



Investor & Analyst Meeting

June 6, 2016



TG Therapeutics

Opening Remarks

Objectives - Agenda

Topic	Presenter
Welcome / Introductions	TG Therapeutics Team
TGR-1202 Monotherapy and TG-1303 Integrated Analysis Review UNITY-CLL High Risk Testing	Anthony Mato, MD
GENUINE Review & Supporting Data Screening Protocol/ High Risk Testing Community Oncologist Perspective	Kathryn Kolibaba, MD
UNITY-DLBCL TG-1303 Experience	Matthew Lunning, DO
Wrap-Up Moderated Q&A	TG Therapeutics Team

Ublituximab (TG-1101), TGR-1202, IRAK4, PD-L1, and GITR represent investigational products and/or targets. These products have not been approved by the FDA.

1. Roschewski M, Staudt LM, Wilson WH. Diffuse large B-cell lymphoma—treatment approaches in the molecular era. *Nature Reviews Clinical Oncology*. 2014;11:12-23.
2. Winiarska M, Glodkowska-Mrowka E, Bil J, Golab J. Molecular mechanisms of the antitumor effects of anti-CD20 antibodies. *Frontiers in Bioscience*. 2011;16:277-306.
3. Vanneman M, Dranoff G. Combining immunotherapy and targeted therapies in cancer treatment. *Nat Rev Cancer*. 2012 Mar 22;12(4):237-51. doi: 10.1038/nrc3237.

NK cell

ADCC cytotoxic granules

ADCC cytotoxic granules

BCR

CD19

SYK

PI3K delta

CD20

BTK

PKC-β

AKT

CARD11

MALT1

BCL-10

mTOR

TLR/IL-1

IRAK4

MYD88

IRAK1

MYD88

TRAF6

NF-κB

IRAK4

TRAF6

IRAK1

Snail

Suppression of growth signaling

GITR

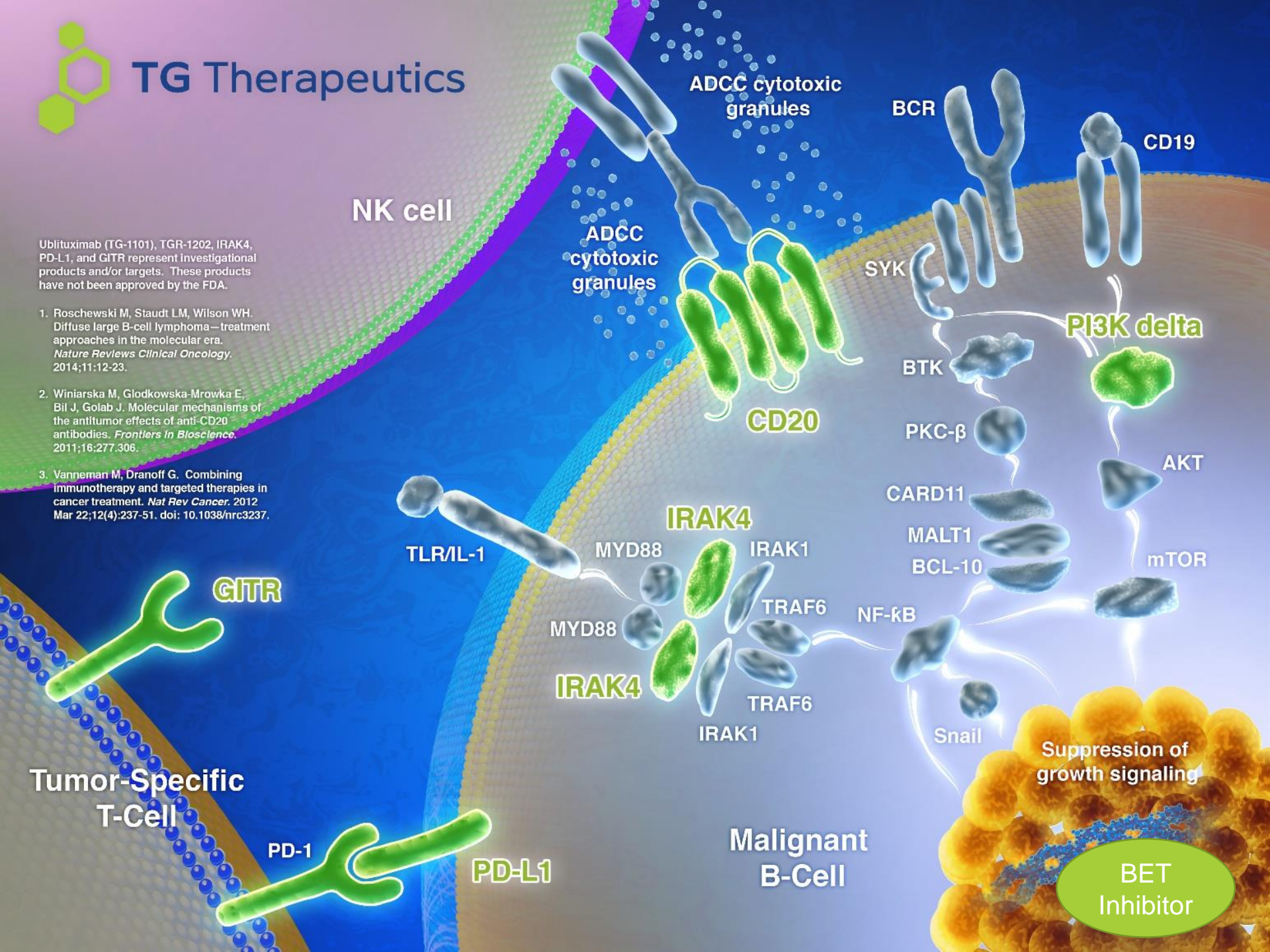
Tumor-Specific T-Cell

PD-1

PD-L1

Malignant B-Cell

BET Inhibitor





TG Therapeutics

Anthony R. Mato, MD

Director, Center for CLL
University of Pennsylvania

Long-term follow-up of the PI3K δ inhibitor TGR-1202 demonstrates a differentiated safety profile and high response rates in CLL and NHL: Integrated-analysis of TGR-1202 monotherapy and combined with ublituximab

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¹Tennessee Oncology, PLLC, Nashville, TN; ²Sarah Cannon Research Institute, Nashville, TN; ³University of Nebraska Medical Center, Omaha, NE; ⁴Department of Lymphoma, MD Anderson Cancer Center, Houston, TX; ⁵University of California Irvine, Orange, CA; ⁶Clearview Cancer Institute, Huntsville, AL; ⁷Florida Cancer Specialists, Sarasota, FL; ⁸Division of Hematology/Oncology, Medical College of Wisconsin, Milwaukee, WI; ⁹Duke University Medical Center, Durham, NC; ¹⁰City of Hope National Medical Center, Duarte, CA; ¹¹Emory University/Winship Cancer Institute, Atlanta, GA; ¹²Department of Leukemia, MD Anderson Cancer Center, Houston, TX ¹³University of Texas Health Science Center at San Antonio, San Antonio, TX; ¹⁴TG Therapeutics, Inc., New York, NY; ¹⁵Center for Lymphoid Malignancies, Columbia University Medical Center, New York, NY

Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: Demographics

Evaluable for Safety (n)	165 (90 Single Agent, 75 Combo with UTX)	
Median Age, years (range)	65 (22 - 86)	
Male/Female	106/59	
Histology	CLL	43
	FL	42
	DLBCL	40
	MZL	11
	HL	11
	MCL	8
	SLL	3
	WM	3
	T-Cell	2
	HCL	1
	Richter's	1
Median ECOG	1	
Prior Therapies, median (range)	3 (0 - 14)	
Patients with ≥ 3 Prior Therapies (%)	94 (57%)	
Patients Refractory to Prior Therapy (%)	85 (52%)	

Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: Safety

All Causality AE's Occurring in $\geq 10\%$ of Patients (n = 165)

Adverse Event	All Grades		Grade 3/4	
	N	%	N	%
Diarrhea	78	47%	5	3%
Nausea	74	45%	2	1%
Fatigue	61	37%	5	3%
Vomiting	44	27%	0	0%
Neutropenia	34	21%	30	18%
Cough	32	19%	0	0%
Dyspnea	30	18%	6	4%
Dizziness	29	18%	0	0%
Headache	28	17%	2	1%
Pyrexia	26	16%	2	1%
Decreased appetite	26	16%	0	0%
Rash	26	16%	6	4%
Sinusitis	25	15%	2	1%
Anemia	24	15%	9	5%
Constipation	24	15%	1	1%
Insomnia	23	14%	0	0%
Hypokalemia	22	13%	5	3%
Back pain	20	12%	1	1%
Abdominal pain	18	11%	4	2%
Upper respiratory infection	18	11%	0	0%

<8% of patients discontinued due to a TGR-1202 related AEs

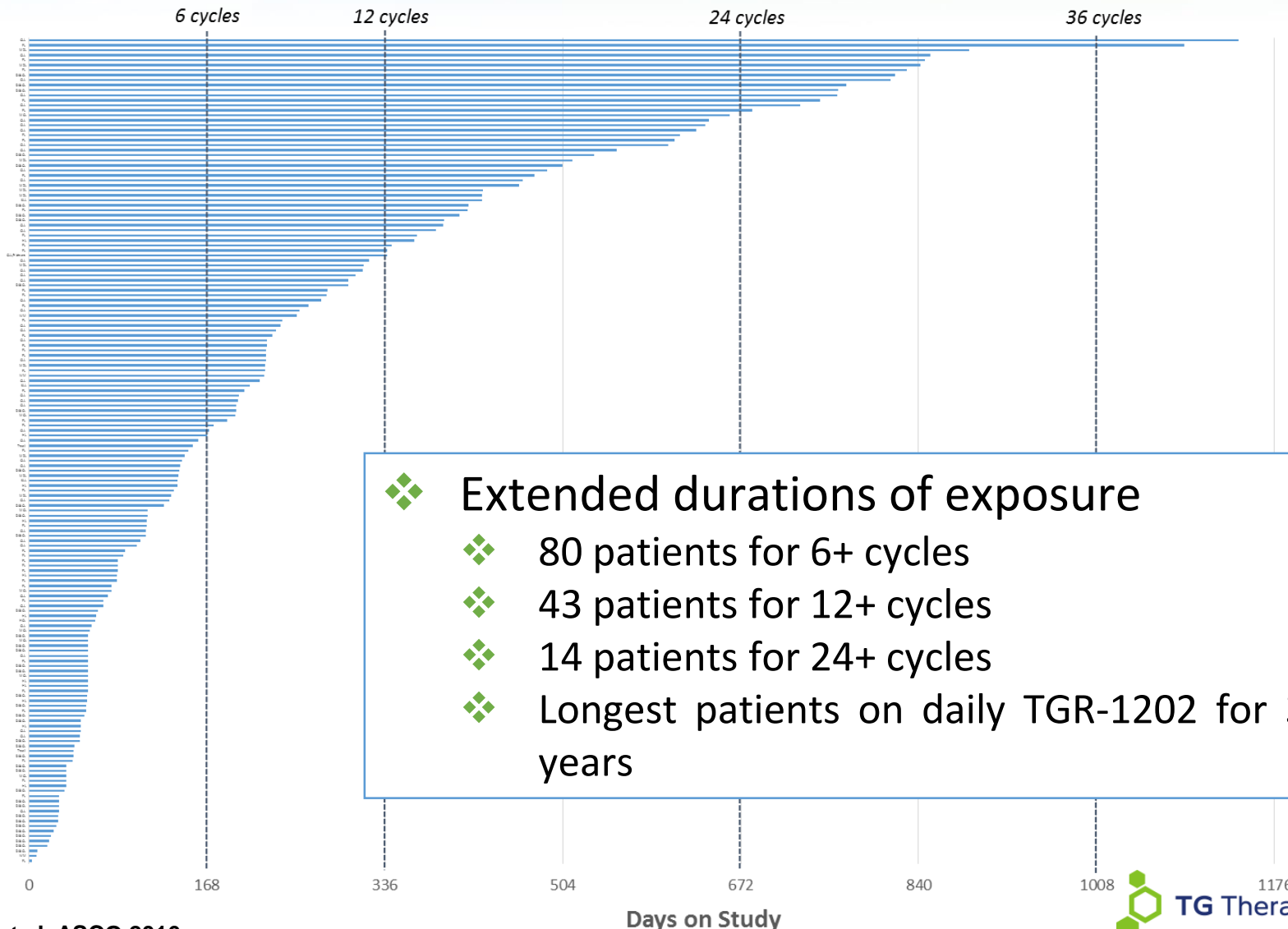
13% of patients had a TGR-1202 dose reduction

Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: Safety

- ❖ Grade 3/4 AST/ALT increase was 3% (8% all grades), predominantly observed above the Phase 3 dose
- ❖ Grade 3/4 pneumonia occurred in 5% of patients (8% all grades); two events of pneumonitis (<1.5%) were reported
- ❖ Two cases of colitis (<1.5%) have been reported at doses exceeding the Phase 3 dose and did not appear to be time dependent (1000 mg and 1200 mg, at 4 mos. and 24 mos., respectively, after initiating therapy).

Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: Efficacy

Duration on Study (n=165)



Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: Efficacy at Phase 3 Dose

Overall Response Rate At Phase 3 Dose

Patients Exposed to TGR-1202 at 800 Micro

Type	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

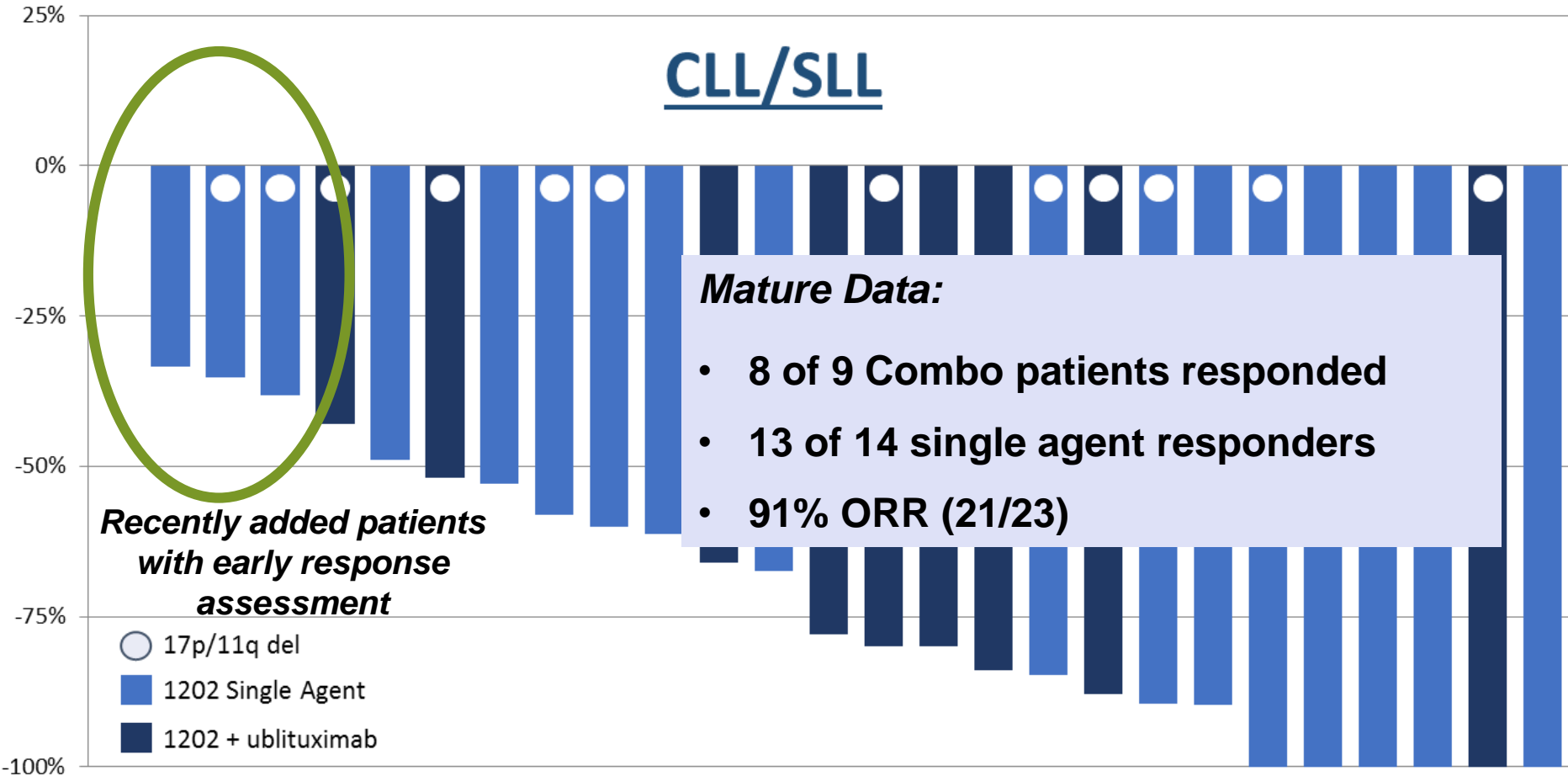
❖ CLL/SLL PR includes 1 patient with persistent lymphocytosis [on single agent TGR-1202]

❖ iNHL = FL & MZL

❖ A strong dose response was observed, with patients exposed to 800 mg of the micronized formulation achieving higher rates of response

Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: CLL/SLL Efficacy

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



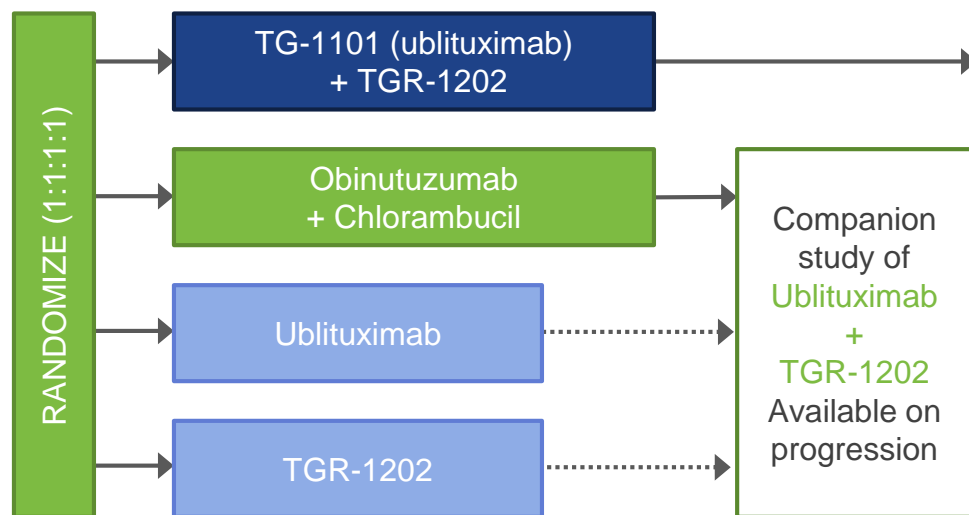
Higher Doses: 1200 mg of the initial formulation, or ≥ 600 mg of the micronized formulation

Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: CONCLUSIONS

- ❖ Discontinuations due to AEs have been limited and AEs generally associated with PI3K delta inhibitors have been rare
- ❖ Safety profile supports additional multi-drug combinations
 - ❖ Ongoing ibrutinib, bendamustine, and pembrolizumab with additional triple therapy studies planned
 - ❖ Study in patients intolerant to kinase inhibitors currently underway

UNITY-CLL Phase 3 Trial

- Design, Endpoints, and Statistics agreed to via Special Protocol Assessment (SPA)
- Enrolling ~450 patients with treatment naïve and previously treated CLL
- Efficacy Endpoints: ORR, PFS
- Study Chair: John Gribben, MD, PhD



TGR-1202 + TG-1101: Ibrutinib Refractory Patients

Ibrutinib Refractory Patients treated with TGR-1202 + TG-1101

Cyto-genetics	# 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 & 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

Prevalence of High Risk Markers

Baseline mutational status of relapsed/refractory CLL patients in clinical studies

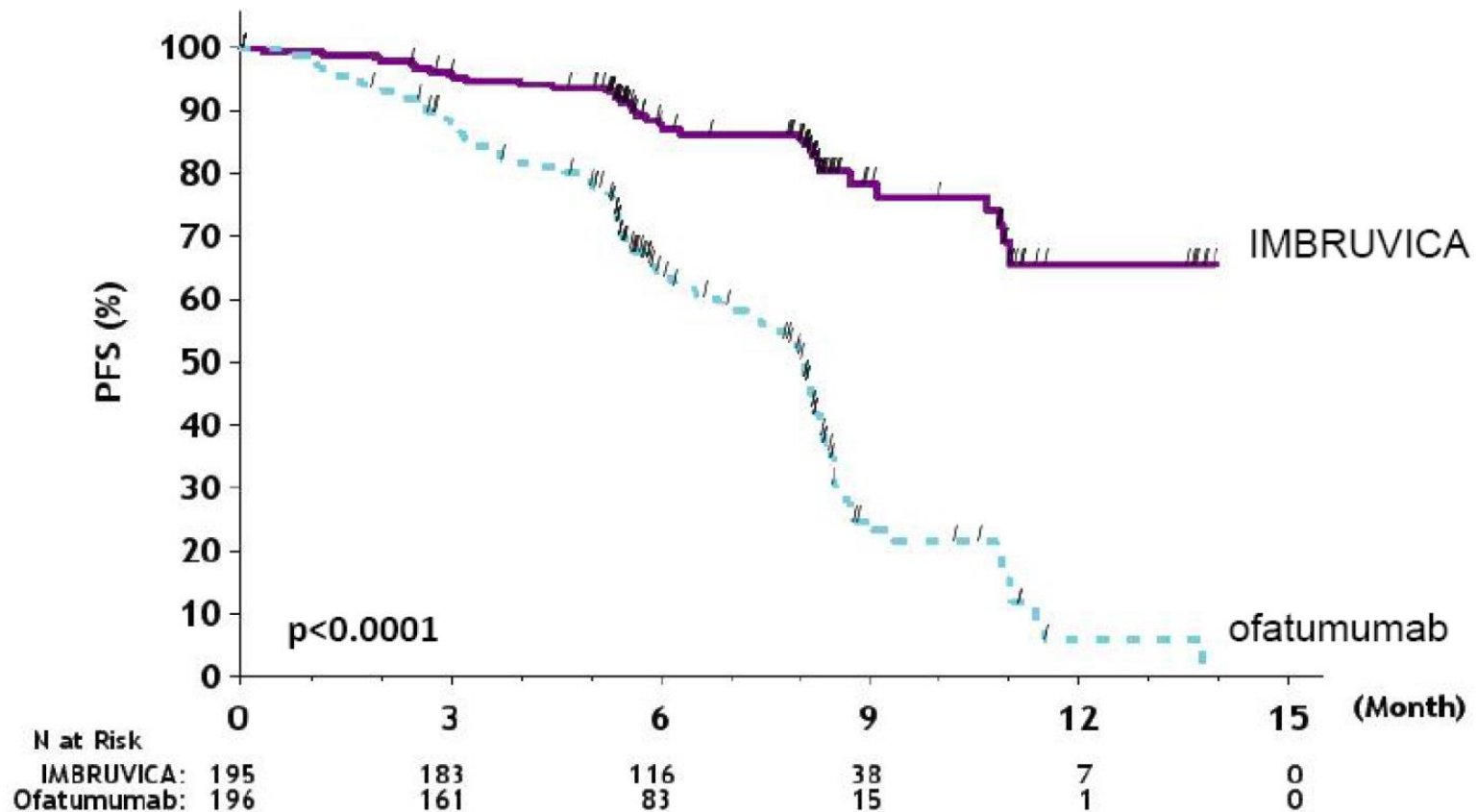
	Idelalisib- Rituxan Phase III Trial (N=220)^{5,6}	RESONATE (N=391)⁷	French CLL Intergroup ICLL01 (N=55)⁸	Ublituximab- Ibrutinib Phase II study (N=39)^{9*}
17p del	26%	32%	27%	30%
p53 mut	18%	N/R	31%	5%
11q del	32%	31%	33%	28%

**Based on prior FISH in patient history*

⬡ Due to overlapping features, it is estimated that over 50% of relapsed/refractory patients may have high-risk cytogenetics

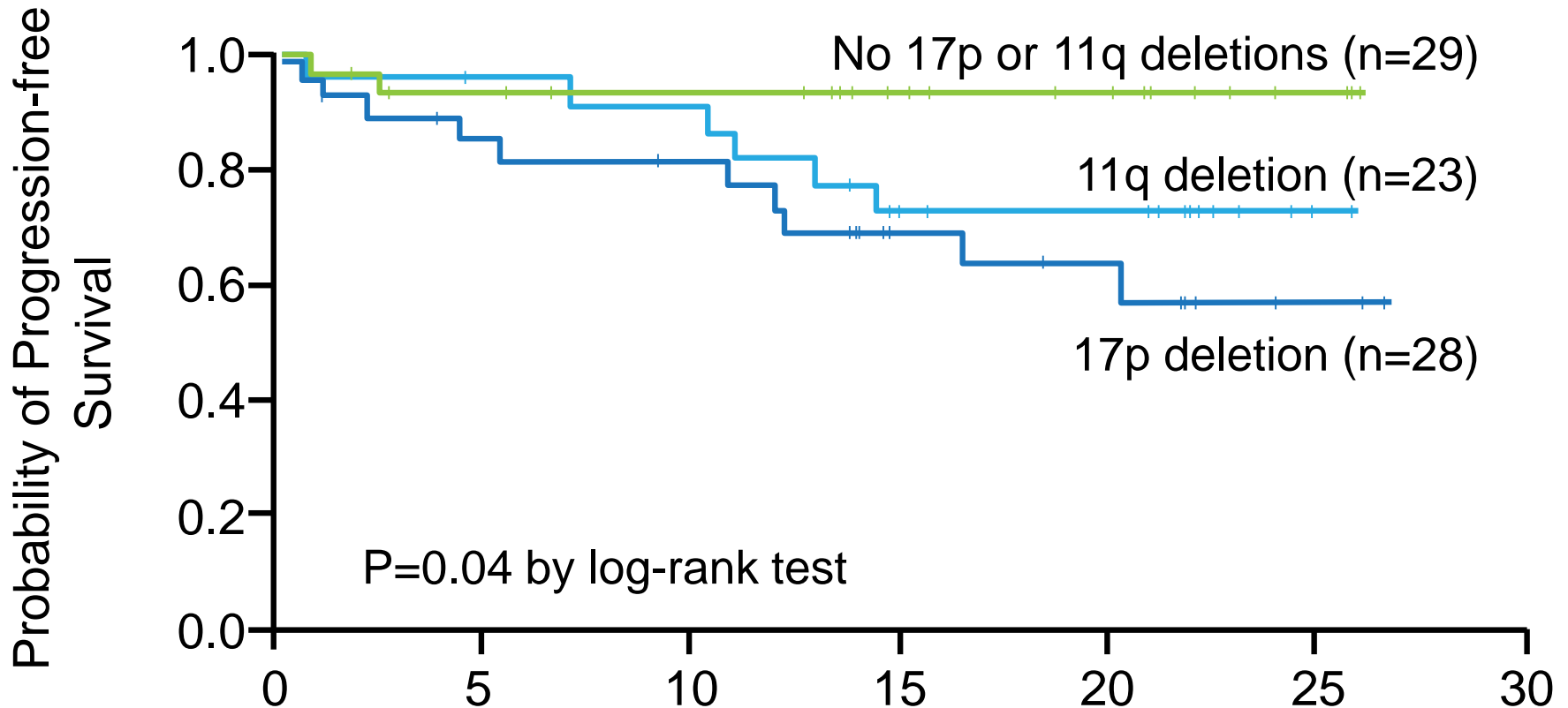
Ibrutinib is not the entire solution!

Phase 3 Ibrutinib vs. Ofatumumab



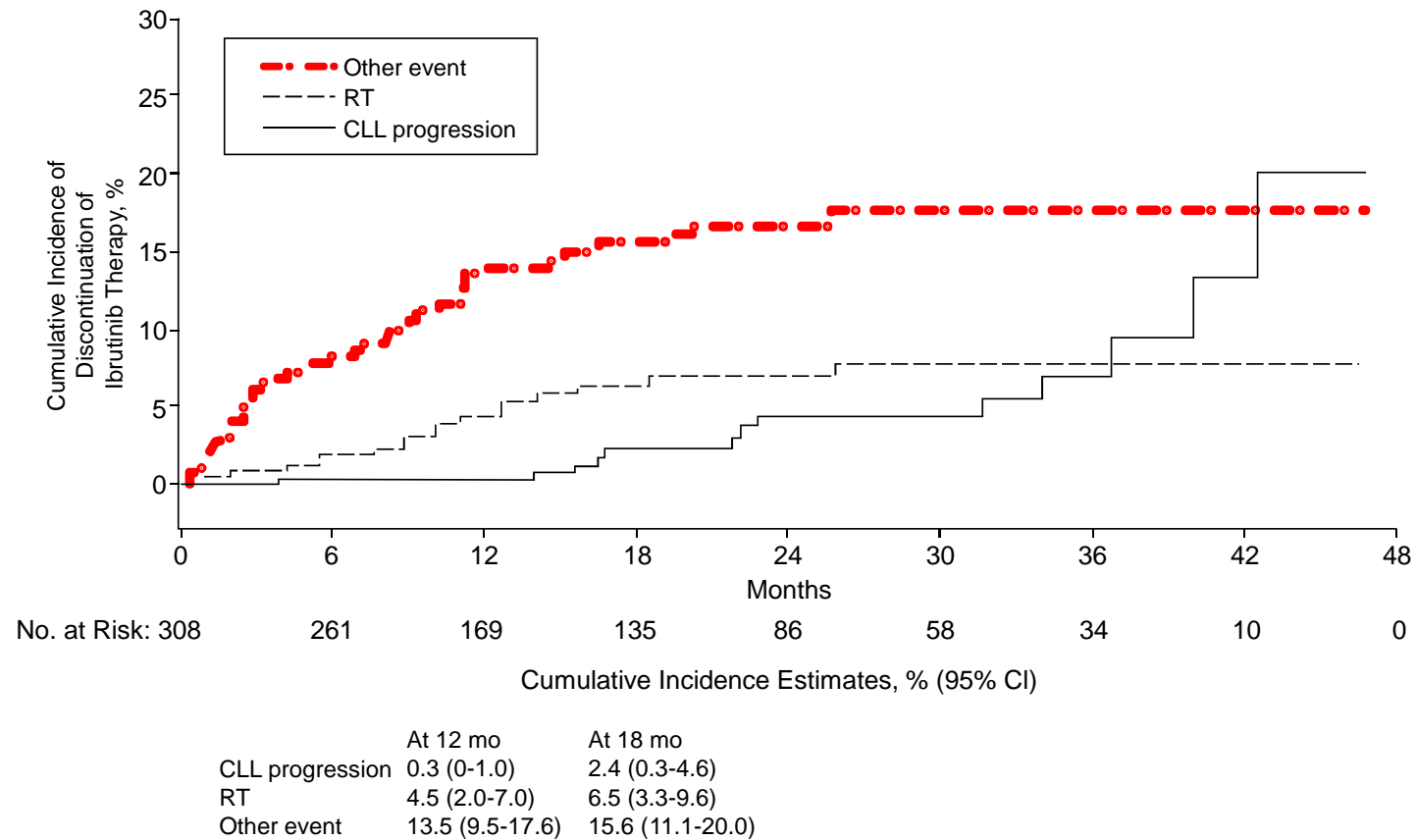
- 32% of patients had 17p deletion

High-Risk Patients Exhibit Poorer PFS



High Incidence of Ibrutinib Discontinuations

Figure. Cumulative Incidence of Discontinuation of Ibrutinib Therapy



Take Home Summary

- High Risk CLL much more common than you think
- Most patients with relapsed CLL are suitable for novel agents, however outcomes for patients with high-risk features continue to be inferior
- Combination biologic therapy will likely lead to improved outcomes for patients with relapsed CLL

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**

Toxicity as Reason for Discontinuation

“Kinase Inhibitor Intolerant” Patients

5 Most Common Toxicities as a Reason for Discontinuation

Ibrutinib (N=66)

Atrial fibrillation 20%

Infection 12%

Hematologic 9%

Bleeding 9%

Pneumonitis 8%

Idelalisib (N=18)

Pneumonitis 33%

Colitis 28%

Rash 17%

Transaminitis 11%

Infection 6%



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Q & A Session



TG-1101 + Ibrutinib, Screening Protocol and Testing Relapsed High-Risk CLL

Kathryn Kolibaba, MD

**Compass Oncology, Vancouver, WA; US Oncology Research,
The Woodlands, TX**

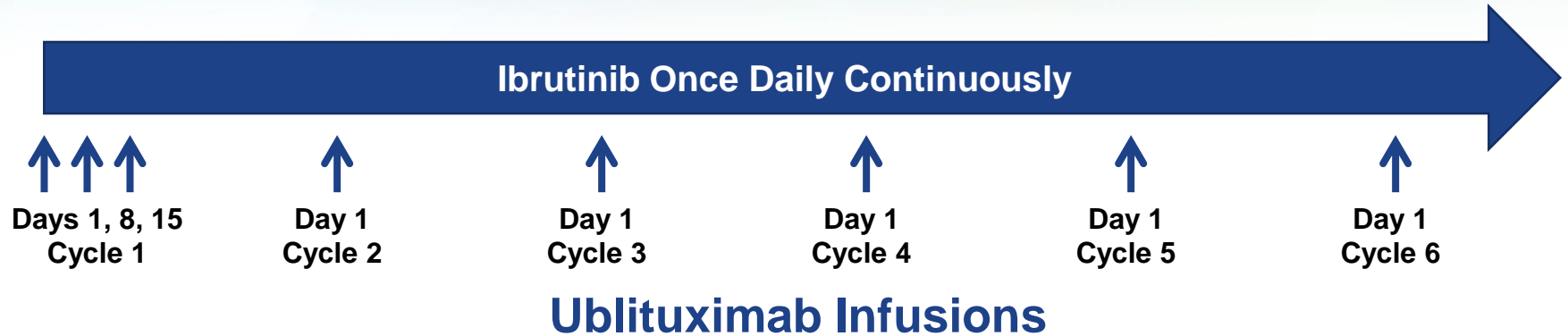
Can Ublituximab Improve Ibrutinib?

UBLITUXIMAB (TG-1101), A NOVEL GLYCOENGINEERED ANTI-CD20 MAB, IN COMBINATION WITH IBRUTINIB ACHIEVES 95% ORR IN PATIENTS WITH HIGH-RISK RELAPSED/REFRACTORY CLL

Jeff Sharman^{1,2}, Charles M. Farber³, Daruka Mahadevan⁴, Marshall T. Schreeder⁵,
Heather D. Brooks^{6,2}, Kathryn S. Kolibaba^{7,2}, Suzanne Fanning^{8,2}, Leonard Klein^{9,2},
Daniel R. Greenwald^{10,2}, Peter Sportelli¹¹, Hari P. Miskin¹¹, Michael S. Weiss¹¹,
John M. Burke^{12,2}

¹Willamette Valley Cancer Institute, Springfield, OR; ²US Oncology Research, The Woodlands, TX; ³Carol G. Simon Cancer Center, Morristown, NJ; ⁴West Cancer Center/UTHSC, Memphis, TN; ⁵Clearview Cancer Institute, Huntsville, AL; ⁶Blue Ridge Cancer Care, Blacksburg, VA; ⁷Compass Oncology, Vancouver, WA; ⁸Greenville Health System Cancer Institute, Greenville, SC; ⁹Illinois Cancer Specialists, Niles, IL; ¹⁰Sansum Clinic, Santa Barbara, CA; ¹¹TG Therapeutics, Inc., New York, NY; ¹²Rocky Mountain Cancer Centers, Aurora, CO

Phase II: Ublituximab + Ibrutinib



- 900mg Ublituximab + 420mg Ibrutinib
- After cycle 6, all patients off study and remained on single agent ibrutinib per investigator discretion

Patient Characteristics – Phase II

Evaluable for Safety, (n)	44
Evaluable for Efficacy, † (n)	40
Median Age, years (range)	71 (39 – 86)
Male/Female	22/22
ECOG, median	1
Prior Regimens, median (range)	2 (1 – 7)
≥ 3 Prior Regimens	16 (36%)
Prior Anti-CD20 (rituximab, ofatumumab, obintuzumab)	41 (93%)
Refractory to anti-CD20	13 (33%)
Prior Alkylating Agent	28 (64%)
Prior Purine Analog	22 (50%)
High-risk (17p del, 11q del, p53 mutated)	21 (48%)

†4 patients not evaluable: 2 patients withdrew consent and 2 patients came off study prior to first disease assessment: 1 due to ibrutinib related AE (diarrhea); 1 due to multiple non-drug related AE's

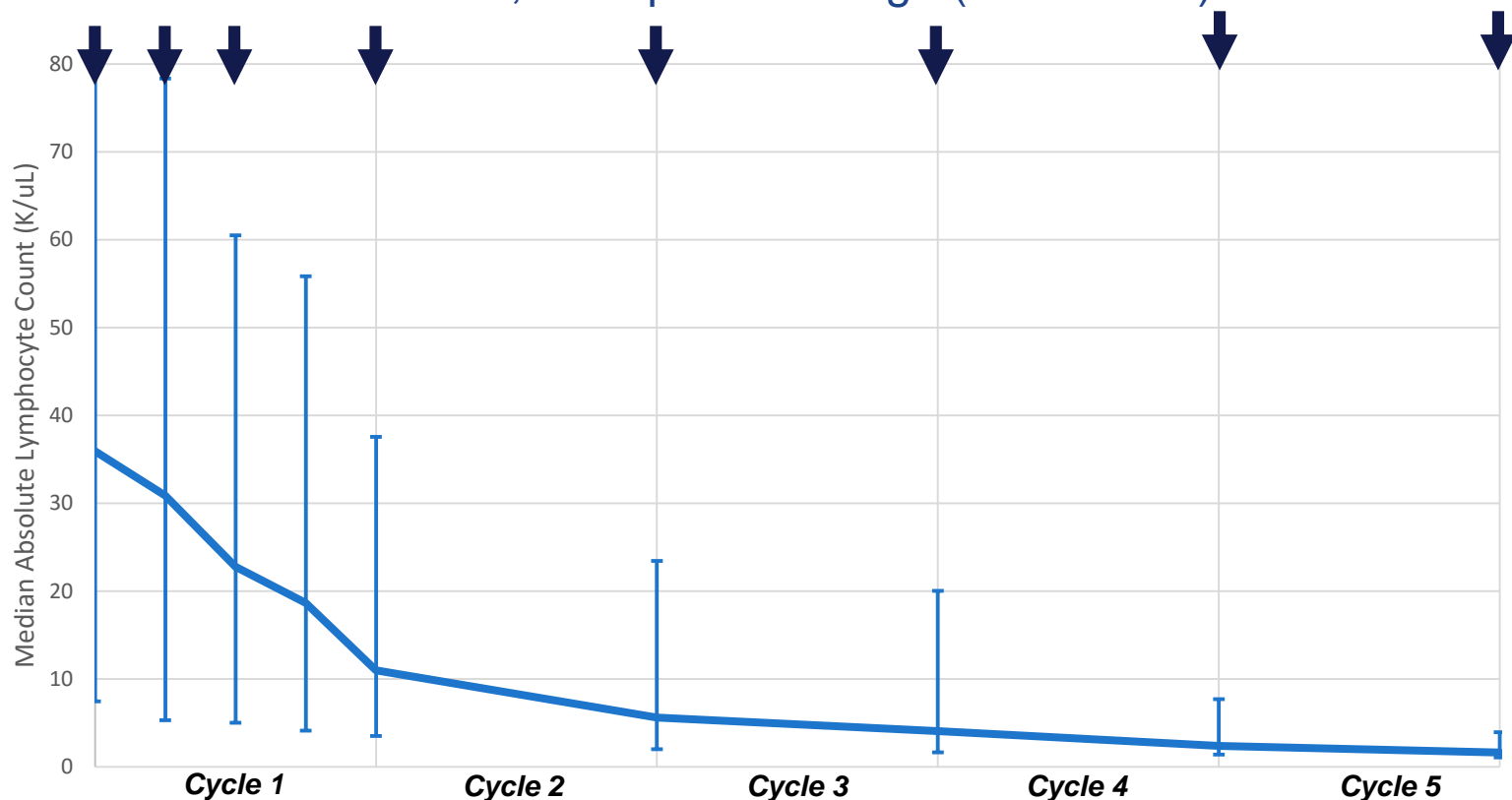
Safety – Phase II

All Causality AE's in > 10% of Patients (n=44)

Adverse Event	All Grades n (%)	Grade 3/4 n (%)
Infusion reaction	20 (45%)	3 (7%)
Diarrhea	16 (36%)	2 (5%)
Fatigue	13 (30%)	1 (2%)
Nausea	11 (25%)	-
Rash	10 (23%)	-
Pyrexia	8 (18%)	-
Arthralgia	7 (16%)	1 (2%)
Constipation	7 (16%)	-
Cough	7 (16%)	-
Muscle Spasms	7 (16%)	-
Peripheral Edema	7 (16%)	-
Upper Respiratory Tract Infection	7 (16%)	-
Dizziness	6 (14%)	-
Anemia	5 (11%)	5 (11%)
Contusion	5 (11%)	-
Headache	5 (11%)	-
Myalgia	5 (11%)	-
Neutropenia	5 (11%)	5 (11%)
Thrombocytopenia	5 (11%)	2 (5%)

Phase II Efficacy: Lymphocytosis

Absolute Lymphocytes in CLL Patients by Month on Treatment Median, Interquartile Range (25% - 75%)



- Median 75% decrease in ALC from baseline by the end of Cycle 3

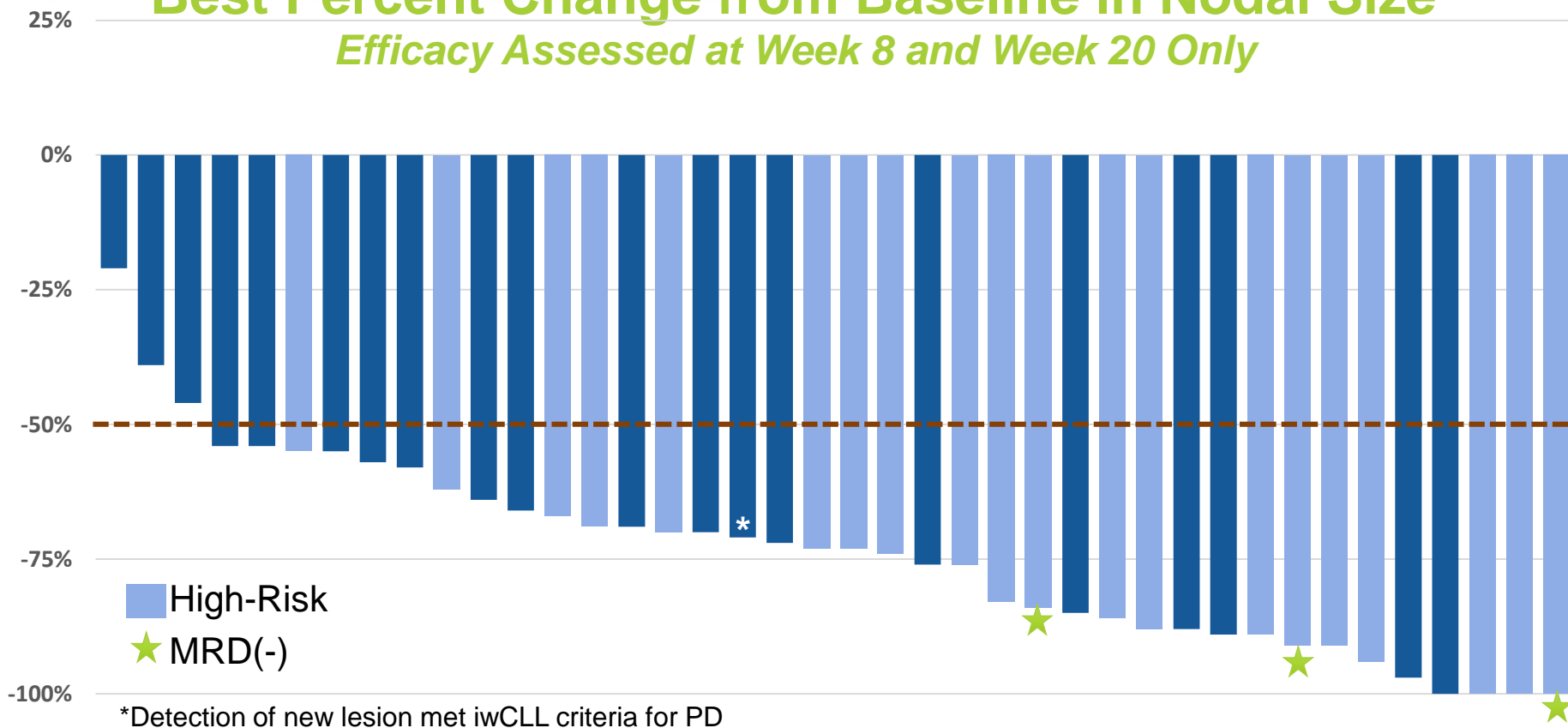
↓ = Ublituximab Infusion

- 70% of CLL patients had ALC in normal range (<4000/uL) within 6 cycles of therapy

Phase II Efficacy: Nodal Reductions

Best Percent Change from Baseline in Nodal Size

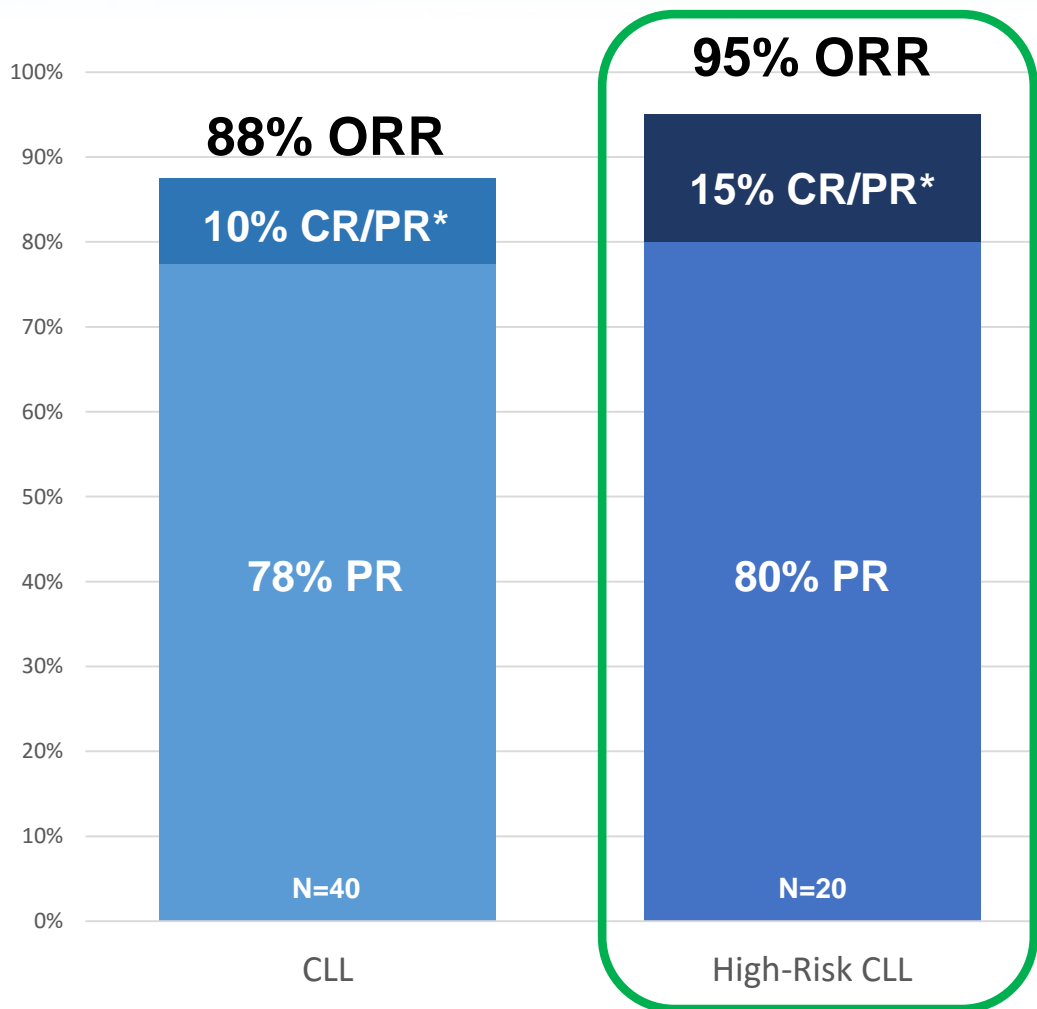
Efficacy Assessed at Week 8 and Week 20 Only



- 37/40 (93%) achieved > 50% reduction in nodal size

Phase 2: Ublituximab + Ibrutinib

Best Overall Response Rate

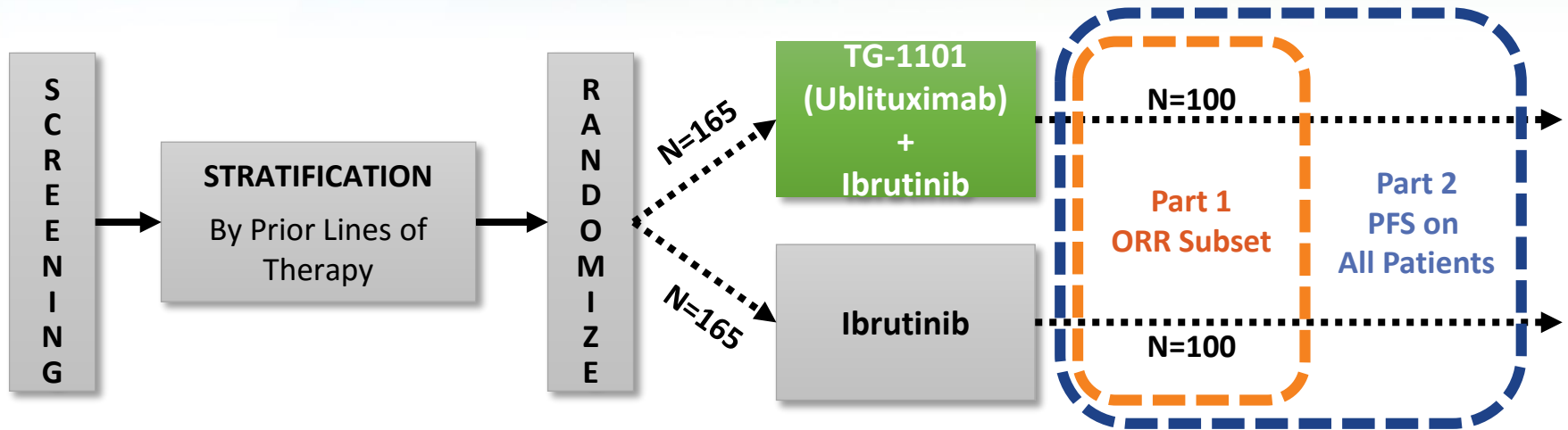


25% of patients were MRD negative or in CR within 6 months of therapy

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

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

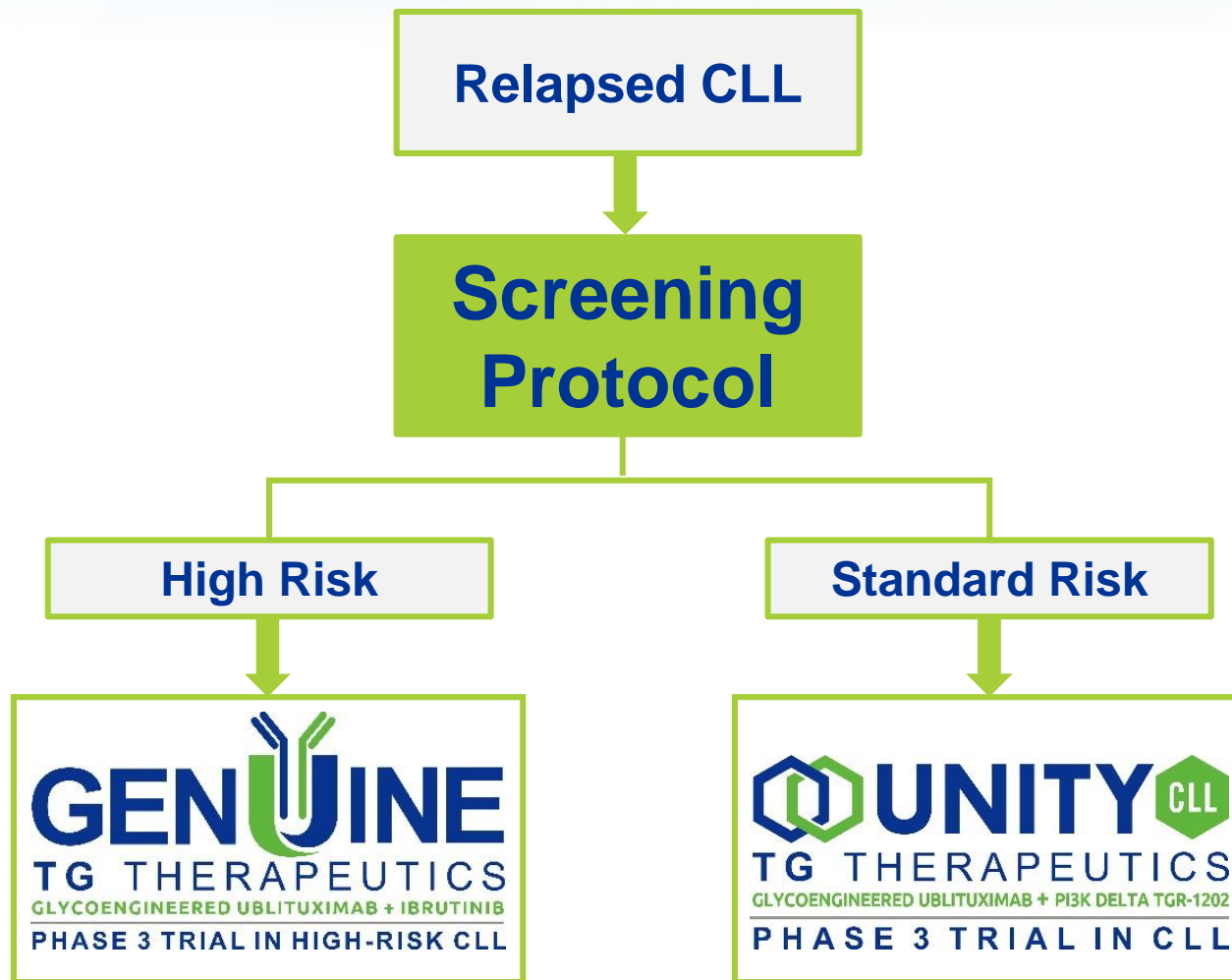
The GENUINE Phase 3 Trial



- 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



Previously Treated CLL Trial Opportunities



Overview

■ Primary Objective

- Identify high-risk genetic features (17p deletion, 11q deletion and/or TP53 mutation) of patients with previously treated Chronic Lymphocytic Leukemia (CLL).

■ This screening protocol is for central testing of a blood sample for **potential enrollment on TG Therapeutics GENUINE trial**

- If not high-risk, result can be used to satisfy FISH requirement for UNITY-CLL

Screening Protocol Benefits

- Results provide "best" treatment option = personalized approach to patient care
- Allows consideration of more than one treatment trial: GENUINE or UNITY- CLL
- Allows deferment of detailed discussion of GENUINE (or UNITY) until risk status is confirmed
- If not high risk, UNITY-CLL a perfect option and Screening Protocol fulfills 17p del testing requirement



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 O'Brien, MD⁷

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	47/24	
Histology	DLBCL	24
	CLL/SLL	19
	FL	19
	MZL	6
	MCL	2
	Richter’s	1
ECOG, 0/1/2	20/47/4	
Prior Therapy Regimens, median (range)	3 (1 – 10)	
Patients with ≥ 3 Prior Therapies (%)	61%	
Prior RTX Based Therapies, 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 $\geq 10\%$ of Patients (n = 71)

Adverse Event	All Grades		Grade 3/4	
	N	%	N	%
Nausea	33	46%	1	1%
Diarrhea	31	44%	2	3%
Fatigue	29	41%	2	3%
Neutropenia	21	30%	18	25%
Infusion related reaction	18	25%	1	1%
Vomiting	17	24%	-	-
Dyspnea	14	20%	2	3%
Back pain	13	18%	-	-
Dizziness	13	18%	-	-
Pyrexia	13	18%	2	3%
Decrease appetite	12	17%	-	-
Insomnia	12	17%	-	-
Sinusitis	11	15%	1	1%
Cough	10	14%	-	-
Anemia	9	13%	1	1%
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%	-	-

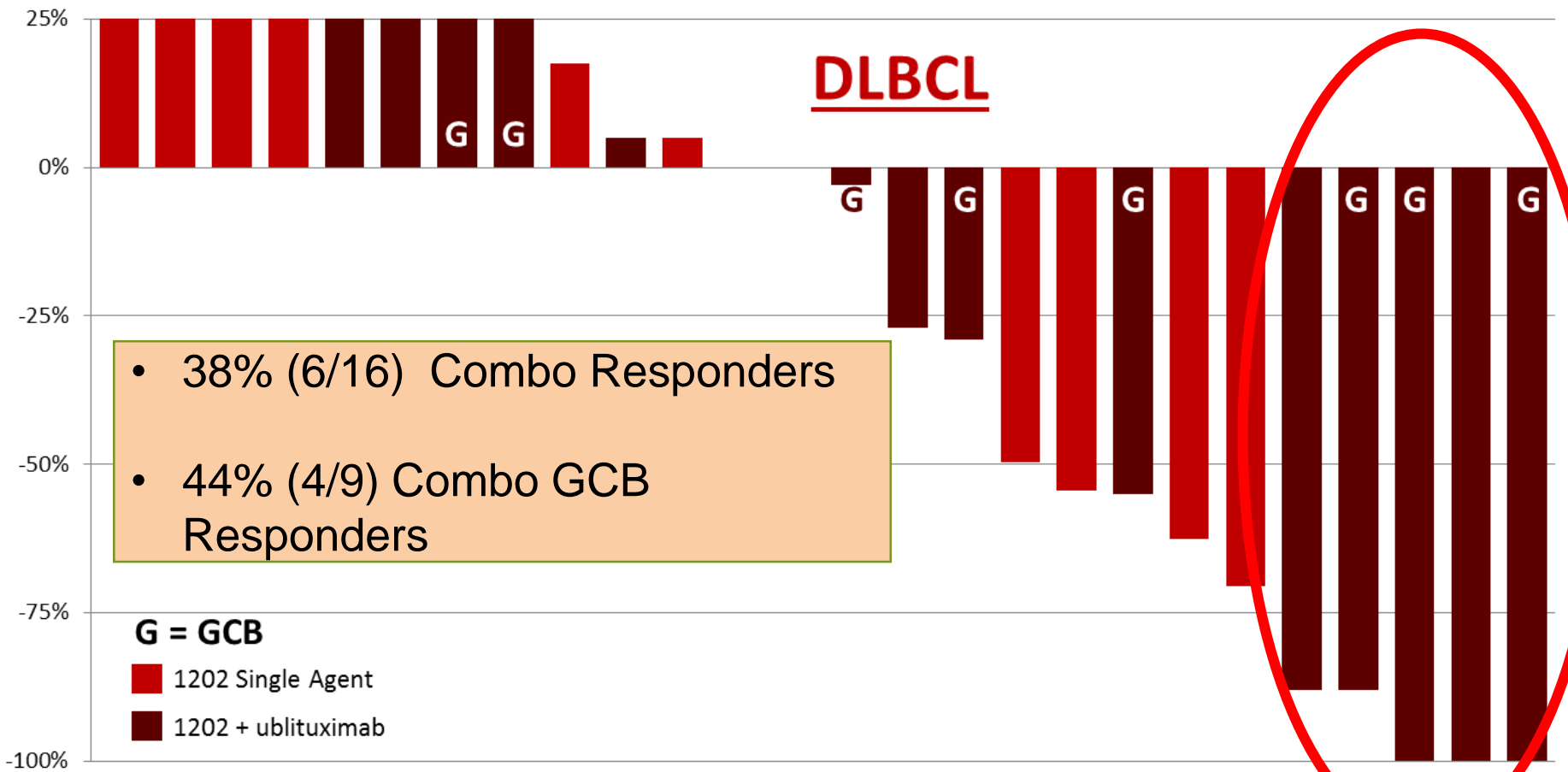
Of the 29 Gr 1/2 Diarrhea, only 11 were Gr.2, and no Gr. 4 events were observed

Data represents events occurring during entire duration on study (upwards of 22 mos.)

- ❖ 6 patients (8%) discontinued due to a TGR-1202 related AE
- ❖ Grade 3/4 AST/ALT increase was 3% (8% all grades)
- ❖ 7 patients (10%) had their TGR-1202 dose reduced; 2 diarrhea, 2 neutropenia, 1 nausea, 1 fatigue, 1 dizziness
- ❖ Colitis has not been reported to date

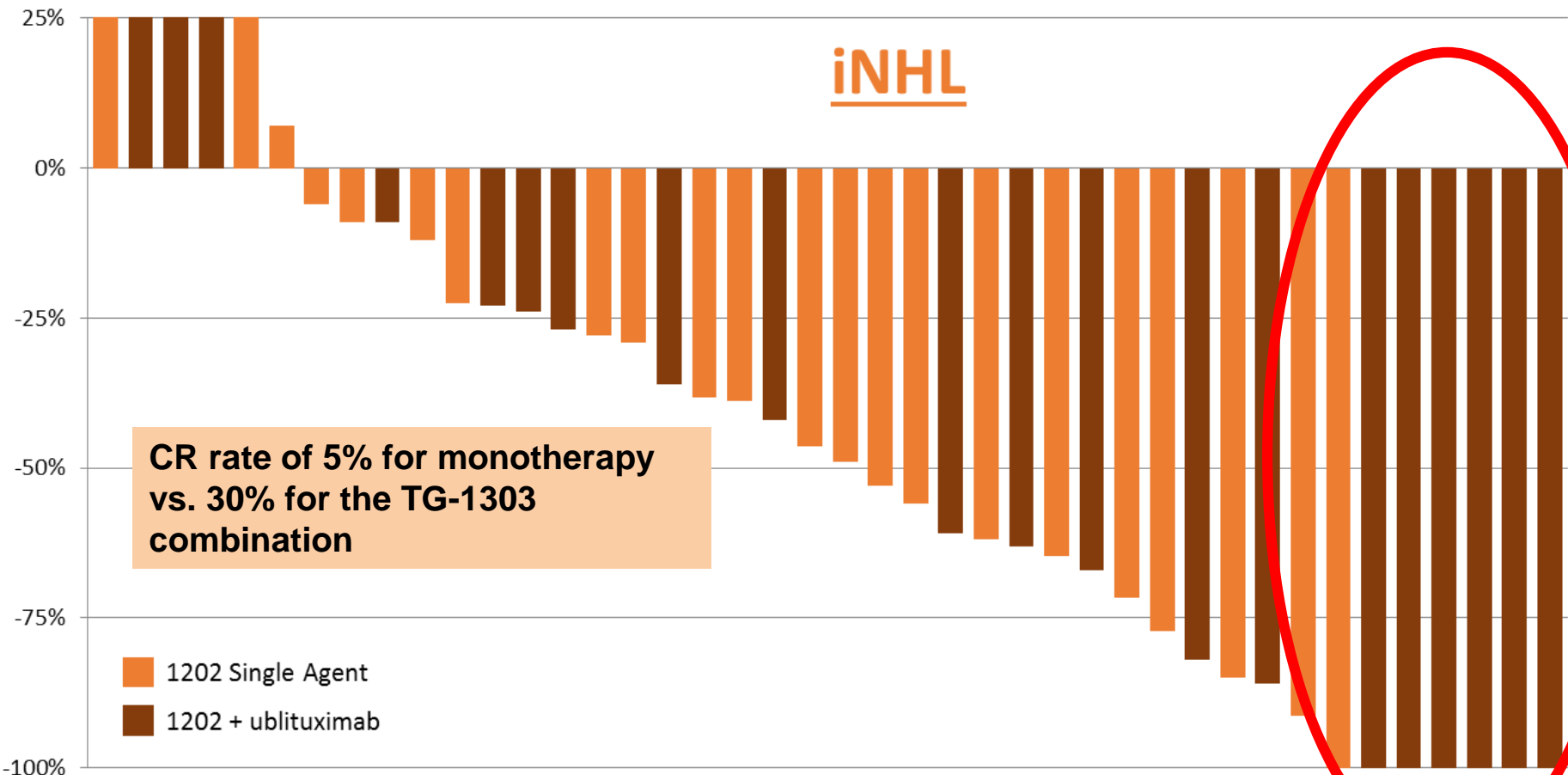
Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: DLBCL Efficacy

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



Integrated Analysis TGR-1202 Monotherapy and TGR-1202 + TG-1101: iNHL Efficacy

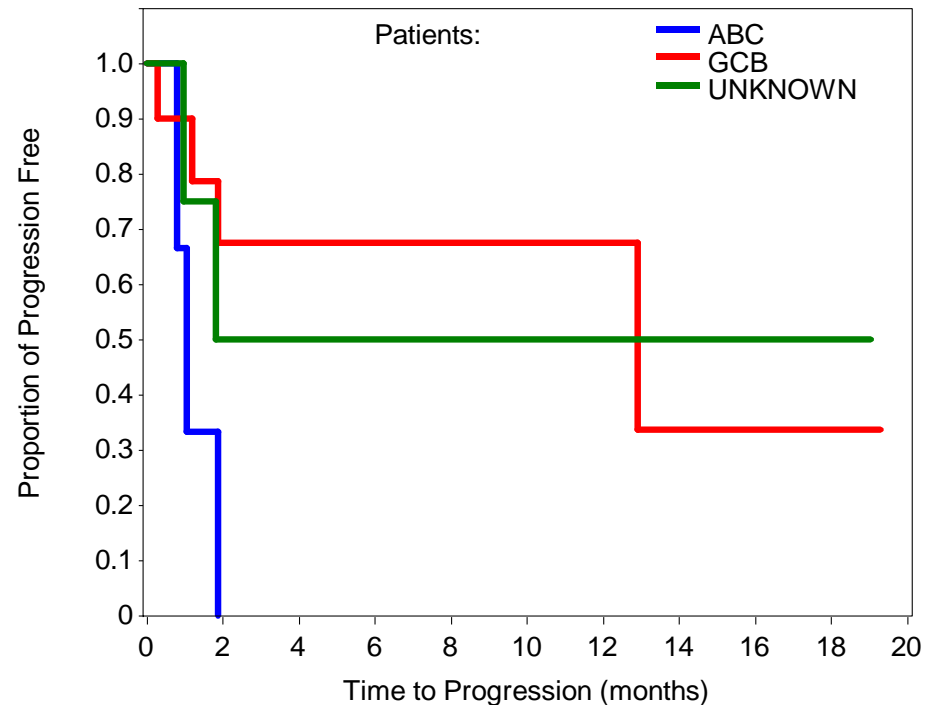
Patients Treated at “Higher Doses” of TGR-1202
Best Percent Change from Baseline in Disease Burden



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

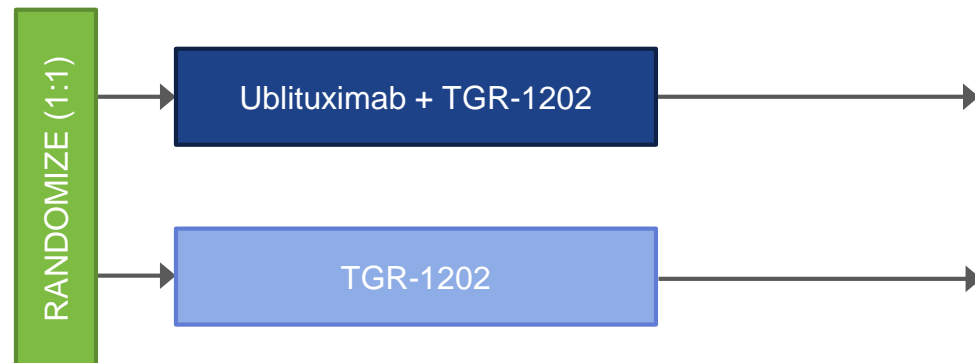


DLBCL Case Study

- 74 yo female
- GCB Subtype
- Received R-CHOP frontline therapy
 - Relapsed within 1 year
- Received R-Gem/Ox
 - Relapsed within 6 months
- Started on TGR-1202 + TG-1101 clinical trial
 - Cycle 3: PR (54% reduction)
 - Cycle 6: PR (71% reduction)
 - Cycle 9: PR (71% reduction)
 - Cycle 12: PR (88% reduction)
- On study treatment for 13+ months

UNITY-DLBCL

- First patient enrolled!
- Phase 2b Randomized Trial of TG-1101 +TGR-1202
- Enrolling patients with previously treated DLBCL of all subtypes
- US Study Chair:
Owen A. O'Connor, MD, PhD
- Ex-US Study Chair:
Pier-Luigi Zinzani, MD, PhD





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Q & A Session
