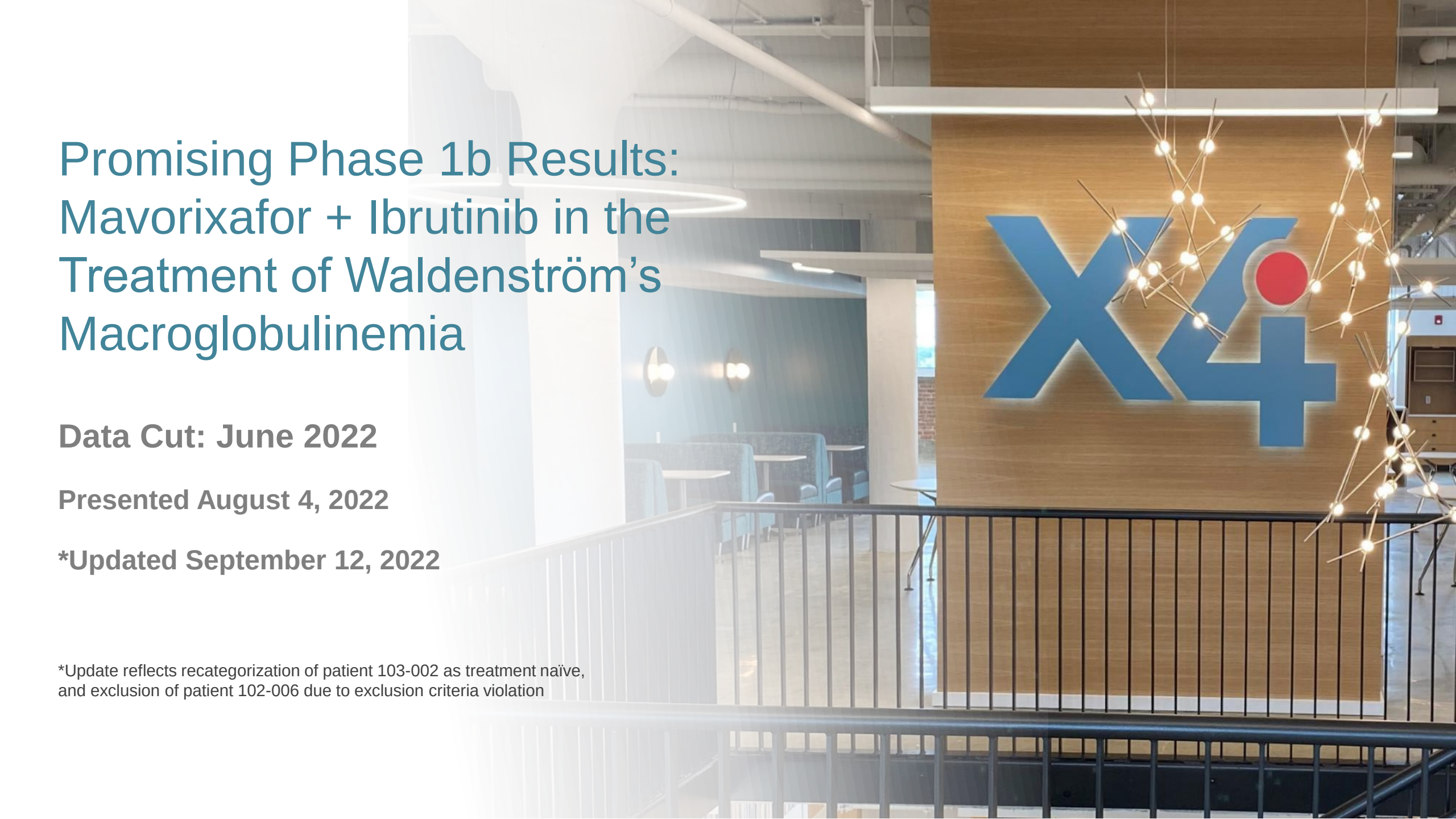
Promising Phase 1b Results: Mavorixafor + Ibrutinib in the Treatment of Waldenström's Macroglobulinemia



Data Cut: June 2022

Presented August 4, 2022

***Updated September 12, 2022**

*Update reflects recategorization of patient 103-002 as treatment naïve, and exclusion of patient 102-006 due to exclusion criteria violation

Forward-Looking Statements

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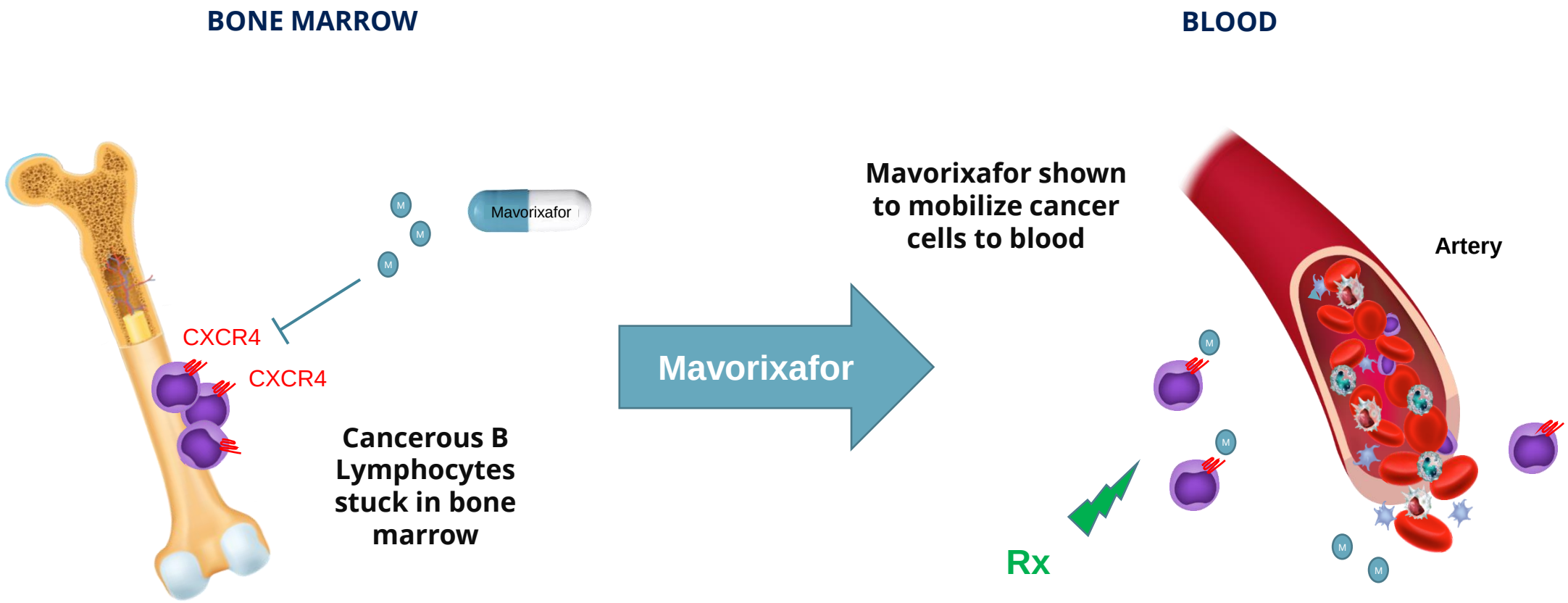
CXCR4 Pathogenesis in B-Cell Lymphomas / MOA of Mavorixafor



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

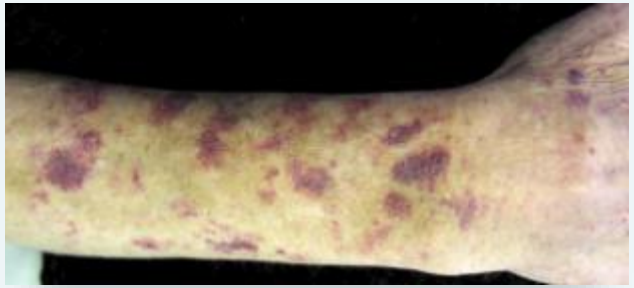
X4 Phase 1b Study

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

1. Burger et al, Blood (2006) 107 (5): 1761–1767. *2. . https://lymphoma.org/aboutlymphoma/nhl/dlbcl/ 3.* https://www.lls.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

About Waldenström's Macroglobulinemia

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[1]

<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[2]

Estimated U.S. other lymphomas

>50,000[3]

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

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

1. Treon *et al,* EHA 2018. 2. *WM Epidemiology Analysis,* The NemetzGroup. 3. See previous slide

Waldenström's Phase 1b Trial: Human Proof of Concept in Patients with CXCR4^{MUT}

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

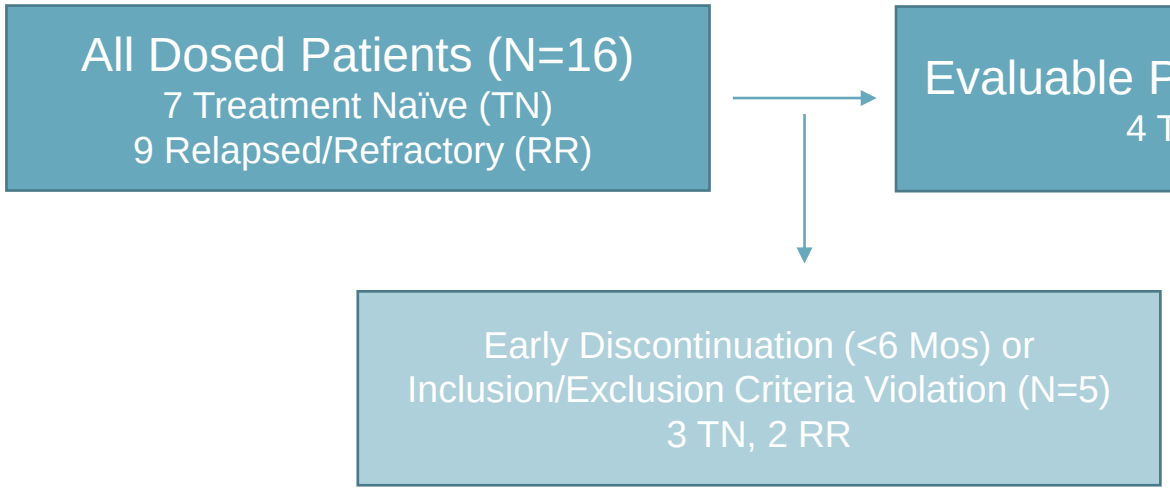
Design: Multi-national Phase 1b trial of mavorixafor in combination with ibrutinib (n=12 to 18)

- **Intrapatient 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

LEUKEMIA & LYMPHOMA SOCIETY®

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

Patient Disposition and Mavorixafor Dose Exposure

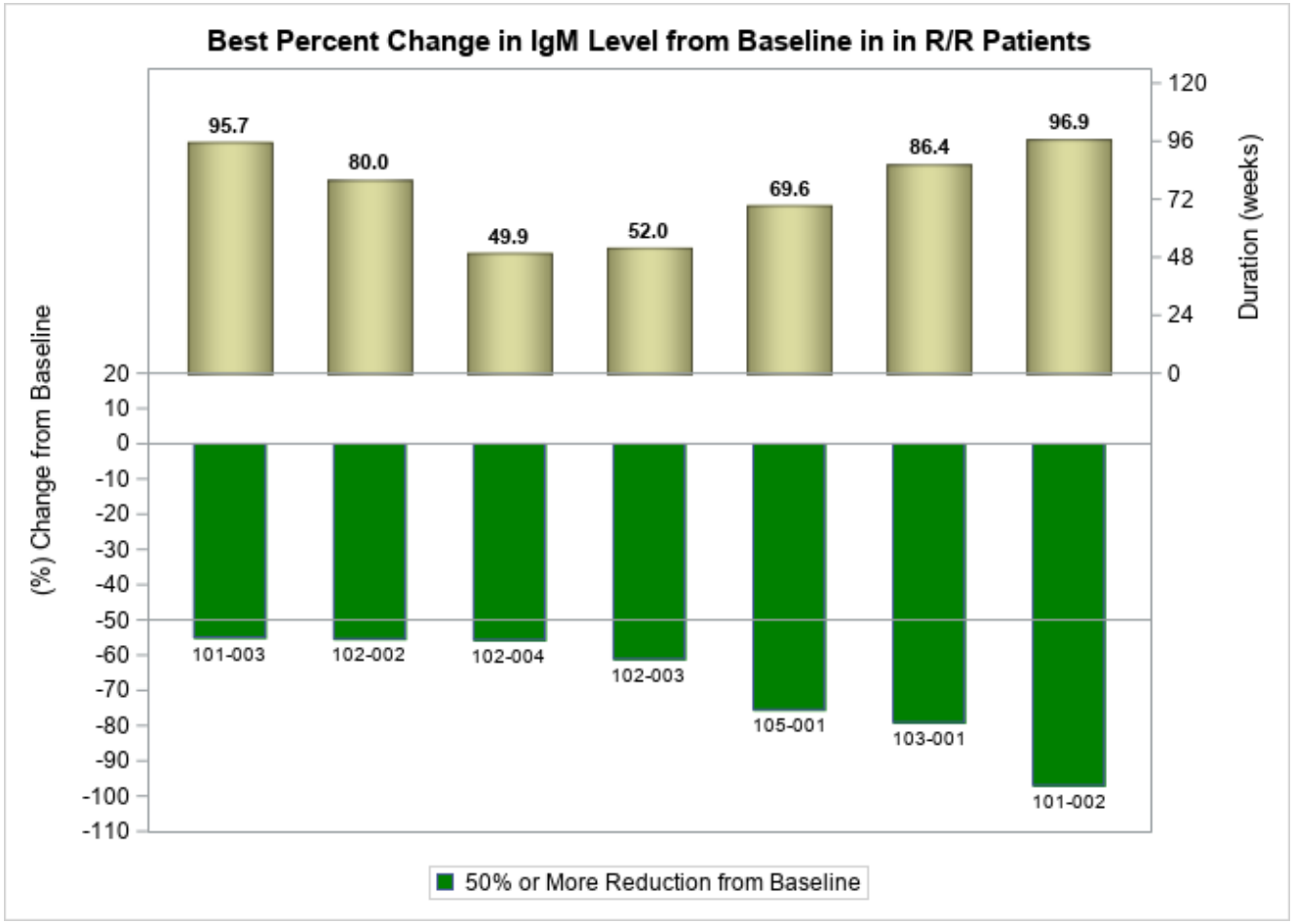


11 patients included in evaluable population as the primary efficacy analysis population

	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.

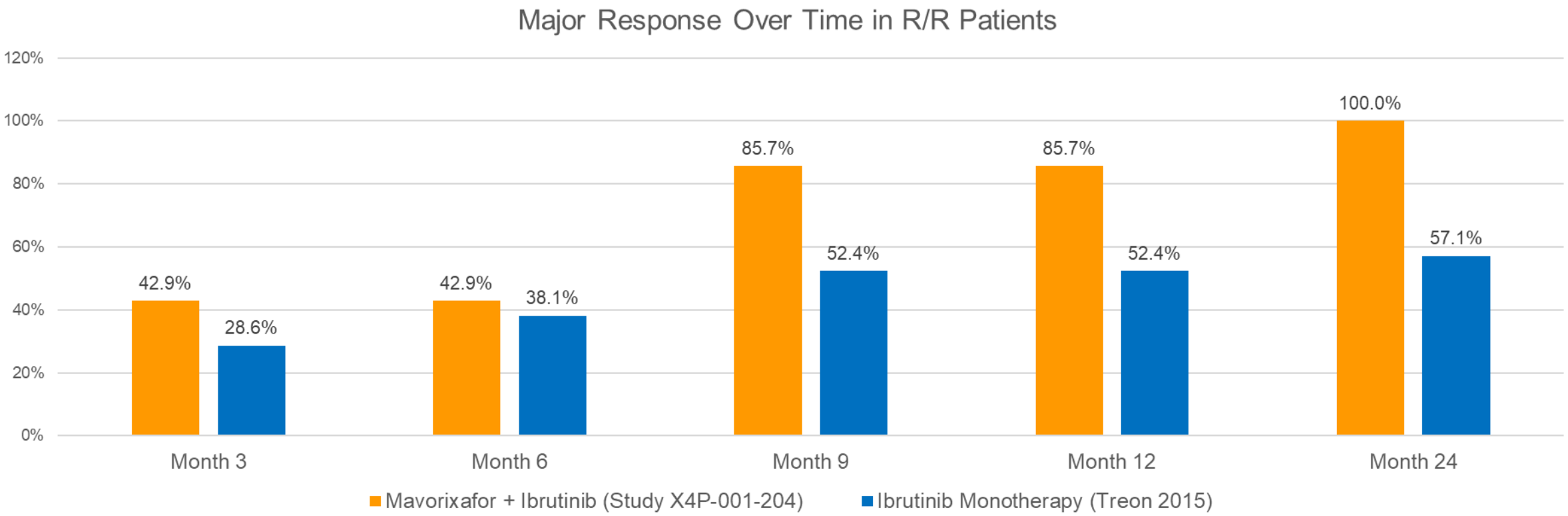
Major Response Achieved in 100% of Relapsed/Refractory Patients



- **100% (7/7) of relapsed/refractory patients achieved ≥50% reduction from baseline in IgM (major response)**
- **In front-line patients (N=4), major responses seen in the 3 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

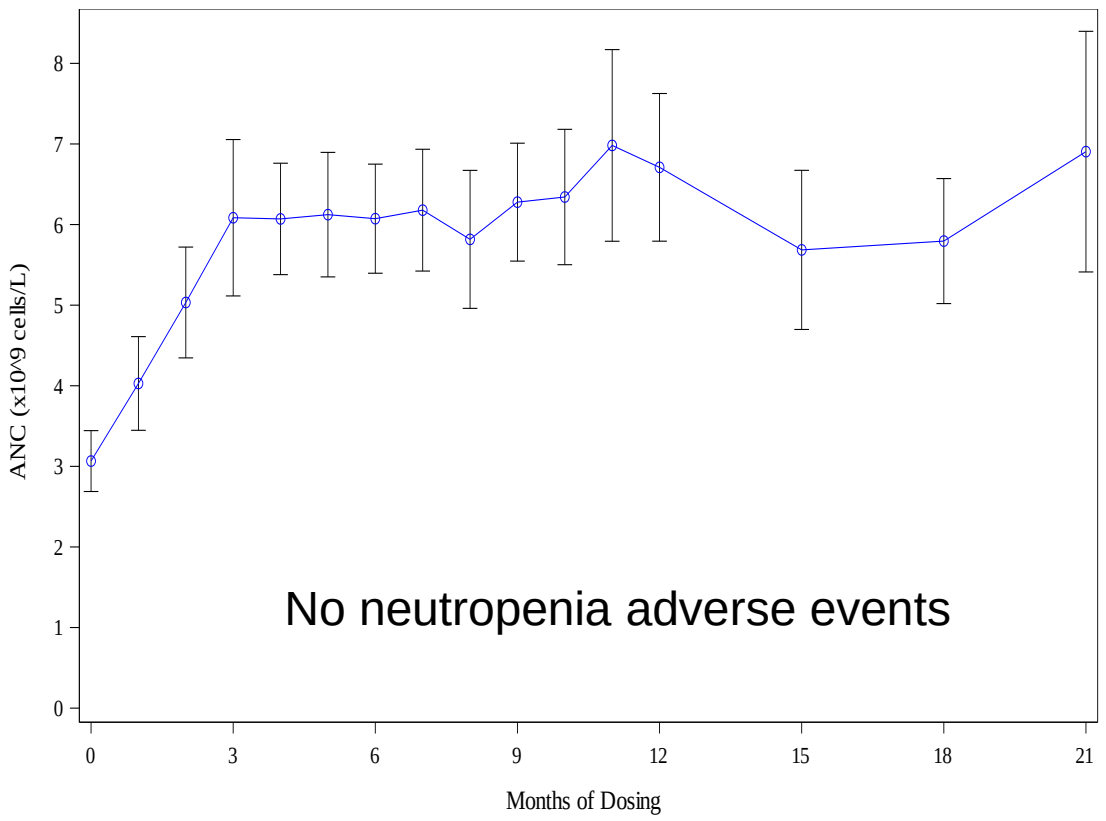


- **Higher major response rate achieved at all timepoints compared to reported values for single agent ibrutinib**
- **Therapeutic effect ≥ 30% above ibrutinib monotherapy observed at 9, 12, and 24 months (Treon, *NEJM* 2015)**

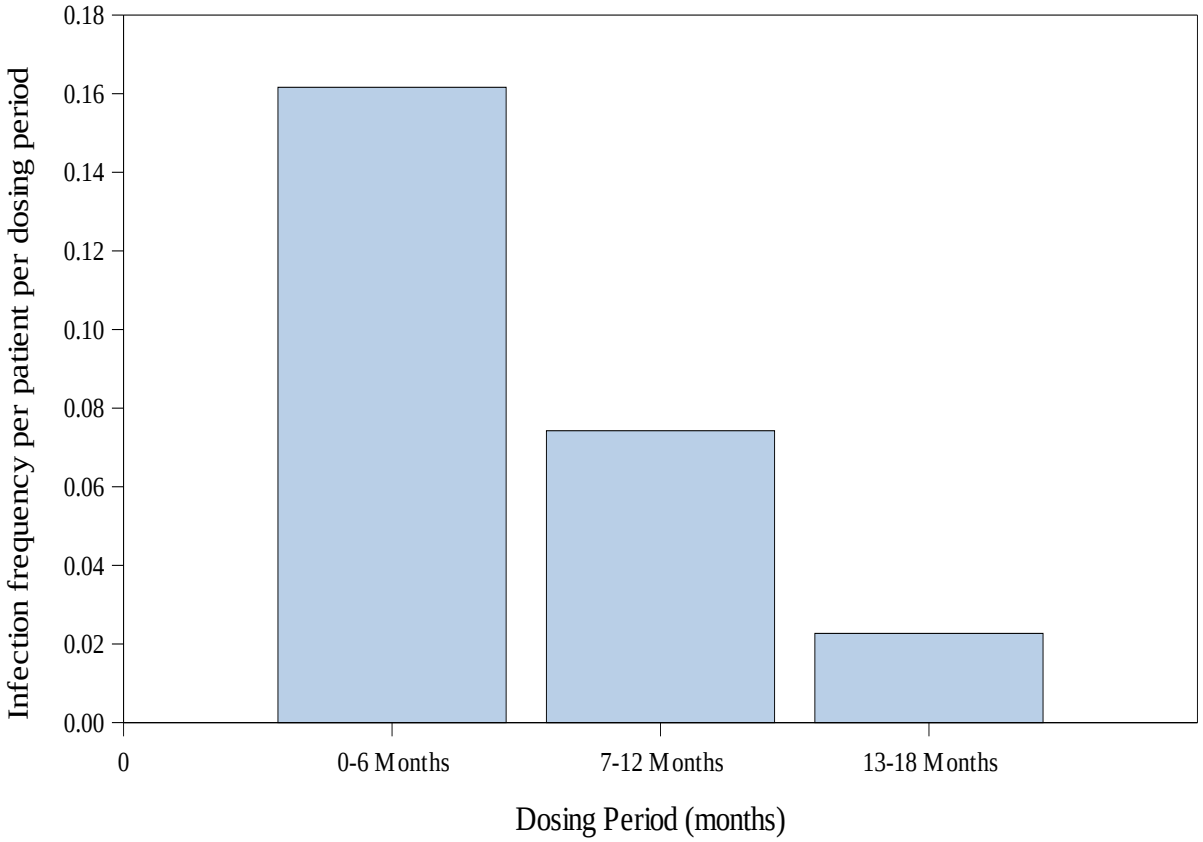
Data Cut as of 12 June 2022, including IgM collected on 05 July 2022 for Subject 101-008.

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

- A total of 16 patients were enrolled in the study (*confirmed MYD88 and CXCR4 mutations*)
- 91% (10/11) of evaluable patients achieved a major response (MR) to therapy (≥ 50% reduction in serum IgM from baseline)
  - 100% (7/7) of relapsed/refractory patients achieved a MR
- In relapsed/refractory patients, mavorixafor + ibrutinib was associated with higher MR rate at all timepoints compared to previously reported MR rates achieved with ibrutinib monotherapy (Treon, *NEJM* 2015)
- Patients achieved elevations in absolute neutrophil count (ANC), with no neutropenic events reported; patients also experienced a reduction in 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, including those escalated to the highest dose of 600 mg (N=8)
- The Phase 1b clinical trial is expected to be completed in the fourth quarter of 2022
- Pre-clinical data (not shown) support the potential of mavorixafor in patients with wild-type CXCR4, suggesting utility across a broad range of lymphomas
- Mavorixafor granted Orphan Drug Designation by the U.S. FDA for the treatment of Waldenstrom's, regardless of CXCR4 mutation status
- Further clinical studies of mavorixafor in oncology indications will now be subject to completing a strategic partnership

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