

# Promising Phase 1b Results: Mavorixafor + Ibrutinib in the Treatment of Waldenström's Macroglobulinemia

**Data Cut: June 2022**

**Presented August 4, 2022**



# Forward-Looking Statements

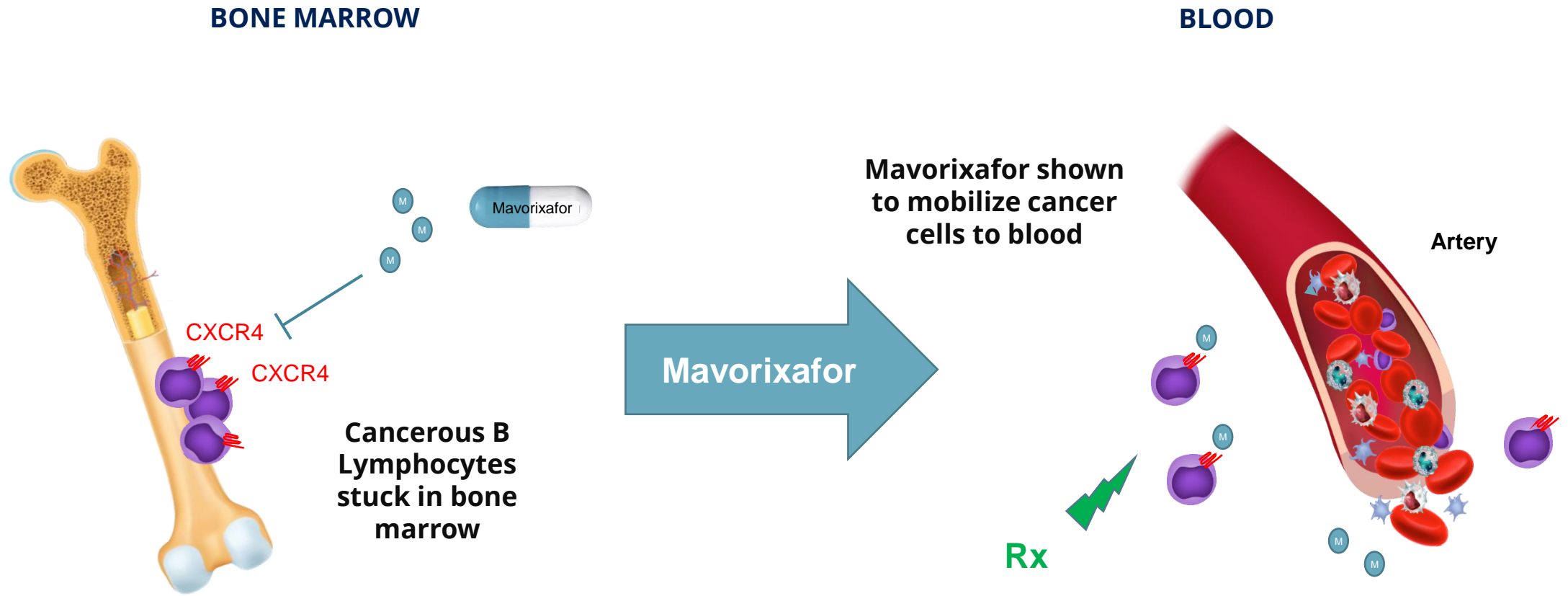


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# CXCR4 Pathogenesis in B-Cell Lymphomas / MOA of Mavorixafor



CXCR4 overexpression in malignant B-cells causes resistance to anti-tumor agents

CXCR4 antagonism demonstrated to increase susceptibility to therapy

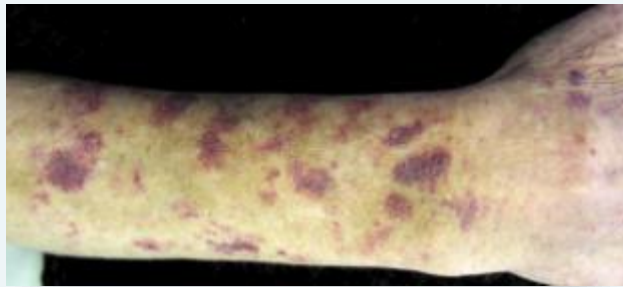
# CXCR4 Inhibition Shows Potential Across Range of B-Cell Lymphomas

X4 Phase 1b Study →

B-Cell Lymphomas	U.S. Prevalence	CXCR4i Combinations in Proof-of-Concept Studies
Waldenström's Macroglobulinemia ( <i>CXCR4</i> -mutation sub-population)	>2,000 <sup>4</sup>	Ulocuplumab + ibrutinib (Clinical) <b>Mavorixafor + Ibrutinib (Phase 1b Clinical)</b>
Waldenström's Macroglobulinemia (non-CXCR4 mutation)	>8,000 <sup>4</sup>	Mavorixafor + SOC (Pre-clinical in WT CXCR4)
Chronic Lymphocytic Leukemia (CLL) <sup>1</sup>	~20,000 <sup>6</sup>	Plerixafor + Rituximab (Clinical)
Diffuse Large B Cell Lymphoma (DLBCL)	~20,000 <sup>2</sup>	Plerixafor + Rituximab (Pre-Clinical)
Mantle Cell Lymphoma (MCL)	>4,000 <sup>3</sup>	Plerixafor + Bortezomib (Pre-Clinical)
Follicular lymphoma (FL)	~10,000 <sup>5</sup>	BKT140 + Bortezomib (Pre-Clinical)

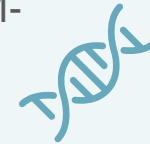
1. Burger et al, *Blood* (2006) 107 (5): 1761–1767. 2. . <https://lymphoma.org/aboutlymphoma/nhl/dlbcl/> 3. [https://www.ils.org/sites/default/files/file\\_assets/mantlecelllymphoma.pdf](https://www.ils.org/sites/default/files/file_assets/mantlecelllymphoma.pdf)  
 4. *WM Epidemiology Analysis* The NemetzGroup. Data on file. 5. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7323888/>.  
 6. <https://www.cancer.org/cancer/chronic-lymphocytic-leukemia/about/key-statistics.html>

A rare B-cell blood cancer of the bone marrow; most often (>90%) caused by mutations in the MYD88 gene, which is involved in innate immune response system



**30-40%**

Patients with identified WHIM-like CXCR4 mutations in addition to MYD88 mutation

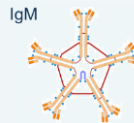


Mean progression-free survival (PFS) in CXCR4-mutation Waldenström's patients versus CXCR4-wild type<sup>1</sup>

**<50%**

## Signs and symptoms

- Elevated IgM
- Hyperviscosity syndrome
- Cryoglobulinemia – IgM clumping
- Pancytopenia, anemia
- Peripheral neuropathy
- Fever, night sweats, weight loss, fatigue



Estimated U.S. Waldenström's patients

**>10,000<sup>2</sup>**

Estimated U.S. other lymphomas

**>50,000<sup>3</sup>**

## Few Current Treatments w/ High Side-Effect Burdens, High Relapse/Refractory Populations

- Ibrutinib, zanubrutinib (BTKi)
- Chemo (bendamustine, R-CHOP)
- Rituximab
- Combinations and others

# Waldenström's Phase 1b Trial: Human Proof of Concept in Patients with CXCR4<sup>MUT</sup>



**Inclusion:** Patients with *MYD88* + *CXCR4* mutations who are naïve to ibrutinib

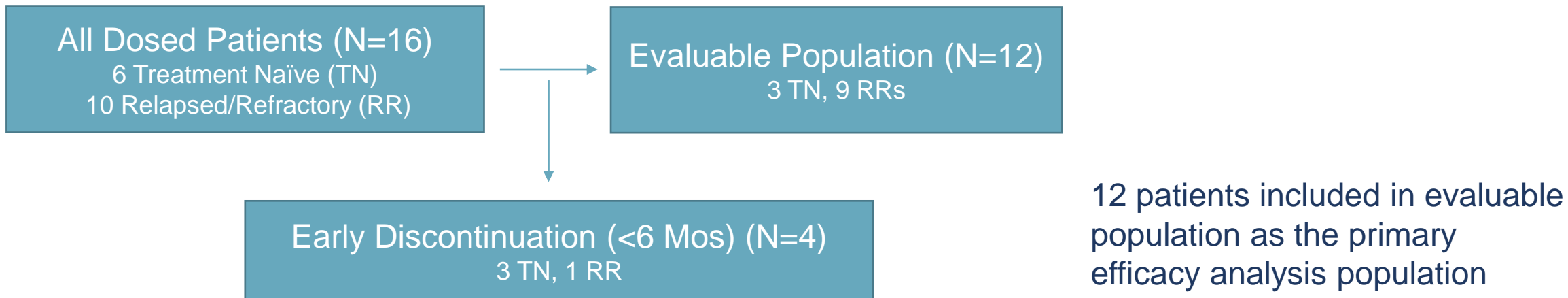
**Design:** Multi-national Phase 1b trial of mavorixafor in combination with ibrutinib (n=12 to 18)

- **Inpatient dose-escalation:** cycles of 200 mg, 400 mg, and 600 mg QD
- **3 cohorts supporting dose selection of mavorixafor:**
  - Cohorts A & B: minimum of 6 patients enrolled in each
  - Cohort C (expansion): potential for additional 6 patients dosed up to 600 mg
- **Endpoints**
  - Safety, PK/PD
  - Assessments of serum IgM levels, hemoglobin, and clinical response



- Strategic collaboration with Leukemia & Lymphoma Society (LLS)
- Selected for LLS' Therapy Acceleration Program

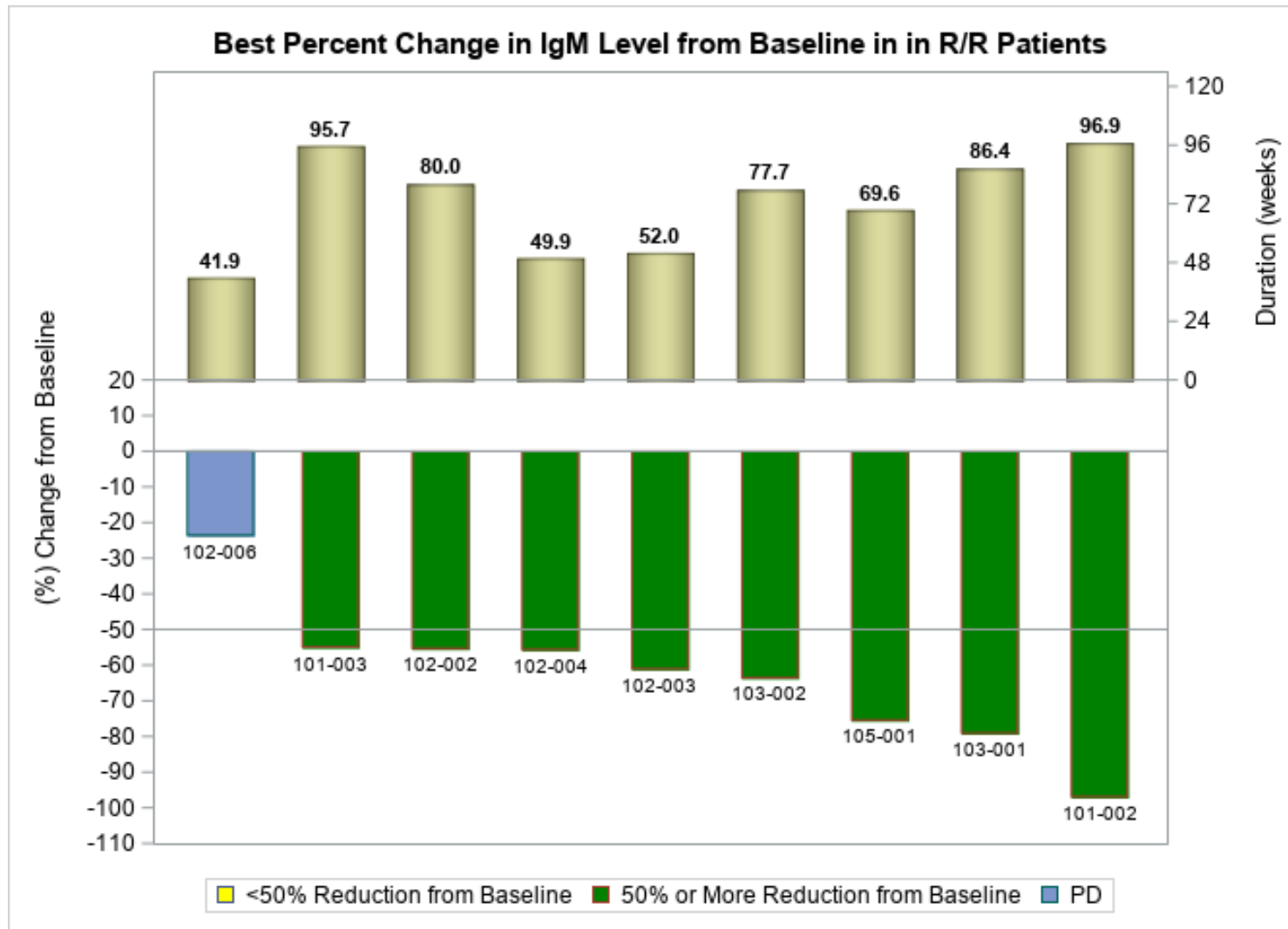
# Patient Disposition and Mavorixafor Dose Exposure



	Mav 200 mg QD	Mav 400 mg QD	Mav 600 mg QD
Number of Subjects Exposed	16	12	8
Person-Years	4.07	7.73	4.74

*Person-Years defined as the sum of time (in years) exposed to a specific dose level over all patients exposed. All patients dosed are summarized in this table, including one patient whose exposure data of 600 mg not entered into the EDC as of data cut.*

# Major Response Achieved in 89% of Relapsed/Refractory Patients



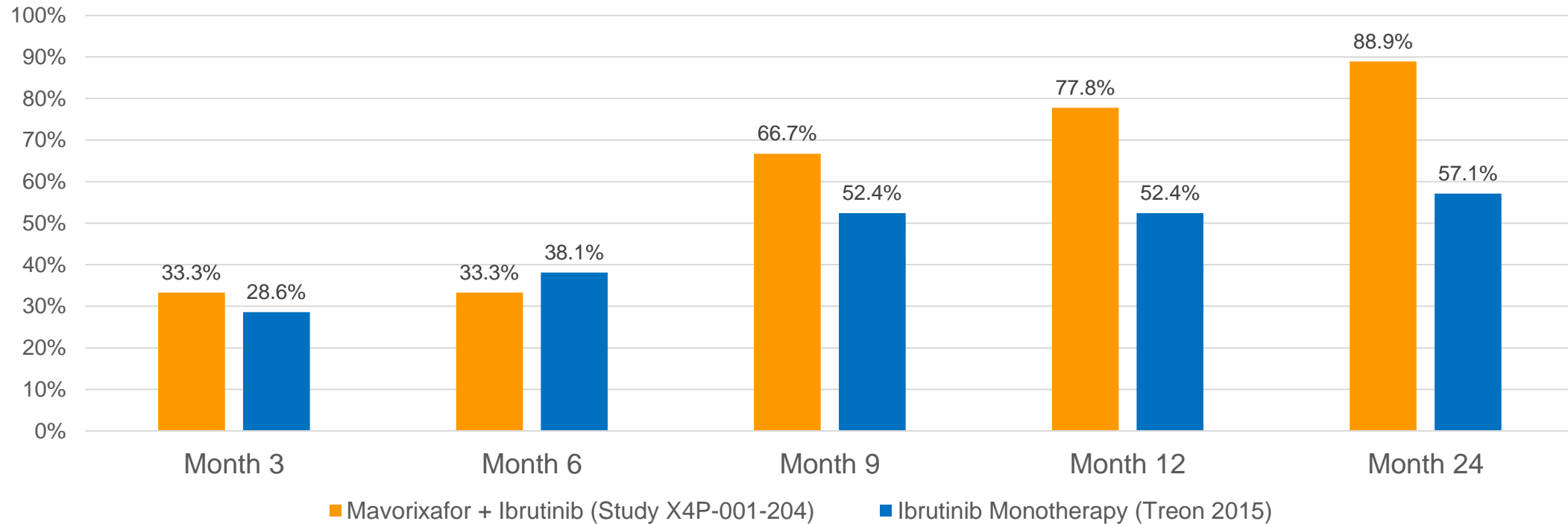
- **89% (8/9) of relapsed/refractory patients achieved  $\geq 50\%$  reduction from baseline in IgM (major response)**
- **In front-line patients (N=6), major responses seen in all patients escalated to >200 mg mavorixafor**

Data Cut as of 12 June 2022, including IgM collected on 05 July 2022 for Subject 101-008  
Duration defined as treatment duration from first dose date to the last dose date or discontinuation date.



# Combination Achieves Greater Response in R/R Group vs. Ibrutinib Monotherapy

## Major Response Over Time in R/R Patients

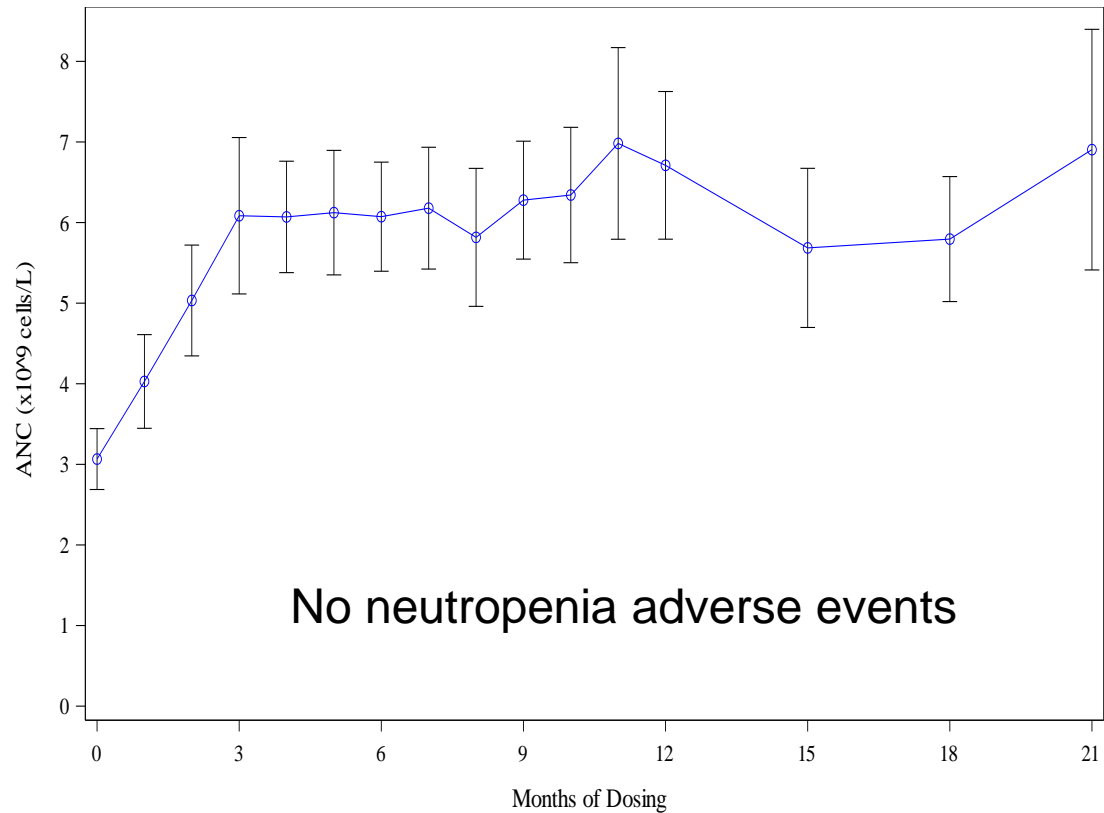


- **Higher major response rate achieved at 9, 12, and 24 months compared to reported values for single agent Ibrutinib**

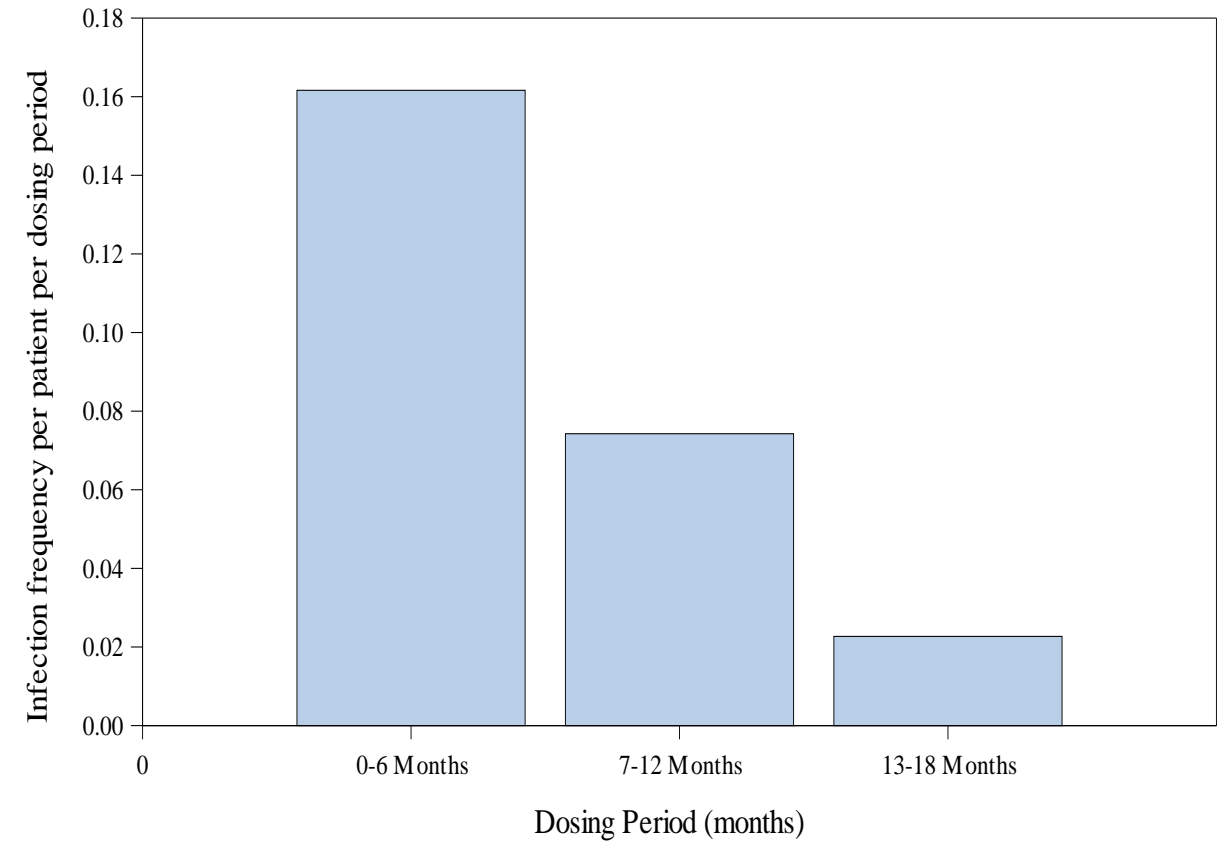
# Mavorixafor-Ibrutinib (QD) Elevates ANC & Reduces Infection Risk in WM Patients



## Mean Absolute Neutrophil Counts (ANC) in Blood of WM Patients Treated with Mavorixafor-Ibrutinib (QD)



## Frequency of Infection Events Per Patient Per Period of Chronic Dosing with Mavorixafor-Ibrutinib (QD)



*Preliminary data as of cutoff July 7, 2022; Study ongoing  
Safety Data & ANC for all 16 patients on study*

# Mavorixafor + Ibrutinib Show Promising Results in Phase 1b Waldenström's Trial

- A total of 16 patients were enrolled in the study
- 10 of 12 evaluable patients (83%) achieved a major response (MR) to therapy ( $\geq$  50% reduction in serum IgM from baseline)
  - 8 of 9 (89%) relapsed/refractory patients achieved a MR
- Mavorixafor + ibrutinib was associated with higher MR rate at 9, 12, and 24 months compared to previously reported MR rates achieved with ibrutinib monotherapy
- Patients achieved elevations in absolute neutrophil count (ANC), with no neutropenic events reported; patients also experienced fewer infections over time with chronic dosing
- Mavorixafor in combination with ibrutinib showed a safety profile similar to ibrutinib monotherapy
  - Mavorixafor well tolerated in all patients escalated to the highest dose of mavorixafor (600 mg) (N=8)
- The Phase 1b clinical trial is expected to be completed in the fourth quarter of 2022
- Mavorixafor granted Orphan Drug Designation by the U.S. FDA for the treatment of Waldenström's, regardless of the CXCR4 mutation status; pre-clinical data support the potential of mavorixafor in patients with wild-type CXCR4, suggesting utility across a broad range of lymphomas
- Further clinical studies in oncology indications will now be subject to completing a strategic partnership



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