SEQUOIA: 5-YEAR FOLLOW-UP

SNEAK PREVIEW

Zanubrutinib vs bendamustine plus rituximab in TN CLL/SLL: 5-year follow-up of the SEQUOIA study

STUDY OVERVIEW

At a median follow-up of 26.2 months, the primary analysis demonstrated that zanubrutinib had a superior progression-free survival (PFS) compared with BR.

Presented here are long-term data with **5 years of overall study follow-up** for cohort 1.

SEQUOIA PHASE 1 2 3

PATIENTS

70 MEDIAN AGE

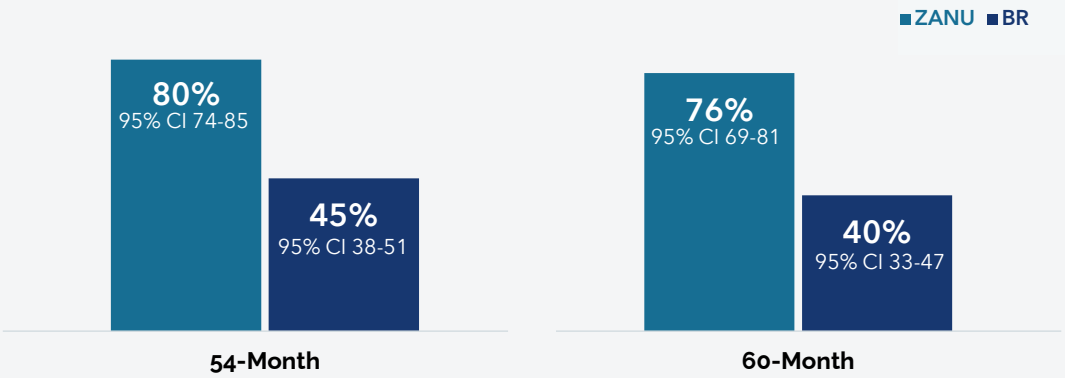
52% Unmutated IGHV

14% Complex karyotype ≥3 abnormalities

ZANUBRUTINIB (n=241) vs BR (n=238)

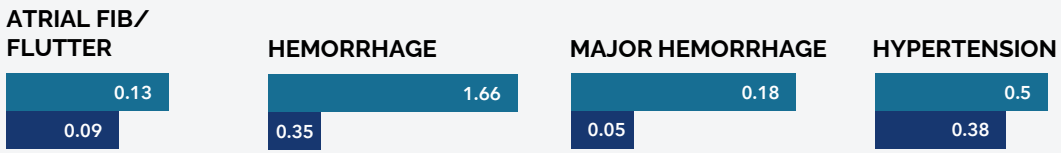
Median follow-up: 61.2 months

PROGRESSION-FREE SURVIVAL



SAFETY: SELECT EAIRs

Person per 100 person-months



KEY TAKEAWAY

Patients with TN CLL without del(17p) treated with zanu had sustained PFS vs BR in this 5-year follow-up of SEQUOIA. Safety and tolerability of zanu was consistent with prior reports; no new safety signals were observed. These long-term data continue to support the use of zanu as a standard frontline treatment for CLL/SLL.

LEARN MORE AT OUR PRESENTATION

Poster 3249, Shadman M et al

Sunday, December 8th,
6-8 PM PST
Convention Center, Halls G-H

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

1124--MRC-051
NCT03336333.

BR=bendamustine plus rituximab, CLL=chronic lymphocytic leukemia, EAIR=exposure-adjusted incident rate, FIB=fibrillation, ORR=overall response rate, SLL=small lymphocytic lymphoma, TN=treatment-naïve, zanu=zanubrutinib.

Zanubrutinib is approved in the EU as a monotherapy for the treatment of adult patients with chronic lymphocytic leukemia (CLL), adult patients with marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy, adult patients with Waldenström's macroglobulinemia (WM) who have received at least one prior therapy or for the first-line treatment of patients unsuitable for chemo-immunotherapy, and in combination with obinutuzumab in adult patients with refractory or relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies. Prescribing information (PI) may vary depending on local approval in each country. Therefore, before prescribing any product, always refer to local authorities concerning reimbursement status and to local materials such as the PI and/or the summary of product characteristics (SmPC) for guidance on prescribing.

BeiGene

LONG-TERM EXTENSION STUDY – BGB-3111-LTE1

SNEAK PREVIEW

Longer-term follow-up of patients with CLL/SLL treated with zanubrutinib (phase 1/2) or zanubrutinib + obinutuzumab (phase 1B)

STUDY OVERVIEW

Eligible patients from two zanubrutinib studies were enrolled for continued treatment or survival follow-up. Here, we report outcomes in patients with CLL/SLL from these two studies with extended follow-up from LTE1.

ZANUBRUTINIB MONOTHERAPY

AU-003 — PHASE: 1 | 2 | 3

ZANUBRUTINIB + OBINUTUZUMAB

6 cycles followed by continuous zanubrutinib monotherapy

GA-101 — PHASE: 1 | 2 | 3

PATIENTS (N=117)

71 MEDIAN AGE
At entry in LTE1

- 75.3% R/R CLL/SLL
- 17.1% del(17p)
- 18.2% TP53 mutation

ZANUBRUTINIB MONOTHERAPY (n=125)

Median follow-up: 76 months

ZANUBRUTINIB + OBINUTUZUMAB (n=45)

Median follow-up: 88 months

OVERALL RESPONSE RATE

TREATMENT-NAÏVE CLL/SLL

100%
95% CI 84.6-100

TREATMENT-NAÏVE CLL/SLL

100%
95% CI 83.2-100

RELAPSED/REFRACTORY CLL/SLL

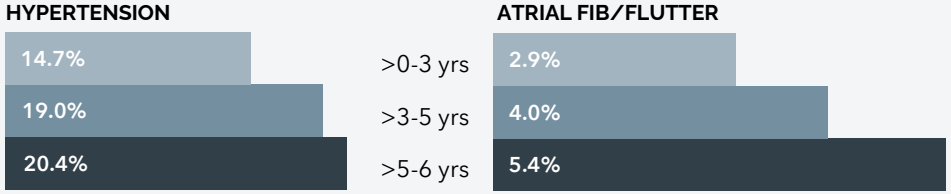
94.2%
95% CI 87.8-97.8

RELAPSED/REFRACTORY CLL/SLL

92.0%
95% CI 74-99

SAFETY: PREVALENCE OF SELECT AEs OF INTEREST

(Both studies combined)



KEY TAKEAWAY

With a median follow-up of 6.5 years, the durable high ORR in patients with CLL/SLL was demonstrated. The tolerability/safety profile of zanubrutinib alone and in combination with obinutuzumab, remained favorable.

LEARN MORE AT OUR PRESENTATION

Poster 3255,
Tam CS et al

Sunday, December 8th,
6-8 PM PST
Convention Center, Halls G-H

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

1124--MRC-051
NCT04170283.
AE=adverse event, CLL=chronic lymphocytic leukemia, FIB=fibrillation, LTE=Long-term extension, ORR=overall response rate, R/R=relapsed/refractory, SLL=small lymphocytic lymphoma, zanu=zanubrutinib.

BeiGene

CaDAnCe-101: WM COHORT

SNEAK PREVIEW

Preliminary efficacy and safety of BGB-16673 in R/R WM: Results from the CaDAnCe-101 study

STUDY OVERVIEW

BGB-16673 is a bivalent small molecule that induces BTK degradation by binding specifically to BTK and the E3 ligase. Preclinically, BGB-16673 degraded WT and mutant BTK associated with cBTKis and ncBTKis, leading to tumor suppression. Here, early results in patients with WM enrolled in the Phase 1 portion of the CaDAnCe-101 study are presented.

CaDAnCe-101 — PHASE 1 | 2 | 3

BGB-16673 is orally dosed once daily in 28-day cycles;
Dose escalation with 6 planned dose levels, 50-600 mg once daily

PATIENTS (N=22)

100 mg, n=4; 200 mg, n=10; 350 mg, n=8

73 MEDIAN AGE

- 23% BTK mutations
- 91% MYD88 mutations
- 36% CXCR4 mutations

BGB-16673 MONOTHERAPY

Median follow-up: 4.3 months | Median number of prior therapies: 3.5

- 100% Prior cBTKis
- 14% Prior ncBTKis

SAFETY SUMMARY

GRADE ≥3 TEAE

45%

NEUTROPENIA/DECREASED NEUTROPHIL COUNT MOST COMMON GRADE ≥3

23%

TEAE LEADING TO DISCONTINUATION OR DOSE REDUCTION

0 patients

TEAE LEADING TO DEATH*

1 patient

No dose-limiting toxicities occurred

OVERALL RESPONSE RATE (n=21)

90%

- **100%** Response at lowest dose: 100 mg (n=4)
- **90.5%** Response in patients previously treated with a cBTKi (n=21)
- **100%** Response in patients previously treated with an ncBTKi (n=3)

KEY TAKEAWAY

Early data from this ongoing, first-in-human study demonstrated that the novel BTK degrader BGB-16673 has a generally tolerable safety profile and showed antitumor activity.

LEARN MORE AT OUR PRESENTATION

Oral Presentation 860, Seymour JF et al

Monday, December 9th,
3 PM PST
Marriott Grand Ballroom 11-13

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

1124--MRC-051
NCT05006716. *septic shock, considered related to disease progression.
BTK=Bruton tyrosine kinase, cBTKi=covalent Bruton tyrosine kinase inhibitor, FIB=fibrillation, ncBTKi=noncovalent Bruton tyrosine kinase inhibitor, TEAE=treatment-emergent adverse events, WT=wild-type, WM=Waldenström macroglobulinemia, zanu=zanubrutinib.
BGB-16673 is an investigational compound for which safety and efficacy have not been established. Because of the uncertainty of clinical trials, there is no guarantee that BGB-16673 will receive regulatory approval and become commercially available for the uses being investigated.

BeiGene

BGB-11417-101: TN CLL COHORT

SNEAK PREVIEW

Sonrotoclax plus zanubrutinib in treatment-naïve CLL: Data from the ongoing Phase 1/1b BGB-11417-101 study

STUDY OVERVIEW

Sonrotoclax, a next-generation BCL2i, was designed to be a more selective and more pharmacologically potent inhibitor of BCL2 than venetoclax. Zanubrutinib, a next-generation BTKi, is highly effective in CLL, including in patients with high-risk disease features. Here, we present updated safety and efficacy data of sonrotoclax + zanubrutinib in patients with TN CLL/SLL in BGB-11417-101.

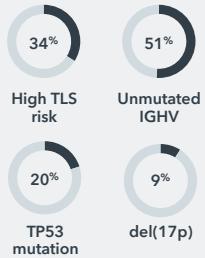
BGB-11417-101 PHASE 1 | 2 | 3

Zanubrutinib (320 mg QD or 160 mg twice daily) for 8-12 weeks; added **sonrotoclax** using a ramp-up schedule (weekly or daily) to the target doses (160 or 320 mg QD) to mitigate risk of TLS.

PATIENTS (N=112)

Sonrotoclax 160 mg QD, n=51; 320 mg QD, n=61

62 MEDIAN AGE



SONROTOCLAX + ZANUBRUTINIB

Median follow-up: 18.3 months

SAFETY SUMMARY

No clinical or laboratory TLS occurred

NEUTROPENIA: MOST COMMON GRADE ≥3

26%

DEATHS

0

DISCONTINUED COMBINATION* (all 160mg)

5 patients

COVID-19: MOST COMMON TEAE RESULTING IN DOSE HOLD

19 patients

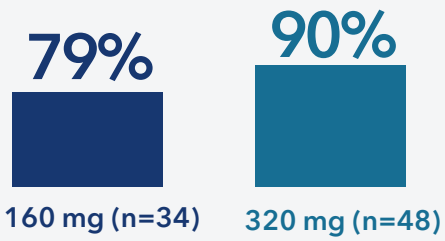
OVERALL RESPONSE RATE (n=108)

100%

41% CR: 160 mg (n=51)

42% CR: 320 mg (n=61)

UMRD4 RATES (WEEK 48)



KEY TAKEAWAY

Sonrotoclax (160 and 320 mg) in combination with zanubrutinib was generally well tolerated in patients with TN CLL/SLL and efficacy was observed. High rates of blood uMRD4 occurred early and were sustained.

LEARN MORE AT OUR PRESENTATION

Oral Presentation 1012, Soumerai JD et al

Monday, December 9th,
5:15 PM PST
Marriott Grand Ballroom 8-9

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

1124--MRC-051

NCT04277637. *1 TEAE (cryptococcal meningitis), 1 PD, 1 patient withdrawal (had CR and uMRD at time of withdrawal). Two patients in uMRD electively discontinued after 96 weeks of treatment.

Sonrotoclax is an investigational compound for which safety and efficacy have not been established. Because of the uncertainty of clinical trials, there is no guarantee that sonrotoclax will receive regulatory approval and become commercially available for the uses being investigated.

BeiGene

CaDAnCe-101: R/R CLL/SLL COHORT

SNEAK PREVIEW

Preliminary efficacy and safety of BGB-16673 in patients with R/R CLL/SLL: Results from phase 1 CaDAnCe-101 study

STUDY OVERVIEW

BGB-16673 is a bivalent small molecule that induces BTK degradation by binding specifically to BTK and the E3 ligase. In preclinical models, BGB-16673 degraded WT and mutant BTK associated with resistance to cBTKis and ncBTKis, leading to tumor suppression. Here, updated results in patients with R/R CLL/SLL enrolled in the phase 1 portion of CaDAnCe-101 are presented.

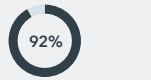
CaDAnCe-101 PHASE 1 | 2 | 3

BGB-16673 dosed QD orally in 28-day cycles
6 planned dose levels, 50-600 mg QD

PATIENTS (N=49)

50 mg, n=1; 100 mg, n=5; 200 mg, n=16; 350 mg, n=15; 500 mg, n=12

70 MEDIAN AGE



Prior cBTKi

del(17p) and/or TP53 mutation (n=49)

Unmutated IGHV (n=39)

BGB-16673 MONOTHERAPY

Median follow-up: 7.9 months | Median number of prior therapies: 4

SAFETY SUMMARY

One dose-limiting toxicity occurred in 1 patient at 200 mg*

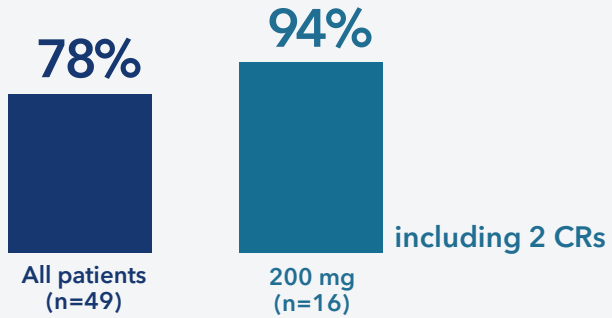
GRADE ≥3 TEAE
57%

TEAE LEADING TO DOSE REDUCTION
3 patients

NEUTROPENIA/DECREASED NEUTROPHIL COUNT MOST COMMON GRADE ≥3
20%

TEAEs LEADING TO DEATH† (not considered related to Tx)
3 patients

OVERALL RESPONSE RATE (N=49)



KEY TAKEAWAY

Emerging data from this ongoing, first-in-human study demonstrated that the novel BTK degrader BGB-16673 has a tolerable safety profile and showed deep overall responses in heavily pretreated patients.

LEARN MORE AT OUR PRESENTATION

Oral Presentation 885, Thompson MC et al

Monday, December 9th,
3:15 PM PST
Marriott Grand Ballroom 5-6

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

1124--MRC-051

NCT05006716. *Grade 3 maculopapular rash on day 27; decreased to grade 1 after 5-day hold; patient continues on treatment;†septic shock, bronchopulmonary aspergillosis/cerebral aspergillosis, and pneumonia in the context of disease progression; n=1 each.
BTK=Bruton tyrosine kinase, cBTKi=covalent Bruton tyrosine kinase inhibitor, CLL=chronic lymphocytic leukemia, CR=complete response, ncBTKis=noncovalent Bruton tyrosine kinase inhibitors, QD=once daily, SLL=small lymphocytic lymphoma, TEAE=treatment-emergent adverse events, Tx=treatment, WT=wild-type.

BeiGene

BGB-3111-215: PHASE 2 STUDY

SNEAK PREVIEW

Zanubrutinib in patients with B-cell malignancies intolerant to prior acalabrutinib treatment

STUDY OVERVIEW

Previous results from this ongoing phase 2 study (BGB-3111-215) showed that zanubrutinib was well tolerated in patients intolerant of ibrutinib and/or acalabrutinib. Here, we report the updated results of the tolerability and efficacy of zanubrutinib in patients intolerant of acalabrutinib (cohort 2).

BGB-3111-215 PHASE 1 | 2 | 3

Zanubrutinib 160 mg twice daily or 320 mg QD

PATIENTS (N=35)

71 MEDIAN AGE

2 Median number of prior therapies

40% Received prior ibrutinib as well

ZANUBRUTINIB

Median follow-up: 18.9 months | Median Tx duration: 14.8 months

SAFETY: SELECT INTOLERANCE EVENTS (N=35)

Acalabrutinib-intolerance events reported: **48**

69% of events
Acalabrutinib-intolerance events (33/48) did not recur with zanubrutinib

66% of patients
Of patients (23/35) did not experience any recurrence of acalabrutinib-intolerance events

4 Patients experienced the same intolerance event with prior ibrutinib and acalabrutinib

2 Patients did not have a recurrence of these events with zanubrutinib, and 2 patients had a recurrence at a lower grade

EFFICACY SUMMARY (n=32)

93.8%
Disease control rate

40.6%
Best response of stable disease

53.1%
Better response

KEY TAKEAWAY

Based on this data, patients with prior intolerance to acalabrutinib may be able to safely and effectively switch to zanubrutinib treatment. Enrollment and follow-up are ongoing.

LEARN MORE AT OUR PRESENTATION

Poster 4632,
Shadman M et al

Monday, December 9th,
6-8 PM PST
Convention Center, Halls G-H

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

1124--MRC-051
NCT04116437.
QD=once daily, Tx=treatment.

BeiGene

LONG-TERM EXTENSION STUDY – BGB-3111-LTE1

SNEAK PREVIEW

Long-term outcomes in patients with WM treated with zanubrutinib in the Phase 3 ASPEN study

STUDY OVERVIEW

ASPEN (BGB-3111-302) compared zanubrutinib and ibrutinib in patients with WM. At end of study, eligible patients could enroll in a long-term extension study (BGB-3111-LTE1); here we report long-term outcomes in patients who received zanubrutinib in the ASPEN study, with extended follow-up from LTE1.

ZANUBRUTINIB MONOTHERAPY	PHASE		
ASPEN	1	2	3
BGB-3111-LTE1	1	2	3

PATIENTS

Received zanu in ASPEN **N=129**
Enrolled in LTE1 **N=75**
Continued treatment **n=72**

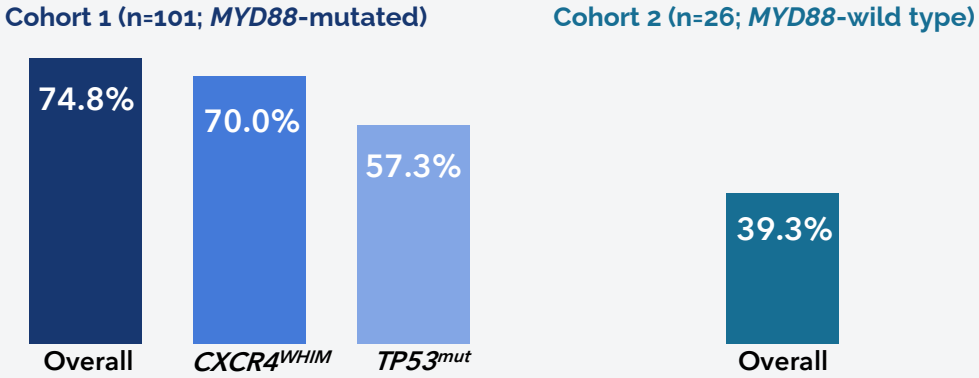
71 MEDIAN AGE
At entry in LTE1

50.6 MONTHS
Median time since zanu treatment initiation

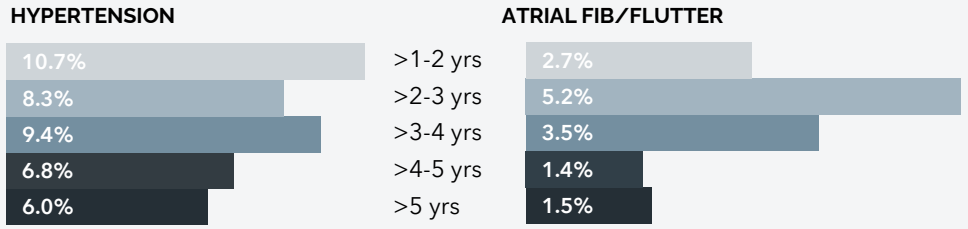
ZANUBRUTINIB

Median treatment duration (ASPEN+LTE1): 73.6 months

60-MONTH EVENT-FREE RATES FOR PFS



SAFETY: PREVALENCE OF SELECT AEs OF INTEREST (N=129)



No Grade ≥3 or serious TEAEs occurred in ≥5% of patients during LTE1

KEY TAKEAWAY

With a median follow-up of 5.8 years, responses in patients with WM treated with zanubrutinib in ASPEN remained durable; furthermore, the tolerability and safety profile of zanubrutinib remained generally favorable.

LEARN MORE AT OUR PRESENTATION

Poster 3031, D'Sa S et al

Sunday, December 8th,
6-8 PM PST
Convention Center, Halls G-H

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

1124--MRC-051
NCT03053440 (ASPEN); NCT04170283 (LTE1)
AE=adverse event, LTE=long-term extension, PFS=progression-free survival, TEAE=treatment-emergent adverse event, WM=Waldenström macroglobulinemia.

BeiGene

US PATIENT PREFERENCE SURVEY: CLL

SNEAK PREVIEW

Patient preference for BTKi treatment and factors affecting decision-making in CLL/SLL in the USA

STUDY OVERVIEW

Understanding and integrating patient perspective in the BTKi treatment selection process is crucial to shared decision-making and attaining optimal treatment outcomes. To understand patients' priorities, a comprehensive quantitative analysis of patient preferences on BTKi treatment attributes was conducted.

Patient Preference Study

Patients responded to DCE questions on attributes related to efficacy, safety (e.g., impacts on QoL), formulation type, and dosing frequency.

PATIENTS (N=200)

61 MEDIAN AGE

CLL DIAGNOSIS AND PRIOR TREATMENT

43% Were diagnosed ≥5 years ago

61% Received ≥3 lines of therapy

89% Reported having experienced ≥1 AE from treatment previously

TREATMENT ATTRIBUTES WITH HIGHEST RELATIVE IMPORTANCE

Patients preferred treatment with higher efficacy, less impact of AEs on QoL, and lower dosing frequency (P<0.001).

24% Impact of atrial fibrillation on QoL

19% Progression-free survival

18% Impact of headache on QoL

KEY TAKEAWAY

Findings from this patient preference survey suggested that impact of atrial fibrillation on QoL, PFS, and impact of headache on QoL were the most important attributes of BTKi treatment for patients with CLL/SLL in the USA.

LEARN MORE AT OUR PRESENTATION

Poster 2265, Ailawadhi S et al

Saturday, December 7th, 5:30–7:30 PM PST
Convention Center, Halls G-H

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

BeiGene

1124--MRC-051

AE=adverse event, BTKi=Bruton tyrosine kinase inhibitor, CLL=chronic lymphocytic leukemia, DCE=discrete-choice experiment, PFS=progression-free survival, QoL=quality of life, SLL=small lymphocytic lymphoma.

US PATIENT PREFERENCE SURVEY: FL

SNEAK PREVIEW

Patient medication preferences in follicular lymphoma in the USA

STUDY OVERVIEW

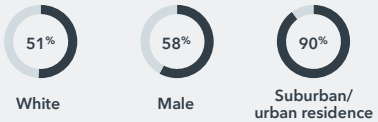
Treatment for R/R FL offers varied levels of efficacy, safety, and convenience, raising a need to understand patient preferences. Therefore, a patient survey using a DCE with quantitative questionnaires was conducted to assess these preferences among patients with R/R FL in the USA

Patient Preference Study

A patient preference survey with the DCE design was conducted. FL treatment attributes were selected based on efficacy, safety, and convenience.

PATIENTS (N=100)

61 MEAN AGE



FL DIAGNOSIS AND PRIOR TREATMENT

28% Were diagnosed ≥5 years ago

82% Received ≥3 lines of therapy

100% Of patients experienced ≥1 AE from Tx

TREATMENT ATTRIBUTES WITH HIGHEST RELATIVE IMPORTANCE

Patients preferred treatments with higher efficacy, less impact of AEs on QoL, and a more convenient mode of administration.

KEY TAKEAWAY

PFS was the most important treatment attribute for patients with R/R FL when making a treatment selection, followed by the impact of CRS on QoL and the mode of administration. Treatment duration was the least important attribute and did not affect patient preferences.

LEARN MORE AT OUR PRESENTATION

Poster 3655, Gaballa S et al

Sunday, December 8th, 6-8 PM PST
Convention Center, Halls G-H

SEE THE FULL ABSTRACT ON THE ASH CONGRESS PAGE

BeiGene

1124--MRC-051

AE=adverse event, CRS=cytokine release syndrome, DCE=discrete-choice experiment, FL=follicular lymphoma, QoL=quality of life, Tx=treatment.