6th Postgraduate lymphoma conference – September 7-9, 2022

Improved biological insight and new agents in Marginal zone lymphoma

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DISCLOSURES

Consultant or advisory role	Bayer, Celgene, Janssen, Roche, Cellectis, Kyte, Novartis,ADC Therapeutics, AstraZeneca, Incyte, Novartis, Sanofi, Takeda, Abbvie, Amgen
Research funding	Roche, Janssen, Hospira, Novartis

Overview

- **Introduction : Epidemiology and recommanded treatment**
- **Biological insights**
- **New agents**
- **Conclusion**

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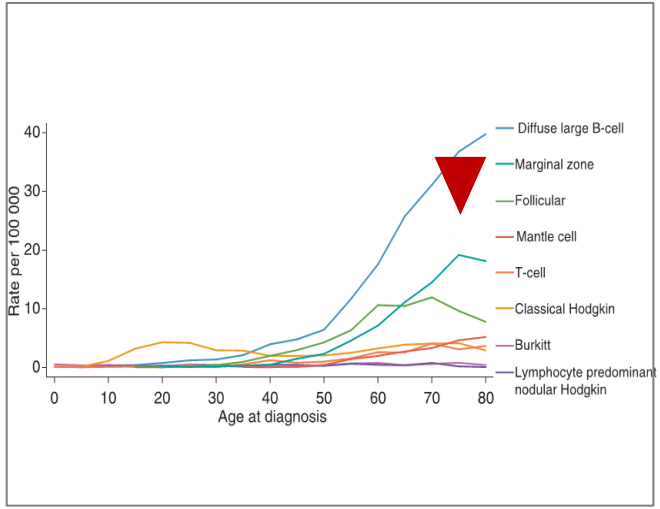
Epidemiology

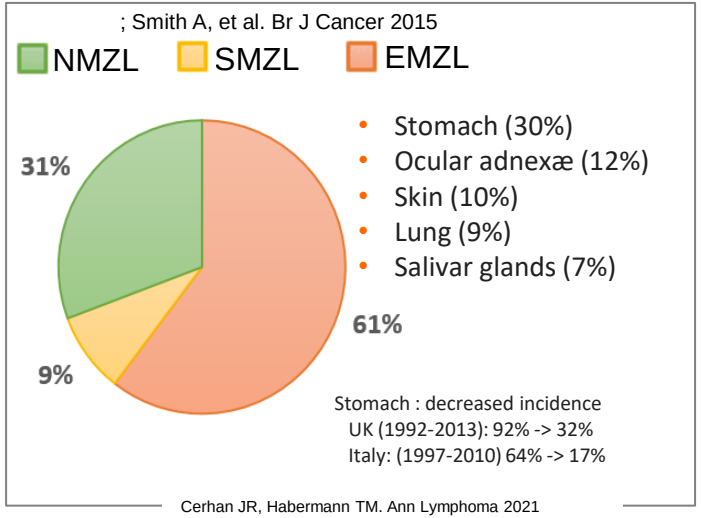
- **7%** of all mature non-Hodgkin lymphomas, with at 3 distinct entities : EMZL, NMZL, SMZL
- Increasing incidence **with age**
- Increased incidence **1-4% per year** over the last 20 years (USA-France: improved diagnosis?)
- **Predisposing conditions** : infectious agent and autoimmune conditions

Increased incidence >60 & >>80



Smith A, et al. Br J Cancer 2015

Three distinct entities



Cerhan JR, Habermann TM. Ann Lymphoma 2021
Monga, Thieblemont, et al. Ann Hematol. 2019;98:175-183;
Sena Gut 2014; Luminari S, et al Ann Oncol 2010

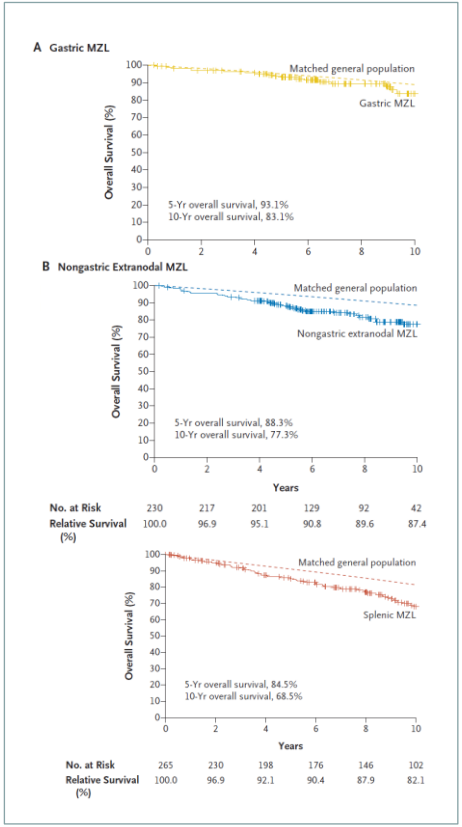
Predisposing conditions

Site of Disease	Infectious Agent	Autoimmune Condition
Stomach	*Helicobacter pylori*	—
Ocular adnexa	*Chlamydia psittaci*	Sjögren's syndrome (in lacrimal gland MZL)
Lung	*Achromobacter xylosoxidans*	Lymphocytic interstitial pneumonia
Intestine	*Campylobacter jejuni*	—
Skin	*Borrelia burgdorferi*	—
Salivary gland	—	Sjögren's syndrome
Thyroid	—	Hashimoto's thyroiditis
Lymph node	Hepatitis C virus	—
Spleen	Hepatitis C virus	—

Rossi D, et al NEJM 2022

Outlines

- Indolent disease, with a risk of transformation < 10%
- No standard treatment in L1 : local or systemic therapy
- Pronostic scores : MALT-IPI, HPLL, ILL
- POD24 + in MZL
- Evaluation criteria : cheson 2014
  - without PET which is still exploratory
  - modified Matutes 2008 for SMZL



-ESMO guidelines . Zucca et al. Ann Oncol 2020.

-First line treatments : Zucca et al. J Clin Oncol 2017; 2.Salar et al. Blood 2017; 3. Kalpadakis C et al. EHA 2017;4. Iannitto et al. ASH 2017; 5

-Pronostic scores : Thieblemont C et al., JCO 2018; Montalban & SMZLSG. Leukemia Lymphoma. 2014; 55:929; Arcaini et al. Blood, 2006;107;4643;

-POD24 : Conconi, Haematologica 2020; Luminari, Blood 2019

-For reviews: Thieblemont C. Blood 2016; Rossi et al. NEJM 2022

Treatment options

Localized MZL	INDICATIONS	TREATMENT	RESULTS
Infectious agent H.pylori - stomach	**Always**	**Antibiotics** [1]	CRR >75%
Amenable to RT e.g. stomach	**Stage IE** gastric EMZL	**RT** [2] 24Gy Involved-site	5y-PFS 90%
Not amenable to RT e.g. lung	Other EMZL	**Consider surgery** [3]	7y-PFS 69% : ocular anexa 7y-PFS ≈75% : lung 5y-/10y-PFS 35%/13% : SMZL

1. Stathis A, Ann Oncol 2009; 2. Quero L& Thieblemont, WJGO 2022; 3. Lenglet & Thieblemont, Leuk Lymphoma 2014; 4. Zucca E et al, JCO 2017; 5. Salar et al. Blood 2017; 6. Kalpadakis et al. Blood 2018 , 7. Iannitto et al. BJH 2018; 8. Rummel et al. Lancet 2013

Treatment options

Disseminated MZL	INDICATIONS	TREATMENT	RESULTS
Disseminated MZL			
EMZL	**MALT-IPI ≥ 1** Age > 70 ans, Ann Arbor III/IV, LDH > N	R-chlorambucil[4] R-bendamustine [5]	5-y PFS : 72 % 7-year PFS 92.8%
SMZL	**Symptoms and cytopenias** hb <10g/dL, plat<80G/L, PNN<1.0G/L +/- auto-immune cytopenias	Rituximab [6] R-Bendamustine [5]	5-year PFS 79% 3y-PFS 90%
NMZL	**High tumor burden** **GELF criteria**	R-Bendamustine [7]	median PFS 69.5 months

1. Stathis A, Ann Oncol 2009; 2. Quero L& Thieblemont, WJGO 2022; 3. Lenglet & Thieblemont, Leuk Lymphoma 2014; 4. Zucca E et al, JCO 2017; 5. Salar et al. Blood 2017; 6. Kalpadakis et al. Blood 2018 , 7. Iannitto et al. BJH 2018; 8. Rummel et al. Lancet 2013

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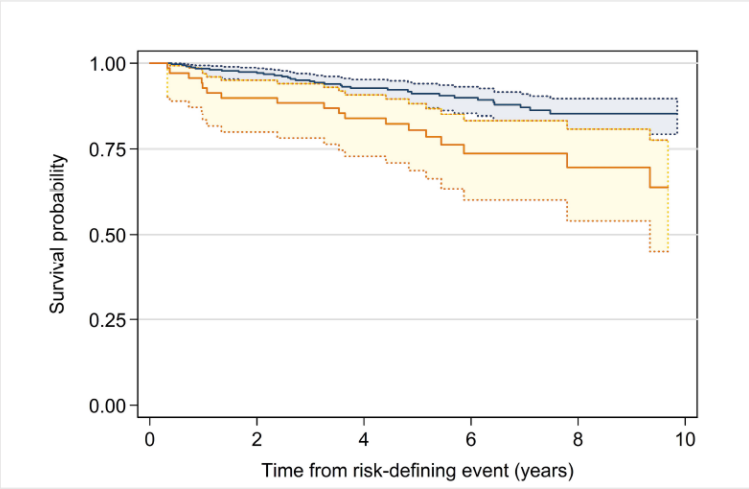
Protocol discontinuation 20%; Dose reduction 15% Grade 3-4 toxicities 89% Lethal toxicity 2%

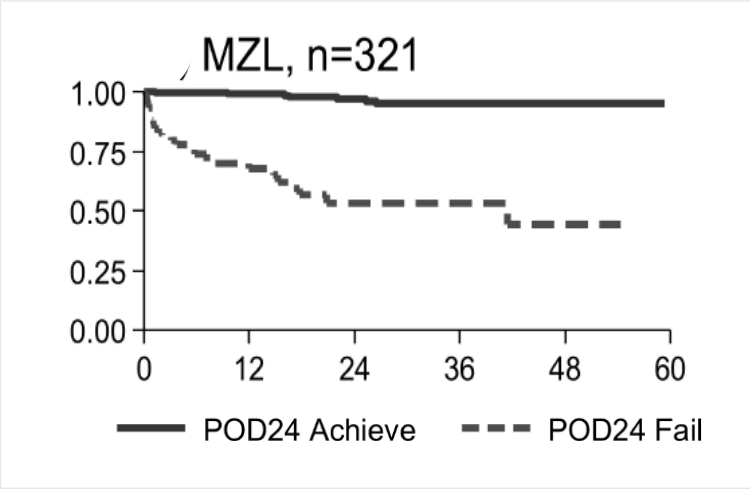
1. Stathis A, Ann Oncol 2009; 2. Quero L& Thieblemont, WJGO 2022; 3. Lenglet & Thieblemont, Leuk Lymphoma 2014; 4. Zucca E et al, JCO 2017; 5. Salar et al. Blood 2017; 6. Kalpadakis et al. Blood 2018 , 7. Iannitto et al. BJH 2018; 8. Rummel et al. Lancet 2013

Maintenance in MZL ?

POD 24 in MZL



Conconi, Haematologica 2020

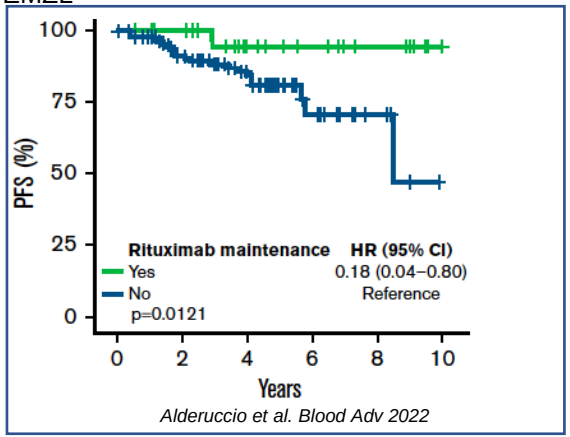


Luminari, Blood 2019

Rituximab maintenance in MZLs

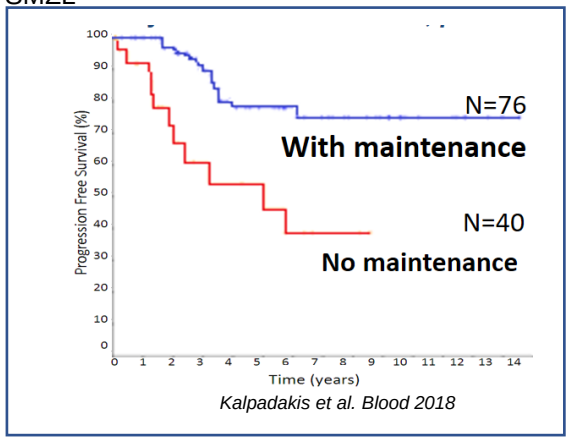
MZL	Study	Rituximab Maintenance	Nber of patients	Results
EMZL	IELSG-38 [1] Prospective Phase 2	**2 years**	109	**CRR** : EOI CR 58% → 1-y 69% → 2-y 80%75%
EMZL	Retrospective multicentric [2]	**2 years**	221	**5y-PFS** 94.4% vs 81.1%, *p*=.0121
SMZL	Prospective multicentric [3]	**1 or 2 years**	108	**7y-PFS** : 75% vs 39%, *p*<.0004
NMZL /SMZL	MAINTAIN [4] phase 2, randomized	**2 years**	104	**median PFS** NR vs 92 months, *p*=.008

EMZL



Alderuccio et al. Blood Adv 2022

SMZL



Kalpadakis et al. Blood 2018

No impact on OS !

1. Stathis et al, IELSG 2021; 2. Alderuccio et al. Blood Adv 2022; 3. Kalpadakis et al. Blood 2018; 4. Rummel et al. ASCO 2018

Overview

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MZL - Biology and genomics

1. IgHV repertory strongly biased & restricted

Site of Disease	Biased Immunoglobulin-Gene Usage†
Stomach	IGHV3–23
Ocular adnexa	IGHV4–34
Salivary gland	IGHV1–69
Thyroid	IGHV3–23
Lymph node	IGHV4–34
Spleen	IGHV1–2*04

Anatomic-site-specific, biaised usage of somatically mutated Ig genes
With ongoing maturation of Ag affinity

Expansion of lymphoma is driven by autoantigens or alloantigens exposed in the tissue microenvironement

Rossi et al NEJM 2022

MZL - Biology and genomics

1. IgHV repertory strongly biased & restricted

2. Genetic changes with specific translocation

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Spleen	IGHV1–2*04

Site of Disease	Recurrent Translocations	Recurrent Copy-No. Aberrations
Stomach	t(11;18)(q21;q21) *BIRC3/MALT1* t(14;18)(q32;q21) *IGH/MALT1* t(1;14)(p22;q32) *BCL10/IGH*	+3, +18
Ocular adnexa	t(14;18)(q32;q21) *IGH/MALT1* t(3;14)(p14.1;q32) *FOXP1/IGH*	+3, +18
Lung	t(11;18)(q21;q21) *BIRC3/MALT1* t(14;18)(q32;q21) *IGH/MALT1*	+3, +18
Intestine	t(11;18)(q21;q21) *BIRC3/MALT1* t(1;14)(p22;q32) *BCL10/IGH*	+3, +18
Skin	t(14;18)(q32;q21) *IGH/MALT1* t(3;14)(p14.1;q32) *FOXP1/IGH*	+3, +18
Salivary gland	t(14;18)(q32;q21) *IGH/MALT1*	+3, +18
Thyroid	t(14;18)(q32;q21) *IGH/MALT1* t(3;14)(p14.1;q32) *FOXP1/IGH*	+3, +18
Lymph node	—	+3, +18
Spleen	t(2;7)(p11;q21) *IGK/CDK6*	+3, +18, del(7q31–32

-> NFκB patchway is activated in the absence of upstream stimulation

Rossi et al NEJM 2022

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2. Genetic changes with specific translocation

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Lymph node	—	+3, +18
Spleen	t(2;7)(p11;q21) *IGK/CDK6*	+3, +18, del(7q31–32

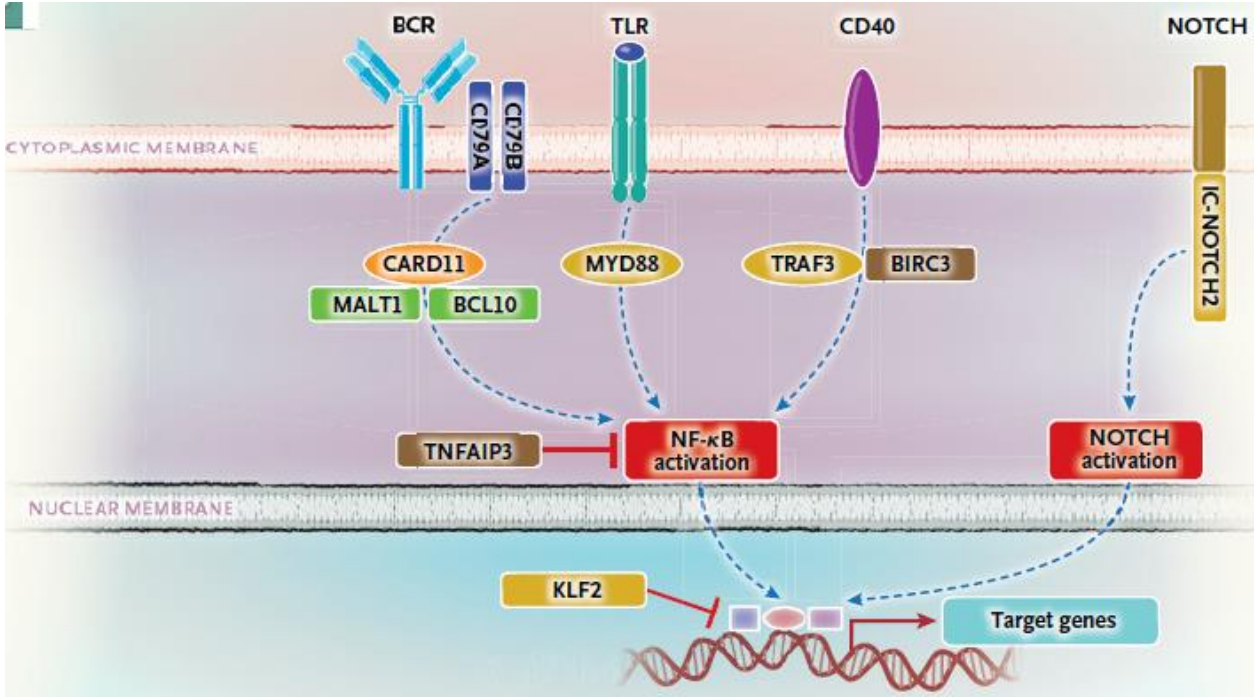
3. Genetic mutations

Site of Disease	Site-Specific Gene Mutations
Ocular adnexa	*TNFAIP3*
Salivary gland	*TBL1XR1*, *GPR34*
Thyroid	*TET2*, *TNFRSF14*, *CD274*
Lymph node	*KLF2*, *NOTCH2*, *PTPRD*
Spleen	*KLF2*, *NOTCH2*

Site-specific mutations

Rossi et al NEJM 2022

Molecules affected by genetic lesions in MZLs



EMZL

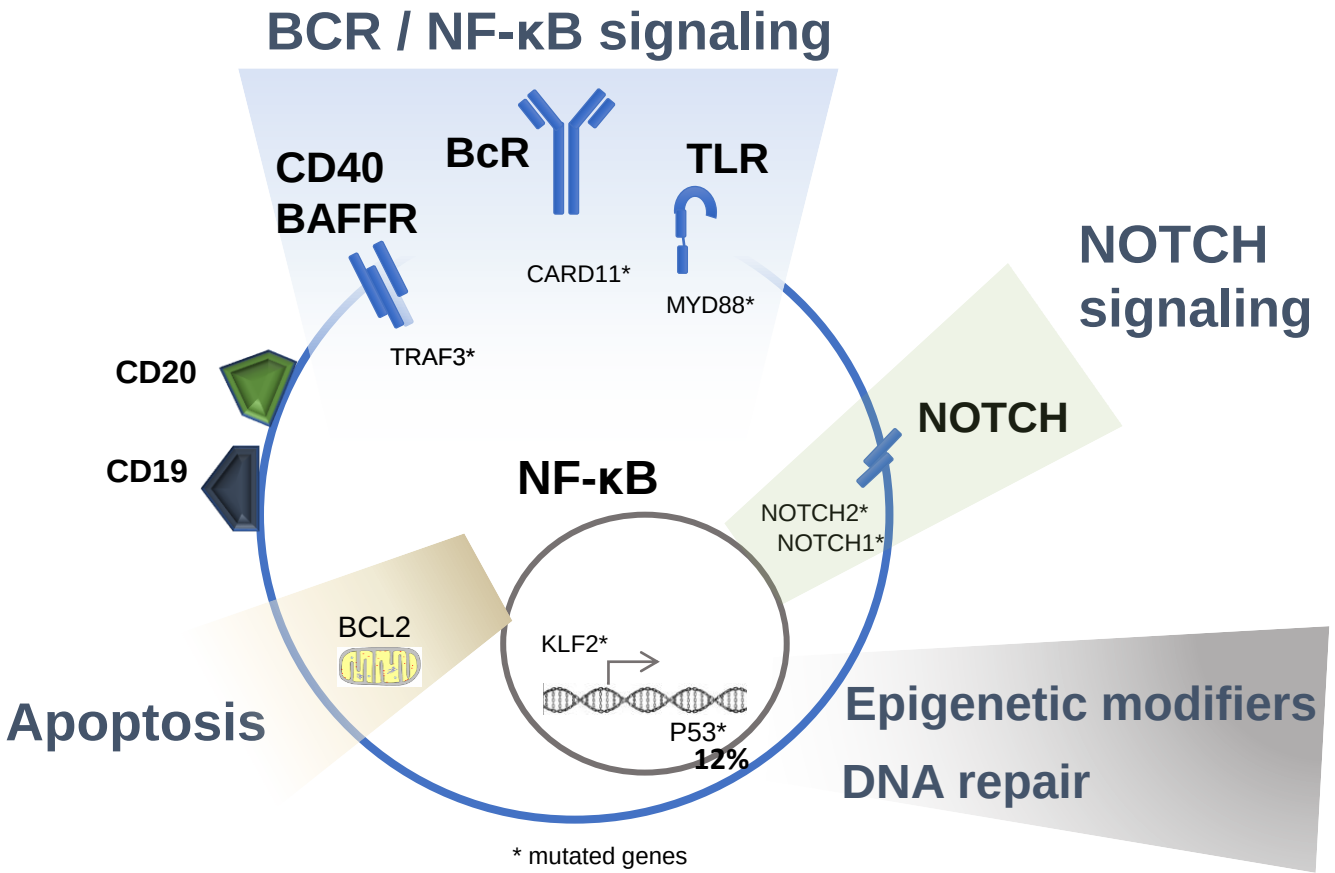
SMZL and NMZL

All MZL

Key activated signaling pathways

Rossi et al NEJM 2022

Oncogenic cooperation with shared altered pathways in MZL



Thieblemont C, 2019 for review

+ SMZL: immunosuppressive or immunosilent microenvironnement

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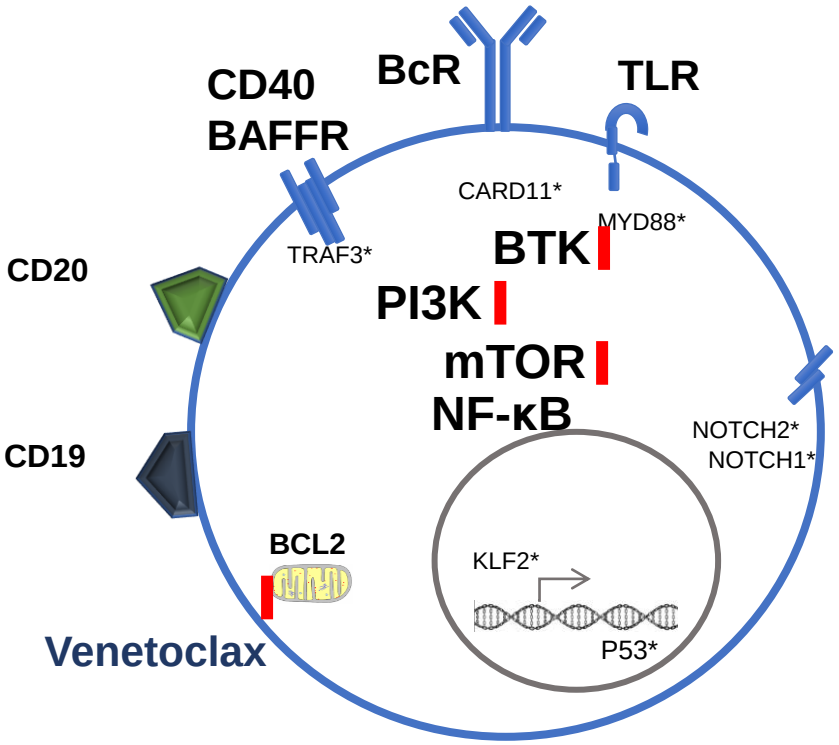
New drugs in MZL



Ibrutinib

Zanubrutinib

Idelalisib
Copanlisib
Umbralisib
Parsaclisib
Duvelisib

Everolimus

Lenalidomide

New drugs in MZL

Anti-CD20 MAb

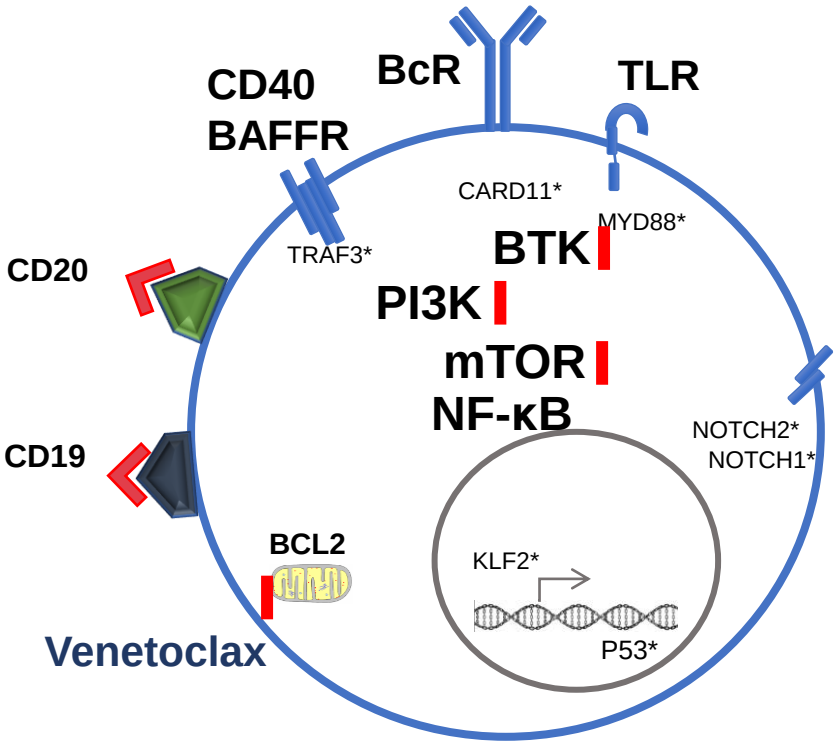
CD20x203 bispecific

Anti-CD19 CAR T-cells

Tafasitamab

Loncastuximab tesirine

Lenalidomide



Ibrutinib

Zanubrutinib

Idelalisib

Copanlisib

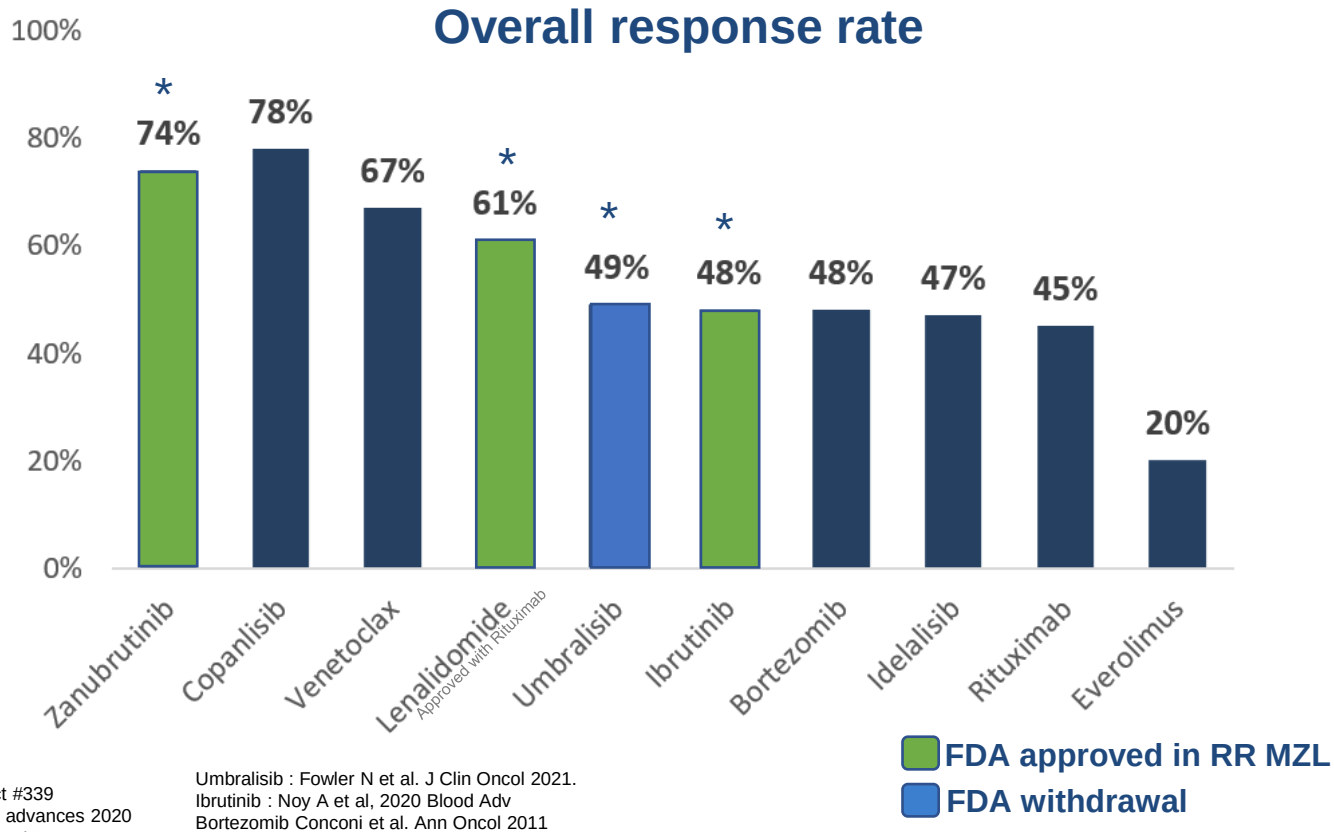
Umbralisib

Parsaclisib

Duvelisib

Everolimus

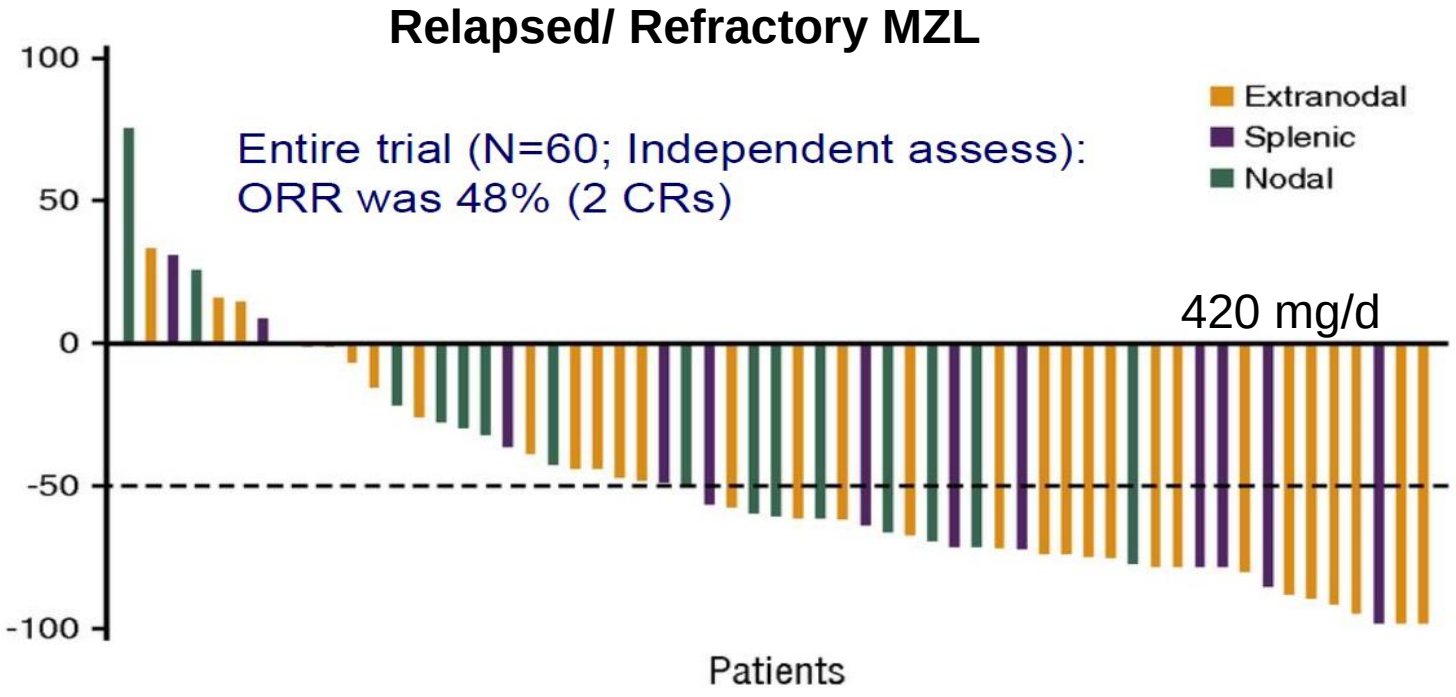
Single Agent Activity in R/R MZL



Zanubrutinib: Opat ASH2020 Abstract #339
Copanlisib : Panayiotidis et al. Blood advances 2020
Venetoclax Davids MA et al J Clin Oncol 2017
Lenalidomide Becnel et al. B J Haematol 2019

Umbralisib : Fowler N et al. J Clin Oncol 2021.
Ibrutinib : Noy A et al, 2020 Blood Adv
Bortezomib Conconi et al. Ann Oncol 2011
Idelalisib : Gopal, et al. NEJM 2014; 370(11):1008-18
Everolimus Conconi et al. Br J Haematol 2014

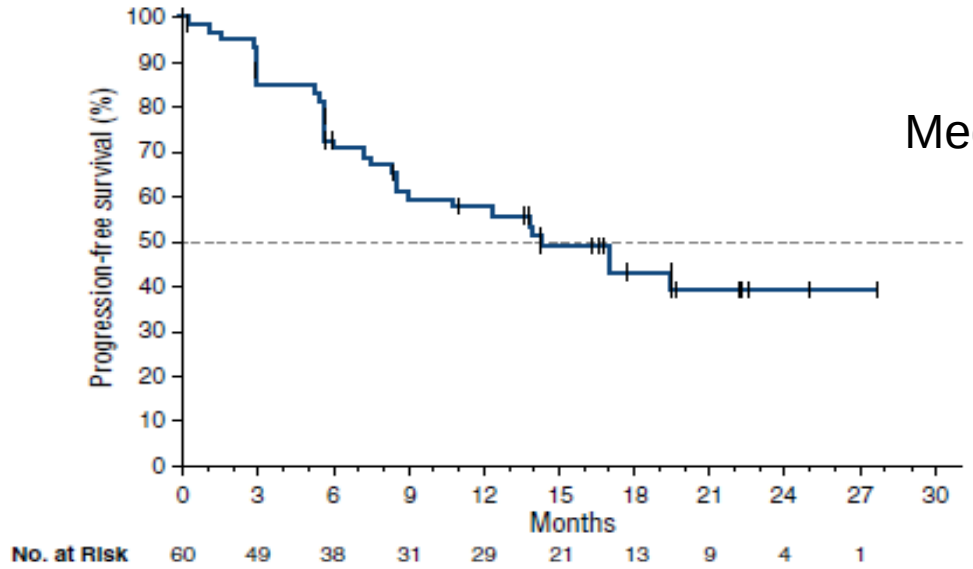
Ibrutinib



FDA approved

Noy et al. Blood 2017;129:2224-2232

Ibrutinib



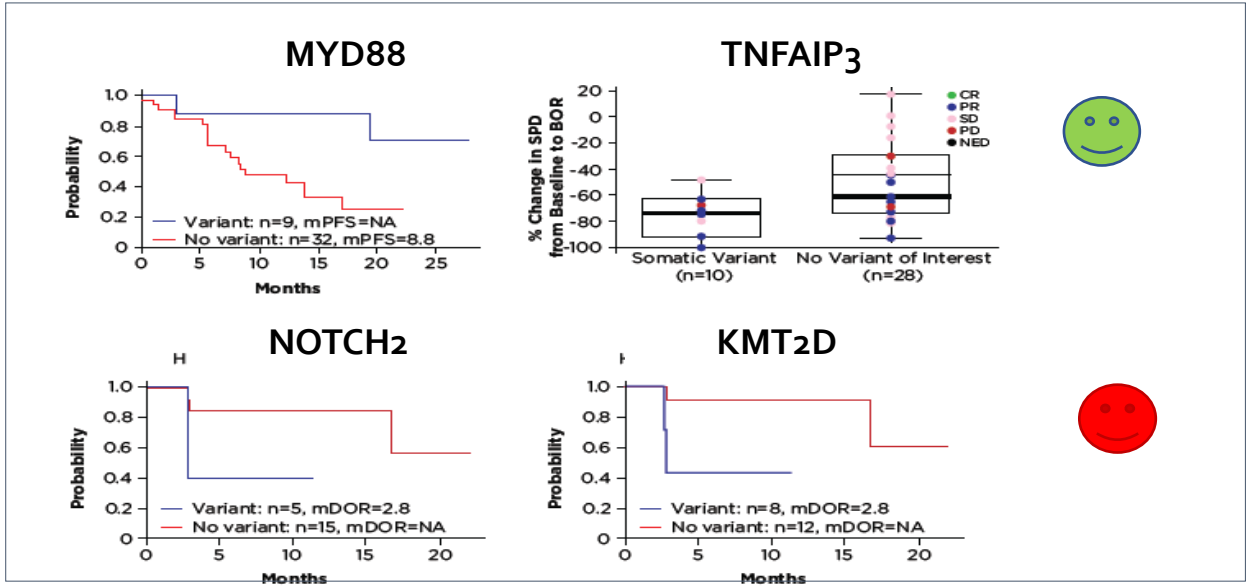
Median PFS = 14.2 mo

*ibrutinib is the **first FDA-approved treatment for MZL**.
= approved in MZL patients who require systemic therapy following ≥1 prior anti-CD20-based therapy

Noy et al. Blood 2017;129:2224-2232

Biomarkers associated in MZL treated with Ibrutinib

N=41 patients

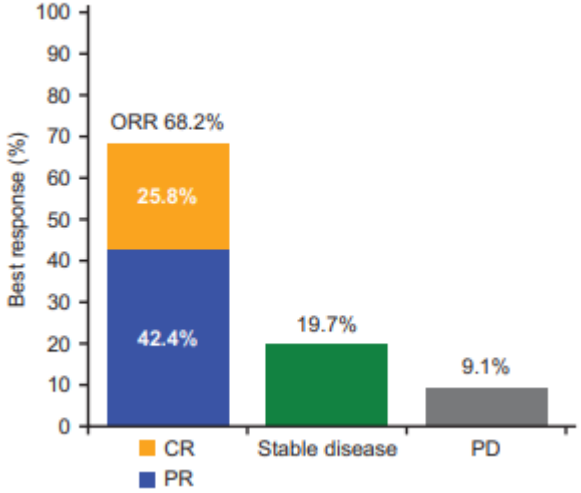


- **Mutation in MYD88** and **TNFAIP3 (A20), which are involved in BCR-NFkB signaling pathway** were positively associated with DOR
- **Mutations in NOTCH2 and KMT2D (MLL2),** which are **not involved** in BCR-NFkB signaling, were negatively correlated with DOR

Chen R et al., ASH 2017 # 3026

Zanubrutinib

- next-generation BTK inhibitor
- Selective and irreversible BTK inhibitor
- Maximize BTK occupancy and minimize off-target inhibition of TEC- and EGFR-family kinases



EMZL(n 25) : 64%

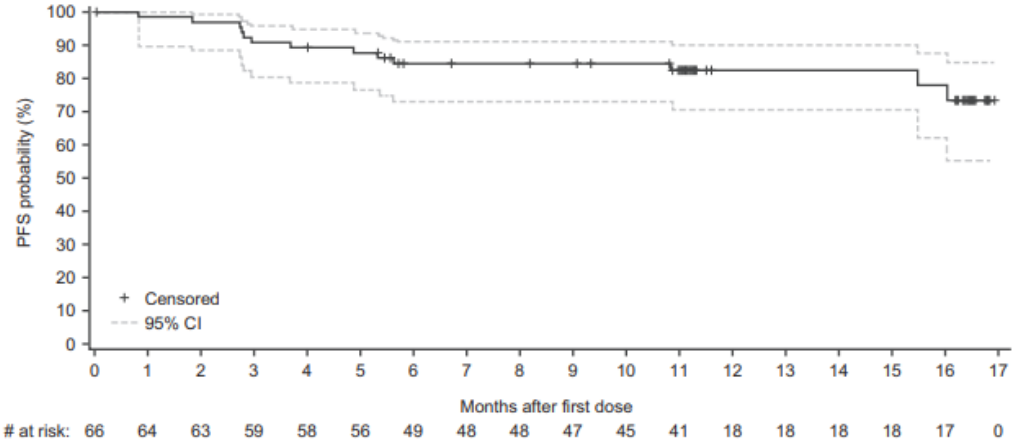
NMZL (n 25) : 76%

SMZL(n 12) : 66.7%

.

Median time to response 2.8 mo

Characteristics	BGB-3111-214 (MAGNOLIA study) R/R MZL (*N* = 68)
Age, years	
Median (range)	70 (37-95)
Age category, *n* (%)	
≥65 years and <75 years	22 (32.4)
≥75 years	19 (27.9)
MZL subtype, *n* (%)	
Extranodal (MALT)	26 (38.2)
Nodal	26 (38.2)
Splenic	12 (17.6)



Opat L et al. Clin Cancer Res 2021

Zanubrutinib in MZL : The MAGNOLIA Trial

AE, *n* (%)	BGB-3111-214 (MAGNOLIA study) (*N* = 68) Any-grade AE	Grade ≥3 AE
Patients with ≥1 AE	65 (95.6)	27 (39.7)
Diarrhea	15 (22.1)	2 (2.9)
Contusion	14 (20.6)	0
Constipation	10 (14.7)	0
Pyrexia	9 (13.2)	2 (2.9)
Abdominal pain	8 (11.8)	
Upper respiratory tract infection	8 (11.8)	1 (1.5)
Back pain	7 (10.3)	0
Nausea	7 (10.3)	0
COVID-19 pneumonia	4 (5.9)	3 (4.4)
Pneumonia	2 (2.9)	2 (2.9)
AE of interest		
Bleeding	25 (36.8)	0
Major hemorrhage[a]	0	0
Atrial fibrillation/flutter	2 (2.9)	1 (1.5)
Hypertension[b]	2 (2.9)	1 (1.5)
Second primary malignancies[c]	5 (7.4)	3 (4.4)
Skin cancers	2 (2.9)	0
Infections	31 (45.6)	11 (16.2)[f]
Opportunistic infections	2 (2.9)	1 (1.5)
Tumor lysis syndrome	0	0
Anemia	4 (5.9)	2 (2.9)
Neutropenia[d]	9 (13.2)	7 (10.3)
Thrombocytopenia[e]	10 (14.7)	3 (4.4)

Most of AEs were Grade 1-2

- diarrhea (22.1%)
- contusion (20.6%)
- constipation (14.7%)
- atrial fibrillation/flutter :2 patients

Grade 3 hypertension : 1 patient

No patient experienced major hemorrhage.

4 patients discontinued treatment due to AEs, none of which were considered treatment-related by the investigators

Opat L et al. Clin Cancer Res 2021

Copanlisib (PI3K-d and PI3K-α inhibitor)

Chronos-1

	No. of patients	ORR	CR	mDOR
Indolent lymphoma	**141**	**59.2%**	**12%**	**22.6 mo** (0–687 days)
• FL	104	–	–	
• MZL (EMZL: 4, SMZL: 4, NZML: 15)	**23**	**70%**	8.7%	Not reached (50–100 days)

TEAEs occuring in >10% of patients with indolent lymphomas	All grades	Grade 3/4
Hyperglycemia	70%	30%
Hypertension	70%	49%
Fatigue	64%	-
Diarrhea / Colitis	36%	5%
Neutropenia	36%	30%

Dreyling M. et al. Am J Hematol. 2019 Dec

Parsasiclib

Citadel 204

	All Treated Patients (N = 100)		
	Nodal MZL (N = 31)	Extranodal MZL (N = 34)	Splenic MZL (N = 35)
Objective response rate, % 95% CI	51.6 33.1–69.8	55.9 37.9–72.8	65.7 47.8–80.9
Best objective response, n (%)			
Complete response	2 (6.5)	3 (8.8)	1 (2.9)
Partial response	14 (45.2)	16 (47.1)	22 (62.9)

	All Treated Patients (N = 100)
Median PFS (95% CI), months	16.5 (13.5–19.6)

Among All Treated Patients:

- Most frequently occurring TEAEs leading to dose interruption were
  - diarrhea (n=14),
  - neutropenia (n=5)
  - pyrexia (n=5)
- Most frequently occurring TEAEs leading to dose reduction were diarrhea (n=5), maculo-popular rash (n=3), colitis and rash (n=2 each)
- Most common TEAEs leading to treatment discontinuation were diarrhea (n=9) and colitis (n=5)

Tycel Phillips ASH 2021

PI3Kδ inhibitors - Summary - Toxicities

	Idelalisib (Zydelig) – USPI (iNHL only)	*Duvelisib*	*TGR 1202*[3]	*TGR 1202 + CD-20*[4]	*Copanlisib*[5]	INCB050465 (ASH '17)
	All grades (≥ grade 3)	All grades (≥ grade 3)	All grades (≥ grade 3)		All grades (≥ grade 3)	All grades (≥ grade 3)
Diarrhea/Colitis	47% (14%)	44%(15%)[1] 5% G3/4 colitis	43%(3%)[10] No colitis	47% (3%) 2 colitis (<1.5%)	36% (5%) 0.7% colitis	36% (10%) 4 colitis (~6%)
Pneumonia	25% (16%) Fatal/serious pneumonitis 4% (combo)	18% (9%)[1] 3 pneumonitis (~2%)	(5%) No pneumonitis	8% (5%) 2 pneumonitis (~1.5%)	~2% 7% pneumonitis and ~1.4% G3/4[11]	10% (5%) 1 pneumonitis (~2%)
ALT Elevations	50% (19%)	14% (6%)[1]	NA	NA	25% (all G1)	24% (0%)
AST Elevations	41% (12%)	NA	NA	NA	26% (all G1)	24% (2%)
ALT/AST Elevations	NA	28% (17%)[2]	4% (2%)	8% (3%)	Mostly Grade 1[6]	N/A
Discontinuations due to AE	20-28%	17%[1]-33%[2]	7%	<8% due to TGR 1202 AE	17%	19% due to AE

1ASH 2016 Abstract #1218 and Presentation Slides n=129 for AE %; 2 Patel et al ASCO 2015 (CLL treatment naïve only); 3 O'Connor et al ASH 2015: ; 4O'Connor et al EHA 2016, Burris ASCO 2016; 5Dreyling et al AACR/ASCO 2017/ICML Safety Summary and USPi; 6Annals of Oncology 27: 1928–1940, 2016; 71 grade 3 event ~ 1 week after INCB050465 discontinuation; all other elevations were grade 1; 8All AST elevations were grade 1; 935% of responders discontinued due to AE as of 01Sep16; 10ASH 2017 Investor Presentation Deck; 11USPI2017

Novel drugs in r/rMZL : high rate of toxicities

Pathway	Drug	Target	Patients n	ORR	CR	Toxicity G3/4
PI3K/AKT/mTOR	**Everolimus**	**mTOR**	**24**	28	4	46%
	Idelalisib	**PI3K-d**	**15**	57	6	27%
	Copanlisib	**PI3K-d &-a**	**23**	70	9	49%
BcR	**Ibrutinib**	**BTK**	**63**	48	3	8%
MicroEnv	**Lenalidomide**	**Immune modulator**	**30**	89	67	35%

Chemo-free association in R/R MZL

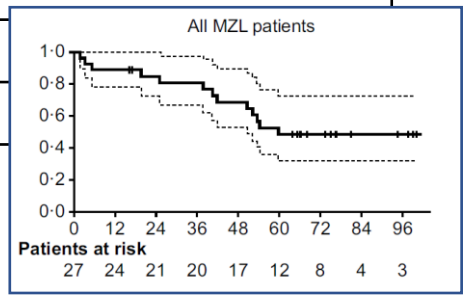
Trial	Combo	status	Phase	ORR*	CR*	Median PFS
AUGMENT*	R-LEN	R/R	III	65%	29%	-
MAGNIFY*	R-LEN	R/R	III	65%	38%	38,4 mo
inMIND	TAFA-R-LEN	**R/R**	III	enrolling		
MALIBU (IELSG47)	R-Ibrutinib	**1rst line**	II	enrolling		
MSKCC	I-R-Len	**1rst line**	II	enrolling		

Lenalidomide in MZL

1rst Line

MZL, n=18 MZL only (1L = 11; RR =7)	
Phase	II
dose	25mg/d, D1-21 /28
ORR	61%
CR	33%
2-y PFS	ND

MZL, among MZL+FL – 1L n=27 /100	
Phase	II
dose	LEN 20 mg/d, D1-21 /28 ; **+ Rituximab** 375 mg/m^2 on D1, continuing in responders for ≥C6–C12
ORR	89%
CR	67%
2-y PFS	83% (FL, MZL, SL)

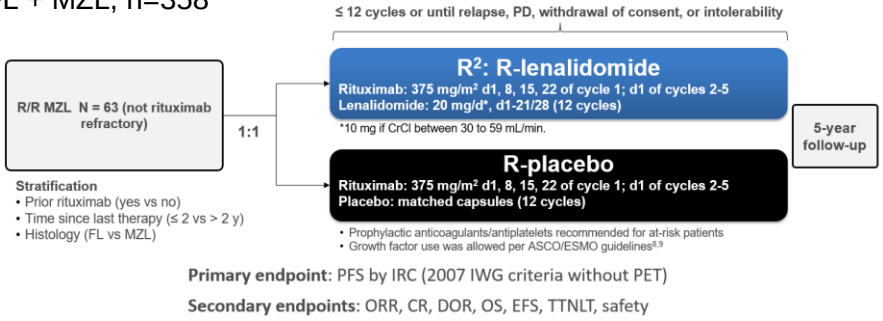


Kiesewetter et al. B Haematologica 2013; 98(3)

Becnel MR et al. Br J Haematol 2019 Jun;185(5):874-882

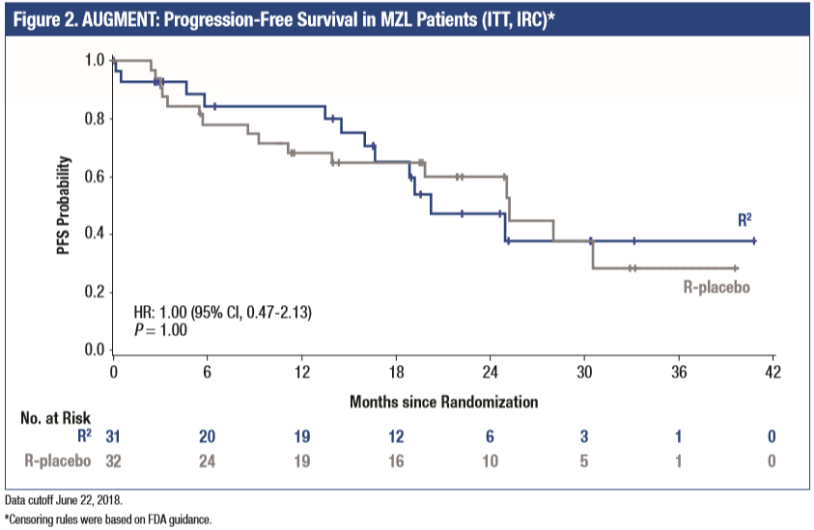
AUGMENT clinical trial : R/R

FL + MZL, n=358



MZL, among MZL+FL – RR **n=63** /358	
Phase	III
dose	20mg/d, D1-21 /28 + R x 12 cycles
ORR	65% vs 44% (p=0,13)
CR	29% vs 13% (p=0,13)
2-y PFS	-

Relapsed MZL

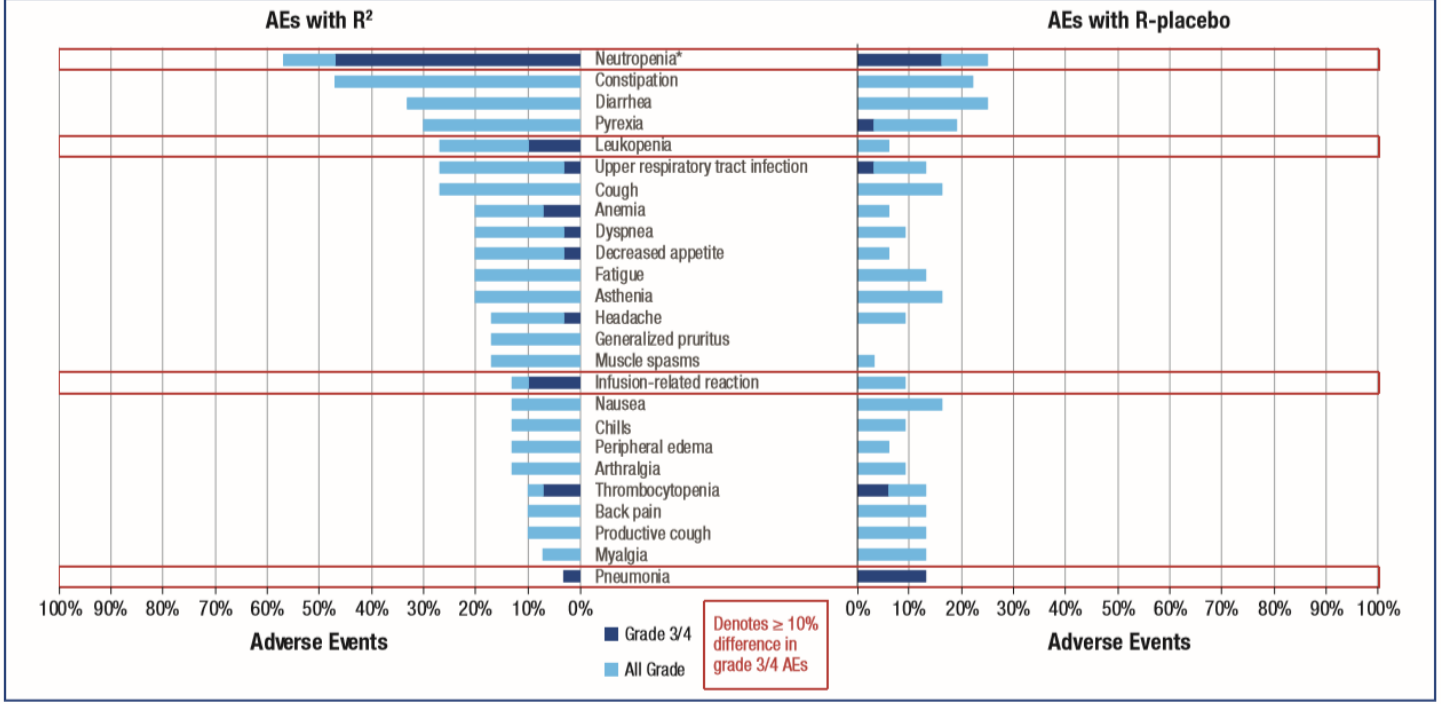


Median PFS for MZL patients : **20.2 mo R2**
vs 25.2 mo R-placebo (HR = 1.00; 95% CI, 0.47-2.13; P = 1.0)

Leonard J et al. J Clin Oncol 2019;37(14):1188-1199 (FL + MZL)
Thieblemont C, EHA 2019: abstract PS1262 (MZL only)

Essai AUGMENT - Toxicities

Figure 3. AUGMENT: All Grade and Grade 3/4 Adverse Events (AEs; > 10% All Grade; Safety Population)



Data cutoff June 22, 2018.
*One R² patient and 0 R-placebo patients had grade 3/4 febrile neutropenia.

Leonard J et al. J Clin Oncol 2019;37(14):1188-1199 (FL + MZL)
Thieblemont C, EHA 2019: abstract PS1262 (MZL only)

MAGNIFY clinical trial : R/R

Median follow-up : 16.7 mo

Multicenter, non-registrational phase IIIb trial in patients with R/R FL grade 1-3a and MZL
Goal : to determine the optimal duration of LEN

Treatment : LEN 20 mg/d, d1-21/28 + R 375 mg/m^2/wk c1 and q8wk c3+ (R^2) -**12 cycles**
followed by 1:1 randomization in patients ≥ SD to continued R^2 vs R maintenance **for 18 months**.

Primary endpoint : ORR by 1999 IWG criteria for induction R^2 in efficacy-evaluable patients receiving ≥ 1 treatment with baseline/post-baseline assessments

	ORR, %	CR, %	Median TTR, mo (range)	Median DOR, mo (95% CI)*	Median PFS, mo (95% CI)*
MZL	65	38	2.7 (1.9-11.1)	35.8 (NR-NR)	38.4 (26.5-38.4)

Grade 3/4 AEs occurring in ≥ 5% of patients
37% neutropenia
3% febrile neutropenia),

8% leukopenia,
6% thrombocytopenia,
5% anemia,
5% fatigue

Results : n=370 patients (80% FL grade 1-3a; **20% MZL)**

Median age of 66 y, 83% stage III/IV disease

Median of 2 prior therapies (95% prior rituximab-containing)

Andorsky DJ., ASCO 2019 – abstract 7513

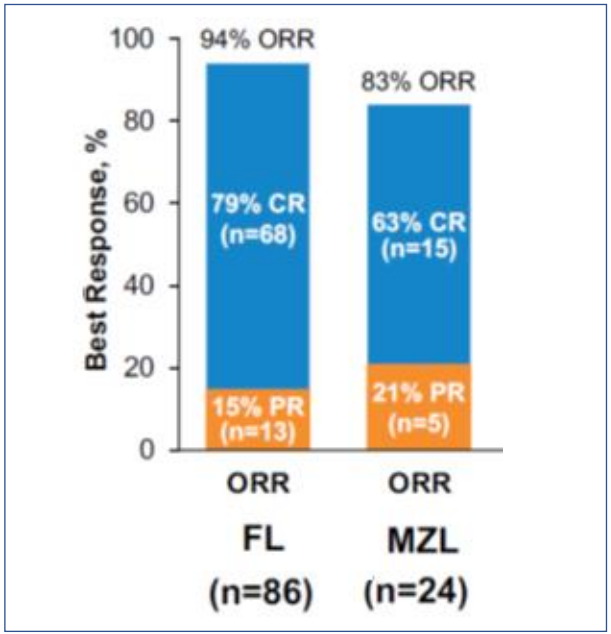
Frederick Lansigan., ASH 2021 – abstract 812

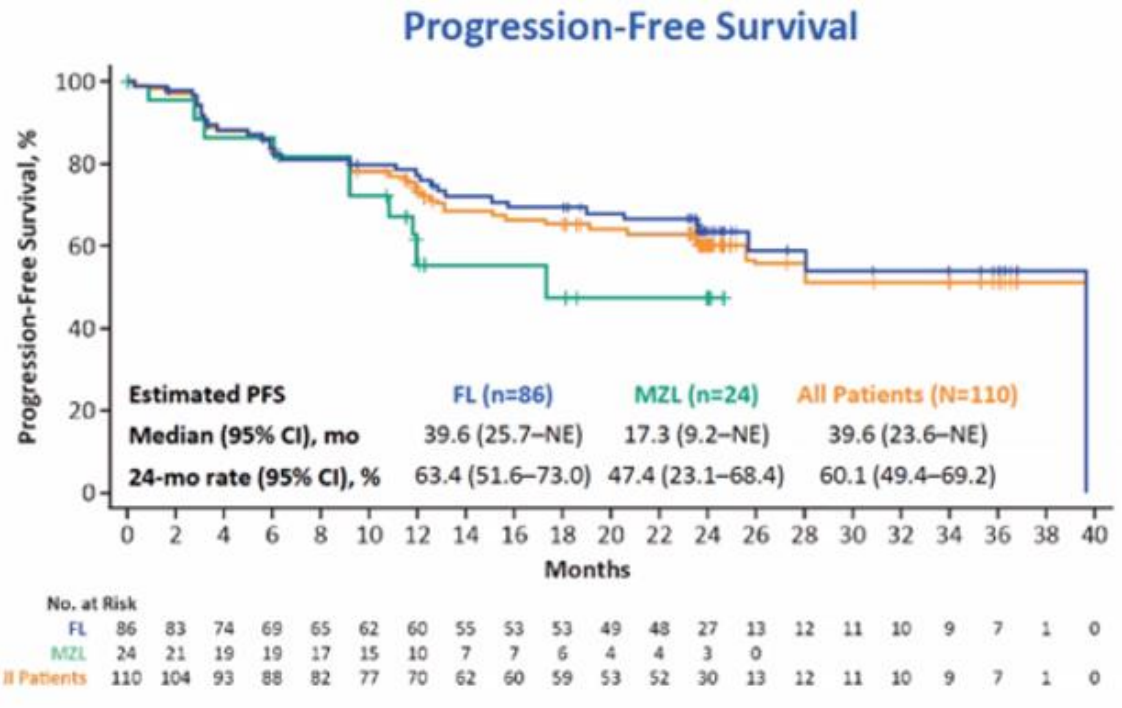
T-cell engagers

Product	drugs	Results	Reference
CAR T-cells	Axicabtagene ciloleucel (ZUMA 5)	- ORR = 83% - CRR = 63% - 12-mo PFS : 45.1%	Neelapu et al. ASH 2021 Abstract #93
CD20xCD3 bispecifics	Epcoritamab Mosunetuzumab	In need of further investigation	

Axicabtagene ciloleucel (ZUMA 5)

Median FU: FL = 30,9 mo – MZL: 23,8 mo





Neelapu et al. ASH 2021 Abstract #93

MARSUN : Phase III, Open-Label, Multicenter, Randomized, Controlled Study Investigating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Mosunetuzumab-Lenalidomide or investigator choices in Patients with Relapsed or Refractory Marginal Zone Lymphoma

Eligibility

- Histologically centralized confirmed diagnosis of MZL
- >=1 prior systemic therapy (antiCD20 +/- chemo)
- N=250 MZL + 10 safety RUN

- Stratification:
  - EMZL SMZL NMZL
  - Time since last treatment <2y vs ≥2y

Safety RUN
M + Len

10 MZL patients (at least 3 with blood involvement)

Dose tolerability

1:1

Arm A
M + Len
N=125 MZL patients

Arm B
Investigator choices
N=125 MZL Patients
R + Len
R + Bendamustin + R
R + CHOP

Endpoints

1° EP: PFS and CR24
2° EP:
- Safety
- OS
- ORR, CR
- DOR
- DOCR
- EFS
- TTNLT
- HT
- Tolerability
- Pharmacokinetics
- Biomarkers Exploratory

Fixed duration of treatment = 1 year

To speed the approval of the right drugs in MZL

Ongoing project

Need for new choices based on

- **Specific entity trials**
- **Establishment of surrogate markers to reduce duration of clinical trials**

MZL Analysis of Surrogate Hypothesis

The MASH project

➢ **To define new surrogate markers in MZL**

Come Bommier, Jérome Lambert, Catherine Thieblemont
Collaboration J. Cerhan, Mayo Clinic, Rochester
E. Zucca, G. Nowaskoski

In conclusion

- Novel strategies in MZL will include MOA, TCE, and targeted treatments
- CAR T-cells are under evaluation
- New surrogate markers for regulatory approvals to reduce duration of clinical trials and give access to innovative treatments

Thank you !

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