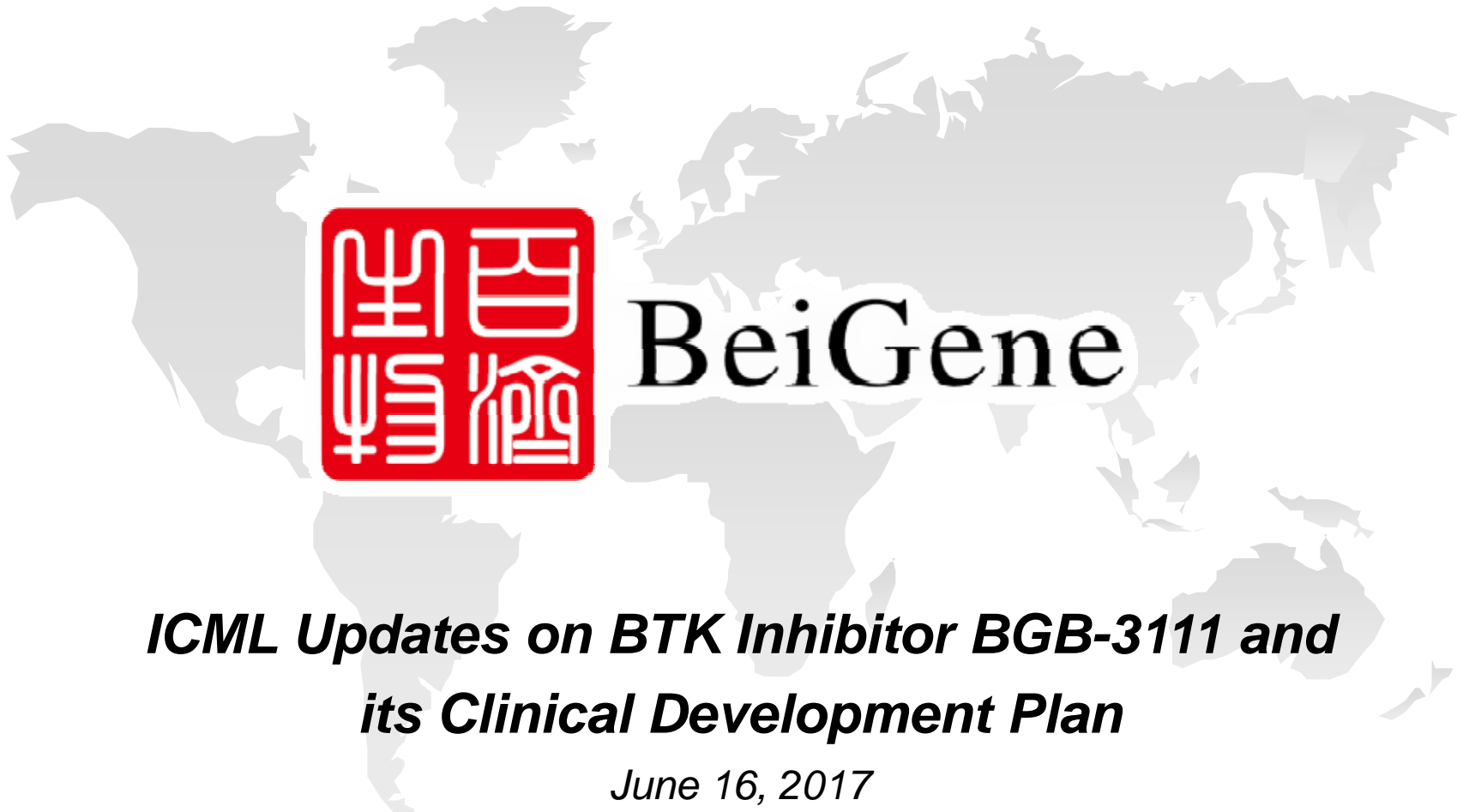


BeiGene



***ICML Updates on BTK Inhibitor BGB-3111 and  
its Clinical Development Plan***

*June 16, 2017*

# Forward Looking Statements

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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.

# Agenda

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- **Pipeline Overview and Summary**

- **14-ICML Presentations**

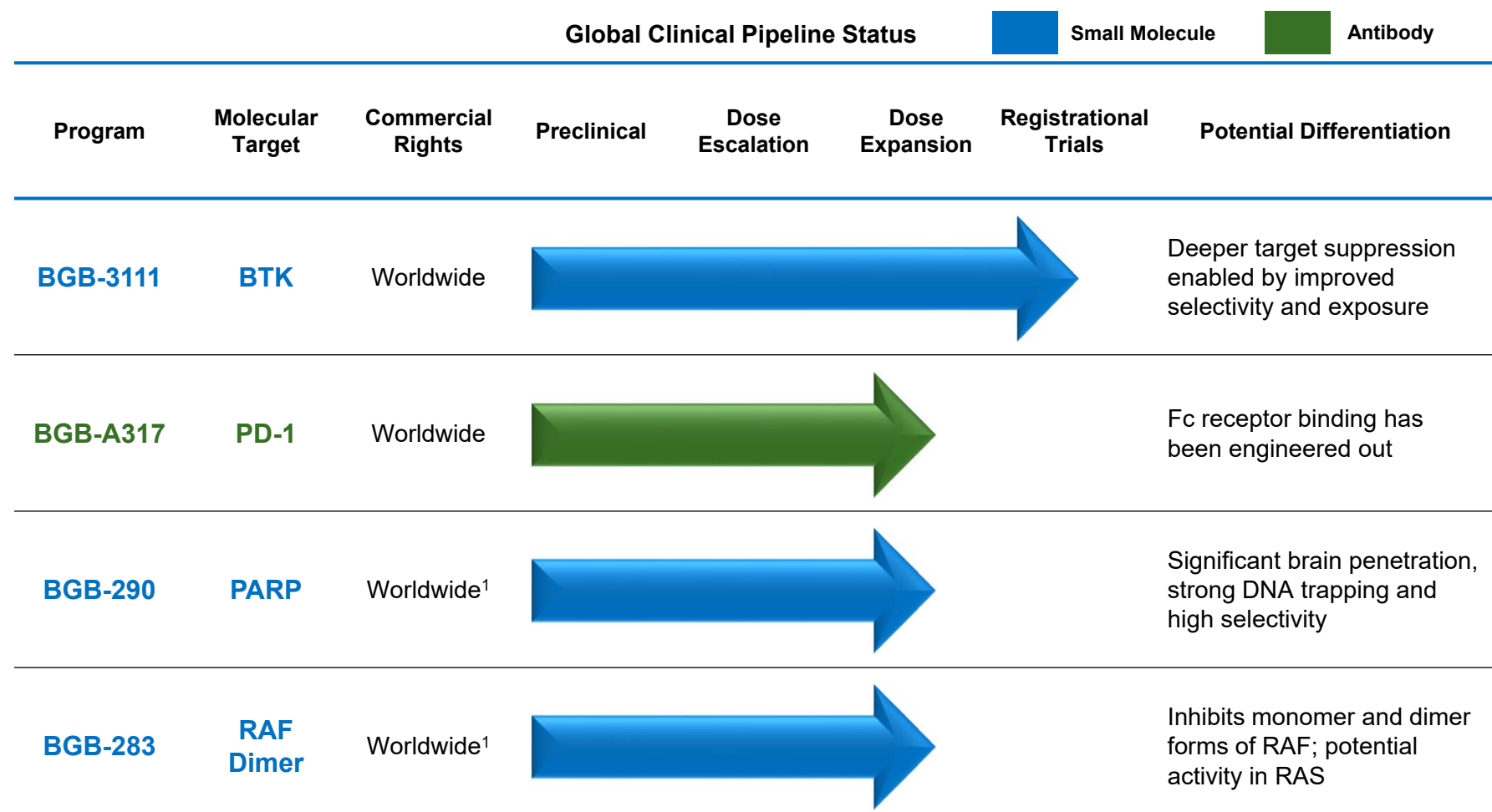
- *Abstract # 059*: Bruton's Tyrosine Kinase (BTK) Inhibitor BGB-3111 Demonstrates High Very Good Partial Response (VGPR) Rate in Patients with Waldenström Macroglobulinemia (WM)
- *Abstract # 237*: High Overall Response Rate With the BTK Inhibitor BGB-3111 in Patients With Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma: an Update on Safety and Activity
- *Abstract # 103*: Safety and Activity of the Highly Specific BTK Inhibitor, BGB-3111 Plus Obinutuzumab in Patients with Follicular Lymphoma and Chronic Lymphocytic Leukemia

- **BGB-3111 Clinical Development Plan**

- **Q&A**

# BeiGene Pipeline: Lead Asset in Global Phase III

Additional Global Pivotal Programs Expected to Start in 2017

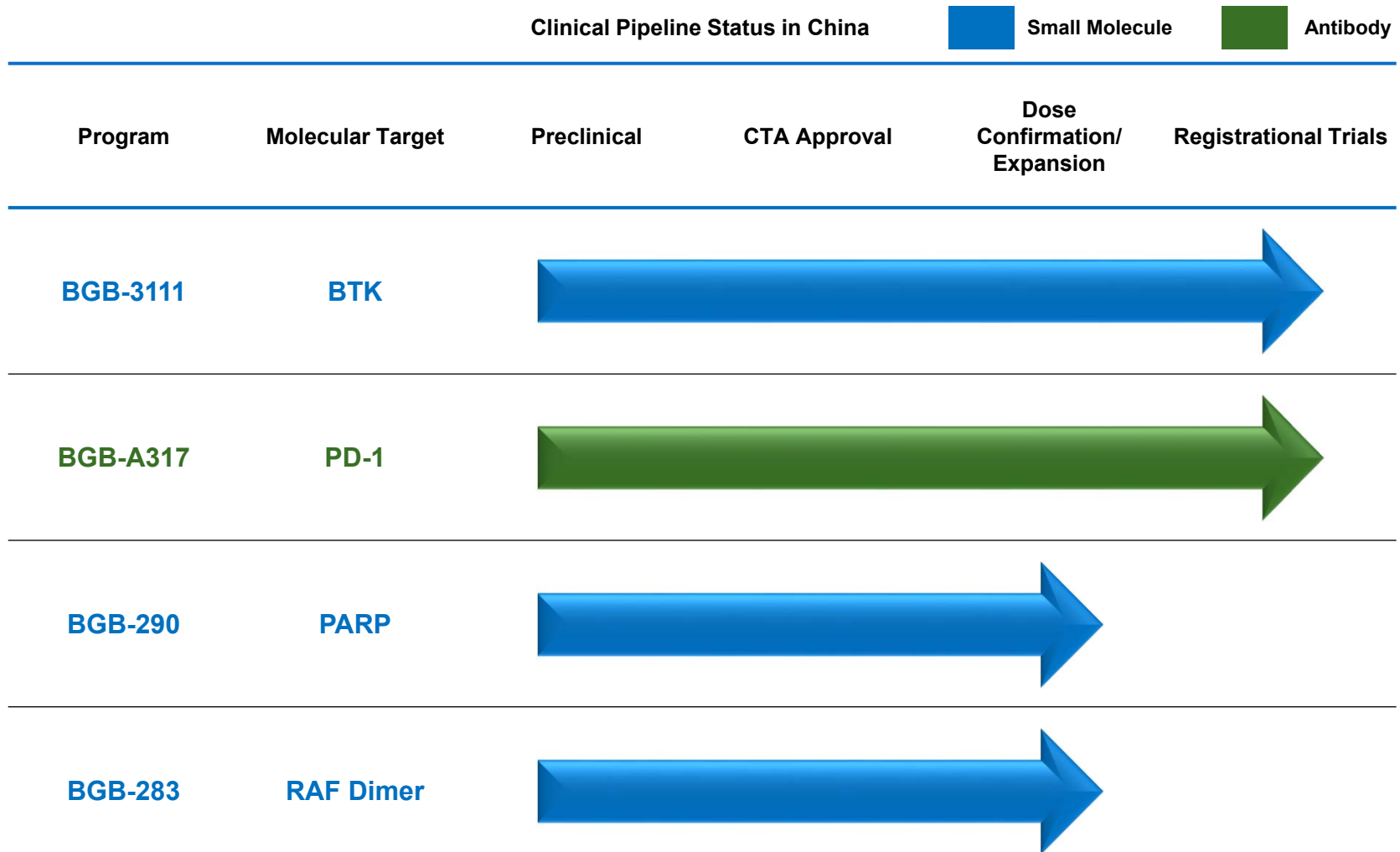


■ In total, over 1,200 patients and healthy adults<sup>2</sup> enrolled across 4 programs including combination trials






# Two Assets in Pivotal Trials in China

## Additional Pivotal Trials Expected to Start in China in 2017



# Combinations in Development

## Broad Internal Portfolio Provides Advantages in Combination Therapy

Combination	Mechanism of Action	Planning for Combination	Dose Escalation	Dose Expansion	Registrational Trials	Differentiation
BGB-3111 + Gazyva®	BTK + CD20					No interference with CD20 antibody activity due to BTK selectivity
BGB-A317 + BGB-290	PD-1 + PARP					Good tolerability due to PARP selectivity
BGB-A317 + BGB-3111	PD-1 + BTK					Good tolerability due to BTK selectivity

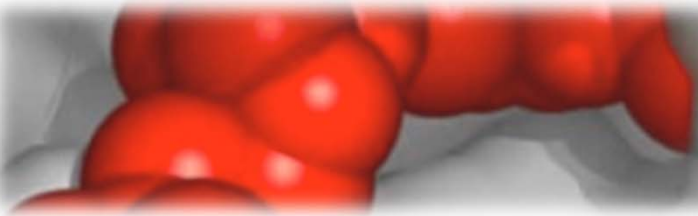
### Combination Potential

- We believe we have the only wholly owned PD-1 and BTK inhibitor combination in clinical testing
- We believe we are one of a small number of companies with internal combinations of PD-1 + PARP inhibitors
- Potential for RAF dimer / PD-1 inhibitor combination based on internal data
- Broad preclinical programs target multiple points in the immunity cycle

# ICML Update on BGB-3111 and Summary

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- **WM monotherapy data: improving VGPR rate (43% vs. 34% at ASH) in a larger number of patients (42 vs. 32 evaluable) further supports ongoing global head-to-head Phase III trial**
- **CLL monotherapy data: continued high ORR (94%) in a larger number of patients (66 vs 46 evaluable at ASH); CRs emerging despite relatively short follow-up; low discontinuation rate due to AE or progression**
  - **Initiating 1L CLL trial vs. BR to address the large population of previously untreated patients who are not eligible for intensive chemo-immunotherapy (FCR)**
- **Combination data with Gazyva: strong early signal in FL (high ORR and CR after a short follow-up) supports expedited development in FL where there is an unmet need as well as a large opportunity for which a BTK inhibitor has not been approved**
- **Continue to show excellent safety and tolerability profile; very low rate of discontinuation**
  - **Nearly 500 patients dosed in BGB-3111 clinical program**



BeiGene

# 14-ICML Presentations



## BGB-3111 Background

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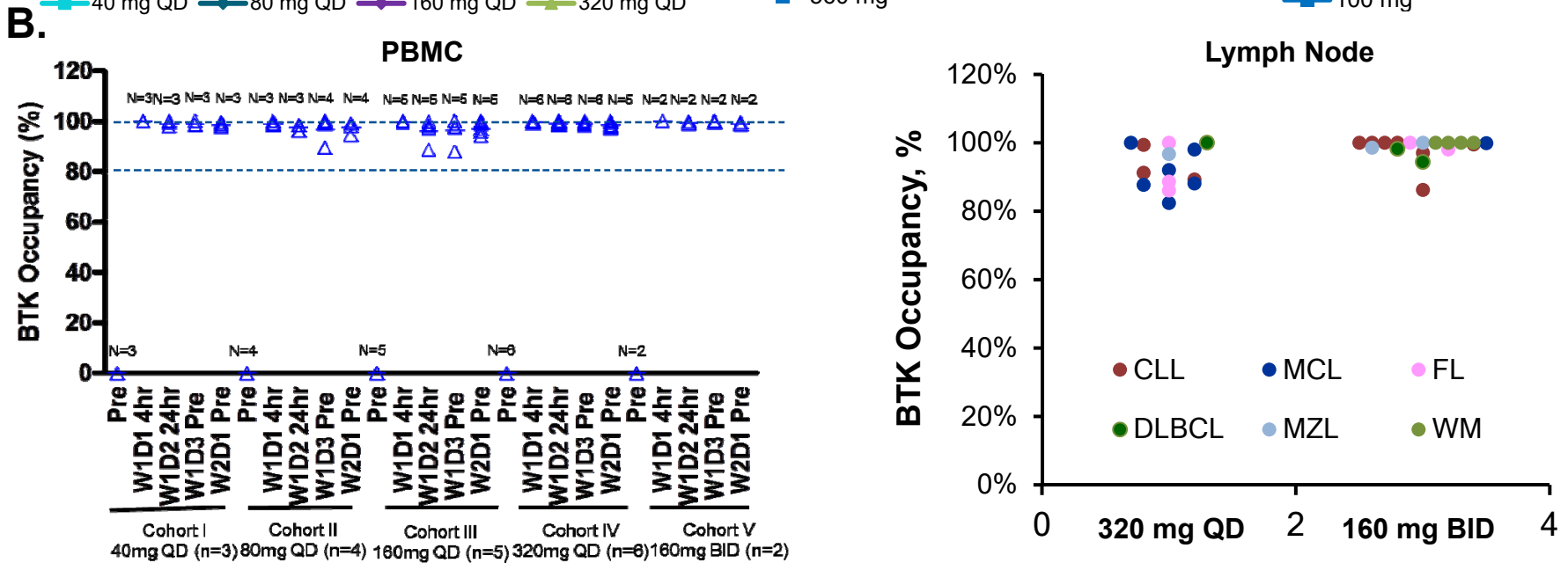
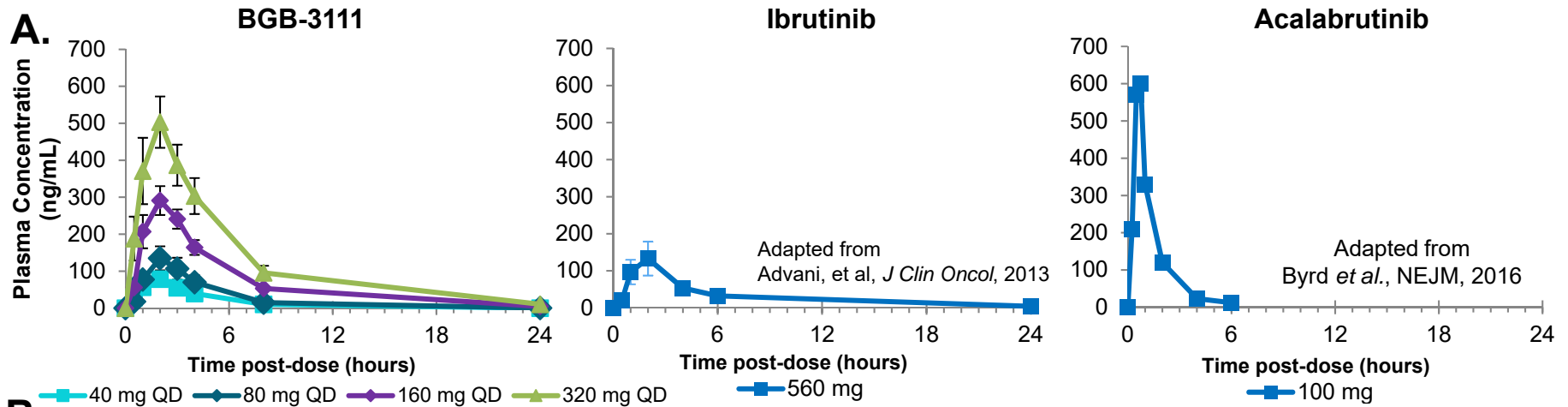
- Bruton's Tyrosine Kinase (BTK), is a critical signaling component of the B-cell receptor, and mediates proliferation, cellular homing, and stromal adhesion in a variety of B cell malignancies
- Ibrutinib, the first generation BTK inhibitor, is currently approved in the following diseases/ treatment settings:
  - CLL/SLL: Survival advantage over ofatumumab (relapsed/ refractory setting) and chlorambucil (treatment-naïve setting)
  - Waldenstrom's macroglobulinemia (WM): single-arm trial (n=63) with major RR 73%, VGPR 15%, 3-year EFS 69%
  - Mantle cell lymphoma and marginal zone lymphoma
- Ibrutinib remains under development, but not yet approved, in other B cell malignancy subtypes, including FL and DLBCL
- BGB-3111 is a potent and specific BTK inhibitor, designed to minimize off target inhibition of TEC- and EGFR-family kinases
  - Favorable pharmacokinetic properties designed to maximize plasma exposure and tissue-independent BTK occupancy

# BGB-3111: Kinase Selectivity Relative to Ibrutinib

Highly selective inhibition of BTK relative to similar tyrosine kinases

Targets	Assays	Ibrutinib IC <sub>50</sub> (nM)	BGB-3111 IC <sub>50</sub> (nM)	Ratio (BGB-3111: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	3,210	9.9
ITK	ITK Occupancy Cellular Assay	189	3,265	17
	p-PLC <sub>γ1</sub> Cellular Assay	77	3,433	45
	IL-2 Production Cellular Assay	260	2,536	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

# Pharmacokinetics of BGB-3111, Ibrutinib and Acalabrutinib<sup>^</sup> (Fig A) and BTK Occupancy for BGB-3111 in Peripheral Blood and Lymph Node (Fig B)



<sup>^</sup> Cross-trial comparison

<sup>1</sup>Tam CS, et al. *Blood*. 2015;126:832. <sup>2</sup>Advani RH, et al. *J Clin Oncol*. 2013;31:88-94. <sup>3</sup>Byrd, et al. *NEJM*. 2016;374:323-32. <sup>4</sup>Tam, et al. ASH 2016 (Abstracts 642 and 1216)

# Bruton's Tyrosine Kinase (BTK) Inhibitor BGB-3111 Demonstrates High Very Good Partial Response (VGPR) Rate in Patients with Waldenström Macroglobulinemia (WM)

Judith Trotman,<sup>1,2</sup> Stephen Opat,<sup>3,4</sup> Paula Marlton,<sup>5</sup> David Gottlieb,<sup>6</sup> David Simpson,<sup>7</sup> Gavin Cull,<sup>8</sup> David Ritchie,<sup>9,10</sup> Emma Verner,<sup>1</sup> Sumita Ratnasingam,<sup>3</sup> Mary Ann Anderson,<sup>10,11</sup> Peter Wood,<sup>5</sup> Lai Wang,<sup>12</sup> Ling Xue,<sup>12</sup> Eric Hedrick,<sup>12</sup> Jane Huang,<sup>12</sup> James Hilger,<sup>12</sup> John F. Seymour,<sup>9,10</sup> Andrew W. Roberts,<sup>10,11</sup> Constantine S. Tam<sup>9,10,13</sup>

<sup>1</sup>Concord Repatriation General Hospital, Concord, Australia; <sup>2</sup>University of Sydney, Concord, Australia; <sup>3</sup>Monash Health, Clayton, Victoria, Australia; <sup>4</sup>Monash University, Clayton, Victoria, Australia; <sup>5</sup>Princess Alexandra Hospital and University of Queensland, Brisbane, Australia; <sup>6</sup>Westmead Hospital, Westmead, Australia; <sup>7</sup>North Shore Hospital, Auckland, New Zealand; <sup>8</sup>Sir Charles Gairdner Hospital, Perth, Western Australia, Australia; <sup>9</sup>Peter MacCallum Cancer Center, East Melbourne, Victoria, Australia; <sup>10</sup>University of Melbourne, Parkville, Victoria, Australia; <sup>11</sup>Melbourne Health, Parkville, Victoria, Australia; <sup>12</sup>Beigene (Beijing) Company Ltd, Beijing, China and Emeryville, CA; <sup>13</sup>St Vincent's Hospital, Fitzroy, Victoria, Australia

## WM: Patient Characteristics

Characteristic	Total (N = 48)
Age, years, median (range)	66 (44-87)
ECOG Performance Status, n (%)	
0	14 (29)
1	34 (71)
Follow-up, months, median (range)	10.6 (1.4-30.5)
Prior Treatment Status, n (%)	
Treatment-naïve	10 (21)
Relapsed/refractory	38 (79)
Number of prior therapies, median (range)	1 (1-8)
Prior rituximab (% R/R pts)	28 (74%)
Genotype	
MYD88 <sup>L265P</sup> / CXCR4 <sup>WT</sup>	21 (43.8)
MYD88 <sup>L265P</sup> / CXCR4 <sup>WHIM</sup>	5 (10.4)
MYD88 <sup>WT</sup>	5 (10.4)
Unavailable	17 (35.4)

## WM: Most Frequent Adverse Events (> 10%) Independent of Causality (Safety Population: N = 48)

Adverse Event	All Grade		Grade 3-4	
	n (pts)	%	n (pts)	%
Petechiae/purpura/contusion	17	35%	0	0%
Upper respiratory tract infection	15	31%	0	0%
Constipation	12	25%	0	0%
Diarrhea	9	19%	1	2%
Epistaxis	9	19%	0	0%
Nausea	8	17%	0	0%
Cough	7	15%	0	0%
Anemia	7	15%	4	8%
Headache	7	15%	1	2%
Neutropenia	6	13%	4	8%
Rash	6	13%	0	0%

## WM: Overview of Adverse Events

Event	All Cause	
	n (pts)	%
Patients with at least one AE Grade $\geq 3$	20	42%
Patients with at least one SAE	18	38% <sup>†</sup>
Events leading to treatment discontinuation	3 <sup>‡</sup>	6%

<sup>†</sup> SAE pos. related to BGB-3111: haemothorax, atrial fib, colitis, febrile neutropenia, headache (all n=1)

<sup>‡</sup> Bronchiectasis, adenocarcinoma of pylori, and prostate adenocarcinoma (all n=1)

AE of Special Interest	All Grade		Grade 3-4	
	n (pts)	%	n (pts)	%
Diarrhea	9	19%	1	2%
Serious hemorrhage <sup>§</sup>	1	2%	1	2%
Atrial fibrillation	3	6%	0	0

<sup>§</sup>Def serious hemorrhage: grade  $\geq 3$ , or CNS hemorrhage of any grade.

## WM: Efficacy Summary (n = 42)

	Total
Median follow-up (range)	12.3 months (4.4-30.5)
Best Response (n = 42)	
CR	0
VGPR	18 (43%)
PR	14 (33%)
MR	6 (14%)
SD	4 (10%)
	90% ORR†
	76% MRR*
IgM reduction (median, %)	32.7 g/L to 6.1 g/L (81.3%)
Hemoglobin change (median)	104.5 g/L to 142 g/L
Lymphadenopathy reduction by CT (n, range)	45.5% (median) (16, 18.2%-81.4%)

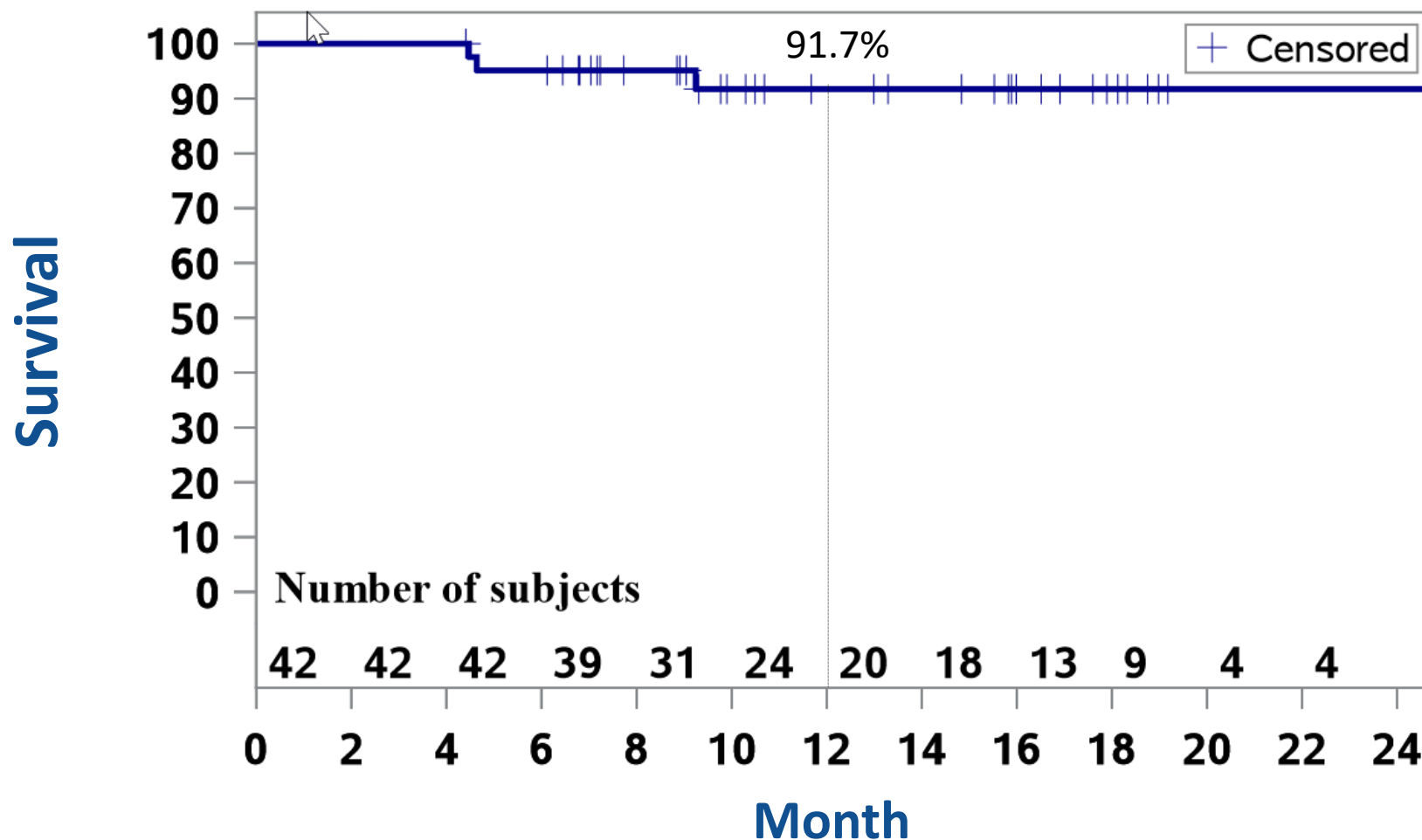
A VGPR and a PR (along with two minor responses) were observed in the 5 patients with MYD88 wild-type status.

† Overall response rate.

\* Major response rate.



# WM: Progression-Free Survival



4 patients have discontinued treatment to date, 1 with progressive disease and 3 with adverse events: exacerbation of bronchiectasis (n=1), prostate adenocarcinoma (n=1), and gastric carcinoma (n=1)

# Conclusions

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- BGB-3111, a highly selective oral BTK inhibitor achieves high plasma concentrations and complete BTK occupancy in blood and lymph nodes
- BGB-3111 is very well tolerated
  - To date: No treatment discontinuation due to BGB-3111 related toxicity
  - One AE-related death (due to pre-existing bronchiectasis, while in VGPR)
- Highly active in WM
  - Overall response rate 90%, with 43% VGPR

# High Overall Response Rate With the BTK Inhibitor BGB-3111 in Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: an Update on Safety and Activity

John F. Seymour<sup>1,2</sup>, Stephen Opat<sup>3,4</sup>, Gavin Cull<sup>5</sup>, Judith Trotman<sup>6,7</sup>, David Gottlieb<sup>8,9</sup>, David Simpson<sup>10</sup>, Paula Marlton<sup>11</sup>, Mary Ann Anderson<sup>1,12</sup>, Matthew Ku<sup>13</sup>, David S. Ritchie<sup>12,14,15</sup>, Sumita Ratnasingam<sup>16</sup>, Bradley Augustson<sup>17</sup>, Won Seog Kim<sup>18</sup>, Lai Wang<sup>19</sup>, Ling Xue<sup>19</sup>, James Hilger<sup>19</sup>, Jane Huang<sup>19</sup>, Eric Hedrick<sup>19</sup>, Andrew W. Roberts<sup>14,20,21</sup>, and Constantine S. Tam<sup>1,22,23</sup>

<sup>1</sup>University of Melbourne, Parkville, Australia; <sup>2</sup>Department of Haematology, Peter MacCallum Cancer Centre, Melbourne, Australia; <sup>3</sup>School of Clinical Sciences at Monash Health, Faculty of Medicine, Nursing & Dentistry, Monash University, Melbourne, Australia; <sup>4</sup>Monash Haematology, Monash Health, Clayton, Australia; <sup>5</sup>Department of Haematology, Sir Charles Gairdner Hospital, Perth, Australia; <sup>6</sup>Department of Hematology, Concord Repatriation General Hospital, Concord, New South Wales, Australia; <sup>7</sup>University of Sydney, Concord, Australia; <sup>8</sup>Blood and Marrow Transplant Service, Westmead Hospital, Sydney, Australia; <sup>9</sup>Sydney Medical School, University of Sydney, Sydney, Australia; <sup>10</sup>North Shore Hospital, Auckland, New Zealand; <sup>11</sup>Princess Alexandra Hospital, University of Queensland School of Medicine, Brisbane, Australia; <sup>12</sup>Department of Clinical Haematology and Bone Marrow Transplantation, The Royal Melbourne Hospital, Parkville, Australia; <sup>13</sup>Austin Health, Melbourne, Australia; <sup>14</sup>University of Melbourne, Melbourne, Australia; <sup>15</sup>Peter MacCallum Cancer Centre, Melbourne, Australia; <sup>16</sup>Department of Haematology, Monash Medical Centre, Monash Health, Melbourne, Australia; <sup>17</sup>Sir Charles Gairdner Hospital, Perth, Australia; <sup>18</sup>Division of Hematology-Oncology Samsung Medical Center, Seoul, Korea; <sup>19</sup>Beigene (Beijing) Company Ltd, Beijing, China; <sup>20</sup>Royal Melbourne Hospital, Melbourne, Australia; <sup>21</sup>Walter and Eliza Hall Institute of Medical Research, Royal Melbourne Hospital, Melbourne, Australia; <sup>22</sup>Peter MacCallum Cancer Centre, Melbourne, Australia; <sup>23</sup>St. Vincent's Hospital, Melbourne, Australia

## CLL/ SLL: Patient Characteristics

Characteristic	Total (N = 69)
Age, years, median (range)	68 (24-87)
ECOG Performance Status, (%)	
0	34 (49)
1	33 (48)
2	2 (3)
Follow-up, months, median (range)	10.3 (0.4-26.8)
Prior treatment status	
Treatment-naïve, n (%)	18 (26)
Relapsed/refractory, n (%)	51 (74)
Number of prior therapies, median (range)	2 (1-7)
Bulky disease*, n (%)	4 (6)
Molecular risk factors, n (%)	
del17p/p53mut (n = 51)	20 (39)
11q- (n = 44)	14 (32)
IgHV unmutated (n = 16)	11 (69)

ECOG, Eastern Cooperative Oncology Group; LN, lesion.

\* Any lymph node >10 cm in maximum diameter.

## CLL/SLL: Most Frequent Adverse Events (> 10%) Independent of Causality (N = 69)

Adverse Event	All Grade		Grade 3-4	
	n (pts)	% (N = 69)	n (pts)	% (N = 69)
Petechiae/purpura/contusion	32	46%	1	1%
Fatigue	20	29%	0	0%
Upper respiratory tract infection	19	28%	0	0%
Cough	16	23%	0	0%
Diarrhea	15	22%	0	0%
Headache	13	19%	0	0%
Hematuria	10	15%	0	0%
Nausea	9	13%	0	0%
Rash	9	13%	0	0%
Arthralgia	8	12%	0	0%
Muscle spasms	8	12%	0	0%
Urinary tract infection	8	12%	0	0%

pts, patients.

## CLL/SLL: Adverse Events of Special Interest

	SAE	n (pts)	% (N = 69)	Grade	Led to Treatment Discontinuation
Purpura (subcutaneous hemorrhage)	Y	1	1%	G3	0
Diarrhea	Y	1	1%	G2	0
Atrial fibrillation	N	1	1%	G2	0

- A total of 18 SAEs were experienced by 13 patients
  - SAE's not listed above (1 each) were also reported: CLL, delirium, febrile neutropenia, Invasive ductal breast carcinoma, lower respiratory tract infection, pleural effusion, renal colic, sepsis, splenectomy, splenomegaly, painful swelling in right neck , cardiac failure, coronary artery stenosis, ventricular extrasystole, pneumonia, and hemorrhoidal infection

# CLL/SLL: Events Leading to Permanent Treatment Discontinuation

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Event	n (pts)	% (N = 69)
Adverse event (Pleural effusion)	1*	1%
Hodgkin's Transformation	1	1%

\* Taken off study prior to first response assessment.

No patients have progressed with a C481S mutation

## CLL/SLL: Response

Response	Treatment Naive (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			
<b>ORR</b>	<b>16 (100%)</b>	<b>46 (92%)</b>	<b>62 (94%)</b>
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%)

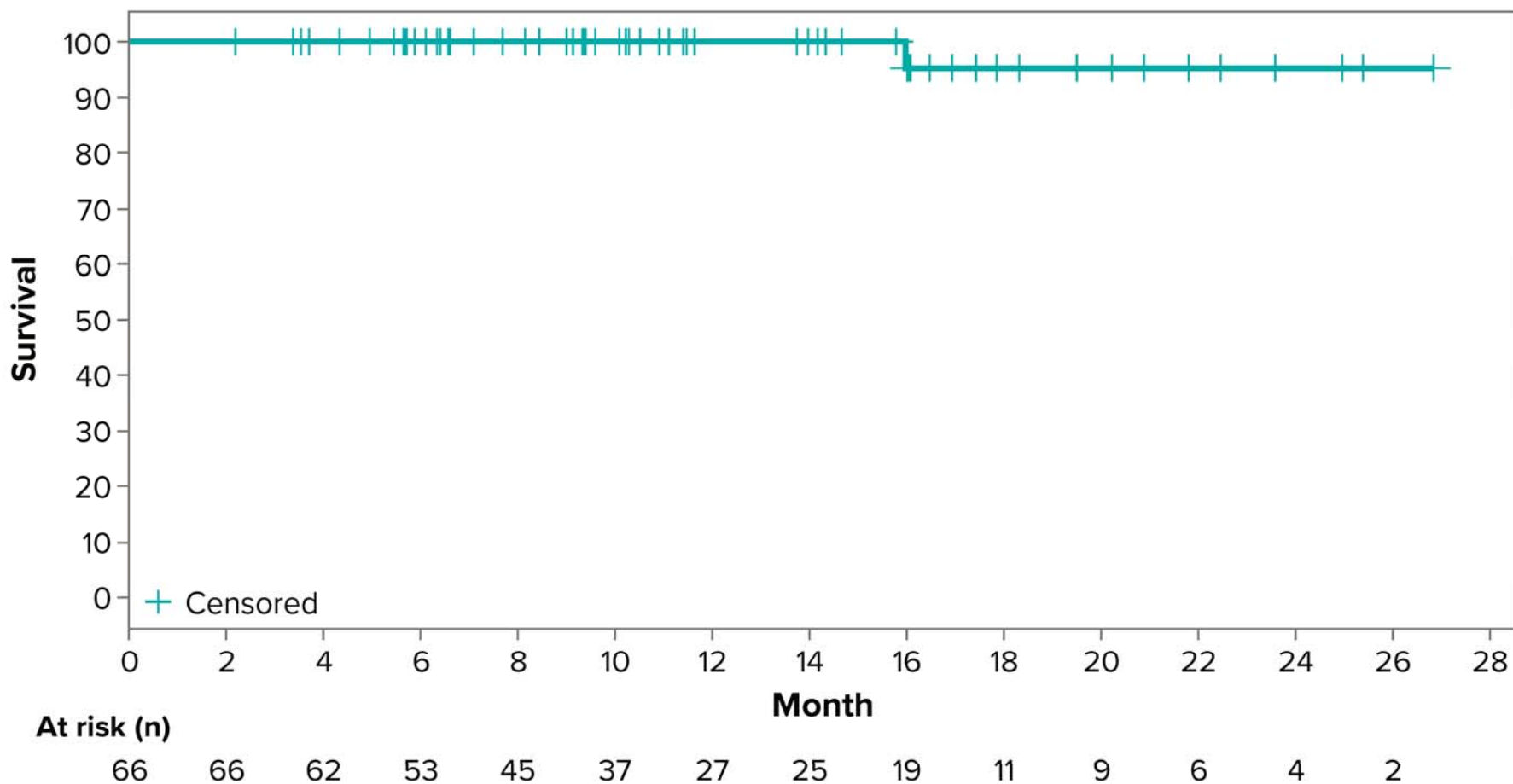
CR, complete response; D/C, discontinuation; ORR, overall response rate; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease.

- The ORR in patients with del17p and/or 11q- (n = 22) was 96%

\* Most patients in this series have yet to reach the protocol-defined marrow reassessment time point for CR assessment



# CLL/SLL: Progression-Free Survival



# Conclusions (CLL/ SLL Phase 1 Update)

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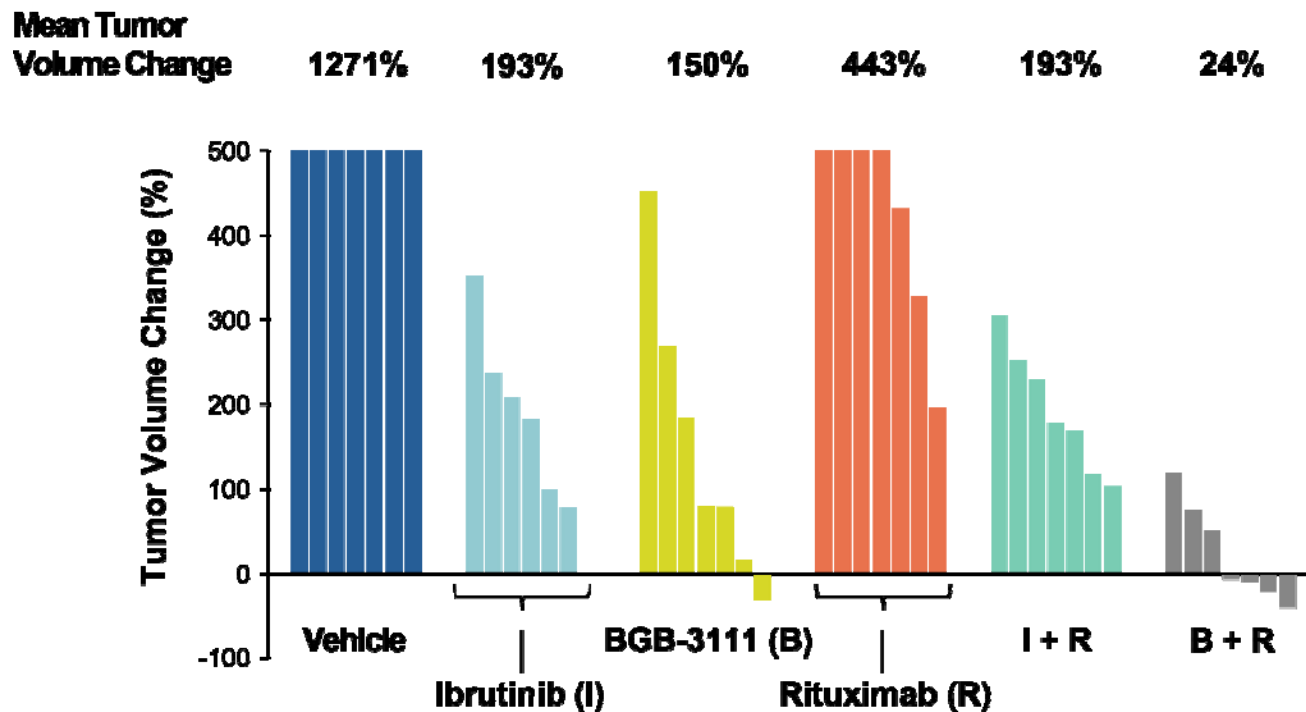
- BGB-3111 is highly active in CLL/SLL
  - Very high rate (94%) of durable response, independent of poor-risk features
  - With a median follow-up of 10.3 months, only one patient has experienced disease progression (Hodgkin's transformation)
- BGB-3111 is safe and well tolerated in CLL/SLL
  - Only one patient with adverse event-related treatment discontinuation
  - Very low incidence of serious diarrhea (1%), and serious bleeding (1%) and atrial fibrillation (1%)
- These updated results support Phase 3 trials of BGB-3111 in a broad population of CLL/SLL patients

# Safety and Activity of the Highly Specific BTK Inhibitor, BGB-3111 Plus Obinutuzumab in Patients with Follicular Lymphoma and Chronic Lymphocytic Leukemia

Constantine S. Tam,<sup>1,2,3</sup> Hang Quach,<sup>1,2</sup> Andrew Nicol,<sup>4</sup> Xavier Badoux,<sup>5</sup> Hannah Rose,<sup>6</sup> Henry Miles Prince,<sup>7</sup> Michael F. Leahy,<sup>8</sup> Richard Eek,<sup>9</sup> Nicholas Wickham,<sup>10</sup> Sushrut Patil,<sup>11</sup> Jane Huang,<sup>12</sup> Xiaoping Zhang,<sup>12</sup> Lai Wang,<sup>13</sup> Eric Hedrick,<sup>12</sup> William Novotny,<sup>12</sup> Ian Flinn<sup>14</sup>

<sup>1</sup>St. Vincent's Hospital, Melbourne, Australia; <sup>2</sup>University of Melbourne, Parkville, Australia; <sup>3</sup>Peter MacCallum Cancer Centre, Melbourne, Australia; <sup>4</sup>Brisbane Clinic for Lymphoma, Myeloma, and Leukaemia, Brisbane, Australia; <sup>5</sup>St. George Hospital, Australia; <sup>6</sup>University Hospital Geelong, Australia; <sup>7</sup>St. Frances Xavier Cabrini Hospital, Australia; <sup>8</sup>Royal Perth Hospital, Australia; <sup>9</sup>Border Medical Oncology Research Unit, Australia; <sup>10</sup>Ashford Cancer Centre Research, Australia; <sup>11</sup>The Alfred Hospital, Australia; <sup>12</sup>BeiGene USA, Cambridge, MA, USA; <sup>13</sup>BeiGene Company Ltd, Beijing, China; and <sup>14</sup>Tennessee Oncology, PLLC, Nashville, TN, USA.

# BGB-3111 Does Not Impair Rituximab-Induced ADCC



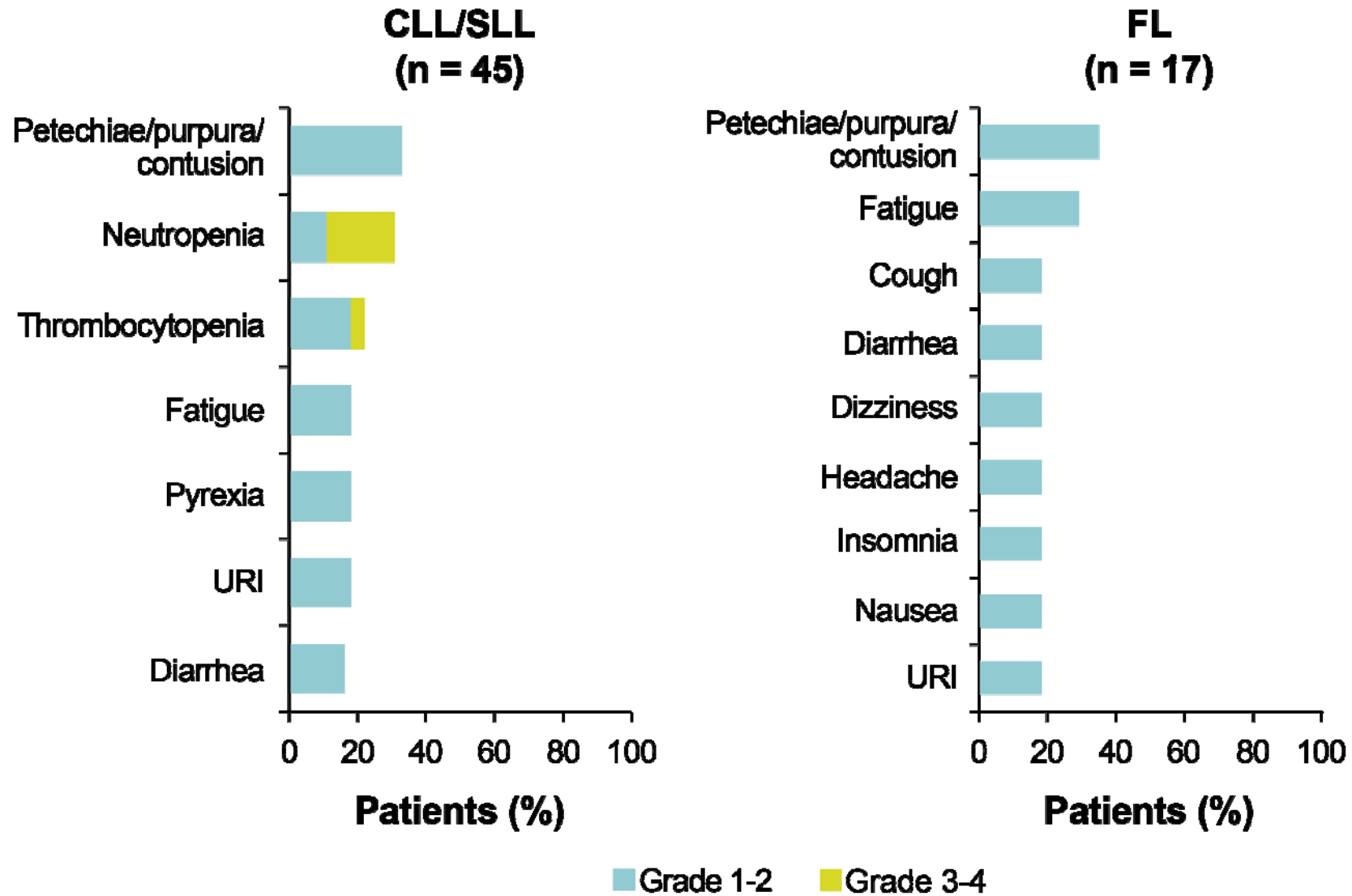
- Published preclinical data suggest that off-target effects of ibrutinib may be detrimental to CD20 mAb-induced ADCC and the activity of the combination
- In a human MCL xenograft model, the combination of BGB-3111 and CD20 antibody demonstrated improved anti-tumor activity as compared to monotherapies and combination of ibrutinib and CD20 antibody

# BGB-3111+Obinutuzumab: Patient and Disease Characteristics

Characteristic	CLL/SLL (n = 45)	FL (n = 17)
Age, years, median (range)	68 (38-82)	56 (41-86)
ECOG Performance Status, (%)		
0	19 (42.2)	14 (82.4)
1	25 (55.6)	2 (11.8)
2	1 (2.2)	1 (5.9)
Follow-up, months, median (range)	6.5 (0.5-14.0)	7.9 (0.1-14.2)
Prior Treatment Status		
Treatment-naïve, n (%)	20 (44.4)	0
Relapsed/refractory, n (%)	25 (55.6)	17 (100)
Number of prior therapies, median (range)	1 (1-4)	3 (1-7)
Bulky Disease*, n (%)	0	2 (11.8)
Molecular Risk Factors, n (%)		
del17p/p53mut (n = 37)	6 (16.2)	N/A
11q- (n = 37)	6 (16.2)	N/A
IGHV unmutated (n = 37)	19 (51.4)	N/A
Complex karyotype (n = 37)	7 (18.9)	N/A

\* Any lymph node >10 cm in maximum diameter.

# BGB-3111+Obinutuzumab: Most Common Adverse Events (Regardless of Causality)



## BGB-3111+Obintuzumab: Adverse Events

Event, n (%)	CLL/ SLL (n = 45)	FL (n = 17)
Patients with at least one AE Grade $\geq$ 3	19 (42.2)	4 (23.5)
Patients with at least one SAE	11 (24.4)	4 (23.5)
Events leading to treatment discontinuation	1 (2.2)*	0

\* Patient with a history of squamous cell carcinoma discontinued due to squamous cell carcinoma

AE of Special Interest, n (%)	CLL/SLL (n = 45)		FL (n = 17)	
	All Grade	Grade 3-4	All Grade	Grade 3-4
Diarrhea	7 (15.6)	0	3 (17.6)	0
Serious hemorrhage*	0	0	0	0
Atrial fibrillation	0	0	0	0
Infusion-related reactions	11 (24.4)	1 (2.2)	1 (5.9)	0

\*  $\geq$ Grade 3 hemorrhage, or central nervous system hemorrhage of any grade.

## BGB-3111+Obinutuzumab: Disease Response

Follow-up and Response	TN CLL/SLL (n = 18)	R/R CLL/SLL (n = 25)	FL (n = 15)
Median follow-up, mo (range)	7.0 (2.8-11.8)	8.0 (3.8-14.0)	6.2 (1.2-10.7)
Best Response			
ORR	<b>16 (88.9)</b>	<b>23 (92.0)</b>	<b>11 (73.3)</b>
CR	4 (22.2)	4 (16.0)	5 (33.3)
PR	12 (66.7)	19 (76.0)	6 (40.0)
PR-L	0	0	N/A
SD	2 (11.1)	1 (4.0)	2 (13.3)
PD	0	1 (4.0)	2 (13.3)

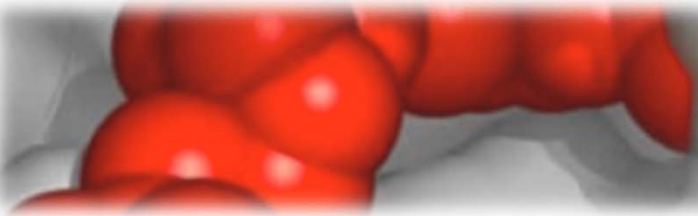
**As of 31 March 2017, all responses (CLL and FL) are ongoing (range 3-12 months)**



# Conclusions

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- The potent and selective BTK inhibitor BGB-3111 and the anti-CD20 antibody obinutuzumab are safe and well-tolerated when given in combination in patients with CLL/SLL and FL
- The combination of BGB-3111 and obinutuzumab is highly active in CLL/SLL and FL
- Early CR rate in CLL/SLL is favorable compared to the expected rate with BTK-inhibitors or anti-CD20 antibodies alone
- Both the frequency and depth of response in FL (overall and complete response rates) are favorable compared to reported data with BTK-inhibitors or anti-CD20 antibodies alone
- BeiGene is planning late-stage trials of this combination in FL



BeiGene

# **BGB-3111**

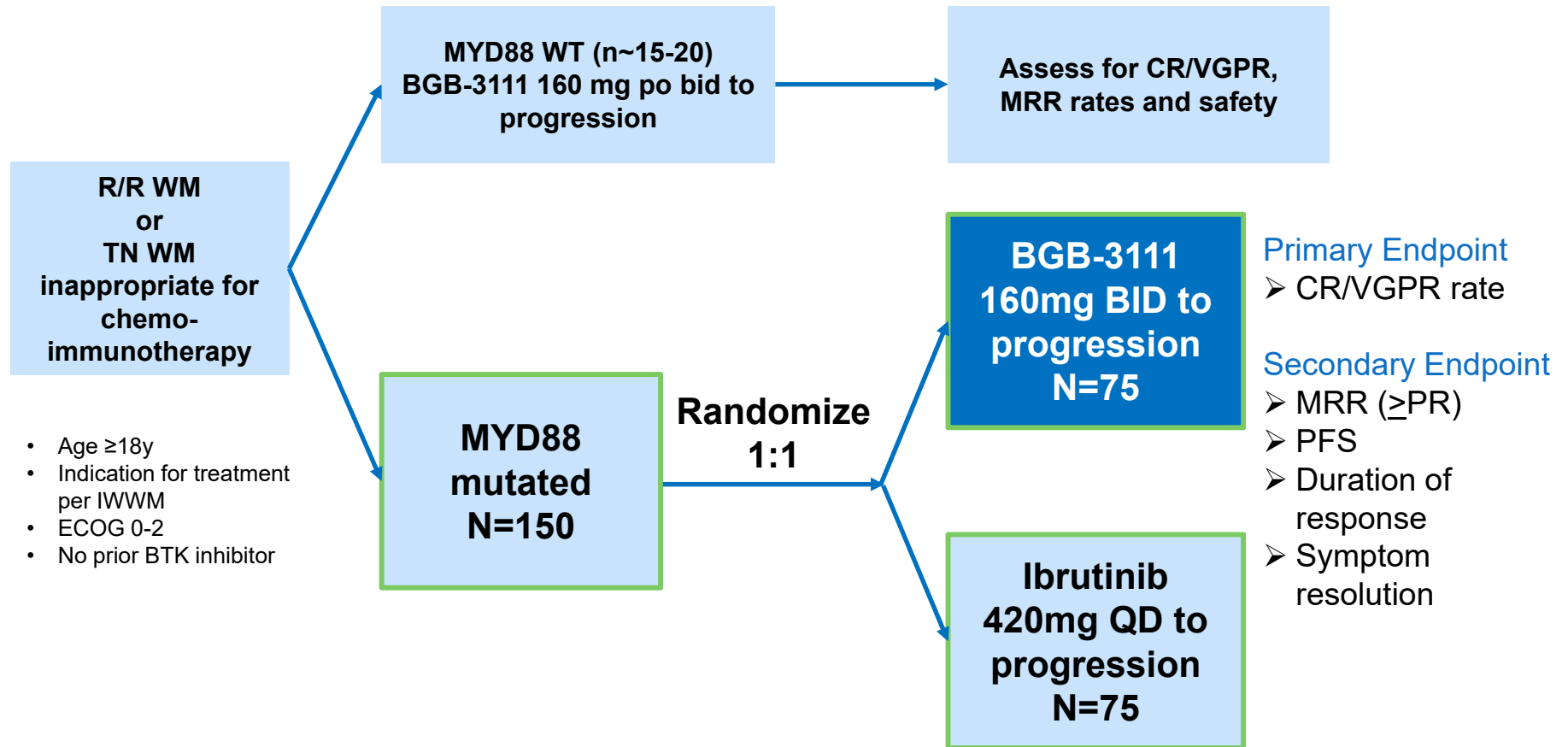
## **Clinical Development Plan Update**

# BGB-3111 Near-Term Development Strategy

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- **Current data suggest potential best-in-class attributes**
  - Response depth, response durability, and tolerability as a monotherapy
  - Preliminary evidence of augmented activity in combination with obinutuzumab
- **BeiGene's overall global plan is to develop BGB-3111 broadly, pursuing approvals in multiple indications and broadly-defined patient populations**
- **Near-term development considerations**
  - WM: maturing monotherapy data continue to support ongoing Phase 3 trial vs. ibrutinib.
  - CLL: The data from the updated Phase 1 monotherapy experience supports approval-directed development in a broad initial treatment CLL population.
  - FL: Unmet medical need exists (failed at least 2 prior lines of therapy and progression within one year of last treatment). Initial efficacy results with BGB-3111+obinutuzumab combination support an expedited development trial in this unmet need population, plus a confirmatory study in a broader (earlier line) FL population.

# BGB-3111 Phase 3 Study Design in WM



- Age ≥18y
- Indication for treatment per IWWM
- ECOG 0-2
- No prior BTK inhibitor

Stratification factors at randomization:

- CXCR4 status (WHIM vs WT)
- No. of lines of prior therapy (0 vs. 1-3 vs. >3)

# BGB-3111 in WM: ICML update continues to support the ongoing global head-to-head pivotal trial

- With a median follow-up of 12.3mo, VGPR of 43% compares very favorably to VGPR of 13-16% of ibrutinib with longer follow up<sup>^</sup>

	BGB-3111 (IWWM 2016)	BGB-3111 (ASH 2016)	BGB-3111 (14-ICML)	Ibrutinib (Treon)	Ibrutinib (PCYC-1127)
n	24	32	42	63	31
Follow-up (med)	8.0 mo	9.6 mo	12.3 mo	19.1 mo*	17.1 mo
VGPR	33%	34% VGPR	43% VGPR	16% VGPR	13% VGPR

- Responses occurred across mutation statuses including patients with MYD88 wild-type background

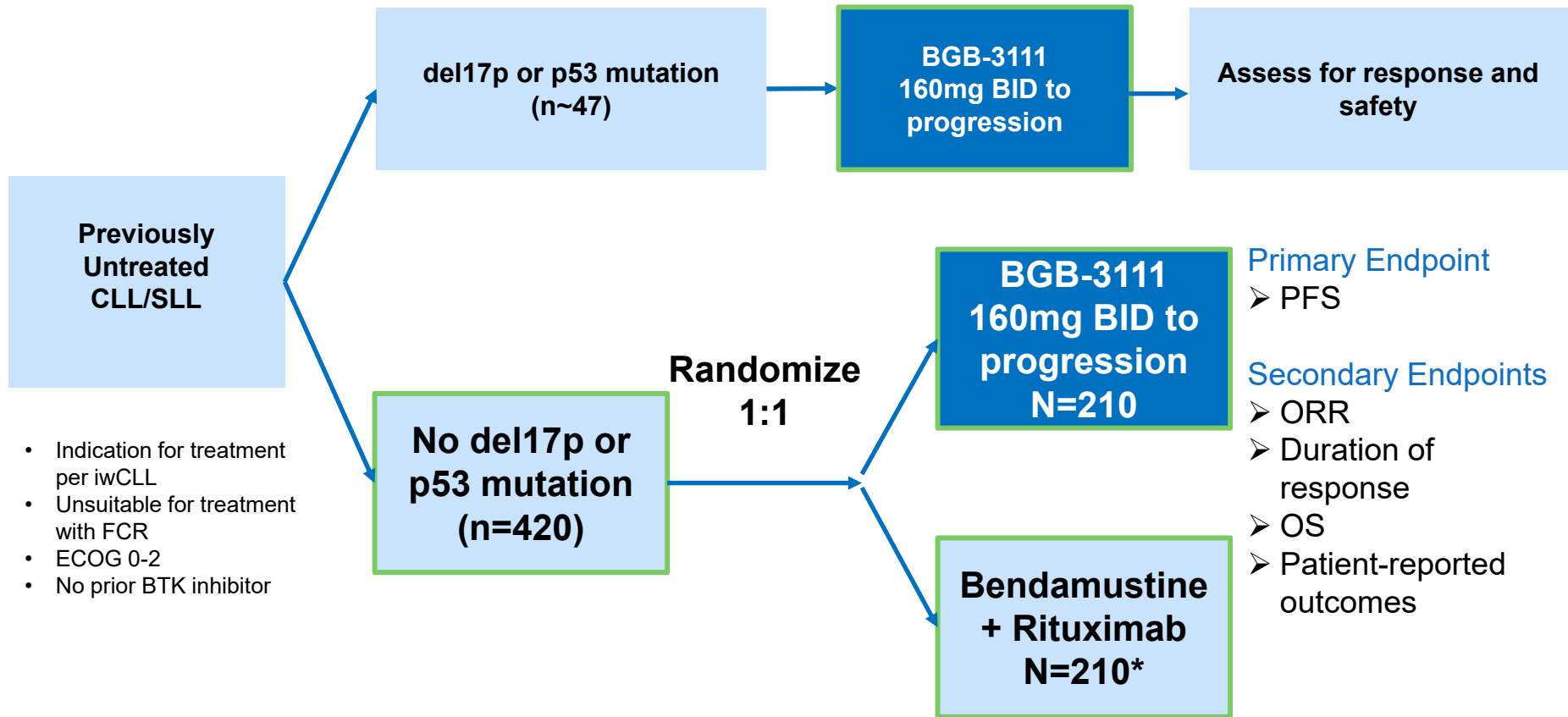
Genotype N=31*	Best Response			
	VGPR	PR	MR	SD
<i>MYD88<sup>L265P</sup>/CXCR4<sup>WT</sup></i> (n = 22)	11 (50%)	7 (32%)	2 (9%)	2 (9%)
<i>MYD88<sup>L265P</sup>/CXCR4<sup>WHIM</sup></i> (n = 4)	1 (25%)	2 (50%)	1 (25%)	0
<i>MYD88<sup>WT</sup></i> (n = 5)	1 (20%)	1 (20%)	2 (40%)	1 (20%)

- Global pivotal trial enrolling well with the opportunity to establish superiority over SOC
  - Estimated 22,500 new cases worldwide each year

Notes: <sup>^</sup> Cross-trial comparison; \* Not reported, treatment duration being 19.1 mo; <sup>†</sup> Genotyping results available for 31 patients

Source: Tam *et al.*, IWWM, 2016; Tam *et al.*, ASH, 2016; Trotman *et al.*, 14-ICML, 2017; Treon *et al.*, NEJM, 2015; Dimopoulos *et al.*, EHA, 2016; Fonseca, *et al.*, Br J Haematol, 2007

# BGB-3111 Phase 3 Study Design in Treatment-Naïve CLL



\*crossover allowed at progression

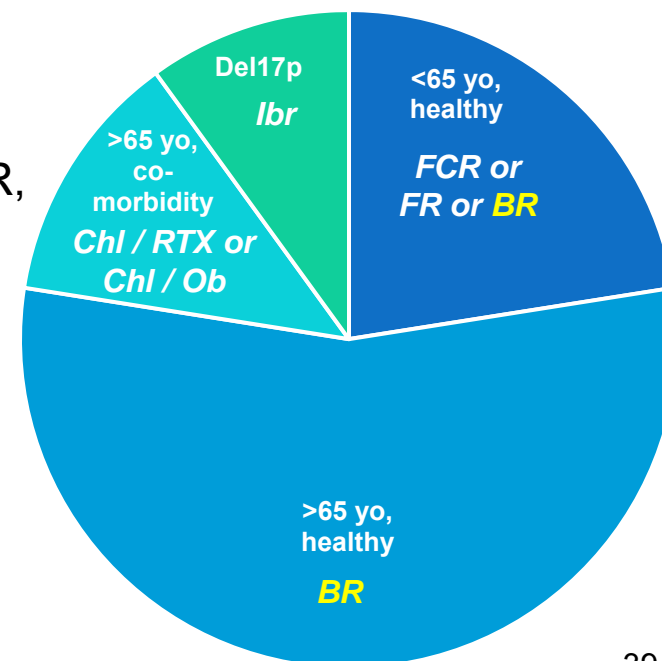
# BGB-3111 for CLL: positioned for broad opportunity in 1L CLL

- ICML update maintains high responses in larger dataset in all treatment settings

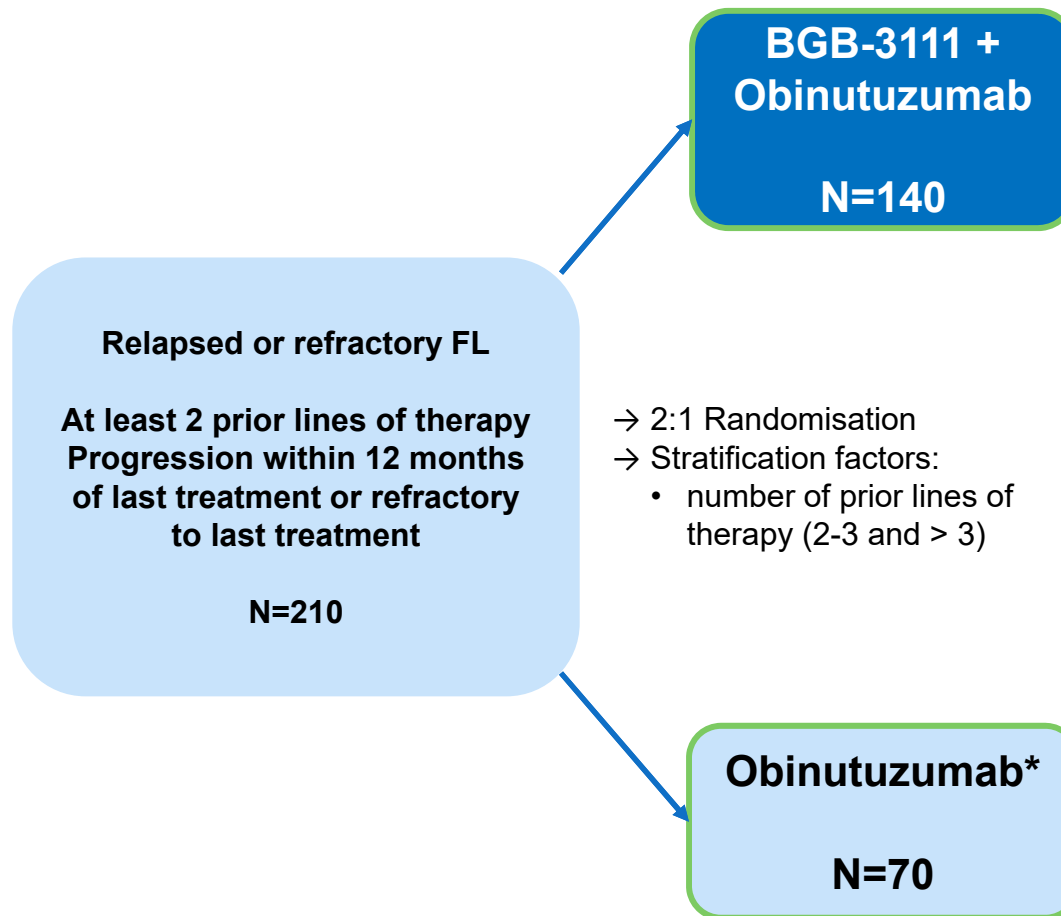
Response	TN (n = 16)	R/R (n = 50)	Total (n = 66)
Median follow-up, mo (range)	7.6 (3.7-11.6)	14.0 (2.2-26.8)	10.5 (2.2-26.8)
<b>ORR</b>	<b>16 (100%)</b>	<b>46 (92%)</b>	<b>62 (94%)</b>

- Very low rate of discontinuation (3%) due to any event, 1 AE and 1 PD out of 69 patients with a median follow-up of 10.5 mo
- Plan to initiate pivotal trial in CLL front line against BR, considered most broadly applicable standard-of-care
  - Estimated 191,000 new cases of CLL and 61,000 deaths worldwide; 20,110 new cases and 4,660 deaths in the U.S. each year
  - BR is frequently used as a SOC for healthy, elderly patients, representing the largest segment of CLL

CLL Patient Subtypes and SOC



# BGB-3111 Phase 2 Pivotal Study Design in Relapsed or Refractory Follicular Lymphoma



- **Study Endpoints:**

- Primary**

- ORR

- Secondary**

- Duration of Response
- PFS
- OS
- Time-to-response

\*option to add BGB-3111 after 12 months if no response



# BGB-3111 for FL: Potential Rapid Entry into a Large Market Segment by Addressing a High Unmet Medical Need

- FL represents a significant market
- Significant unmet medical need: patients failed at least 2 prior lines of therapy and progression within one year of last treatment
- BGB-3111/ obinutuzumab combination highly active in a treatment setting where ibrutinib is not yet approved
- Early frequency and depth of responses in FL (73% ORR and 33% CR) compares favorably to reported data with BTK inhibitors or anti-CD20 antibodies alone<sup>^</sup>

## Significant Market (FL)<sup>1,2</sup>

- Accounts for ~35% of NHLs, one of the most common forms
- Estimated **140,000 new cases** worldwide each year
- Estimated **25,000 new cases** in the U.S. each year
- ~50% of blockbuster drug Rituximab oncology revenue reported to come from FL

	BGB-3111 & Obinutuzumab	Ibrutinib <sup>3</sup>	Obinutuzumab <sup>4</sup>	Idelalisib <sup>5</sup>
n	15	110	40	72
Population	Prior alkylator and CD20, mixed Rituxan-sensitive and -refractory	Prior alkylator and CD20, last response <12 months	Mixed Rituxan-sensitive and -refractory	Alkylator and Rituxan-refractory relapse
Follow-up (med)	7.9 mo	27.7 mo	33.7 mo	NR
ORR	73%	21%	50%	54%
CR	33%	11%	18%	6%

Notes: <sup>^</sup> cross-trial comparison



Source: Tam *et al.*, 14-ICML, 1 SEER, 2 GLOBOCAN; 3 Gopal, *et al* ASH 2016; 4 Salles, *et al* J Clin Oncol 2013; 5 Gopal, *et al* N Engl J Med 2014 41



# BGB-3111 Near-Term Development Plan

	Global Monotherapy	Global Combination	China
<b>Current</b> 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 1L WM	Phase 1b 3111 + A317 FL, DLBCL+, 1° CNS lymphoma	Phase 2 Mono in RR MCL
<b>Future</b> 2017-2021	Phase 3 3111 vs BR 1L CLL	Phase 2 3111+G vs G R/R FL	Phase 2 Monotherapy RR WM
		Phase 3 Confirmatory Trial in Earlier-line treatment of FL	Phase 2 Monotherapy RR DLBCL
			Phase 3 3111 vs chlorambucil in 1L CLL/SLL
			Phase 1b 3111 + rituximab

	Proof-of-Concept Trial
	Registrational Trial

# BGB-3111 Clinical Development Summary

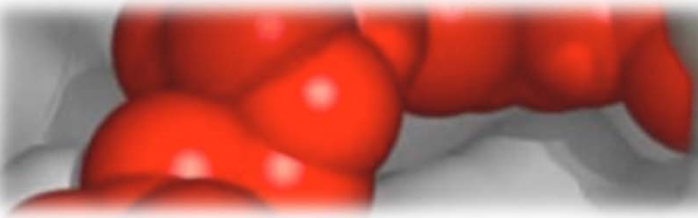
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- **Expanding program with close to 500 patients treated to date**
- **2017 Phase 3/ Registrational Programs**
  - China- accelerated programs in relapsed/ refractory CLL and MCL
    - On track for 2018-2019 filing
  - Best-in-class Phase 3 Trial in Waldenstrom macroglobulinemia
    - Superiority comparison (VGPR) with ibrutinib
  - First-in-class registrational opportunity in follicular lymphoma (in combination with obinutuzumab)\*
  - Phase 3 trial in broad first-line CLL population\*
- **Broad Phase 2/ proof-of-concept program ongoing, including:**
  - BGB-3111/ BGB-A317 (anti-PD1) combination
  - DLBCL (including molecular characterization studies)
  - Other B cell malignancies (MCL, MZL, etc.)

# BeiGene – Near-term Milestones

Event	Expected Timing
<b>BGB-3111 (BTK Inhibitor)</b>	
<ul style="list-style-type: none"> <li>Present data from the combination study with BGB-A317 at a medical conference</li> <li>Present additional data from the dose-expansion phase of the Phase I monotherapy study</li> <li>Present data from the China Phase I study</li> </ul>	<ul style="list-style-type: none"> <li>2017</li> <li>2017</li> <li>2017</li> </ul>
<b>BGB-A317 (PD-1 Antibody)</b>	
<ul style="list-style-type: none"> <li>Present data from the Phase Ia/Ib study in patients with advanced hepatocellular carcinoma at the ESMO 18<sup>th</sup> World Congress on Gastrointestinal Cancer</li> <li>Present additional clinical combination data</li> <li>Present data from the dose-expansion phase of the ongoing Phase I trials</li> </ul>	<ul style="list-style-type: none"> <li>June 28-July 1, 2017</li> <li>2017</li> <li>2017</li> </ul>
<b>BGB-290 (PARP Inhibitor)</b>	
<ul style="list-style-type: none"> <li>Present updated Phase I monotherapy study data</li> </ul>	<ul style="list-style-type: none"> <li>2017</li> </ul>

***Initiate additional registrational trials globally and in China with our portfolio compounds in 2017***



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# Q&A



BeiGene

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# Appendix

# BGB-3111 Phase 1 Trial Design

## DOSE ESCALATION

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

## RP2D

320 mg QD  
or  
160 mg BID

## DOSE EXPANSION

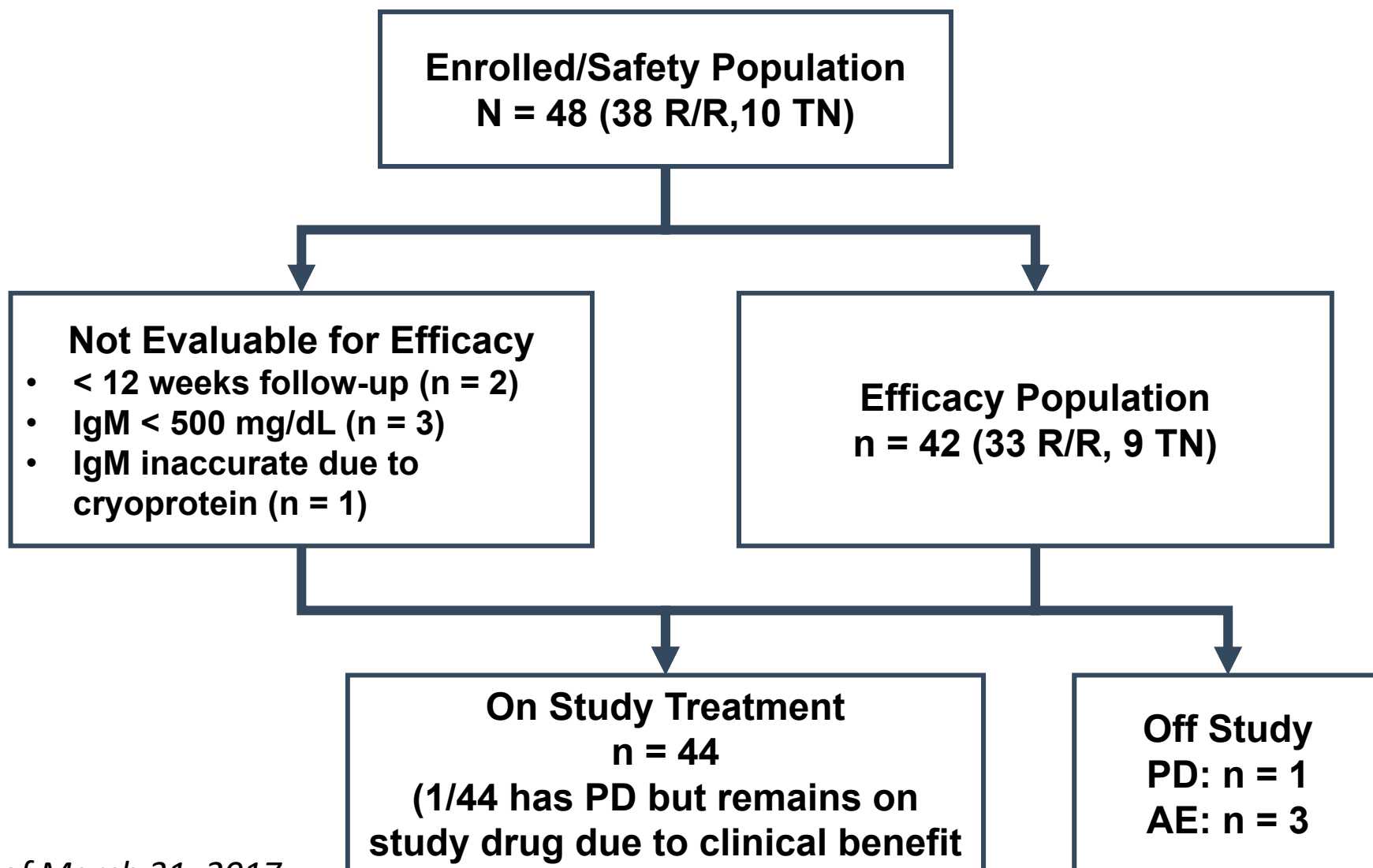
Population	RP2D Dose	Disease	Planned (WM enrolled)
Relapsed/Refractory	BID or QD	MCL, MZL, FL, GCB DLBCL, WM	40 (2)
Relapsed/Refractory	BID	Non-GCB DLBCL	40
Relapsed/Refractory	BID	CLL/SLL	70
Relapsed/Refractory	BID	WM	20 (20)
Relapsed/Refractory	QD	CLL/SLL	20
Relapsed/Refractory or Treatment-naïve	BID or QD	WM	50 (22)
Relapsed/Refractory	BID or QD	MCL	20
Treatment-naïve	BID or QD	CLL/SLL	20
Treatment-naïve	BID or QD	MCL	20
Relapsed/Refractory	BID or QD	HCL	10
Relapsed/Refractory	BID	iNHL	40
Relapsed/Refractory	BID	Richter Transform.	15
Relapsed/Refractory from prior btk-i	BID	WM	15

### Eligibility:

- ≥1 prior therapy (relapsed cohorts only)
- No available higher priority treatment
- ECOG 0-2
- ANC >1,000/μl, PLT >50,000/μl

## WM: Patient Disposition

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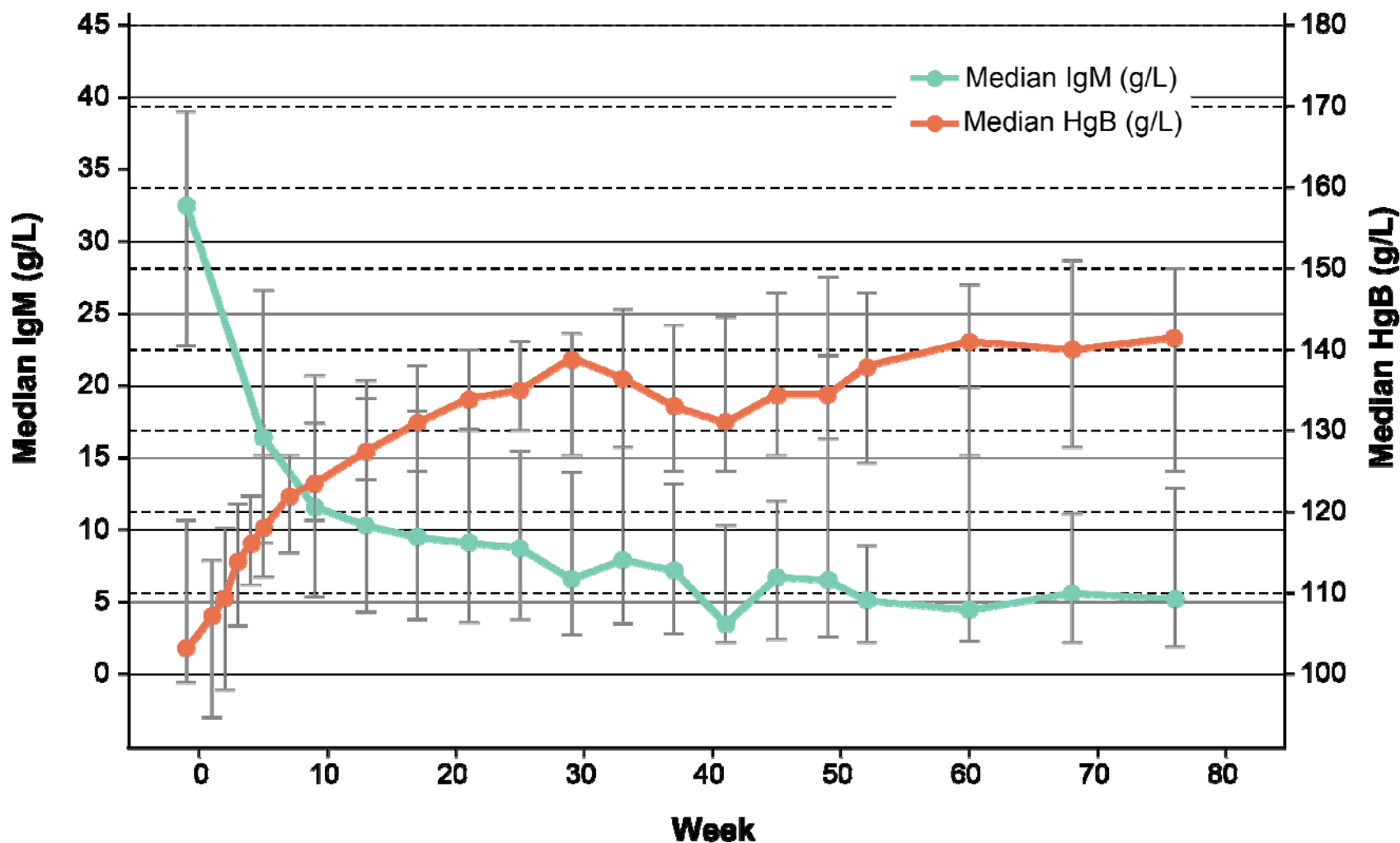
*As of March 31, 2017*



# WM: Modified IWWM Response Criteria

Category	Criteria
Complete Response (CR)	<ul style="list-style-type: none"> <li>• Normal serum IgM values</li> <li>• Disappearance of monoclonal protein by immunofixation</li> <li>• No histological evidence of bone marrow involvement</li> <li>• Complete resolution of lymphadenopathy/splenomegaly (if present at baseline)</li> </ul>
Very Good Partial Response (VGPR)	<ul style="list-style-type: none"> <li>• <math>\geq 90\%</math> reduction of serum IgM from baseline <b>or normal IgM values</b></li> <li>• <b>Reduction</b> in lymphadenopathy/splenomegaly (if present at baseline)</li> </ul>
Partial Response (PR)	<ul style="list-style-type: none"> <li>• <math>\geq 50\%</math> reduction of serum IgM from baseline</li> <li>• Reduction in lymphadenopathy/splenomegaly (if present at baseline)</li> </ul>
Minor Response (MR)	<ul style="list-style-type: none"> <li>• At least 25% but <math>&lt; 50\%</math> reduction of serum IgM from baseline</li> </ul>
Stable Disease (SD)	<ul style="list-style-type: none"> <li>• Not meeting criteria for CR, VGPR, PR, MR, or progressive disease</li> </ul>
Progressive Disease (PD)	<p>At least one of the following:</p> <ul style="list-style-type: none"> <li>• Confirmed <math>\geq 25\%</math> increase in serum IgM and <b>total increase of <math>\geq 500</math> mg/dL from nadir (on treatment)</b></li> <li>• New lymph nodes <math>&gt; 1.5</math> cm, or <math>\geq 50\%</math> increase from nadir in SPD of <math>&gt; 1</math> node, or <math>\geq 50\%</math> increase in longest diameter of previously identified node <math>&gt; 1</math> cm in short axis</li> <li>• New splenomegaly or <math>\geq 50\%</math> increase from nadir in enlargement</li> <li>• New extranodal disease</li> <li>• New or recurrent involvement in bone marrow</li> <li>• New symptomatic disease</li> </ul>

# WM: Decreased IgM and Improved Hemoglobin Levels over time



At risk (n)

IgM	39	38	36	38	39	35	36	34	27	26	23	21	22	20	16	14	11
HgB	42	42	42	42	42	39	38	37	32	31	27	24	22	21	19	15	12

# WM: Response Rate By *MYD88* Mutation Status

## Preliminary Results

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Genotype N=31*	Best Response			
	VGPR	PR	MR	SD
<i>MYD88</i> <sup>L265P</sup> / <i>CXCR4</i> <sup>WT</sup> (n = 22)	11 (50%)	7 (32%)	2 (9%)	2 (9%)
<i>MYD88</i> <sup>L265P</sup> / <i>CXCR4</i> <sup>WHIM</sup> (n = 4)	1 (25%)	2 (50%)	1 (25%)	0
<i>MYD88</i> <sup>WT</sup> (n = 5)	1 (20%)	1 (20%)	2 (40%)	1 (20%)

\* Patients evaluable for response with mutation data

## WM: Efficacy by Prior Treatment

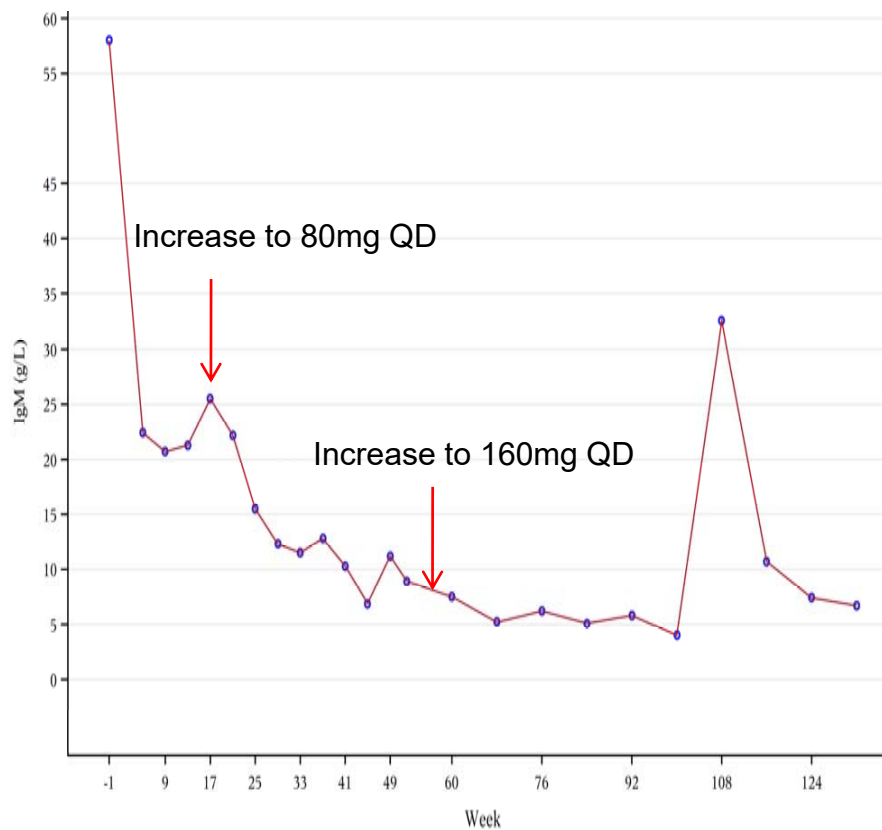
	Treatment-naive N=9	Relapsed/refractory N=33	Total N=42
Median follow-up (range)	9.3 months (6.1-11.7)	15.5 months (4.4-30.5)	12.3 months (4.4-30.5)
Best Response			
CR	0	0	0
VGPR	2 (22%)	16 (49%)	18 (43%)
PR	5 (56%)	9 (27%)	14 (33%)
MR	2 (22%)	4 (12%)	6 (14%)
SD	0	4 (12%)	4 (10%)
			90% ] 76% ORR† MRR*

\* Major response rate.

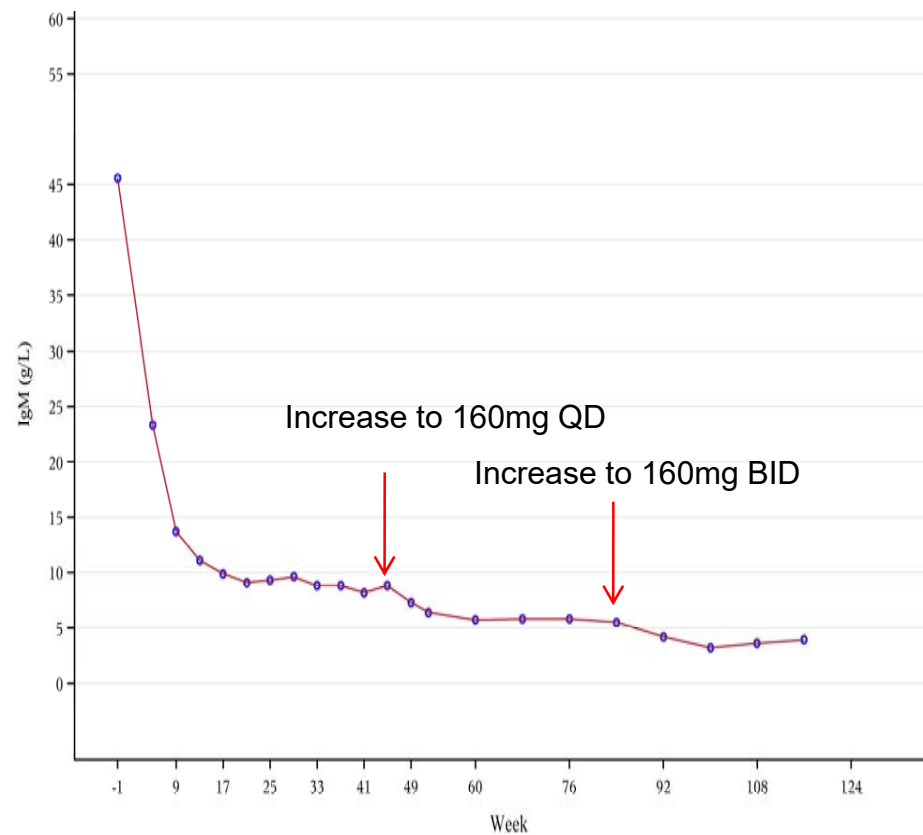
† Overall response rate.

# WM: Inpatient Dose Escalation

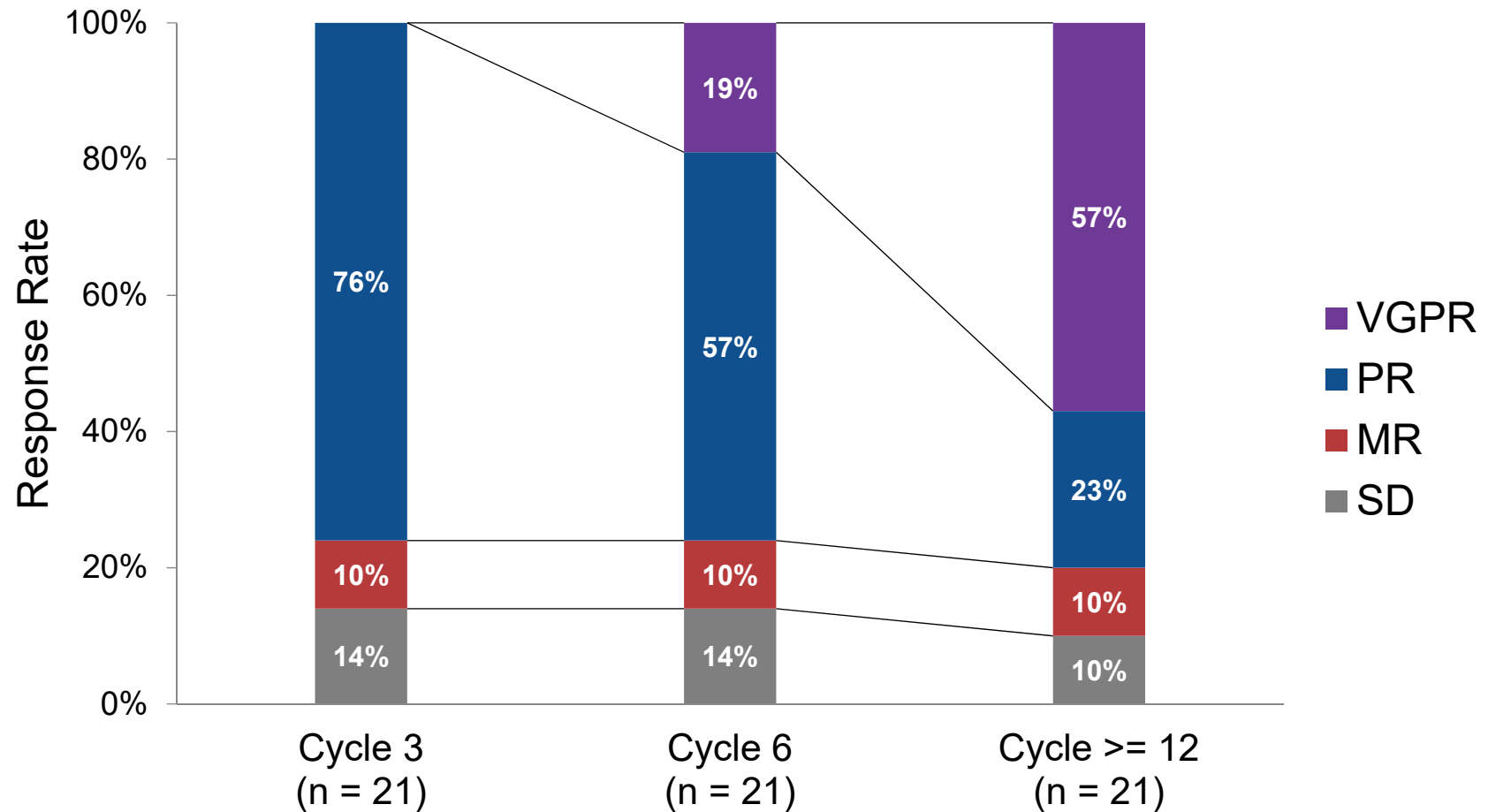
## S401: Initial dose 40mg QD



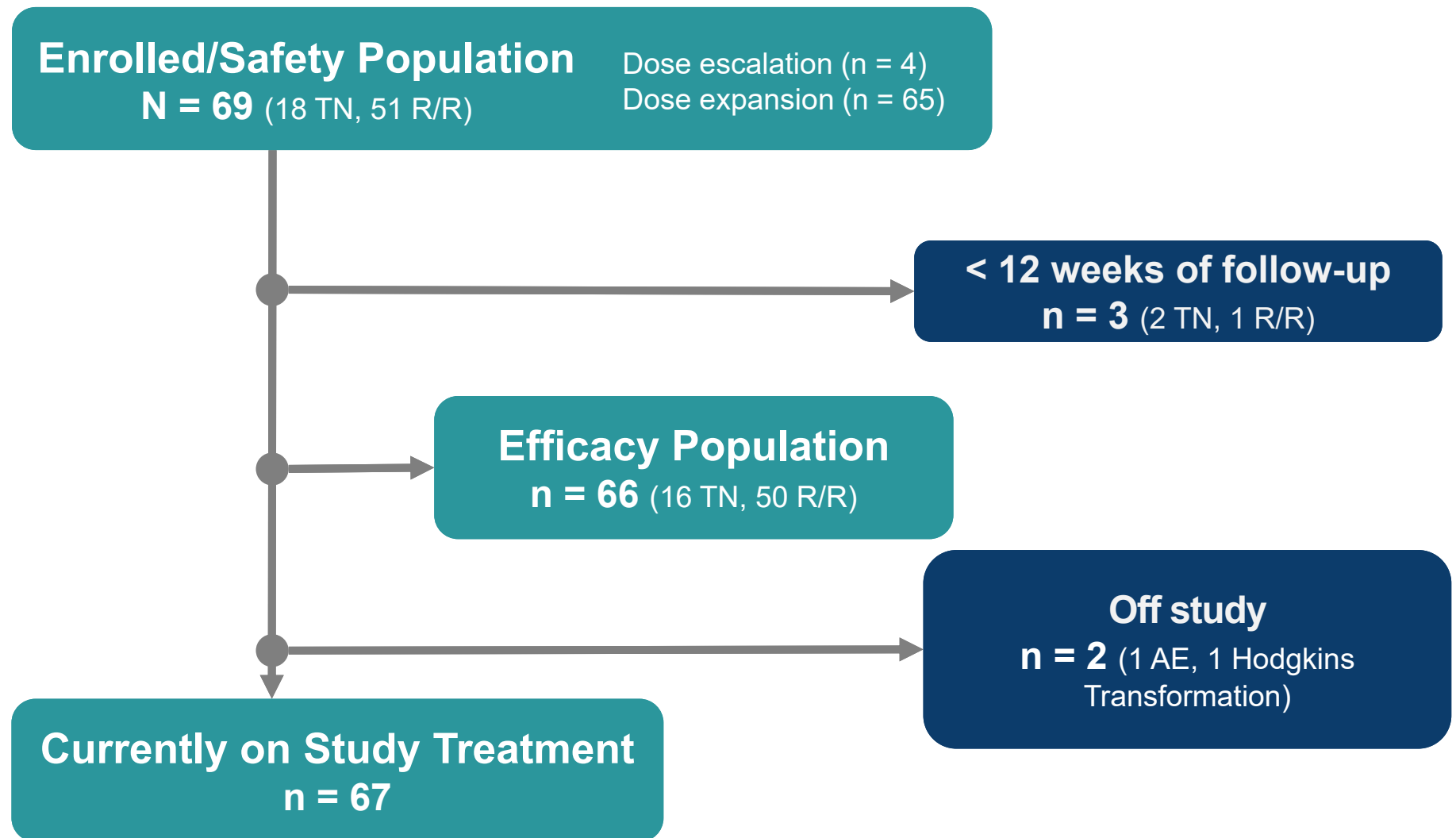
## S101: Initial dose 80mg QD



# WM: IWWM Response Over Time on Treatment: 21 patients on study >12 months



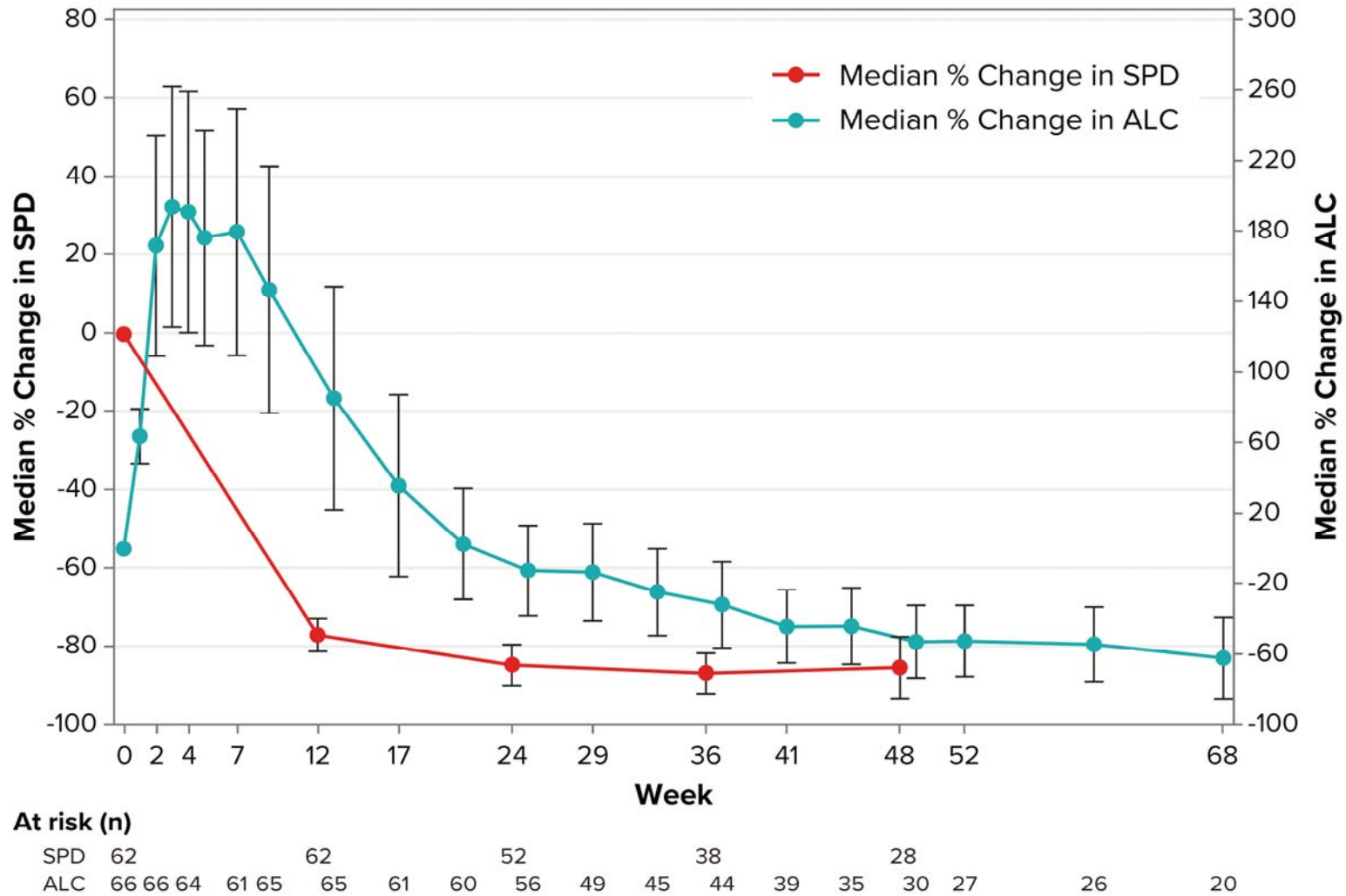
# CLL/ SLL: Patient Disposition



As of March 31, 2017

AE, adverse event; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; R/R, relapsed/refractory; TN, treatment naïve.

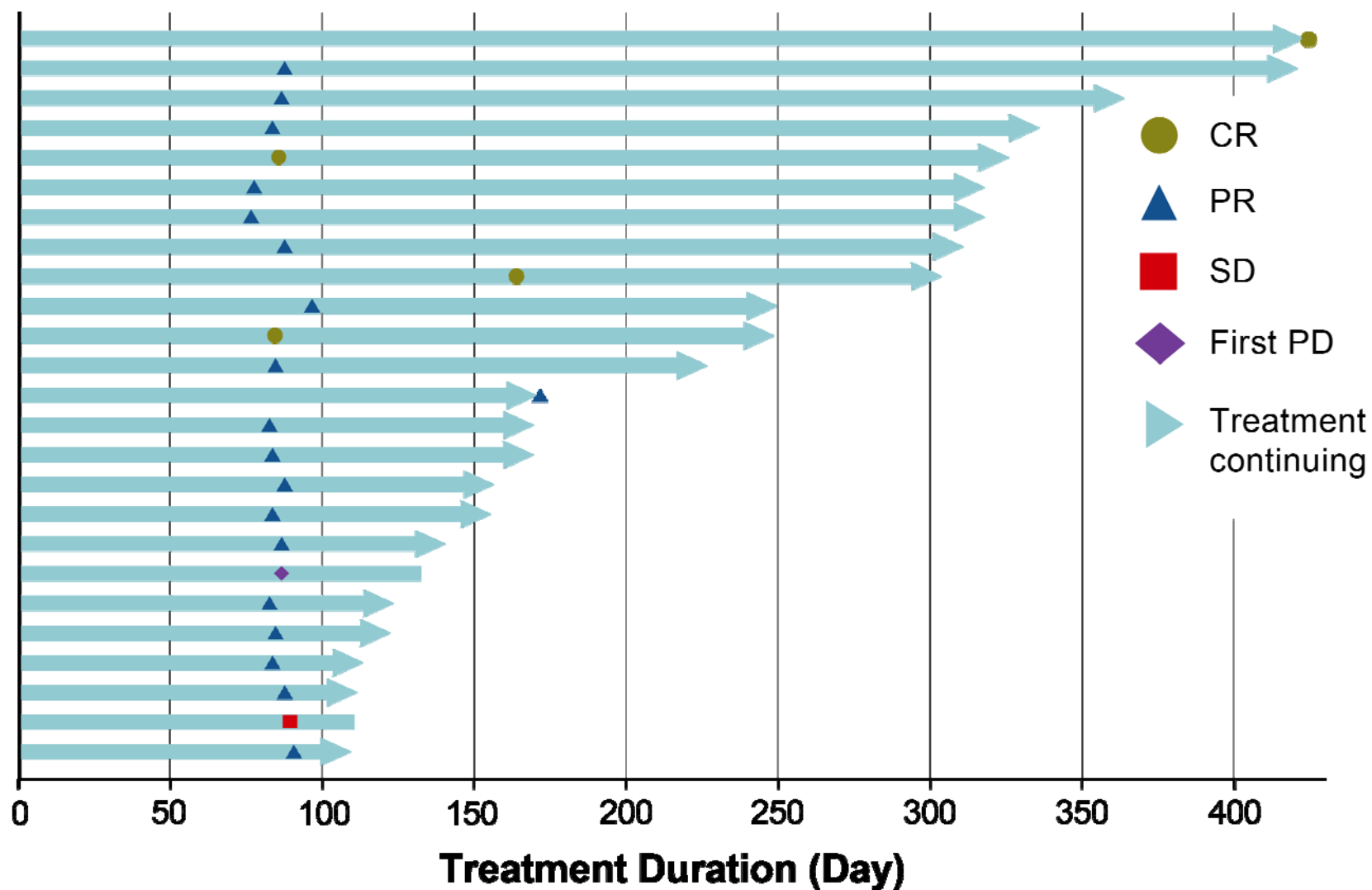
# CLL: Kinetics of ALC and SPD Response



Note: Error bars represent 95% confidence intervals; 4 patients with SPD data at week 37 were combined with 34 patients with SPD data at week 36; 2 patients with SPD data at week 49 were combined with 26 patients with SPD data at week 48. ALC, absolute lymphocyte count; SPD, sum of the products of lymph node diameters by CT scan.



# BGB-3111+Obinutuzumab in R/R CLL/SLL: Duration of Treatment



# Study Design: BGB-3111 in Combination with Obinutuzumab

## DOSE ESCALATION

Cohort	BGB-3111* (D1-28/28-day cycles)	Obinutuzumab	Patients Dosed
1a	320 mg QD	Cycle 1 D2: 100 mg Cycle 1 D3: 900 mg	4
1b	160 mg BID	Cycle 1 D9 and D16: 1000 mg Cycles 2-6 D1: 1000 mg	5

\* BGB-3111 treatment continued until progression, death, or unacceptable toxicity.

† Cohort -1a and -1b will be opened if 2 or more DLTs are observed in Cohorts 1a and 1b.

### Eligibility:

- WHO defined B cell lymphoid malignancy
- ≥1 prior therapy (relapsed cohorts only)
- No available higher priority treatment
- ECOG 0-2
- ANC >1,000/μl, platelets >40,000/μl‡
- Adequate renal and hepatic function
- No significant cardiac disease§

‡ Growth factor/transfusion allowed.

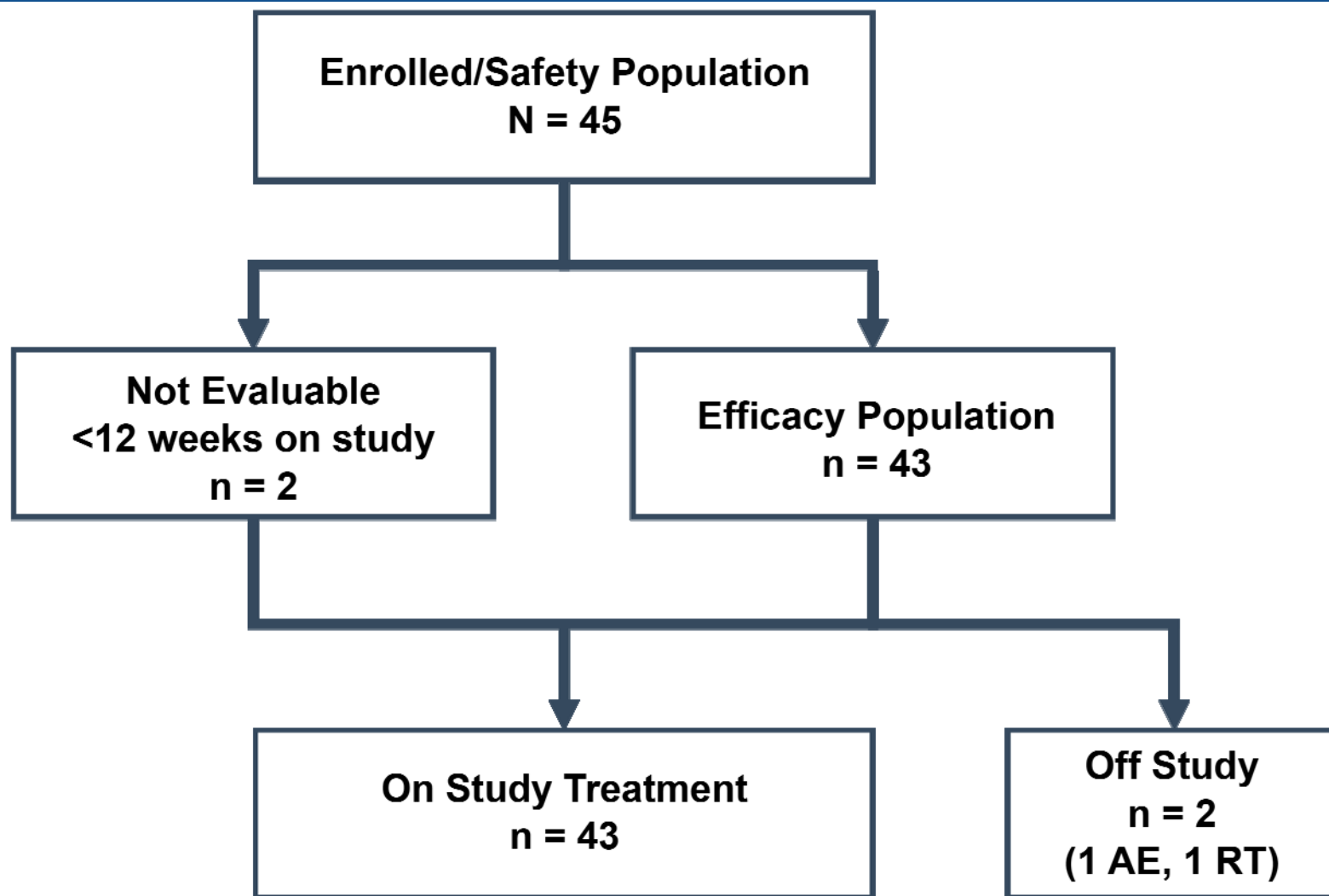
§Anti-coagulation allowed.

## DOSE EXPANSION

Pop	Disease	Planned
TN	CLL/SLL	20
R/R	CLL	20
R/R	non-GCB DLBCL	20
R/R	FL, MCL, MZL, and WM	20
R/R	FL	40

# BGB-3111+Obinutuzumab: CLL/SLL Patient Disposition

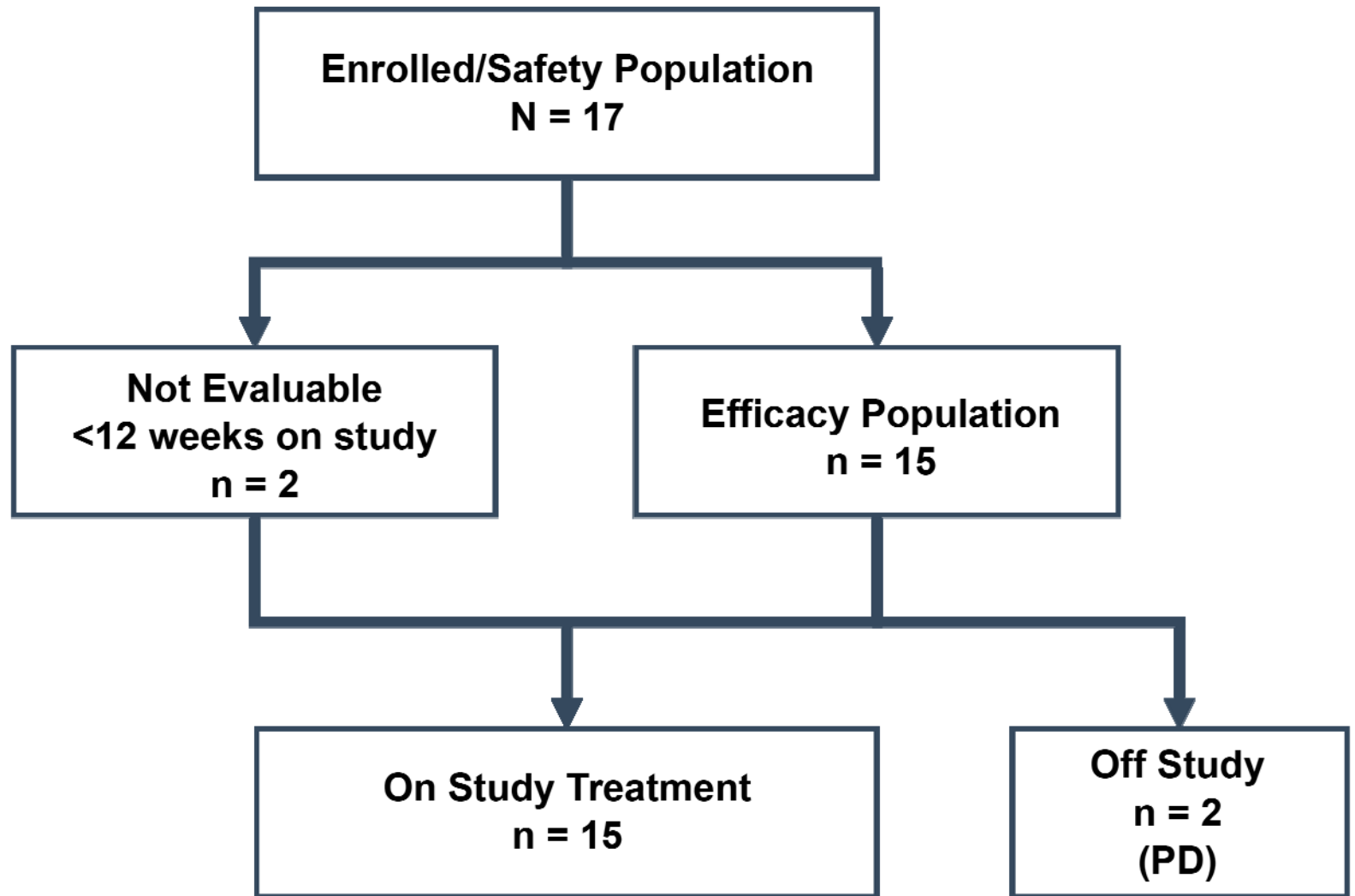
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*As of March 31, 2017*

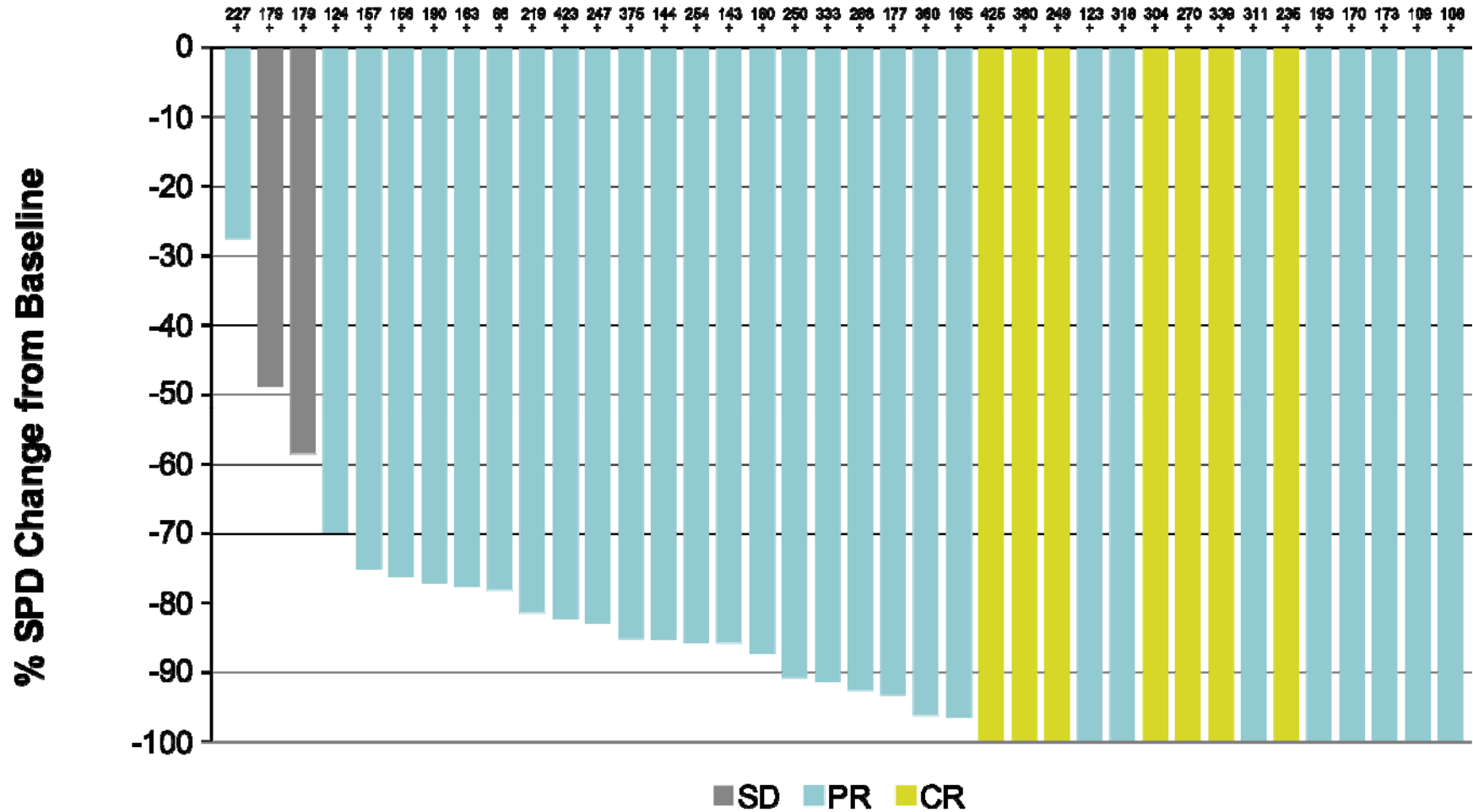
# BGB-3111+Obinuzumab: FL Patient Disposition

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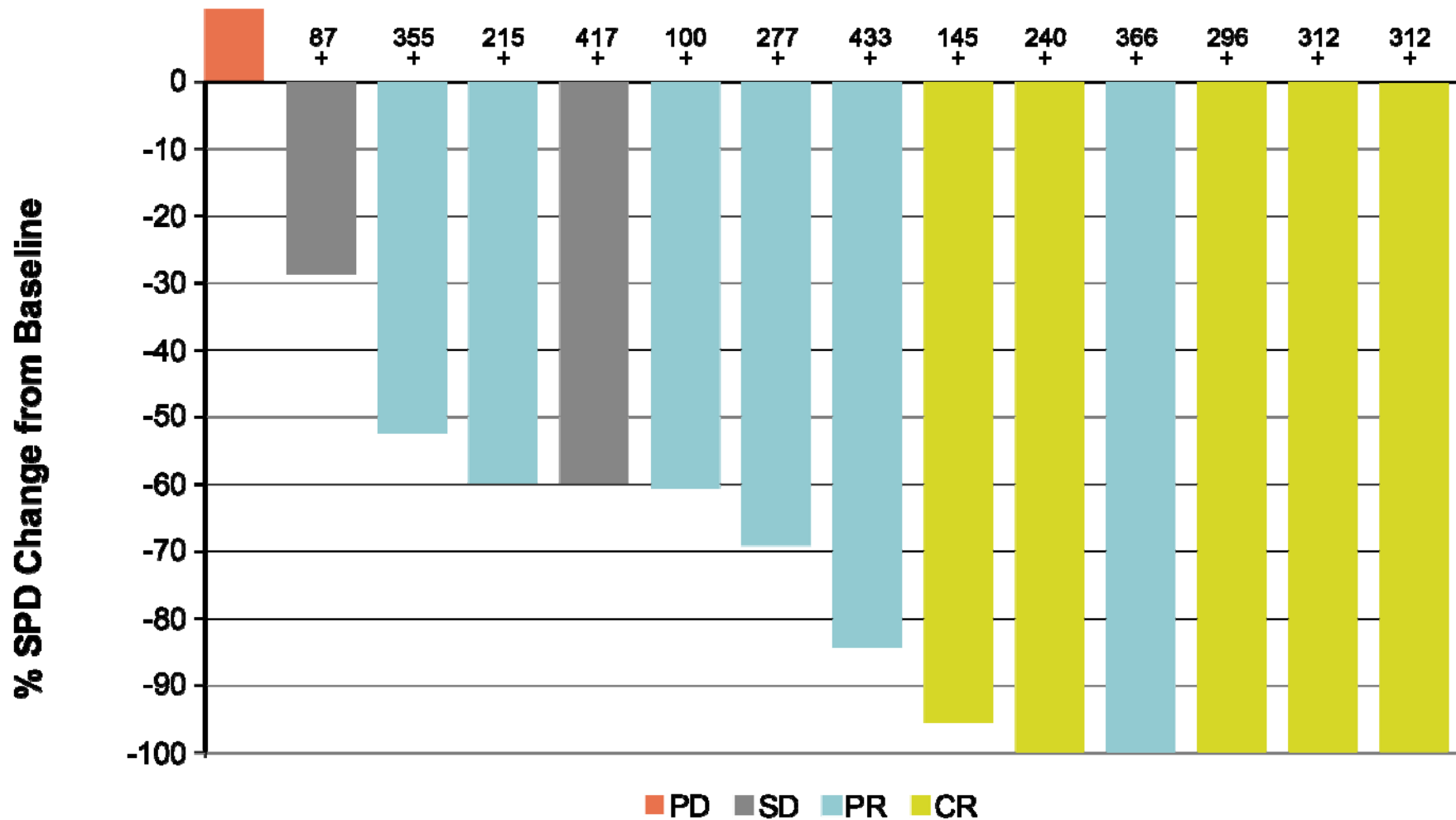


*As of March 31, 2017*

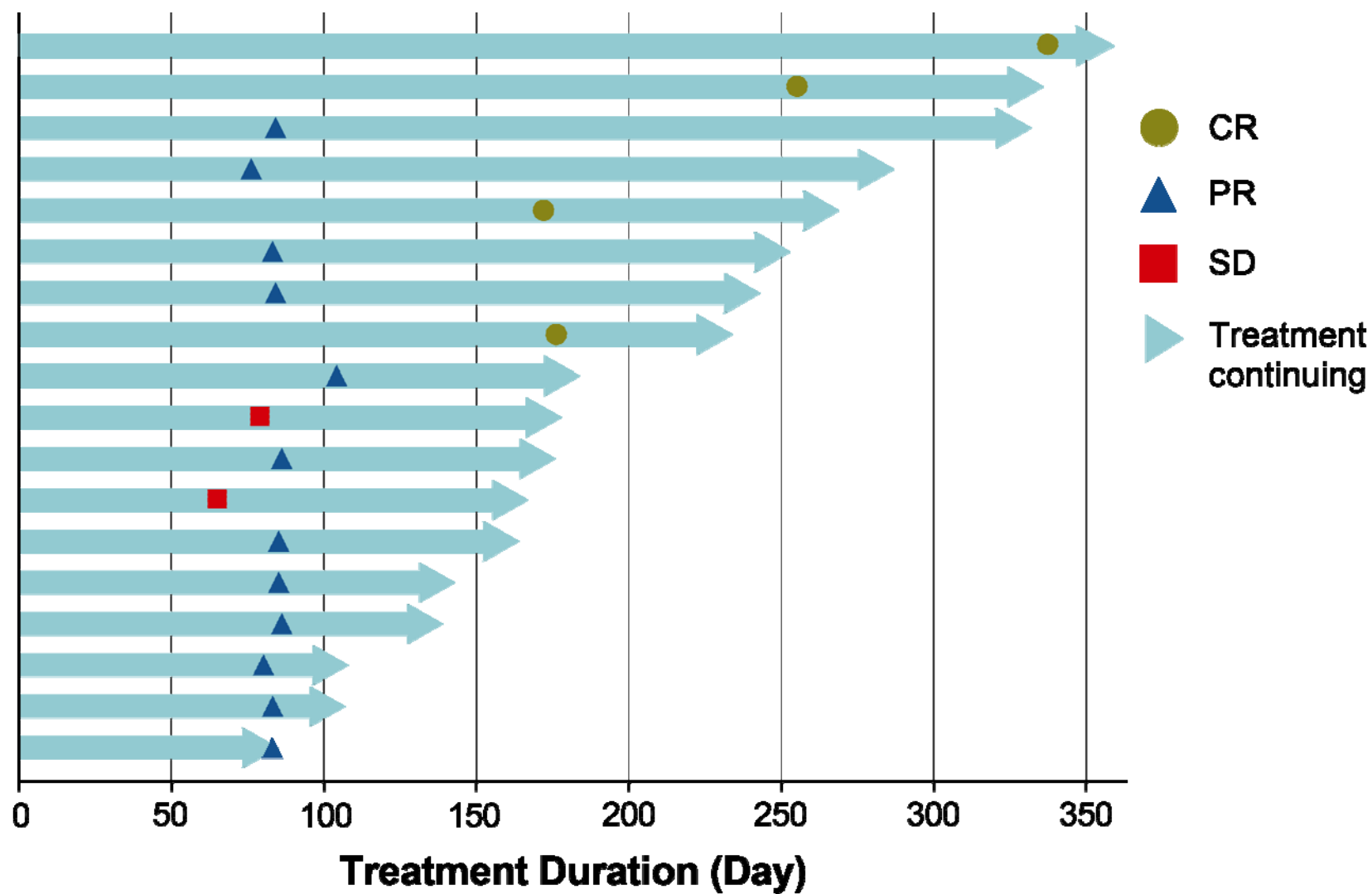
# BGB-3111+Obinuzumab in CLL/SLL: Maximum Improvement in SPD



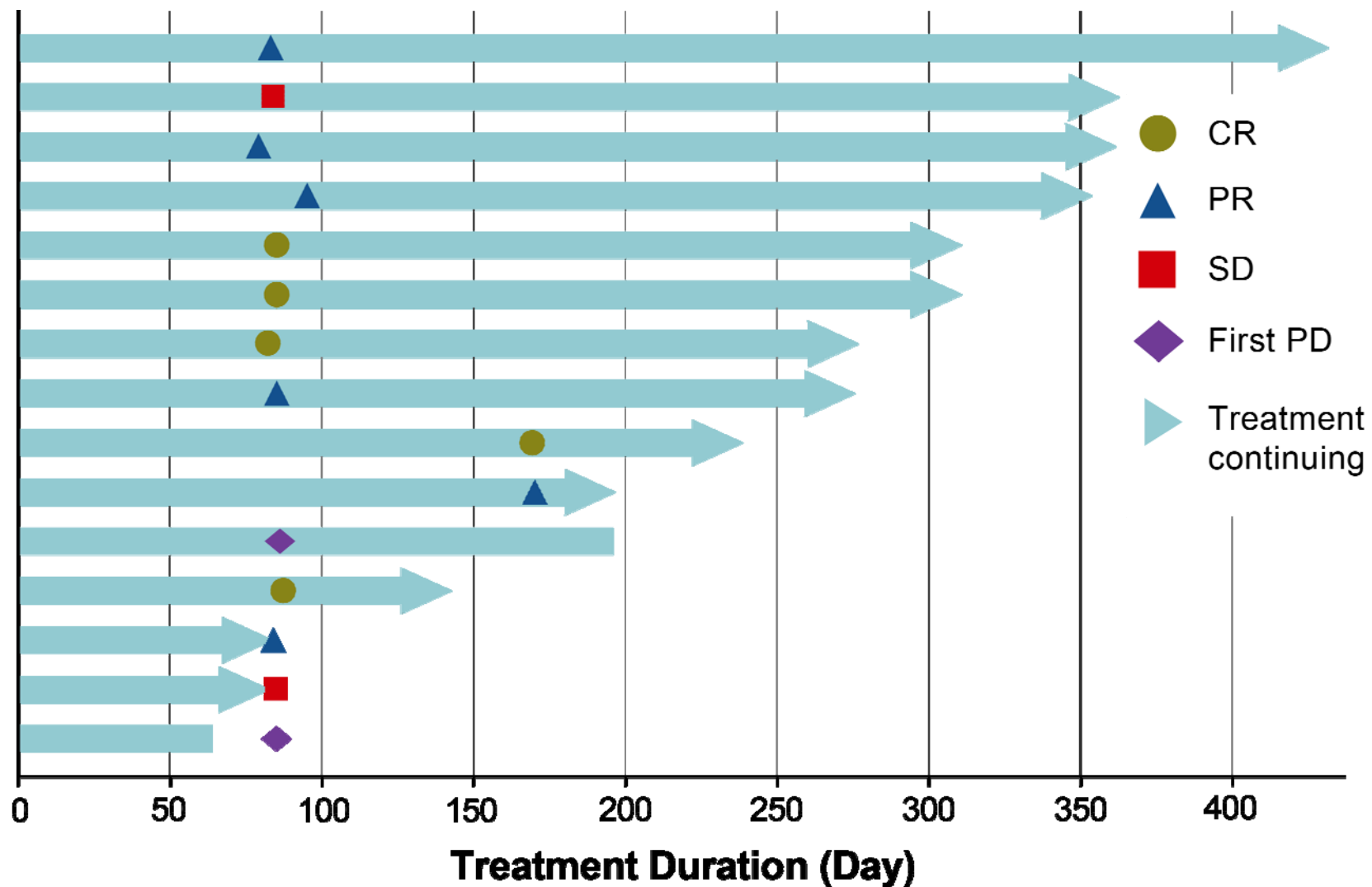
# BGB-3111+Obinuzumab in FL: Maximum Improvement in SPD



# BGB-3111+Obinutuzumab in TN CLL/SLL: Duration of Treatment



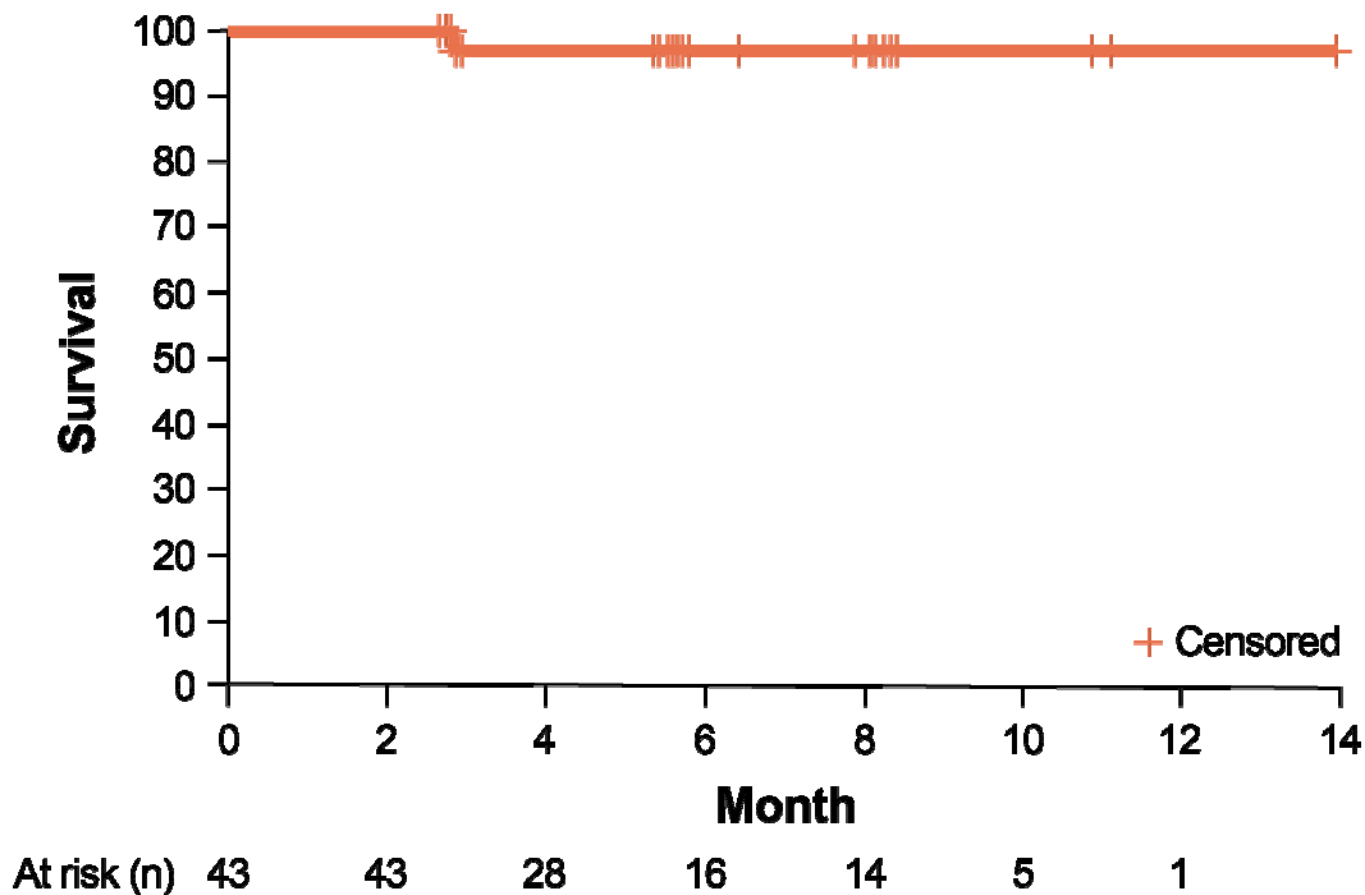
# BGB-3111+Obinutuzumab in FL: Duration of Treatment





# BGB-3111+Obinutuzumab in CLL/SLL: Progression-Free Survival

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# BGB-3111+Obinutuzumab in FL: Progression-Free Survival

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