Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

EHA2023 HYBRID

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Expert:innen berichten zu Lymphomen & Leukämien

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Morbus Waldenström (WM) & Marginalzonen-Lymphom (MZL)

Disclosures – Philipp Staber, MD PhD

Research Support	Takeda-Millenium, Genactis, Roche Diagnostics
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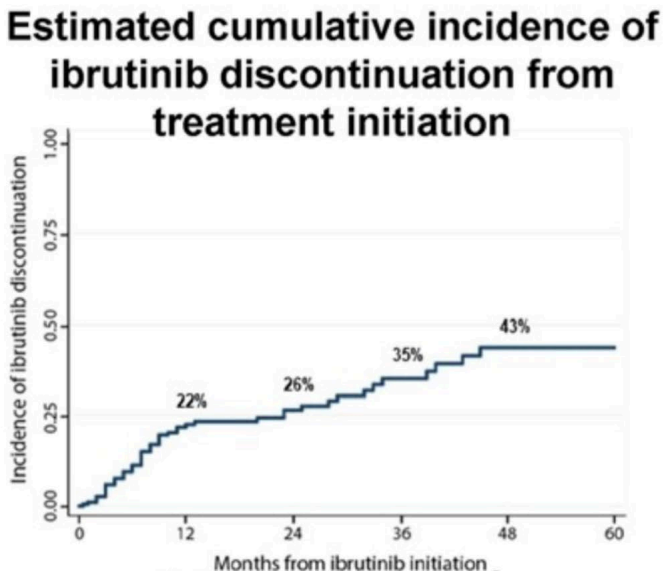
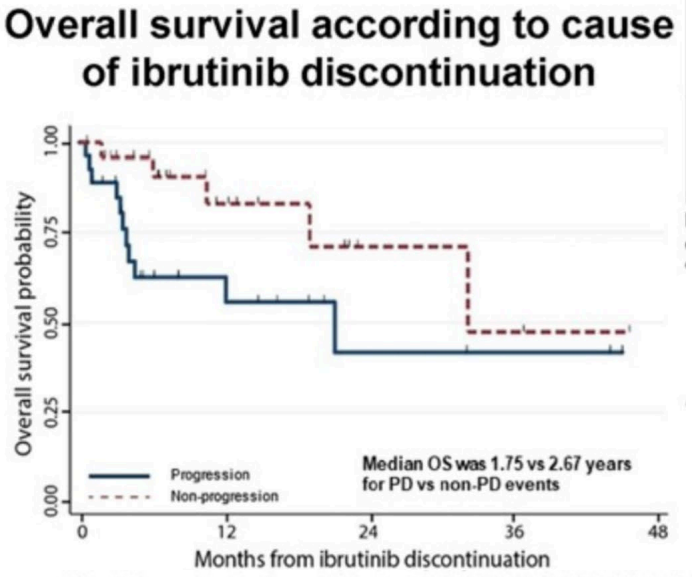
Scientific Advisory Board	Amgen, Roche, Janssen, Gilead, BeiGene, Incyte, Abbvie, CTI, Takeda,

Kapitel 1 WALDENSTRÖM MACROGLOBULINEMIA

Therapieoptionen nach BTKi Versagen?





Gustine et al. *Am J Hematol.* 2018;93:511-517.

Morbus Waldenström Ansprechkriterien:

Major RR	Komplette Remission (CR)	• kein Nachweis des monoklonalen IgM in der Immunfixation im Serum und • normaler IgM Spiegel im Serum und • komplette Rückbildung vergrößerter Lymphknoten und einer Splenomegalie, wenn vor Therapie vorhanden und • Knochenmarkaspirat und –biopsie normal
	Sehr gute partielle Remission (VGPR)	• Monoklonales IgM nachweisbar und • ≥ 90% Reduktion des IgM Spiegels im Serum, ausgehend vom Befund vor Therapie und • keine neuen Krankheitszeichen oder Symptome
	Partielle Remission (PR)	• Monoklonales IgM nachweisbar und • ≥ 50%, aber < 90% Reduktion des IgM Spiegels im Serum, ausgehend vom Befund vor Therapie und • Rückgang von Lymphadenopathie / Splenomegalie, wenn vor Therapie vorhanden und • keine neuen Krankheitszeichen oder Symptome
	Minor Response (MR)	• Monoklonales IgM nachweisbar und • ≥ 25%, aber < 50% Reduktion des IgM Spiegels im Serum, ausgehend vom Befund vor Therapie und • keine neuen Krankheitszeichen
	Stabile Erkrankung (SD)	• Monoklonales IgM nachweisbar und • < 25% Reduktion und < 25% Anstieg des IgM Spiegels im Serum, ausgehend vom Befund vor Therapie und • keine neuen Krankheitszeichen

Onkopedia Leitlinie: Christian Buske, Dominik Heim, Michael Herold, Philipp Staber, Martin Dreyling

P1108 EFFICACY OF PIRTOBRUTINIB, A HIGHLY SELECTIVE, NON-COVALENT (REVERSIBLE) BTK INHIBITOR IN RELAPSED/REFRACTORY WALDENSTRÖM MACROGLOBULINEMIA: RESULTS FROM THE PHASE 1/2 BRUIN STUDY

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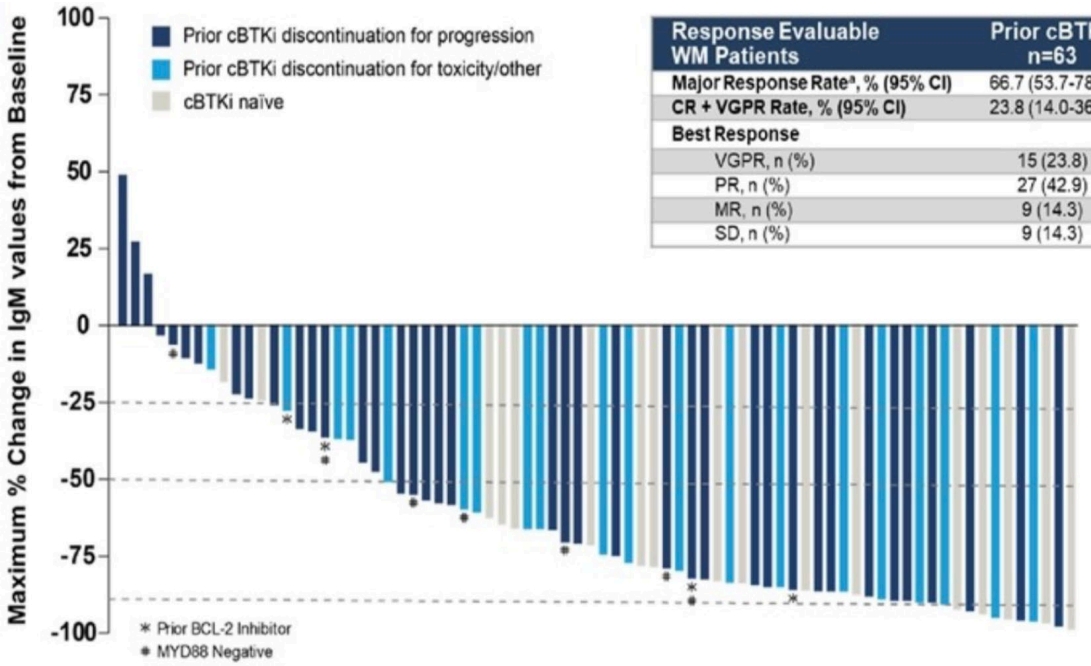
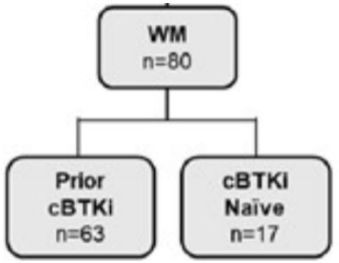
NON-COVALENT BTKi, PIRTOBRUTINIB in R/R WM

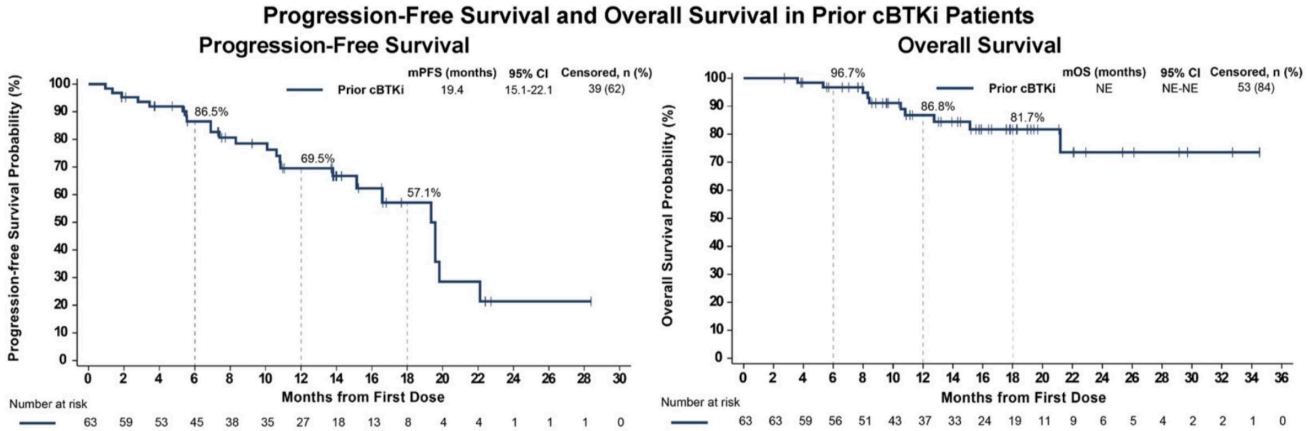


Response Evaluable WM Patients	Prior cBTKi n=63	cBTKi Naïve n=17
Major Response Rate[a], % (95% CI)	66.7 (53.7-78.0)	88.2 (63.6-98.5)
CR + VGPR Rate, % (95% CI)	23.8 (14.0-36.2)	29.4 (10.3-56.0)
Best Response		
VGPR, n (%)	15 (23.8)	5 (29.4)
PR, n (%)	27 (42.9)	10 (58.8)
MR, n (%)	9 (14.3)	0 (0)
SD, n (%)	9 (14.3)	2 (11.8)



Pirtobrutinib Safety Profile

	All Doses and Patients (N=773)			
	Treatment-Emergent AEs, (≥15%), %		Treatment-Related AEs, %	
Adverse Event (AEs)	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Fatigue	28.7%	2.1%	9.3%	0.8%
Diarrhea	24.2%	0.9%	9.3%	0.4%
Neutropenia[a]	24.2%	20.4%	14.7%	11.5%
Contusion	19.4%	0.0%	12.8%	0.0%
Cough	17.5%	0.1%	2.3%	0.0%
Covid-19	16.7%	2.7%	1.3%	0.0%
Nausea	16.2%	0.1%	4.7%	0.1%
Dyspnea	15.5%	1.0%	3.0%	0.1%
Anemia	15.4%	8.8%	5.2%	2.1%
AEs of Special Interest[b]	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Bruising[c]	23.7%	0.0%	15.1%	0.0%
Rash[d]	12.7%	0.5%	6.0%	0.4%
Arthralgia	14.4%	0.6%	3.5%	0.0%
Hemorrhage/Hematoma[e]	11.4%	1.8%	4.0%	0.6%
Hypertension	9.2%	2.3%	3.4%	0.6%
Atrial fibrillation/flutter[f,g]	2.8%	1.2%	0.8%	0.1%



Median Follow-up: 14 months
After cBTKi: major RR: 67% … mPFS 19.4 months
Naïve cBTKi: major RR: 88%
Very well tolerated with low rates of Grade 3 or 4 AEs

P1097 CD20 CAR-T THERAPY WITH MB-106 FOR BTK INHIBITOR-REFRACTORY WALDENSTRÖM MACROGLOBULINEMIA (WM)/ LYMPHOPLASMACYTIC LYMPHOMA (LPL) – SINGLE INSTITUTION STUDY

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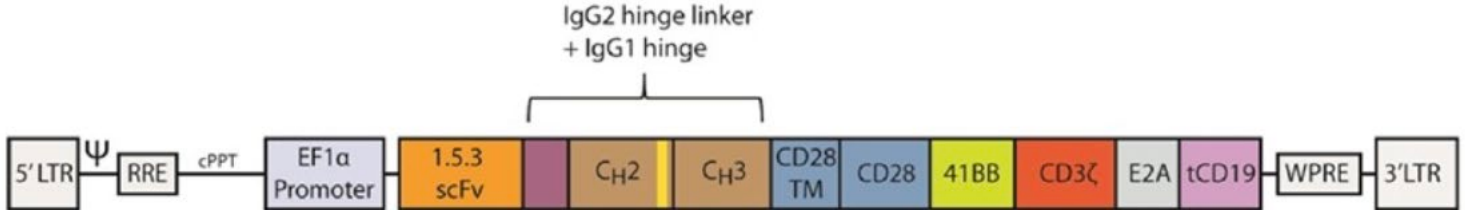
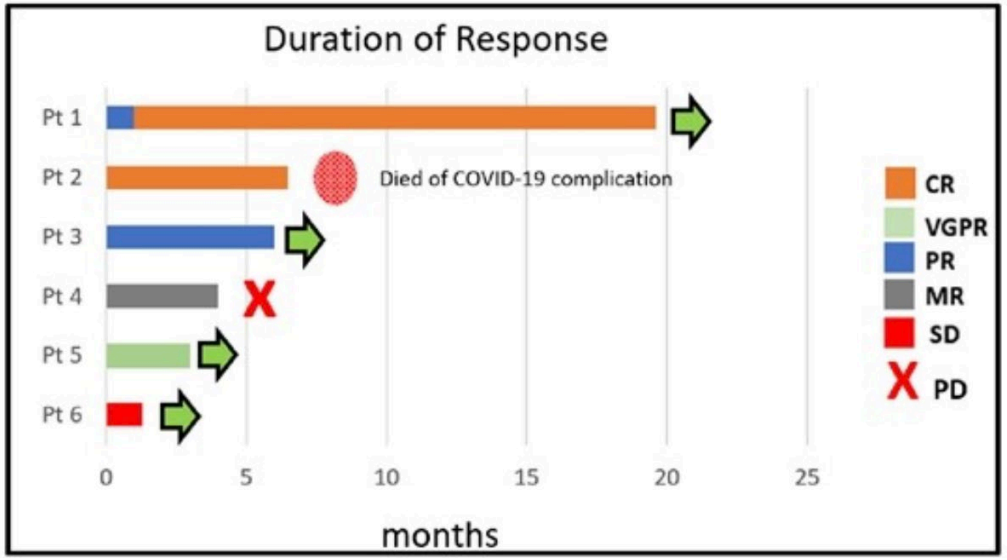
CD20 CAR-T, MB-106 in BTKi R/R WM

fully human 3rd gen. CD20 CAR-T with 2 costimulatory domains: 4-1BB and CD28



Major RR

Baseline (N = 6)	
Age, median (range)	69 (51-79)
Female sex, n (%)	2 (33%)
Prior lines of therapy, m(range)	7.5 (2-12)
Prior BTKi treatment Ibrutinib Acalabrutinib zanubrutinib	6 (100%) 5 1 2
BTKi progression	6 (100%)
BTKi intolerant	2 (33%)
MYD88^{L265P} mutation	6 (100%)



Sum: Short FU
Major RR: 4/6, 2CR, 1VGPR
safe, outpatient setting

Adverse events:
Outpatient treatment
No grade 3 or 4 CRS or ICANS

	Grade 3	Grade 4	Grade 3 or 4
Leukopenia	1 (16%)	4 (66%)	5 (83%)
Neutropenia	2 (32%)	4 (66%)	6 (100%)
Lymphopenia	3 (50%)	2 (33%)	5 (83%)
Thrombocytopenia	2 (33%)	-	2 (33%)
Hypotension	2 (33%)	-	2 (33%)
Hypertension	1 (16%)	-	1 (16%)
Fatigue	1 (16%)	-	1 (16%)
Elevated ALT	1 (16%)	-	1 (16%)
Elevated AST	1 (16%)	-	1 (16%)

FDA granted orphan drug designation
WM is one of the priority disease for MB-106

Kapitel 2

MARGINAL ZONE LYMPHOMA (MZL

P1084 LONG-TERM EFFICACY AND SAFETY OF ZANUBRUTINIB (ZANU) IN PATIENTS (PTS) WITH RELAPSED/REFRACTORY (R/R) MARGINAL ZONE LYMPHOMA (MZL): FINAL ANALYSIS OF THE MAGNOLIA (BGB-3111-214) TRIAL

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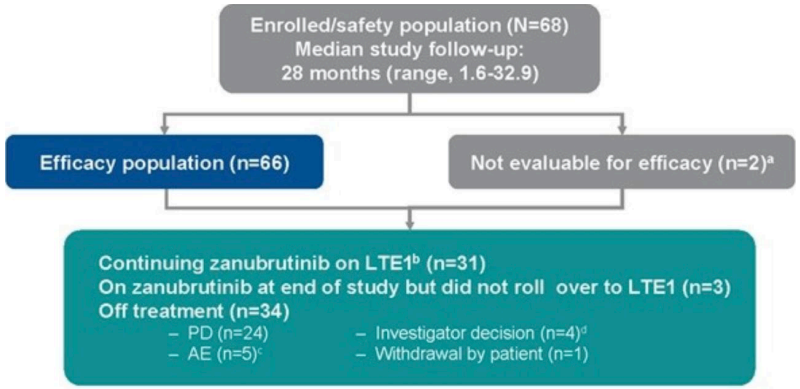
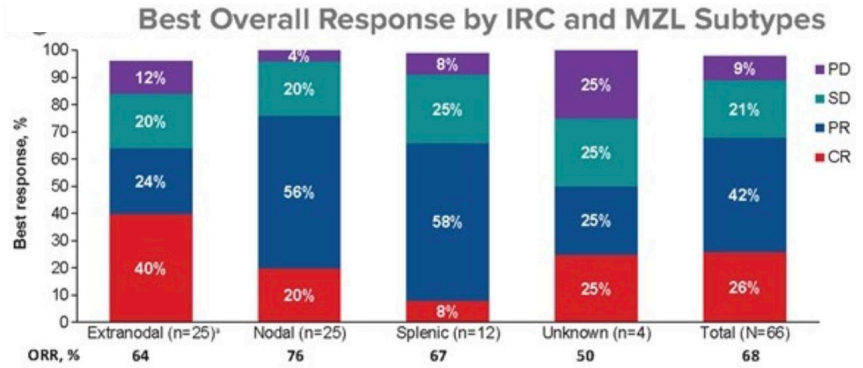
ZANUBRUTINIB in R/R MZL

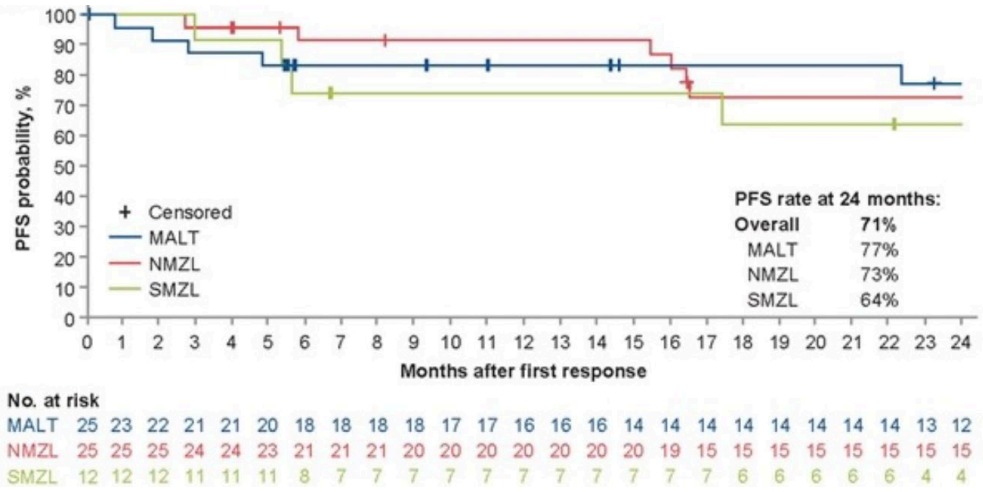
FINAL ANALYSIS OF THE MAGNOLIA (BGB-3111-214) TRIAL





TEAEs of clinical interest, n (%)	All grade	Grade ≥3
Infections	38 (56)	15 (22)[d]
Hemorrhage	28 (41)	1 (1.5)[e]
Cardiac		
Hypertension	3 (4)[f]	2 (3)
Atrial fibrillation/flutter	2 (3)[g]	1 (1.5)
Ventricular extrasystole	1 (1.5)[h]	0
Second primary malignancy	5 (7)[i]	3 (4)

Characteristics	Total (N=68)
Age, median (range), years	70 (37-95)
≥65 years, n (%)	41 (60)
≥75 years, n (%)	19 (28)
Male, n (%)	36 (53)
ECOG PS 0 or 1, n (%)[a]	63 (93)
MZL subtypes, n (%)	
Extranodal	26 (38)
Nodal	26 (38)
Splenic	12 (18)
Unknown	4 (6)
Disease status, n (%)	
Relapsed	44 (65)
Refractory	22 (32)
Stage III/IV, n (%)	59 (87)
FDG avid (by IRC), n (%)	61 (90)
Extranodal site involvement, n (%)	53 (78)
Bone marrow infiltration, n (%)	29 (43)
Prior lines of systemic therapy, median (range)[b]	2 (1-6)
Immunochemotherapy, n (%)	61 (90)[b]
Rituximab monotherapy, n (%)	7 (10)



- Median Follow-Up 28 months
- ORR 68%
- 24mo-PFS 71%
- Well tolerated

Zusammenfassung | Take-Home-Messages

- WM-R/R, aus BRUIN Studie, R/R nach cBTKi:
  Pirtobrutinib major RR: 67% … mPFS 19.4 mo

- WM-R/R, 3rd gen. CD20-CAR-T, R/R nach cBTKi:
  outpatient setting, keine Gr3 oder 4 CRS, NCANs
  MB-106 major RR: 4/6 (67%) … kurzes Follow-up

- MZL-R/R, Finale Analyse der Magnolia Studie:
  Zanubrutinib ORR 68%, 24mo-PFS 71%

Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2023

Für den Inhalt verantwortlich:

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Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

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Expert:innen berichten zu Lymphomen & Leukämien

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