TG Therapeutics

2015 ASCO Analyst & Investor Event

May 31, 2015

Forward Looking Safe Harbor Statement

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Event Agenda & Speakers

AGENDA	SPEAKER
Overview & Introductions	Michael S. Weiss, CEO of TGTX
TG-1101 & TGR-1202 Overview	Dr. Owen A. O'Connor
TG-1101 & TGR-1202 in NHL	Dr. Nathan Fowler
TG-1101 & TGR-1202 in CLL	Dr. Anthony Mato
Q&A Session	Dr.'s O'Connor, Fowler & Mato
Closing Remarks	

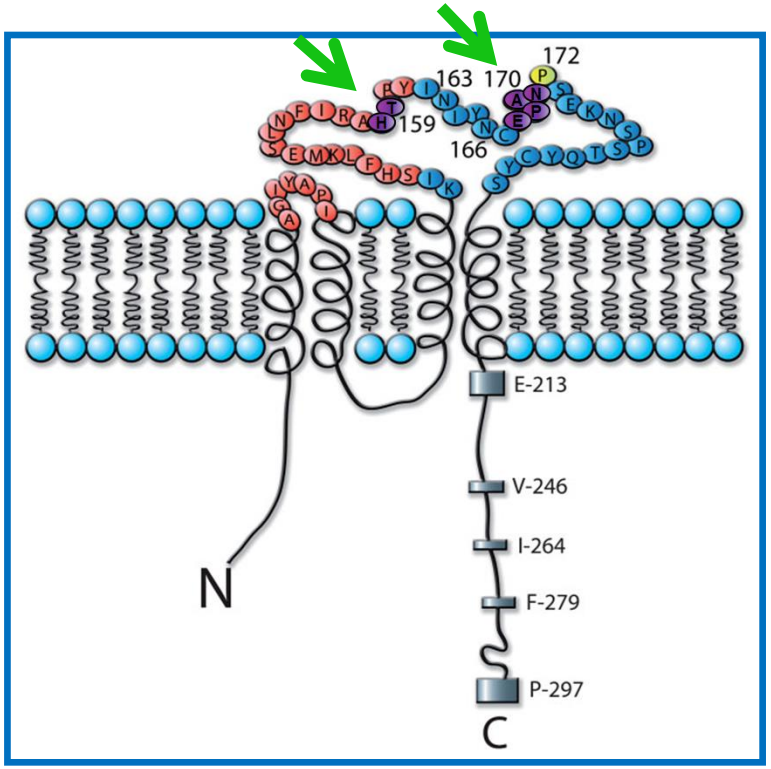
Owen A. O'Connor, MD, PhD
Professor of Medicine and Experimental Therapeutics
Director of the Center for Lymphoid Malignancies
Columbia University Medical Center

TG-1101 & TGR-1202 Single Agent

TG-1101 (UBLITUXIMAB)

Ublituximab: A Novel Glycoengineered Anti-CD20 mAb

- Unique protein sequence
- Type 1 Chimeric IgG1 mAb
- Potential advantages over current standard of care:
  - Glycoengineered for significantly enhanced ADCC
  - Activity in “low” CD20 expressing cell lines, a characteristic of rituximab resistance
  - Binds to a novel epitope on CD20



Safety of Ublituximab

- Day 1 Infusion Related Reaction most common adverse event
  - manageable with infusion interruptions only and recovered without sequelae
- Infusion times decreased to an average of 90 minutes for the 4th and all subsequent infusions

At Least Possibly Related AE's

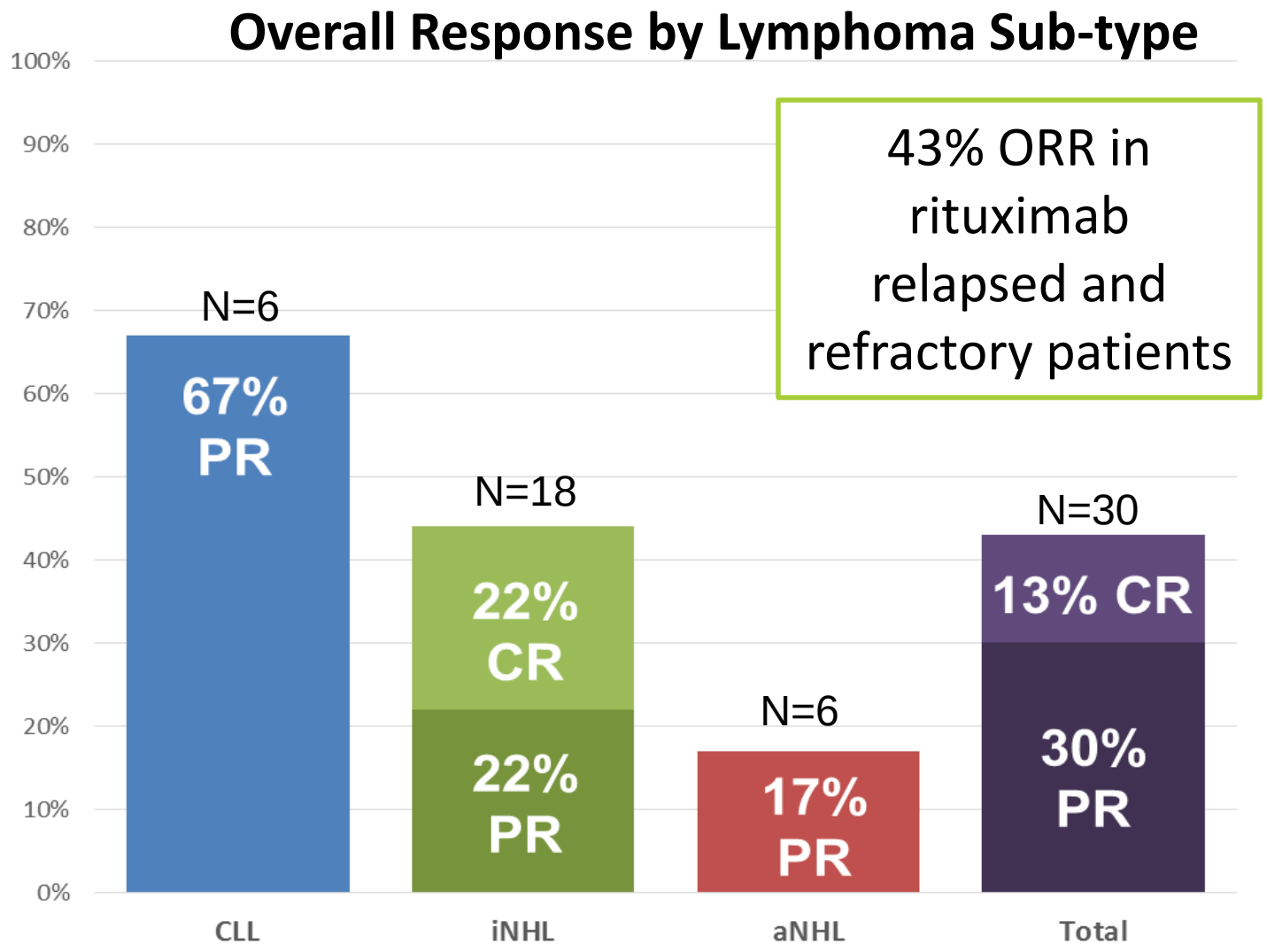
All Patients (n = 35)		
AE	All Grades n (%)	Grade 3/4 n (%)
Infusion Related Reaction*	10 (29%)	0
Fatigue	5 (14%)	1 (3%)
Diarrhea	4 (11%)	0
Pain (General)	4 (11%)	0
Dysgeusia	3 (9%)	0
Bilirubin Increase	2 (6%)	0
Pruritus	2 (6%)	0

At Least Possibly Related Lab Abnormalities

AE	CLL (n=8)		NHL (n=27)	
	Grade 1/2 n	Grade 3/4 n	Grade 1/2 n	Grade 3/4 n
Neutropenia	1	3	0	0
Thrombocytopenia	1	1	0	0
Anemia	0	0	0	1

Demonstrated single agent activity:

TG-1101 Phase 1 Efficacy Results ASCO/EHA 2014



Ublituximab – Take Home Messages

- Well tolerated with minimal IRR complications
- Promising activity in both rituximab relapsed and rituximab refractory patients across all histologies
  - Interesting activity in iNHL—e.g. one rituximab refractory MZL patient transition from hospice to durable (2+ year) Complete Response
- 11 of 30 evaluable patients remained on study >1 year with no complications (2 patients on study >2 years)

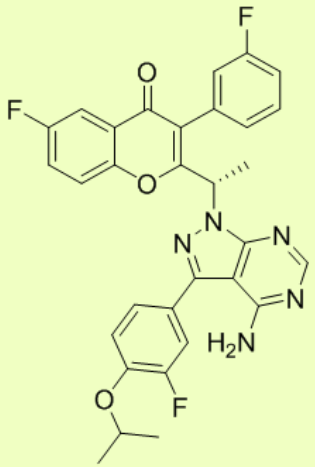
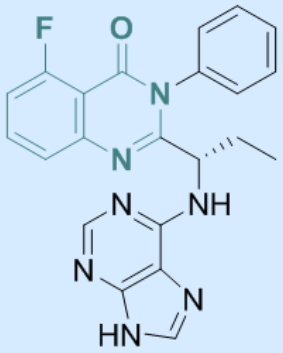
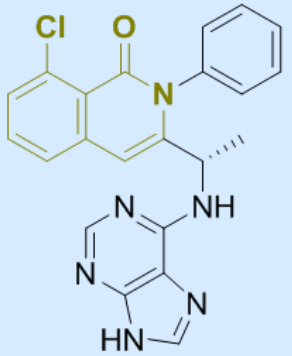
TGR-1202
SINGLE AGENT

Clinical activity and safety profile of TGR-1202, a novel once daily PI3Kδ inhibitor, in patients with CLL and B-cell lymphoma.

Howard A. Burris III, MD[1,2], Manish R. Patel, MD[1,3], Timothy S. Fenske, MD[4], Owen A. O'Connor, MD, PhD[5], Changchun Deng, MD, PhD[5], Danielle M. Brander, MD[6], Martin Gutierrez, MD[7], Suzanne Jones, PharmD[1], John Kuhn, PharmD[8], Hari P. Miskin, MS[9], Peter Sportelli[9], Swaroop Vakkalanka, PhD[10] and Ian Flinn[1,11]

[1]Sarah Cannon Research Institute, Nashville, TN; [2]Tennessee Oncology, PPLC, Nashville, TN; [3]Florida Cancer Specialists, Sarasota, FL; [4]Medical College of Wisconsin, Milwaukee, WI; [5]Columbia University Medical Center, New York, NY; [6]Duke University Medical Center, Durham, NC; [7]John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; [8]University of Texas Health Science Center at San Antonio, San Antonio, TX; [9]TG Therapeutics, Inc., New York, NY; [10]Rhizen Pharmaceuticals SA, La Chaux-de-Fonds, Switzerland; [11]Tennessee Oncology, PLLC, Nashville, TN

TGR-1202: Novel PI3K delta Inhibitor

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

- PK profile that allows once-daily oral dosing
- 93% nodal PR rate in patients with rel/ref CLL[1]

[1]Burris et al, ASCO 2015, Abstract # 7069

Demographics

Evaluable for Safety (n)	66	
Evaluable for Efficacy (n)	51	
Median Age, years (range)	66 (22 – 85)	
Male/Female	46/20	
Histology	20 CLL	5 MCL
	17 FL	3 MZL
	10 DLBCL	1 HCL
	9 HL	1 WM
ECOG 0/1/2	22/43/1	
Prior Therapies, median (range)	3 (1 – 14)	
Patients with ≥ 3 Prior Therapies (%)	36 (55%)	
Patients Refractory to Prior Therapy	34 (52%)	

† Patient's evaluable for efficacy included only patients treated with 800 mg of initial formulation or higher, and any micronized dose level of which the following were excluded: 4 were Too Early To Evaluate, 2 Non-Compliant (both at 1800 mg Fasted), 1 removed per investigator discretion, and 1 Failed Inclusion/Exclusion (Richter's Transformation prior to entry)

Safety

Adverse Events in TGR-1202 Treated Patients

All Events in >10% of Pts (N=66)				
AE	All Grades		Gr. 3/4	
	N	%	N	%
Nausea	27	41%	0	0%
Diarrhea	21	32%	1	2%
Fatigue	21	32%	2	3%
Headache	15	23%	0	0%
Vomiting	15	23%	0	0%
Cough	14	21%	0	0%
Decreased Appetite	11	17%	0	0%
Rash	11	17%	3	5%
Constipation	9	14%	1	2%
Hypokalemia	9	14%	3	5%
Anemia	8	12%	5	8%
Dizziness	8	12%	0	0%
Dyspnea	8	12%	3	5%
Neutropenia	8	12%	7	11%
Pyrexia	8	12%	0	0%
Abdominal Pain	7	11%	0	0%

- Limited Gr. 3/4 events and no significant dose or time dependent trends in AEs observed with 31 patients on study 6+ months
- **3 patients (< 5%) have discontinued due to an adverse event, none of which for hepatic toxicity, colitis, or pneumonitis**

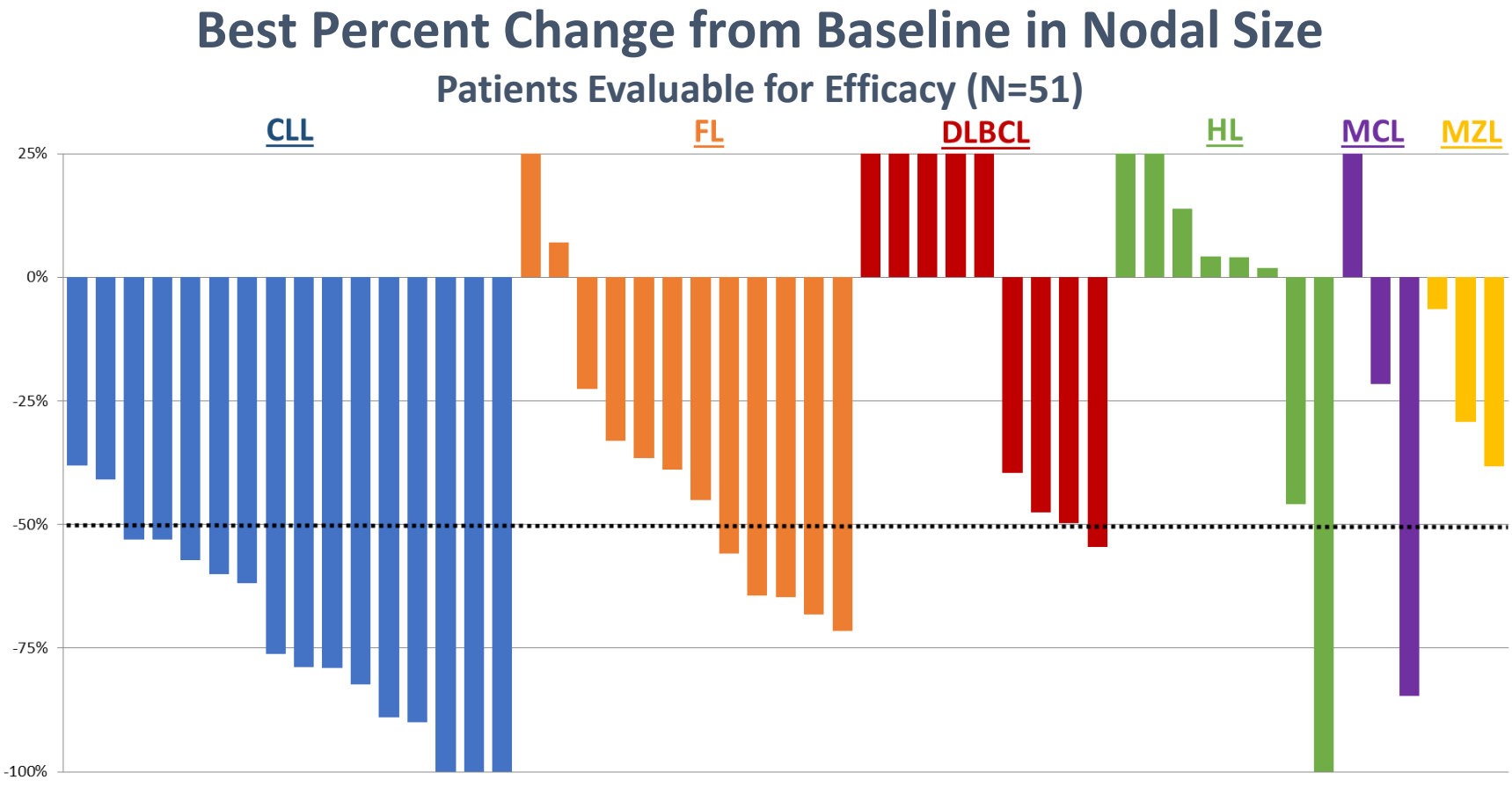
PI3K-Delta Class AE Profile

	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)
	All Grades (≥Gr 3)	All Grades (≥Gr 3)	All Grades (≥Gr 3)	All Grades (≥Gr 3)
Diarrhea/ Colitis	**49%** (20%)	**78%** (22%)	**36%** (10%)	**26%** (1%)**
Pneumonia	**17%** (13%)	N/A	**24%** (16%)	**7%** (4%)
ALT Elevations	N/A	N/A	**43%** (11%)	**2%** (2%)
AST Elevations	N/A	N/A	**34%** (7%)	**4%** (2%)
ALT/AST Elevations	**35%** (13%)	**28%** (17%)	N/A	**3%** (2%)
Discontinuations due to AE	**31%**	**33%**	**12%**	**4%**

** No observed instances of colitis

[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

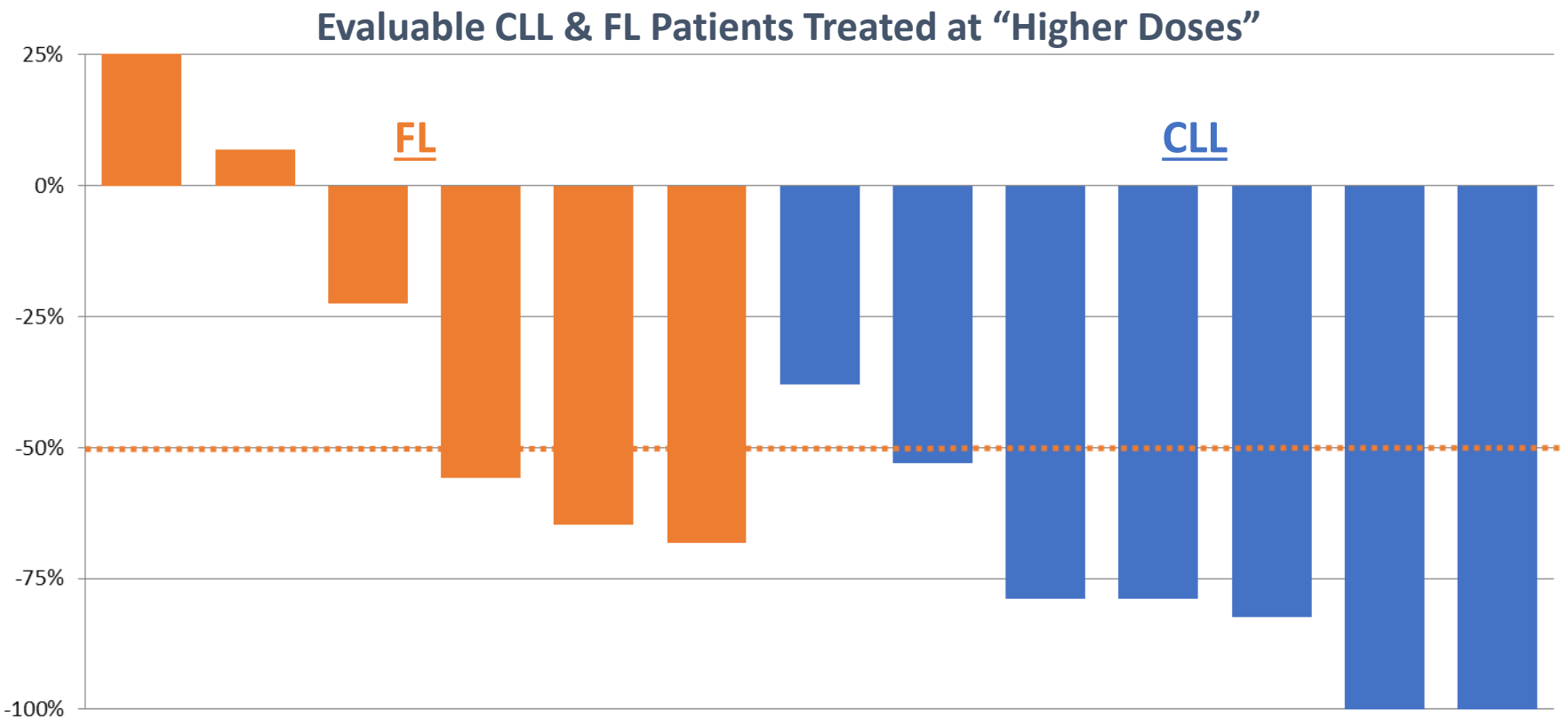
Overall Efficacy



- High level of activity demonstrated across a wide variety of hematologic malignancies

Efficacy

Best Percent Change from Baseline in Nodal Size



- "Higher Doses" of TGR-1202 (1200 mg initial formulation, or ≥ 600 mg micronized) demonstrated rapid and profound responses

TGR-1202 Take Home Messages

- Once-daily PI3Kδ inhibitor with single agent activity across B-cell malignancies
  - 88% nodal response rate in rel/ref CLL;
  - 42% ORR in rel/ref FL
  - Patients remaining on therapy pending further efficacy assessments
- Differentiated safety profile from other PI3Kδ inhibitors
  - Hepatic toxicity
  - Diarrhea/colitis
  - Pneumonia/pneumonitis
  - Discontinuations due to AE's have been rare

Nathan Fowler, MD
Associate Professor
Lead, New Drug Development
MD Anderson Cancer Center

Combination of TG-1101 & TGR-1202

"TG-1303"

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

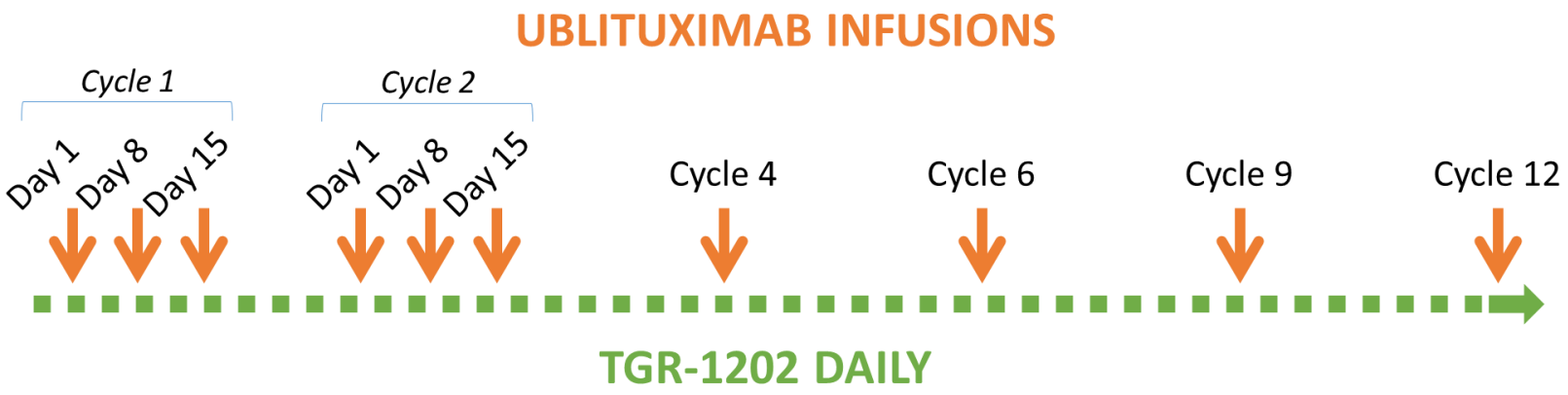
Matthew Lunning, DO[1], Julie Vose, MD[1], Nathan Fowler, MD[2], Loretta Nastoupil, MD[2], Jan A. Burger, MD[2], William G. Wierda, MD[2], Marshall T. Schreeder, MD[3], Tanya Siddiqi, MD[4], Christopher Flowers, MD[5], Jonathon Cohen, MD[5], Susan Blumel, RN, BSN[1], Myra Miguel, RN[2], Emily K. Pauli, PharmD[3], Kathy Cutter, RN[3], Brianna Phye, BS[4], 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]University of Nebraska Medical Center, Omaha, NE; [2]MD Anderson Cancer Center, Houston, TX; [3]Clearview Cancer Institute, Huntsville, AL; [4]City of Hope National Medical Center, Duarte, CA; [5]Emory University/Winship Cancer Institute, Atlanta, GA; [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, Orange, CA

Study Design

Cohort	Ublituximab NHL Dose	Ublituximab CLL Dose	TGR Dose (QD)
1	900 mg	600 mg	800 mg
2	900 mg	600 mg	1200 mg
3	900 mg	900 mg	400 mg (micronized)
4	900 mg	900 mg	600 mg (micronized)
5	900 mg	900 mg	800 mg (micronized)
6	900 mg	900 mg	1200 mg (micronized)
Expansion	*Currently Enrolling Expansion Cohorts with TGR-1202 at 800 mg and 1200 mg micronized*		

Treatment Schedule:



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%)	

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

Safety

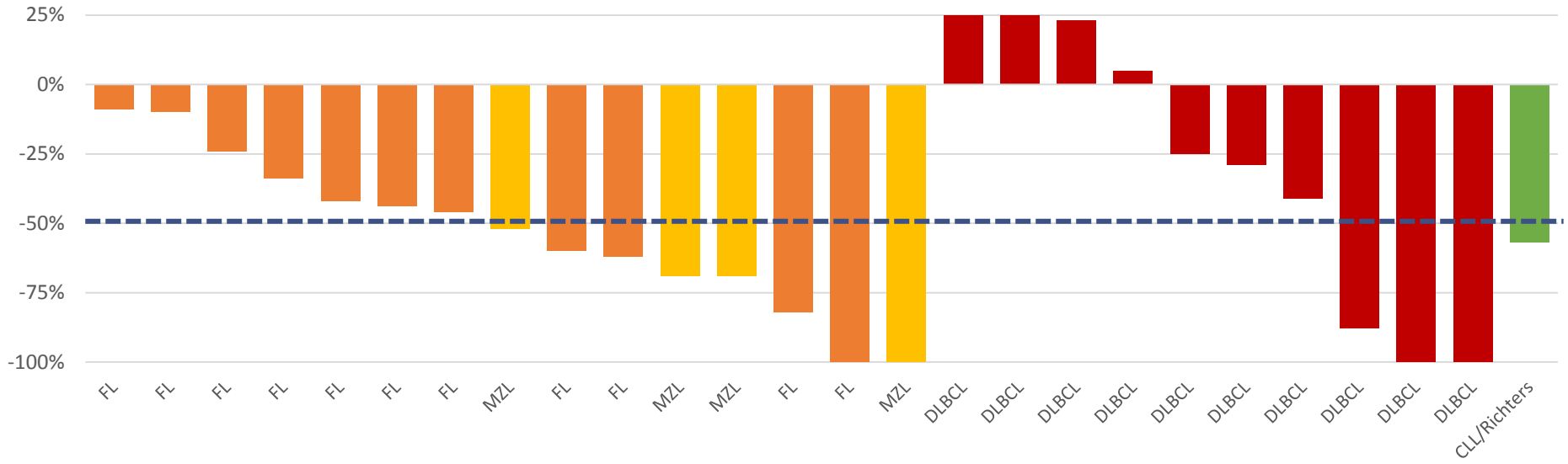
Related AE's Occurring in ≥ 5% of Patients (n = 55)

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%**	-	**-**

- 3 patients (~5%) have come off study due to an adverse event, none related to hepatic toxicity or colitis

TG-1101 + TGR-1202 – NHL

Best Percent Change from Baseline in Nodal Size



Type	TGR-1202 Higher* Doses						Type	TGR-1202 Lower** Doses					
	Pts (n)	CR (n)	PR (n)	ORR n (%)	SD (n)	PD (n)		Pts (n)	CR (n)	PR (n)	ORR n (%)	SD (n)	PD (n)
CLL/SLL	6	-	5	**5 (83%)**	1	-	CLL/SLL	7	1	3	**4 (57%)**	3	-
DLBCL	7	2	1	**3 (43%)**	3	1	DLBCL	3	-	-	**-**	1	2
FL/MZL	11	2	5	**7 (64%)**	4	-	FL/MZL	4	-	1	**1 (25%)**	3	-
Richter's	1	-	1	**1 (100%)**	-	-	Richter's	-	-	-	**-**	-	-
Overall	25	4	12	**16 (64%)**	8	1	Overall	14	1	4	**5 (36%)**	7	2

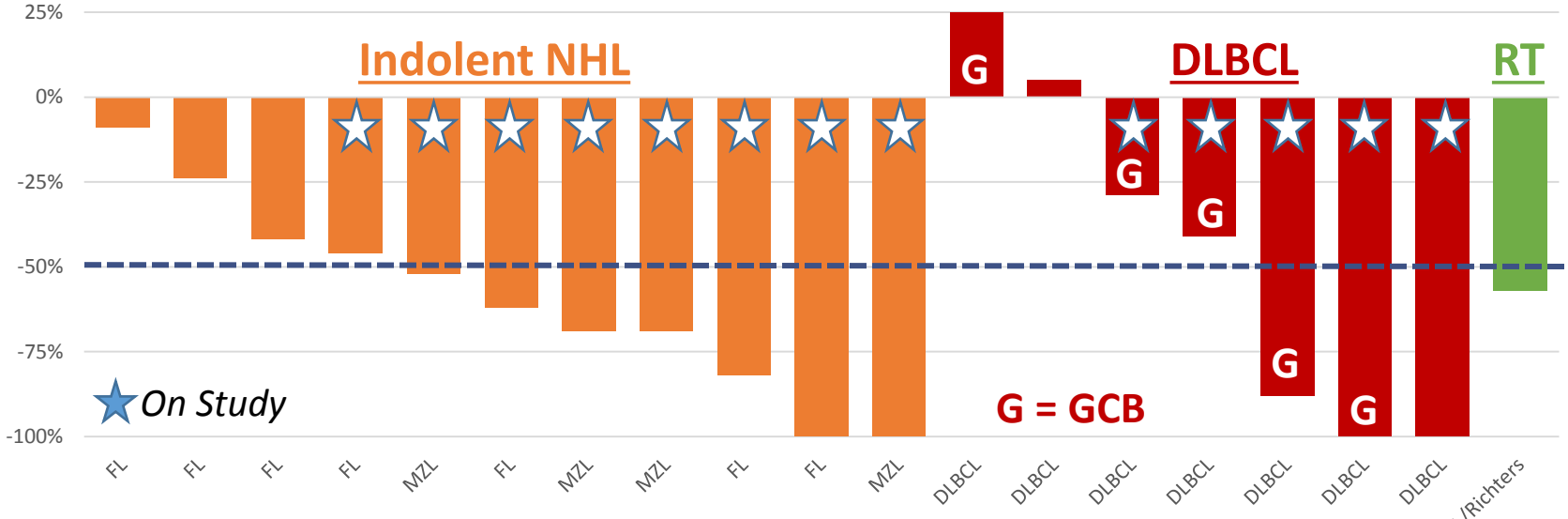
*Higher Dose = 1200 original formulation and 600 or > micronized

**Lower Dose = 800 original formulation and 400 micronized

TG-1101 + TGR-1202 – Higher Doses NHL

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

Best Percent Change from Baseline in Nodal Size



Type	TGR-1202 Higher* Doses					
	Pts (n)	CR (n)	PR (n)	ORR n (%)	SD (n)	PD (n)
CLL/SLL	6	-	5	**5 (83%)**	1	-
DLBCL	7	2	1	**3 (43%)**	3	1
FL/MZL	11	2	5	**7 (64%)**	4	-
Richter's	1	-	1	**1 (100%)**	-	-
Overall	25	4	12	**16 (64%)**	8	1

*Higher Dose = 1200 original formulation and 600 or > micronized

TG-1101 + TGR-1202 Take Home Messages

- Combination is well tolerated
  - Grade 3/4 AE's and discontinuations due to AE's have been limited (~5%)
- Activity of the combination has been observed in indolent NHL, and GCB-DLBCL
- Safety profile supports additional multi-drug combination regimens
  - TG-1101 + TGR-1202 + Ibrutinib, oral presentation Monday, June 1, 2015

ASH 2014: TGR-1202 + Ublituximab + Ibrutinib

- Initial cohorts for both NHL and CLL (n=5)

Ublituximab 900mg + **TGR-1202** 400 mg micronized + **Ibrutinib** CLL: 420mg NHL: 560mg

Histology	Description	Prior # Rx	Prior Ibrutinib	Rel/Ref	Rituximab Refractory	Response	% ↓
Follicular	Stage IV	4	Refractory	Refractory	Yes	PR	74%
MCL	Advanced	2	No	rAuto txp	No	CR	PET -
Richter's	17p	3	No	Refractory	Yes	PD	N/A
CLL	17p	2	No	Refractory	Yes	Too Early	N/A
Follicular	Stage IV	1	No	Refractory	Refractory	Too Early	N/A

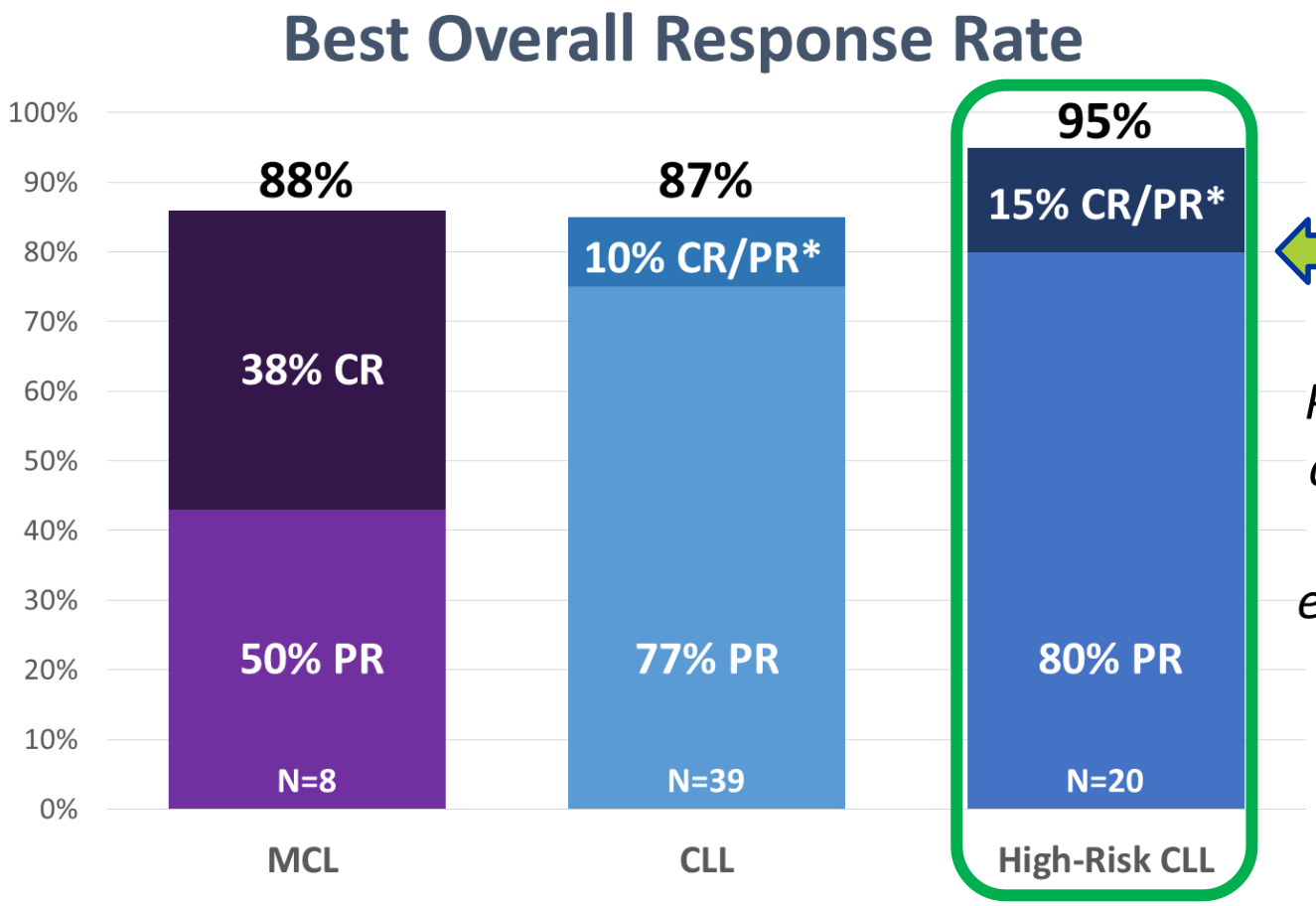
- Tomorrow's update to include additional patients evaluable for safety and efficacy

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

The GENUINE Phase 3 Study
&
TGR-1202 + TG-1101 Combination

GENUINE PHASE 3 STUDY

Phase II: Ublituximab + Ibrutinib
Overall Efficacy



GENUINE
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB PLUS IBRUTINIB

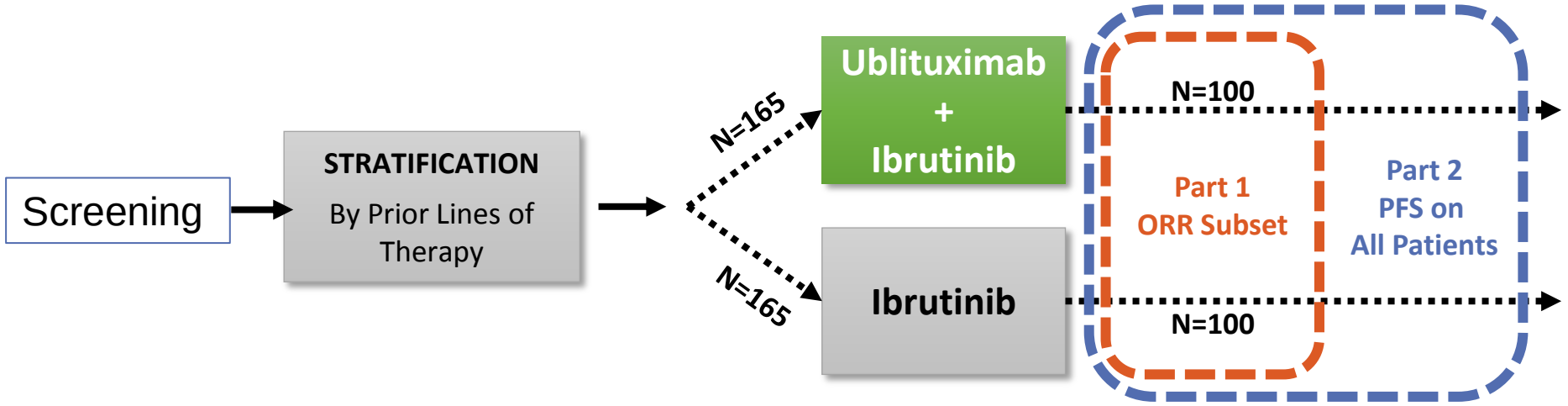
Per study design, all patients were evaluated for efficacy at Month 2 and 5 only

CLL assessed by iwCLL (Hallek 2008) Criteria; MCL/SLL assessed by Cheson, 2007 Criteria

PR = Complete Response per iwCLL criteria, pending bone marrow confirmation*

Sharman et al, ASH 2014

The GENUINE Phase 3 Trial



- Design, Endpoints, and Statistics agreed to via Special Protocol Assessment (SPA)
- Enrolling ~330 patients with high-risk CLL

GENUINE
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB PLUS IBRUTINIB

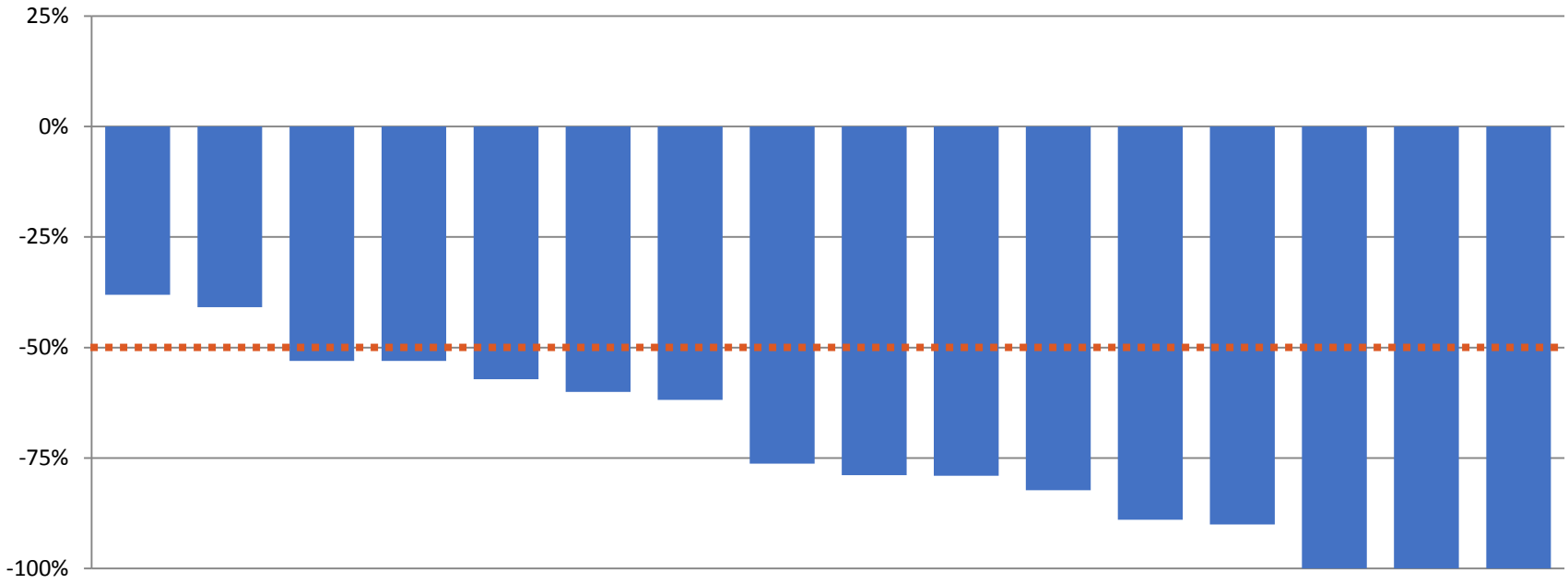
- **Part 1**: ORR among first 200 patients
- **Part 2**: PFS of all 330 patients
  - Part 1 to be analyzed following full enrollment of study

TGR-1202 SINGLE AGENT & TG-1101 + TGR-1202 IN CLL

TGR-1202 Single Agent – CLL

Best Percent Change from Baseline in Nodal Size

Patients Evaluable for Efficacy (N=16)

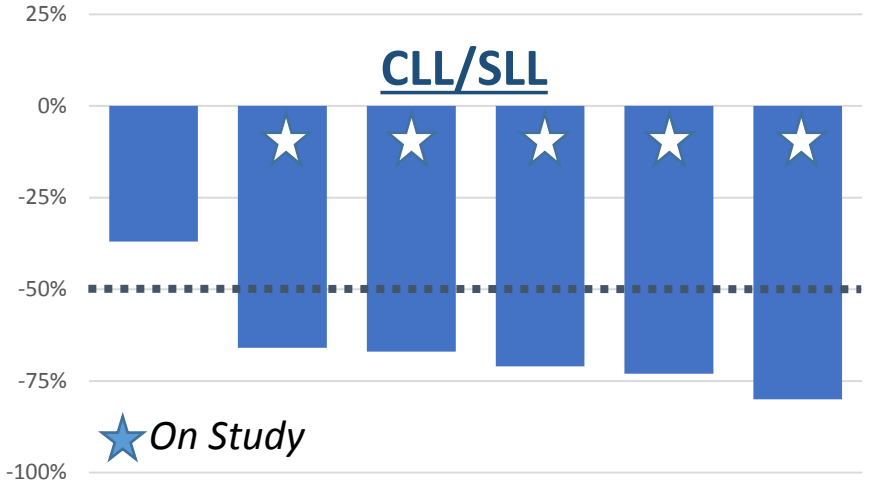


- 88% of CLL patients (14/16) achieved a nodal PR, remaining 2 patients still on study pending further evaluation
- 63% of CLL patients (10/16) achieved a response per iwCLL (Hallek 2008) criteria

TG-1101 + TGR-1202 – CLL

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

Best Percent Change from Baseline in Nodal Size



70% of CLL patients had high-risk cytogenetics (17p del and/or 11q del)

Type	TGR-1202 Higher* Doses						Type	TGR-1202 Lower** Doses					
	Pts (n)	CR (n)	PR (n)	ORR n (%)	SD (n)	PD (n)		Pts (n)	CR (n)	PR (n)	ORR n (%)	SD (n)	PD (n)
CLL/SLL	6	-	5	**5 (83%)**	1	-	CLL/SLL	7	1	3	**4 (57%)**	3	-
DLBCL	7	2	1	**3 (43%)**	3	1	DLBCL	3	-	-	**-**	1	2
FL/MZL	11	2	5	**7 (64%)**	4	-	FL/MZL	4	-	1	**1 (25%)**	3	-
Richter's	1	-	1	**1 (100%)**	-	-	Richter's	-	-	-	**-**	-	-
Overall	25	4	12	**16 (64%)**	8	1	Overall	14	1	4	**5 (36%)**	7	2

*Higher Dose = 1200 original formulation and 600 or > micronized

**Lower Dose = 800 original formulation and 400 micronized

TG-1101 + TGR-1202
Safety supports further combination studies

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%**	-	**-**

- ~5% have come off study due to an adverse event
- No patients at ≥800 mg micronized TGR-1202 have discontinued due to an AE

Newest Triple Combination Study

Phase I/II study of pembrolizumab in combination with TG-1101 (ublituximab) and TGR-1202 in patients with relapsed-refractory CLL

A unique opportunity to correct immunological defects which allow CLL to escape immune surveillance

A research collaboration between University of Pennsylvania, Center for CLL and TG Therapeutics

Study Rationale: PD-1 Blockade and CLL

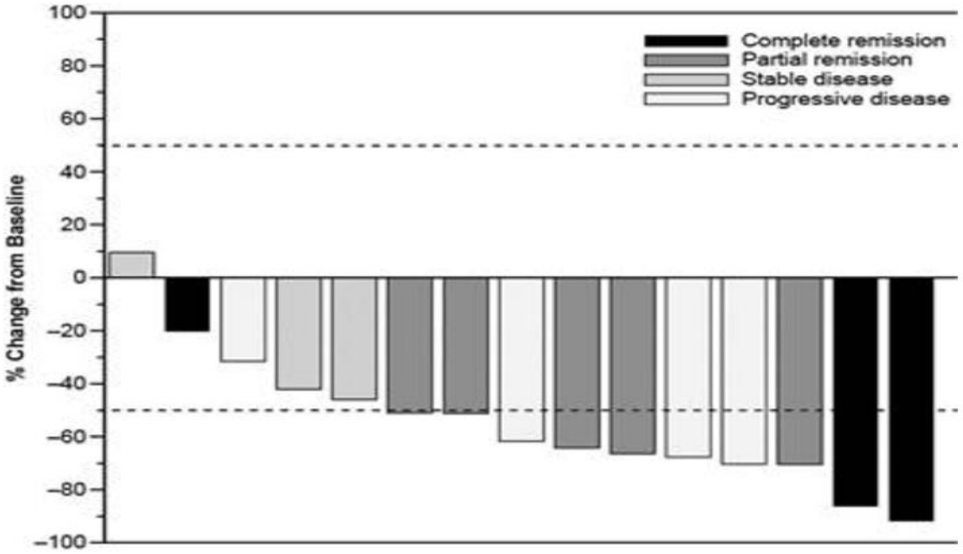
- Malignant cells utilize PD-1 receptor-ligand pathway to evade immune surveillance by inactivating cytotoxic T cells via PD-L1 expression.
- CLL: Preclinical data demonstrates the importance PD-1 / PD-L1 signaling
  - PD-1 expression is significantly higher in CLL patients (T cells) vs. healthy donors.
  - CLL cells expresses higher PD-L1 and PD-1 vs. circulating B lymphocytes from healthy donors.
  - CD4+/PD-1+ T lymphocytes are found to be in close contact with PD-L1+ CLL cells.
  - In vivo data demonstrate that early PD-L1 blockade effectively controls CLL development in TCL1 murine model for CLL.

Pembrolizumab is a highly selective, humanized IgG4/kappa monoclonal antibody that binds PD-1, and prevents its interaction with its ligands.

Haematologica. 2013;98(6):953-963.

*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)

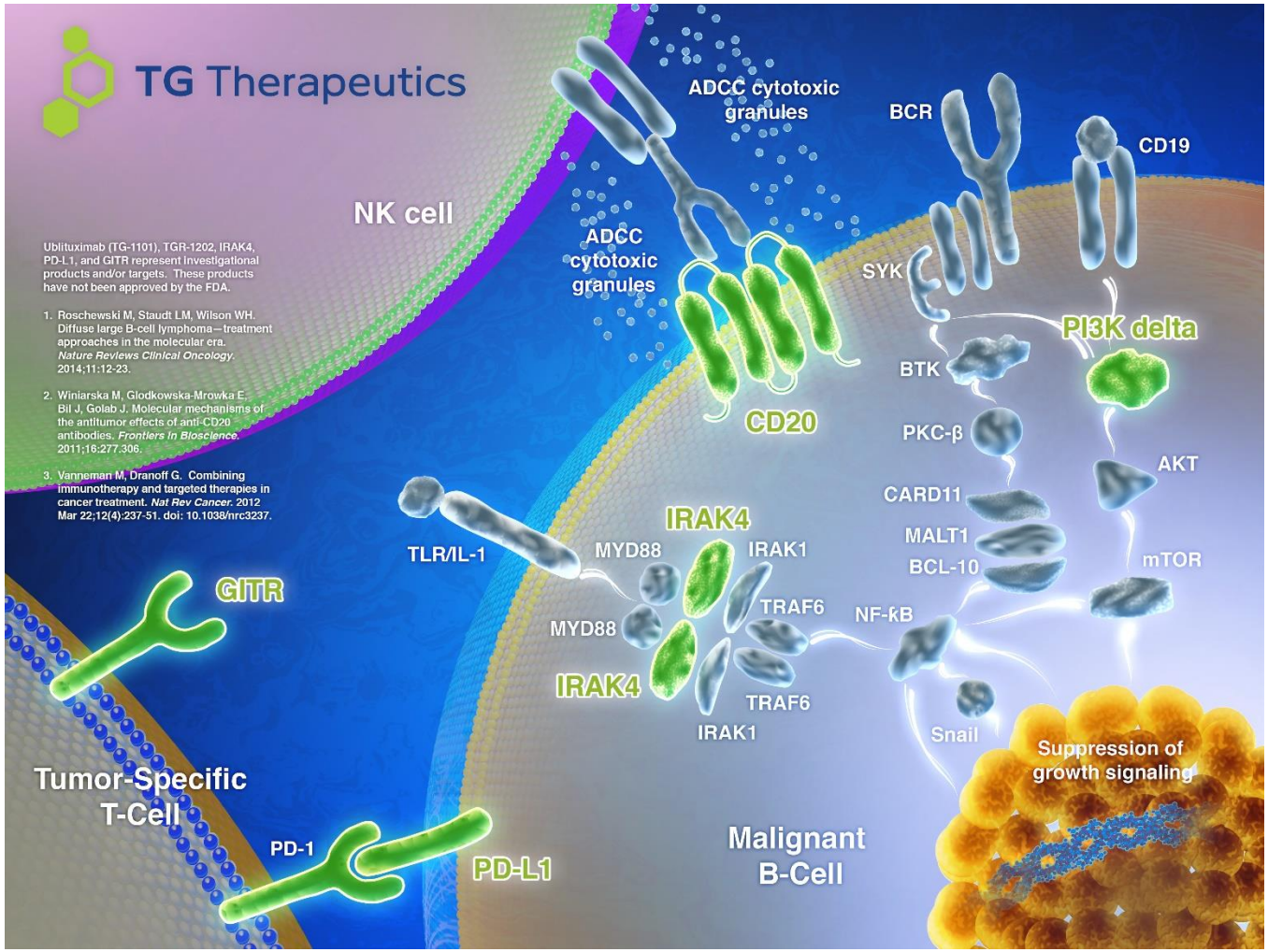


Response rate in HD
- 3 patients (20%) = CR
- 5 patients (33%) = PR
- Best ORR = 53%

Lesokhin et al. ASH 2014, Abstract 291.

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

Hypothesis



TG1101 + TG1202 doublet is an ideal platform for combination with anti-PD1 therapy based on clinical activity and non overlapping safety profile.

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

Objectives

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

Q&A

Questions?

TG Therapeutics

2015 ASCO Analyst & Investor Event

May 31, 2015