

Investor & Analyst Meeting December 7, 2015







TG Therapeutics

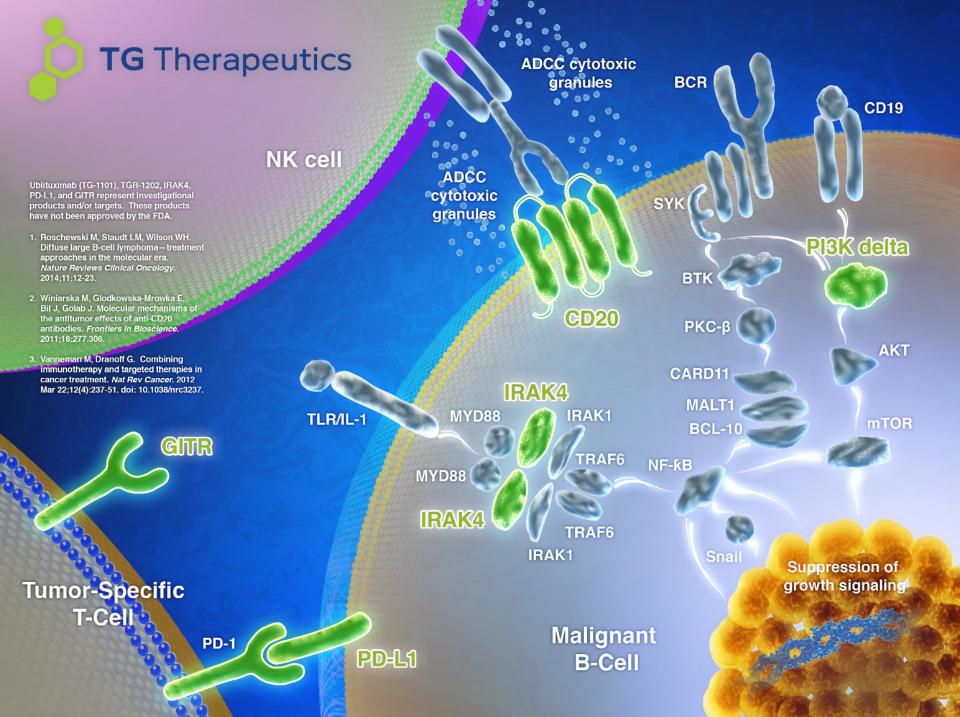
Opening Remarks

Michael S. Weiss, CEO

Objectives - Agenda

Topic	Presenter
Welcome / Introductions	Michael S. Weiss
GENUINE Review TG-1101 + Ibrutinib TG-1303 + Pembrolizumab	Anthony Mato, MD
TGR-1202 Single Agent Review	Owen O'Connor, MD, PhD
TG-1303	Matthew Lunning, DO
UNITY-CLL	Jon Gribben, MD, PhD
Wrap-Up Moderated Q&A	Michael Weiss





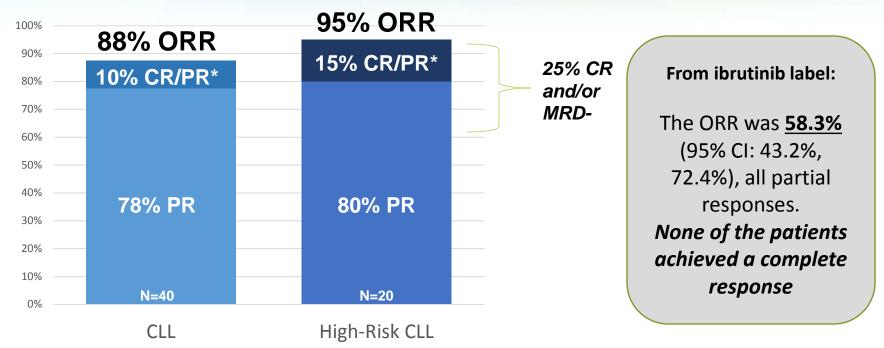


TG Therapeutics

Anthony R. Mato, MD

Director, Center for CLL University of Pennsylvania

Phase II: TG-1101 + ibrutinib Safety & Efficacy

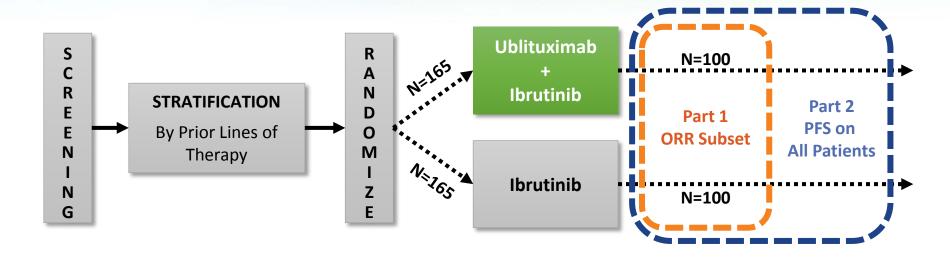


^{* 2} patients had CR per iwCLL criteria without bone marrow confirmation

- 33% of patients were considered anti-CD20-refractory, including to Rituxan®, Ofa or GA-101
- Only 3 Grade 3/4 adverse events were observed in > 5% of patients: neutropenia, anemia & IRR
- Only 7% of CLL patients (3/44) discontinued from the study due to an adverse event
- Aside from day 1 IRR, the addition of TG-1101 to ibrutinib did not appear to alter the safety and tolerability profile of ibrutinib



The GENUINE Phase 3 Trial



- Design, Endpoints, and Statistics agreed to via Special Protocol Assessment (SPA)
- Enrolling ~330 patients with high-risk CLL
- Part 1: ORR among first 200 patients—file for Accelerated Approval
- Part 2: PFS of all 330 patients—file for full approval
 - Part 1 to be analyzed following full enrollment of study



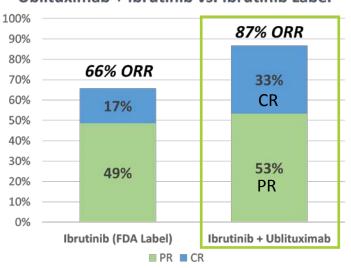
Ublituximab (TG-1101), a Novel Glycoengineered Anti-CD20 Monoclonal Antibody, in Combination with Ibrutinib Is Highly Active in Patients with Relapsed and/or Refractory Mantle Cell Lymphoma: Results of a Phase II Trial

Kathryn S. Kolibaba^{1,2}, John M. Burke^{3,2}, Heather D. Brooks^{4,2}, Daruka Mahadevan⁵, Jason Melear^{6,2}, Charles M. Farber⁷, Suzanne Fanning^{8,2}, Marshall T. Schreeder⁹, Ralph Boccia¹⁰, Peter Sportelli¹¹, Hari P. Miskin¹¹, Michael S. Weiss¹¹, and Jeff Sharman^{12,2}

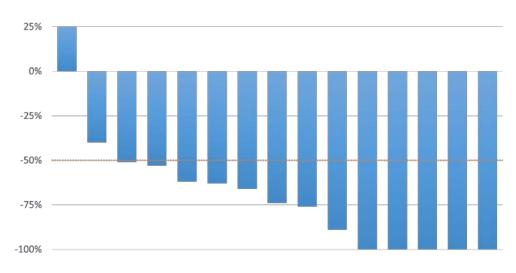
¹Compass Oncology, Vancouver, WA; ²US Oncology Research, The Woodlands, TX; ³Rocky Mountain Cancer Centers, Aurora, CO; ⁴Blue Ridge Cancer Care, Blacksburg, VA; ⁵West Cancer Center/UTHSC, Memphis, TN; ⁶Texas Oncology, Austin, TX; ⁷Carol G. Simon Cancer Center, Morristown, NJ; ⁸Greenville Health System Cancer Institute, Greenville, SC; ⁹Clearview Cancer Institute, Huntsville, AL; ¹⁰Center for Cancer and Blood Disorders, Bethesda, MD; ¹¹TG Therapeutics, Inc., New York, NY; ¹²Willamette Valley Cancer Institute, Springfield, OR

TG-1101 plus Ibrutinib: Efficacy

Investigator Assessed Overall Response Rate and CR rate
Ublituximab + Ibrutinib vs. Ibrutinib Label



Best % Change in Disease Burden from Baseline



- 87% ORR (33% CR, 53% PR)
- 93% (14 of 15) of patients achieved some reduction in tumor burden on study
- One patient, refractory to prior anti-CD20 therapy, and refractory to prior ibrutinib progressed in Cycle 3

Phase I/II study of pembrolizumab in combination with ublituximab and TGR-1202 in patients with relapsed-refractory CLL

Anthony R. Mato, MD University of Pennsylvania



Recent data highlight the activity and immense potential of anti PD-1 antibodies in patients with Hodgkin lymphoma and B cell lymphoproliferative disorders.

Response Rates	Objective Response Rate, n (%)	Complete Responses, n (%)	Partial Responses, n (%)	Stable Disease n (%)
B-Cell Lymphoma* (n=29)	8 (28)	2 (7)	6 (21)	14 (48)
Follicular Lymphoma (n=10)	4 (40)	1 (10)	3 (30)	6 (60)
Diffuse Large B-Cell Lymphoma (n=11)	4 (36)	1 (9)	3 (27)	3 (27)

Lesokhin et al. ASH 2014, Abstract 291.

Moscowitz et al, Blood. 2014;124(21):290-290.

834 PD-1 Blockade with Pembrolizumab (MK-3475) in Relapsed/Refractory CLL Including Richter Transformation: An Early Efficacy Report from a Phase 2 Trial

- 4 / 5 RS patients responded to therapy.
 - 1 CR
 - 1 PR
 - 2 PD (transient)
 - 3 SD (1 RT and 2 CLL)

Wei Ding, MD, PhD et al, ASH 2015, Abs 834



Hypothesis and Objectives

TG1101 + TGR1202 doublet is an ideal platform for combination studies with an anti PD1 antibody therapy based on its clinical activity and non overlapping safety profile.

Pembrolizumab will enhance the efficacy of host T cells to induce apoptosis in CLL following TG-1101 and TGR-1202 induction.

Primary objective: Determine the safety of pembrolizumab + ublituximab + TGR-1202 following ublituximab and TGR-1202 in patients with relapsed-refractory CLL.

Secondary objectives:

- Describe the clinical efficacy of pembrolizumab triplet combination therapy in patients with relapsed-refractory CLL.
- Describe changes T cell repertoire and PD-1 / PD-L1 expression in subjects at planned time points pre and post pembrolizumab

Phase 2 Study to Assess the Safety and Efficacy of TGR-1202 in Patients with CLL who are Intolerant to Prior BTK or PI3K Inhibitor Therapy

Anthony R. Mato, MD
Center for CLL
University of Pennsylvania

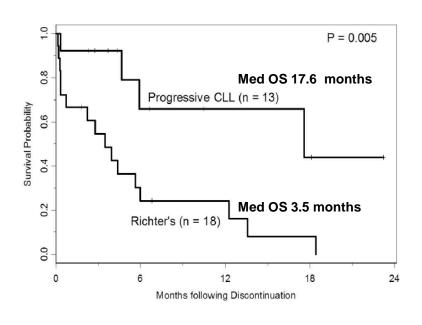


OSU Experience Ibrutinib discontinuation series

 Identified 76 discontinuation patients (25%) from 4 clinical trials (N=308)

Reason for Discontinuation (N=76)					
RT	18 (24%)				
CLL Progression	13 (17%)				
Infection	28 (37%)				
Other AEs	8 (11%)				
Other	9 (12%)				

OS following disease progression on ibrutinib



Estimated incidence of progression at 18 months = 8.9% Estimated incidence of non relapse discontinuation at 18 months = 15.6%

Reasons for Discontinuations

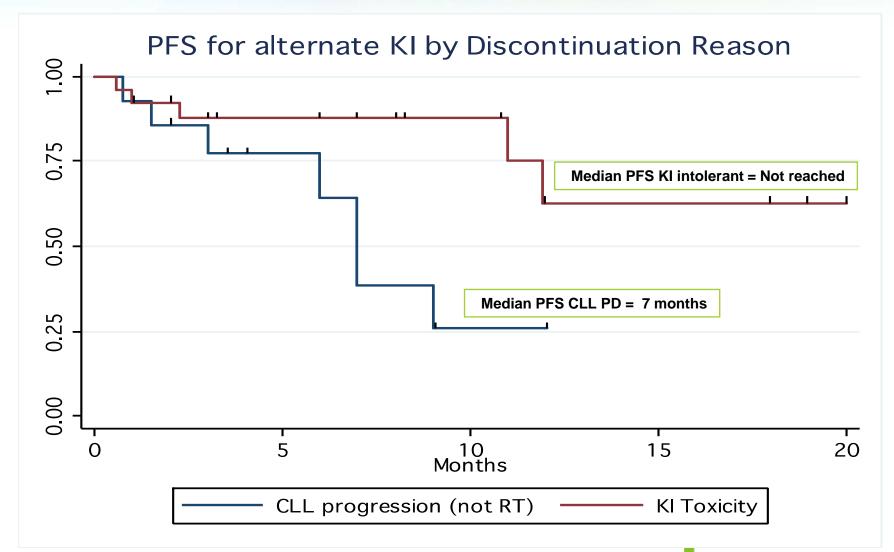
Most Common Reasons for KI Discontinuation				
	Ibrutinib	Idelalisib		
Toxicity	51%	52%		
CLL progression	28%	31%		
Richter's transformation	8%	6%		
SCT / CAR-T	2%	0%		
Unrelated death or other	11%	11%		

Toxicity as Reason for Discontinuation

"Kinase Inhibitor Intolerant" Patients

5 Most Common Toxicities as a Reason for Discontinuation				
Ibrutinib (N=66)	Idelalisib (N=18)			
Atrial fibrillation 20%	Pneumonitis 33%			
Infection 12%	Colitis 28%			
Hematologic 9%	Rash 17%			
Bleeding 9%	Transaminitis 11%			
Pneumonitis 8%	Infection 6%			

Progression-Free Survival





Director of the Center for Lymphoid Malignancies Columbia University Medical Center

Clinical Activity and Safety Profile of TGR-1202, a Novel Once-Daily Pl3Kδ Inhibitor, in Patients with CLL and B-Cell Lymphoma

Owen A. O'Connor, MD, PhD¹, Ian W. Flinn, MD, PhD²,³, Manish R. Patel, MD²,⁴, Timothy S. Fenske, MD⁵, Changchun Deng, MD, PhD¹, Danielle M. Brander, MD⁶, Martin Gutierrez, MD⁶, Suzanne Jones, PharmD², John G Kuhn, Pharm.D.⁶, Hari P. Miskin, MS⁶, Peter Sportelli⁶, Swaroop Vakkalanka, PhD¹⁰ and Howard A. Burris III, MD²,³

¹Center for Lymphoid Malignancies, Columbia University Medical Center, New York, NY, ²Sarah Cannon Research Institute, Nashville, TN, ³Tennessee Oncology, PLLC, Nashville, TN, ⁴Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, ⁵Division of Hematology & Oncology, Medical College of Wisconsin, Milwaukee, WI, ⁶Duke University Medical Center, Durham, NC, ⁷John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ, ⁸University of Texas Health Science Center at San Antonio, San Antonio, TX ⁹TG Therapeutics, Inc., New York, NY, ¹⁰Rhizen Pharmaceuticals SA, La Chaux-de-Fonds, Switzerland

TGR-1202: Novel PI3K delta Inhibitor

TGR-1202	Idelalisib (GS-1101)	Duvelisib (IPI-145)
F N N N N N N N N N N N N N N N N N N N	F O N NH N	CI O NH
Delta	Delta	Delta/Gamma
QD	BID	BID

PK profile that allows <u>once-daily oral</u> dosing

TGR-1202: Safety

All Even	its in >10% o	f Pts (N=81	L)		
AE	All G	irades	Gr.	Gr. 3/4	
AL	N	%	N	%	
Nausea	34	42%	1	1%	
Diarrhea	33	41%	2	2%	
Fatigue	25	319′	3	4%	
Rash	22	279	4	5%	**
Headaches	20	250		10/	
Cough	19	Of the 31 Gr 1/2 Diarrhea, o			
Vomiting	18	were G	3r.2 and	d no Gr.	4 eve
Constipation	12		were o	bserved	
Decreased Appetite	12				
Hypokalemia	12	Da	ata repres	sents ev	ents
Anemia	11	occurr	ing durin	g entire	dura
Dizziness	11	on stu	dy (upwa	ards of 2	.5 ye
Dyspnea	11	11/0	•	5 /0	
Pyrexia	10	12%	0	0%	
Abdominal Pain	9	11%	0	0%	
Arthralgia	9	11%	0	0%	
Insomnia	9	11%	0	0%	

38 patients have been on study over 6 cycles, and 22 patients have been on study over 12 cycles

Grade 3/4 AST/ALT rease was 2% (4% all hea, only 5 des) r. 4 events

> atients (7%) have come study due to an erse event

the 81 pts treated, no **2.5 years)** events of colitis have been observed to date

re duration

PI3K-Delta Class AE Profile

	Idela + Ofa (ASCO '15) ¹ (n=173)	Idela +BR (ASH '15 Abstract) ² (n=207)	Idelalisib Label (CLL & NHL) ³ (n=256)	TGR-1202 (ASH '15) ⁴ (n=152)
	All Grades (<u>></u> Gr 3)	All Grades (<u>></u> Gr 3)	All Grades (<u>></u> Gr 3)	All Grades (<u>></u> Gr 3)
Diarrhea/ Colitis	49% (20%)	N/A (7.2%)	36% (10%)	42% (2%)**
Pneumonia	17% (13%)	N/A	24% (16%)	6% (5%)
ALT Elevations	N/A	60% (21%)	43% (11%)	N/A
AST Elevations	N/A	52% (16%)	34% (7%)	N/A
ALT/AST Elevations	35% (13%)	N/A	N/A	6% (3%)
Discontinuations due to AE	31%	N/A	12%	8%

** No observed instances of colitis

¹Jones et al, ASCO 2015

² Zelenetz et al, ASH 2015

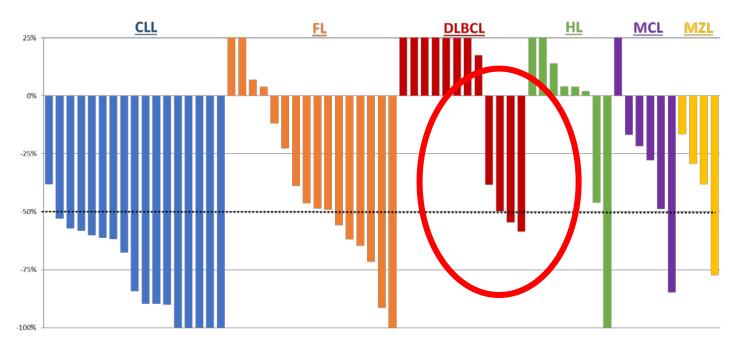
³ Aggregated from Idelalisib Prescribing Information

⁴ Aggregated from O'Connor et al, Lunning et al, ASH 2015

TGR-1202: Efficacy

Best Percent Change from Baseline in Disease Burden

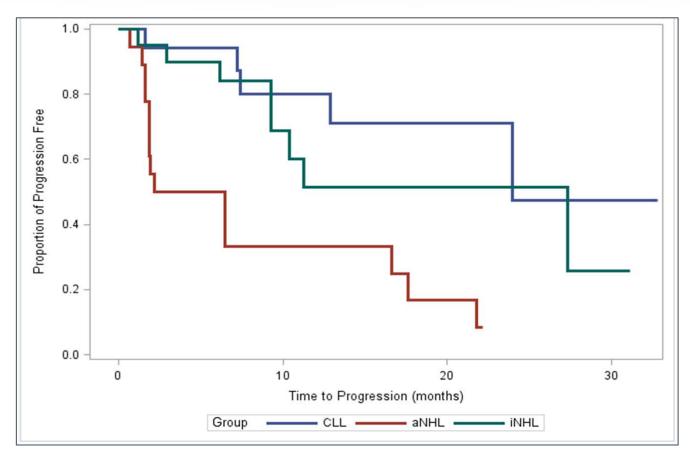
Patients Evaluable for Efficacy (N=63)



- ❖ 94% of CLL patients (16/17) achieved a nodal PR, remaining patients still on study pending further evaluation
- 59% of CLL patients (10/17) achieved a response per iwCLL (Hallek 2008) criteria
- Similar to activity seen in CLL, tumor reductions in indolent lymphoma have shown improvement over time

TGR-1202: Efficacy

Kaplan-Meier Plot of PFS



Median PFS:

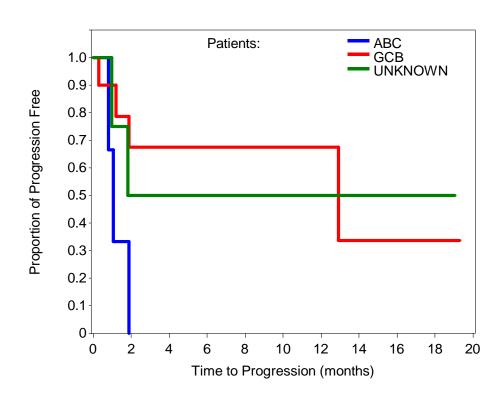
- CLL: 23.98 months (95% CI: 7.4, NR)
- * iNHL (FL & MZL): 27.3 months (95% CI: 9.28, NR)
- aNHL (DLBCL & MCL): 4.33 months (95% CI: 1.88, 16.6)



TG-1101 (ublituximab) +TGR-1202: Efficacy

Patients with DLBCL

- 16 DLBCL patients evaluable:
- ORR: 33% (3/9) GCB, 0%
 (0/3) ABC, 50% (2/4) subtype
 unknown
- Notable activity has been observed particularly in patients with GCB DLBCL
- UNITY-DLBCL randomized study opening soon



Coming Soon: For Previously Treated DLBCL Patients



- Owen O'Connor, Study Chair
- Phase 2b randomized trial TG-1101 +TGR-1202
- Expected to open in 1H2016
- Targeting centers in the US and Ex-US

Disruption of the mTOR-eIF4F Axis by Selectively Targeting PI3K δ and Proteasome Potently Inhibits Cap Dependent Translation of c-Myc in Aggressive Lymphomas

Changchun Deng, M.D., Ph.D.
Mark Lipstein, B.S.
Luigi Scotto, Ph.D.
Michael Mangone, Ph.D.
Owen A. O'Connor, M.D., Ph.D.

Columbia University Medical Center
Department of Medicine
Center for Lymphoid Malignancies









TG Therapeutics

Matthew Lunning, DO

Assistant Professor, Division of Hematology University of Nebraska Medical Center

Ublituximab + TGR-1202 Demonstrates Activity and a Favorable Safety Profile in Relapsed/Refractory B-Cell NHL and High-Risk CLL: Phase I Results

Matthew Lunning, DO¹, Julie Vose, MD¹, Nathan Fowler, MD², Loretta Nastoupil, MD², Jan A. Burger, MD², William G. Wierda, MD², Marshall T. Schreeder, MD³, Tanya Siddiqi, MD⁴, Christopher R. Flowers, MD⁵, Jonathon B. Cohen, MD⁵, Susan Blumel, RN, BSN¹, Myra Miguel, RN², Emily K. Pauli, PharmD³, Kathy Cutter, RN³, Christine McCarthy⁴, Ryan Handy, BS⁵, Peter Sportelli⁶, Hari P. Miskin, MS⁶, Michael S. Weiss⁶ and Susan OʻBrien, MD⁵

¹University of Nebraska Medical Center, Omaha, NE; ²MD Anderson Cancer Center, Houston, TX; ³Clearview Cancer Institute, Huntsville, AL; ⁴City of Hope National Medical Center, Duarte, CA; ⁵Emory University/Winship Cancer Institute, Atlanta, GA; ⁶TG Therapeutics, Inc., New York, NY; ⁷University of California Irvine, Orange, CA



TG-1101 (ublituximab) +TGR-1202 ("1303"): Demographics

Evaluable for Safety (n)	71		
Evaluable for Efficacy [†] (n)	58		
Median Age, years (range)	65 (26 – 86)		
Male/Female	47/2	24	
	DLBCL	24	
Histology	CLL/SLL	19	
	FL	19	
	MZL	6	
	MCL	2	
	Richter's	1	
ECOG, 0/1/2	20/47	7/4	
Prior Therapy Regimens, median (range)	3 (1 – 10)		
Patients with ≥ 3 Prior Therapies (%)	61%		
Prior RTX Based Therapies, median (range)	es, median (range) 3 (1 – 7)		
Refractory to Prior Therapy, n (%)	41 (58%)		

^{†13} Patients not evaluable (9 too early, 2 non-related AE, 1 removed per investigator discretion, 1 for SAE, 1 ineligible)



TG-1101 (ublituximab) +TGR-1202 ("1303"):

Safety

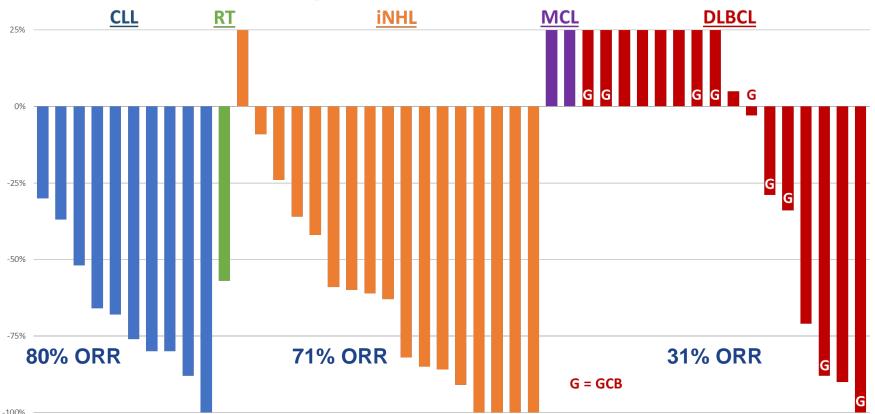
All Causality AE's Occurring in ≥ 10% of Patients (n = 71)

Adverse Event	All (Grades	Grade	e 3/4		
Adverse Event	N	%	N	%		
Nausea	33	46%	1	1%		
Diarrhea	31	44%	2	3%		
Fatigue	29	41/0	າ	3/0	4 6 patients (8	3%) discontinued
Neutropenia	21	30%	18	25%	due to a TGI	R-1202 related AE
Infusion related reaction	18	25%	1	1%		
Vomiting	17	24%			Grada 2/1 A	ST/ALT increase
Dyspnea	14	20%	Of the	e 29 Gr 1	/2 Diarrhea, only	II grades)
Back pain	13	18%	11 \	were Gr.2	2, and no Gr. 4)(()
Dizziness	13	18%	e [,]	vents we	ere observed	%) had their
Pyrexia	13	18%				se reduced; 2
Decrease appetite	12	17%	Da	ata repre	sents events	eutropenia, 1
Insomnia	12	17%	occurr	ing durir	ng entire duration	gue, 1 dizziness
Sinusitis	11	15%	on stu	udy (upw	ards of 22 mos.)	
Cough	10	14%				ot been reported
Anemia	9	13%	1	1%	to date	
Constipation	8	11%	-	-		
Headache	8	11%	-	-		
Vitamin D decrease	8	11%	-	-		
Hypophosphatemia	7	10%	1	1%		
Peripheral edema	7	10%	1	1%		
Rash	7	10%	-	-	<u> </u>	G Thorapoutics 24

TG-1101 (ublituximab) +TGR-1202 ("1303"): Efficacy

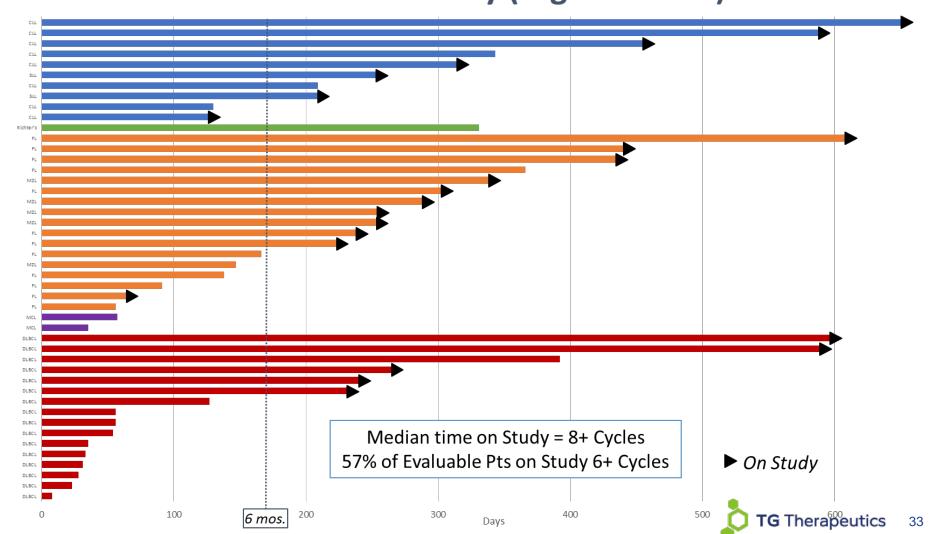
Patients Treated at the "Higher Doses" of TGR-1202

Best Percent Change from Baseline in Disease Burden



TG-1101 (ublituximab) +TGR-1202 ("1303"): Efficacy

Duration on Study (Higher Doses)





TG Therapeutics

Jon Gribben, MD, PhD

Centre Lead, Centre for Hemato-Oncology, Barts Cancer Institute, London UK

TGR-1202 Meta Analysis

Safety and efficacy data from 2 datasets as follows:

- Single Agent TGR-1202
- Combination of TG-1101(ublituximab) + TGR-1202 ("1303")

Fuelushia fee Cafety (v)	152		
Evaluable for Safety (n)	Single agent (81) / Combo (71)		
	121	l	
Evaluable for Efficacy (n)	Single agent (63)	/ Combo (58)	
	CLL/SLL	40	
	DLBCL	38	
	FL	41	
Histology	MZL	11	
	HD	9	
	MCL	8	
	Other	5	



TGR-1202 Meta Analysis: Safety

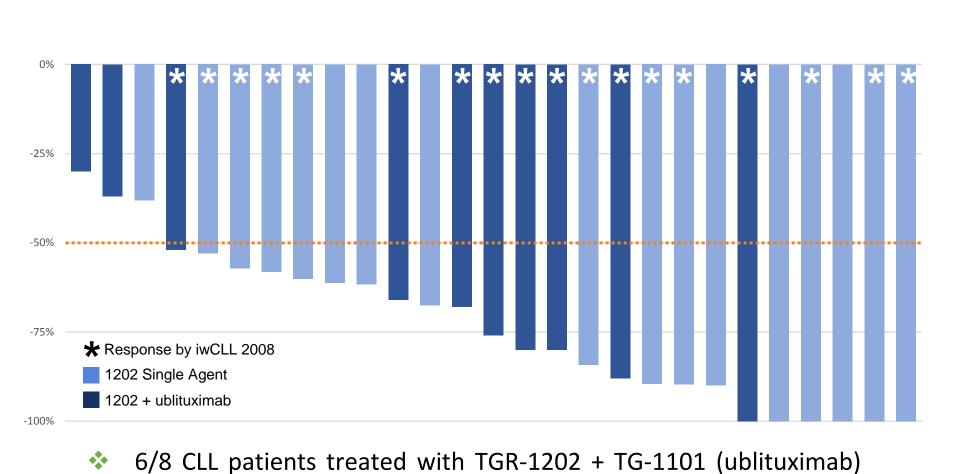
All Causality AE's Occurring in ≥ 10% of Patients (n = 152)

Advance French	All G	irades	Grade	e 3/4
Adverse Event	N	%	N	%
Nausea	67	44%	2	1%
Diarrhea	64	42%	3	2%
Fatigue	54	36%	5	3%
Vomiting	35	23%	0	0%
Neutropenia	29	19%	25	16%
Cough	29	19%	0	0%
Headache	28	18%	1	< 1%
Rash	27	18%	4	3%
Dyspnea	25	16%	6	4%
Dizziness	24	16%	0	0%
Decrease appetite	24	16%	0	0%
Pyrexia	23	15%	2	1%
Insomnia	21	14%	0	0%
Anemia	20	13%	7	5%
Constipation	20	13%	1	< 1%
Abdominal pain	15	10%	4	3%
URT infection	15	10%	0	0%
AST/ALT elevation	9	6%	4	3%
Pneumonia	9	6%	7	5%
Pneumonitis	2	1%	1	<1%
Colitis	0	0%	0	0%

- 64 patients have been on study over 6 cycles and 33 patients have been on study over 12 cycles
- 12 patients (8%) discontinued due to a TGR-1202 related AE
- Of the 25 patients with G
 3/4 neutropenia, 7 (28%)
 were on single agent TGR 1202

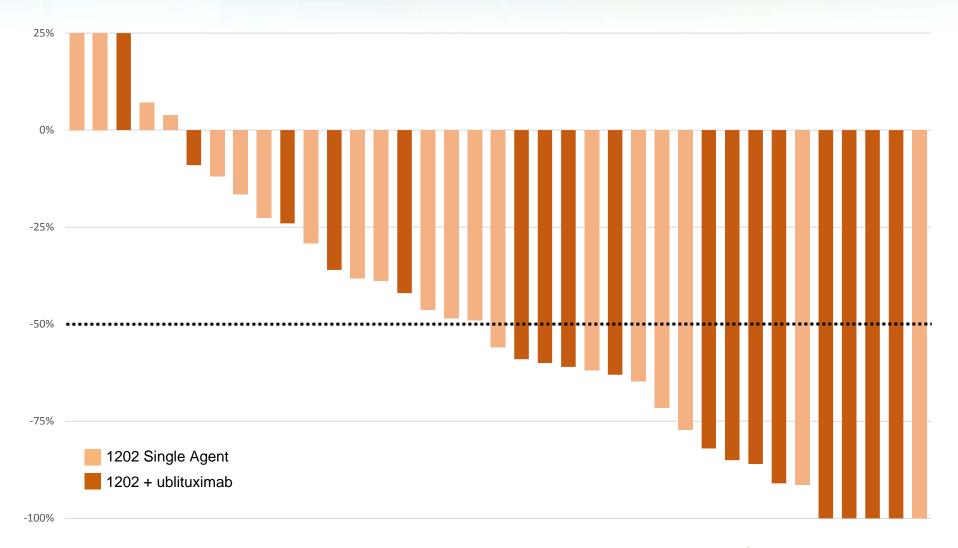
Meta-Analysis: Efficacy in CLL/SLL

25%

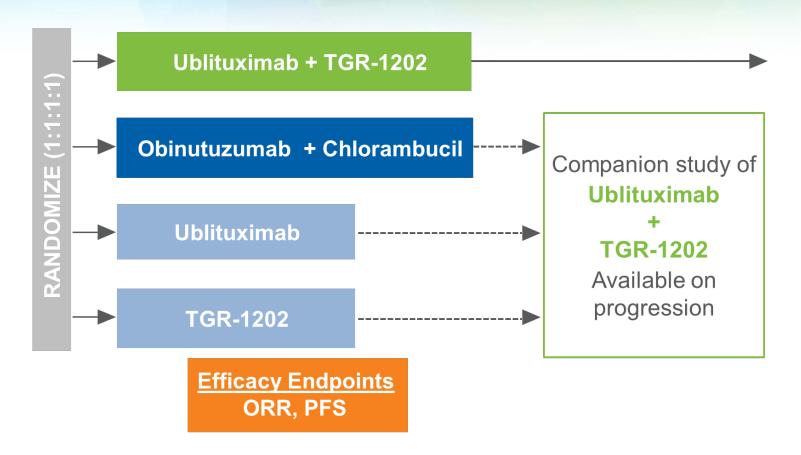


had del 17p and/or 11q

Meta-Analysis: Efficacy in iNHL (FL & MZL)



UNITY-CLL – Phase 3 Trial



- Design, Endpoints, and Statistics agreed to via Special Protocol Assessment (SPA)
- Enrolling ~450 patients with previously treated and previously untreated CLL
- Primary Endpoint: PFS



TG Therapeutics

Closing Remarks

Michael S. Weiss

Executive Chairman & Interim CEO

TGR-1202 Meta Analysis: Safety

Still Concerned about Colitis?

Including all studies presented at ASH 2015*:

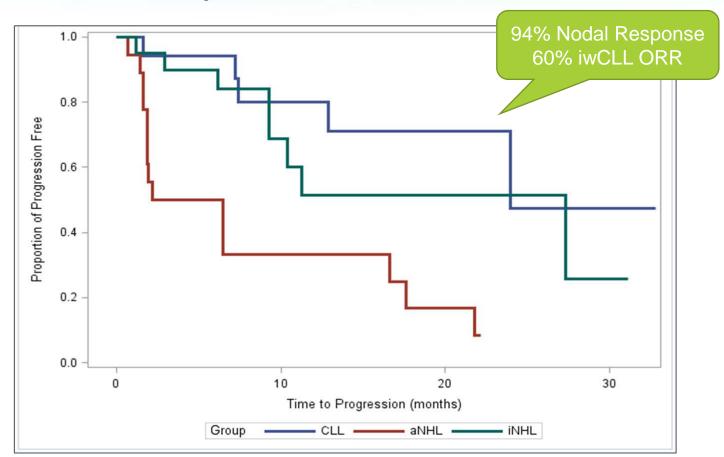
- 80 patients have been on study over 6 months
- 41 patients have been on study over 12 months

95% Binomial Confidence Interval: 0% - 4.5%

^{*} Includes study of TGR-1202 plus Gazyva plus chlorambucil

TGR-1202-101: Efficacy

Kaplan-Meier Plot of PFS



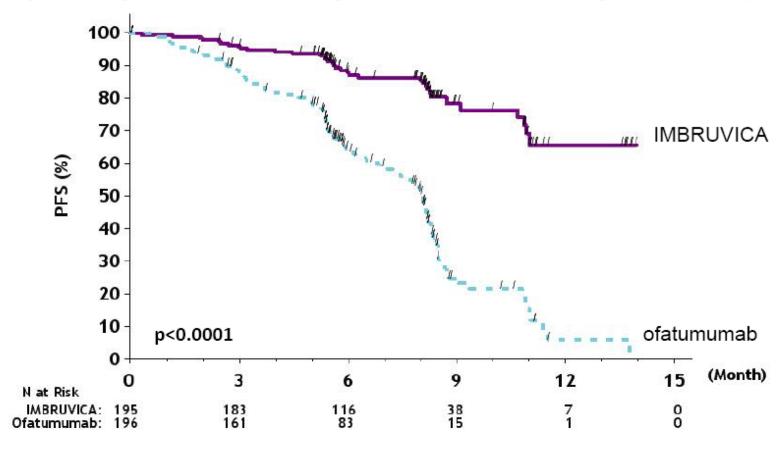
Median PFS:

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

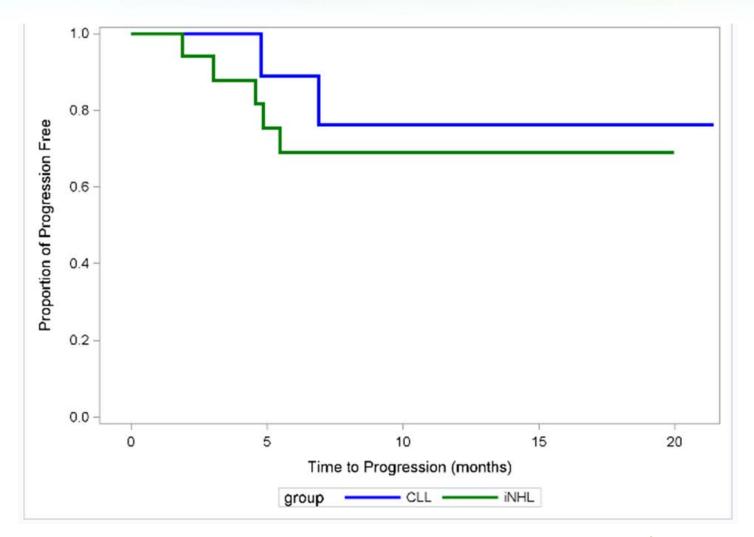


TGR-1202: Efficacy

Figure 1: Kaplan-Meier Curve of Progression-Free Survival (ITT Population) in Study 2



1303 Efficacy: PFS



TGR-1202 + Gazyva: PRESENTATION HIGHLIGHTS

- 100% (15 of 15) ORR in treatment naïve CLL patients, with 33% of patients achieving a CR, and 47% of patients achieving MRD negativity
- Notably different safety profile than TG-1303, specifically regarding neutropenia (78% vs. 30%), thrombocytopenia (78% vs. <10%), and transaminase elevations (39% vs. 8%)
 - Neutropenia was high but infections were low
 - A lot of the neutropenia occurred in cycle 1 when growth factor support was restricted
- The median PFS has not been reached, with the longest patient on study now 20+ months on TGR-1202 daily maintenance at 800mg

