Supplemental Slides

ASH 2021: Data from ongoing Phase 1b clinical trial in double-mutation patients with Waldenström's Macroglobulinemia

December 16, 2021

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Waldenström's Phase 1b Trial: Generating PoC 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)

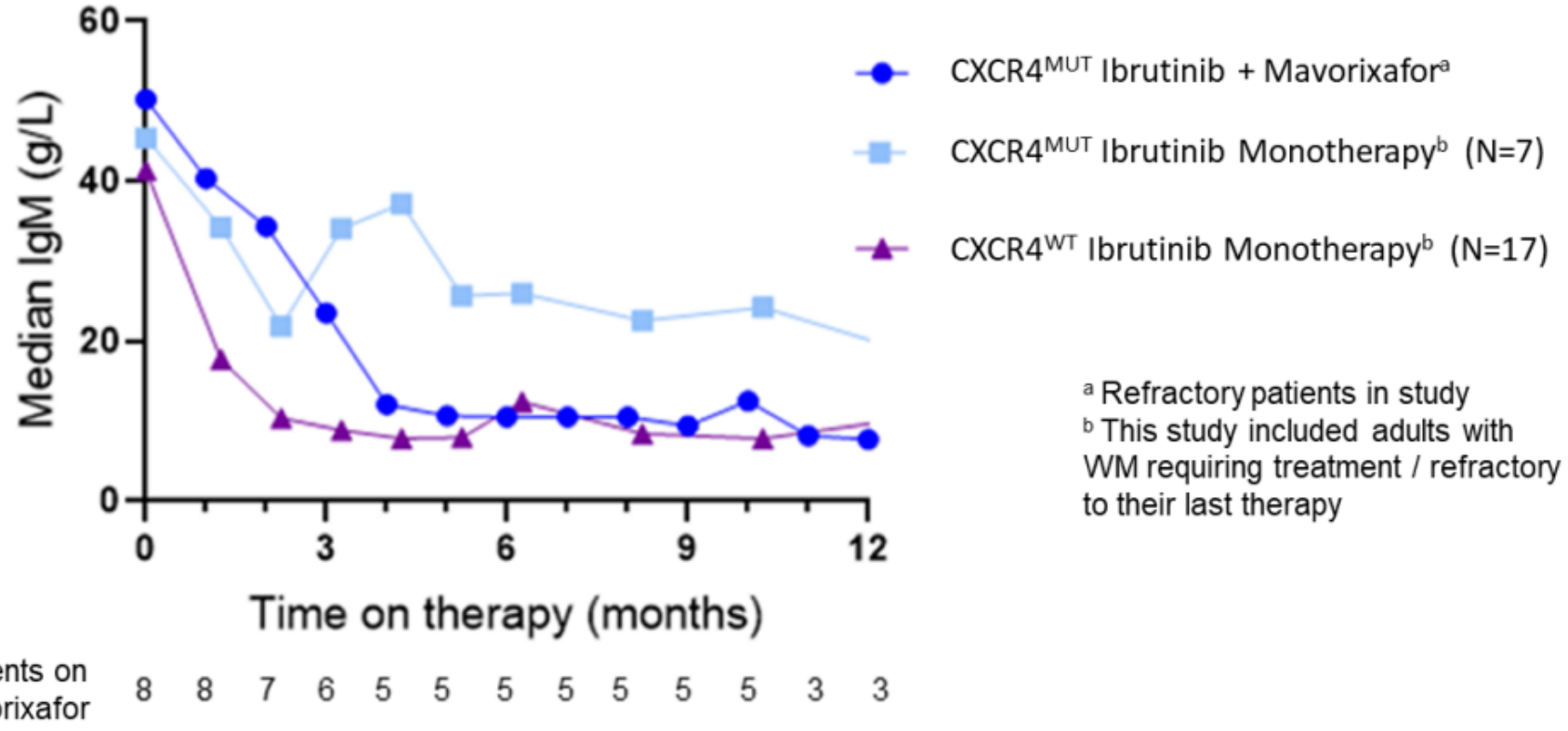
- **Intrapatient dose-escalation:** cycles of 200 mg, 400 mg, and 600 mg QD
- **3 cohorts supporting dose selection of mavorixafor:**
  - Cohorts A & B: minimum of 6 patients enrolled in each
  - Cohort C (expansion): potential for additional 6 patients dosed up to 600 mg
- **Endpoints**
  - Safety, 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

ASH 2021: Data Support Mavorixafor Proof-of-Concept in Waldenström's Particularly in Refractory Patient Population

Refractory Patients' Serum IgM Levels After Treatment with Mavorixafor + Ibrutinib vs. Ibrutinib Monotherapy With or Without CXCR4 Mutations



[a] Refractory patients in study
[b] This study included adults with WM requiring treatment / refractory to their last therapy

Adapted from *The Lancet Oncology*, 18, Dimopoulos MA, 241-250, © 2017, with permission from Elsevier

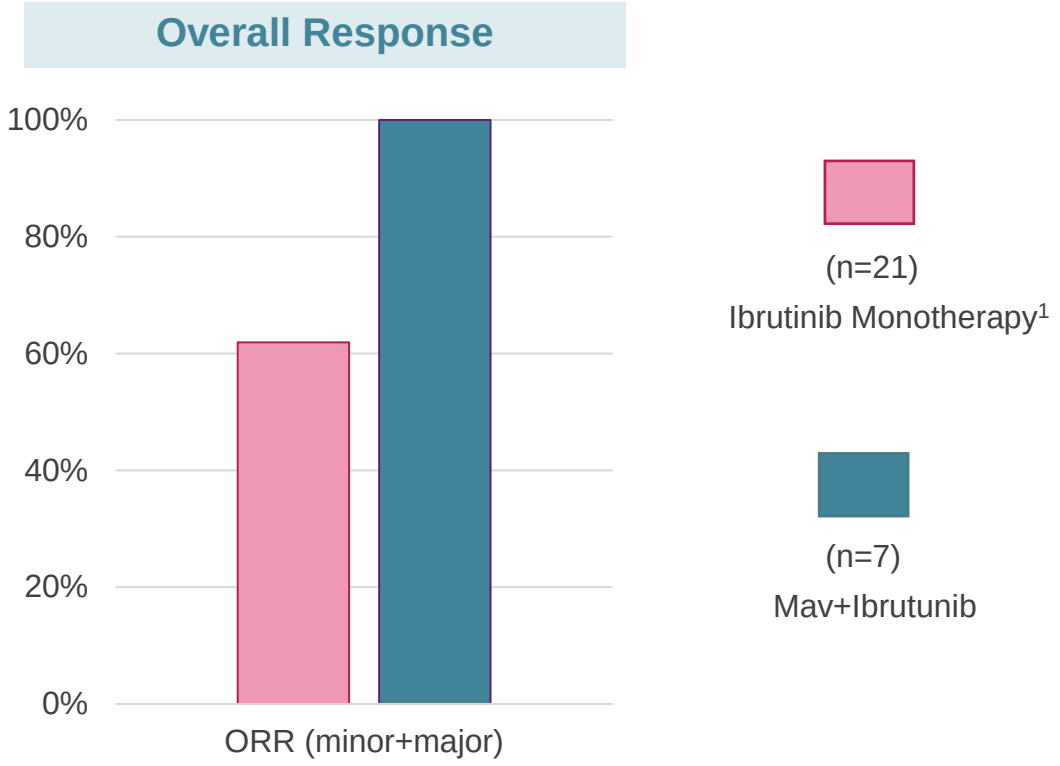
Response Rate: X4 ASH Data vs. **Benchmarks of Ibrutunib Monotherapy**
*After 6-Months of Treatment in **R/R Patients with CXCR4 Mutations***

X4 ASH 2021 Poster

Table 3. Clinical Response Rates

Response Category	Overall (n=10)	Frontline (n=3)	Relapse/Refractory (n=7)
ORR, n (%)	10 (100)	3 (100)	7 (100)
Major response (CR+VGPR+PR), n (%)	4 (40)	1 (33)	3 (43)
VGPR n (%)	1 (10)	0 (0)	1 (14)
PR n (%)	3 (30)	1 (33)	2 (29)
MR n (%)	6 (60)	2 (67)	4 (57)

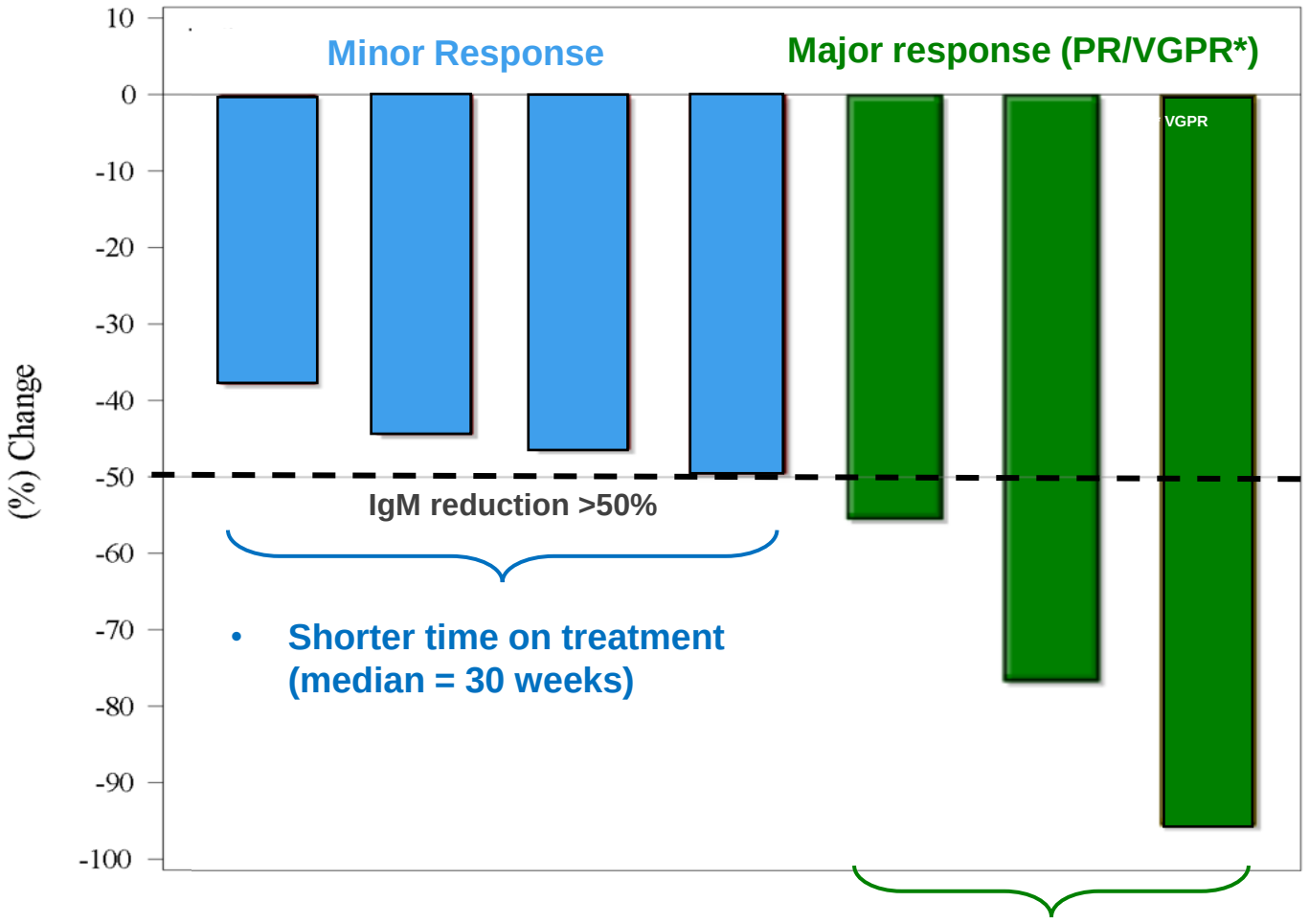
X4 ASH 2021 Vs. Benchmarks



1. Treon S et al. *NEJM*, 2015. – Figure S1(A and B) at Cycle 6 ; Note: VGPR Data are not provided; no benchmark available.

Additional Patient-Level Data from X4's Trial

Clinical Responses in Individual R/R Patients (N=7)
(based on Best IgM Response)



- Major Responses achieved after median 52 weeks on treatment
- Additional patients treated for median 30 weeks; all remain on treatment
- Highest dose (600 mg QD) is being evaluated
- Ibrutinib monotherapy benchmark = 38% major response at 6 months[1]

Major Response IgM Threshold

1. Treon S et al. *NEJM*, 2015

Patient Specific Information Related to Reported Safety in WM Phase 1b Trial

Patient with Grade 5 Fatality: 81 yo with relapsing disease

- Prior to study, **patient required plasmapheresis** and red blood cell transfusion
  - Rapidly rising IgM/cancer progression required plasmapheresis, which removes antibody and other blood components, making it harder to fight infections
- Patient entered the study with history of **recurrent respiratory infections including lung infections**
  - Resulted in prior discontinuation of rituximab
- Patient was on treatment for **less than 4 weeks** and at the lowest dose of Mavorixafor and highest dose of ibrutinib.
  - Median time of treatment for other patients was 39 weeks; most at twice the dose (400 mg QD) – no sepsis identified

Patient with Cryptococcal Infection: 71 yo

- Crypto-positive lung lesion identified before treatment
  - Demonstrating pre-existing infection
- Patient was treated for crypto and restarted study medications
- Patient **remains on-study at lower dose**

Known Safety Issues w/ Ibrutinib

- Serious infections are a risk of ibrutinib
- >50 cases of crypto reported (via FDA database)
- Aspen WMs trial: 3% (3/98) had sepsis on ibrutinib; 2/3 were fatal

No Impact to Mavorixafor Ongoing Trials

- FDA has reviewed all data including fatality; no changes recommended to any ongoing trial
- Independent Data Monitoring Committee reviewed all WM safety; no changes, dose-escalation supported
- >200 patients dosed with mavorixafor; no evidence of sepsis or cryptococcal infections
- WHIM Phase 2 study demonstrates a >60% reduction in infections while on treatment

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