BeiGene

Update on BTK Inhibitor Zanubrutinib (BGB-3111) and the Clinical Development Program

December 9, 2017

Forward Looking Statements

Certain statements contained in this presentation, other than statements of fact that are independently verifiable at the date hereof, may constitute forward-looking statements. Examples of such forward-looking statements include those regarding investigational drug candidates and clinical trials and the status and related results thereto, as well those regarding continuing and further development efforts. Such statements, based as they are on the current analysis and expectations of management, inherently involve numerous risks and uncertainties, known and unknown, many of which are beyond BeiGene's control. Such risks include but are not limited to: the impact of general economic conditions, general conditions in the pharmaceutical industries, changes in the global and regional regulatory environments in the jurisdictions in which BeiGene does business, market volatility, fluctuations in costs and changes to the competitive environment. Consequently, actual future results may differ materially from the anticipated results expressed in the forward-looking statements. In the case of forward-looking statements regarding investigational drug candidates and continuing further development efforts, specific risks which could cause actual results to differ materially from BeiGene's current analysis and expectations include: failure to demonstrate the safety, tolerability and efficacy of our drug candidates, final and quality controlled verification of data and the related analyses, the expense and uncertainty of obtaining regulatory approval, including from the FDA, CFDA and EMA, and the possibility of having to conduct additional clinical trials. Further, even if regulatory approval is obtained, pharmaceutical products are generally subject to: stringent on-going governmental regulation, challenges in gaining market acceptance and competition. These statements are also subject to a number of material risks and uncertainties that are described in BeiGene's filings with the Securities and Exchange Commission. The reader should not place undue reliance on any forward-looking statements included in this presentation. These statements speak only as of the date made, and BeiGene is under no obligation and disavows any obligation to update or revise such statements as a result of any event, circumstances or otherwise, unless required by applicable legislation or regulation.

Clinical data in this presentation relating to BeiGene's investigational drug candidates is from early phase, single-arm trials. When such data are presented in relation to other investigational or marketed drug products, the presentation and discussion are not based on head-to-head trials between BeiGene's investigational drug candidates and other products. BeiGene is still conducting clinical trials and, as additional patients are enrolled and evaluated, data on BeiGene's investigational drug candidates may change.

This presentation and the accompanying oral presentation contains data and information obtained from third-party studies and internal company analysis of such data and information. BeiGene has not independently verified the data and information obtained from these sources. Forward-looking information obtained from these sources is subject to the same qualifications noted above.

Agenda

- Welcome and Introduction, John Oyler, CEO and Dr. Jane Huang, CMO for Hematology, BeiGene
- ASH 2017 Data Review by Dr. Constantine Tam:
  - *Abstract # 152: Safety and Activity of the Highly Specific BTK Inhibitor BGB-3111 in Patients with Indolent and Aggressive Non-Hodgkin's Lymphoma*
  - *Abstract # 1745: BGB-3111 in Combination with Obinutuzumab in Patients with Chronic Lymphocytic Leukemia and Follicular Lymphoma*
  - *Abstract # 4057: Safety and Activity of the Highly Specific BTK Inhibitor BGB-3111 in Combination with the PD-1 Inhibitor BGB-A317 in Patients with B-Cell Lymphoid Malignancies*
- Zanubrutinib Development Program, Dr. Eric Hedrick, Chief Advisor, BeiGene
- Q&A with Dr. Christian Buske, Dr. Judith Trotman, Dr. Constantine Tam, Dr. Jane Huang, and Dr. Eric Hedrick

Introduction to BeiGene

Global oncology company **born and initially raised** ***in China*** **with commitment to science and quality for China and the world**

- Dramatic ***reform at CFDA*** **has** ***opened China*** **to global trials**
  - New access to 20%+ of world's cancer patients
  - Strategically important for global oncology development, timing & Asian prevalent cancers
  - But very few have ability to operate effectively in China
- BeiGene
  - Has built a unique, world-class ***global clinical oncology organization of 300+*** with experience and capabilities to operate in China for global and vice versa
    - Team: US (150+); China (140+); AU (10+)
    - Over 30 oncology developers from Genentech
  - Internally developed ***three late-stage clinical assets***, each with demonstrated proof-of-concept and potentially differentiated profile
    - **Zanubrutinib (BGB-3111)**, potentially best-in-class BTKi, in pivotal trials globally and in China
    - **Tislelizumab (BGB-A317)**, PD-1 mAb, in pivotal trials in China and recently partnered with Celgene to accelerate late-stage global development
    - **Pamiparib (BGB-290)**, PARPi, entering late-stage development
  - Is commercializing Abraxane, Revlimid, and Vidaza in China

Introduction to Zanubrutinib

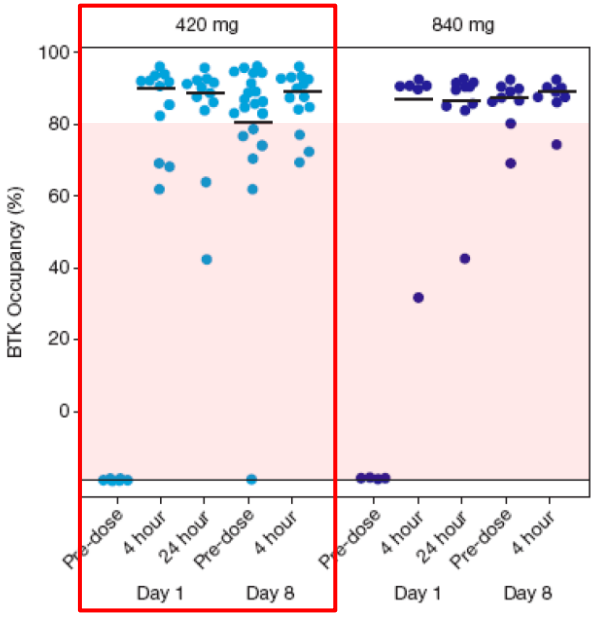
- Bruton's tyrosine kinase (BTK) plays a critical role in B-cell receptor signaling, which mediates B-cell proliferation, migration, and adhesion[1-3]
  - *The BCR pathway is an established therapeutic target in multiple subtypes of non-Hodgkin's lymphoma (NHL)*[4,5]
- Based on preclinical data, zanubrutinib was shown to be a potent, highly specific, and irreversible BTK inhibitor, with greater selectivity for BTK vs. other TEC- and EGFR-family kinases and demonstrates favorable pharmacokinetic and pharmacodynamic properties
- Zanubrutinib achieved complete and sustained BTK occupancy in peripheral blood mononuclear cells and lymph nodes in patients treated at 160 mg BID in this Phase 1 trial[6]

Source: 1. Rickert RC. Nat Rev Immunol. 2013;13:578-591. 2. Choe H, Ruan J. Oncology (Williston Park). 2016;30:847-858. 3. Aalipour A, Advani RH. Br J Haematol. 2013;163:436-443. 4. ten Hacken E, Burger JA. Clin Cancer Res. 2014;20:548-556. 5. Krysiak K, et al. Blood. 2017;129:473-483. 6. Tam CS, et al. ASH 2016.

Ibrutinib: Target Inhibition Appears *Incomplete* and *Compartment-Dependent*

Clinical data show borderline target inhibition by ibrutinib in the blood at approved dose

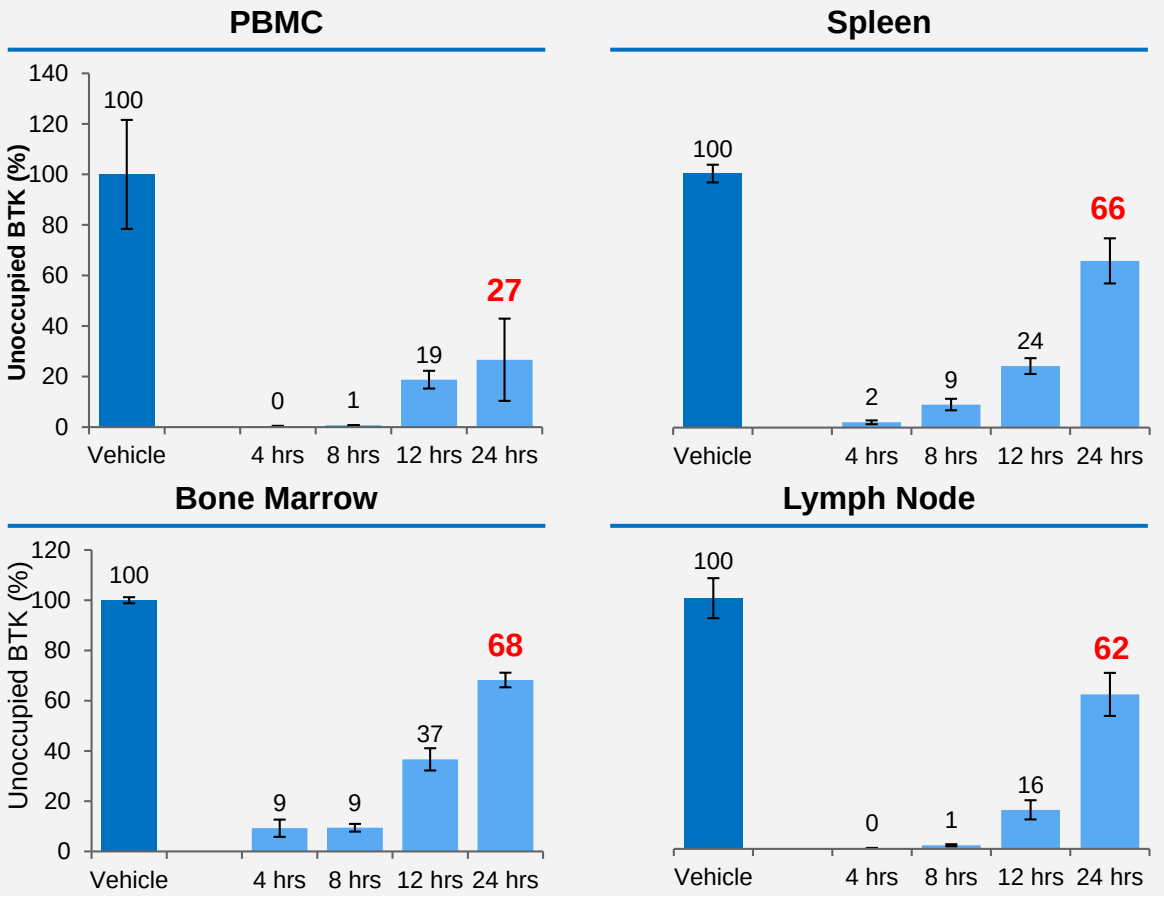
Ibrutinib Clinical Data in Blood



Approved Ibrutinib Doses: 420mg for CLL and WM; 560mg for MCL

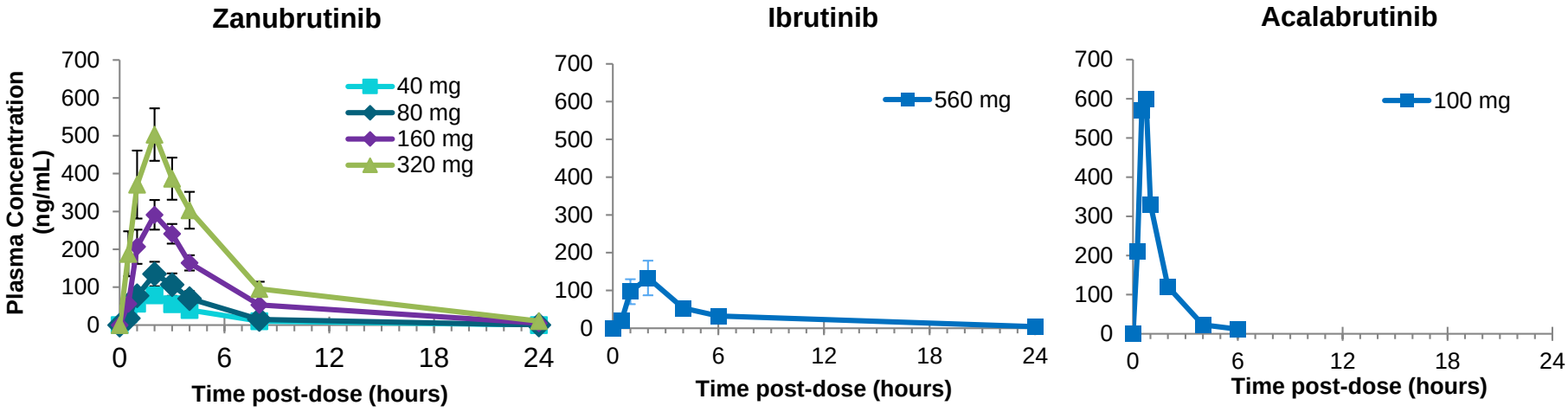
Byrd *et al.*, NEJM, 2013

Preclinical models* show significant recovery of target occupancy in disease relevant tissues for ibrutinib

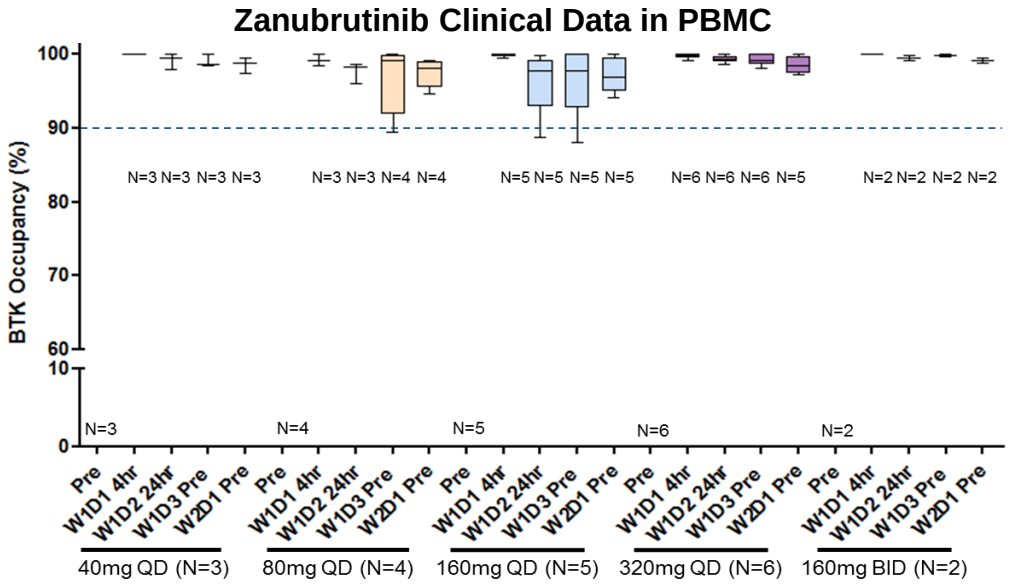


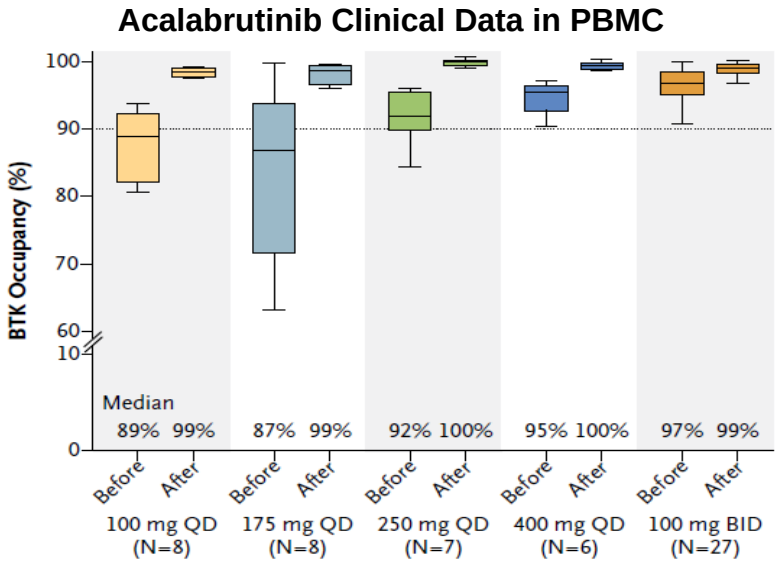
Note: PBMC = Peripheral Blood Mononuclear Cell; Source: BeiGene data and Byrd et al, NEJM, 2013
*Animal studies

Zanubrutinib: PK and Target Occupancy



Adapted from Advani, et al, *J Clin Oncol*, 2013; Byrd *et al*., NEJM, 2015





Adapted from Byrd *et al*., NEJM, 2016

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Data are from independent studies
Source: Tam *et al.*, ASH, 2015; Byrd *et al.*, NEJM, 2016; Lannutti *et al.*, AACR, 2015,

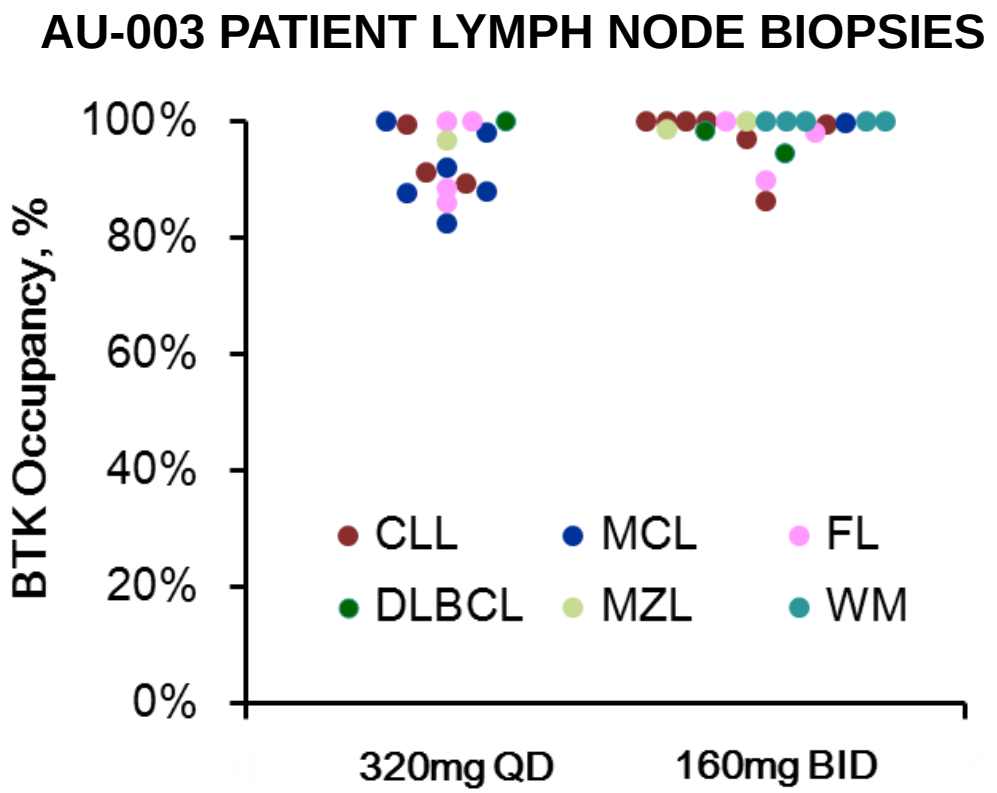
Zanubrutinib: Highly Potent and Selective BTK Inhibitor

In Preclinical Studies, Equipotent against BTK compared to ibrutinib
Higher selectivity vs EGFR, ITK, JAK3, HER2 and TEC

Targets	Assays	Ibrutinib IC_{50} (nM)	Zanubrutinib IC_{50} (nM)	Ratio (Zanubrutinib:Ibrutinib)
BTK	BTK-pY223 Cellular Assay	3.5	1.8	0.5
	Rec-1 Proliferation	0.34	0.36	1.1
	BTK Occupation Cellular Assay	2.3	2.2	1.0
	BTK Biochemical Assay	0.20	0.22	1.1
EGFR	p-EGFR HTRF Cellular Assay	101	606	6.0
	A431 Proliferation	323	3210	9.9
ITK	ITK Occupancy Cellular Assay	189	3265	17
	p-$PLC_{\gamma 1}$ Cellular Assay	77	3433	45
	IL-2 Production Cellular Assay	260	2536	9.8
	ITK Biochemical Assay	0.9	30	33
JAK3	JAK3 Biochemical Assay	3.9	200	51
HER2	HER2 Biochemical Assay	9.4	661	70
TEC	TEC Biochemical Assay	0.8	1.9	2.4

BTK, Bruton's tyrosine kinase; EGFR, epidermal growth factor receptor; IC50, drug concentration causing 50% inhibition of the desired activity; ITK, interleukin-2 inducible T-cell kinase; JAK3, Janus kinase 3.

Zanubrutinib: Sustainable, Near-Complete Target Inhibition in Lymph Nodes



- Paired lymph node biopsies were collected during screening and pre-dose on day 3
- Median trough occupancy: 100% (160mg BID) vs 94% (320mg QD), p=0.002
- Proportion ≥90% trough occupancy: 94% (160mg BID) vs 58% (320mg QD), p=0.027

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Source: Tam *et al.* ASH 2016 (abstracts 642 and 1216)

Dr. Constantine Tam

Disease Group Lead for Low Grade Lymphoma and Chronic Lymphocytic Leukemia at Peter MacCallum Cancer Centre, Director of Haematology at St. Vincent's Hospital, Australia

- Leads the Low Grade Lymphoma and CLL programs at Peter MacCallum Cancer Centre
- Leukemia Fellowship at MD Anderson
- Recipient of Herman Fellowship in Translational Cancer Research, University of Melbourne
- Principal Investigator of first global study to combine ibrutinib and venetoclax
- Published 139 peer-review articles

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Safety and Activity of the Highly Specific BTK Inhibitor Zanubrutinib (BGB-3111) in Patients with Indolent and Aggressive Non-Hodgkin's Lymphoma

Constantine S. Tam[1], David Simpson[2], Stephen Opat[3], Won Seog Kim[4], Michael Wang[5], Gavin Cull[6], Patrick B Johnston[7], Javier Munoz[8], WonSik Lee[9], Paula Marlton[10], David Gottlieb[11], Lai Wang[12], Jane Huang[12], James Hilger[12], Ling Xue[12], Sunhee Ro[12], and Judith Trotman[13]

[1]Peter MacCallum Cancer Centre & St. Vincent's Hospital, Melbourne, Australia; [2]North Shore Hospital, Auckland, New Zealand; [3]Monash Medical Centre, Monash Health, Clayton, Australia; [4]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South); [5]Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX; [6]Department of Haematology, Sir Charles Gairdner Hospital, Nedlands, Australia; [7]Division of Hematology, Mayo Clinic, Rochester, MN; [8]Banner MD Anderson Cancer Center, Gilbert, AZ; [9]Inje University Busan Paik Hospital, Busan, Korea, Republic of (South); [10]Princess Alexandra Hospital, University of Queensland School of Medicine, Brisbane, Australia; [11]Westmead Hospital, Westmead Institute of Medical Research University of Sydney, Sydney, Australia; [12]BeiGene, San Mateo, CA; [13]Concord Repatriation General Hospital, Sydney, Australia

Trial Design: First-in-Human, Open-label, Multicenter, Phase 1b Study of Zanubrutinib in Patients With B-cell Malignancies

DOSE ESCALATION

Dose		Enrolled (indolent, aggressive)
40 mg	QD	4 (0, 1)
80 mg	QD	5 (0, 1)
160 mg	QD	6 (0, 2)
320 mg	QD	6 (0, 1)
160 mg	BID	4 (0, 2)

RP2D

320 mg QD

or

160 mg BID

DOSE EXPANSION

Population	RP2D Dose	Disease	Planned
R/R	BID, QD	MCL, MZL, FL, GCB DLBCL	40
R/R	BID	Non-GCB DLBCL	40
R/R	BID	CLL/SLL	70
R/R	BID	WM	20
R/R	QD	CLL/SLL	20
R/R, TN	BID, QD	WM	50
R/R	BID, QD	MCL	20
TN	BID, QD	CLL/SLL	20
TN	BID, QD	MCL	20
R/R	BID, QD	HCL	10
R/R	BID	iNHL	40
R/R	BID	Richter Transform.	15
R/R or intolerant	BID	BTK-R/R WM	15

Eligibility:

- World Health Organization-defined B-cell malignancy
- No available higher priority treatment
- Eastern Cooperative Oncology Group 0-2
- ANC >1,000/µL, platelets >100,000/µL*
- Adequate renal and hepatic function
- No significant cardiac disease†

*Growth factor/transfusion allowed. †Anti-coagulation allowed.
BID, twice daily; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma;
DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; GCB, germinal center B-cell–like; HCL, hairy cell leukemia; iNHL, indolent non-Hodgkin lymphoma;
MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; Pop, population; RP2D, recommended phase 2 dose; QD, once daily; WM, Waldenström macroglobulinemia.

Patient Characteristics

Characteristic	Indolent (FL, MZL) n = 34	Aggressive (DLBCL, MCL) n = 65	Total N = 99
Age, years, median (range)	65 (41-79)	70 (20-86)	68 (20-86)
ECOG Performance Status, (%) 0 1 2	 16 (47) 15 (44) 3 (9)	 28 (43) 29 (45) 8 (12)	 44 (44) 44 (44) 11 (11)
Prior treatment status Treatment-naïve, n (%) Relapsed/refractory, n (%) Number of prior therapies, median (range)	 0 34 (100) 2 (1-8)	 2 (3) 63 (97) 2 (1-10)	 2 (2) 97 (98) 2 (1-10)
Bulky disease,* n (%)	0	3 (5)	3 (3)
Stage at Study Entry (per disease type) I II III IV	 2 (6) 3 (9) 7 (21) 22 (65)	 2 (3) 7 (11) 12 (18) 43 (66)	 4 (4) 10 (10) 19 (19) 65 (66)
LDH at baseline, median (range) in µkat/L	4.1 (2.2-23.1)	4.4 (2-77.6)	4.2 (2-77.6)
DLBCL: GCB vs. non-GCB†	-	4 vs. 23	-

* Any lymph node >10 cm in maximum diameter. †Defined by Hans algorithm.

DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; GCB, germinal center B-cell like; LDH, lactate dehydrogenase; LN, lesion.

Most Frequent Adverse Events

Adverse Event	Indolent (FL, MZL) n = 34		Adverse Event	Aggressive (DLBCL, MCL) n = 65	
	All Grade n (%)	Grade 3-5 n (%)		All Grade n (%)	Grade 3-5 n (%)
Petechiae/purpura/ contusion	8 (24)	0	Petechiae/purpura/ contusion	16 (25)	0
Upper respiratory tract infection	7 (21)	0	Diarrhea	15 (23)	1 (2)
Nausea	6 (18)	1 (3)	Constipation	14 (22)	0
Pyrexia	5 (15)	0	Fatigue	12 (18)	0
Anemia	4 (12)	3 (9)	Upper respiratory tract infection	12 (18)	1 (2)
Headache	4 (12)	0	Anemia	11 (17)	7 (11)
Rash	4 (12)	0	Cough	10 (15)	0
Urinary tract infection	3 (9)	2 (6)	Pyrexia	10 (15)	2 (3)
Abdominal pain	3 (9)	2* (6)	Thrombocytopenia	10 (15)	6 (9)
Neutropenia	3 (9)	3 (9)	Neutropenia	8 (12)	6 (9)
			Pneumonia	6 (9)	4** (6)

*1 Grade 5 event, **1 Grade 5 event, both cases are in the context of disease progression and considered not treatment-related by investigators

Selected Adverse Events

Event, n (%)	Indolent (FL, MZL) n = 34	Aggressive (DLBCL, MCL) n = 65
Patients with ≥1 AE Grade ≥3	13 (38)	39 (60)
Patients with ≥1 serious AE	11 (32)	26 (40)
Events leading to treatment discontinuation	2 (6)	8 (12)
Fatal AE	1* (3)	6† (9)
AE of special interest		
Petechiae/purpura/contusion	8 (24)	16 (25)
Diarrhea	2 (6)	15 (23)
Hypertension	1 (3)	5 (8)
Severe hemorrhage‡	1 (3)	2 (3)
Atrial fibrillation	0	2 (3)

*Abdominal pain in the context of progressive disease.

†n=2 pneumonia, n=1 congestive cardiac failure, cerebral infarction, multi-organ failure, septic shock, unknown causes. Pneumonia and septic shock from same patient. All in the context of progressive disease except for cardiac failure and cerebral infarction

‡≥G3: gastrointestinal hemorrhage, hematuria, renal hematoma.

Indolent Lymphoma: Best Responses

Response (based on CT for majority of pts)	FL n = 17	MZL n = 9	Indolent Total N = 26
Median efficacy follow-up, mo (range)	7.8 (1.9-22.3)	7 (2.8-22)	7.5 (1.9-22.3)
Best Response, n (%)			
ORR	**7 (41)**	**7 (78)**	**14 (54)**
CR	3 (18)	0	3 (12)
PR	4 (24)	7 (78)	11 (42)
SD	7 (41)	2 (22)	9 (35)
PD	1 (6)	0	1 (4)
NE*	2 (12)	0	2 (8)

CR, complete response; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease.
* Both due to withdrawal of consent.

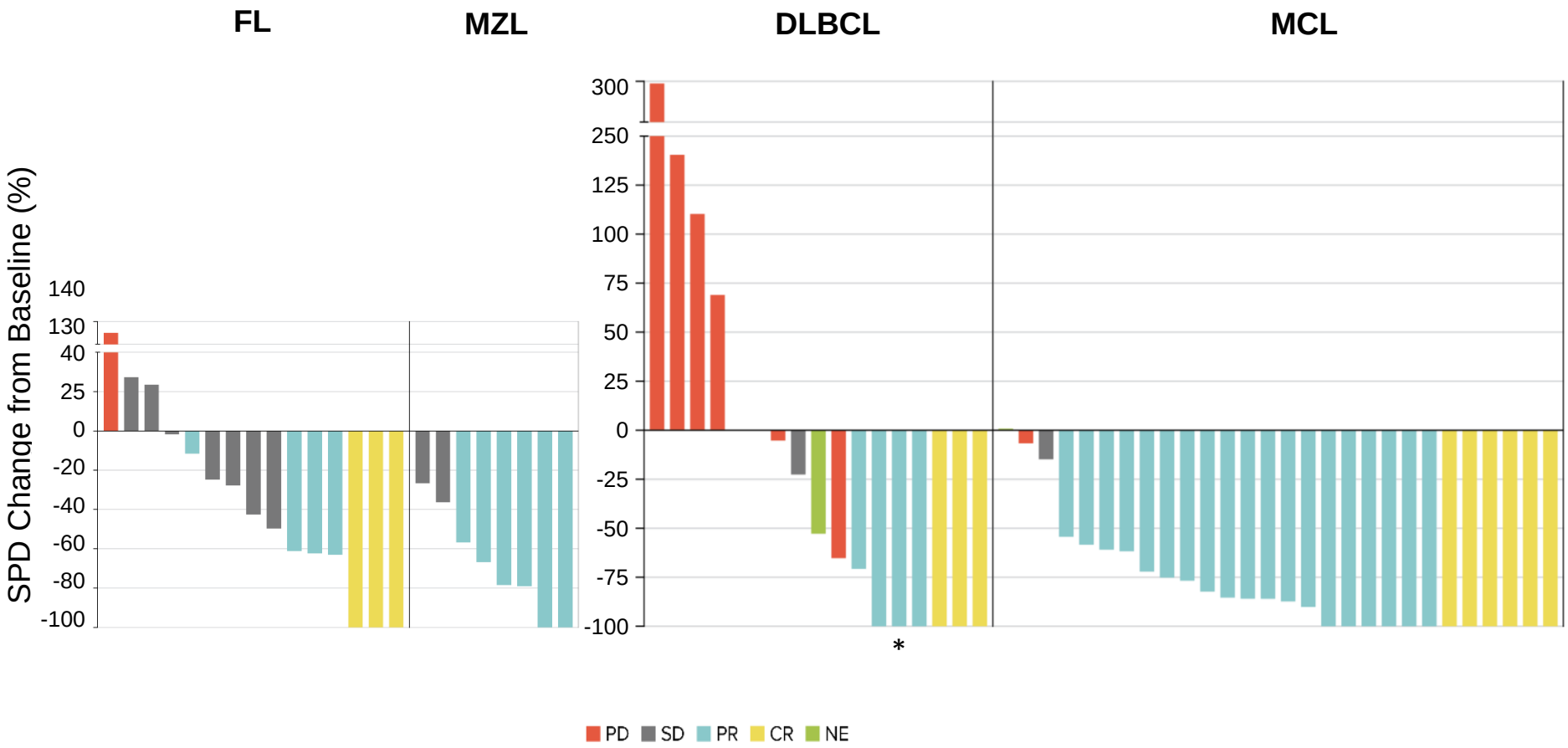
Aggressive Lymphoma: Best Responses

Response (based on CT for majority of pts)	DLBCL* n = 26	MCL*** n = 32	Aggressive Total N = 58
Median efficacy follow-up, mo (range)	4.2 (0.1-24)	9.5 (0.8-31.9)	5.6 (0.1-31.9)
Best Response, n (%)			
ORR	**8 (31)**	**28 (88)**	**36 (62)**
CR	4 (15)	8 (25)	12 (21)
PR	4 (15)	20 (63)	24 (41)
SD	4 (15)	1 (3)	5 (9)
PD	13 (50)	1 (3)	14 (24)
NE**	1 (4)	2 (6)	3 (5)

CR, complete response; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease.
*ORR was 25% (1 of 4) and 32% (7 of 22) for GCB (n=4) and non-GCB, respectively.
** n=1 DLBCL withdrew consent, n=2 MCL off study for adverse event before response assessment
***ORR in patients treated with at least 320 mg/d : 93% with a 27% CR rate

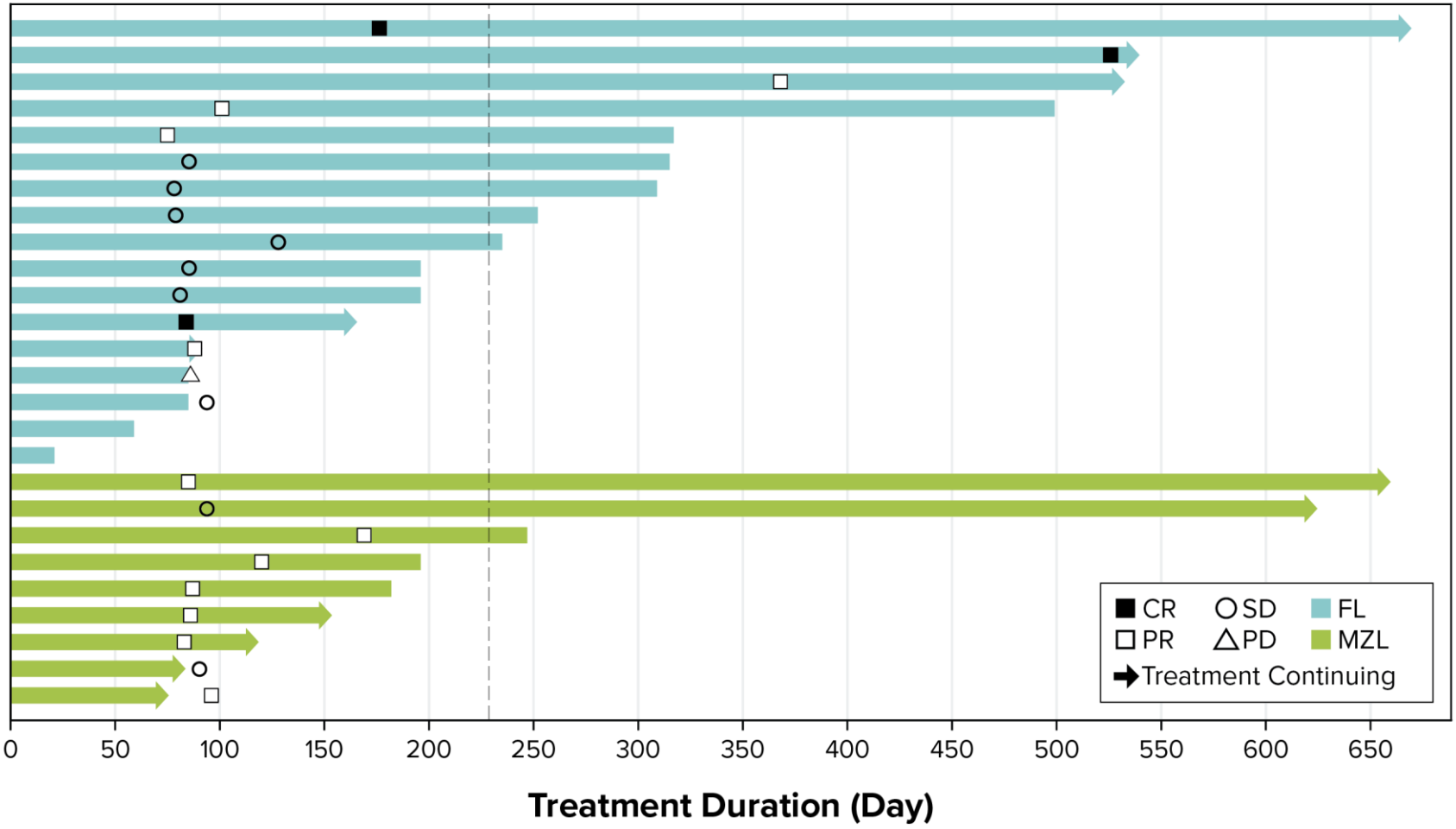
PET scanning not mandated for trial

Lymph Node Responses



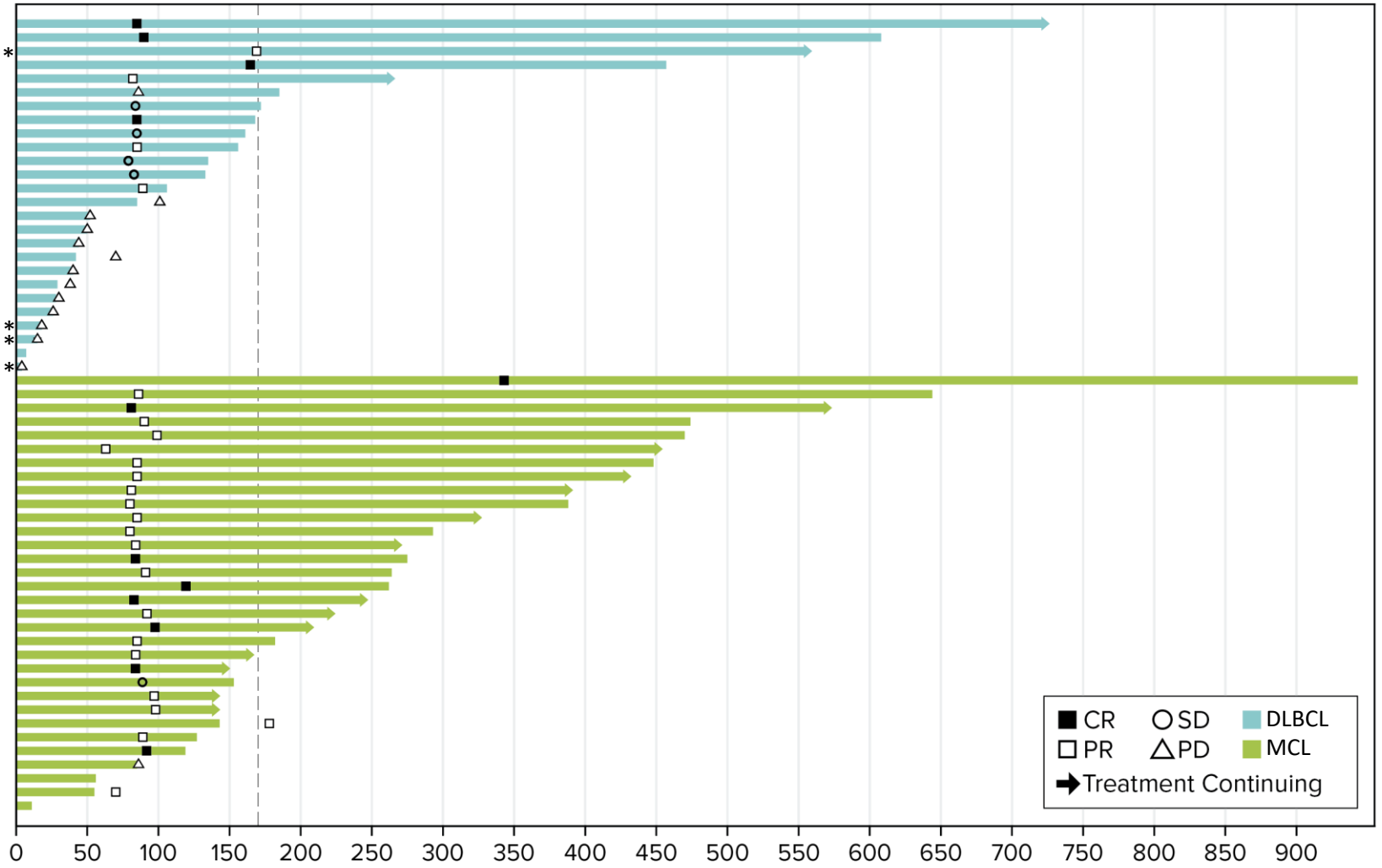
*Patient had GBC-DLBCL.
Note: 1 subject had no measurable lesions at baseline, 13 subjects did not have a post baseline scan in indolent lymphoma cohort; 4 subjects had no measurable lesions at baseline, 9 subjects did not have a post baseline scan in the aggressive lymphoma cohort.
SPD, sum of the products of lymph node diameters by CT scan.

Treatment Duration: Indolent Lymphoma (FL, MZL)



Note: symbols indicate best response.
Dashed line = median follow-up (7.5 months)

Treatment Duration: Aggressive Lymphoma (DLBCL, MCL)



*Patients had GCB-DLBCL.
Note: symbols indicate best response.
Dashed line = median follow-up (5.6 months)

Conclusions

- Zanubrutinib (BGB-3111) was well tolerated in multiple NHL subtypes
  - Adverse events led to discontinuation in 10% of patients overall
- Encouraging activity across multiple aggressive and indolent NHL subtypes
  - ORR of 88% (28/32 pts) in MCL and 78% (7/9 pts) in MZL
  - Durable response observed across a variety of histologies
- Supports ongoing development of zanubrutinib
  - Monotherapy: in registrational trials in WM and CLL
  - Combination: in registrational trial in combination with obinutuzumab
  - Additional registrational trials planned

Summary: Favorable Responses on Zanubrutinib Monotherapy Across Tumor Types

- Data presented include a total of 192 patients at 14-ICML and ASH 2017
- Encouraging activities across tumor types suggest that zanubrutinib is a highly active BTK inhibitor

Zanubrutinib	TN CLL	R/R CLL	WM	MZL	MCL	FL	DLBCL
Source	14-ICML	14-ICML	14-ICML	ASH17	ASH17	ASH17	ASH17
n	16	50	42	9	32	17	26
Follow-up (med)	7.6 mo	14.0 mo	12.3 mo	7.0 mo	9.5 mo	7.8 mo	4.2 mo
Prior Lines (med)	0	2 (1-7)	1 (1-8)	2 (1-8)	2 (1-10)	2 (1-8)	2 (1-10)
ORR	**100%**	**92%**	**90%**	**78%**	**88%**	**41%**	**31%**
CR	6%	2%	0	0	25%	18%	15%
VGPR	--	--	43%	--	--	--	--
PR/PR-L	94%	90%	33%	78%	63%	24%	15%
MR	--	--	14%	--	--	--	--

Zanubrutinib (BGB-3111) in Combination with Obinutuzumab in Patients with Chronic Lymphocytic Leukemia and Follicular Lymphoma

Constantine S. Tam[1], Hang Quach[1], Andrew Nicol[2], Xavier Badoux[3], Hannah Rose[4], H. Miles Prince[1], Michael F. Leahy[5], Richard Eek[6], Nicholas Wickham[7], Sushrut S. Patil[8], Jane Huang[9], Xiaoping Zhang[9], Lai Wang[9], Eric Hedrick[9], William Novotny[9], and Ian W. Flinn[10]

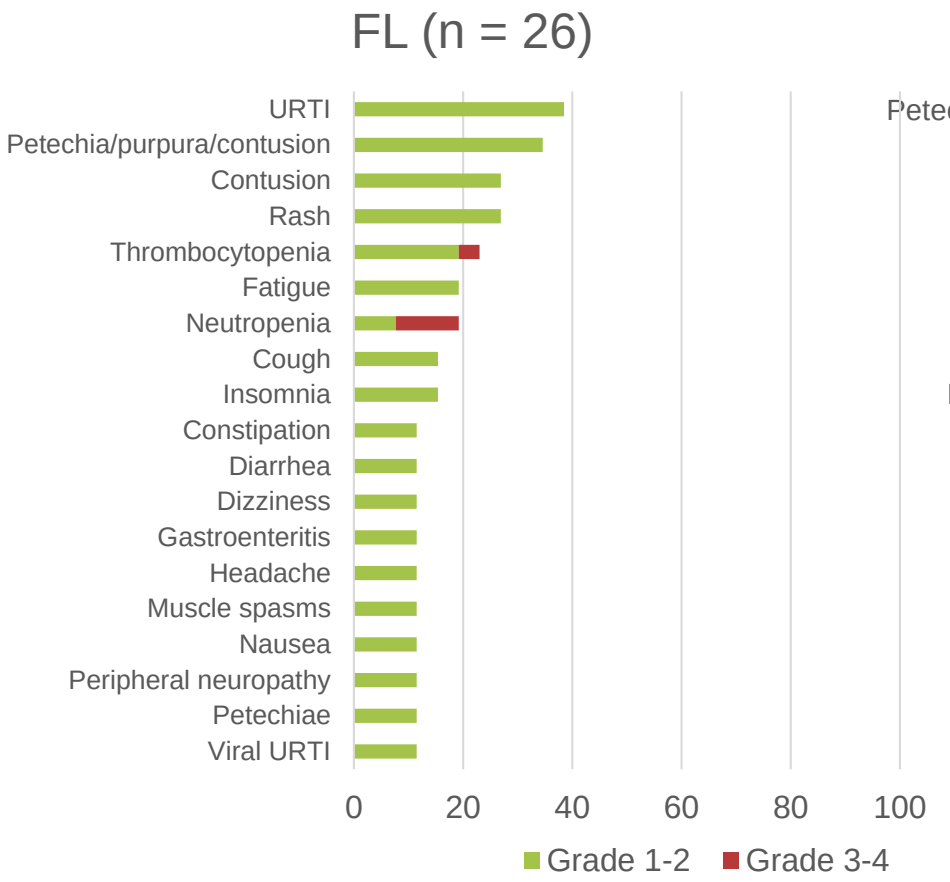
[1]Peter MacCallum Cancer Centre & St. Vincent's Hospital, Melbourne, Australia; [2]Brisbane Clinic for Lymphoma, Myeloma, and Leukaemia, Brisbane, Australia; [3]St. George Hospital, Sydney, Australia; [4]University Hospital, Geelong, Australia; [5]Royal Perth Hospital, Perth, Australia; [6]Border Medical Oncology, Wodonga, Australia; [7]Ashford Cancer Centre Research, Adelaide, Australia; [8]The Alfred Hospital, Melbourne, Australia; [9]BeiGene, San Mateo, CA; [10]Tennessee Oncology PLLC, Nashville, TN

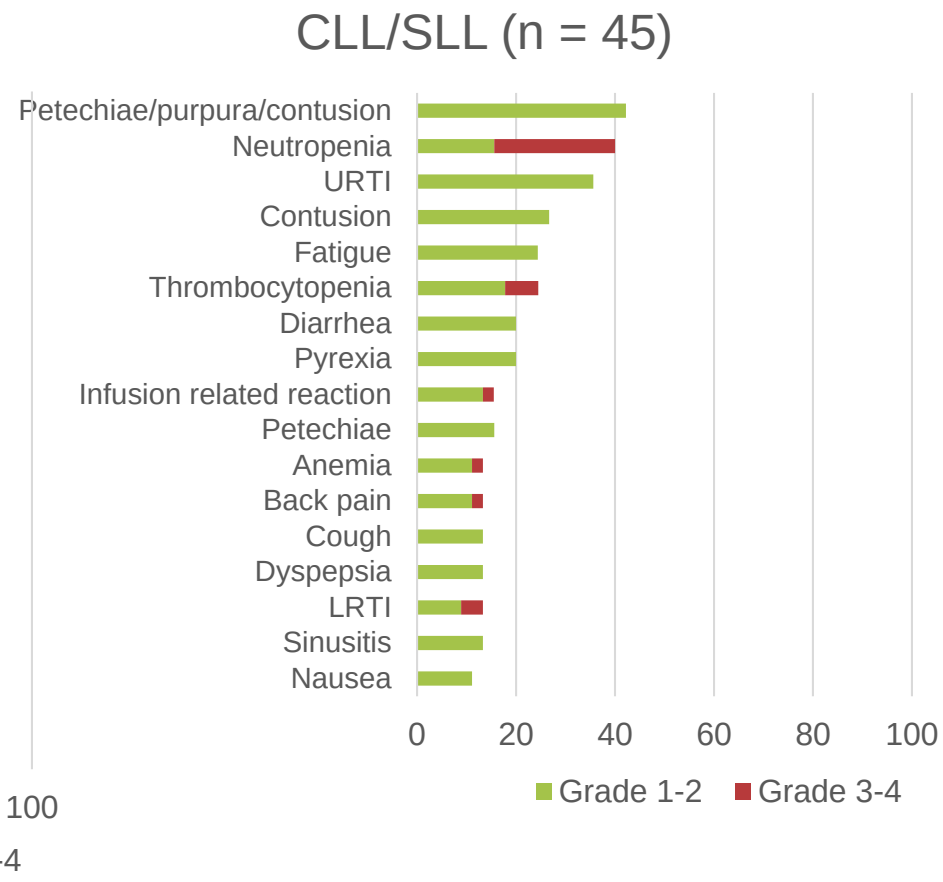
Patient and Disease Characteristics

Characteristic	CLL/SLL (n = 45)	FL (n = 26)
Age, years, median (range)	68 (38-82)	60 (41-86)
ECOG performance status, (%) 0 1 2	 20 (44.4) 24 (53.3) 1 (2.2)	 19 (73.1) 6 (23.1) 1 (3.8)
Median follow-up, mo (range)	11.8 (6.0-19.5)	8.6 (0.3-19.7)
Prior treatment status Treatment-naïve, n (%) Relapsed/refractory, n (%) Number of prior therapies, median (range)	 20 (44.4) 25 (55.6) 1 (1-4)	 0 26 (100) 9 (34.6) 2 (1-7)
Bulky Disease*, n (%)	0	2 (7.7)
Molecular risk factors (n = 37), n (%) del17p/p53mut del11q Unmutated *IGHV* Complex karyotype	 6 (16.2) 6 (16.2) 19 (51.4) 7 (18.9)	 N/A N/A N/A N/A

* Any lymph node >10 cm in maximum diameter.

Most Common Adverse Events Regardless of Causality





LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection.

Safety Summary

Event, n (%)	CLL/SLL (n = 45)	FL (n = 26)
Patients with ≥ 1 Grade ≥ 3 AE	26 (57.8)	7 (26.9)
Patients with ≥ 1 SAE	15 (33.3)	5 (19.2)
Patients with events leading to treatment discontinuation	1 (2.2)*	0
Patients with fatal AE	1 (2.2)*	0

* Patient with a history of squamous cell carcinoma discontinued and died due to squamous cell carcinoma. This case is considered not treatment-related by investigators.
AE, adverse event; SAE, serious adverse event.

Adverse Events of Special Interest				
Event, n (%)	CLL/SLL (n = 45)		FL (n = 26)	
	All Grade	Grade ≥ 3	All Grade	Grade ≥ 3
Diarrhea	9 (20.0)	0	3 (11.5)	0
Serious hemorrhage*	0	0	0	0
Atrial fibrillation	0	0	0	0
Hypertension	3 (6.7)	1 (2.2)	1 (3.8)	1 (3.8)
Infusion-related reactions	11 (24.4)	1 (2.2)	2 (7.7)	0

* ≥ Grade 3 hemorrhage, or central nervous system hemorrhage of any grade.

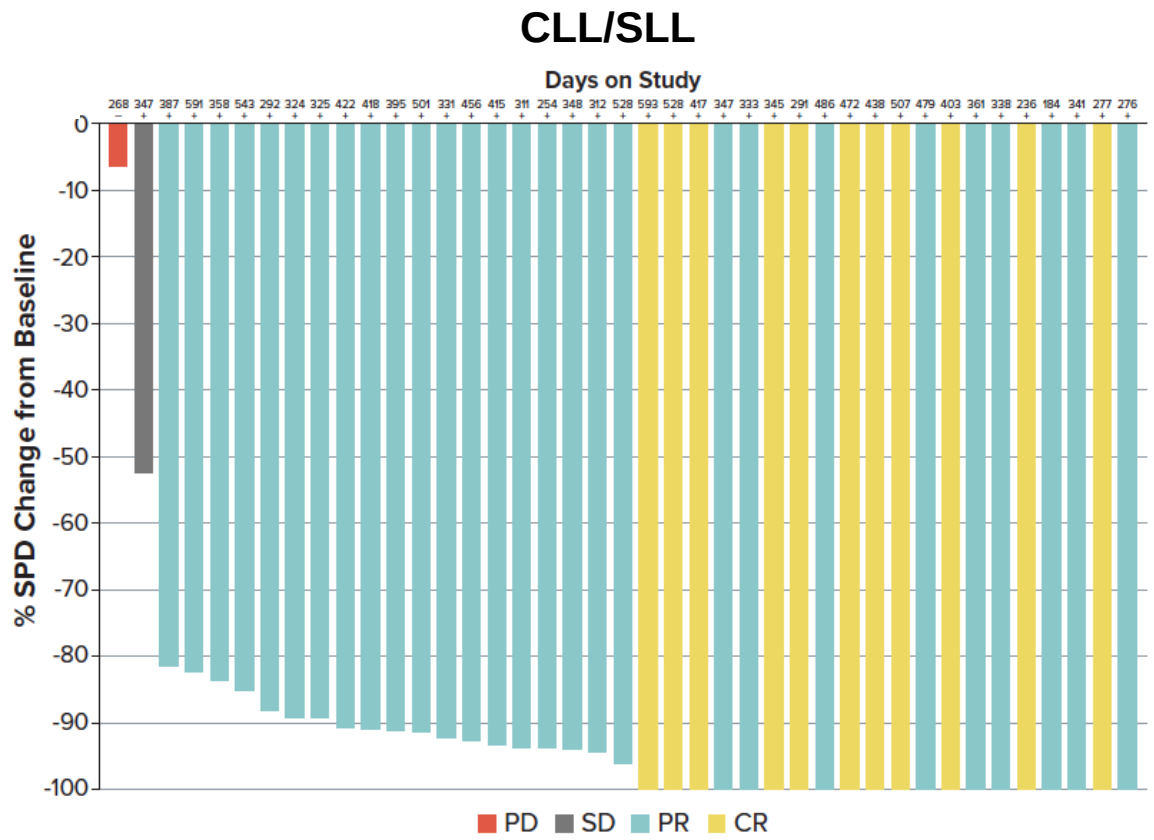
Disease Response

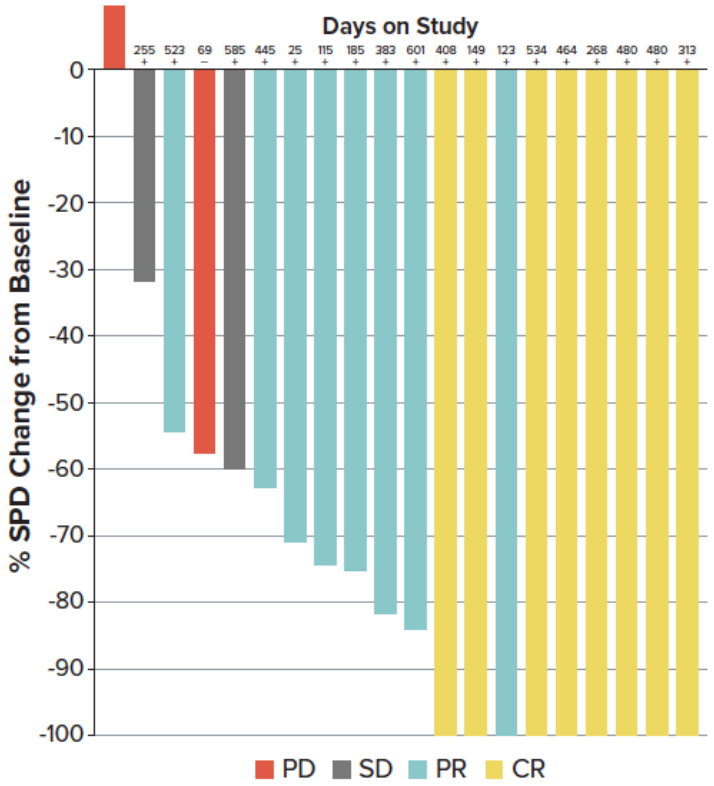
	TN CLL/SLL (n = 20)	R/R CLL/SLL (n = 25)	FL (n = 21)
Median follow-up, mo (range)	11.4 (6.0-17.3)	12.7 (7.9-19.5)	12.1 (0.8-19.7)
Best Response, n (%)			
ORR	**19 (95.0)**	**23 (92.0)**	**16 (76.2)**
CR	7 (35.0)	5 (20.0)	8 (38.1)
PR	12 (60.0)	18 (72.0)	8 (38.1)
SD	1 (5.0)	1 (4.0)	2 (10.0)
PD	0	1 (4.0)	3 (15.0)

CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; CR, complete response; FL, follicular lymphoma; ORR, overall response rate; PD, progressive disease; PR, partial response; PR-L, partial response with lymphocytosis; R/R, relapsed/refractory; SD, stable disease; TN, treatment-naïve.

- ORR in patients with high-risk CLL/SLL
  - del17p/p53mut (n = 6): 83.3%
  - del11q (n = 6): 100%
  - Unmutated *IGHV* (n = 19): 94.7%

Maximum Lymph Node Response in Patients With CLL/SLL and FL

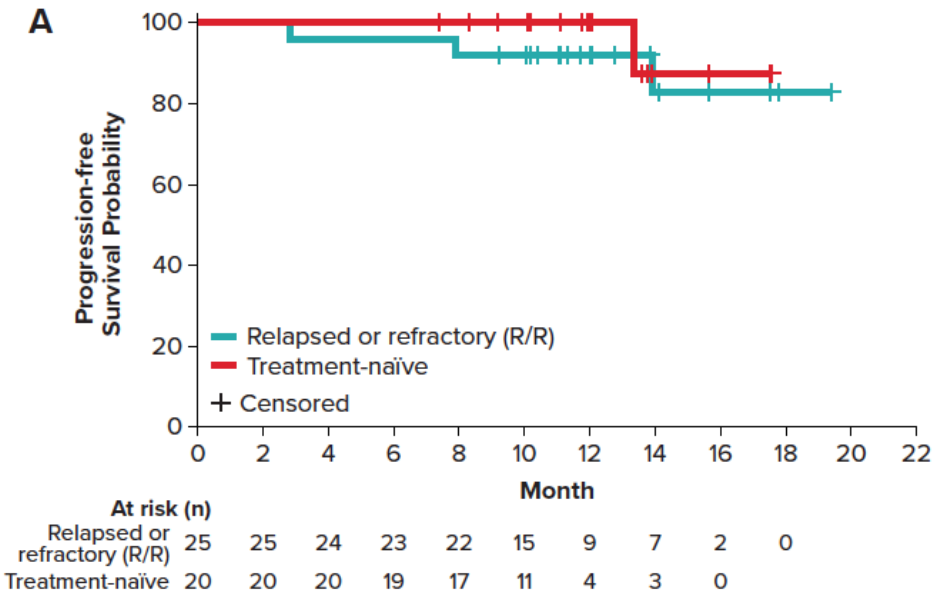




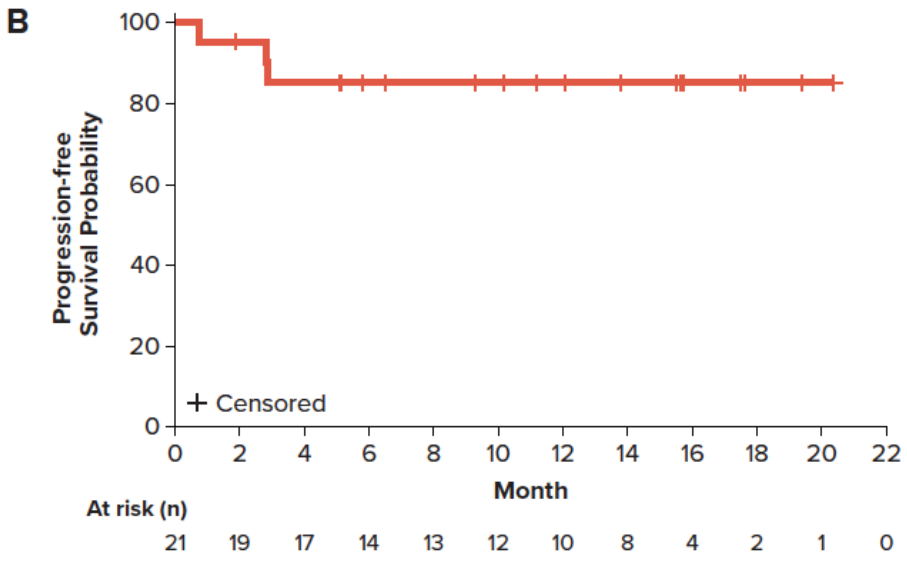
*Patients with no target lesions at baseline are not shown.

Progression-Free Survival

CLL/SLL



FOLLICULAR LYMPHOMA



Conclusions

- Updated results from the Phase 1b trial suggest that BTK inhibitor zanubrutinib (BGB-3111) and the anti-CD20 antibody obinutuzumab were generally well-tolerated when given in combination in patients with CLL/SLL and FL
- Compared to the expected rates with BTK-inhibitors or anti-CD20 antibodies alone:
  - CR rate in CLL/SLL was favorable
  - Frequency and depth of response (ORR and CR rate) in FL were favorable
- A pivotal randomized Phase 2 trial of the zanubrutinib + obinutuzumab combination in FL (≥2 prior therapies) is ongoing

Safety and Activity of BTK Inhibitor Zanubrutinib (BGB-3111) in Combination with the PD1 Inhibitor Tislelizumab (BGB-A317) in Patients with B-Cell Lymphoid Malignancies

Gavin Cull[1], Stephen Opat[2], Judith Trotman[3], James Hilger[4], Xiaoping Zhang[4], Sibaou Feng, PhD[4], Sunhee Ro[4], Jane Huang[4], Constantine S. Tam[5]

[1]Department of Haematology, Sir Charles Gairdner Hospital, Perth, Australia; [2]Department of Haematology, Monash Medical Centre, Monash Health, Melbourne, Australia; [3]Department of Hematology, Concord Repatriation General Hospital, Concord, New South Wales, Australia; [4]BeiGene, San Mateo, CA; [5]St. Vincent's Hospital and Peter MacCallum Cancer Center, Melbourne, Australia

Abstract # 4057

Safety and Activity of the Highly Specific BTK Inhibitor BGB-3111 in Combination with the PD-1 inhibitor BGB-A317 in Patients with B-cell lymphoid malignancies

Gavin Cull[1], Stephen Opat, FRACP, FRCPA[2], Judith Trotman, MBChB, FRACP, FRCPA[3*], James Hilger[4*], Xiaoping Zhang[4*], Shibao Feng, PhD[4*], Sunhee Ro, PhD[4*], Jane Huang, MD[4] and Constantine S. Tam, MBBS (Hons), MD, FRACP, FRCPA[5]

[1]Department of Haematology, Sir Charles Gairdner Hospital, Nedlands, Australia; [2]Monash Medical Centre, Monash Health, Clayton, Australia; [3]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia; [4]BeiGene, San Mateo, CA; [5]St. Vincent's Hospital and Peter MacCallum Cancer Centre, Melbourne, Australia

Session Name: 623. Mantle Cell, Follicular, and Other Indolent B-Cell Lymphoma — Clinical Studies: Poster III

Date: Monday, December 11, 2017

Presentation Time: 6:00 PM - 8:00 PM EST

Location: Georgia World Congress Center, Bldg A, Lvl 1, Hall A2

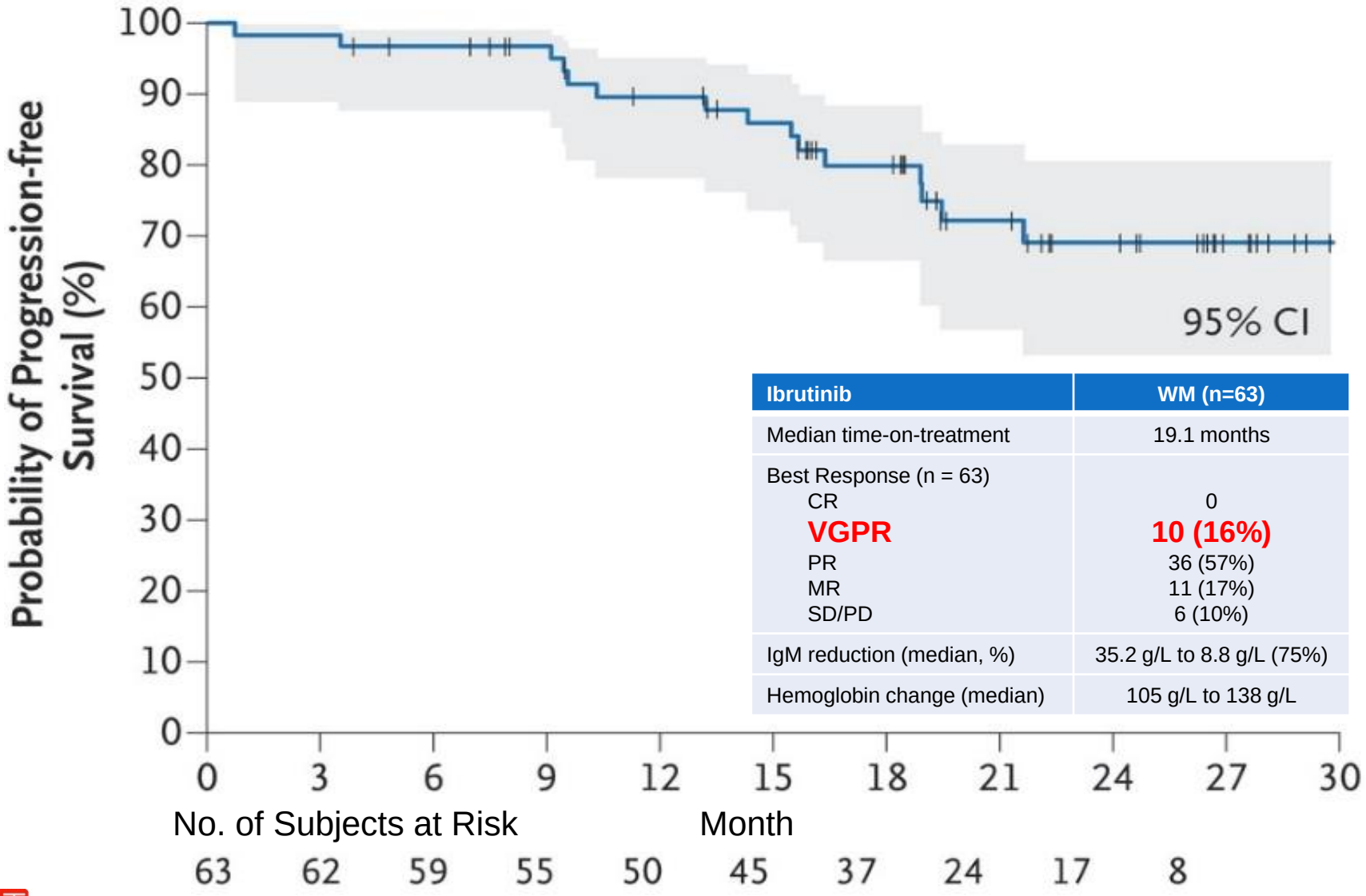
Agenda

- Welcome and Introduction, John Oyler, CEO and Dr. Jane Huang, CMO for Hematology, BeiGene
- ASH 2017 Data Review by Dr. Constantine Tam:
  - *Abstract # 152: Safety and Activity of the Highly Specific BTK Inhibitor BGB-3111 in Patients with Indolent and Aggressive Non-Hodgkin's Lymphoma*
  - *Abstract # 1745: BGB-3111 in Combination with Obinutuzumab in Patients with Chronic Lymphocytic Leukemia and Follicular Lymphoma*
  - *Abstract # 4057: Safety and Activity of the Highly Specific BTK Inhibitor BGB-3111 in Combination with the PD-1 Inhibitor BGB-A317 in Patients with B-Cell Lymphoid Malignancies*
- Zanubrutinib Development Program, Dr. Eric Hedrick, Chief Advisor, BeiGene
- Q&A with Dr. Christian Buske, Dr. Judith Trotman, Dr. Constantine Tam, Dr. Jane Huang, and Dr. Eric Hedrick

Zanubrutinib: Hypothesis, Results to Date, and Current Development Plans

- Pre-clinical data suggested pharmacological advantages over ibrutinib
  - Hypothesis - Selectivity and exposure advantages may afford qualitative advantages, relative to ibrutinib, in disease response, as well as improvement in regard to safety *and* tolerability
- Clinical experience to date supports our hypothesis
  - Strong suggestion of better response depth in WM
  - Favorable response rate and durability and in WM, CLL (and across different histologies)
  - Paucity of treatment discontinuations for adverse events
  - Encouraging evolving data on rate of events of particular interest for BTKi therapy: atrial fibrillation, serious hemorrhage, and severe diarrhea
- Broad development program designed to establish zanubrutinib as a best-in-class BTK inhibitor
  - Head-to-head Phase 3 trial versus ibrutinib in WM ongoing, head-to-head Phase 3 in relapsed/refractory CLL planned

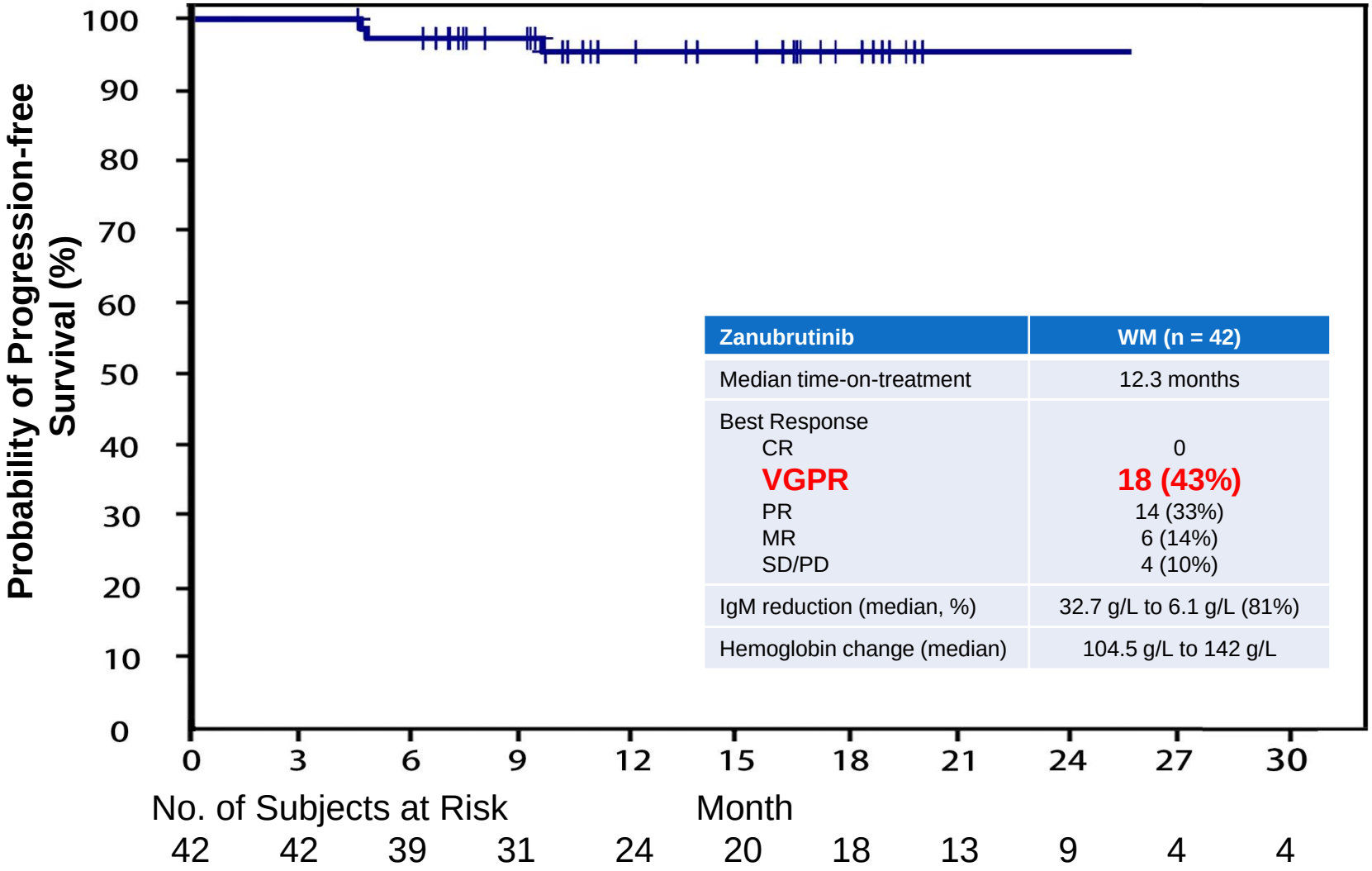
Ibrutinib in WM



Ibrutinib	WM (n=63)
Median time-on-treatment	19.1 months
Best Response (n = 63)	
CR	0
VGPR	**10 (16%)**
PR	36 (57%)
MR	11 (17%)
SD/PD	6 (10%)
IgM reduction (median, %)	35.2 g/L to 8.8 g/L (75%)
Hemoglobin change (median)	105 g/L to 138 g/L

Source: Treon *et al.*, NEJM, 2015

Zanubrutinib in WM



Zanubrutinib	WM (n = 42)
Median time-on-treatment	12.3 months
Best Response	
CR	0
VGPR	**18 (43%)**
PR	14 (33%)
MR	6 (14%)
SD/PD	4 (10%)
IgM reduction (median, %)	32.7 g/L to 6.1 g/L (81%)
Hemoglobin change (median)	104.5 g/L to 142 g/L

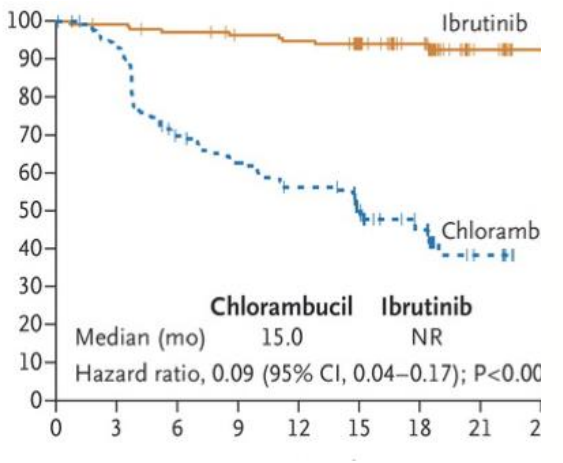
BeiGene

Source: Trotman *et al.* 14-ICML (abstract 059) presentation based on data cutoff of Mar 31, 2017

Ibrutinib in CLL

Treatment-Naive

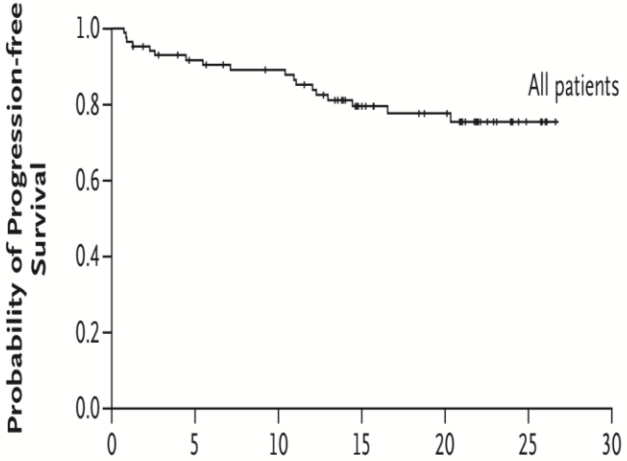
Burger JA et al. NEJM 2015



n = 136	
Median follow-up (months)	18.4
ORR	**117 (86%)**
CR	5 (4%)
PR	105 (55%)
PR-L	5 (4%)
SD	NR
PD	NR

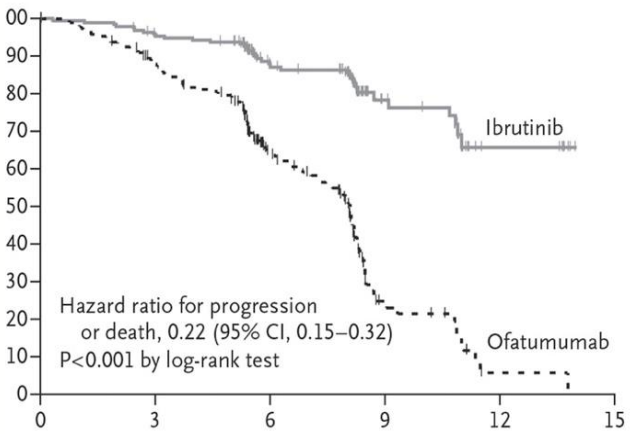
Relapsed/Refractory

Byrd JC et al. NEJM 2013



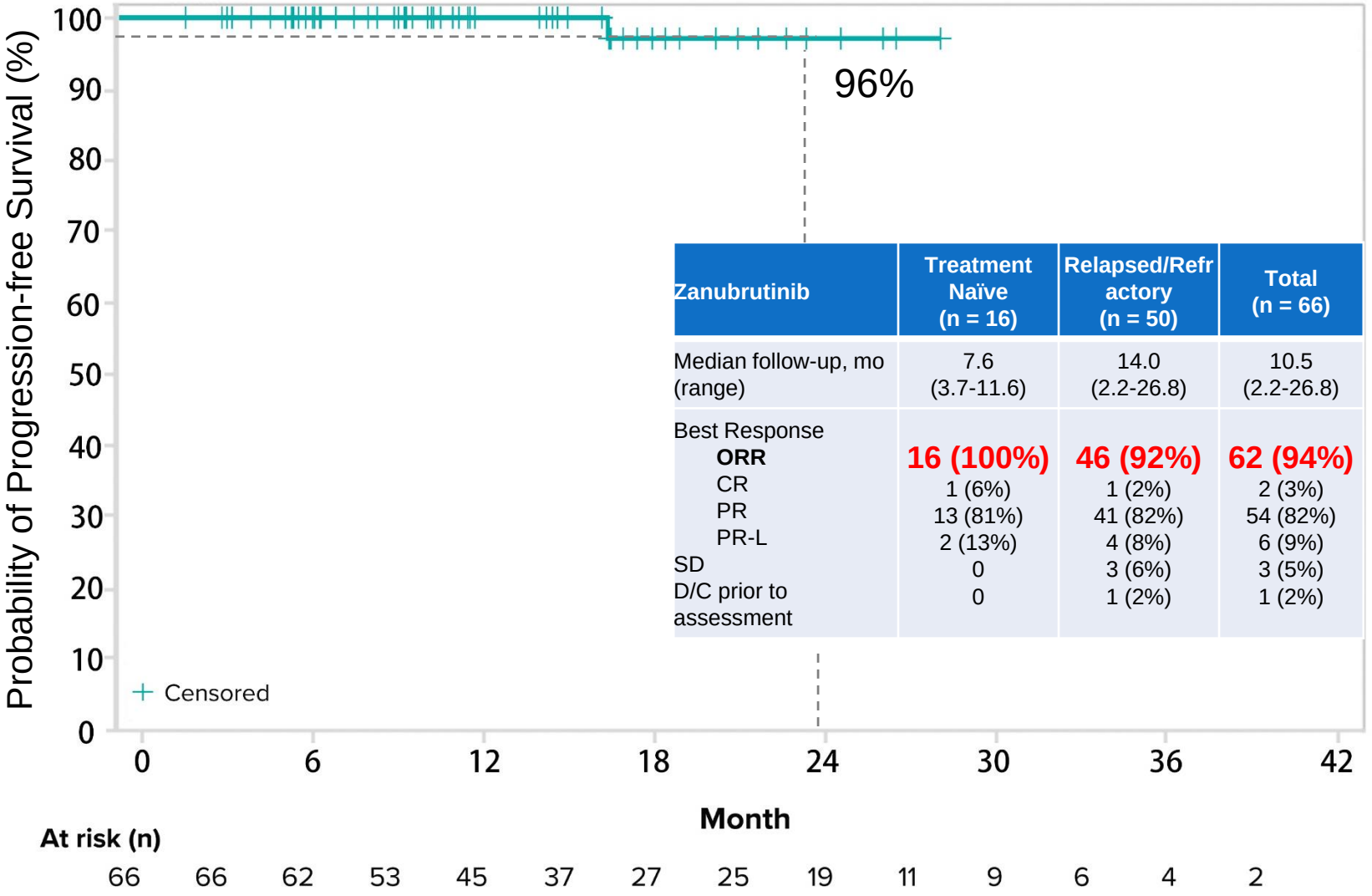
n=85	
Median follow-up (months)	20.9
ORR	**75 (88%)**
CR	2 (2%)
PR	58 (68%)
PR-L	15 (18%)
SD	NR
PD	NR

Byrd JC et al. NEJM 2014



n=195	
Median follow-up (months)	9.4
ORR	**117 (83%)***
CR	4 (2%)
PR	132 (68%)
PR-L	40 (4%)
SD	22 (11%)
PD	2 (1%)

Zanubrutinib in All CLL Patients: Response Rate and PFS



Zanubrutinib	Treatment Naïve (n = 16)	Relapsed/Refractory (n = 50)	Total (n = 66)
Median follow-up, mo (range)	7.6 (3.7-11.6)	14.0 (2.2-26.8)	10.5 (2.2-26.8)
Best Response			
ORR	**16 (100%)**	**46 (92%)**	**62 (94%)**
CR	1 (6%)	1 (2%)	2 (3%)
PR	13 (81%)	41 (82%)	54 (82%)
PR-L	2 (13%)	4 (8%)	6 (9%)
SD	0	3 (6%)	3 (5%)
D/C prior to assessment	0	1 (2%)	1 (2%)

Source: Seymour *et al.* 14-ICML 2017 (abstract 237) poster based on data cutoff of Mar 31, 2017

Activities of Zanubrutinib + Obinutuzumab Combination in FL

	Zanubrutinib & Obinutuzumab	Zanubrutinib	Ibrutinib[1]	Obinutuzumab[2]	Idelalisib[3]
n	**21**	17	110	40	72
Population	**Prior alkylator and CD20, mixed Rituxan-sensitive and –refractory**	Median 2 prior lines of therapy, range 1-8	Prior alkylator and CD20, last response <12 months	Mixed Rituxan-sensitive and -refractory	Alkylator and Rituxan-refractory relapse
Follow-up (med)	**8.6 mo**	7.8 mo	27.7 mo	33.7 mo	NR
ORR	**76%**	41%	21%	50%	54%
CR	**38%**	18%	11%	18%	6%

Notes: ^ cross-trial comparison
Source: Tam *et al.*, 14-ICML, 1 Gopal, et al ASH 2016; 2 Salles, et al J Clin Oncol 2013; 3 Gopal, et al N Engl J Med 2014

Ibrutinib: Frequency of Treatment Discontinuation in CLL

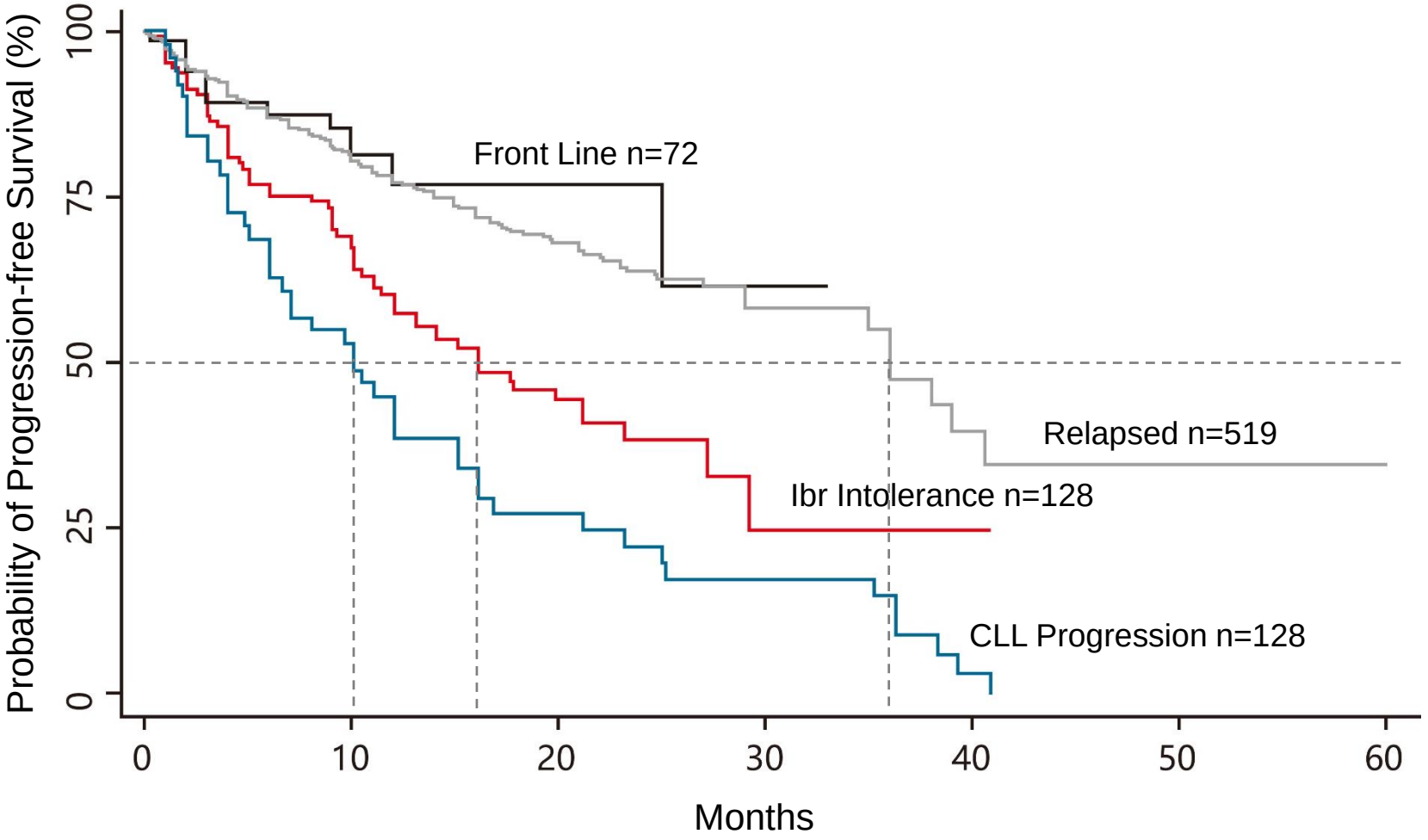
CLL	Treatment-Naïve (n=80)	Relapsed/ Refractory (n=536)
Median Follow up	14.5 months	
Total Treatment D/C	**19 (24%)**	**231 (43%)**
Toxicity/ Tolerability	**12 (15%)**	**117 (22%)**
CLL Progression	**3 (4%)**	**49 (9%)**
Transformation (RT or HD)	**0**	**10 (2%)**
Death Unrelated to Treatment	1 (1%)	28 (5%)
Physician or Patient Decision	2 (2%)	15 (3%)
Transplant	0	8 (1.5%)
Financial Concerns	0	1 (0.2%)
Secondary Malignancy	1 (1%)	2 (0.5%)

Approximately one-third of patients are off-treatment by 1.5 years. More frequently for toxicity or tolerability issues than disease progression or transformation

BeiGene

Source: Mato ASH 2016

Ibrutinib: Treatment Discontinuation (All Causes) Compromises PFS in CLL



Source: Mato, Blood, 2016

Zanubrutinib: Frequency of Treatment Discontinuation

CLL	Treatment-Naïve (n=18)	Relapsed/ Refractory (n=51)
Median Follow up	10.3 months	
Total Treatment D/C	**0**	**2 (4%)**
Toxicity/ Tolerability	**0 (0%)**	**1 (2%)**
CLL Progression	**0 (0%)**	**0 (0%)**
Transformation (RT or HD)	**0**	**1 (2%)**

Seymour, ICML 2017

Zanubrutinib Safety: Adverse Events of Interest
Experience in 641 Patients

AE of Interest (All Causes)	Zanubrutinib (Including Pt Enrolled in Combo Studies)
Patient Number	N = 641
Mean Exposure Time	7.7 mo
Atrial Fibrillation	**1.7%**
Serious Hemorrhage	**1.9%**

AE of Interest (All Causes)	Zanubrutinib (Single Agent Only)
Patient Number	N = 424
Mean Exposure Time	8.1 mo
Diarrhea (All Gr)	**14.2%**
Diarrhea (Gr 3-5)	**0.7%**

Source: pooled safety analysis of ongoing zanubrutinib clinical trials, data cut-off September 2017, n=641

Zanubrutinib Clinical Development Program

Expanding Breadth of Indications and Best-in-Class Opportunities

BGB-3111-302: Waldenströms Phase 3 Trial Design

Cohort 1: R/R or TN* WM with *MYD88* mutation

*TN must be unsuitable for standard chemoimmunotherapy

MYD88^{MUT} WM patients
(N=150)

→ R 1:1

Arm A
Zanubrutinib
160 mg BID until PD
(n = 75)

Arm B
Ibrutinib
420mg QD until PD
(n = 75)

Stratification factors:
- *CXCR4* mutational status (*CXCR4^{WHIM}* vs *CXCR4^{WT}*)
- No. of prior lines of therapy (0 vs 1-3 vs > 3)

Primary Endpoint: CR/VGPR rate

Secondary Endpoint: MRR (≥PR), PFS, duration of response, symptom resolution

Cohort 2: WM with wild type MYD88; present in ~10% of enrolled patients

MYD88^{WT} WM patients
(N = 15-20)

→

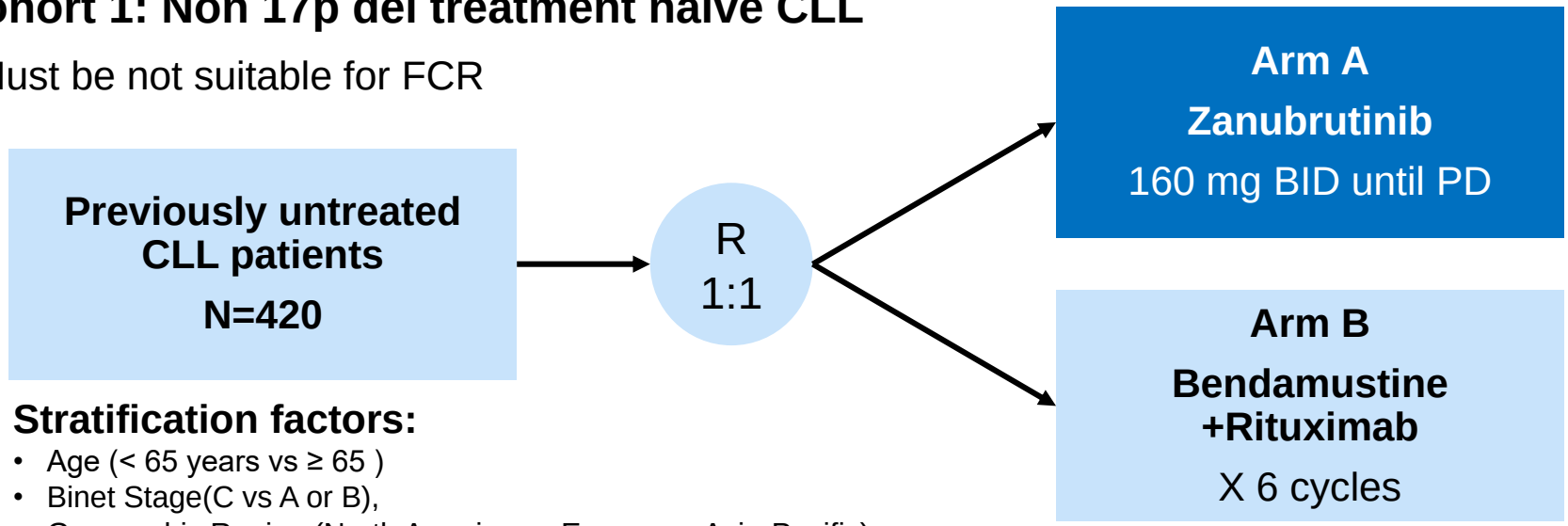
Arm C
Zanubrutinib
160 mg BID until PD

This study is registered at ClinicalTrials.gov (NCT03053440)

BGB-3111-304: CLL Phase 3 Trial Design

Cohort 1: Non 17p del treatment naïve CLL

*Must be not suitable for FCR



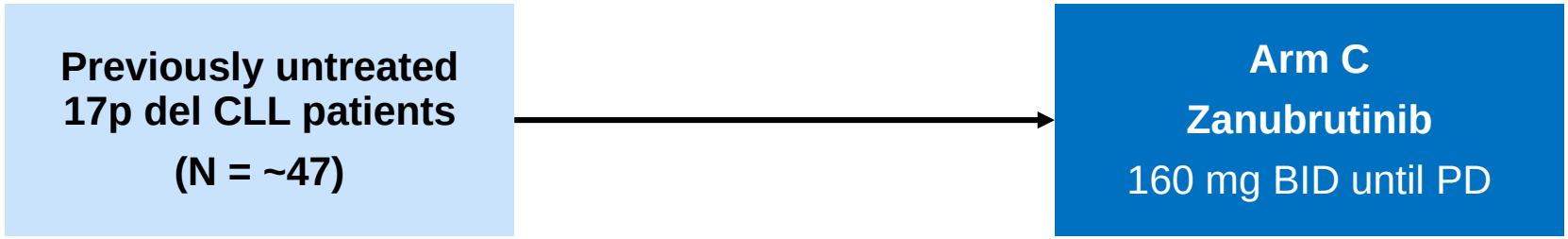
Stratification factors:

- Age (< 65 years vs ≥ 65)
- Binet Stage(C vs A or B),
- Geographic Region (North America vs Europe vs Asia-Pacific)
- IgHV mutational status (Mutated vs Unmutated)

Primary Endpoint: PFS

Secondary Endpoint: ORR, duration of response, OS, patient-reported outcomes

Cohort 2: 17p del treatment naïve CLL

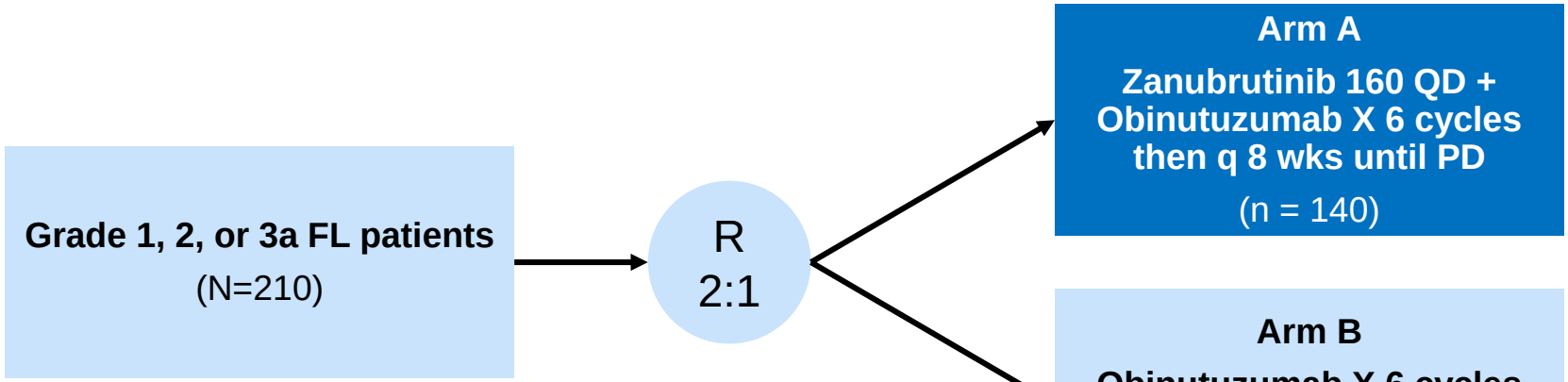


This study is registered at ClinicalTrials.gov (NCT03336333)

BGB-3111-212: Relapsed FL Phase 2 Trial Design

Relapsed/Refractory FL (Received ≥2 prior treatments*)

*Must have received prior treatment with rituximab and an alkylator; relapsed <12 months from end of last treatment OR Refractory to last treatment (no CR, no PR)



Stratification factors:

- No. of prior lines of therapy (2-3 vs > 3)
- Rituximab refractory status (yes/no)

Primary Endpoint: ORR
Secondary Endpoint: duration of responses, PFS, OS, time-to-response

Option to add zanubrutinib after 12 months if no response OR at PD

This study is registered at ClinicalTrials.gov (NCT02569476)

Planned Phase 3 Trial of Zanubrutinib vs Ibrutinib in R/R CLL

- A Phase 3 comparison of zanubrutinib versus ibrutinib in relapsed or refractory CLL is being planned to initiate in 2018
- Intent is to study a broad and representative relapsed or refractory population
- Design will be detailed at the time of trial initiation

Zanubrutinib Clinical Development Plan

	Global Monotherapy	Global Combination	China
Current *2014-2017*	Phase 1 **CLL, WM, MCL, DLBCL, FL, MZL, HCL, RT**	Phase 1b **3111 + GA101** **CLL, FL, DLBCL, NHL**	Phase 1 **B-cell Malignancies**
	Phase 3 **3111 vs ibrutinib** **WM**	Phase 1b **3111 + A317** **FL, DLBCL+,** ***1° CNS lymphoma***	Phase 2 **Monotherapy R/R DLBCL**
	Phase 3 **3111 vs BR[1]** **1L CLL/SLL**	Phase 2 **3111+G vs G[2]** **R/R FL**	Phase 2 **Mono in R/R MCL**
			Phase 2 **Mono in R/R CLL/SLL**
			Phase 2 **Mono in R/R WM**
Currently Planned *2017-2021*		Phase 3 **3111 vs. ibrutinib** **2L CLL/SLL**	Phase 1b **3111 + rituximab**
		Phase 3 **Confirmatory Trial in FL**	

Proof-of-Concept Trial

Pivotal Trial

Key: [1] BR = Bendamustine + rituxumab; [2] G = Gazyva (obinutuzumab)

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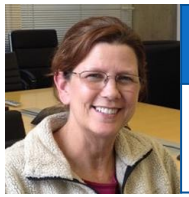

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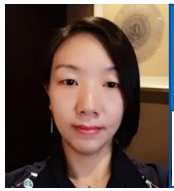

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Clinical Pipeline: Lead Assets in Global Phase 3

Additional Pivotal Programs Expected to Start in Q1 2018

China Global

Program (Molecular Target)	Commercial Rights	Pre-clinical	Dose Escalation	Dose Expansion*		Pivotal**	
			Phase 1a	Phase 1b	Phase 2	Phase 2	Phase 3
Zanubrutinib *(BTK)*	Worldwide		*Waldenstrom's macroglobulinemia (WM)*				
			Treatment-naïve chronic lymphocytic leukemia (CLL)				
			B-cell malignancies				
			Relapsed/refractory (R/R) mantle cell lymphoma				
			R/R CLL				
			WM				
			R/R diffuse large B-cell lymphoma (DLBCL)				
			B-cell malignancies				
Tislelizumab *(PD-1)*	Worldwide (Heme Malignancies); Asia ex-Japan (Solid Tumors)[1]		*Solid tumors*				
			2/3 L non-small cell lung cancer				
			*1 L Hepatocellular carcinoma (HCC)****				
			R/R Hodgkin's lymphoma				
			2L+ urothelial carcinoma				
			Solid tumors				

- **In total, over 2,000 patients and healthy adults[2] enrolled across four programs, including combination trials**

*Some indications will not require a non-pivotal Phase 2 clinical trial prior to beginning pivotal Phase 2 or 3 clinical trials.
Confirmatory clinical trials post approval are required for accelerated approvals. * Plan to initiate

[1] Celgene has the rights to develop and commercialize tislelizumab in solid tumors in the United States, European Union, Japan and the rest-of-world outside of Asia. [2] As of November 20, 2017.

Clinical Pipeline: Lead Assets in Global Phase 3

Additional Pivotal Programs Expected to Start in Q1 2018

China Global

Program *(Molecular Target)*	Commercial Rights	Pre-clinical	Dose Escalation	Dose Expansion*		Pivotal**	
			Phase 1a	Phase 1b	Phase 2	Phase 2	Phase 3
Pamiparib *(PARP)*	Worldwide[1]		*Solid tumors*				
			Solid tumors				
Lifirafenib *(RAF Dimer)*	Worldwide[1]		*B-RAF- or K-RAS/N-RAS-mutated solid tumors*				
			B-RAF- or K-RAS/N-RAS-mutated solid tumors				

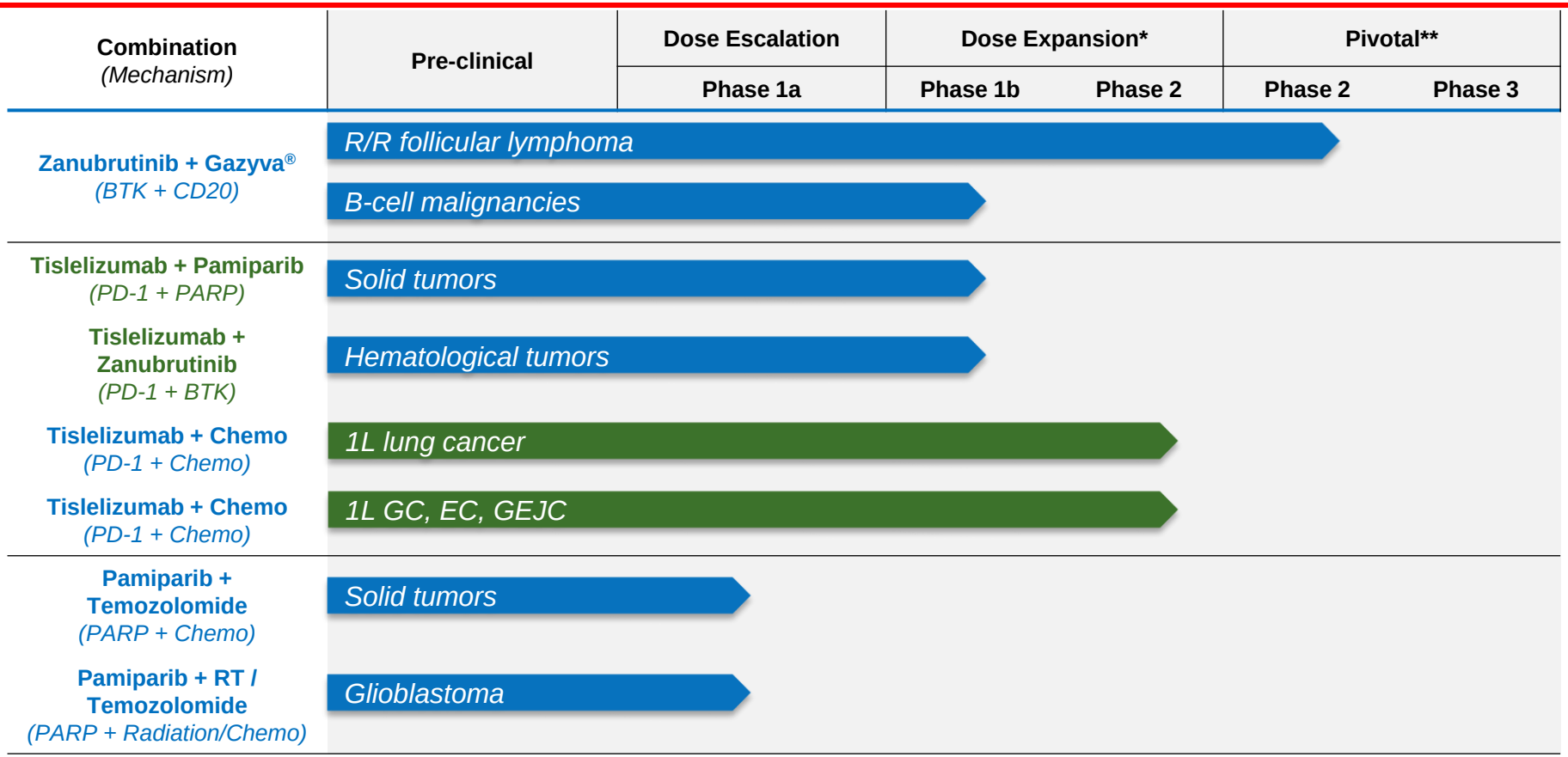
- **In total, over 2,000 patients and healthy adults[2] enrolled across four programs, including combination trials**

*Some indications will not require a non-pivotal Phase 2 clinical trial prior to beginning pivotal Phase 2 or 3 clinical trials.
**Confirmatory clinical trials post approval are required for accelerated approvals.
[1] Limited collaboration with Merck KGaA [3] As of November 20, 2017.

Combinations in Development

Broad Internal Portfolio Provides Advantages in Combination Therapy

China Global



GC-gastric cancer, EC-esophageal cancer, GEJC-gastroesophageal junction cancer

*Some indications will not require a non-pivotal Phase 2 clinical trial prior to beginning pivotal Phase 2 or 3 clinical trials.
**Confirmatory clinical trials post approval are required for accelerated approvals.
Celgene has the rights to develop and commercialize tislelizumab in solid tumors in the United States, European Union, Japan and the rest-of-world outside of Asia.

Agenda

- Welcome and Introduction, John Oyler, CEO and Dr. Jane Huang, CMO for Hematology, BeiGene
- ASH 2017 Data Review by Dr. Constantine Tam:
  - *Abstract # 152: Safety and Activity of the Highly Specific BTK Inhibitor BGB-3111 in Patients with Indolent and Aggressive Non-Hodgkin's Lymphoma*
  - *Abstract # 1745: BGB-3111 in Combination with Obinutuzumab in Patients with Chronic Lymphocytic Leukemia and Follicular Lymphoma*
  - *Abstract # 4057: Safety and Activity of the Highly Specific BTK Inhibitor BGB-3111 in Combination with the PD-1 Inhibitor BGB-A317 in Patients with B-Cell Lymphoid Malignancies*
- Zanubrutinib Development Program, Dr. Eric Hedrick, Chief Advisor, BeiGene
- Q&A with Dr. Christian Buske, Dr. Judith Trotman, Dr. Constantine Tam, Dr. Jane Huang, and Dr. Eric Hedrick

Dr. Christian Buske

Attending Physician, Professor and Medical Director, Comprehensive Cancer Center, Institute of Experimental Cancer Research, University Hospital Ulm, Germany

- President Elect, German Lymphoma Alliance
- Steering Committee German Low Grade Study Group
- Coordinator ‘European Consortium for Waldenstrom’s Macroglobulinemia
- Prior posts at the University Hospital Gottingen, British Columbia Cancer Agency, Vancouver and University Hospital Grosshadern, Munich
- Recipient of the Young Investigator Award International Society for Experimental Hematology
- Published in leading journals including Nature Medicine, Cell Stem Cell, Cancer Cell, Blood, Leukemia

Dr. Judith Trotman

Attending Physician, Associate Professor and Director, Clinical Research Unit, The University of Sydney and Concord Hospital, Sydney, Australia

- Chair of the Low Grade Lymphoma Committee of the Australian Leukaemia and Lymphoma Group
- Author of international guideline of staging and response assessment of lymphoma
- Lead author of paper that demonstrated the predictive power of PET-CT response assessment after first-line therapy in PRIMA and GALLIUM
- Principal Investigator for two global studies in lymphoma
- Published in leading journals including NEJM, Blood, JCO and The Lancet Haematology

Q&A

Dr. Christian Buske
Dr. Judith Trotman
Dr. Constantine Tam

Dr. Jane Huang, BeiGene
Dr. Eric Hedrick, BeiGene