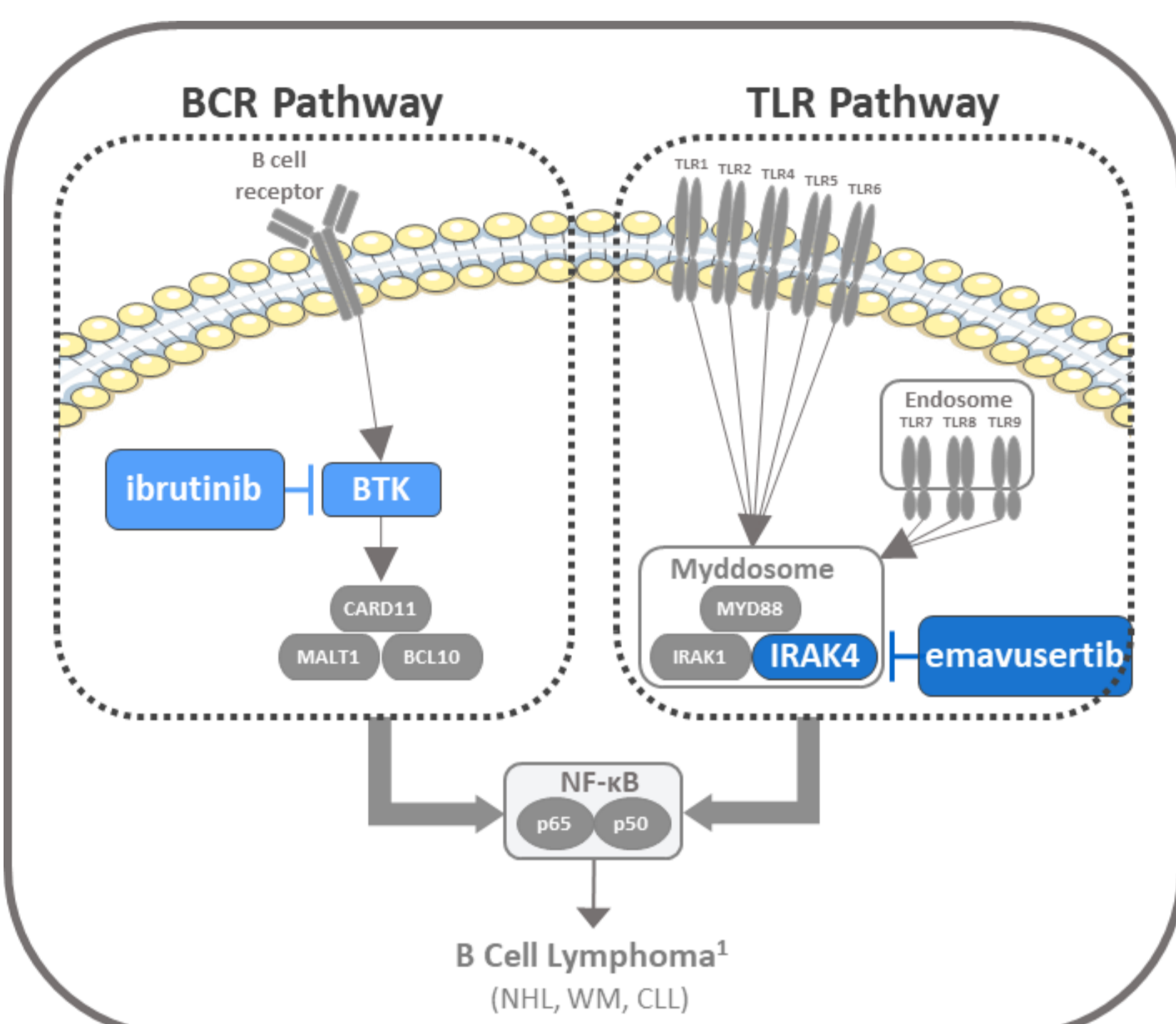


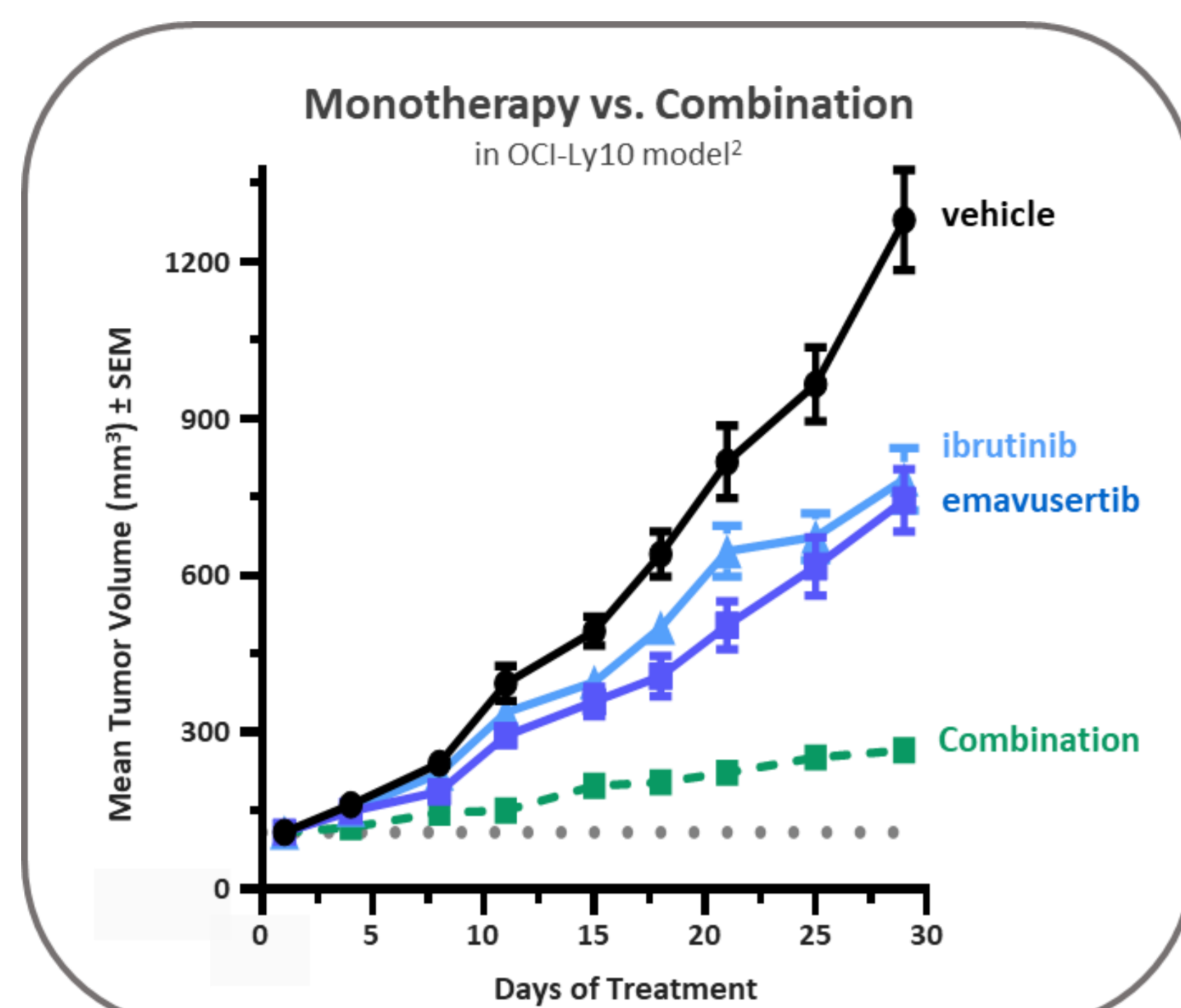
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## INTRODUCTION



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)

Interleukin-1 receptor associated kinase 4 (IRAK4) is essential for TLR and IL-1R signaling in B-cell proliferation. It forms a Myddosome complex with MYD88 adaptor protein and drives overactivation of NF-κB, causing inflammation and tumor growth<sup>(1,2)</sup>

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

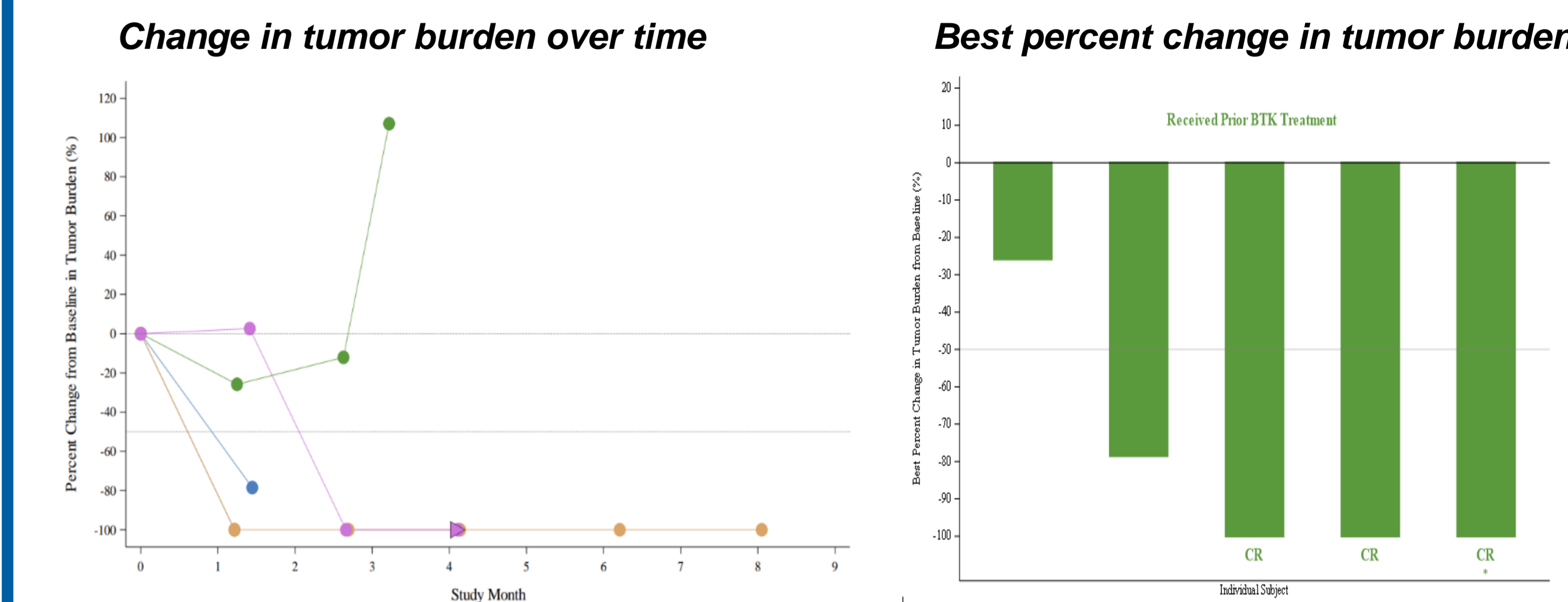
- Demonstrated an acceptable long term safety profile in monotherapy cohort of TakeAim Lymphoma trial, showing single agent activity in R/R NHL patients<sup>(3)</sup>
- Demonstrated the ability to overcome tumor resistance to ibrutinib and PI3K inhibitors in preclinical studies<sup>(4)</sup>
- Crossed 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<sup>(5)</sup>
- Shown in-vivo synergy in B-cell NHL in combination with BTK inhibitors, including ibrutinib, acalabrutinib, and zanubrutinib, potentially enhancing patient sensitivity to BTK inhibitor therapy and promoting resensitization to BTKi treatment<sup>(6,7)</sup>

## BASELINE CHARACTERISTICS

	Total (N=19)	Grade 3+ Treatment-Related Adverse Event Occurred in >1 Patient	100 mg BID+IBR (N=2)	200 mg BID+IBR (N=10)	300 mg BID+IBR (N=7)	Total (N=19)
Female n : Male n	8: 11					
Age (yrs): median (range)	64.0 (5, 72)					
<b>Diagnosis</b>						
CNSL	7		1 (50)	7 (70)	6 (86)	14 (74)
MZL	3			2 (20)	1 (14)	3 (16)
CLL	2					
MCL	2					
DLBCL	2			1 (10)	1 (14)	2 (11)
WM	2			1 (10)	1 (14)	2 (11)
FL	1					
Prior lines of therapy: median (range)	3.0 (1 - 10)					
Prior BTK inhibitor	11		1 (50)	1 (10)		2 (11)

- As of October 12<sup>th</sup> 2023, 19 heavily pretreated NHL patients have received emavusertib at 100, 200 and 300 mg BID in combination with prescribed ibrutinib doses
- Median number of prior lines of anti-cancer therapies is 3.0 (range 1-10) and 11 patients had failure to previous BTKi treatment
- Emavusertib in combination with ibrutinib is, in general, well tolerated with an acceptable safety profile
- No DLTs observed at 100mg or 200mg and 2 reversible DLTs observed at 300mg (stomatitis and syncope)
- No cases of Grade 3 or higher rhabdomyolysis were reported in the patients treated with emavusertib at 200mg BID in combination with ibrutinib

## PCNSL EMAVUSERTIB + IBRUTINIB EFFICACY



- 5 evaluable PCNSL patients previously treated with BTKi showed promising anti-cancer activity, with 3 patients achieving CR and one patient having a durable response for approximately 7 months

Data extracted October 12<sup>th</sup>, 2023

## CONCLUSIONS

- The combination of emavusertib plus ibrutinib is well tolerated with an acceptable and manageable safety profile.
- Emavusertib in combination with ibrutinib showed promising efficacy with several objective responses in heavily pretreated patients, including BTKi naïve and experienced patients.
- Patients who have progressed on prior BTKi treatment are re-sensitized to BTKi treatment in combination with emavusertib.
- Based on these promising results, the combination emavusertib + ibrutinib is being explored in an expansion cohort of PCSNL patients at 200 mg BID.

## ACKNOWLEDGEMENTS

We would like to thank the patients, their families and caregivers for their invaluable contribution and participation in this study.

## CONTACT INFORMATION

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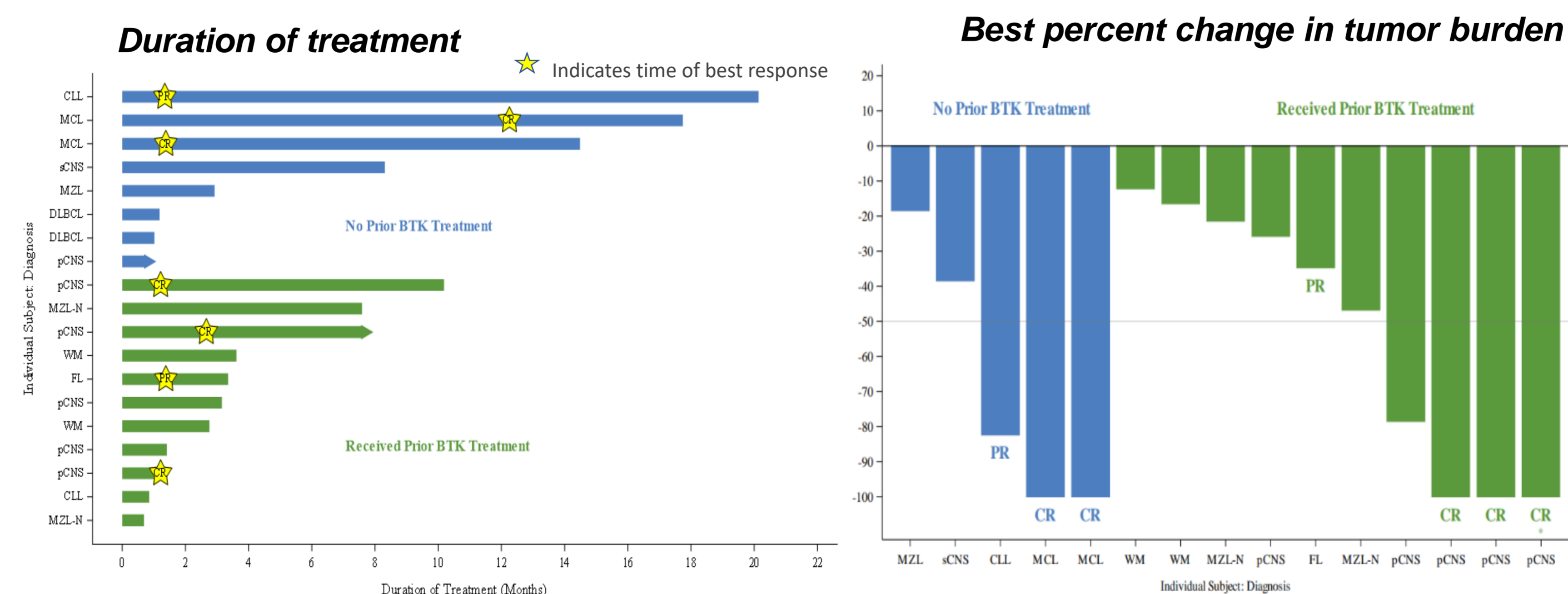
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Data extracted October 12<sup>th</sup>, 2023

## RESULTS

### 19 NHL Patients treated with emavusertib + ibrutinib



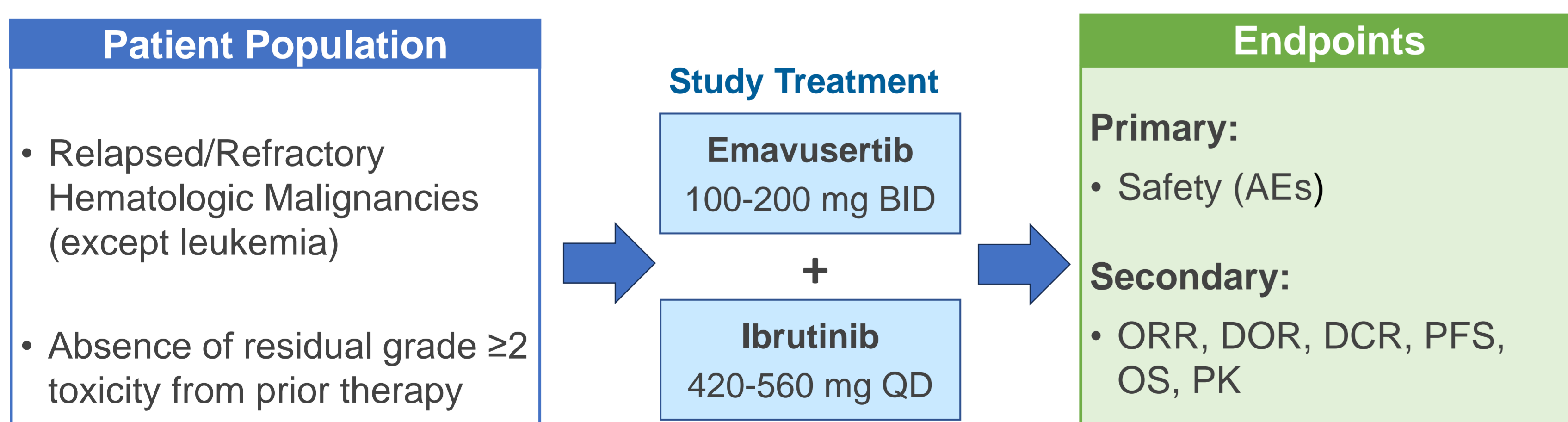
- From 19 treated patients, 11 patients had received prior BTKi treatment and showed promising anti-cancer activity with 5 CRs.
- Median treatment duration was 96 days (range 21-613 days), suggesting acceptable safety and tolerability.
- Majority of patients had decreases in tumor burden or stable disease over time.
- The preliminary efficacy data of 16 evaluable patients in combination with ibrutinib showed 5 CR (2 MCL, 3 PCNSL).

Data extracted October 12<sup>th</sup>, 2023

## STUDY DESIGN

### TakeAim-Lymphoma (NCT03328078)

Part A2: Dose escalation of emavusertib in combination with ibrutinib



- Endpoints include safety, tolerability, and anti-cancer activity evaluation

### 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), Chronic lymphocytic leukemia (CLL), Follicular Lymphoma (FL), Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), Duration of Response (DOR), Disease Control Rate (DCR), Progression-Free Survival (PFS), Adverse Event (AE), twice daily (BID), once daily (QD).