
**Ublituximab, a Novel Glycoengineered Anti-CD20 mAb,
In Combination with TGR-1202,
a Next Generation Once Daily PI3K δ Inhibitor,
Demonstrates Activity in Heavily Pre-Treated and
High-Risk Chronic Lymphocytic Leukemia and
B-Cell Lymphoma**

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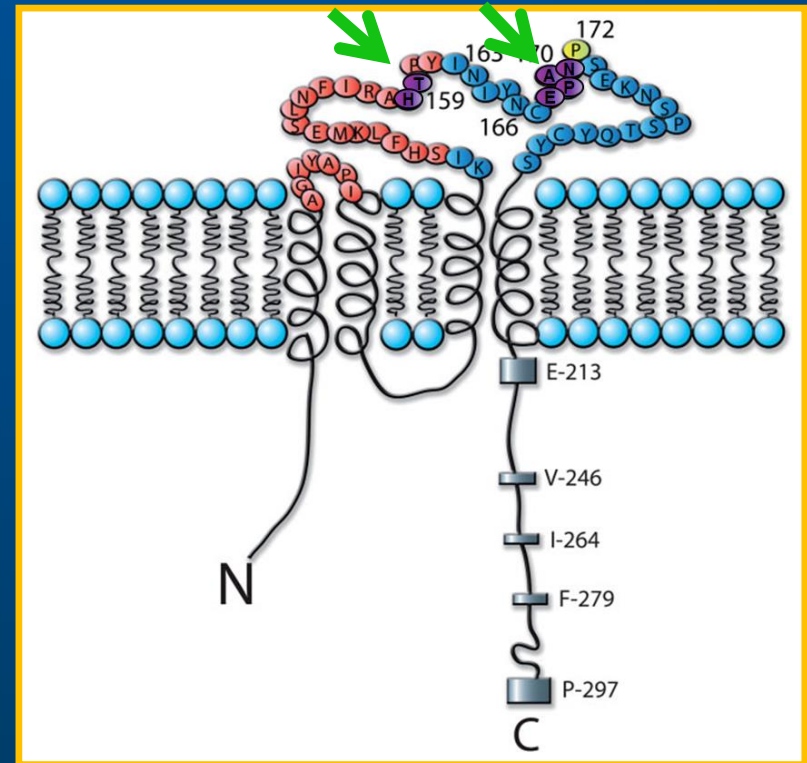
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Disclosures

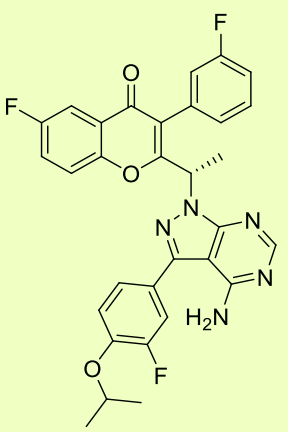
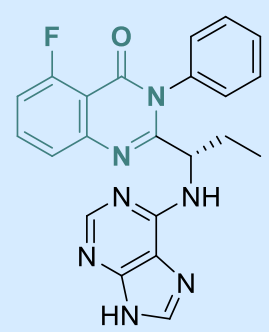
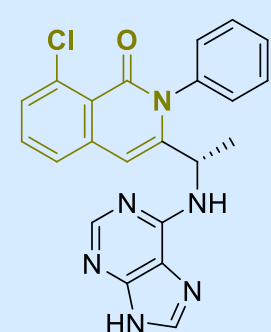
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Ublituximab: Glycoengineered Anti-CD20 mAb

- Type 1 chimeric IgG1 mAb
- Unique binding sequence on CD20 (Green arrows in figure)
- Potential advantages over current standards of care:
 - Glycoengineered for enhanced ADCC
 - Demonstrated activity in “low” CD20 expressing cell lines:
 - CLL/SLL
 - Refractory B-NHL
 - Single agent responses observed in rituximab refractory patients¹



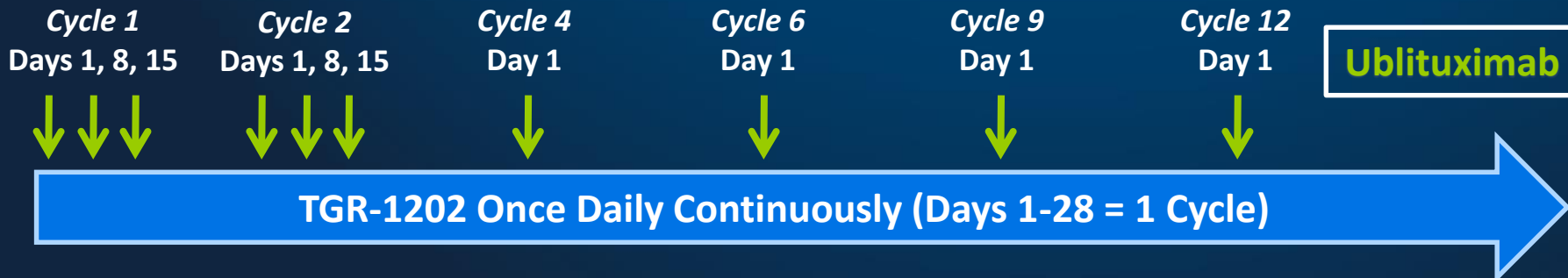
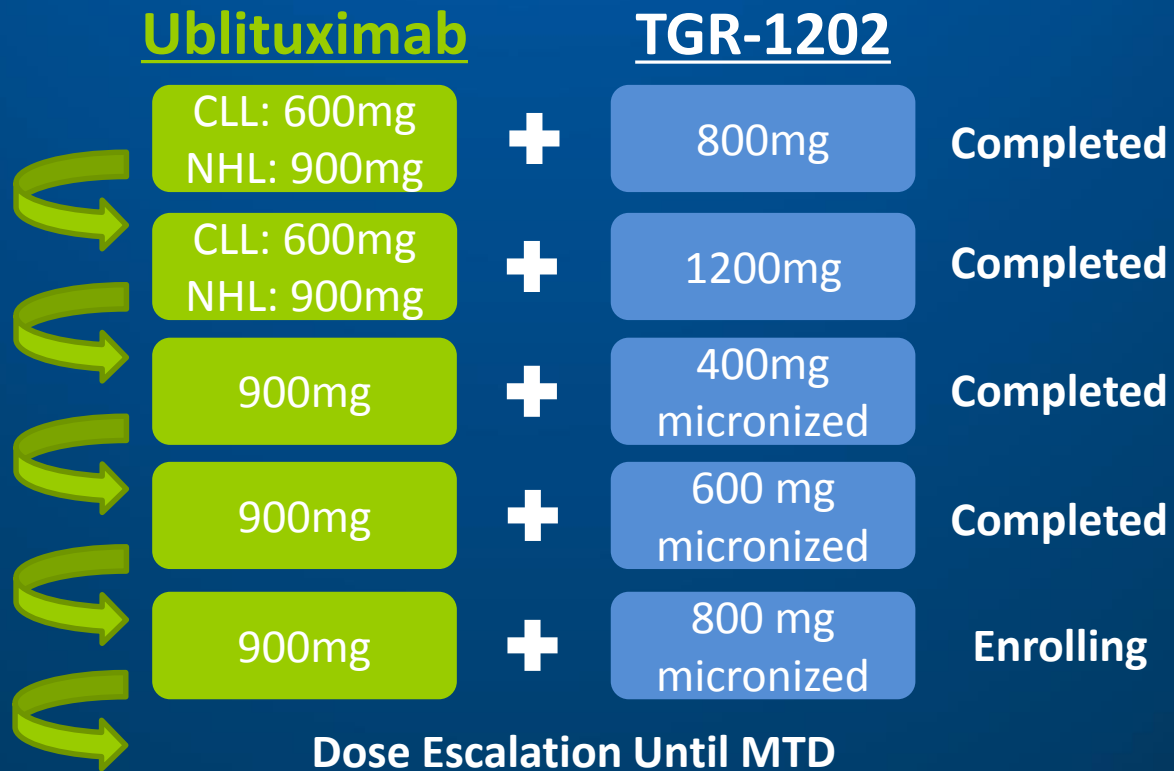
TGR-1202: Novel PI3K δ (delta) Inhibitor

TGR-1202	Idelalisib (GS-1101)	Duvelisib (IPI-145)
 <p>The chemical structure of TGR-1202 features a central pyrazole ring. One nitrogen of the pyrazole is substituted with a 4-fluorophenyl group. The other nitrogen is substituted with a 2-amino-5-(4-fluorophenyl)-2H-tetrazol-3-yl group. The pyrazole ring also has a methyl group and a 2-(4-fluorophenyl)oxyethyl group attached to it.</p>	 <p>The chemical structure of Idelalisib (GS-1101) consists of a pyridine ring fused to a pyrimidine ring. The pyridine ring has a fluorine atom at the 6-position and a benzyl group at the 2-position. The pyrimidine ring has a methyl group at the 4-position and a 2-amino-5-(4-fluorophenyl)-2H-tetrazol-3-yl group at the 5-position.</p>	 <p>The chemical structure of Duvelisib (IPI-145) features a pyridine ring fused to a pyrimidine ring. The pyridine ring has a chlorine atom at the 6-position and a benzyl group at the 2-position. The pyrimidine ring has a methyl group at the 4-position and a 2-amino-5-(4-fluorophenyl)-2H-tetrazol-3-yl group at the 5-position.</p>
Delta	Delta	Delta/Gamma
QD	BID	BID

- PK profile that allows once-daily oral dosing
- Absence of hepatic toxicity in rel/ref hematologic malignances¹
- 93% nodal PR rate in patients with rel/ref CLL¹
- Dose escalation ongoing—dose-response relationship observed¹

Trial Design: TGR-1202 + Ublituximab

- Enrolling B-cell NHL and CLL/SLL
- No limit on prior therapies
- Allows for prior BTK and/or PI3K inhibitors use
- 3+3 Dose escalation



Demographics: TGR-1202 + Ublituximab

Evaluable for Safety (n)	27	
Evaluable for Efficacy [†] (n)	26	
Median Age, years (range)	65 (35 – 82)	
Male/Female	17/10	
ECOG, 0/1/2	12/15/0	
Prior Therapies, median (range)	3 (1 – 9)	
Histologies	CLL/SLL, n	9/1
	Follicular, n	9
	DLBCL, n	7
	Richter's, n	1
≥ 2 Prior R-Chemo Regimens, n	18 (67%)	
Refractory to Prior Therapy, n	11 (41%)	

- 67% of CLL had 17p and/or 11q del
- Median Prior Tx in FL: 5 (range 1 – 9)
- 5/7 DLBCL with Germinal Center (GCB) Subtype

Safety: TGR-1202 + Ublituximab

Adverse Events in $\geq 10\%$
(All Causality) n=27

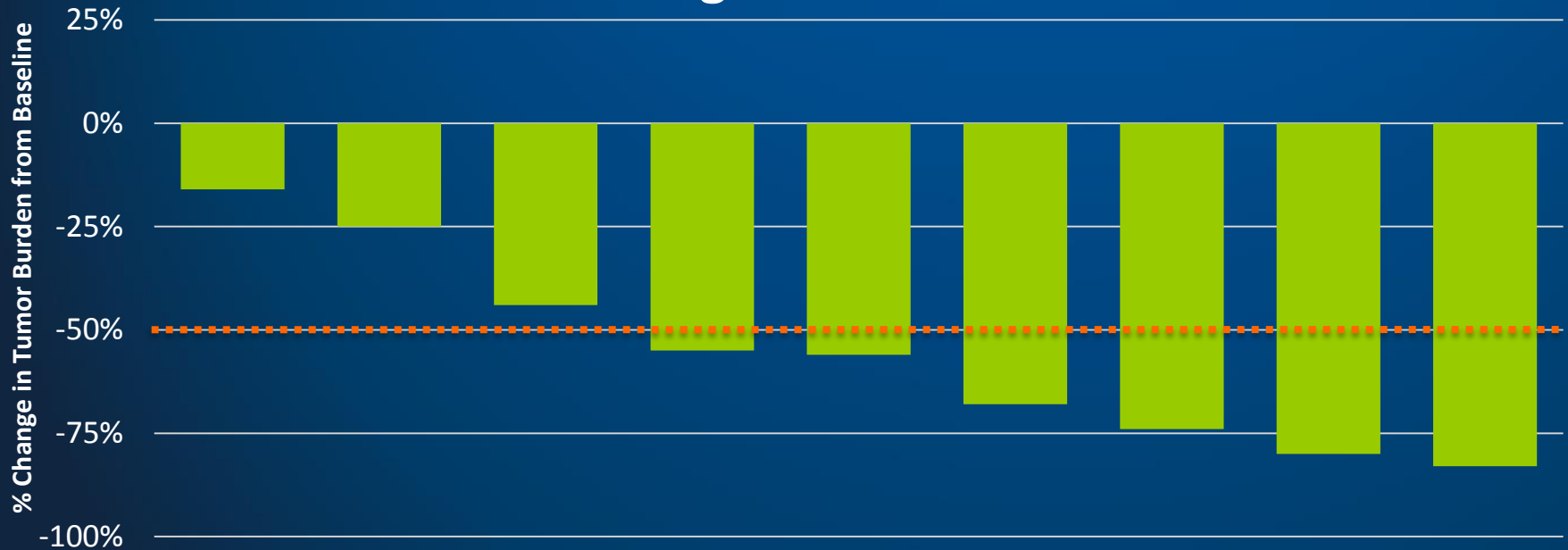
Adverse Event	All Grades n (%)	Grade 3/4 n (%)
Infusion reaction	14 (52)	1 (4)
Neutropenia	11 (41)	9 (33)
Nausea	10 (37)	-
Diarrhea	9 (33)	-
Fatigue	8 (30)	-
Insomnia	8 (30)	-
Dyspnea	6 (22)	1 (4)
Cough	5 (19)	-
Back Pain	4 (15)	-
Constipation	4 (15)	-
Sinusitis	4 (15)	-
Vomiting	4 (15)	-
Abdominal Pain	3 (11)	1 (4)
Fever	3 (11)	2 (7)
Upper Resp Inf	3 (11)	-

- IRR mostly on Day 1
- 3 patients enrolled with Gr 3 neutropenia
 - 2 improved & 1 worsened (DLT)
 - GCSF restricted in Cycle 1
- TGR-1202 dose reduced in 1 patient in Cycle 5
 - Grade 1 diarrhea
- Notably, no hepatic toxicity observed

Activity in CLL/SLL: TGR-1202 + Ublituximab

Interim Data From Early Dose Escalation Cohorts

% Change in Nodal Size



- 67% PR rate iwCLL (Hallek 2008)
- 6/9 patients with 17p and/or 11q
- All CLL patients remain on study (3+ to 9+ months)

TGR-1202 + Ublituximab: Activity in CLL

Mean Change in ALC from Baseline

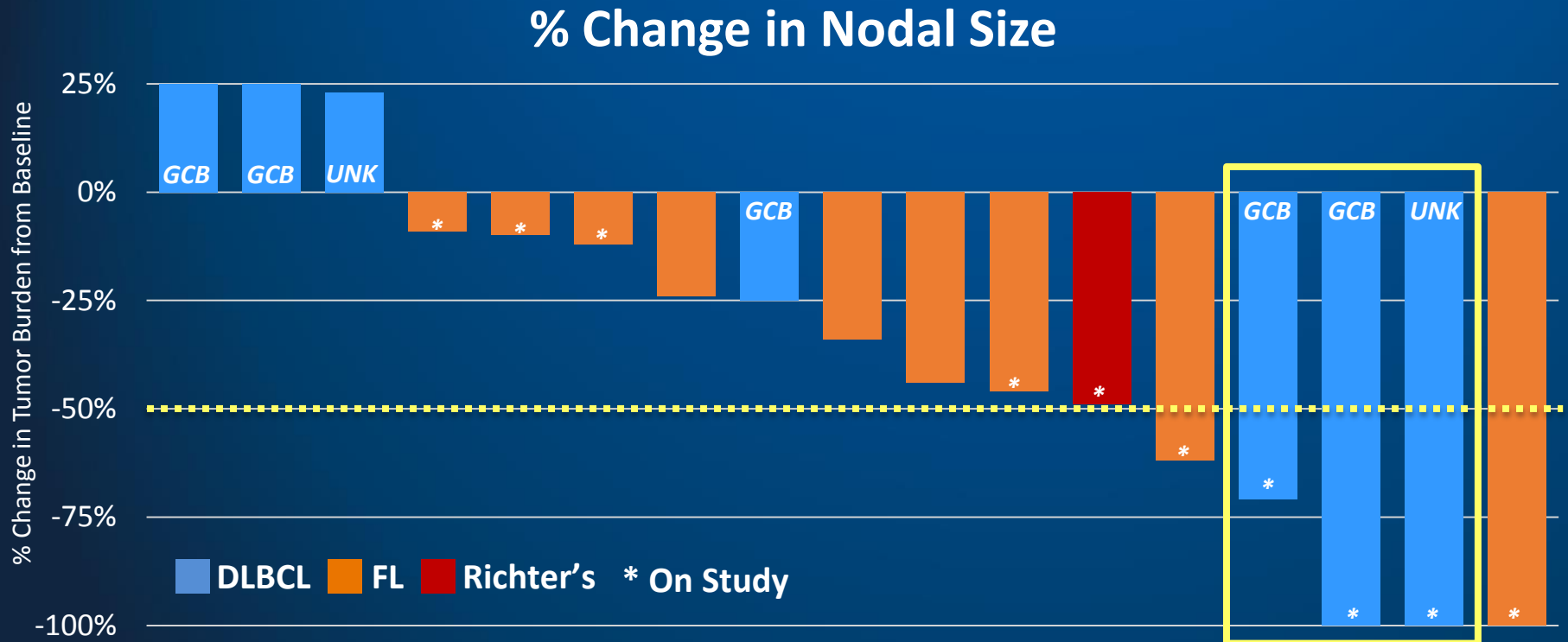


■ End of Cycle 3:

- All patients achieved >50% reduction of ALC
- 88% achieved ALC <5000/uL

Activity in NHL: TGR-1202 + Ublituximab

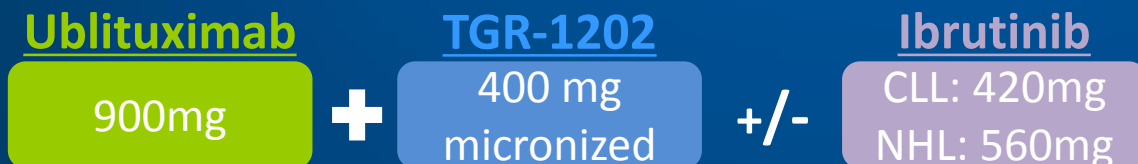
Interim Data From Early Dose Escalation Cohorts



- **FL: 1 PET(-) CR and 1 PR**
 - 78% of FL (N=9) patients have not progressed on study
- **DLBCL: ORR 43% (3/7);**
 - 2 CR's confirmed by independent radiologic review
 - 3 patients remain on study > 7 months

“Triplet”: TGR-1202 + Ublituximab + Ibrutinib

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



- Ongoing enrollment with 600 mg dose of TGR-1202 in NHL cohort
- Safety: All Grade 1/2 AEs (no Grade 3/4 events to date)
 - AEs included IRR, nausea, fatigue, and diarrhea
 - No dose reductions or delays with patients treated up to 4+ months

Clinical Response at First Assessment (8 Weeks)

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

Conclusions

- **Ublituximab and TGR-1202 has significant activity:**
 - **CLL:** ORR 67% iwCLL (Hallek 2008)
 - **FL:** 78% have not progressed on study
 - **DLBCL:** ORR 43%, with 2 confirmed CRs (activity in GCB)
- **Favorable toxicity profile**
 - No hepatic toxicity to date in 87 pts
 - 32 pts in current study + 55 pts in single agent TGR-1202 Ph 1
- **Both the “Doublet” and “Triplet” continue to accrue**
 - [Clinicaltrials.gov: NCT02006485](https://clinicaltrials.gov/ct2/show/study/NCT02006485)

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- **Families**

- **Patients**