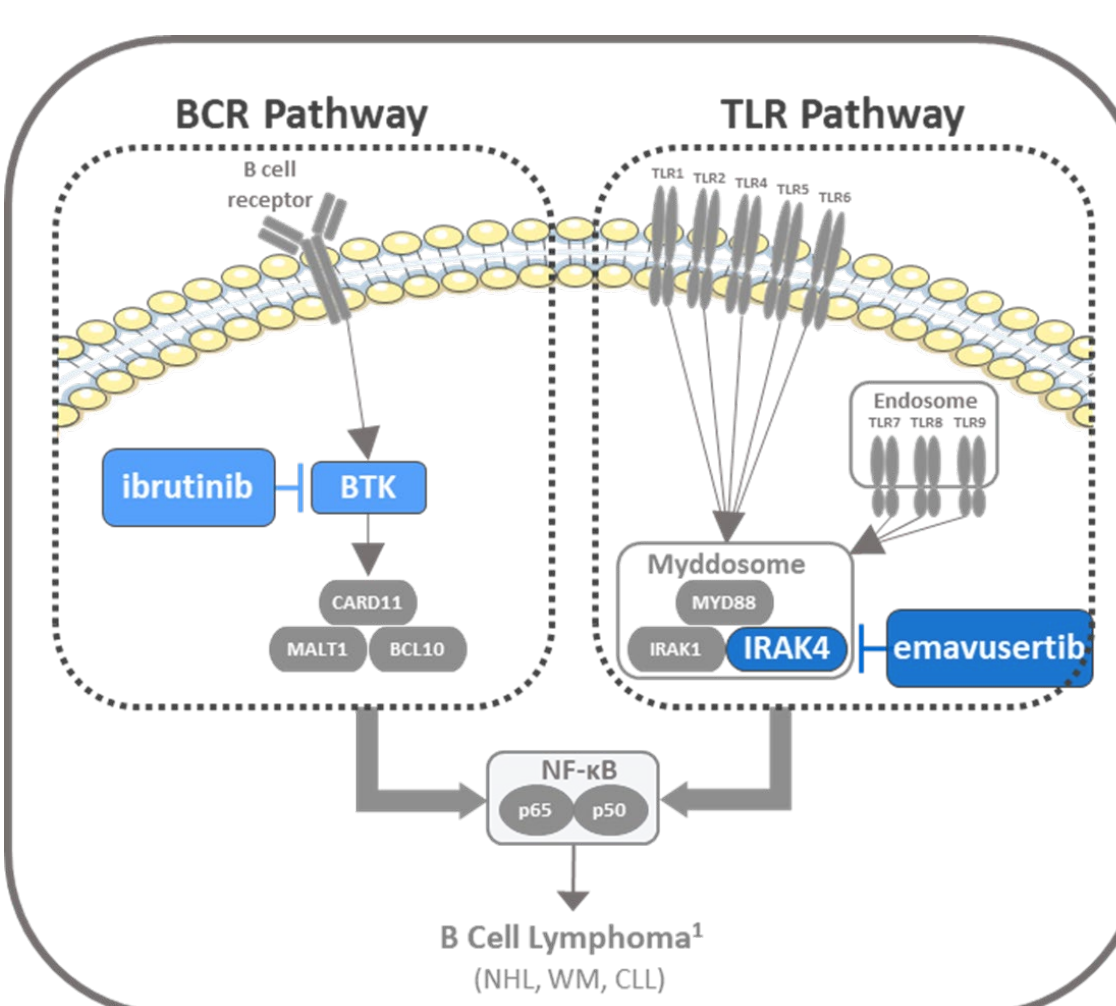


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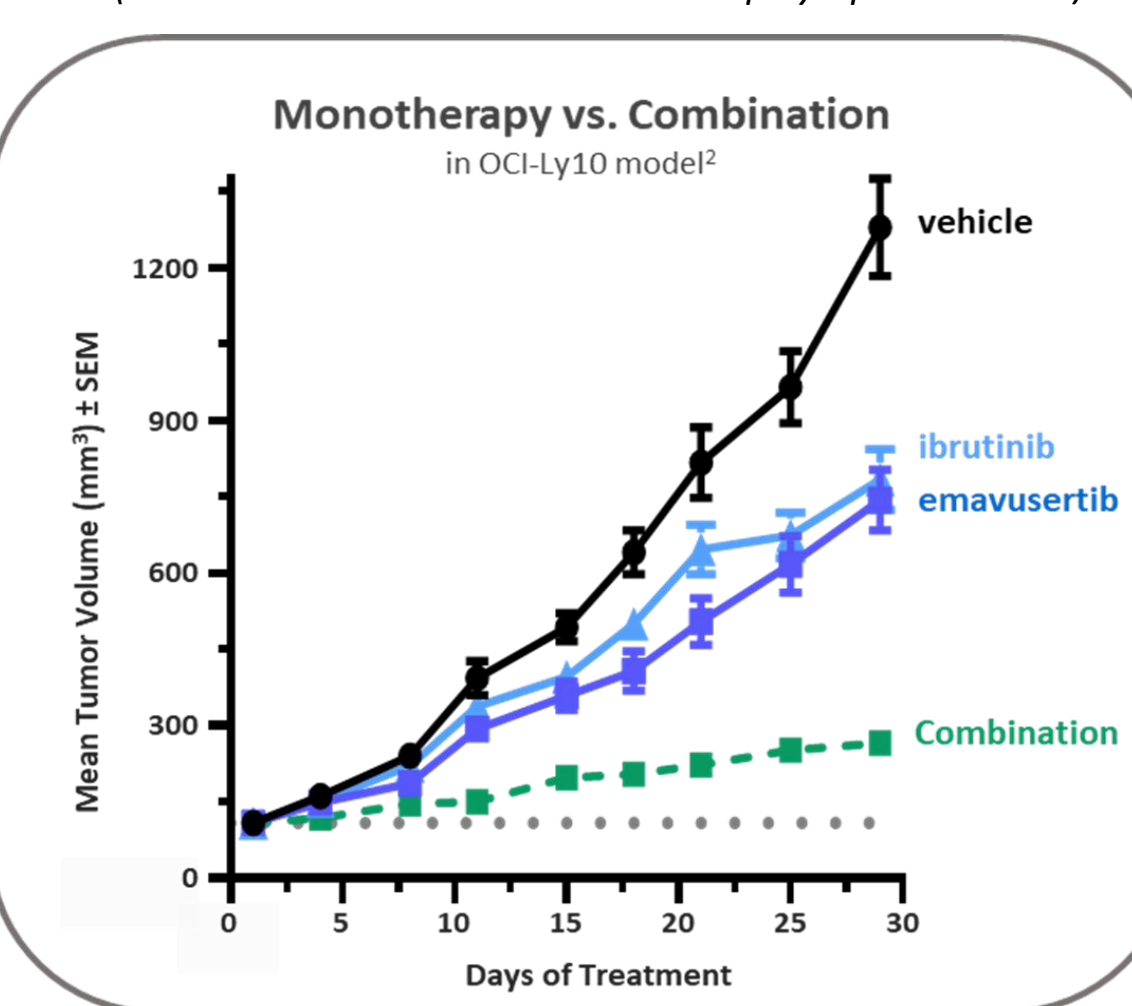
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INTRODUCTION

BCR and TLR Pathways independently drive NF-κB overactivity (IMBRUVICA Package Insert, Rev 08/2018)



In preclinical testing, blocking both IRAK4 and BTK drove tumor reduction better than blocking either one alone (Booher et al. Waldenström Roadmap Symposium 2019)



IRAK4 is essential for TLR and IL-1R signaling in B-cell proliferation forming multiprotein complexes causing inflammation and tumor growth (1, 2)

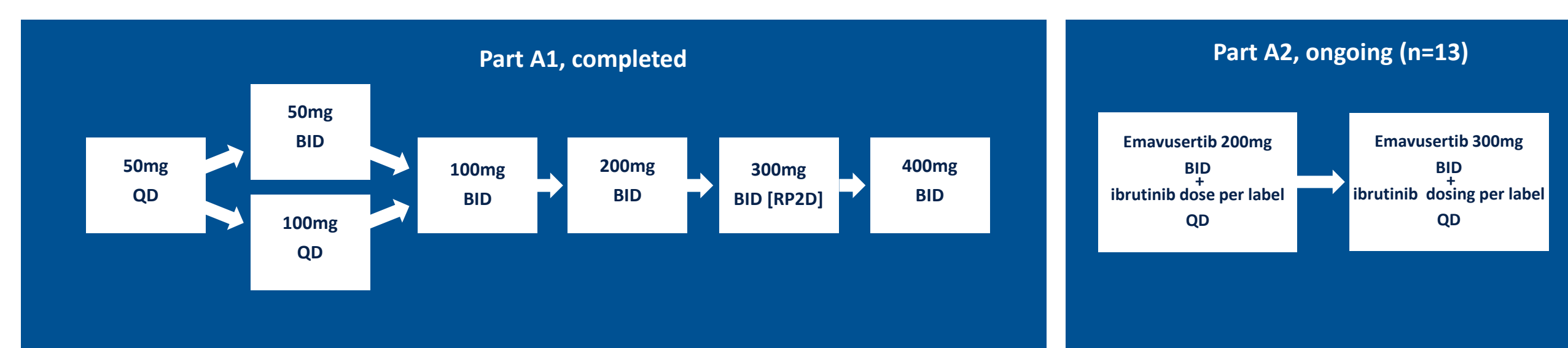
Emavusertib, a novel oral IRAK4 inhibitor, dosed twice daily has previously shown:

- Single agent activity in R/R non-Hodgkin Lymphoma patients (3)
- Demonstrated in preclinical studies to overcome tumor resistance to ibrutinib and PI3K inhibitors (4)
- Crossed the blood-brain barrier, reversed IRAK4 pathway activity and caused tumor regression, including cure in a murine PDX model with transplanted A20 NHL to the brain (5)
- Showed in-vivo synergy in B-cell NHL in combination with ibrutinib (6)

STUDY DESIGN

TakeAim-Lymphoma (NCT03328078)

- Part A1:** dose escalation of emavusertib as monotherapy
- Part A2:** dose escalation of emavusertib in combination with ibrutinib
 - Endpoints of Part A1 and A2 include safety, tolerability, and RP2D
 - Treatment: Oral, once-daily (QD), or twice-daily (BID), dosing in continuous 21-day cycles
- Part B:** expansion cohorts of emavusertib in combination with ibrutinib (not yet initiated)



Abbreviations
Relapsed/Refractory (R/R), Marginal Zone Lymphoma (MZL), Diffuse Large B-Cell Lymphoma (DLBCL), Primary Central Nervous System Lymphoma (PCNSL), Non-Hodgkin Lymphomas (NHL), Mantle Cell Lymphoma (MCL), Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), Recommended Phase II Dose (RP2D)

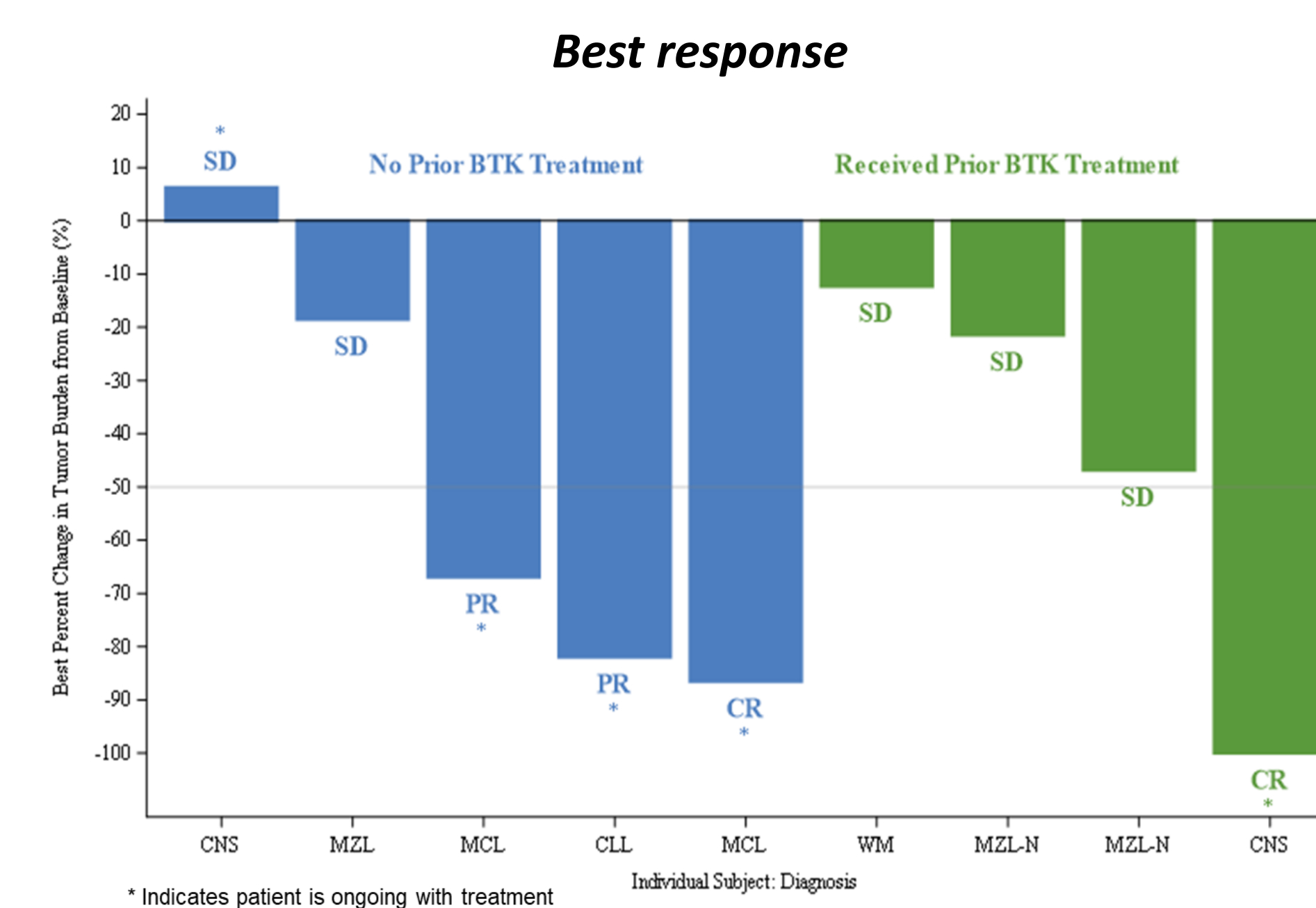
RESULTS

- 13 patients received emavusertib + ibrutinib combination therapy: 8 patients discontinued treatment due to adverse event (2), PD (3), and other (3)
- Emavusertib in combination with ibrutinib is well tolerated
- No DLTs observed at 200mg, 2 DLTs observed at 300mg (Stomatitis and Syncope)

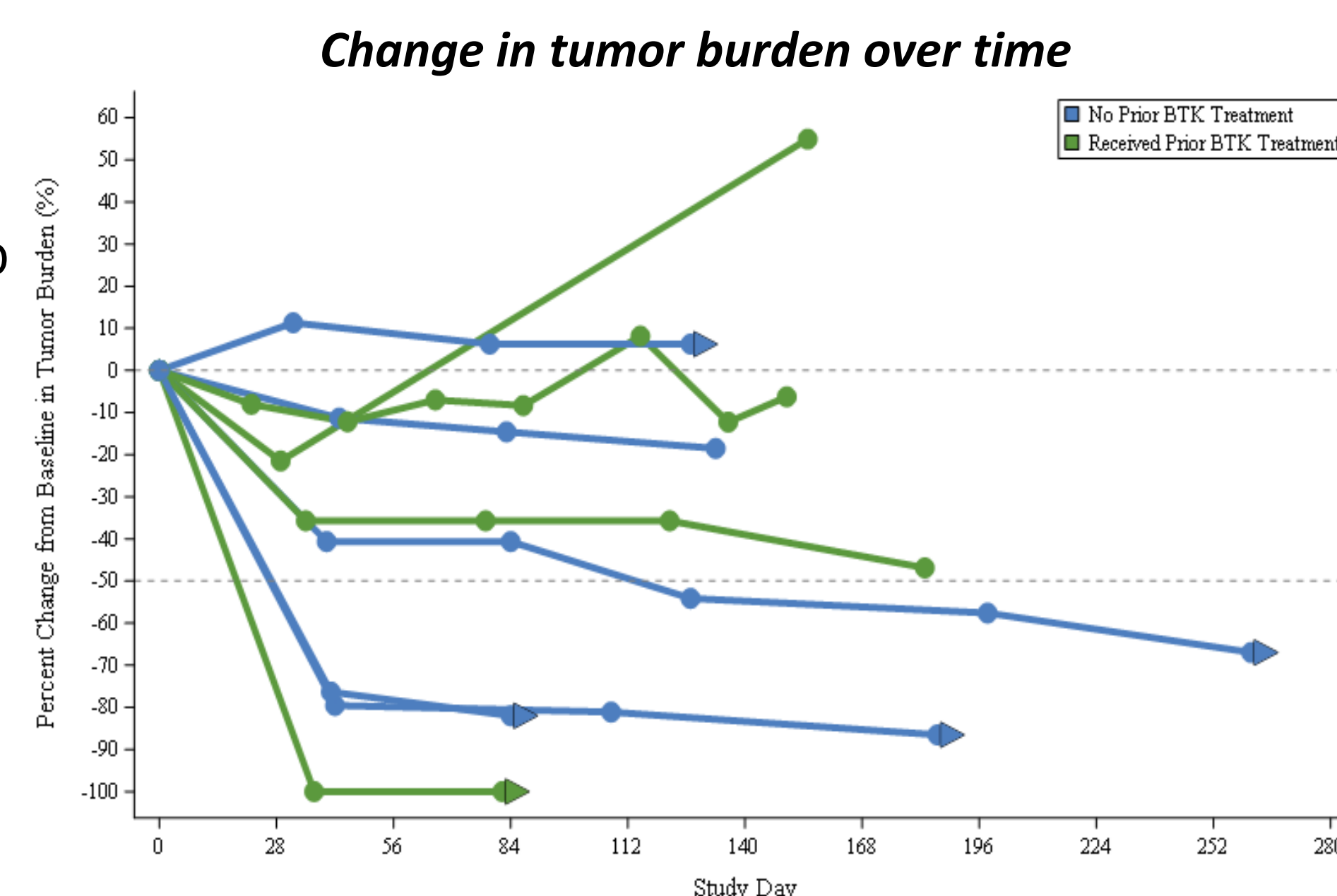
Combination therapy	Total (N = 13)	Safety			
		Emavusertib 200 mg BID		Emavusertib 300 mg BID	
		ibrutinib 420 mg QD (N = 1)	ibrutinib 560 mg QD (N = 5)	ibrutinib 420 mg QD (N = 3)	ibrutinib 560 mg QD (N = 4)
Female n : Male n	6 : 7	# patients having grade 3+ TRAEs			
Age (yrs): median (range)	66 (56, 92)	Platelet count decreased			
Diagnosis		Alanine aminotransferase increased			
		Anaemia			
CLL	2	Aspartate aminotransferase increased			
PCNSL	2	Asthenia			
DLBCL	2	Blood alkaline phosphatase increased			
MCL	2	Diarrhea			
MZL	3	Fatigue			
WM	2	Hyponatraemia			
Prior lines of therapy: median (range)	3 (1-8)	Lipase increased			
		Muscular weakness			
Prior BTK inhibitor	6	Pain			
		Stomatitis			
		Syncope			
		Thrombocytopenia			
		Vomiting			

Evaluable Patients treated with emavusertib + ibrutinib

- 4 patients that received prior BTK treatment show promising anti-cancer activity (SD/CR)
- 4/13 patients were not evaluable for tumor burden; 1 patient progressed without evaluable tumor burden; 3 patients had no response assessments prior to discontinuation of treatment (1 due to adverse event, 1 died, 1 other)

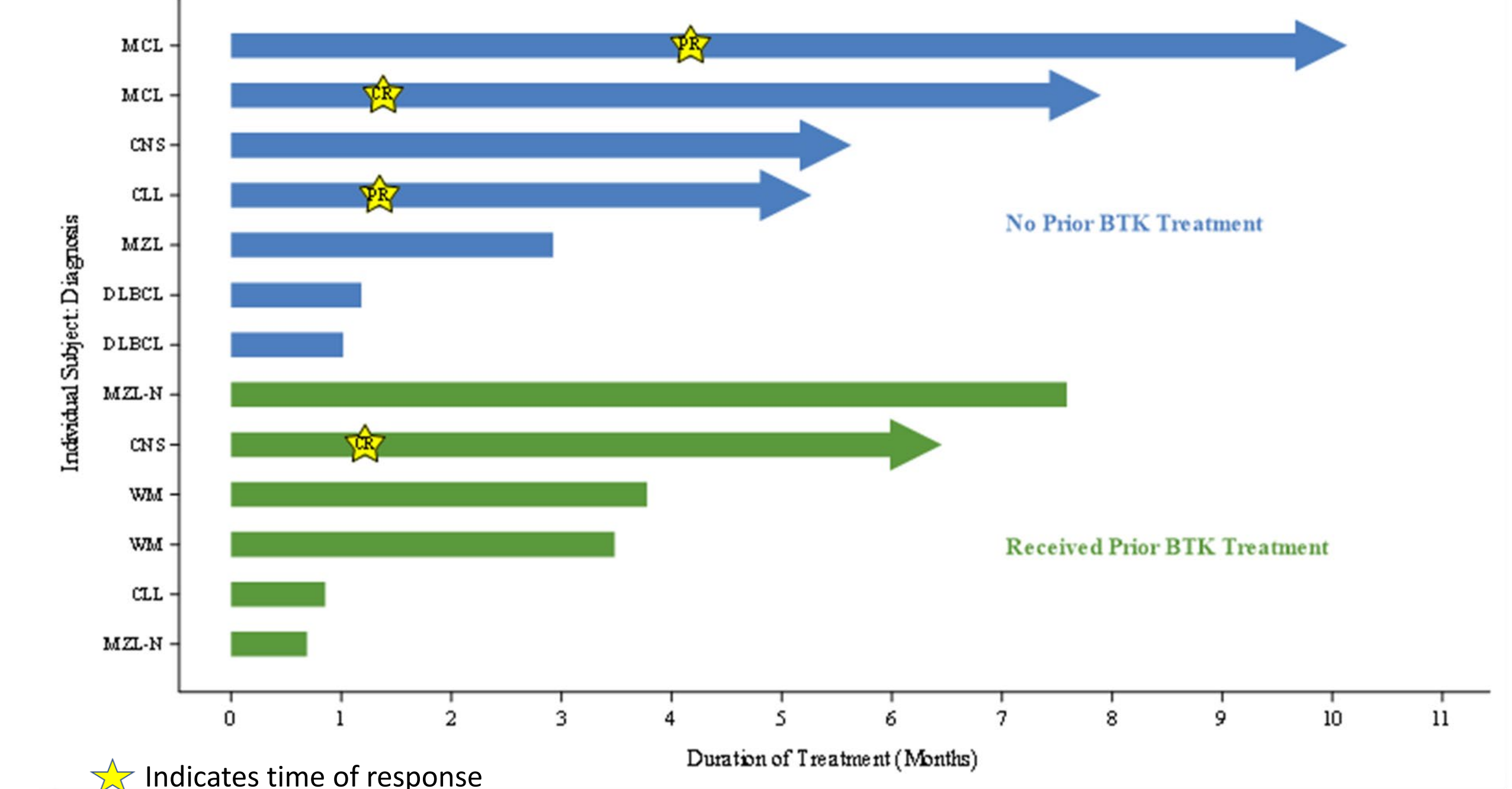


- Majority of patients had decreases in tumor burden or SD over time



RESULTS

Preliminary Efficacy Data From Patients with Combination Therapy



Data extracted May 6th, 2022

SUMMARY

- In prior clinical studies oral emavusertib monotherapy appears to be well tolerated with an acceptable long term safety profile
- Preliminary data suggest that combination therapy may overcome ibrutinib resistance in hematological malignancies
- Objective responses occurred at both 200mg and 300mg BID dose levels. All responding patients are presently being treated at 200mg BID of emavusertib with full dose of ibrutinib

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