MCL, with no DLTs observed and an RP2D of 800 mg daily

- The toxicities of TGR-1202 + ibrutinib are manageable and comparable to the additive toxicity profiles of the two agents given individually

- The preliminary efficacy results show a high response rate in both diseases
    - CLL patient achieved CR at 1 yr, several others approaching CR

- Correlative studies in progress

- The CLL arm has now completed accrual, MCL patients continue to accrue to this ongoing study (NCT02268851)

Safety and Activity of the Chemotherapy-free Triplet of Ublituximab, TGR-1202, and Ibrutinib in Relapsed B-cell Malignancies

Loretta Nastoupil, MD[1], Nathan Fowler, MD[1], Matthew Lunning, DO[2], Julie Vose, MD[2], Tanya Siddiqi, MD[3], Christopher Flowers, MD[4], Jonathon Cohen, MD[4], Jan Burger, MD, PhD[1], Marshall T. Schreeder, MD[5], Myra Miguel, RN[1], Susan Blumel, RN, BSN[2], Brianna Phye, BS[3], Emily K. Pauli, PharmD[5], Kathy Cutter, RN[5], Peter Sportelli[6], Hari P. Miskin, MS[6], Michael S. Weiss[6], Swaroop Vakkalanka, PhD[7], Srikant Viswanadha, PhD[8] and Susan O'Brien, MD[9]

[1]MD Anderson Cancer Center, Houston, TX; [2]University of Nebraska Medical Center, Omaha, NE; [3]City of Hope National Medical Center, Duarte, CA; [4]Emory University/Winship Cancer Institute, Atlanta, GA; [5]Clearview Cancer Institute, Huntsville, AL; [6]TG Therapeutics, Inc., New York, NY; [7]Rhizen Pharmaceuticals S.A, La Chaux-de-Fonds, Switzerland; [8]Incozen Therapeutics, Hyderabad, India; [9]University of California Irvine Cancer Center, Orange, CA.

Demographics: TGR-1202 + Ublituximab + Ibrutinib

Evaluable for Safety (n)		16
Evaluable for Efficacy† (n)		13
Median Age, years (range)		63 (51 – 85)
Male/Female		12/4
ECOG, 0/1/2		5/8/3
Prior Treatment Regimens, median (range)		4 (1 – 5)
Histologies	4 CLL	1 SLL
	4 Follicular	1 MZL
	3 DLBCL	2 MCL
	1 Richter's Transformation	
≥ 2 Prior R–Chemo Regimens, n		13 (81%)
Refractory to Prior Therapy, n		8 (50%)

†1 removed per investigator discretion and 2 too early to evaluate

- 100% of CLL had 17p and/or 11q del
- 4/5 FL/MZL pts had ≥ 4 prior lines of treatment
  - 1 ibrutinib refractory
  - 1 duvelisib refractory
- 2/3 DLBCL were ABC subtype and had ≥ 4 prior lines of treatment

Safety: TGR-1202 + Ublituximab + Ibrutinib

Cohort Summary

- CLL and NHL cohorts evaluated separately

					NHL Pts	# DLT	CLL Pts	# DLT
1:	Ublituximab 900mg	Ibrutinib 420/560mg	+	TGR-1202 400 mg	3	0	5	1*
2:	Ublituximab 900mg	Ibrutinib 420/560mg	+	TGR-1202 600 mg	4	0	0	0
3:	Ublituximab 900mg	Ibrutinib 420/560mg	+	TGR-1202 800 mg	4	0	0	0

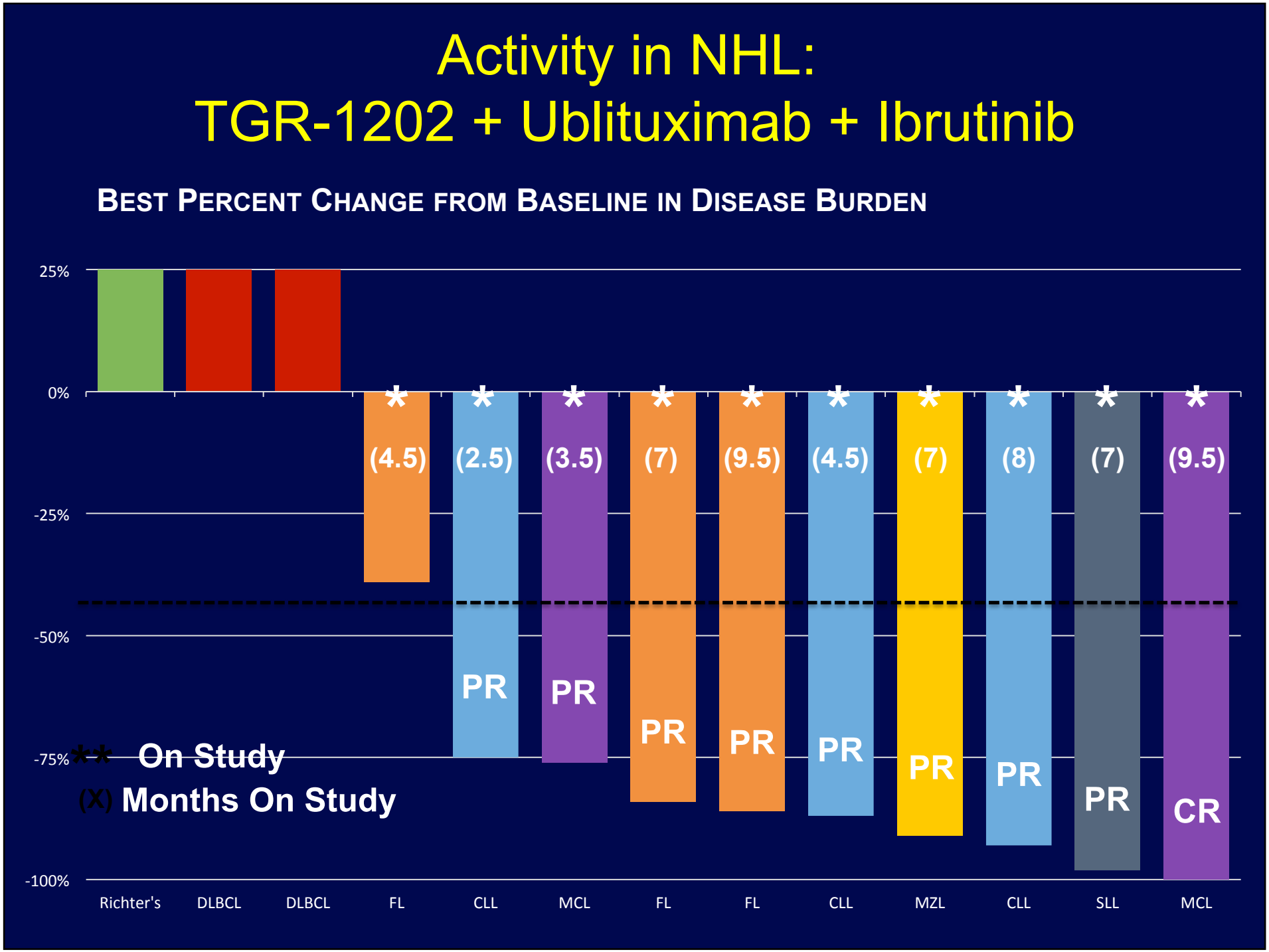
**DLT of reactivated varicella zoster – no additional DLT's to date in CLL cohort*

- Median time on study = 4 mos (range 1 – 9 mos)
- DLT in CLL 400 mg cohort
- 800 mg TGR-1202 cohort cleared in NHL

Safety:
TGR-1202 + Ublituximab + Ibrutinib

AE's (at least possibly related) in > 1 Patient N=16		
Adverse Event	**All Grades** n (%)	**Grade 3/4** n (%)
Infusion reaction	4 (25%)	-
Diarrhea	3 (19%)	-
Nausea	3 (19%)	-
Fatigue	3 (19%)	-
Rash	3 (19%)	-
Anemia	2 (13%)	-
Neutropenia	2 (13%)	1 (6%)
Leukopenia	2 (13%)	1 (6%)
Insomnia	2 (13%)	-

Activity in NHL: TGR-1202 + Ublituximab + Ibrutinib



Activity in NHL: TGR-1202 + Ublituximab + Ibrutinib

Clinical Response at First (8 week) and Second (20 week) Assessment

(All patients who had second assessment shown)

* Durable PR (9+ months) in an ibrutinib refractory Follicular patient

Conclusions

- The biologic combination of Ublituximab, TGR-1202 + Ibrutinib is safe in patients with relapsed B cell malignancies.
  - 800 mg cohort of TGR-1202 in NHL enrolled
  - 400mg cohort of TGR-1202 in CLL continues to enroll
    - One DLT was observed in a CLL for re-activated varicella
      - patient resumed treatment
  - The majority of patients remain on study

- The combination appears highly active in B-cell malignancies
  - CLL/SLL: ORR 100% in all patients with high risk features (n=4)
  - Responses were rapid in the majority of patients
    - 76% reduction in nodal disease noted at first assessment in responders.

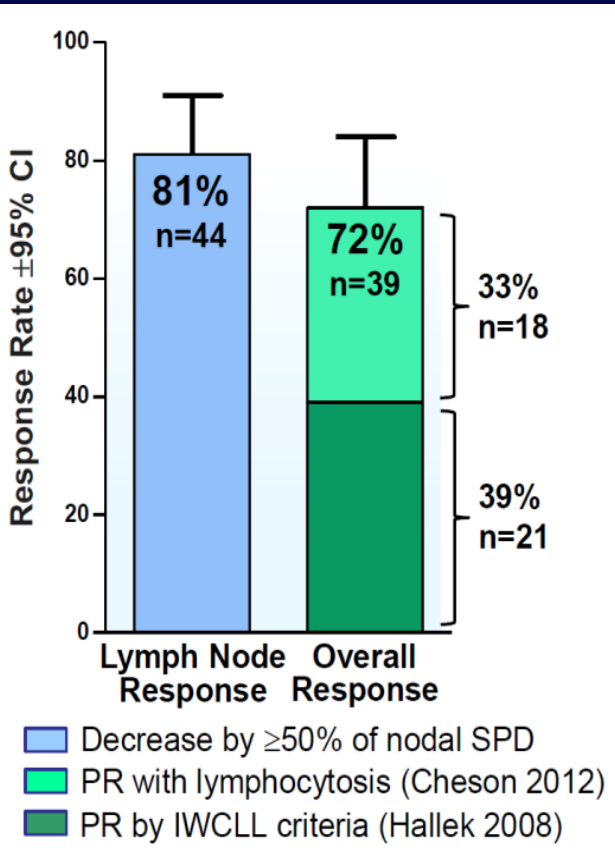
- Triplet combination continues to accrue, with dose expansion planned at 800mg.
  - Clinicaltrials.gov: NCT02006485

- Phase II studies are planned in multiple histologies.

Clinical Activity in CLL

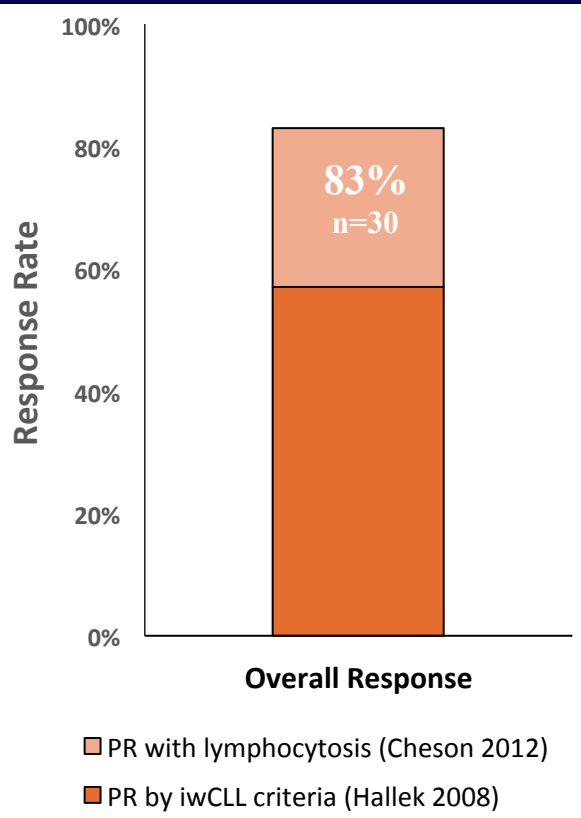
Phase I **Idelalisib** in R/R CLL

(Brown et al, iwCLL 2013)



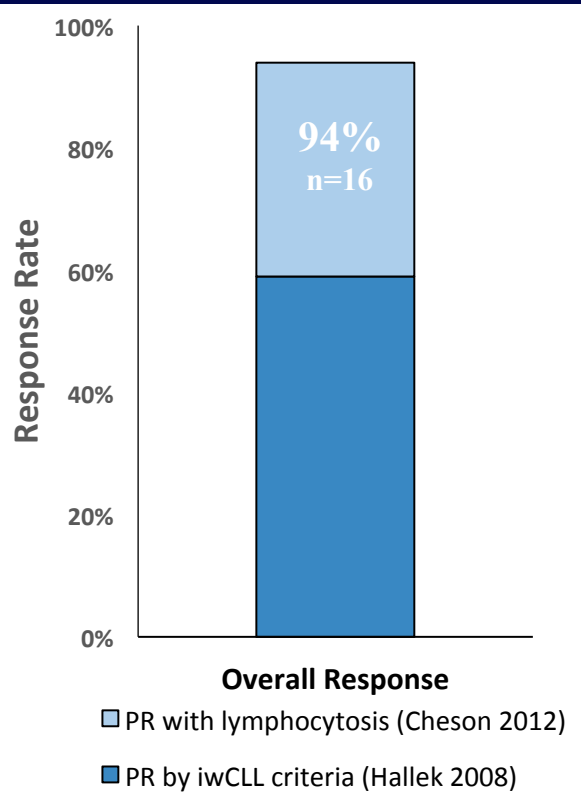
Phase I **Duvelisib** in R/R CLL

(O'Brien et al, ASH 2014)



Phase I **TGR-1202** in R/R CLL

(O'Connor et al, ASH 2015)



Comparison of Safety Profiles of Other PI3K Inhibitors

	Idela + Ofa (ASCO '15)[2] (n=173)	Duvelisib (ASCO '15)[3] (n=18)	Idelalisib Label (CLL & NHL)[1] (n=256)	TGR-1202 All Studies (ASCO 2015)[4] (n=137)
	Grade 3/4	Grade 3/4	Grade 3/4	Grade 3/4
Diarrhea/ Colitis	20%	22%	10%	1%**
Pneumonia	13%	N/A	16%	4%
ALT Elevations	N/A	N/A	11%	2%
AST Elevations	N/A	N/A	7%	2%
ALT/AST Elevations	13%	17%	N/A	2%
Discontinuations due to AE	31%	33%	12%	4%

**No Cases of Colitis Reported with TGR-1202

[1]Aggregated from Idelalisib Prescribing Information; [2]Jones et al, ASCO 2015; [3]Patel et al, ASCO 2015; [4]Aggregated from Burris et al, Lunning et al, Fowler et al, ASCO 2015

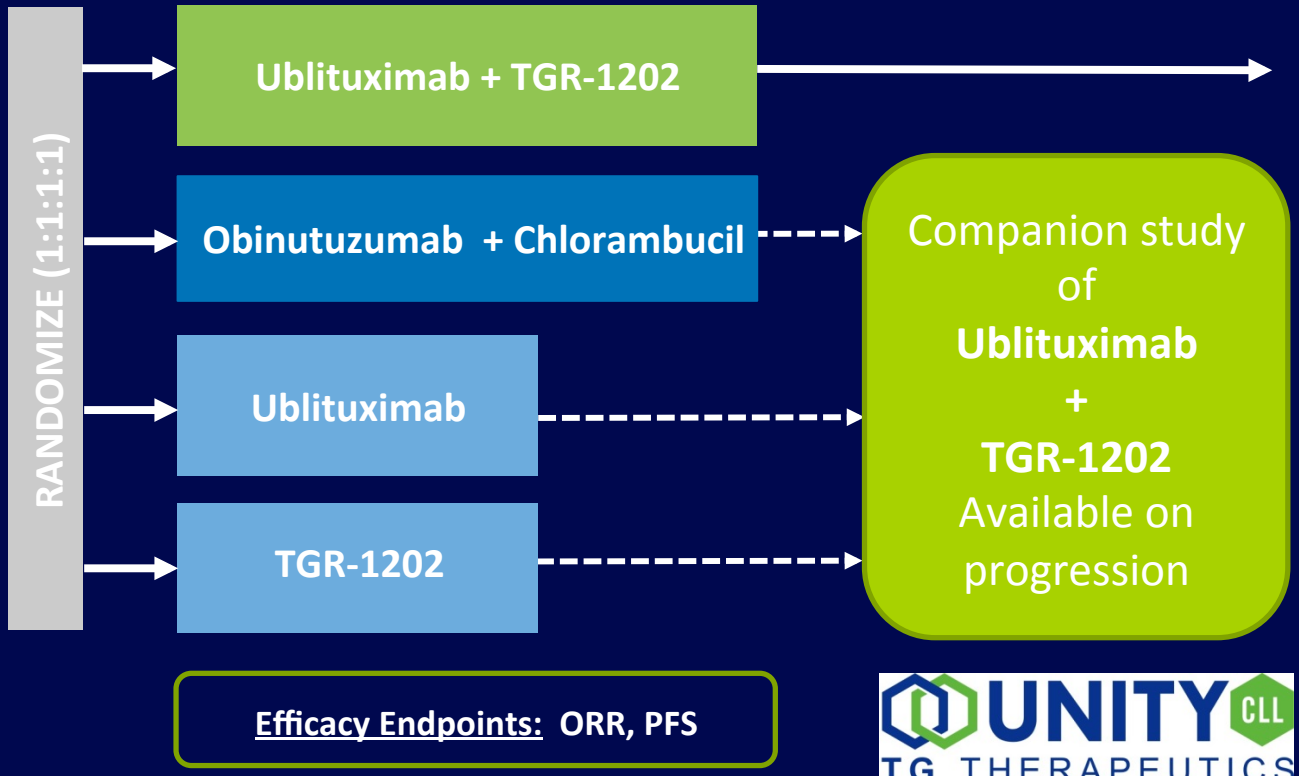
UNITY-CLL 304: Phase 3 Trial for Patients with CLL
Treatment-naïve or Previously Treated

A Multi-center, **Phase 3,** Study of **Ublituximab**, a Glycoengineered Anti-CD20 mAb**, in Combination with TGR-1202,** an Oral PI3Kδ Inhibitor, Compared to Obinutuzumab + Chlorambucil, and Compared to Ublituximab or TGR-1202 Alone, in Patients with **Treatment-naïve or Previously Treated Chronic Lymphocytic Leukemia (CLL)**

Key Eligibility Criteria:

- No limit on the number of prior lines of therapy
- ECOG Status 0, 1, or 2
- No prior exposure to a PI3K inhibitor
- No prior exposure to obinutuzumab and/or chlorambucil

- Global Study Chair: John Gribben, Barts, UK



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

Ublituximab and TGR-1202 are investigational drugs and are not yet approved.
No claims on the safety or efficacy of these drugs are supported by the FDA.