Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

65th ASH Meeting 2023

San Diego & virtuell

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

Prof. Dr. med. Christian Buske
Universitätsklinikum Ulm

Morbus Waldenström (WM) Marginalzonen-Lymphom (MZL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2023 wird in Kooperation mit acht unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	--
Beratungs-/ Gutachtertätigkeit	Roche, Janssen, AbbVie, Novartis, Bayer, Celltrion, Incyte, Beigene, BMS, Sobi
Besitz von Geschäftsanteilen, Aktien oder Fonds	--
Patent, Urheberrecht, Verkaufslizenz	--
Honorare	Roche, Janssen, AbbVie, Novartis, Bayer, Celltrion, Incyte, Beigene, BMS, Sobi
Finanzierung wissenschaftlicher Untersuchungen	Roche, Janssen, Bayer, Celltrion, MSD, Amgen, AbbVie
Andere finanzielle Beziehungen	--
Immaterielle Interessenkonflikte	--

Kapitel 1

Morbus Waldenström assozierte Neuropathie – Neuigkeiten in der Behandlung?

Prospective Study of Acalabrutinib with Rituximab in Patients with Symptomatic Anti-MAG Mediated IgM Peripheral Neuropathy

Shayna Sarosiek, Andrew R Branagan, Christopher T Doughty, Catherine A Flynn, Megan Little, Katherine Stockman, Timothy White, Kirsten Meid, Steven P Treon, Jorge J Castillo

Abstract No 213

Dana-Farber
Cancer Institute

IgM and neuropathy

- 20-25% of patients with an IgM paraprotein have peripheral neuropathy
- Multiple potential etiologies, such as amyloidosis, cryoglobulinemia, POEMS, or anti-myelin associated glycoprotein (MAG) antibodies
- 40-50% of patients with IgM-associated neuropathy have anti-MAG antibodies

Yeung, et al. J Neurol 1991
Nobile-Orazio, et al. Neurology 1987
Ramchandren, et al Curr Neurol Neurosci Rep 2012
Stork, et al J Neuroimmunol 2014

Anti-MAG neuropathy

- Chronic, symmetric, length-dependent sensorimotor demyelinating polyneuropathy
- Progressive neuropathy, up to 50% of patients will develop significant disability within 10-15 years after diagnosis, severely affect QOL and functional status

Castillo, et al. Am J Hematol 2021
Campagnolo, et al. J Peripher Nerv Syst 2019
Latov N Ann Neurol 1995
Nobile-Orazio, et al Brain 2000

Treatment of anti-MAG neuropathy

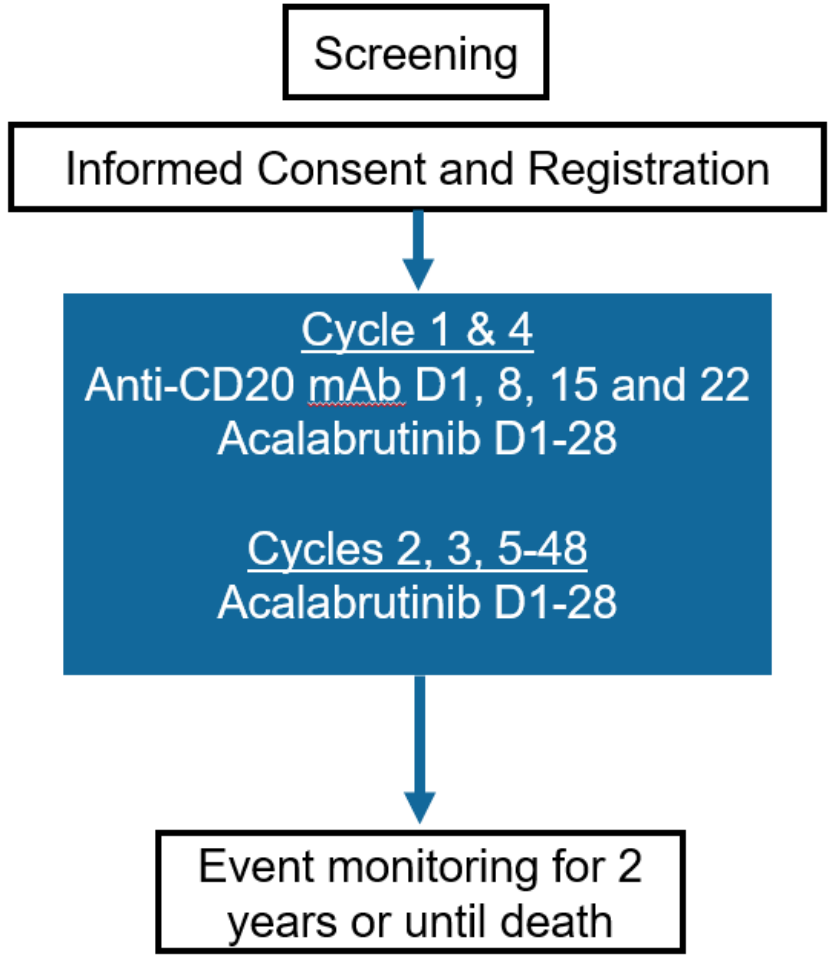
- IVIG
- Single-agent Rituximab
  - Mixed results in case series and small randomized trials
  - Low response rate, delayed responses
- Chemoimmunotherapy
  - Fludarabine or cyclophosphamide
  - Faster responses than rituximab alone, but added toxicity
- Ibrutinib
  - Three-patient case series

Dalakas, et al Ann Neurol 2009
Iancu Ferfoglia, et al J Peripher Nerv Syst 2016
Leger, et al Neurology 2013
Hospital, et al Haematologica 2013
Castellani, et al. Neurol Neuroimmunol Neuroinflamm 2020

www.clinicaltrials.gov:
NCT05065554

Acalabrutinib-Rituximab study

- Single-arm open label Phase II trial
- Includes patients with anti-MAG neuropathy and either IgM monoclonal gammopathy or WM
- Acalabrutinib 100 mg twice daily
- Rituximab (biosimilar or ofatumumab)



Key Inclusion Criteria

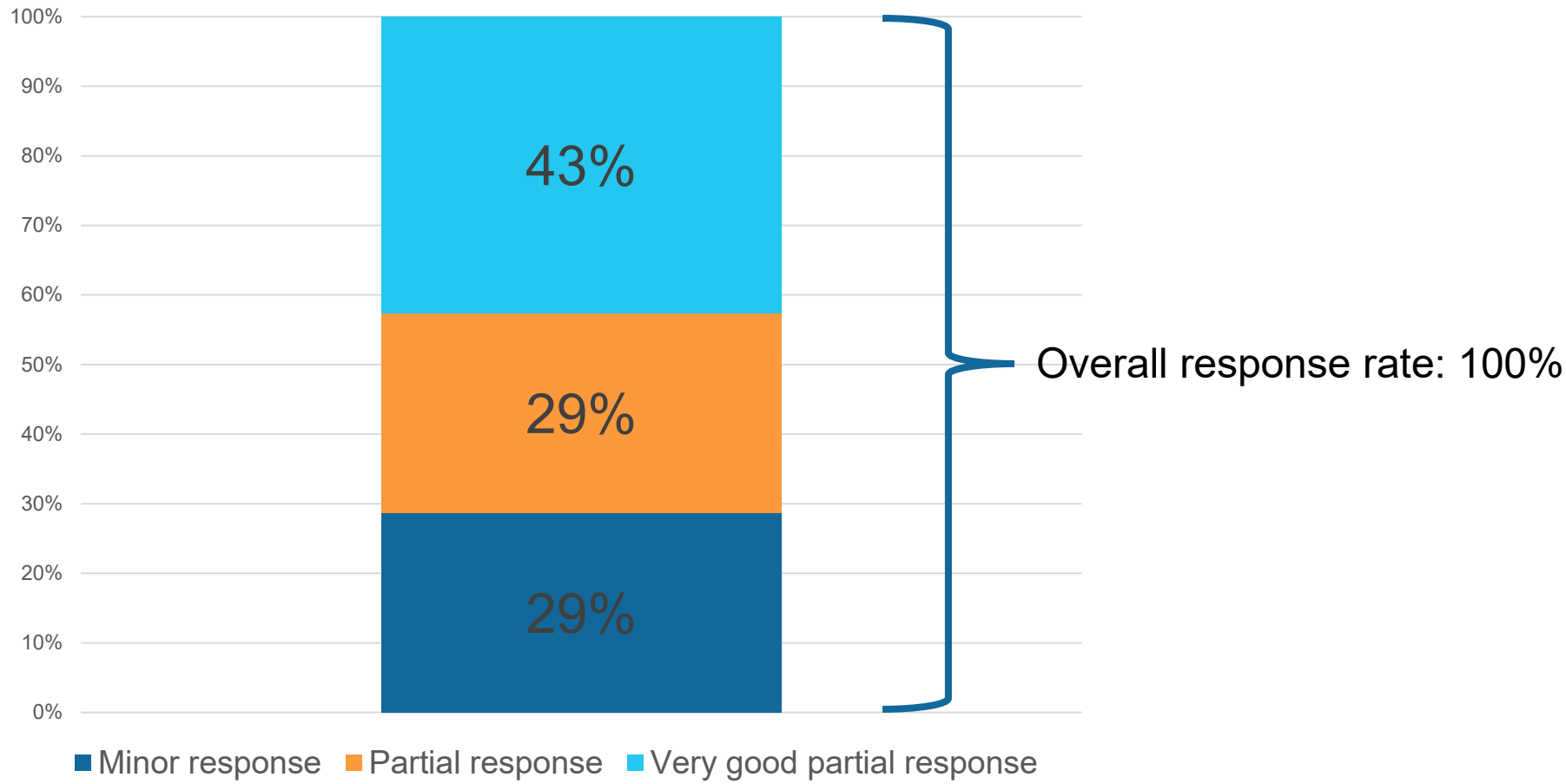
- IgM monoclonal protein
- Presence of anti-MAG antibodies
- Sensory neuropathy with predominantly demyelinating features on nerve conduction studies
- Modified Rankin Scale score of 1 with progressing symptoms or ≥2

MODIFIED RANKIN SCALE

0: no neuropathy
1: neuropathy with no significant disability
2: neuropathy with slight disability
3: neuropathy with moderate disability
4: neuropathy with moderately severe disability
5: neuropathy with severe disability; bedridden

Hematologic responses (7 evaluable patients)

Median of 11 months on treatment (range, 6 to 18 months)



Neurologic assessment (7 evaluable patients)

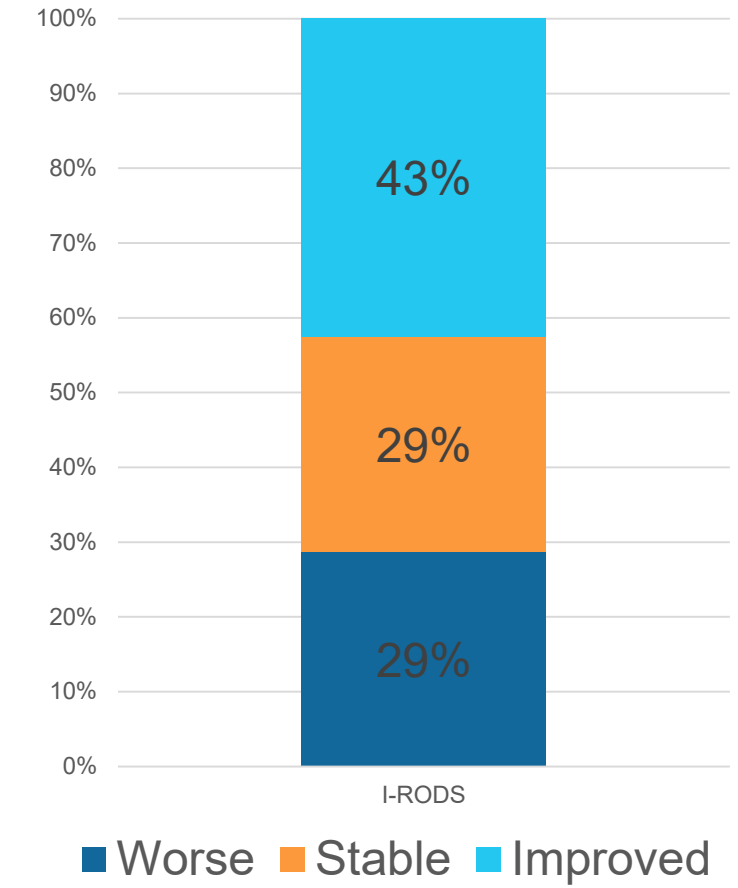
I-RODS

Scored by patient
- (0) impossible
- (1) performed with difficulty
- (2) easily performed

Total score of 0 (severe limitations) to 48 (no limitation)

Baseline median score: 38.1 (range 23-47)

1. Read a newspaper/book
2. Eat
3. Brush your teeth
4. Wash upper body
5. Sit on a toilet
6. Make sandwich
7. Dress upper body
8. Wash lower body
9. Move a chair
10. Turn a key in a lock
11. Go to a general practioner
12. Take a shower
13. Do the dishes
14. Do the shopping
15. Catch an object (e.g. ball)
16. Bend and pick up an object
17. Walk 1 flight of stairs
18. Travel by public transport
19. Walk and avoid obstacles
20. Walk outdoors > 1km
21. Carry and put down a heavy object
22. Dance
23. Standing for hours
24. Run



Median score change: improvement of 1.4

Neurologic assessment (7 evaluable patients)

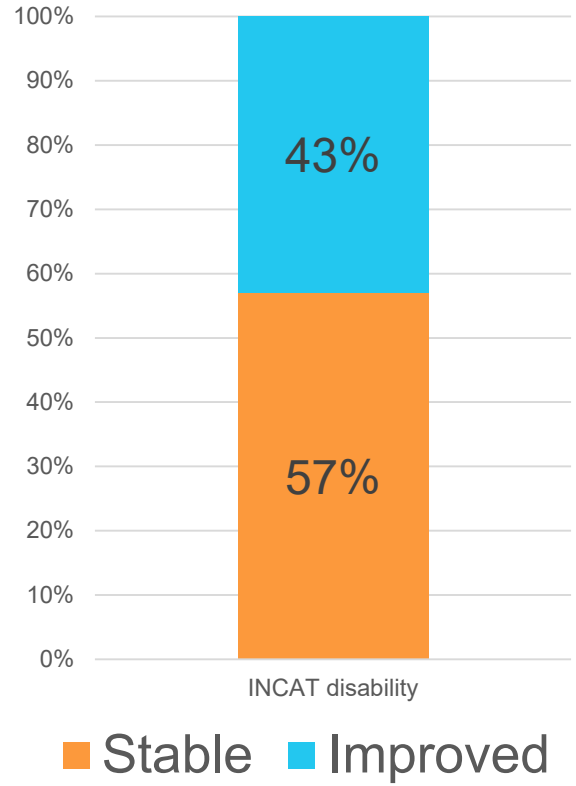
INCAT Disability Score

Scored by physician

Total score of 0 (normal) to 10 (severe disability)

Baseline median score: 2.3 (range 1-3)

0	1	2	3	4	5
No upper limb problems	Symptoms, in one or both arms, not affecting the ability to perform any of the following functions: doing all zips and buttons; washing or brushing hair; using a knife and fork together;	Symptoms, in one arm or both arms, affecting but not preventing any of the previously mentioned functions	Symptoms, in one arm or both arms, preventing one or two of the previously mentioned functions	Symptoms, in one arm or both arms, preventing three or all of the functions listed, but some purposeful movements still possible	Inability to use either arm for any purposeful movement



Median score change: improvement of 0.4

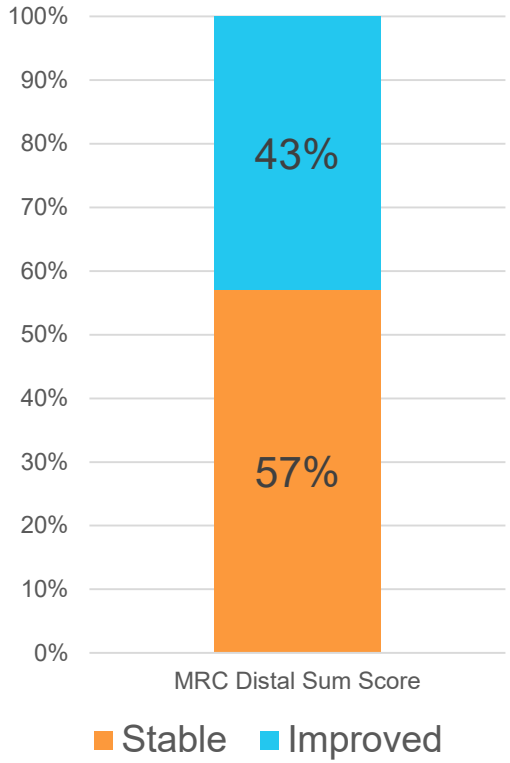
Neurologic assessment (7 evaluable patients)

MRC Distal Sum Score

Scored by physician
- Measures muscle contraction
- Fingers, wrist, ankles and toe

Total score of 0 (no muscle contraction) to 80 (normal)

Baseline median score: 75.6 (range 68-80)



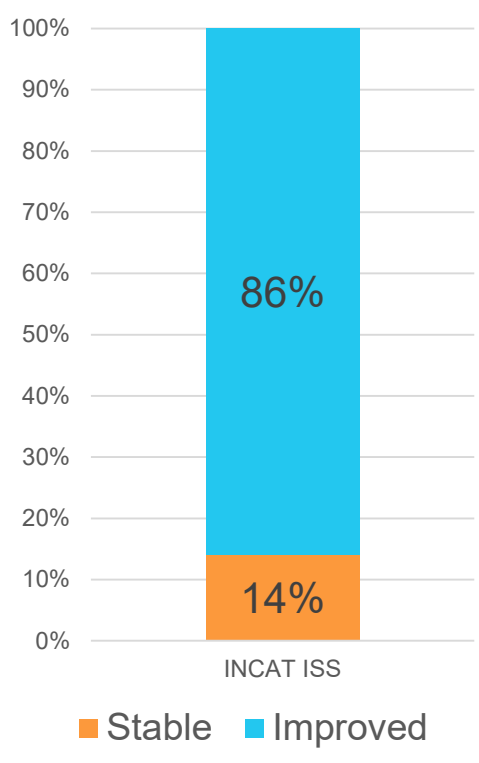
Median score change: improvement of 1.4

INCAT ISS

Scored by physician
- Pinprick / vibration in arm and leg
- Two-point discrimination

Total score of 0 (normal) to 20 (severe deficit)

Baseline median score: 7.6 (range 4-10)



Median score change: improvement of 2.7

Conclusions

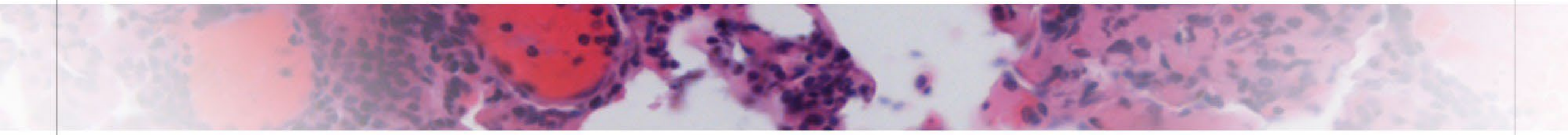
- Preliminary results show 100% hematologic response
- Preliminary results show stability or improvement on multiple neurologic scales, including physician and patient-reported scoring systems
- Ideal neurologic assessment tool yet to be determined
- Clinical trial enrollment is ongoing and final outcomes are pending

Kapitel 2

Morbus Waldenström BTKi Therapie – Switching?

American Society of Hematology
Helping hematologists conquer blood diseases worldwide

Abstract No 3043

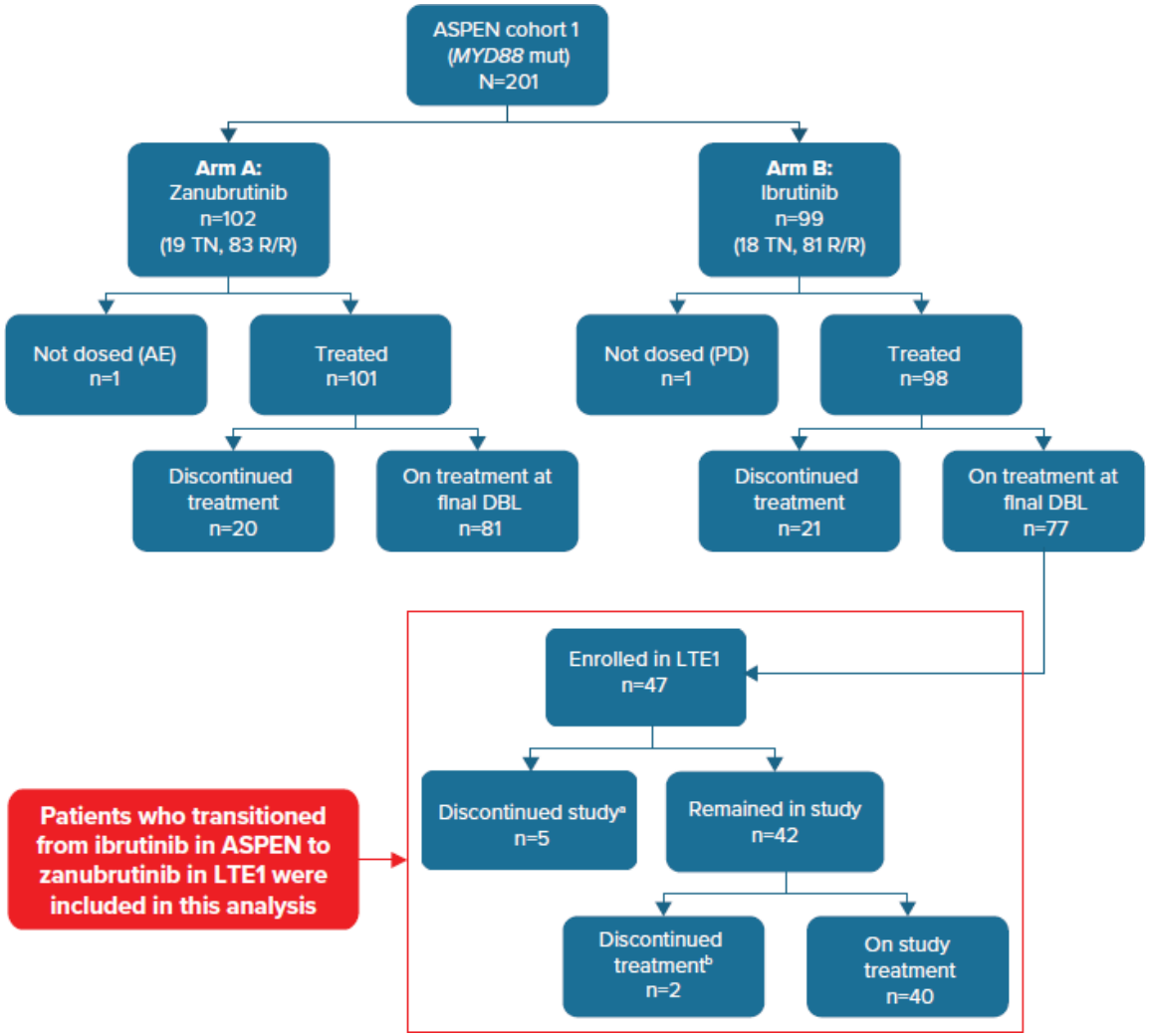


Clinical Outcomes in Patients With Waldenström Macroglobulinemia Receiving Ibrutinib on the Phase 3 ASPEN Study ≥1 Year After Transitioning to Zanubrutinib

Ramon Garcia-Sanz,[1] Roger Owen,[2] Wojciech Jurczak,[3] Meletios Dimopoulos,[4] Helen McCarthy,[5] Gavin Cull,[6] Stephen Opat,[7] Jorge J. Castillo,[8] Marie José Kersten,[9] Bjorn Wahlin,[10] Sebastian Grosicki,[11] Radha Prathikanti,[12] Tian Tian,[12] Heather Allewelt,[12] Aileen Cohen,[12] Constantine Tam[13]

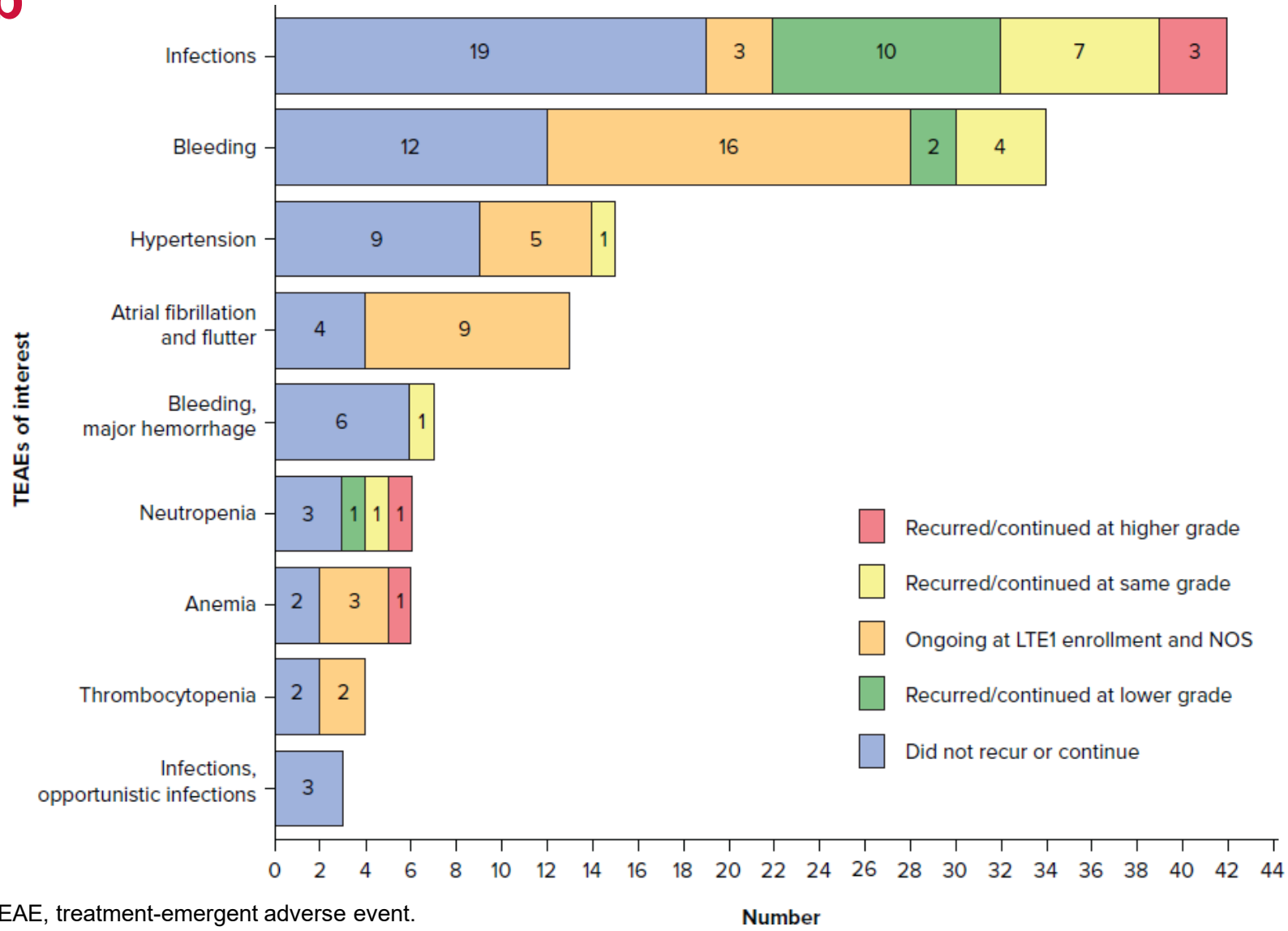
[1]Hospital Universitario de Salamanca, Salamanca, Spain; [2]St. James's University Hospital, Leeds, UK; [3]MSC National Research Institute of Oncology, Krakow, Poland; [4]General Hospital of Athens-Alexandra, Llisia, Greece; [5]Royal Bournemouth Hospital, Bournemouth, UK; [6]Sir Charles Gairdner Hospital, Nedlands, Australia; [7]Monash Health, Victoria, Australia; [8]Dana-Farber Cancer Institute, Boston, MA, USA; [9]Amsterdam University Medical Centers, Location University of Amsterdam, Amsterdam, the Netherlands; [10]Karolinska Universitetssjukhuset Solna, Solna, Sweden; [11]Medical University of Silesia Katowice, Poland; [12]BeiGene USA, Inc, San Mateo, CA, USA; [13]Alfred Hospital and Monash University, Melbourne, Victoria, Australia

Patients With WM Tolerating Ibrutinib on ASPEN were Switched to Zanubrutinib on LTE1



[a] Reasons for study discontinuation (5 patients): death (n=3); lost to follow-up (n=1); and withdrawal (n=1).
[b] Reasons for treatment discontinuation (5 patients who left the study plus 2 who remained in the study): ''other'' reasons (n=3); AEs (n=2); PD (n=1); and withdrawal (n=1).
AE, adverse events; DBL, database lock; *MYD88*, Myeloid differentiation primary response 88; PD, progressive disease; RR, relapsed/refractory.

Recurrence or Continuation of Ibrutinib TEAEs on Zanubrutinib



NOS, not otherwise specified; TEAE, treatment-emergent adverse event.

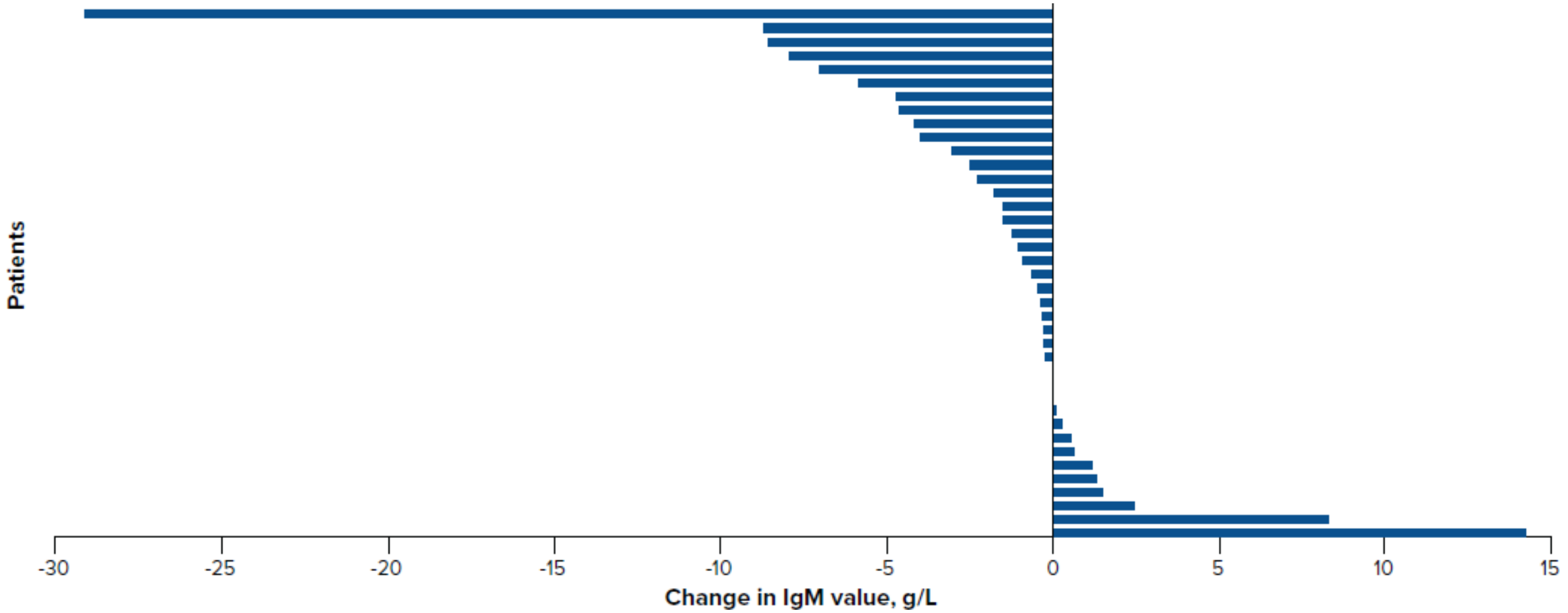
Efficacy Results

Overall Response Assessment by PI	ASPEN BOR	ASPEN Last RA	LTE1 BOR
	n (%); N=47		
CR	0	0	2 (4.3)
VGPR	15 (31.9)	13 (27.7)	17 (36.2)
PR	31 (66)	27 (57.4)	23 (48.9)
MR	1 (2.1)	3 (6.4)	3 (6.4)
IgM flare	N/A	1 (2.1)	N/A
PD	N/A	2 (4.3)	N/A
Not evaluable	N/A	1 (2.1)	N/A
No evidence of PD	N/A	N/A	1 (2.1)
Discontinued prior to assessment	N/A	N/A	1 (2.1)

[a]Grouped terms.

BOR, best overall response; CR, complete response (negative immunofixation, not confirmed by bone marrow biopsy); IgM, immunoglobulin M; MR, minor response; N/A, not applicable; PD, progressive disease; PI, principal investigator; PR, partial response; RA, response assessment; VGPR, very good partial response.

Change in [IgM] From Last Response Assessment in ASPEN Study to BOR in LTE1 Study



BOR, best overall response; IgM, immunoglobulin M.

Conclusions

- The majority of ibrutinib-emergent adverse events did not recur or continue with zanubrutinib treatment, despite advanced and increasing age
- WM disease response was maintained or improved in 96% of efficacy-evaluable patients (44/46)
- While limited by sample size and nonrandomized/ad hoc analysis, data suggest that patients who are tolerating ibrutinib may switch to zanubrutinib without compromising, and may improve upon, safety or efficacy; long-term follow-up is ongoing

BTKi, Bruton's tyrosine kinase inhibitor; TEAE, treatment-emergent adverse events; WM, Waldenström macroglobulinemia .

Kapitel 3

Morbus Waldenström - CAR-Ts bei sekundärer Transformation?

CD19-TARGETING CAR T-CELL THERAPY IN TRANSFORMED WALDENSTRÖM MACROGLOBULINEMIA/LYMPHOPLASMACYTIC LYMPHOMA: A DESCAR-T AND US COLLABORATIVE STUDY

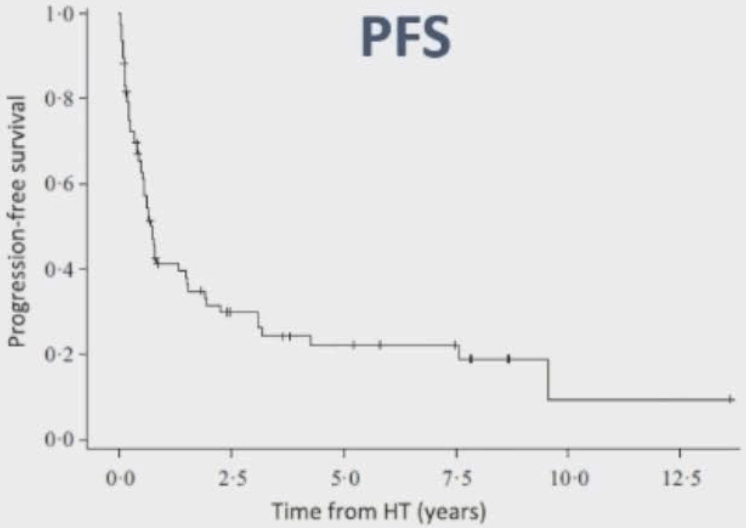
Eric Durot[1], Damien Roos-Weil[2], Adrien Chauchet[3], Justine Decroocq[4], Roberta Di Blasi[5], Thomas Gastinne[6], Hedi Bensaber[7], Morgane Cheminant[8], Caroline Jacquet[9], Stéphanie Guidez[10], François-Xavier Gros[11], Emmanuel Bachy[12], Pascale Cony-Makhoul[13], Steven P. Treon[14], Alain Delmer[1], Ran Reshef[15], Steven Le Gouill[16], Jorge J. Castillo[14], and **Roch Houot[17]**

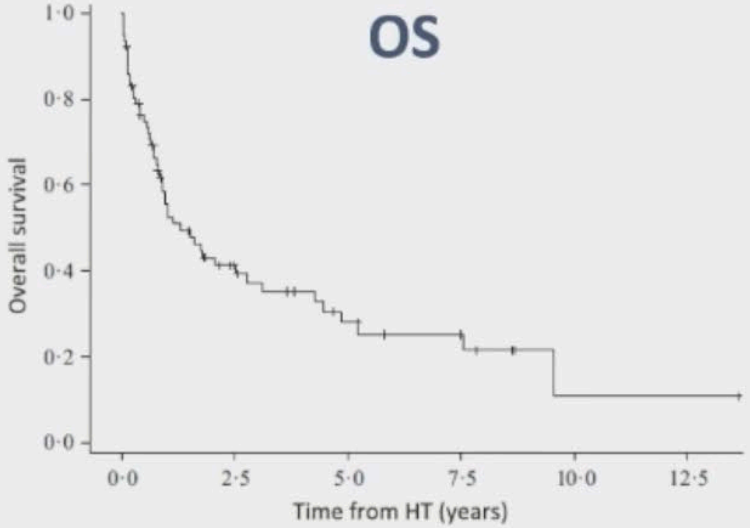
[1]CHU de Reims, France, [2]Pitié-Salpêtrière Hospital and Sorbonne University, UPMC Paris, GRECHY, France, [3]CHU de Besançon, France, [4]Hôpital Cochin, Paris, France, [5]Hôpital Saint-Louis, Paris, France, [6]CHU de Nantes, France, [7]CHU de Clermont-Ferrand, France, [8]Hôpital Necker, Paris, France, [9]CHU de Nancy, France, [10]CHU de Poitiers, France, [11]CHU de Bordeaux, France, [12]Hospices Civils de Lyon, Pierre Bénite, Lyon, France, [13]Medical and Scientific Department, LYSARC, Hôpital Lyon-Sud, Pierre-Bénite, France, [14]Bing Center for Waldenström Macroglobulinemia, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA, [15]Division of Hematology/Oncology and Columbia Center for Translational Immunology, Columbia University Irving Medical Center, New York, USA, [16]Institut Curie, Paris, France, [17]CHU de Rennes, France

Abstract 616

Background

- **Histological transformation (HT)** of Waldenström macroglobulinemia (WM) to large B-cell lymphoma (LBCL) is a **rare event** (< 5%)[1]
- Most patients present with **extranodal involvement and elevated LDH at HT**[1,2,3]
- HT carries a **poor prognosis** (OS = 1.5 to 2.7 years after HT) despite the use of LBCL-directed chemoimmunotherapy due to **refractory disease, short duration of response and frequent CNS relapses**[1-5]





[1]Castillo et al., Am J Hematol, 2016
[2]Zanwar et al., Am J Hematol, 2020
[3]Durot et al., Br J Haematol, 2017
[4]Durot et al., Haematologica, 2021
[5]Durot et al., Blood Adv, 2022

Background

- **CD19-targeted chimeric antigen receptor (CAR) T-cell therapies can lead to durable responses in relapsed/refractory (R/R) LBCL** and are approved for transformed follicular lymphoma (FL)[1,2]
- However, **patients with transformed indolent lymphoma were largely underrepresented in pivotal studies**, in particular non-FL transformed lymphoma
- To our knowledge, **only 3 cases** of patients with transformed WM treated with CAR T-cell have been reported :
  - 2 patients (among 18 non-FL transformed lymphomas) in the TRANSCEND study : 1 patient in PR[3]
  - 1 case report : CR at 1 year[4]

vimeo

→ Objective : evaluate the efficacy and safety of CAR T-cells in transformed WM

[1]Neelapu et al., NEJM, 2019, [2]Schuster et al., NEJM, 2019, [3]Abramson et al., The Lancet, 2020, [4]Bansal et al., Leuk and Lymph, 2019

Patients and Methods

Patient population

- ≥ 18 years
- R/R transformed WM/lymphoplasmacytic lymphoma
- Biopsy-proven LBCL
- Treated with commercial CAR T-cells
- From 13 DESCAR-T centers (18 patients) and 2 US centers (4 patients)

Endpoints

- Primary endpoint : best complete response rate (CR)
- Secondary endpoints :
  - Best overall response rate (OR)
  - PFS (from infusion)
  - OS (from infusion)
  - Safety (CRS, ICANS, hematological toxicity, infections)

Patient characteristics at HT

Characteristics	Total (n=22)
Median age at HT (yrs, range)	65 (41-81)
Median time from WM to HT (yrs, range)	4.5 (0-32)
Histology	
DLBCL NOS	21 (95%)
HGBL (*MYC* and *BCL6* translocations)	1 (5%)
Hans algorithm	
non-GC	3 (15%)
GC	17 (85%)
Extranodal involvement	19 (86%)
CNS involvement	3 (14%)
Elevated LDH	11/17 (65%)
Median serum IgM level (g/L, range)	5.8 (0-31.1)
Stage III-IV	21 (95%)
IPI ≥ 3	9/19 (47%)

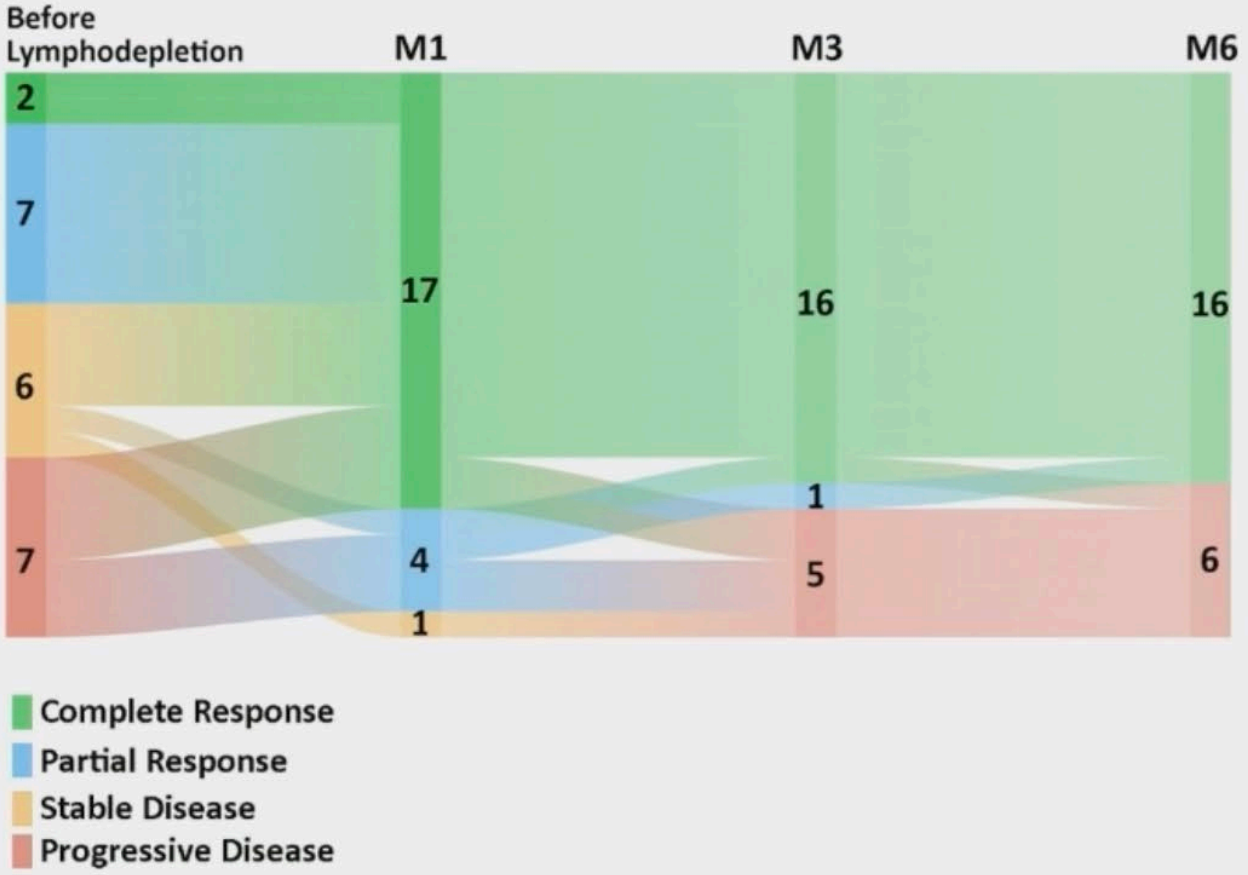
Patient characteristics at lymphodepletion

Characteristics	Total (n=22)
Median age at LD (yrs, range) > 70 years	66 (41-82) 8 (36%)
Median time from HT diagnosis to CAR T-cell infusion (months, range)	26 (3-90)
Median number of lines from WM (range)	3 (2-7)
Median number of lines from HT (range)	2 (1-4)
Prior autologous SCT	7 (32%)
Prior allogeneic SCT	1 (4%)
Refractory to last therapy	11 (50%)
ECOG PS ≥ 2	5/21 (24%)
Elevated LDH	11 (50%)
Stage III-IV	12/15 (80%)
CNS involvement	2/22 (9%)

Characteristics	Total (n=22)
Bridging therapy	16 (73%)
Response to bridging therapy (n = 16)	
CR	2 (12%)
PR	3 (19%)
SD	5 (31%)
PD	6 (38%)
Lymphodepleting chemotherapy	
Flu/Cy	20 (91%)
Bendamustine	2 (9%)
CAR T-cell product	
Axicabtagene-ciloleucel	13 (59%)
Tisagenlecleucel	9 (41%)

Response

Response	Total (n=22)	Axi-cel (n = 13)	Tisa-cel (n = 9)
Best OR*	**95%****	92%	100%
Best CR*	**86%****	85%	89%
OR			
1 month	95%	92%	100%
3 months	78%	69%	89%
6 months	73%	69%	78%
CR			
1 month	77%	77%	78%
3 months	73%	62%	89%
6 months	73%	69%	78%

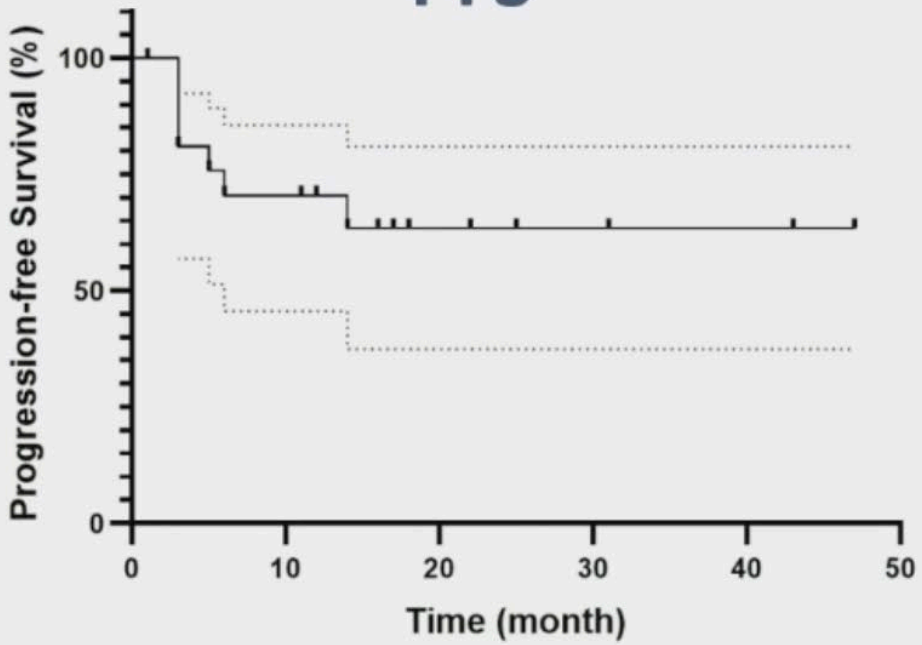


*According to Lugano 2014 classification

**The 2 CNS+ patients achieved a CR at 1 mo: 1 relapsed at 3 mo and 1 remains in CR at 12 mo

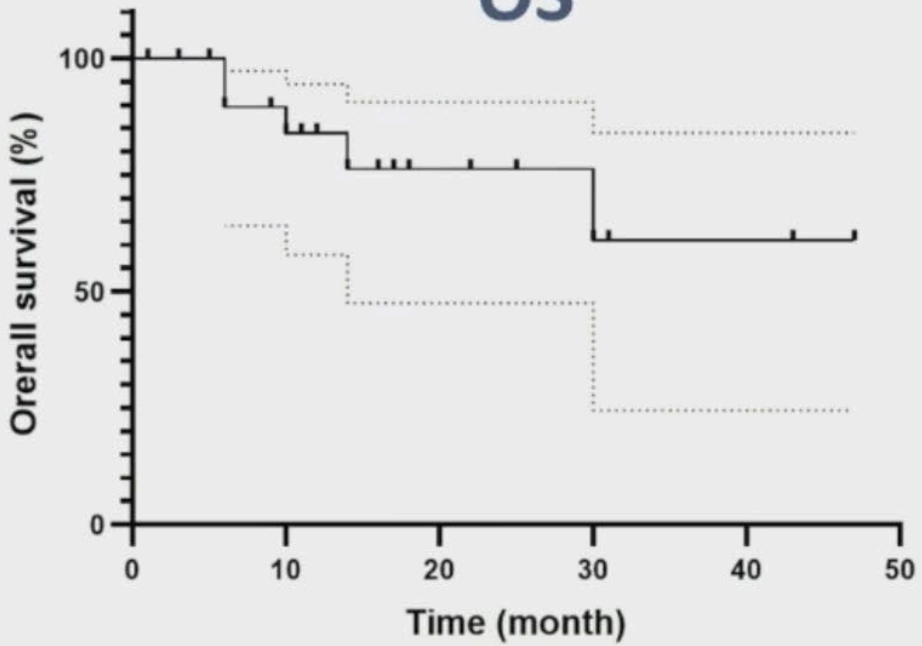
Survival

PFS



6-months PFS = 70.5% (95% CI, 50-89)
12-months PFS = 70.4% (95% CI, 46.1-85.8)
24-months PFS = 63.8% (95% CI, 37.8-81.2)

OS



6-months OS = 89.6% (95% CI, 64.4-97.2)
12-months OS = 84.1% (95% CI, 58.3-94.7)
24-months OS = 75.9% (95% CI, 48.2-89.9)

Median follow-up : 17 months (range, 1-47)
5 deaths : lymphoma (4), COVID-19 infection (1)

Safety

Toxicity	Total (n=22)	Axi-cel (n=13)	Tisa-cel (n=9)
CRS			
All grade	17 (78%)	9 (69%)	8 (89%)
≥ grade 3	2 (9%)	2 (15%)	0 (0%)
Use of tocilizumab	10/17 (59%)	5/9 (56%)	5/8 (63%)
ICANS			
All grade	9 (41%)	6 (46%)	3 (33%)
≥ grade 3	2 (9%)	2 (15%)	0 (0%)
Infection			
All grade	8 (36%)	4 (31%)	4 (44%)
≥ grade 3	4 (18%)	3 (23%)	1 (11%)
Grade ≥ 3 prolonged cytopenia*			
Neutropenia	7 (32%)	3 (23%)	4 (44%)
Anemia	5 (23%)	1 (8%)	4 (44%)
Thrombocytopenia	8 (36%)	4 (31%)	4 (44%)
Non relapse mortality	1 (5%)**	0 (0%)	1 (11%)**

**Grade ≥ 3 cytopenia not resolved 30 days after CAR T-cell infusion; **COVID-19 infection*

Conclusions

- Largest study to date reporting the efficacy and safety of CD19 CAR T-cell therapy in patients with R/R transformed WM
- High efficacy of CD19 CAR T-cell therapy in heavily pre-treated R/R transformed WM (OR=95%, CR=86%, 12mo-PFS=70%, 12mo-OS=84%)
- No unexpected toxicity
- Our results support the use of CAR T-cells in this population of patients
- Longer follow-up is needed to confirm the long-term efficacy of CAR T-cells in transformed WM

Kapitel 4

Marginalzonenlymphom: neue Therapieansätze?

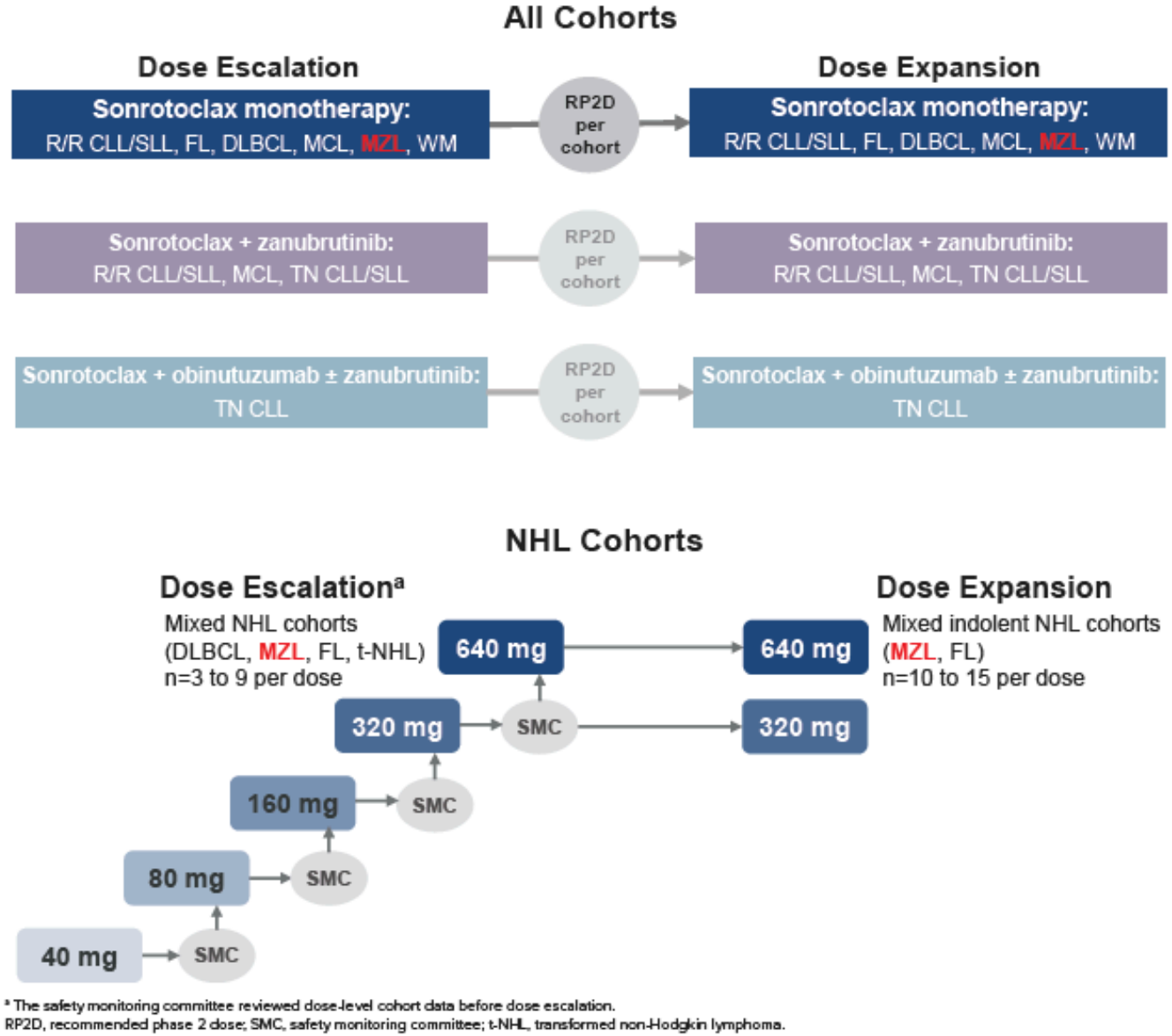
Monotherapy With Second-Generation BCL2 Inhibitor Sonrotoclax (BGB-11417) is Well Tolerated with High Response Rates in Patients with Relapsed/Refractory Marginal Zone Lymphoma: Data from an Ongoing Phase 1 Study

Alessandra Tedeschi,[1] Chan Y. Cheah,[2-4] Stephen Opat,[5,6] Emma Verner,[7,8] Laura Magnano,[9] Narendranath Epperla,[10] James Hilger,[11] Yiqian Fang,[11] David Simpson,[11] Haiyi Guo,[11] and Mary Ann Anderson[12]

[1]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [2]Department of Haematology, Sir Charles Gairdner Hospital and PathWest Laboratory Medicine, Nedlands, WA, Australia; [3]Medical School, University of Western Australia, Crawley, WA, Australia; [4]Linear Clinical Research, Nedlands, WA, Australia; [5]Monash University, Clayton, VIC, Australia; [6]Monash Health, Clayton, VIC, Australia; [7]Concord Repatriation General Hospital, Concord, NSW, Australia; [8]University of Sydney, Sydney, NSW, Australia; [9]Hospital Clínic de Barcelona, Barcelona, Spain; [10]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [11]BeiGene (Shanghai) Co, Ltd, Shanghai, China, and BeiGene USA, Inc, San Mateo, CA, USA; [12]Peter Mac Callum Cancer Centre, Melbourne, VIC, Australia

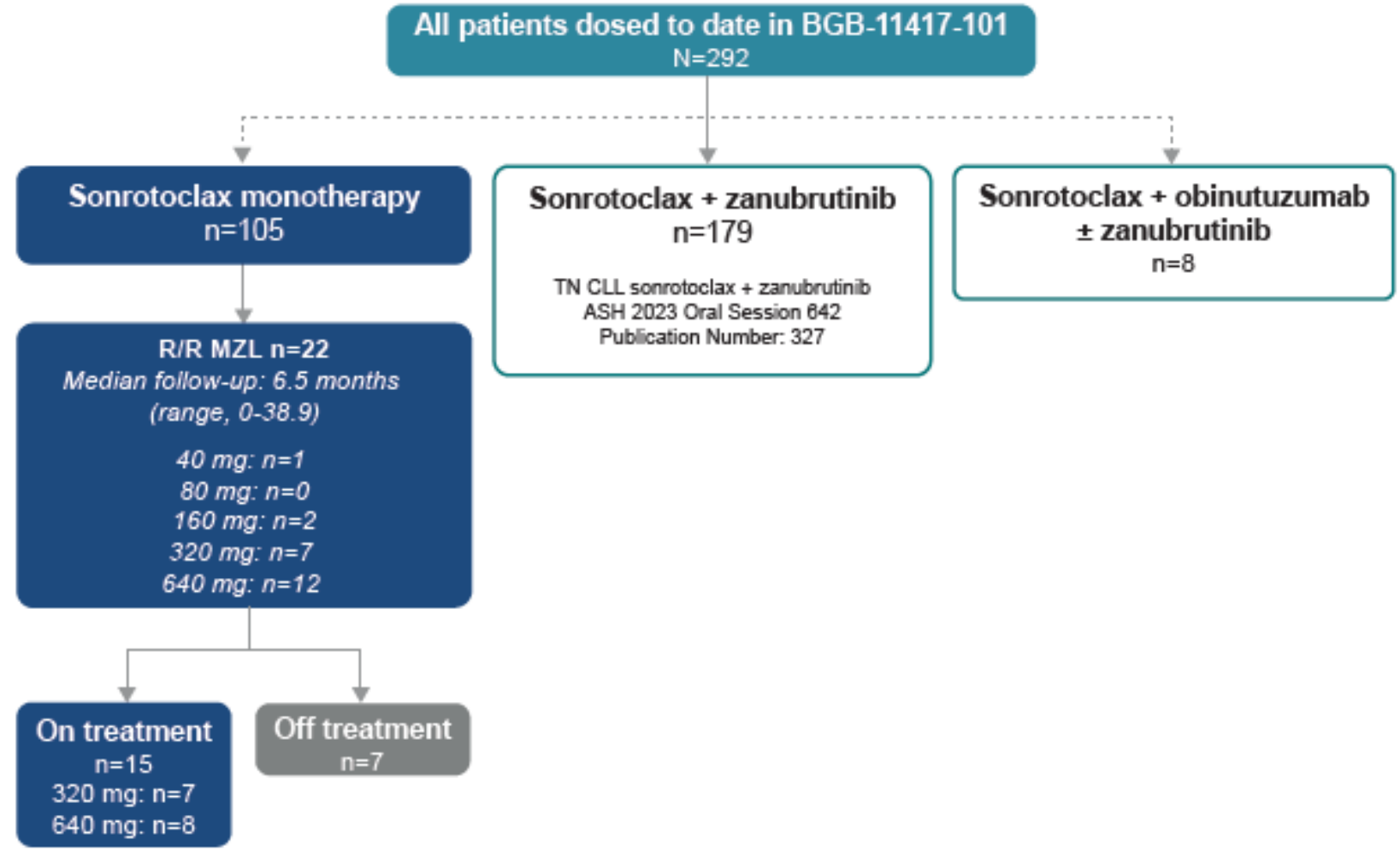
Abstract No 3032

Figure 1. BGB-11417-101 Study Design



[a] The safety monitoring committee reviewed dose-level cohort data before dose escalation.
RP2D, recommended phase 2 dose; SMC, safety monitoring committee; t-NHL, transformed non-Hodgkin lymphoma.

Figure 2. Patient Disposition



Data cutoff date: August 14, 2023.
R/R, relapsed/refractory; TN, treatment naïve.

Table 1. Baseline Patient Characteristics

Characteristic	640 mg (n=12)	All patients with MZL (N=22)
Age, median (range), years	72.5 (54-84)	74.5 (54-85)
Sex, n (%)		
Male	6 (50.0)	10 (45.5)
Female	6 (50.0)	12 (54.5)
ECOG PS		
0	7 (58.3)	12 (54.5)
1	3 (25.0)	8 (36.4)
2	2 (16.7)	2 (9.1)
Prior therapy		
No. of prior lines of therapy, median (range)	1.5 (1-3)	2 (1-6)
Time from last systemic therapy to first dose, median (range), months	11.5 (0.2-158.1)	11.5 (0.1-158.1)
Prior BTKi (BTKi as last prior therapy), n	4 (3)	10 (8)
Prior BTKi duration, median (range), months	17.8 (7.9-41.8)	22.8 (12.1-42.6)
Prior rituximab use, n (%)	12 (100)	22 (100)
Prior CHOP-like regimens, n (%)	7 (58.3)	16 (72.7)
Prior bendamustine, n (%)	6 (50.0)	10 (45.5)

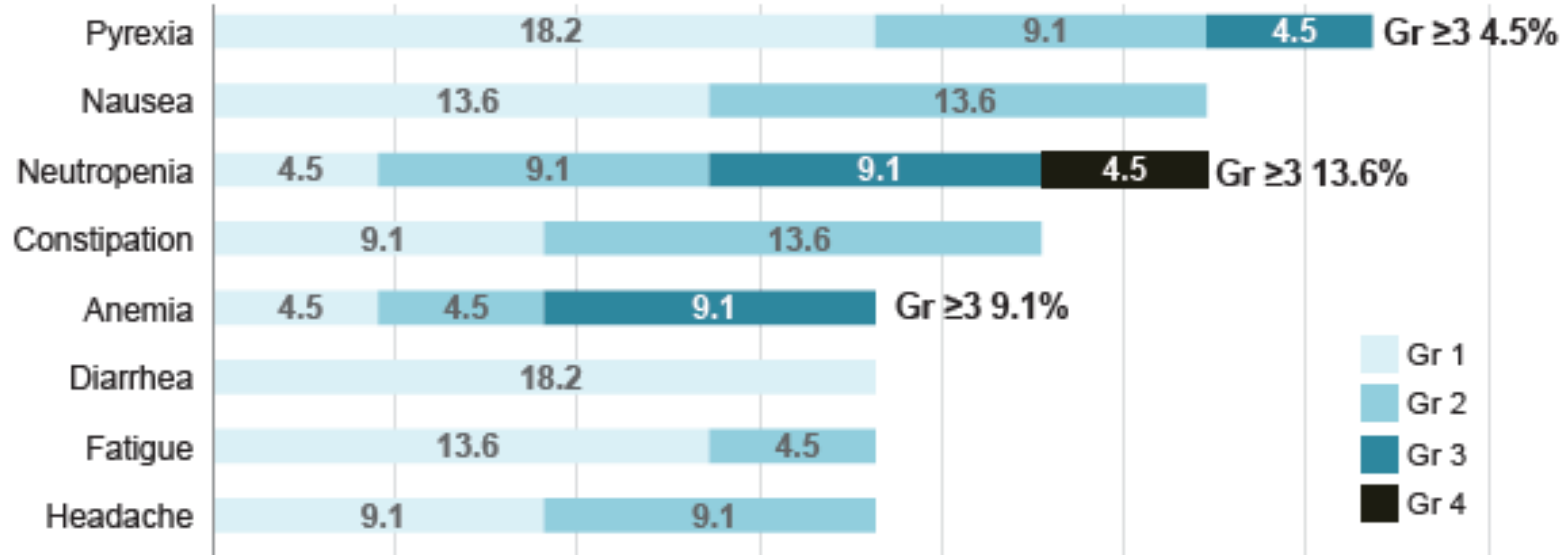
BTKi, Bruton tyrosine kinase inhibitor; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; ECOG PS, Eastern Oncology Group Performance Status.

Table 2. Adverse Event Summary

Patients, n (%)	640 mg (n=10)	All patients with MZL (N=22)
Any AEs	12 (100)	21 (95.5)
Grade ≥3	6 (50.0)	10 (45.5)
Serious AEs	5 (41.7)	8 (36.4)
Leading to death[a]	1 (8.3)	1 (4.5)
Leading to discontinuation of sonrotoclax	1 (8.3)	1 (4.5)
Leading to dose interruption of sonrotoclax	3 (25.0)	3 (13.6)
Leading to dose reduction of sonrotoclax	0	0

[a] Patient with lymphopenia and low immunoglobulin levels at baseline developed PML and died 8 months after starting treatment with 640 mg sonrotoclax. Prior treatments included rituximab, bendamustine and a PI3K inhibitor.
PI3K, phosphoinositide-3-kinase; PML, progressive multifocal leukoencephalopathy

Figure 3. TEAEs in ≥2 Patients



- **TLS:**
  - No clinical TLS
  - Two patients experienced laboratory TLS

Table 3. Response Rates

	40 mg (n=1)	160 mg (n=2)	320 mg (n=7)	640 mg (n=12)	All patients with MZL (N=22)
Median follow-up (range), months	38.9 –	27.7 (27.4-28.1)	1 (0-3.4)	7.2 (2.1-15.4)	6.5 (0-38.9)
Efficacy-evaluable patients, n	1	2	–	10	13
ORR, n (%)	0	1 (50)	–	7 (70)	8 (62)
CR, n (%)	0	0	–	4 (40)	4 (31)
PR, n (%)	0	1 (50)	–	3 (30)	4 (31)
SD, n (%)	1 (100)	0	–	2 (20)	3 (23)
PD, n (%)	0	1 (50)	–	1 (10)	2 (15)

BOR, best overall response; ORR, overall response rate.

CONCLUSIONS

- Sonrotoclax doses as high as 640 mg QD are well tolerated, and the MTD was not determined
- Sonrotoclax demonstrated promising single-agent activity in patients with MZL
  - An ORR of 70% (including a CR rate of 40%) was seen with the expansion dose of 640 mg; efficacy data from the 320 mg expansion dose level is forthcoming
- Laboratory TLS was only seen in patients with high baseline levels of circulating cells, and resolved quickly without need for dose modification
- Further studies of sonrotoclax in combination with other active agents in MZL (eg, zanubrutinib and rituximab) are warranted

Zusammenfassung | Take-Home-Messages

- Morbus Waldenström
  - Beim Morbus Waldenström bleibt die Neuropathie eine therapeutische Herausforderung. Die Wirksamkeit von BTK Inhibitoren muss in unabhängigen Studien validiert werden.
  - Switching von Ibrutinib zu Zanubrutinib ist sehr gut möglich, und zum Teil mit einer Verbesserung von Symptomen und Krankheitskontrolle assoziiert.
  - CAR-T Zellen hocheffektiv bei transformierten WM

- Marginalzonenlymphom
  - Die Therapieoptionen beim rezidiverten MZL sind limitiert. Möglicherweise bieten BCL2 Inhibitoren der zweiten Generation neue Therapiechancen

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2023

Für den Inhalt verantwortlich:

Prof. Dr. med. Christian Buske

Universitätsklinikum Ulm

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

Das Informationsprojekt wird unterstützt von den Firmen:

abbvie

AMGEN

AstraZeneca

BeiGene

Bristol Myers Squibb™

GSK

HEXAL

A Sandoz Brand

janssen

PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Diese hatten keinen Einfluss auf die Inhalte.