Disclosures

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Advisory Boards :

Sandoz Novartis, Roche, Janssen, Acerta, Abbvie, TG Therapeutics, Teva, Takeda, Spectrum, NovoNordisk, Mundipharma,

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Jak leczę chłoniaka z komórek płaszcza ?

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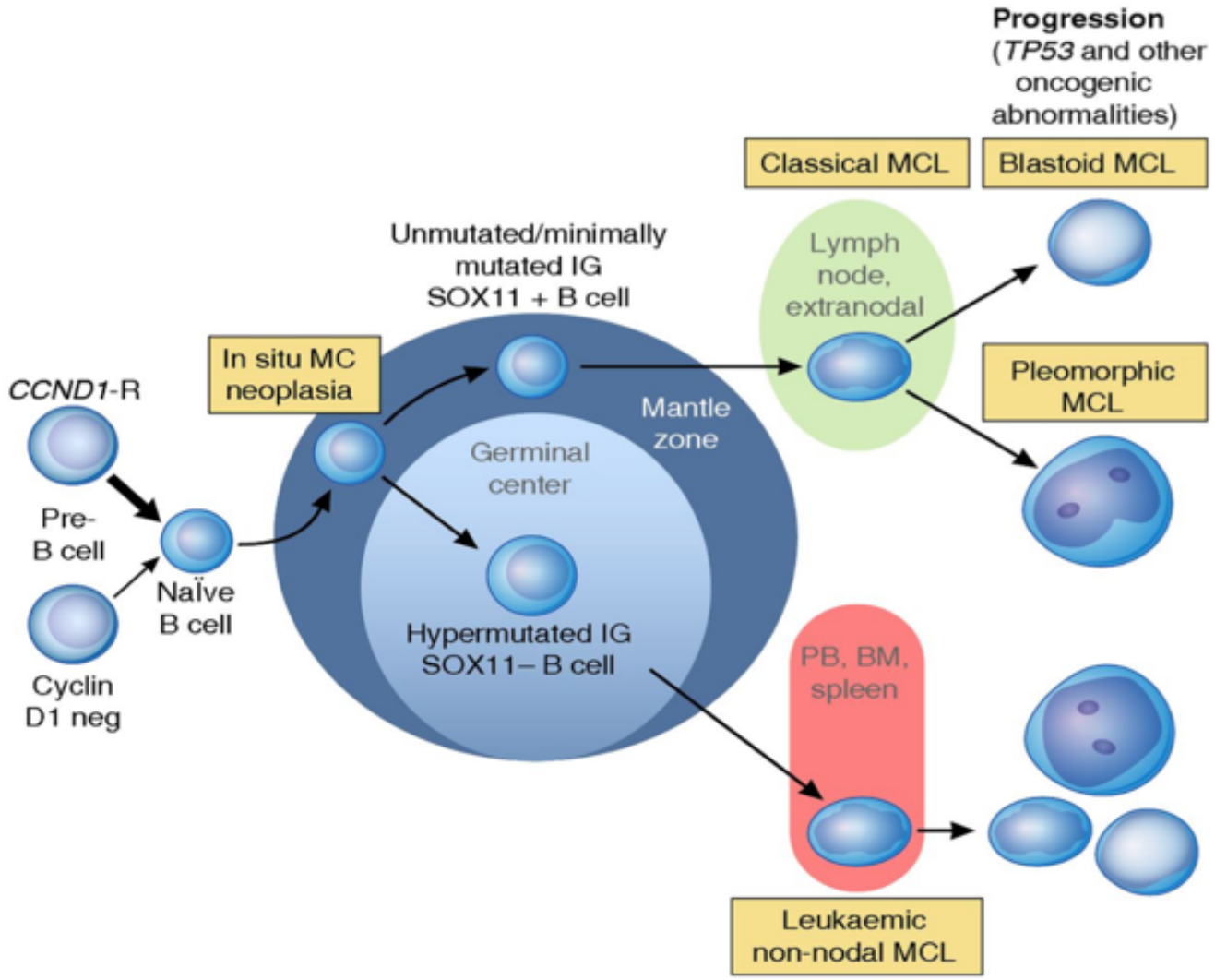
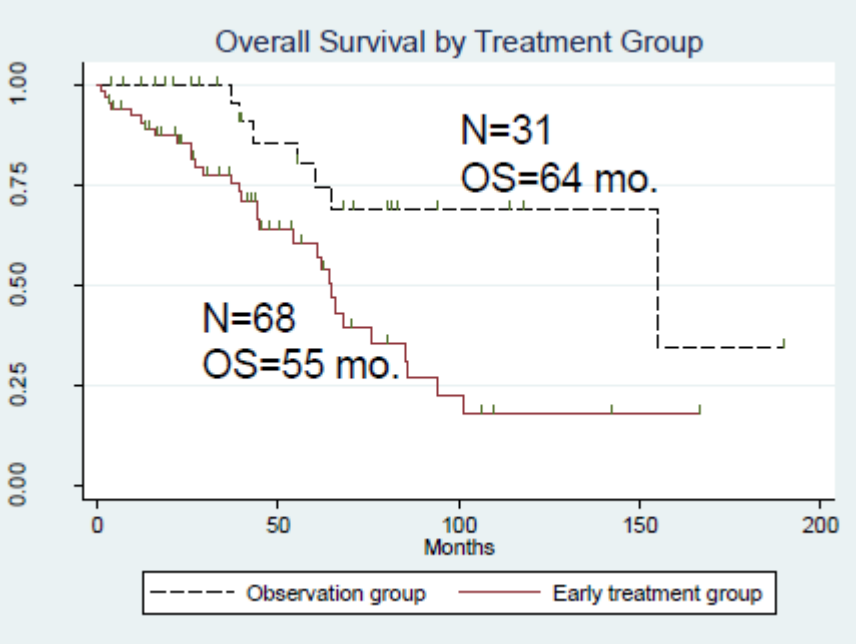
MCL – the disease we know better and better



Courtesy of E Campo

Outcomes of Deferred Therapy in MCL
- Successful identification of low risk patients



What characteristics are define these patients?

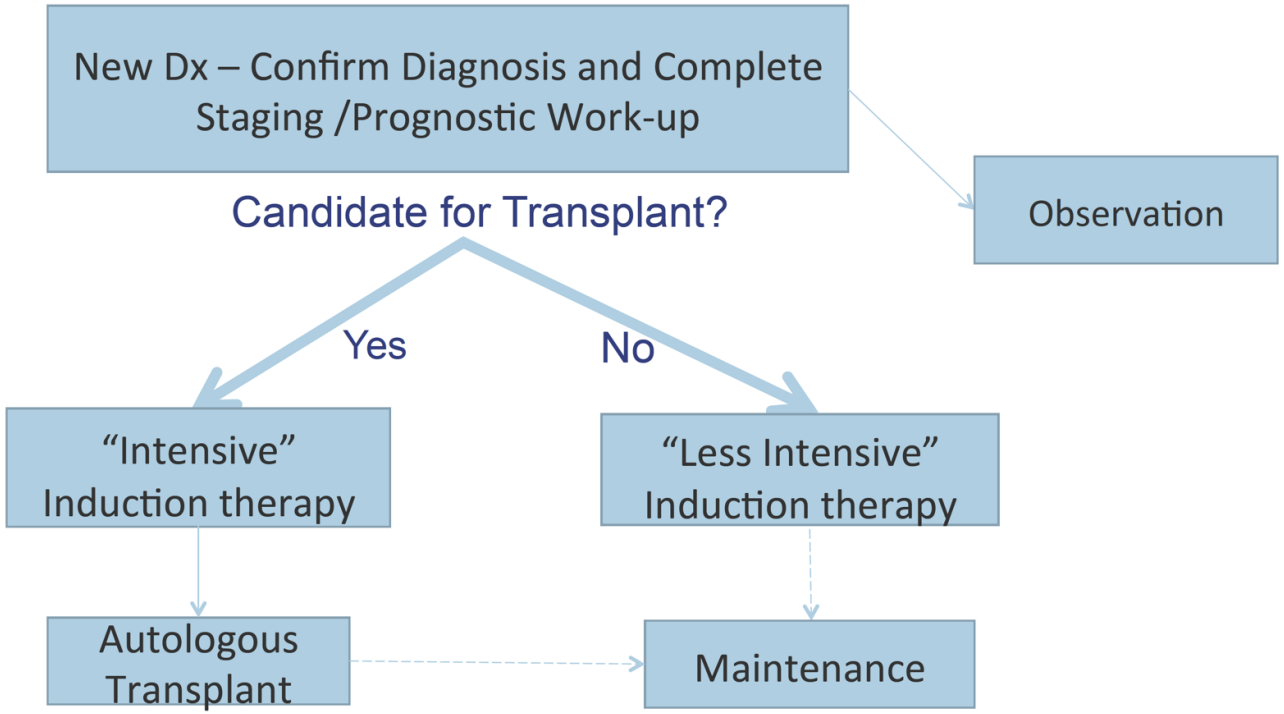
- **Not blastoid morphology[1]**
- **Normal LDH[2]**
- **Ki67 <30%[3]**
- **No B symptoms[4]**
- **Mutated IGHV[5]**
- **SOX11-**
- **Non-nodal[6]**
- **MIPI is NOT a defining characteristic**

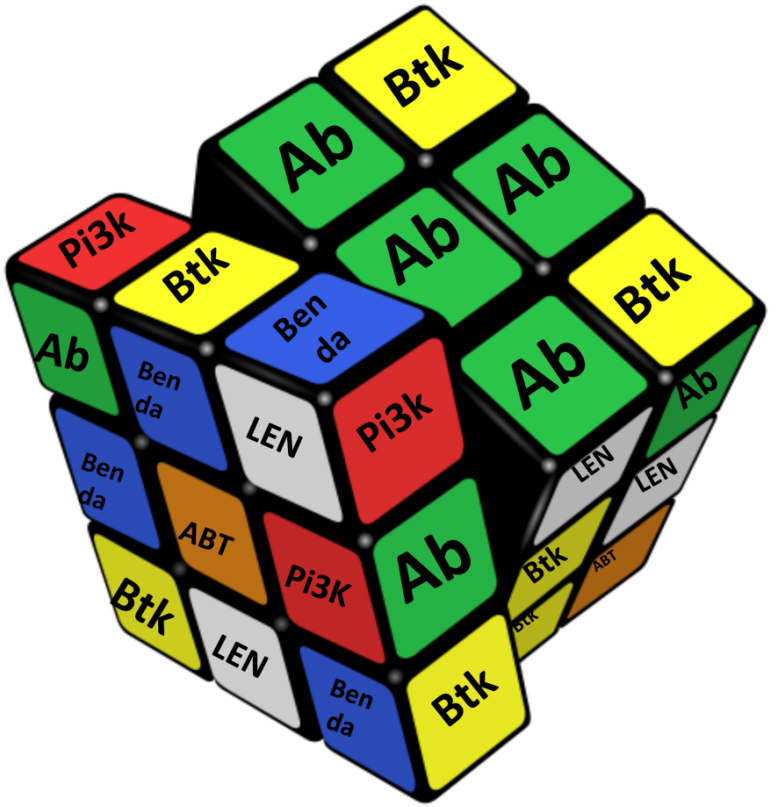
1-Martin JCO 2009, 2-Abrahamsson Blood 2014, 3-Abrisqueta ASH abstract 2015, 4-Cohen ASH abstract 2015, 5-Orchard Blood 2003, 6-Ondrejka Haematologica 2011, 7-Eve JCO 2009

Outcomes of Deferred Therapy in MCL
- Successful identification of low risk patients

Series	Number of Deferred Patients (%)	Median time to treatment (Range)	Median OS (Deferred Pts)	Median OS (Immediate Pts)
Martin 2009 (Cornell)	31 / 97 (32)	12 months (4-128)	Not Reached (4.6 years)	5.3 years
Abrisqueta 2017 (B.C.)	74 / 439 (17)	35.5 months (5-79)	5.5 years	4.2 years
Cohen 2016 (NCDB)	492 / 8029 (6)	4 months (3-38)*	6.6 years	-
Kumar 2015 (MSKCC)	91 / 404 (23)	23 months	10.6 years	9.4 years
Calzada 2016 (Multicenter)	72 / 395 (18)	7.8 months (3-121)*	11.8 years	11.6 years

“Traditional” vs „Targeted” Approaches in MCL





Courtesy of S.Rule

MCL – present European standard of care

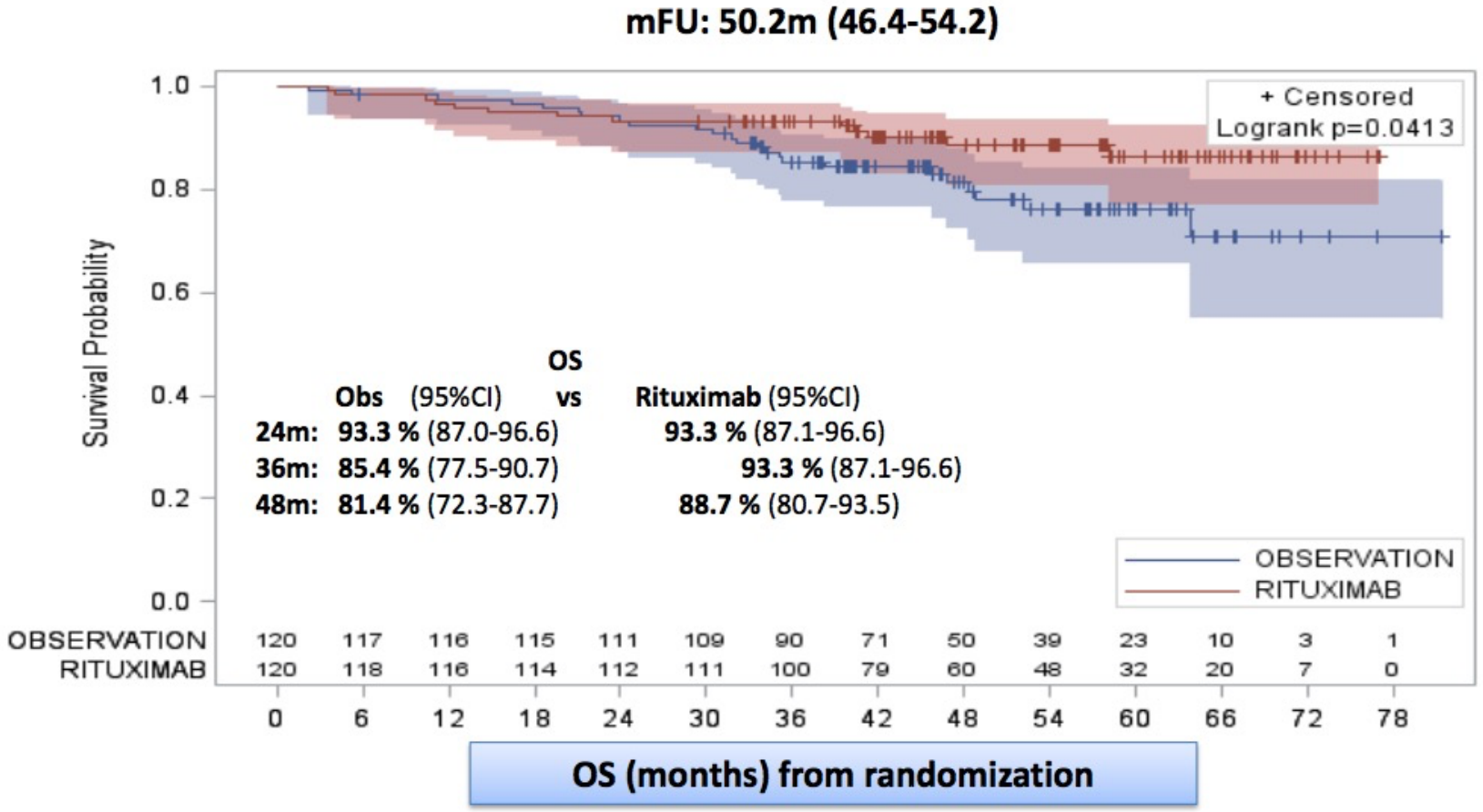
Young Patients (<65)	Elderly (>65)	„Compromised”
I line therpy		
Dose-intensified (R-CHOP + R-high dose Ara-C → ASCT) + Rit Maintenance	Conventional Immuno-chemotherapy (e.g. R-CHOP, BR, VR-CAP,) + Rit maintenance	Best supportive care R-Chlorambucil BR (dose reduced) R-CVP
1 relapse		
Immuno-chemotherapy (e.g. R-BAC, BR) or targeted approaches Discuss: - Rit maintenance - Allo SCT	Immuno-chemotherapy (e.g. R-BAC, BR) or targeted approaches Discuss: - Rit maintenance - Radioimmunotherapy - Autologous SCT	Immuno-chemotherapy (e.g. BR) or targeted approaches
Higher relapse		
Targeted approaches (Ibrutynib, Lenalidomide, Temsirolimus, Bortezomib (preferably in Combinations) Alternatively – repeat previous therapy if in long remissions		

Dreyling, ESMO 2017

„Younger” MCL patients - necessity of maintenance after ASCT

FRENCH INNOVATIVE LEUKEMIA ORGANIZATION

LyMa trial



Le Gouill et al. NEJM 2017

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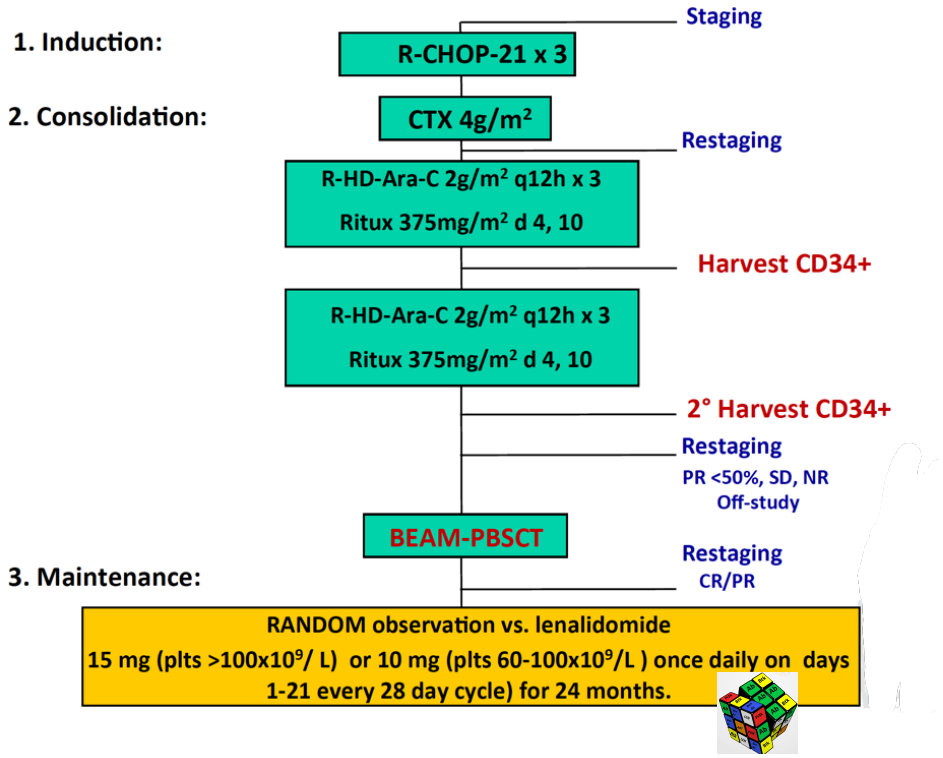
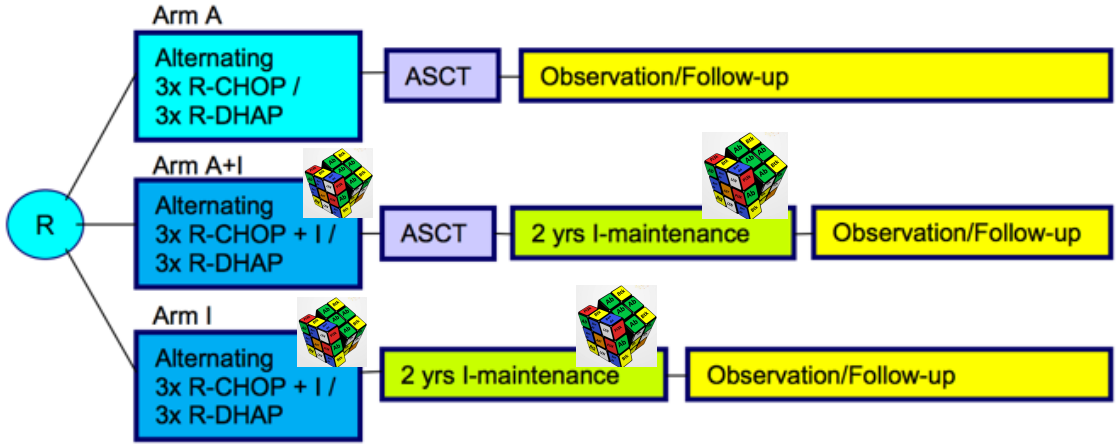
„Younger” MCL patients - necessity of maintenance after ASCT *(≠)*

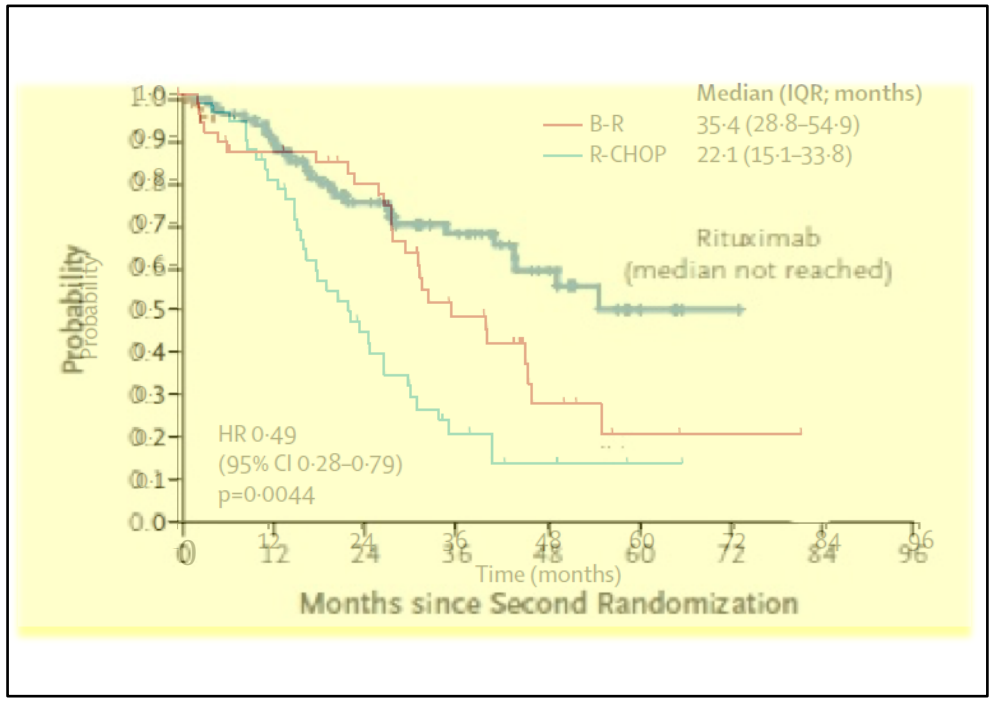
MCL0208 study



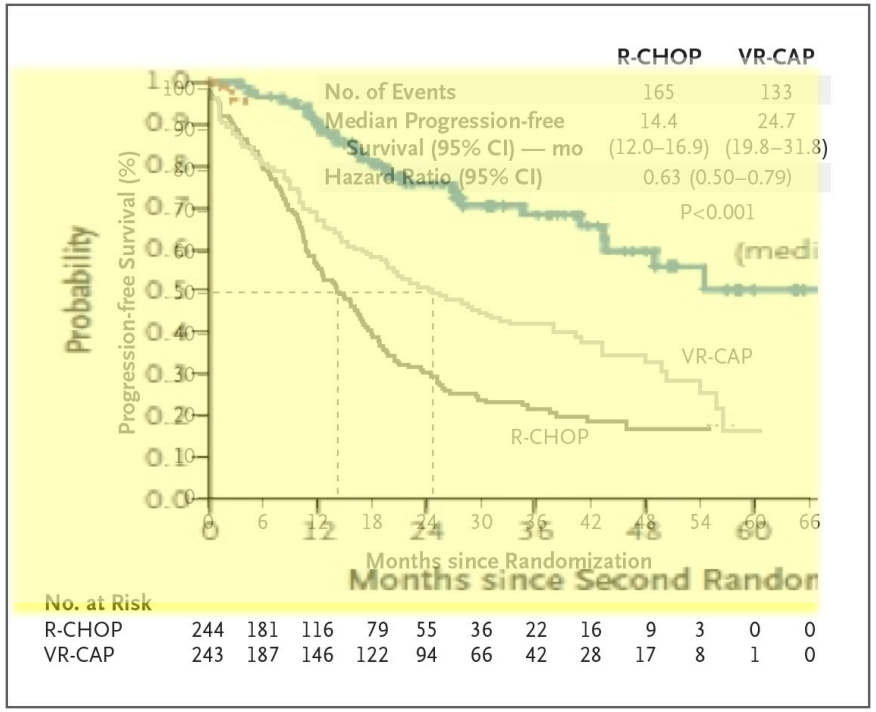
„Triangle” study



I line immuno-chemotherapy in elderly MCL patients



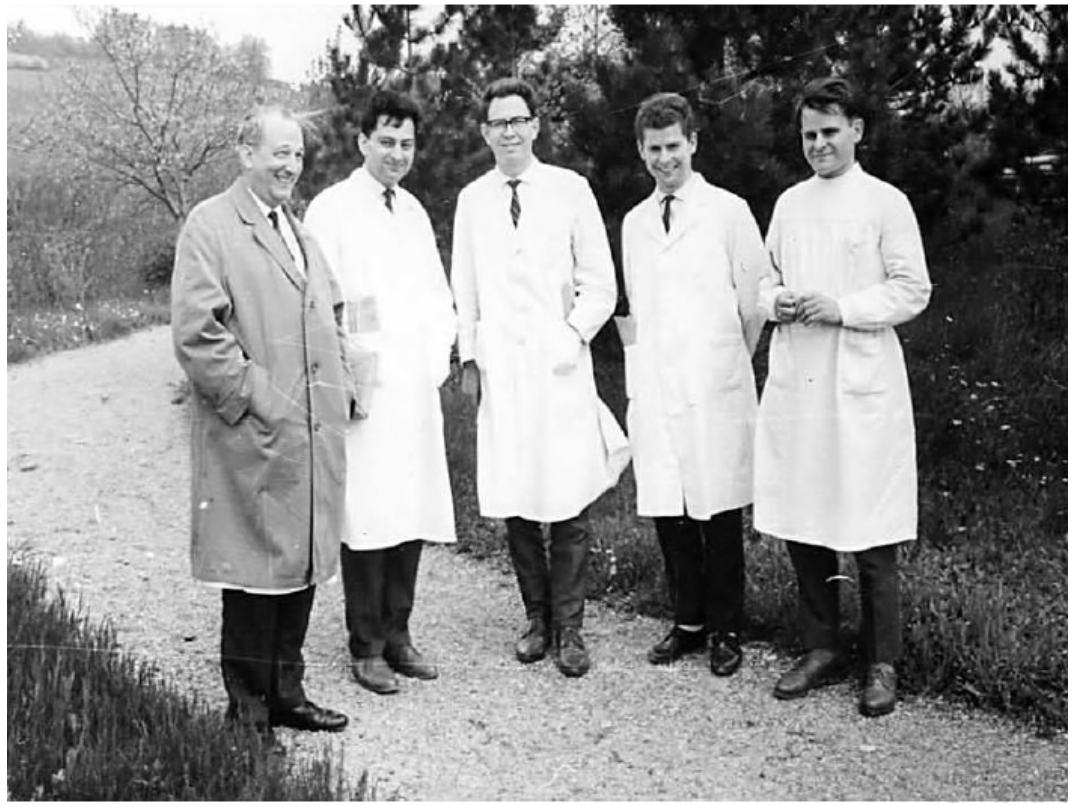
Rummel et al, Lancet 2013

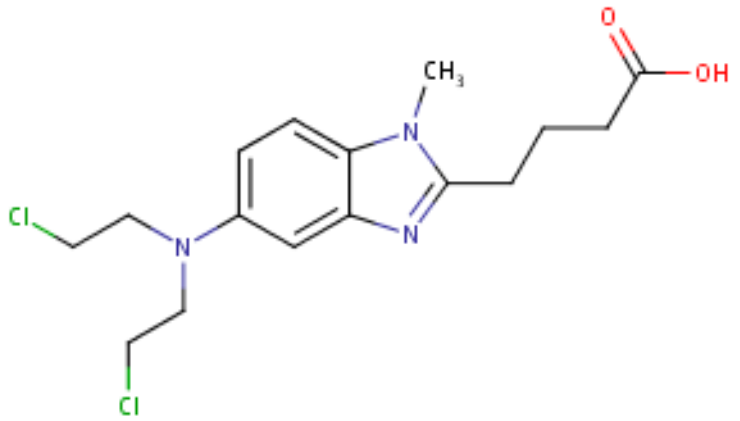


Robak et al, NEJM 2015

R-CHOP + Rituximab maintenance was however always better

Bendamustine: An ‘agent’ with a long history

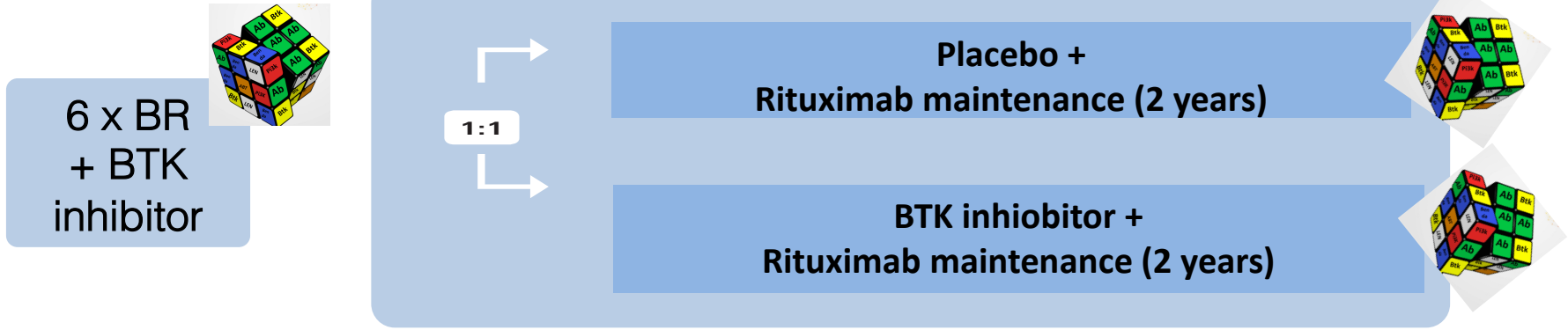




Synthesis : W.Ozegowski, D.Krebs, Institute of Microbiology and Experimental Therapy, Jena (1962)

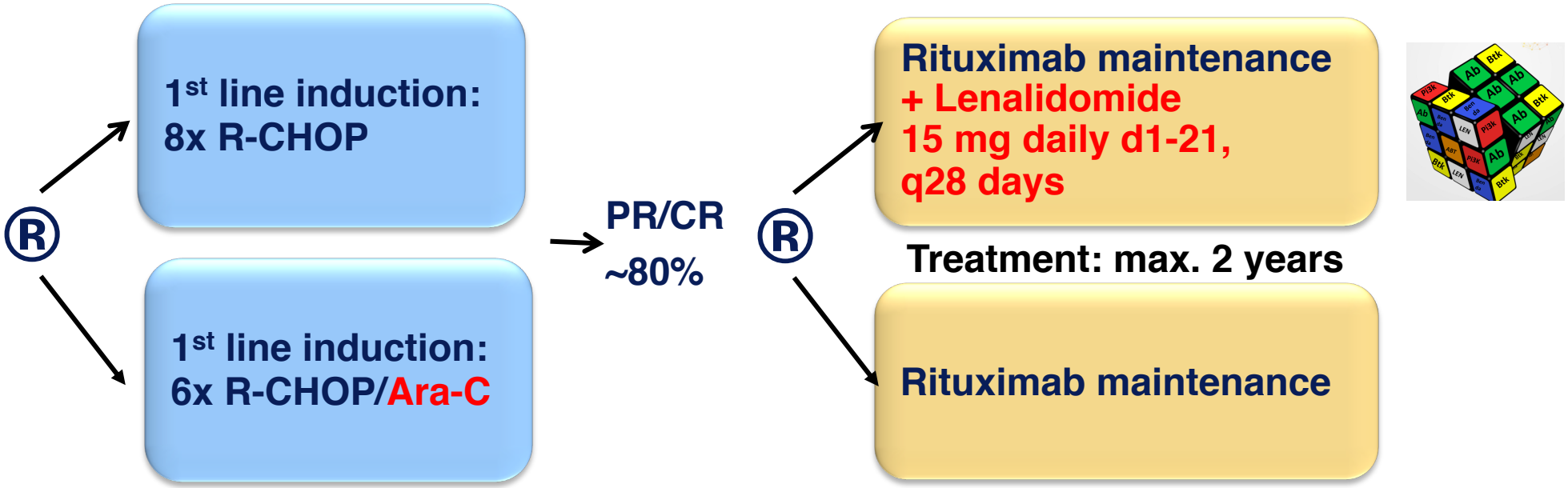
Praktische Chemie, Vol. 20, issue 3-4, 1963

BR and Rituximab maintenance +/- BTK inhibitor *(≠)*



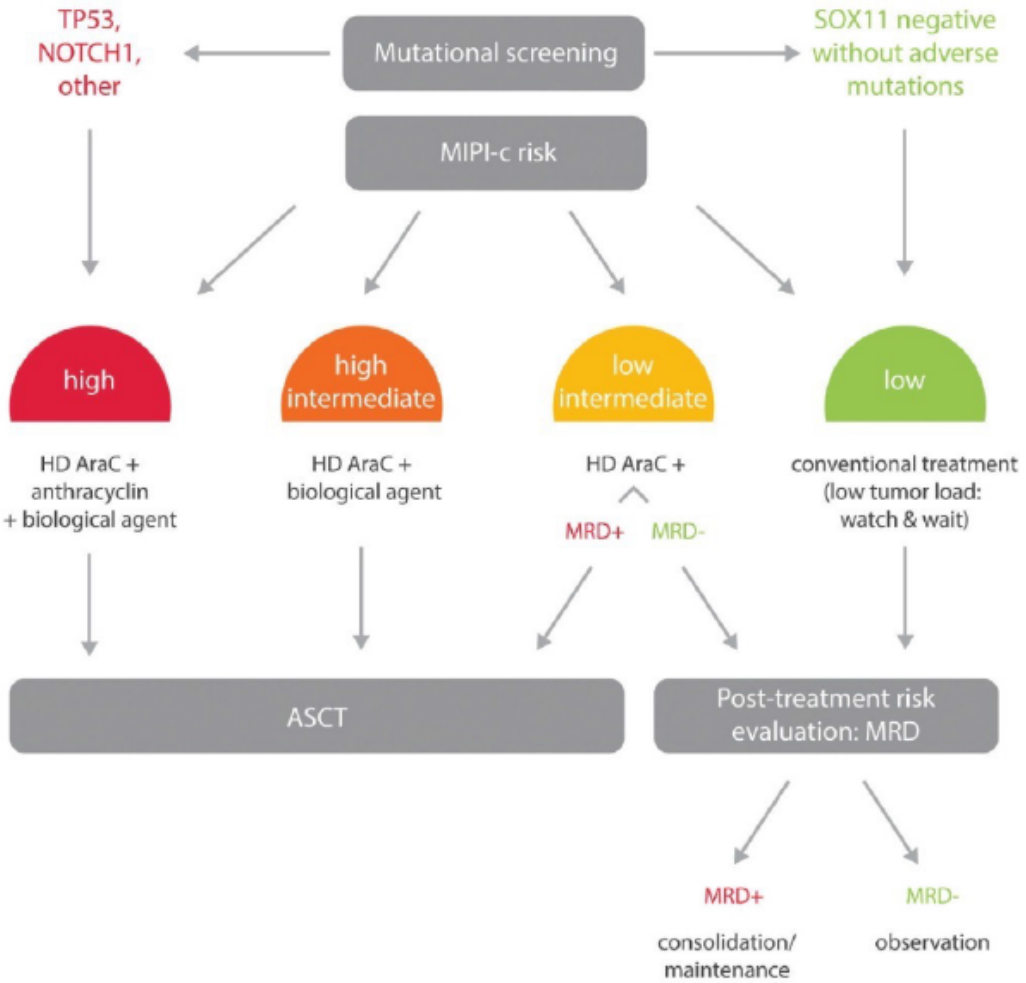
Study	SHINE PCI-32765MCL3002	Acerta 196	Acerta 306
Study details	N=520 Phase III Ibrutinib	N=48 Phase I Acalabrutinib	N=546 Phase III Acalabrutinib
Recruitment status	completed	completed	On - going
Primary Objective	PFS		PFS
Secondary Objectives	**OS**, RR, CR, DOR, Safety		**OS**, RR, CR, DOR

I line immuno-chemotherapy in elderly MCL patients (≠)



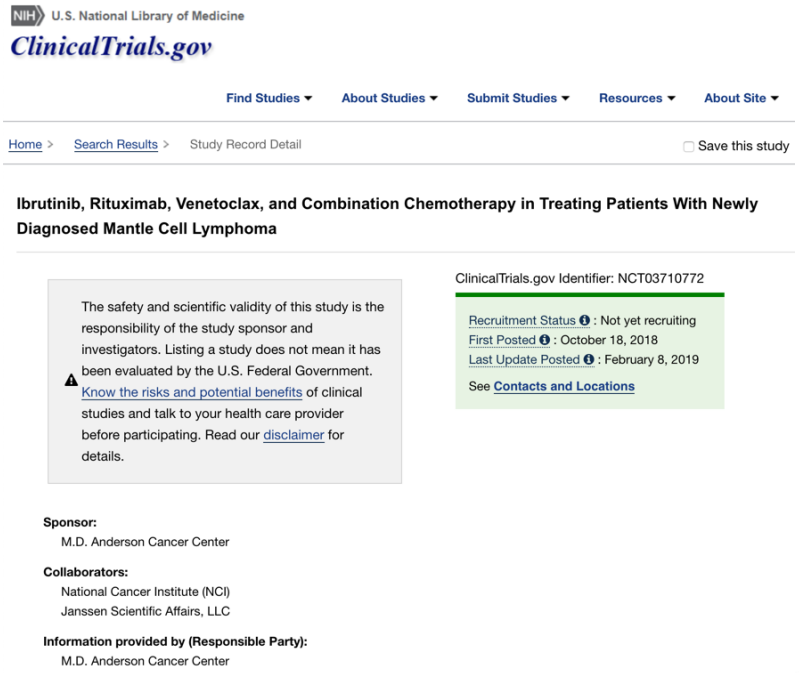
Are we ready for first line … (≠)

……risk adopted therapy ?



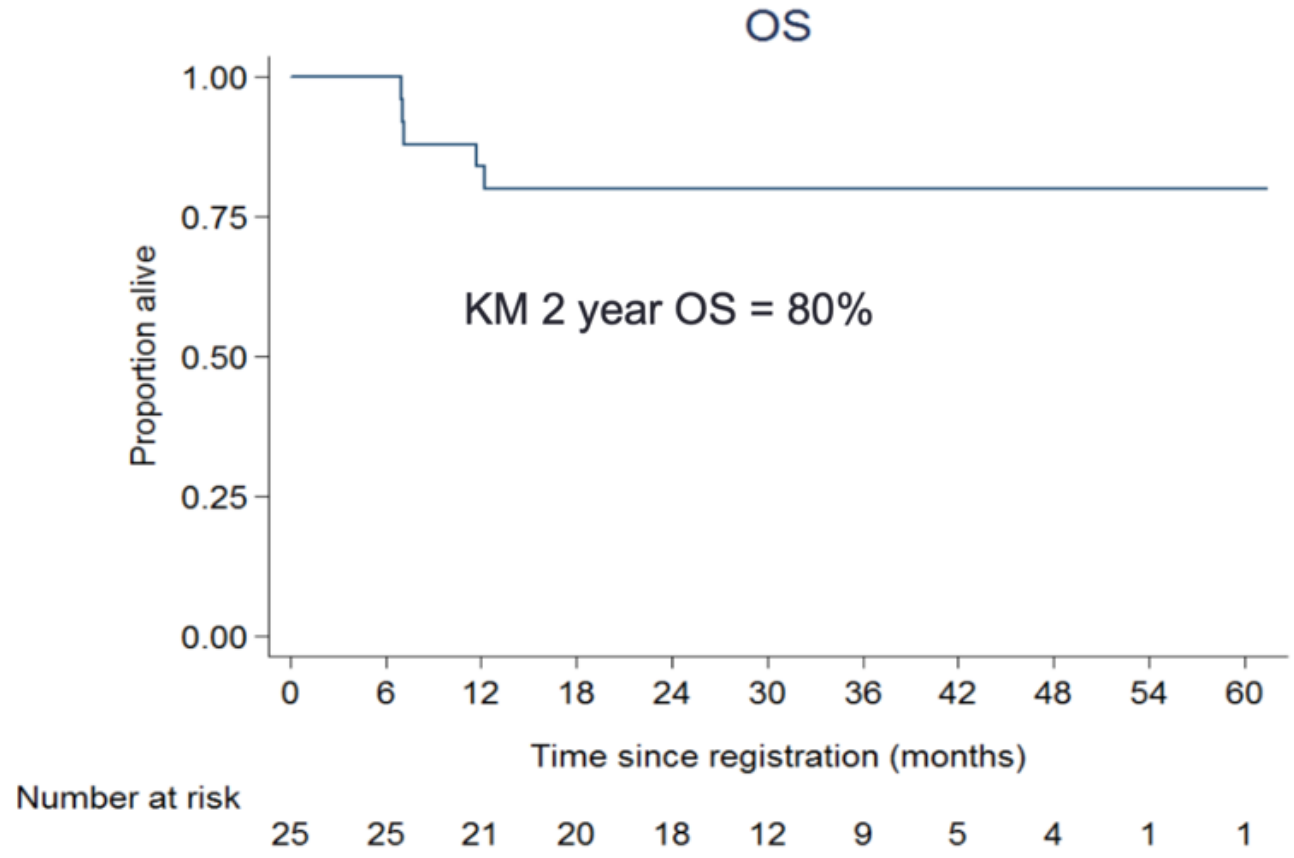
…… non chemo option ?

- R^2 (Rituximab + Lenalidomide)
- Rituximab, Ibrutinib, Venetoclax



Are we ready for first line … *(≠)*

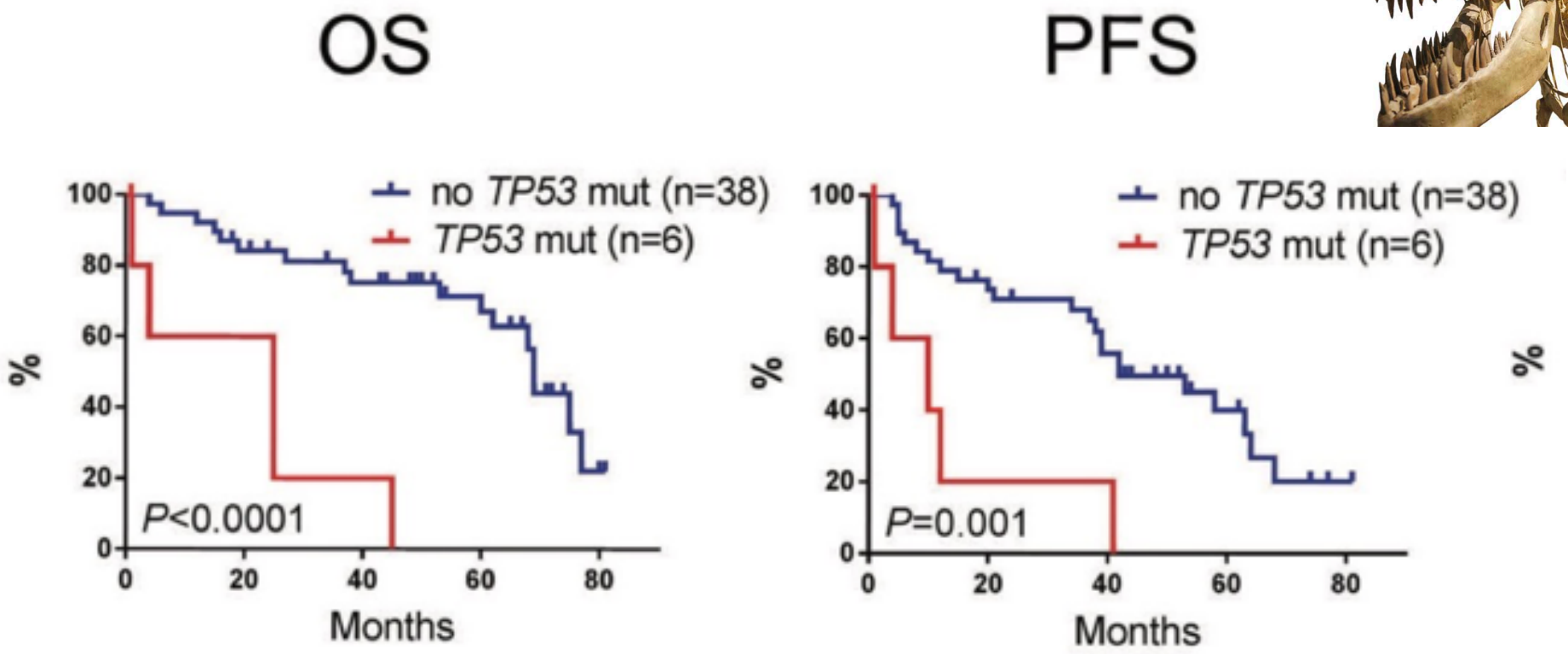
….mini allo (II phase study, Cruk: C7627/A9080)



Peggs et al

Relapsing/Refractory MCL

TP53 mutation is an independent RF in R/R MCL

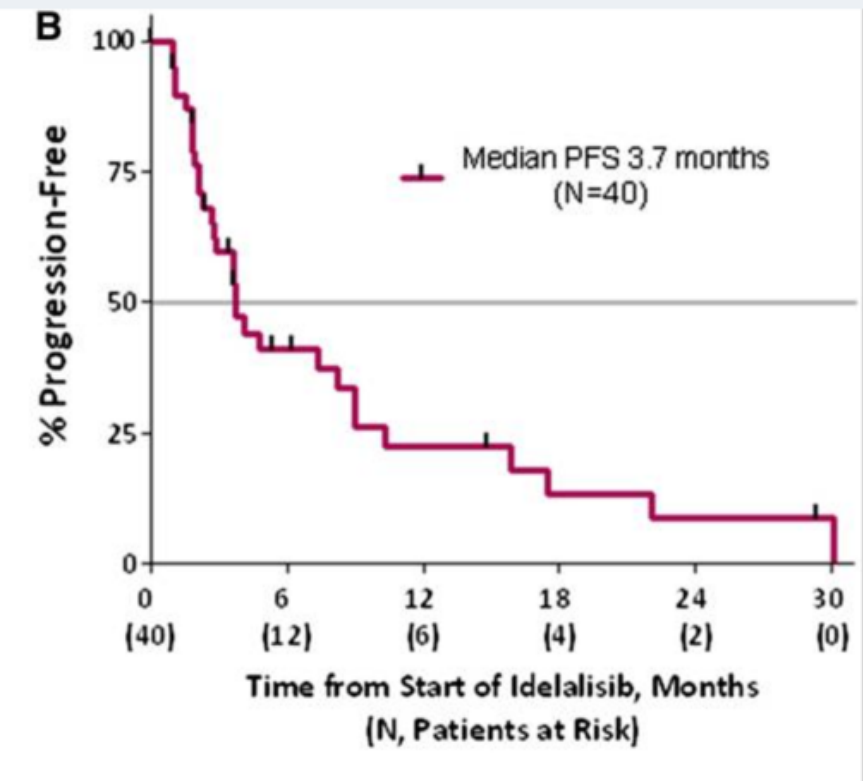


Eskelund et al., Haematologica 2018

Novel Agents - results in relapsing/refractory (‡)

Regimen	N	ORR% (CR%)	mPFS (months)	mOS	Reference
Idelalisib	40	40 (5)	**3.7**	n/a	Kahl, Blood 2014
Temsirolimus	54	22 (2)	**4.8**	12.8	Hess, JCO 2009
Everolimus	35	20 (6)	**5.5**	n/a	Wang, BJH 2014
Bortezomib	141	33 (8)	**6.7**	23.5	Fisher, JCO 2006
Lenalidomide	134	28 (8)	**8,6**	19	Trneny, Lancet O 2016
Ibrutinib	110	68 (21)	**13.9**	n/a	Wang, NEJM 2013

Efficacy of PI3kinase inhibition in R/R MCL (≠)



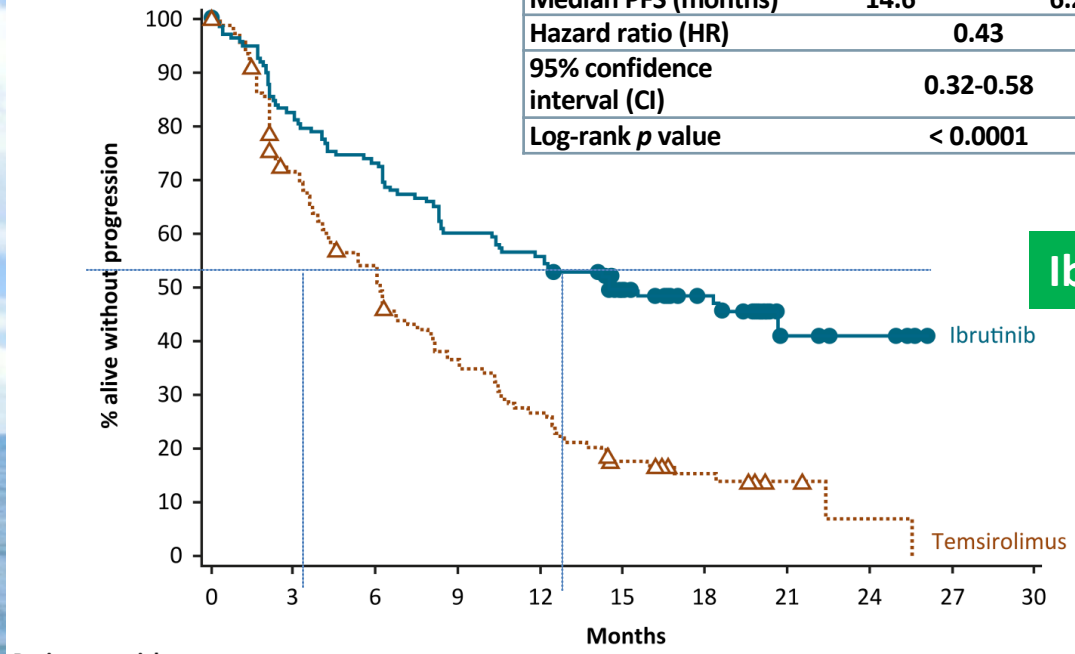
- 40 patients with relapsed/refractory MCL were treated with **Idelalisib**
- 17/40 (43%) were refractory to bortezomib
- ORR was 16/40 (40%), with CR in 2/40 (5%) patients.
- ORR 69% in patients getting 150 mg twice daily or higher
- Median DOR was 2.7 months, median PFS was 3.7 months
- 1-year PFS was 22%.

Kahl et al. Blood. 2014; 123(22):3398-405.

Temsirolimus is approved in EC for R/R MCL

Hess et al., JCO 2009,
Jurczak et al. Leuk Lymph 2017

	Ibrutinib	Temsirolimus
Median PFS (months)	14.6	6.2
Hazard ratio (HR)	0.43	
95% confidence interval (CI)	0.32-0.58	
Log-rank *p* value	< 0.0001	



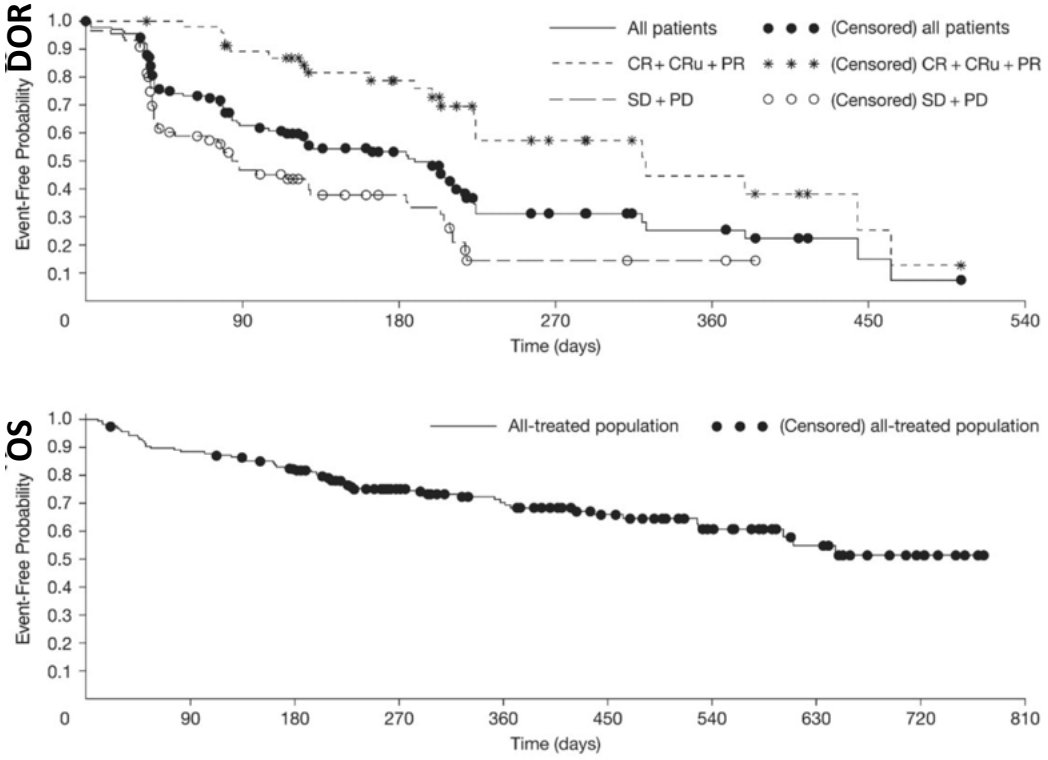
Ibrutynib

Patients at risk

Ibrutinib	139	114	101	83	77	45	34	8	5	0	0
Temsirolimus	141	93	69	45	33	19	11	3	1	0	0

Dreyling, Jurczak et al, Lancet 2016

Bortezomib in Relapsed MCL

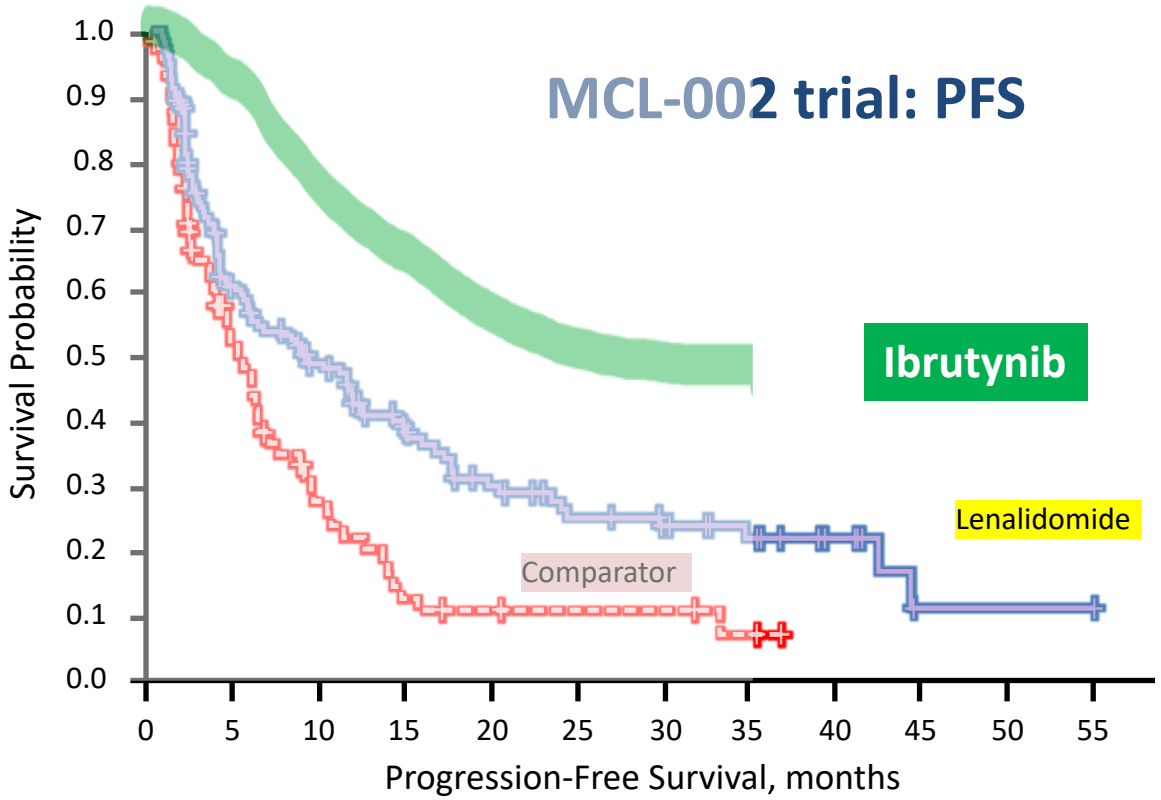


- 155 relapsing/refractory pts
- in 141 patients **RR was 33% including 8% CRs.**
- **Median DOR was 9.2 months**.
- Median TTP was 6.2 months.
- Median OS not reached after a median follow-up of 13.4 mo.

Approved in US:
- **In R/R MCL**
- **BR-CAP as I line therapy**

Fisher R I et al. JCO 2006;24:4867-4874

Lenalidomide in R/R MCL



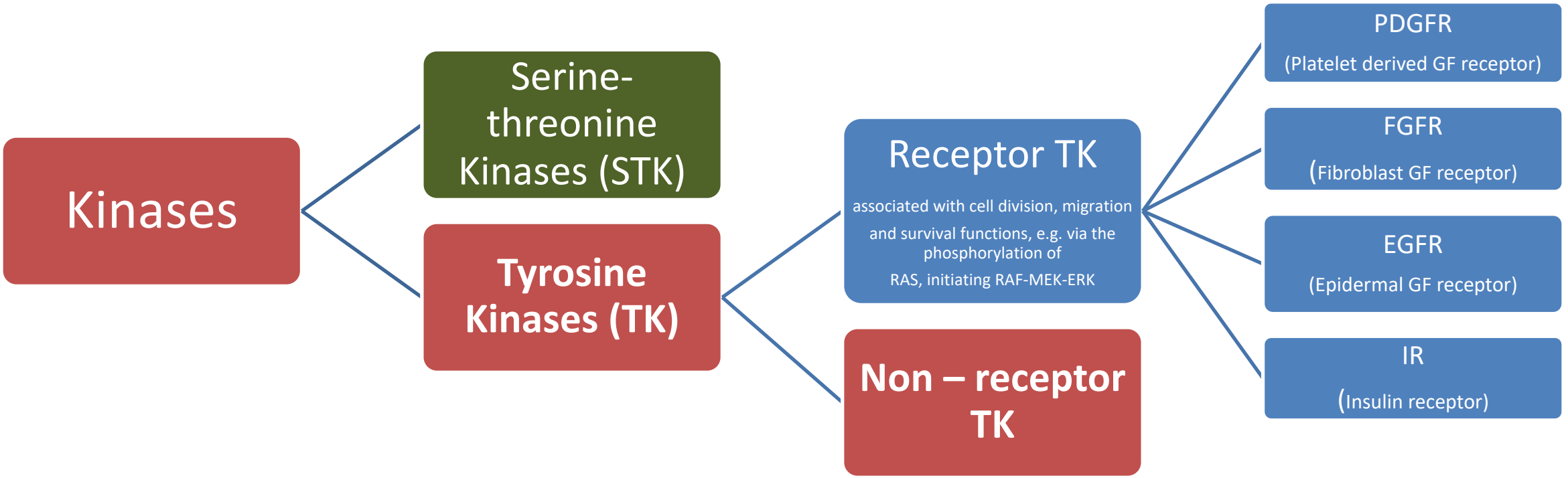
	Lenalidomide (n = 170)	IC (n = 84)
Median PFS, mo (95% CI)	8.6 (5.5-12.1)	5.2 (3.6-6.9)
HR (95% CI)	0.61 (0.44-0.84); P = 0.004	

Lenalidomide vs IC showed a 39% reduction in the risk of PD or death, reflected as an estimated improvement in median PFS of 3.4 months

Regimen	N	ORR% (CR%)	mPFS	mOS	Reference
Lenalidomide	**134**	**28 (8)**	**8,6**	**19**	**Trneny, L.Oncol 2016**
Len + R	**52**	**56 (36)**	**11.1**	**24.3**	**Wang, Lancet 2012**
Thal+R+PEPC	**25**	**73 (32)**	**10**	**45%@2y**	**Ruan, Cancer 2010**

Trneny et al, Lancet Oncology 2016

Kinases



Siveen et al., Mol Cancer 2018

Non – receptor tyrosine kinases

SRC kinase (membrane associated)

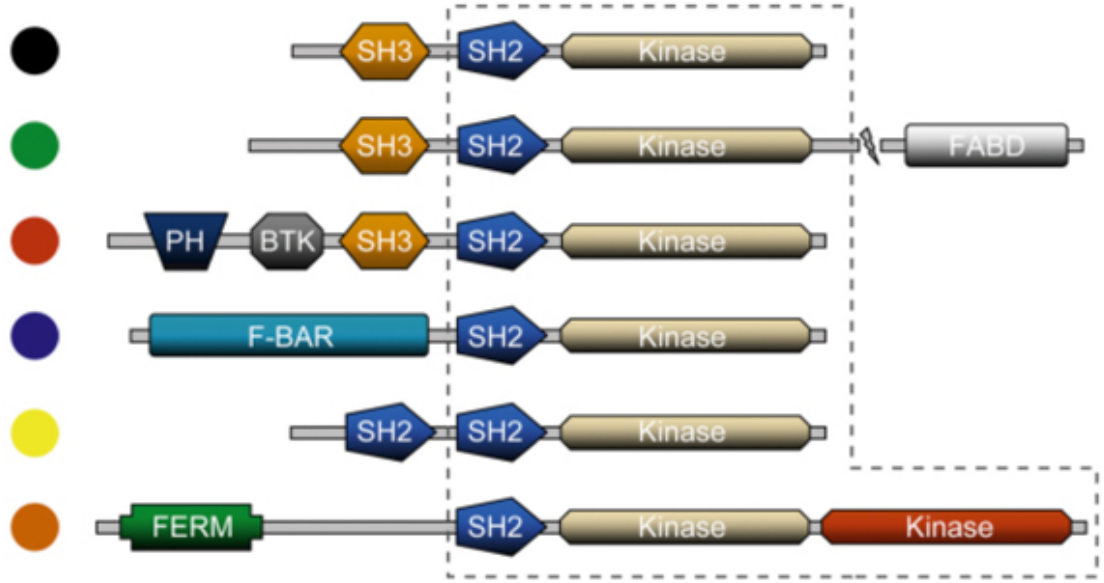
Abl (Abelson kinases family)

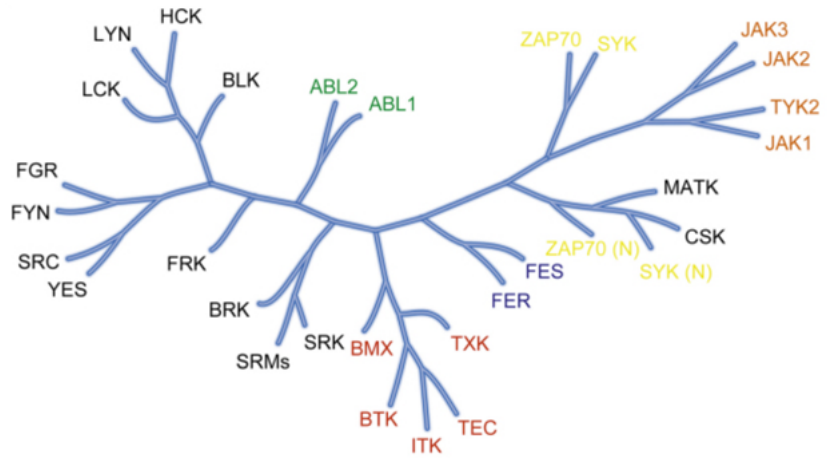
TEC kinases

FES (Feline Sarcoma kinases)

SYK (spleen Thyrosine kinase)

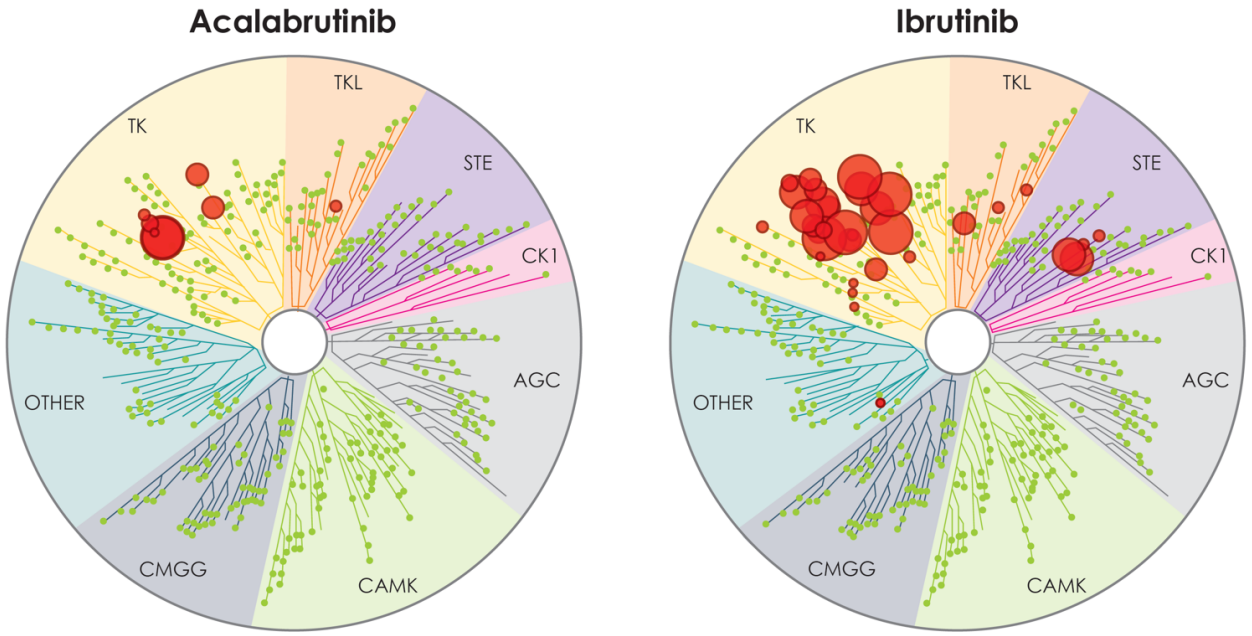
JAK (Janus kinase activating STAT)





Siveen et al., Mol Cancer 2018

How selective BTK inhibitors are ?



Larger red circles represent stronger inhibition

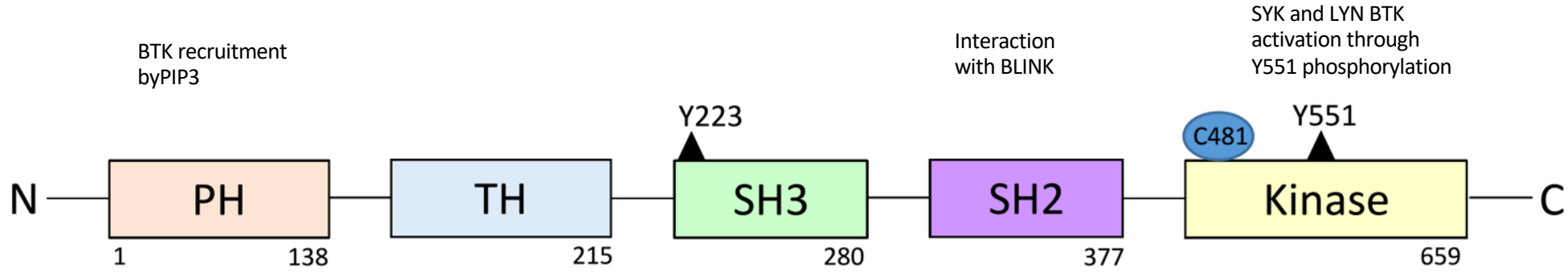
Kinase Inhibition Average IC_{50} (nM)[4]										
Kinase	BTK	TEC	ITK	BMX	TXK	EGFR	ERBB2	ERBB4	BLK	JAK3
Acalabrutinib	5.1	126	>1000	46	368	>1000	~1000	16	>1000	>1000
Ibrutinib	1.5	10	4.9	0.8	2.0	5.3	6.4	3.4	0.1	32

Barf et al. Jnl of Pharmacol and Exp Therap 2017

TEC kinases: non-receptor tyrosine kinases with a highly conserved carboxyl-terminal kinase domain:

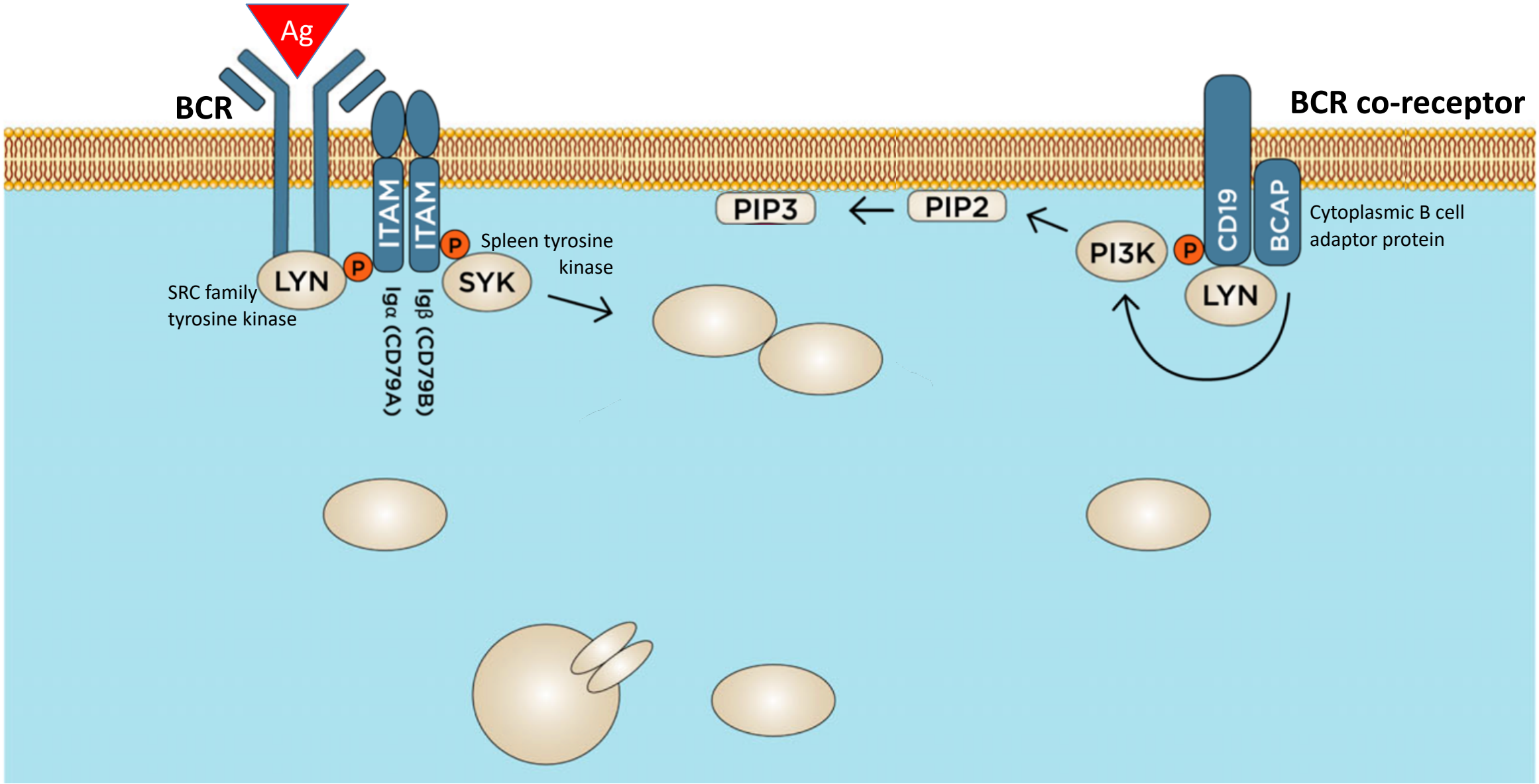
- **BTK (Bruton Tyrosine kinase)**
- **BMX (bone marrow tyrosine kinase on chromosome X)**
- **TXK (tyrosine-protein kinase)**
- **ITK (interleukin 2-inducible T-cell kinase)**
- **TEC (tyrosine kinase expressed in hepatocellular carcinoma)**

Bruton Tyrosine Kinase

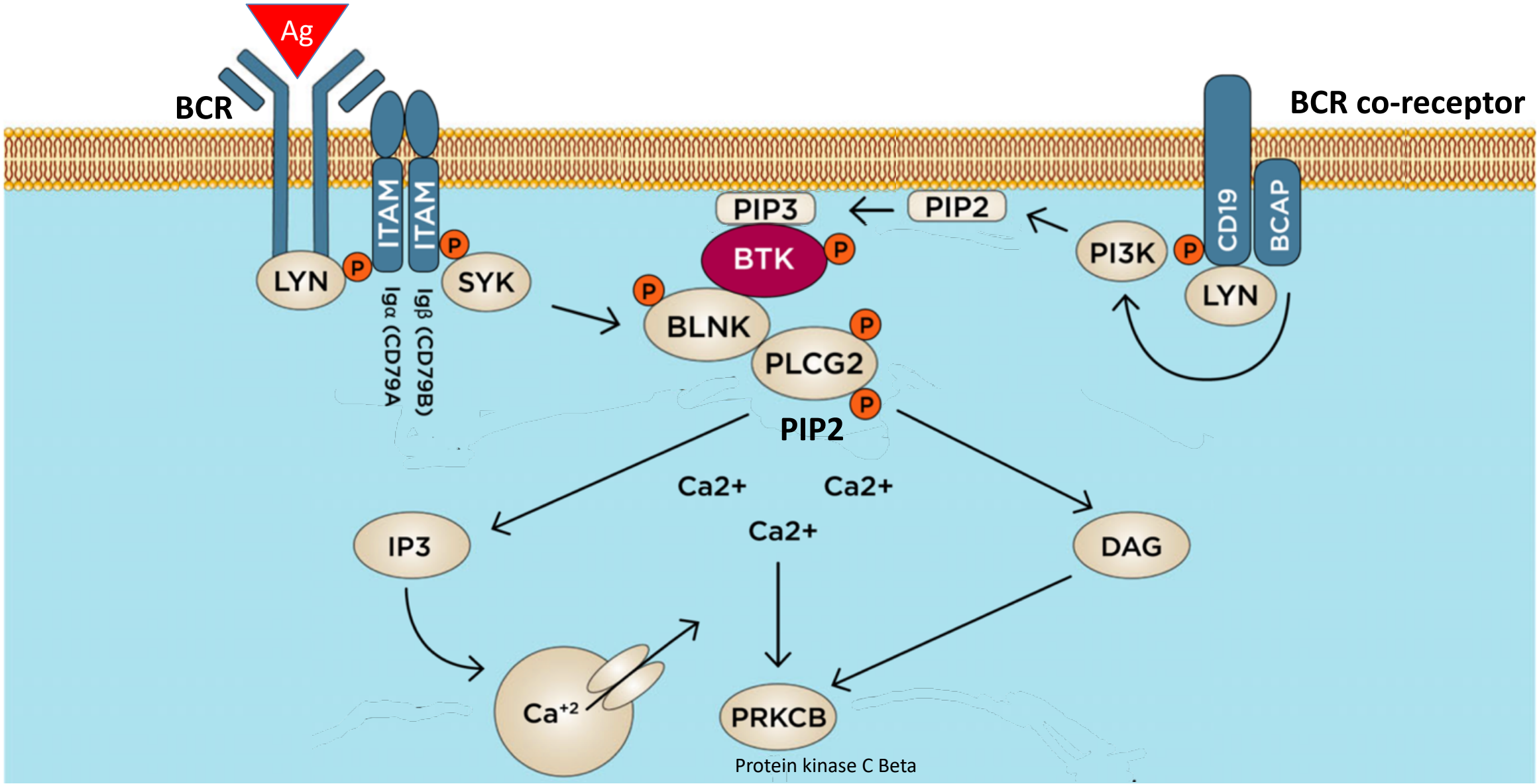


- **BCR signalling**
- CD19, CD38, CD40, G-protein coupled receptors and chemokine receptors, TNF, Toll like receptor signalling

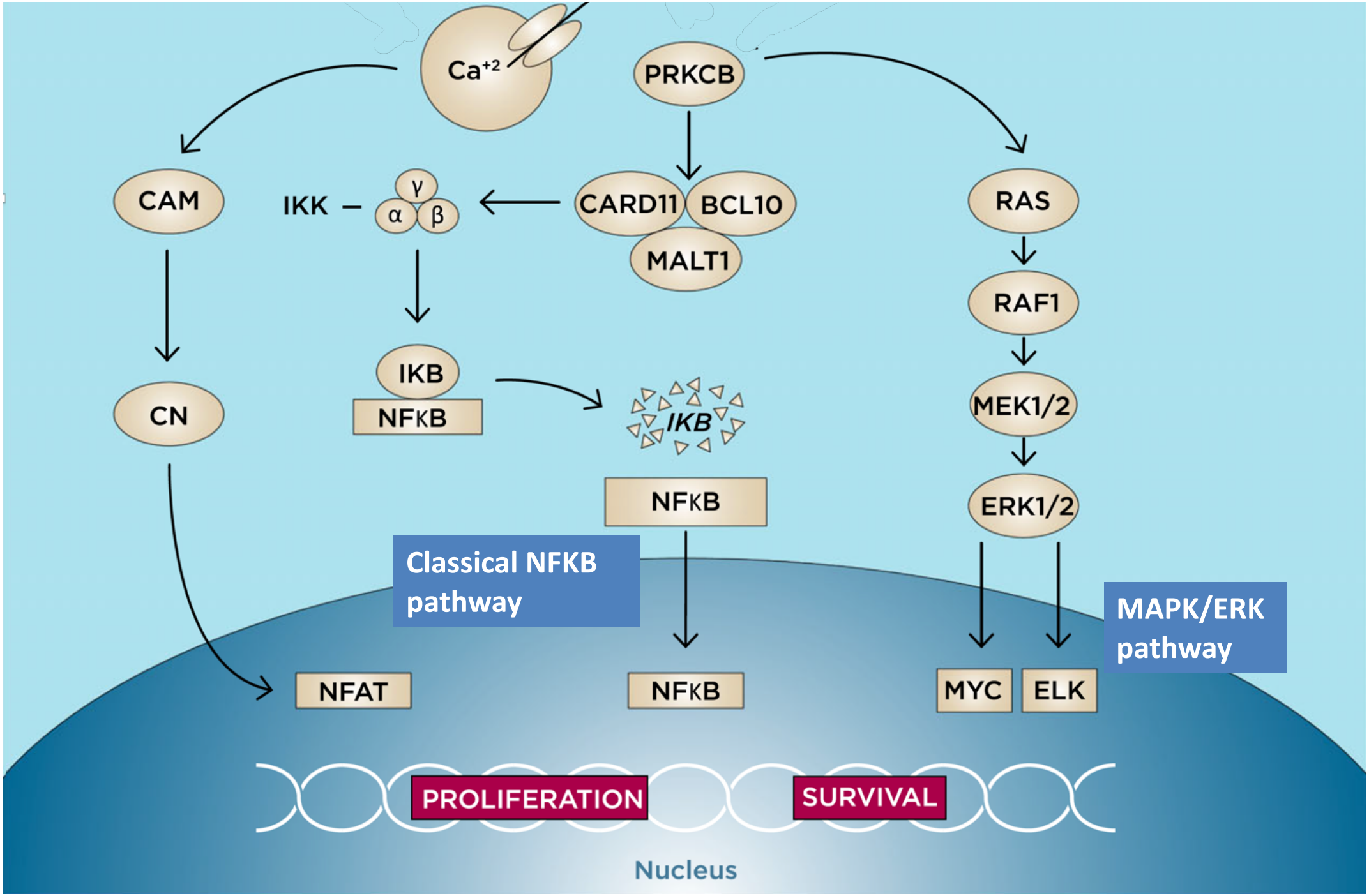
- BTK is essential for B cell maturation, formation of germinal centres, plasma cell proliferation
- BTK activation may provoke autoantibody production and auto-immunopathy
- BTK is defective in primary immunodeficiency X-linked agammaglobulinemia (XLA)

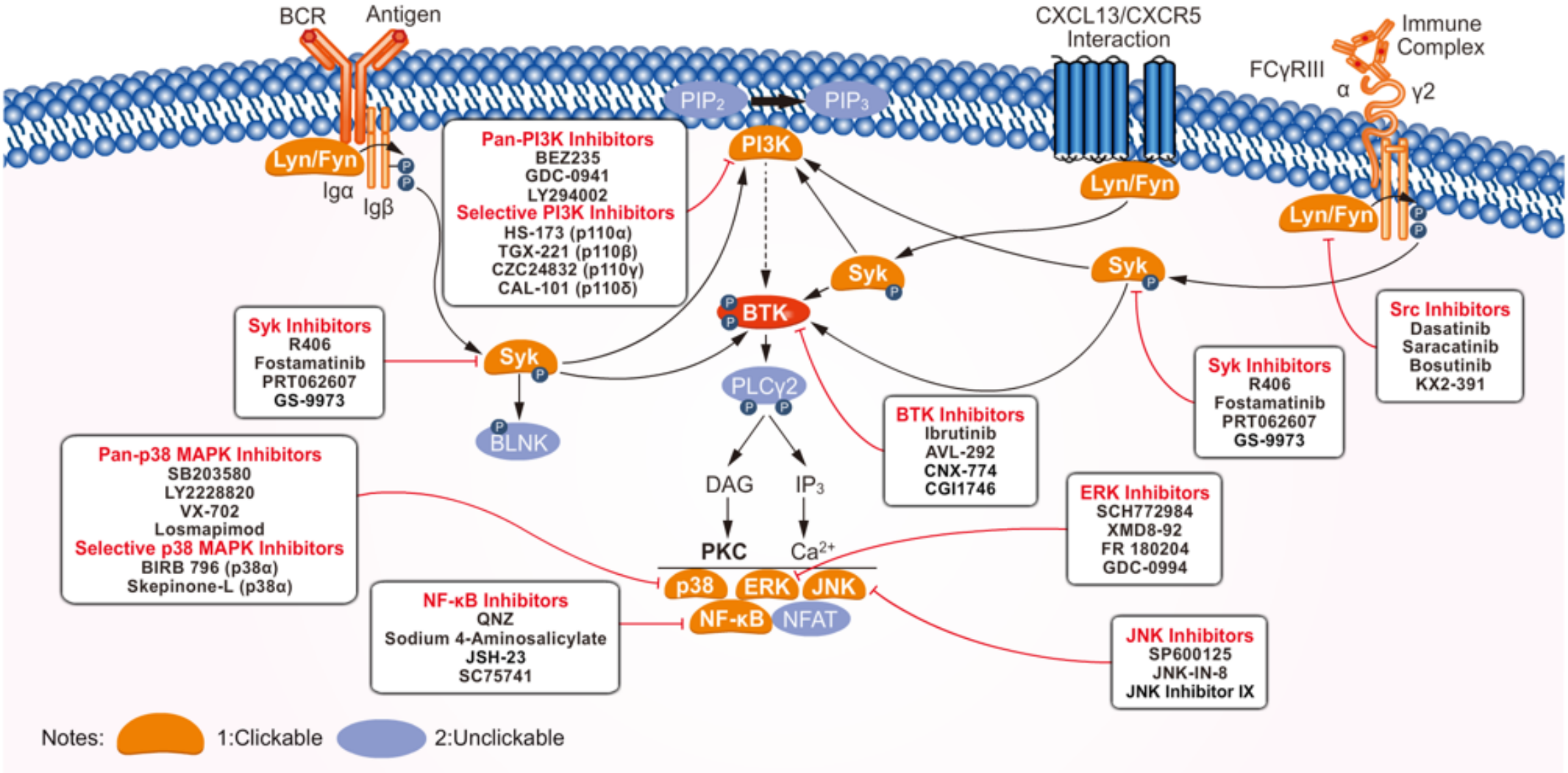


Hershkovitz-Rokah et al., BJH 2018



Hershkovitz-Rokah et al., BJH 2018

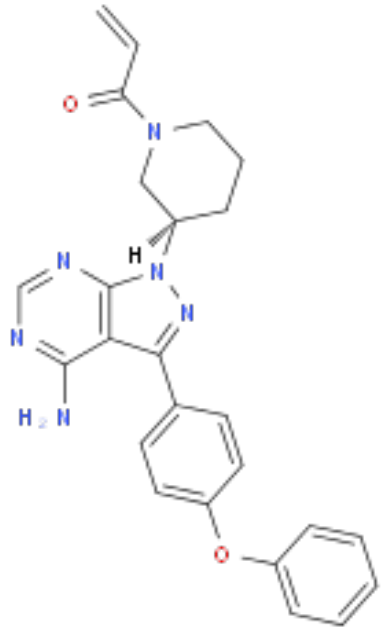

Ca+2
PRKCB
CAM
IKK
γ
α
β
CARD11
BCL10
MALT1
RAS
RAF1
MEK1/2
ERK1/2
IKB
NFKB
CN
IKB
NFKB
NFKB
Classical NFKB pathway
MAPK/ERK pathway
NFAT
NFKB
MYC
ELK
PROLIFERATION
SURVIVAL
Nucleus



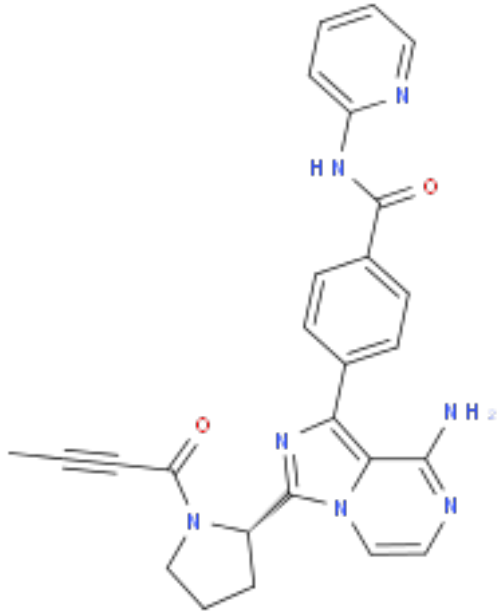
https://www.selleckchem.com

Comparison of BTK inhibitors

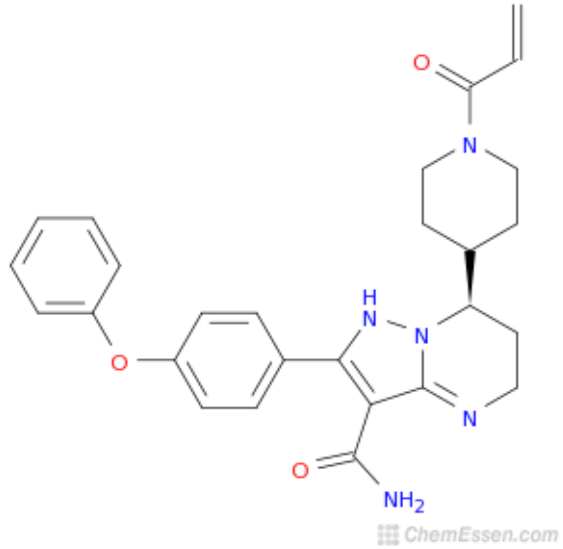
Ibrutynib (PCI 32765)



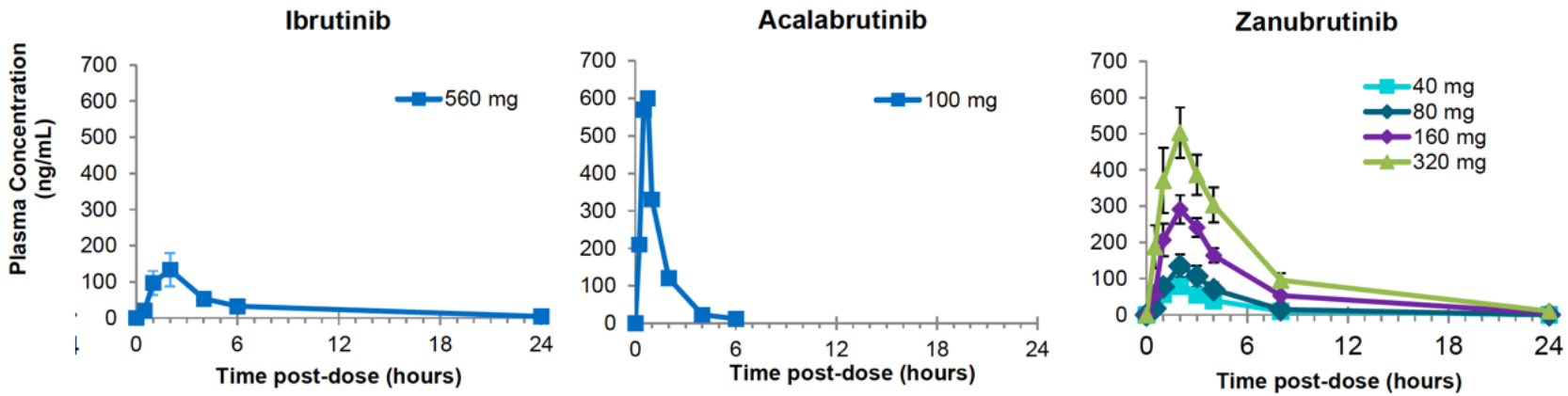
Acalabrutinib (ACP-196)



Zanubrutynib (BGB-311)



Comparison of BTK inhibitors - Plasma Exposure By Dose

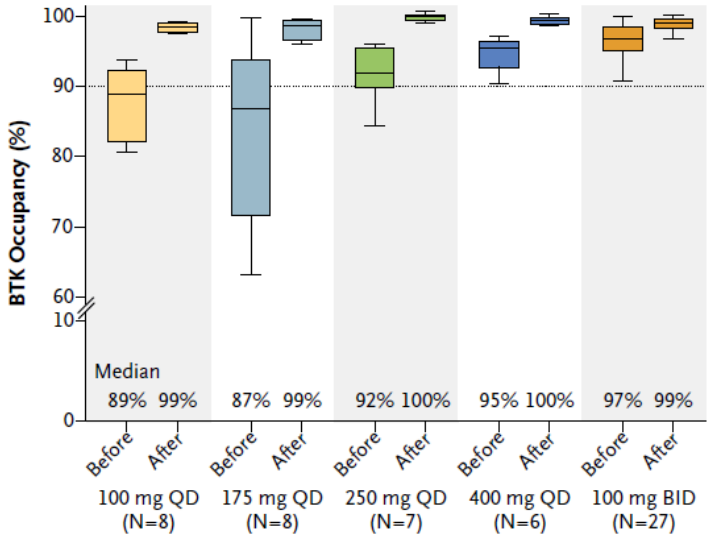


in vitro BTK inhibition IC50 relative to Ibrutinib:	1	3.4-7.2	1
Dose in MCL:	1 x 560 mg	2 x 100 mg	2 x 160 mg

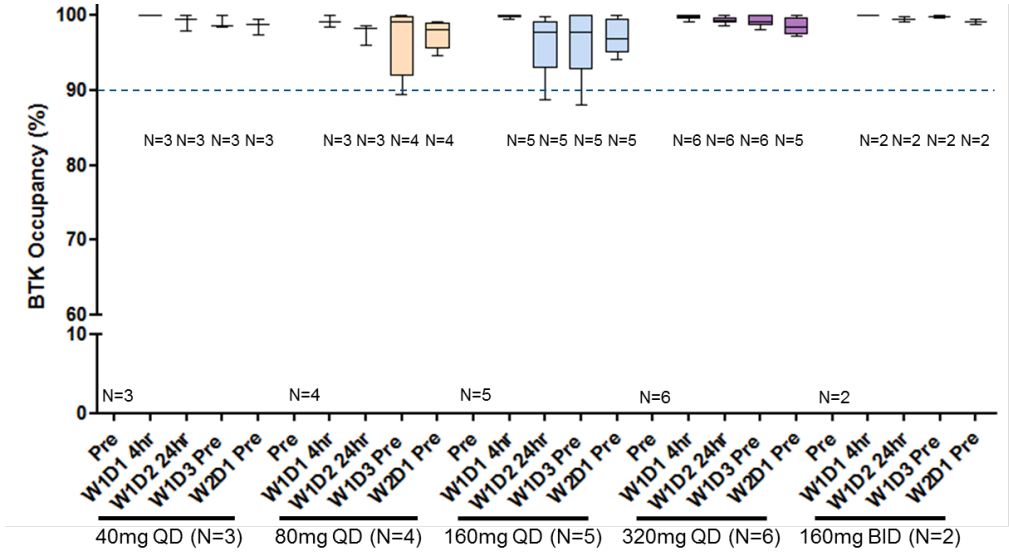
Advani et al., JCO 2013; Byrd et al. NEJM 2015,

Comparison of BTK inhibitors – Target Occupancy

Acalabrutinib (ACP-196)



Zanubrutynib (BGB-311)



Advani et al., JCO 2013; Byrd et al. NEJM 2015,

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Two uncomparable clinical studies

	PCYC-1104-CA	ACE-LY-004
Study Name	Safety and Efficacy of PCI-32765 in Participants with Relapsed/Refractory MCL	An Open-label, Phase 2 Study of ACP-196 in Subjects with MCL
Study Timeline	February 2011 – January 2014	March 2015 - February 2017
Inclusion Criteria: • Men and women ≥ 18 years of age. • Pathologically confirmed MCL, with documentation of monoclonal B cells that have a chromosome translocation t(11;14)(q13;q32) and/or overexpress cyclin D1 and measurable disease on cross sectional imaging that is ≥ 2 cm in the longest diameter and measurable in 2 perpendicular dimensions • Relapsed/refractory after at least 1, but no more than 5, prior treatment regimens for MCL • Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2.		
Number of patients, median age	115, median age 68	124, median age 68

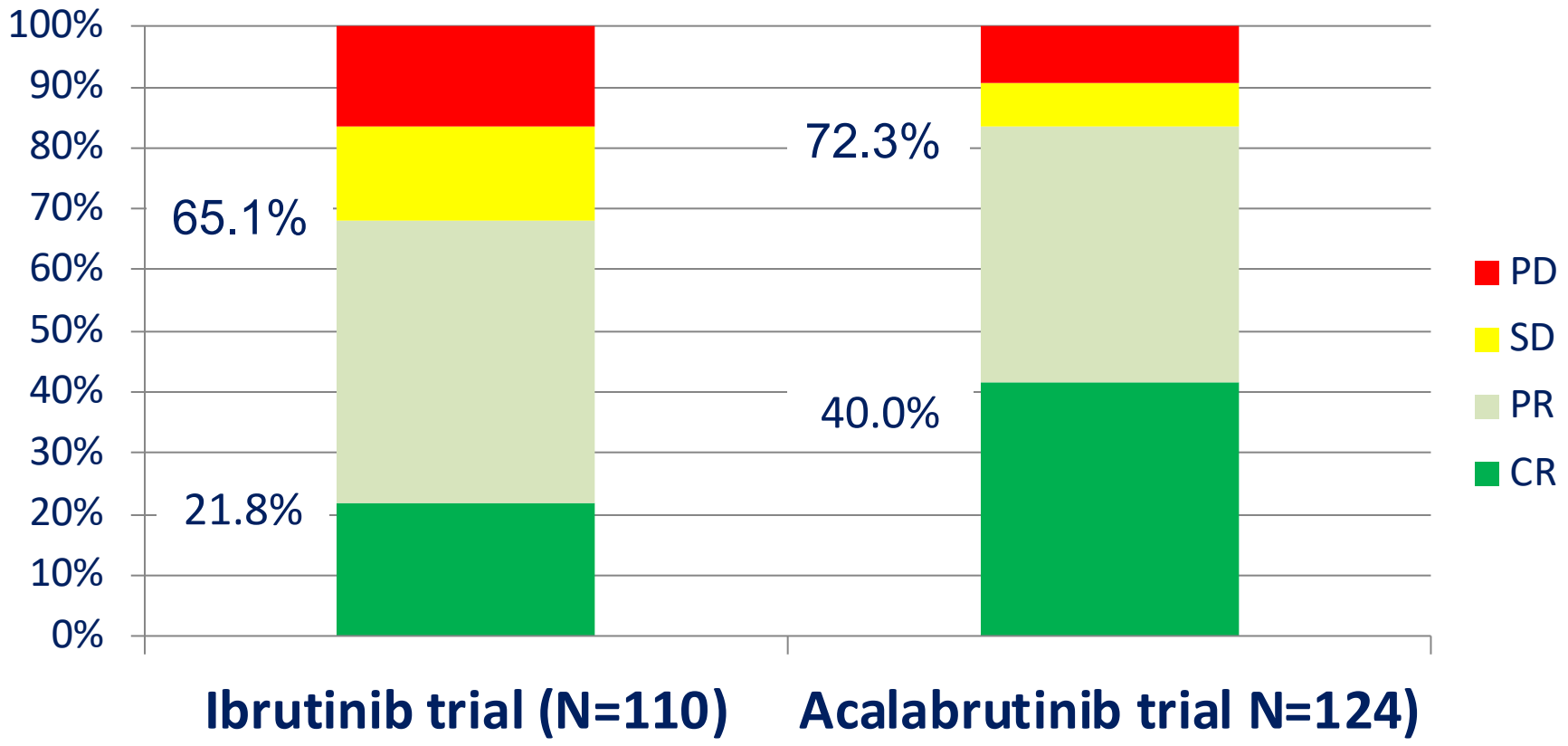
Wang et al., NEJM 2013; Wang et al. Lancet 2018

Two uncomparable clinical studies

	PCYC-1104-CA	ACE-LY-004
Number of previous therapies	**3 (1-5)**	2 (1-5)
Previous ASCT	11%	**18%**
% of patients with intermediate-or high-risk (MIPI)	**86%**	60%
Refractory disease	**45%**	24%
Bulk > 5 and > 10 cm	39% and 8% respectively	37% and 8% respectively
Primary endpoint - ORR (*):	ORR – 68% CR - 21% PR - 47%	**ORR - 81%** **CR - 40%** PR - 41%
Median time to initial response (months)	1.9 (range 1.4-13.7)	1.9 (range 1.5-4.4)
Median time to CR (months)	5.5 (range 1.7-24.7)	**3.4** (range 1.9–5.5)
Duration of Response (DOR)	median - 17.5 months	**72% at 12 months**
Progression Free Survival (PFS)	median - 13.9 months	**67% at 12 months**
Overall Survival (OS)	58% at 18 months	**87 at 12 months**

Wang et al., NEJM 2013; Wang et al. Lancet 2018

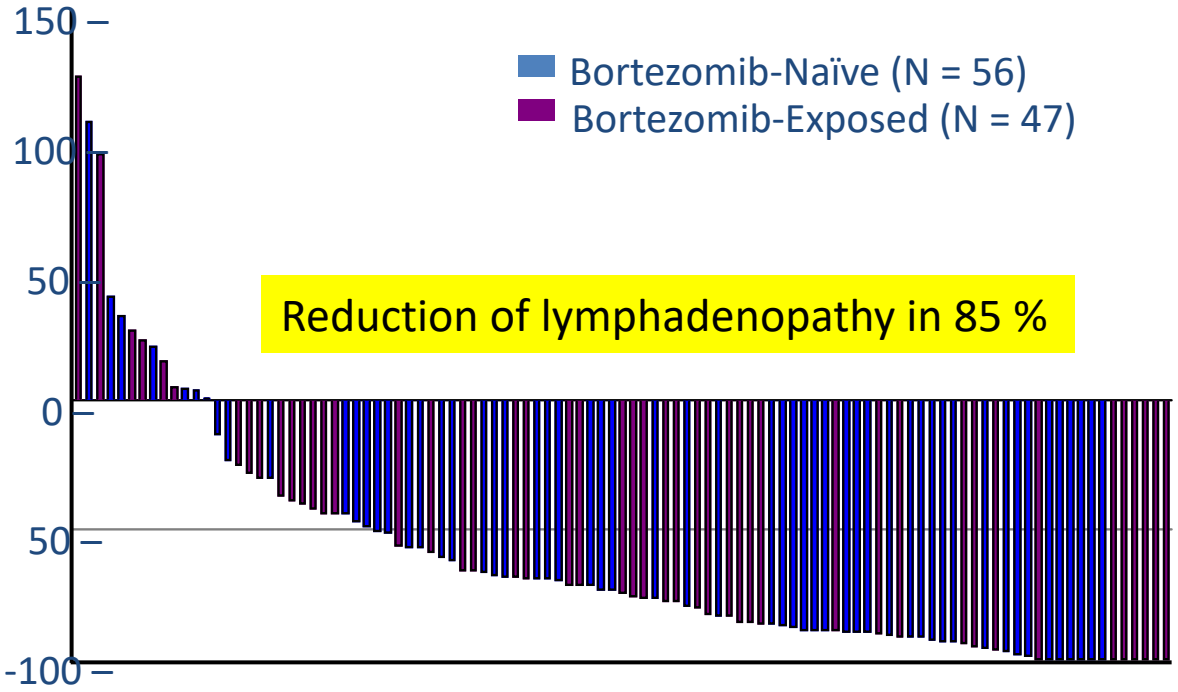
BTK inhibitors in R/R MCL - Response to therapy



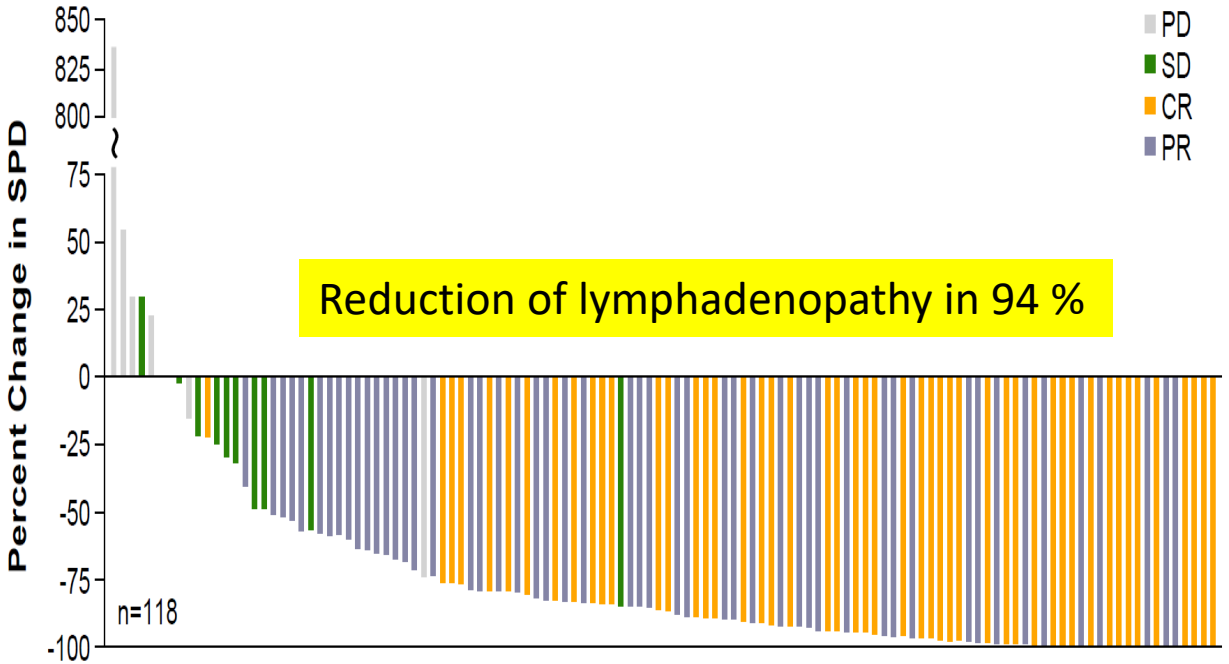
CT based follow-up
PET and BM only in CT CR

PET based follow-up
BM only in PET CR

BTK inhibitors in R/R MCL - Response to therapy (SPD)



Ibrutinib trial

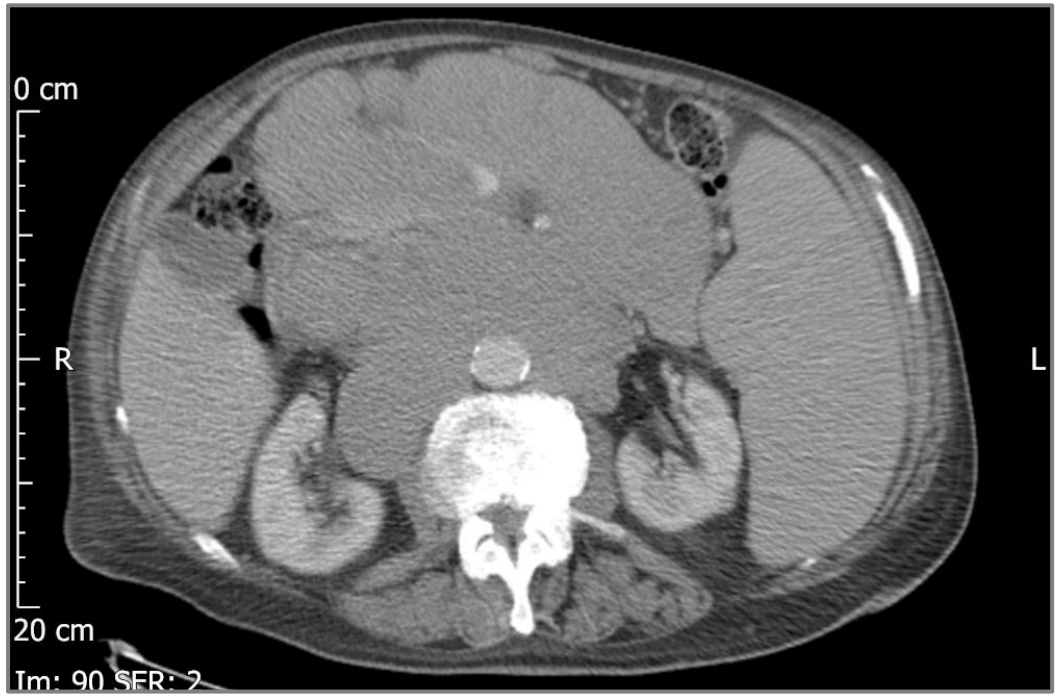


Acalabrutinib trial

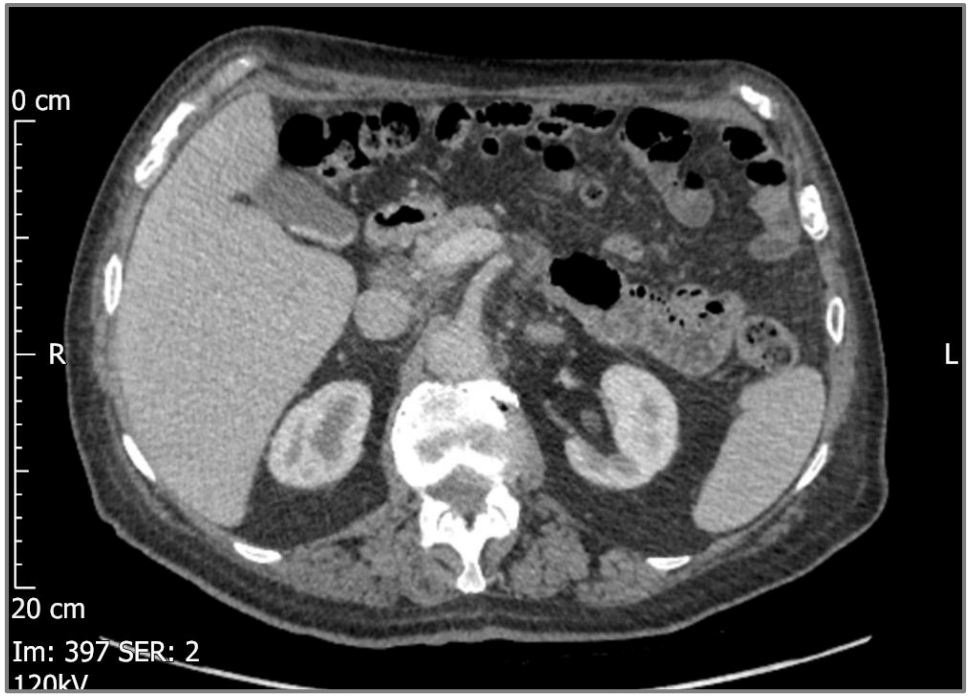
CT Scans of Tumor Response to Acalabrutinib

- Axial images of a 92-year-old male with chemorefractory MCL treated with acalabrutinib

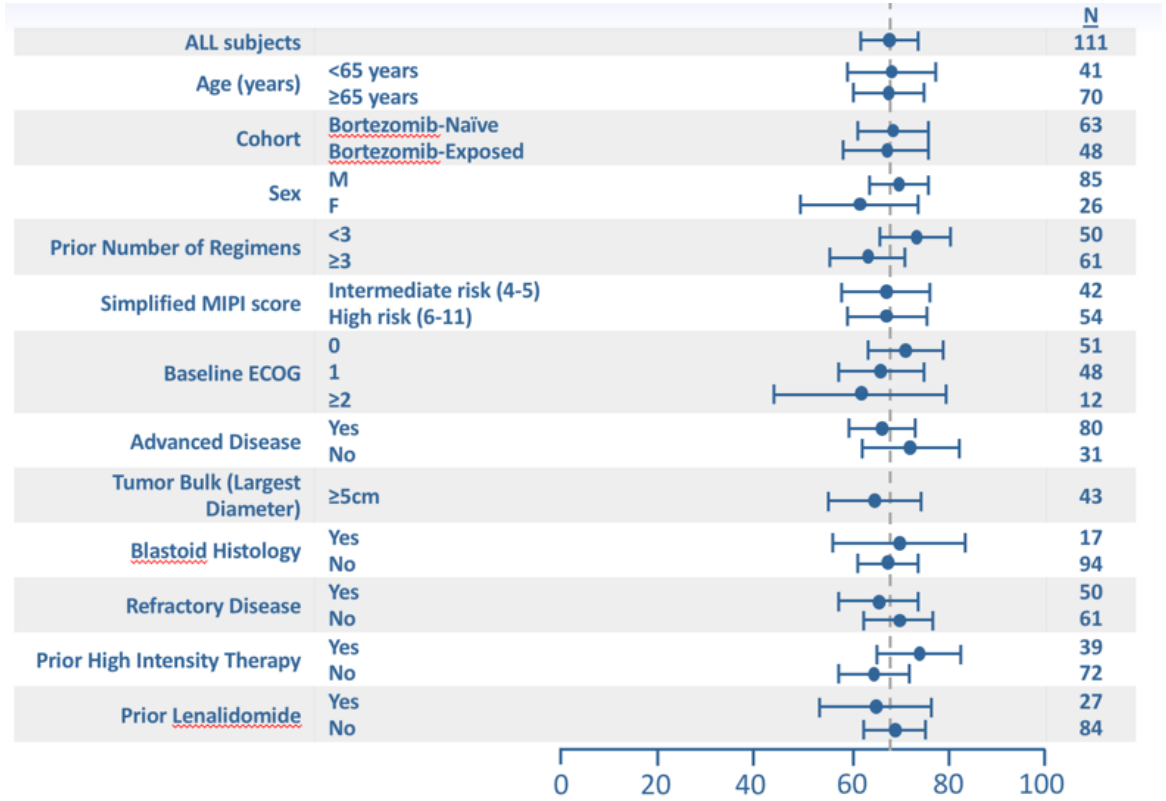
Before Treatment



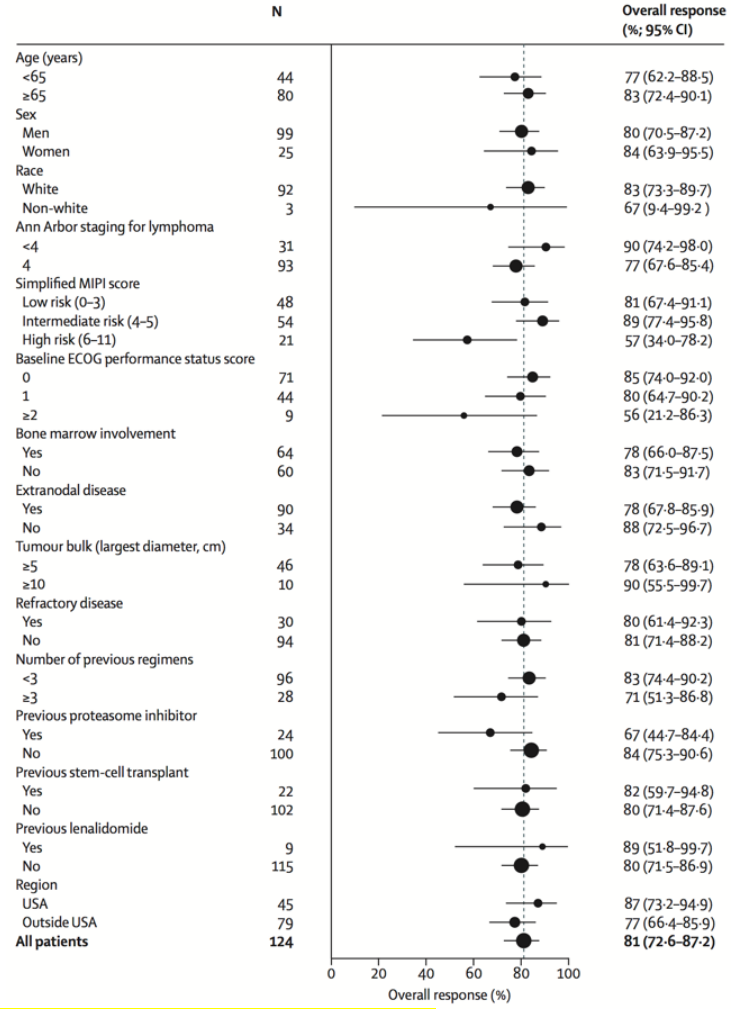
After 7 Months of Treatment



Response to BTK inhibitors is Independent of Patient Characteristics and Risk Factors

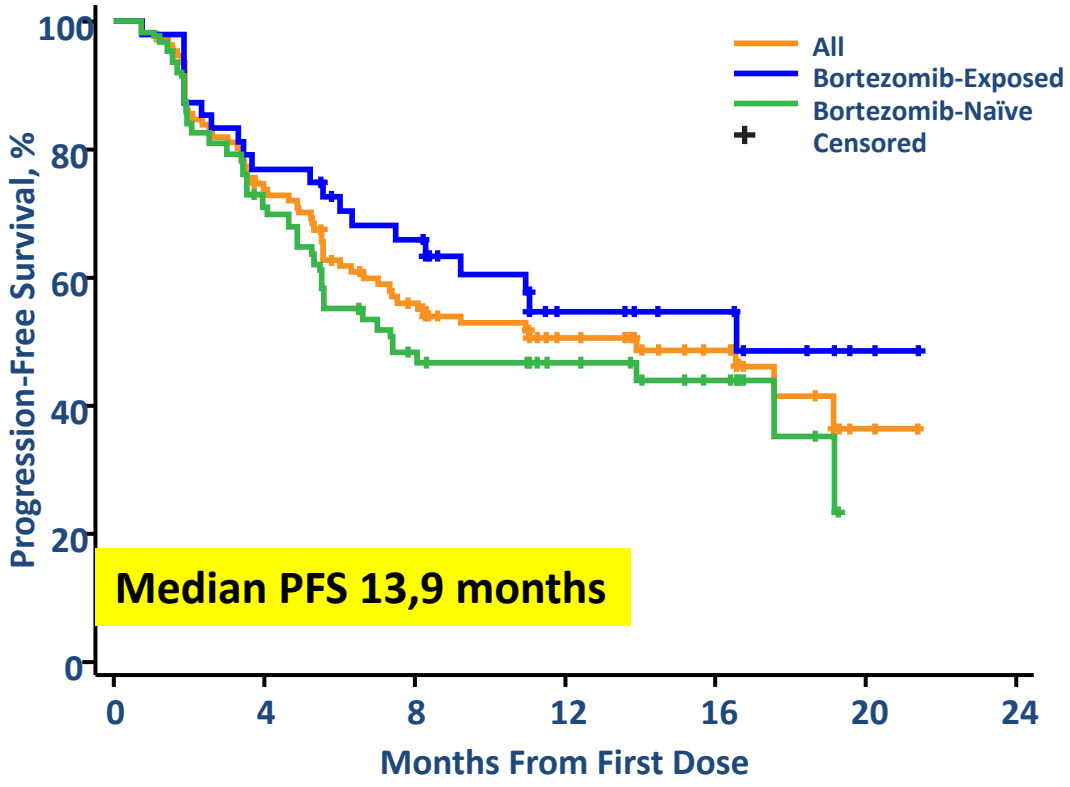


Ibrutinib trial



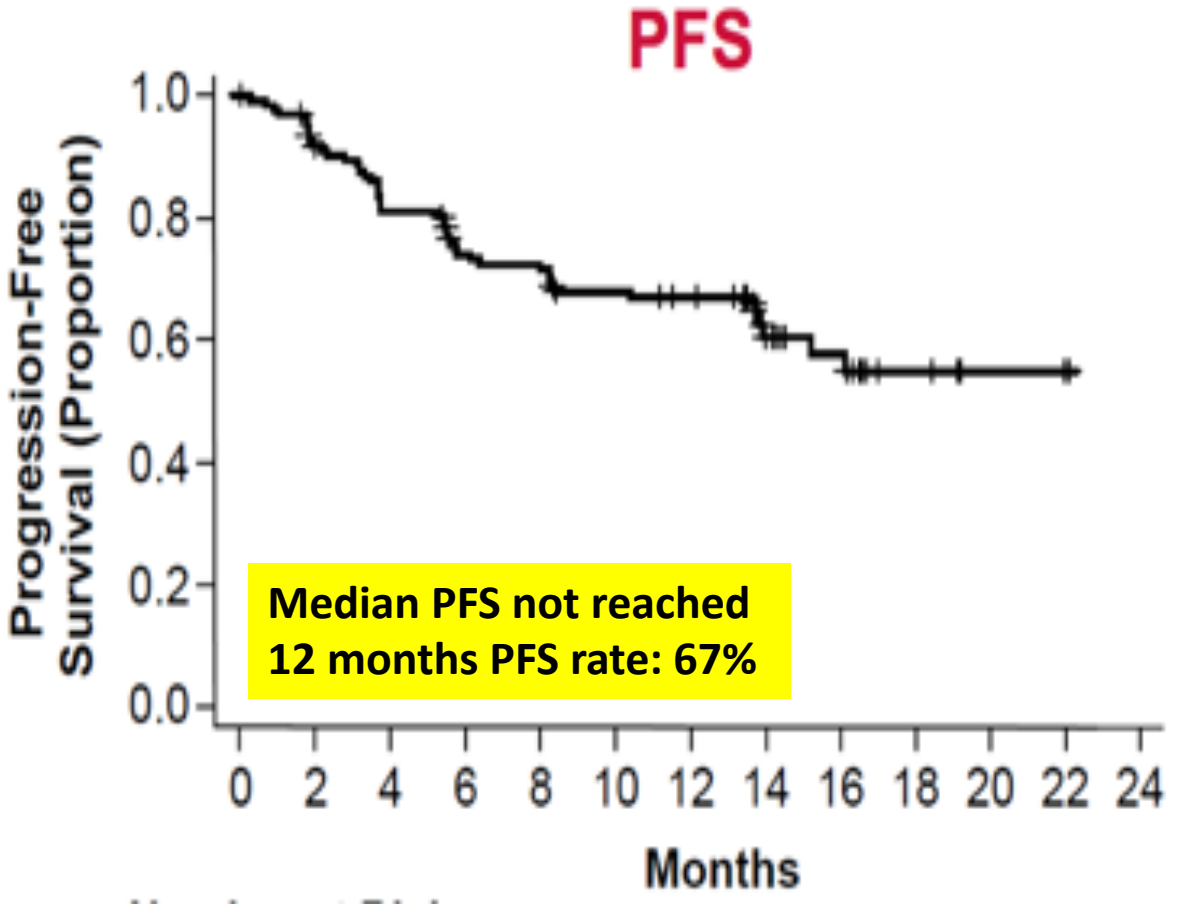
Acalabrutinib trial

BTK inhibitors in R/R MCL - PFS



Median PFS 13,9 months

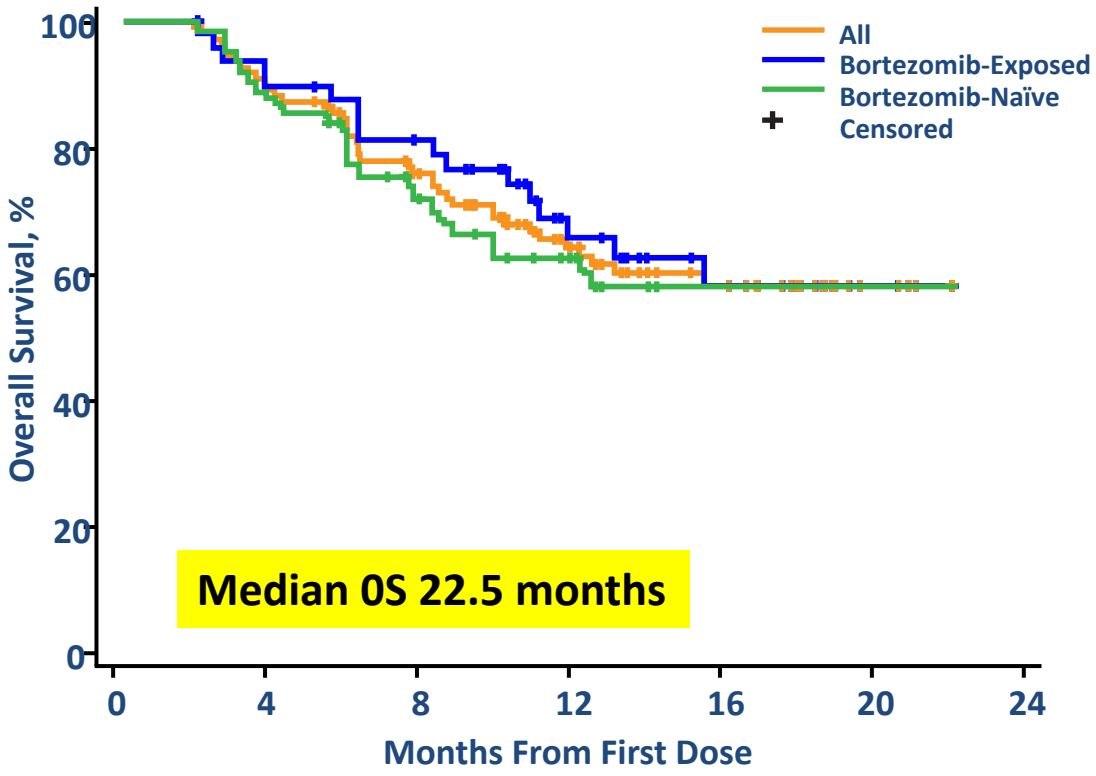
Ibrutinib trial



Median PFS not reached
12 months PFS rate: 67%

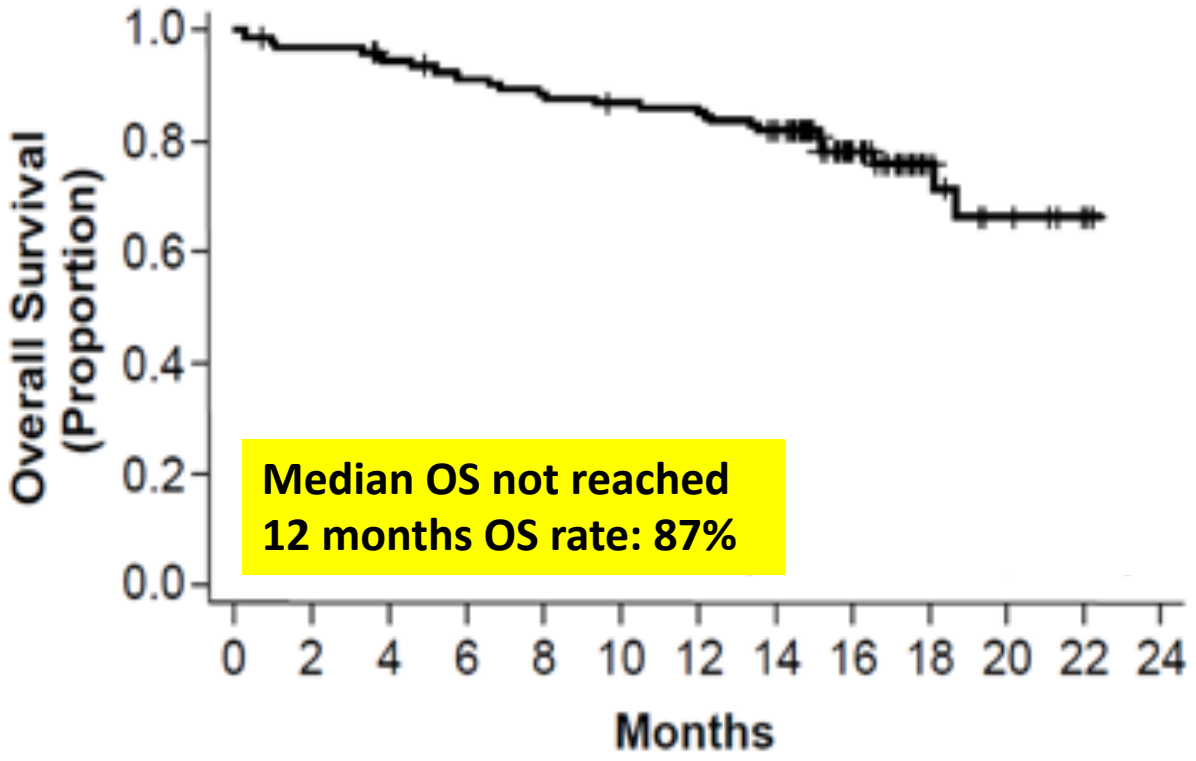
Acalabrutinib trial

BTK inhibitors in R/R MCL - OS



Median 0S 22.5 months

Ibrutinib trial



Median OS not reached
12 months OS rate: 87%

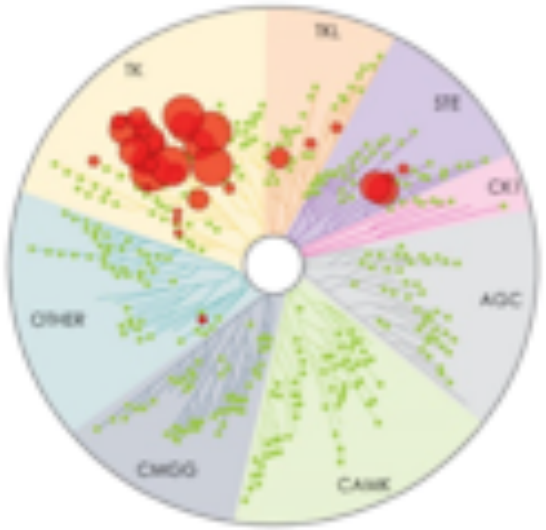
Acalabrutinib trial

Two uncomparable clinical studies

	PCYC-1104-CA	ACE-LY-004
Hematological AE: any /3-4 grade (%):		
Neutropenia	17 /16	14/14
Anemia	11 / 10	15/11
Thrombocytopenia	**13 /11**	**<5%**
Most Common AE any grade/grade 3-4 (%):		
Headache	0	**38/2**
Diarrhea	**53/6**	31/3
Fatigue	**49/5**	27/1
Myalgia	**17/0**	21/1
Nausea	**33/1**	18/1
AE of special interest any grade/grade 3-4 (%)		
Pneumonia	7 / 6	7/6
Atrial fibrillation	**7/ 6**	0/0
Bleeding events	**41/6**	31/1
Patients discontinuing therapy due to AE (%)	**11**	6

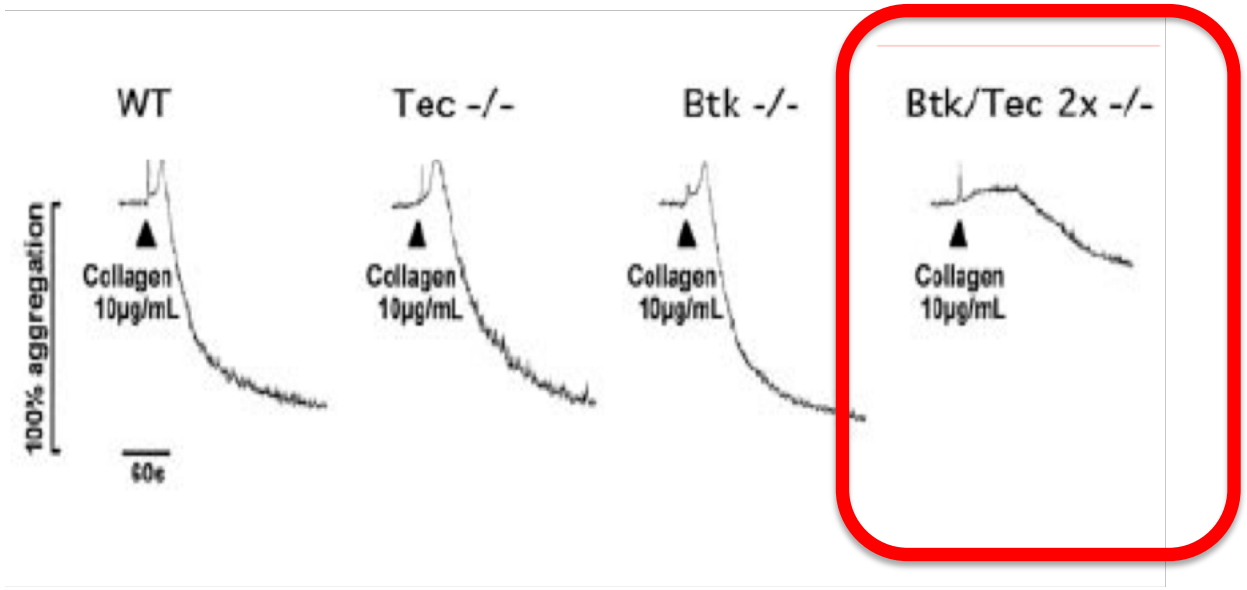
Wang et al., NEJM 2013; Wang et al. Lancet 2017

Ibrutinib - Concurrent BTK/TEC inhibition disrupts collagen-mediated platelet aggregation



Kinase Inhibition IC_5 (nmol/L)[1]

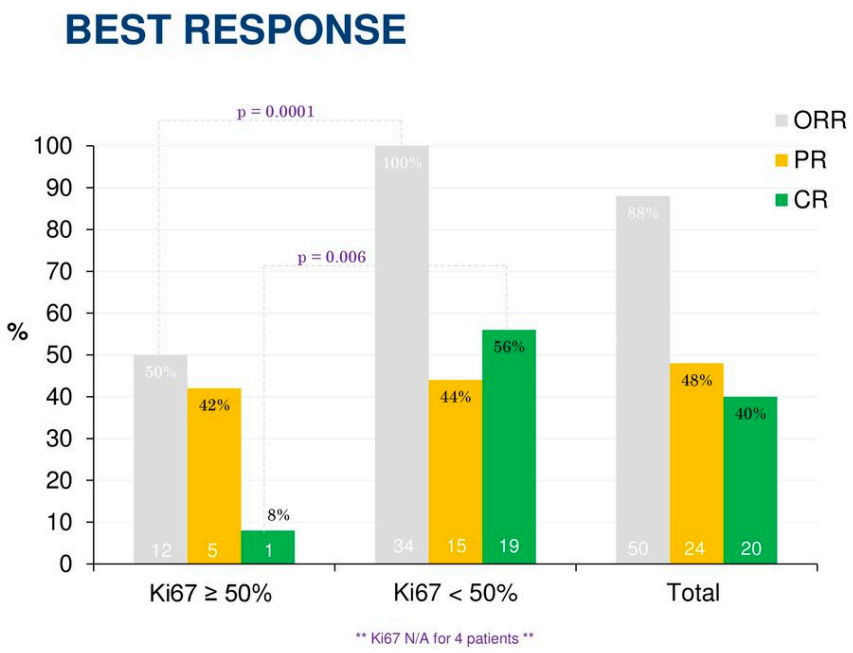
Kinase	Ibrutinib
BTK	1.5
TEC	7.0
BMX	0.8
TXK	2.0
ERBB2	6.4
EGFR	5.3
ITK	4.9
JAK3	32
BLK	0.1

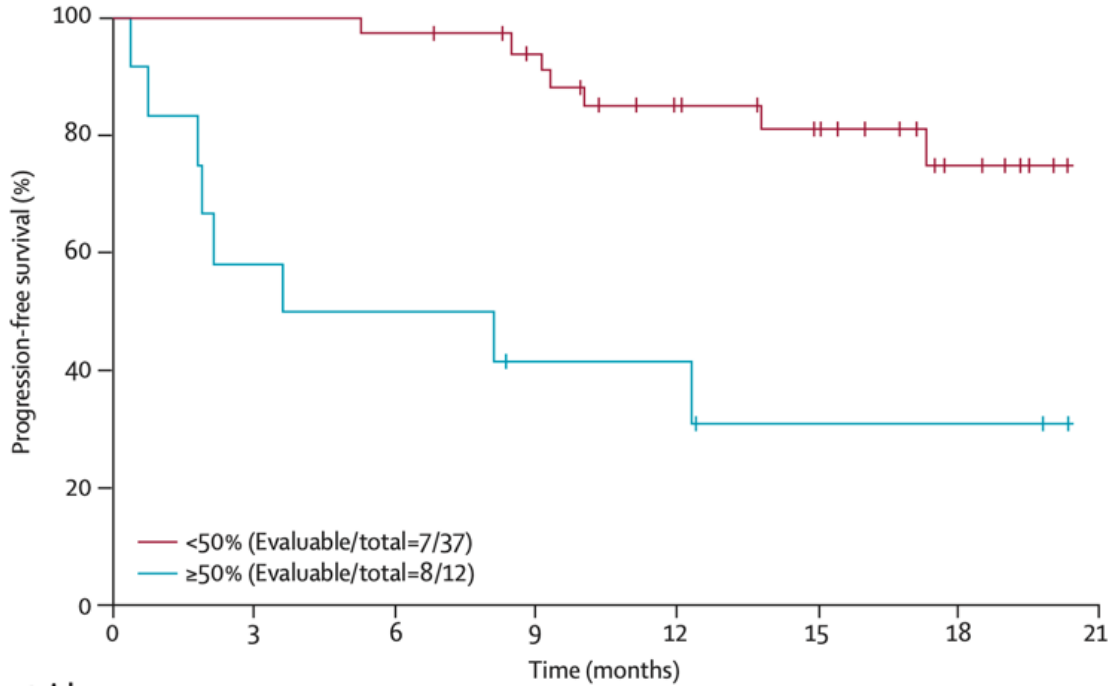


Atkinson et al, 2003

Ibrutinib + Rituximab in R/R MCL (≠)

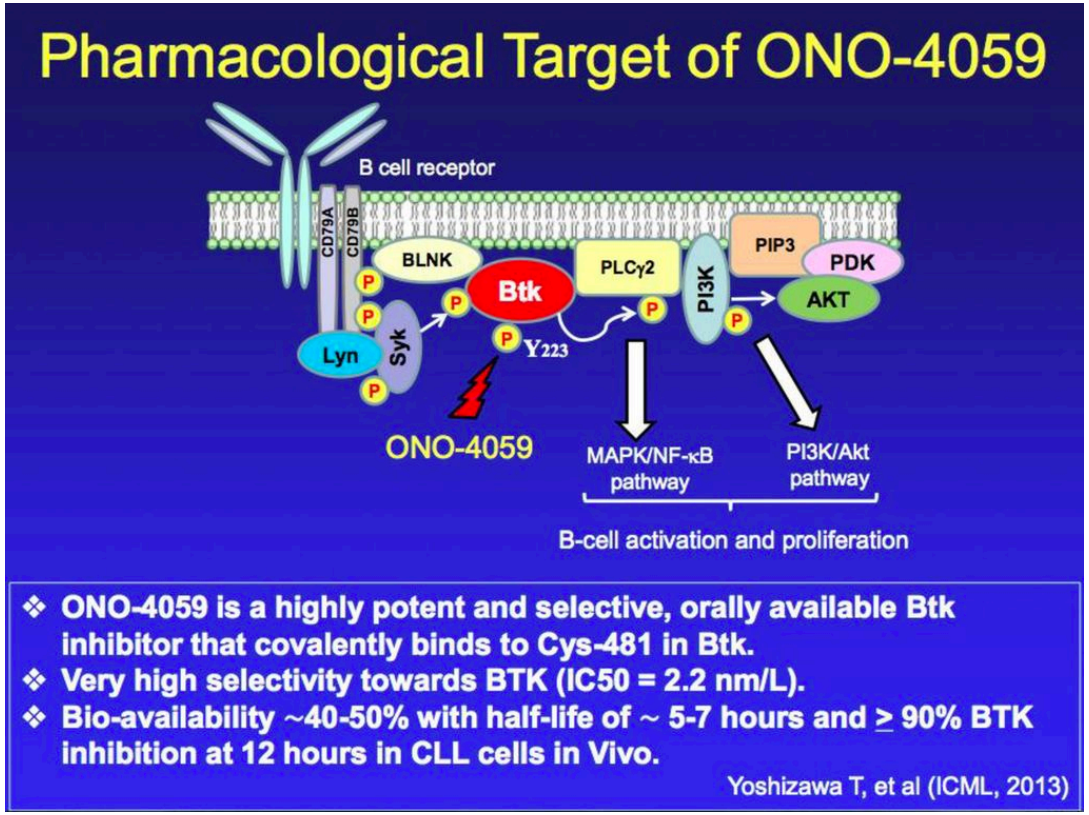
Very promising results in those with ki67 expression < 50 %

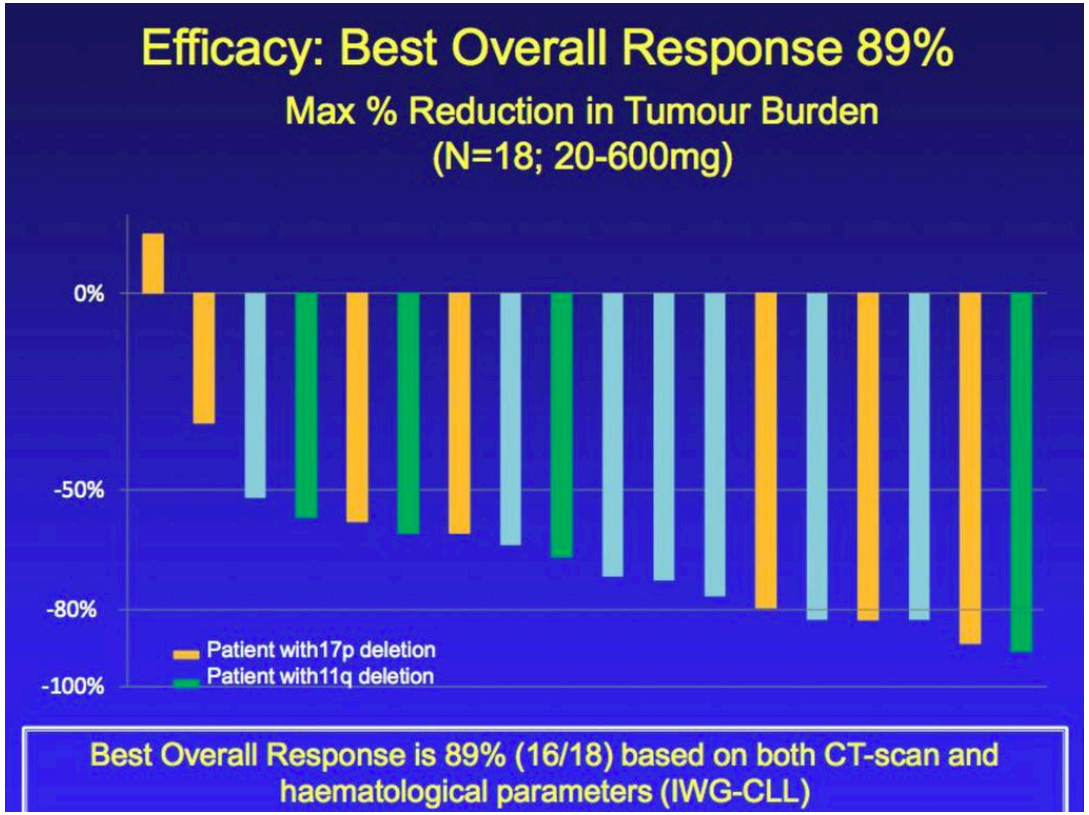




Wang et al.; Lancet Oncol 2016

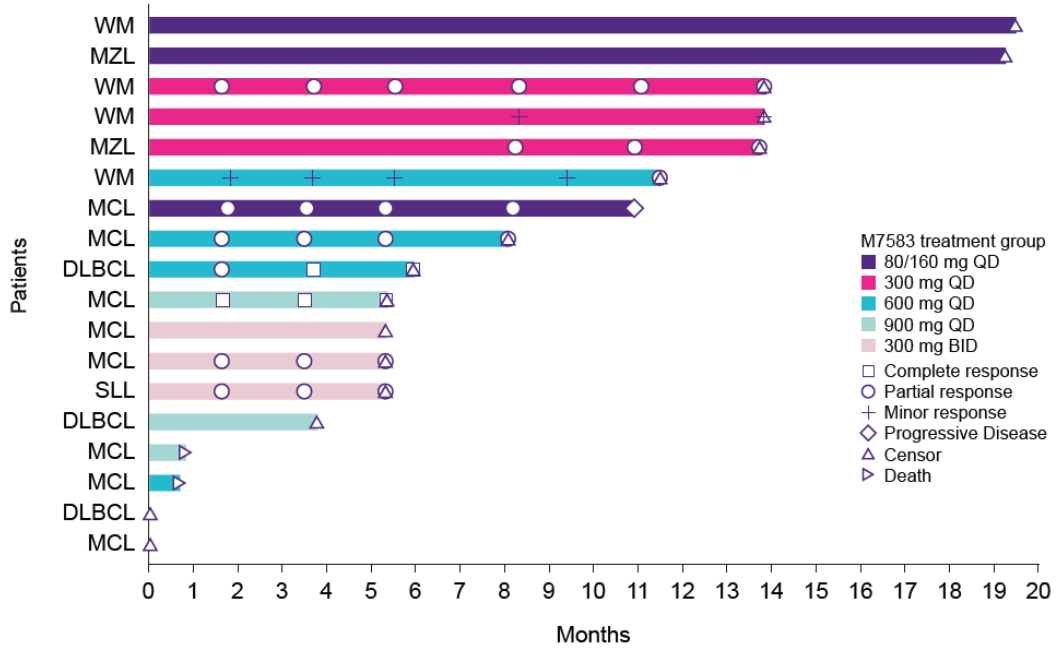
ONO-4059 in MCL *(≠)*





Yoshizawa et al., ICML 2013

M7583 in R/R B cell NHL *(≠)*



Jurczak et al., ESMO 2018

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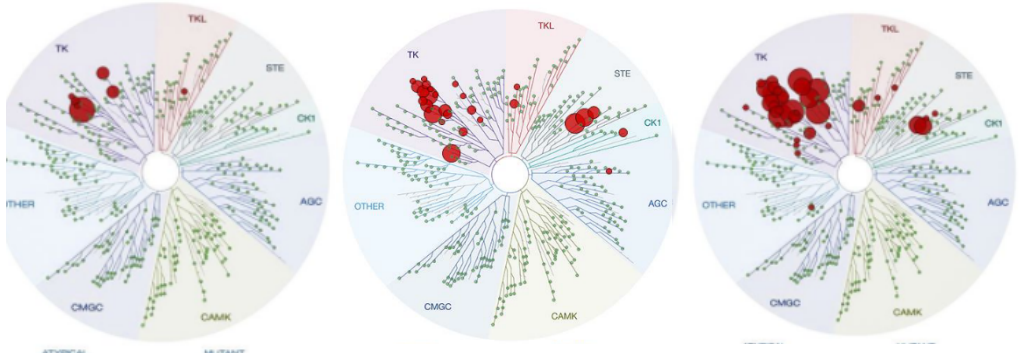
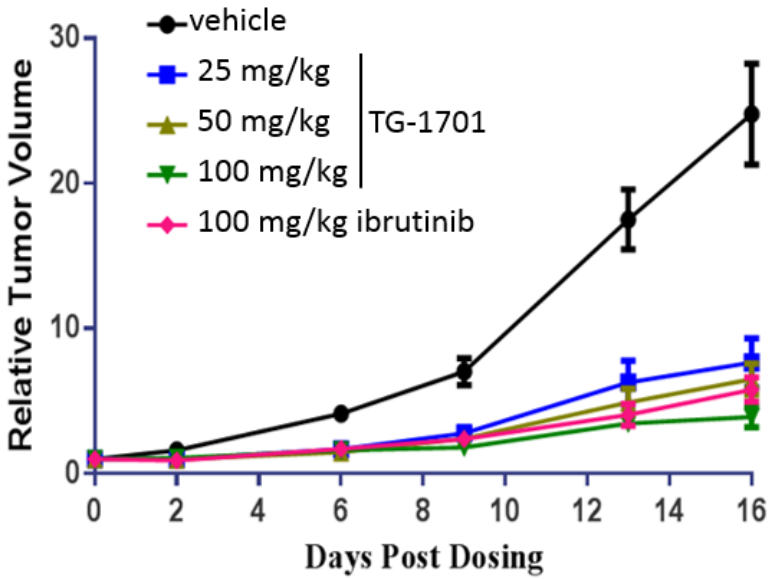
TG-1701 in MCL and WM *(≠)*

Acalabrutinib TG-1701 ibrutinib



Larger red circles represent stronger inhibition

kinase	acalabrutinib	TG-1701	ibrutinib
BTK	5.1	3	1.5
TEC	93	4	7
BMX	46	72% at 1000	0.8
TXK	368	136	2
ERBB2	1000	> 3000	6.4
EGFR	> 1000	270	5.3
ITK	> 1000	> 3000	4.9
JAK3	> 1000	> 3000	32
BLK	> 1000	54% at 1000	0.1



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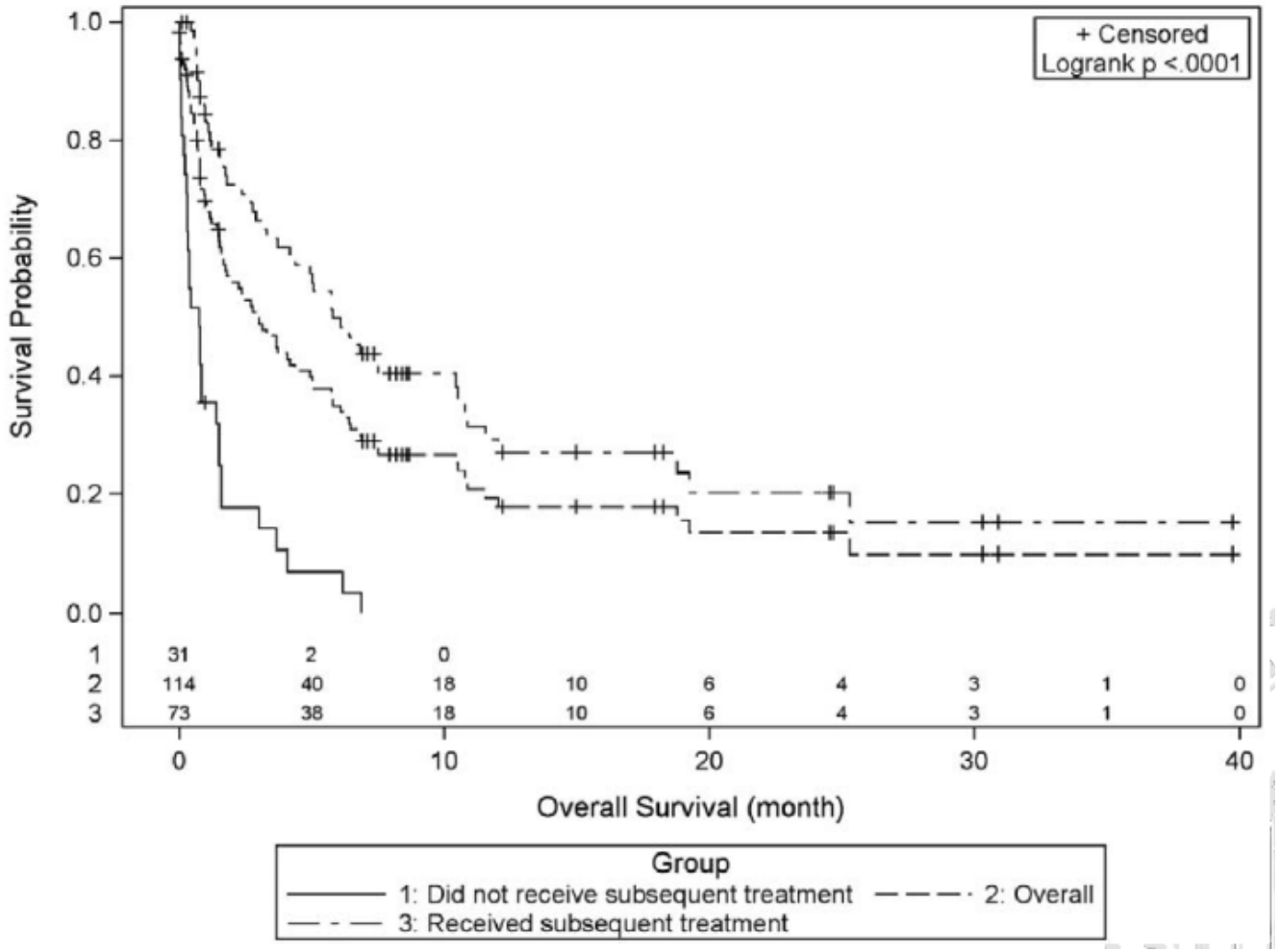
Clinical trials with Ibrutinib in R/R MCL

	Wang et al (2013b)	Cheah et al (2015)	Martin et al (2016)	Dreyling et al (2016)	Epperla et al (2017)
Study design	Prospective, phase 2 (2011–12)	Retrospective (2011–14)	Retrospective (NA)	Prospective, phase 3, (2012–13)	Retrospective (2013–2015)
Sites, n	18	1	15	21	8
Patients, n	111	78	114	280 (139 on Ibrut.)	97
Median prior treatments (range)	3 (1–5)	2 (1–8)	3 (0–10)	2 (1–9)	2 (1–8)
Median Ibrutinib (cycles/duration)	9 cycles	6-5 cycles	4-7 months	14-4 months	NA
CR	NA	30%	11%	NA	NA
ORR to ibrutinib	68%	NA	55%	72%	65%
Median DOR to ibrutinib	17-5 months	6 months	NA	NR	17 months
Ibrutinib discontinuation	58%	54%	NA	53%	50%
Progression (%)	45%	35%	100%	40%	25% PD, 10% SD
Primary resistance	**32%**	**10%**	**32%**	**28%**	**35%**
Acquired resistance	**NA**	**25%**	**54%**	**NA**	**17%**

How to treat MCL after BTKi failure ?



Martin et al., Blood 2016

ABSOLUTELY NO IDEA
But it almost certainly depends on when it is used
……Simon Rule

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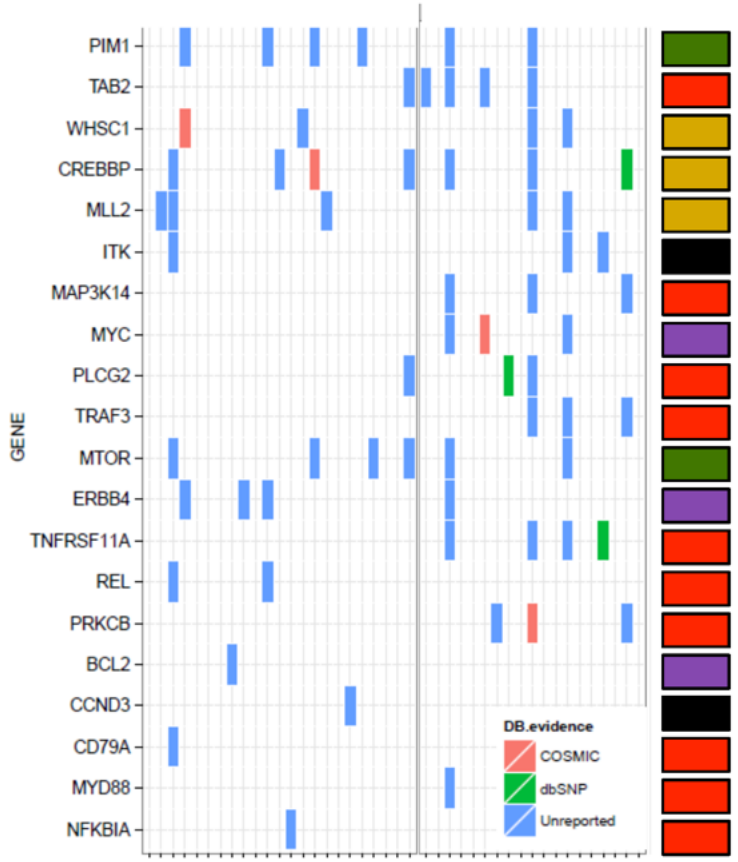
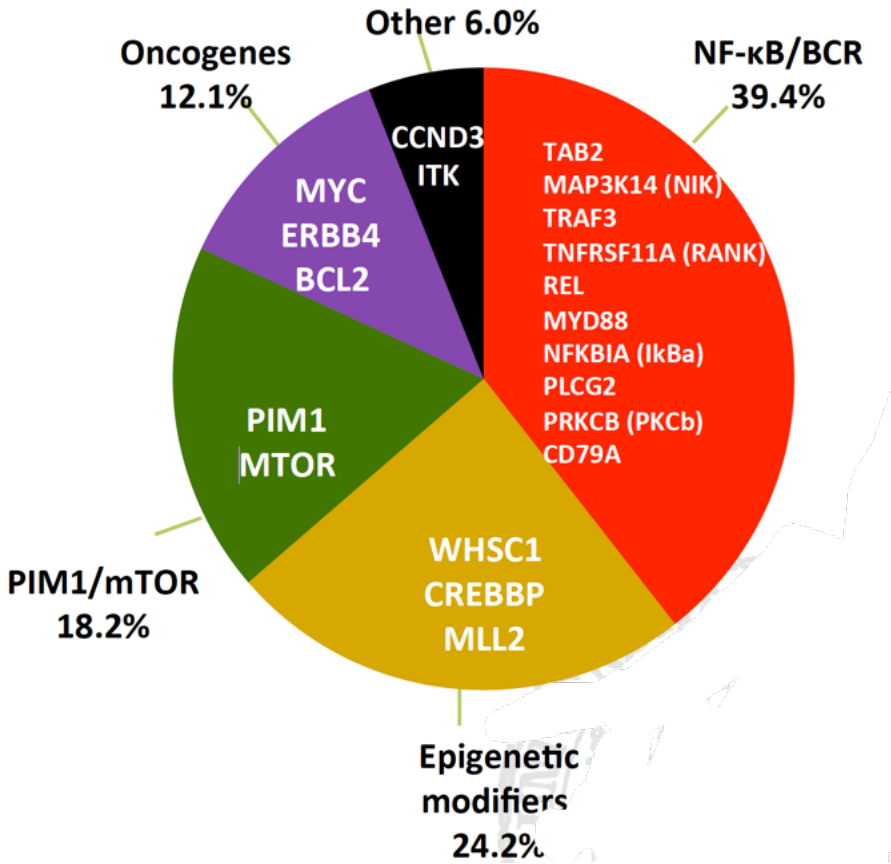
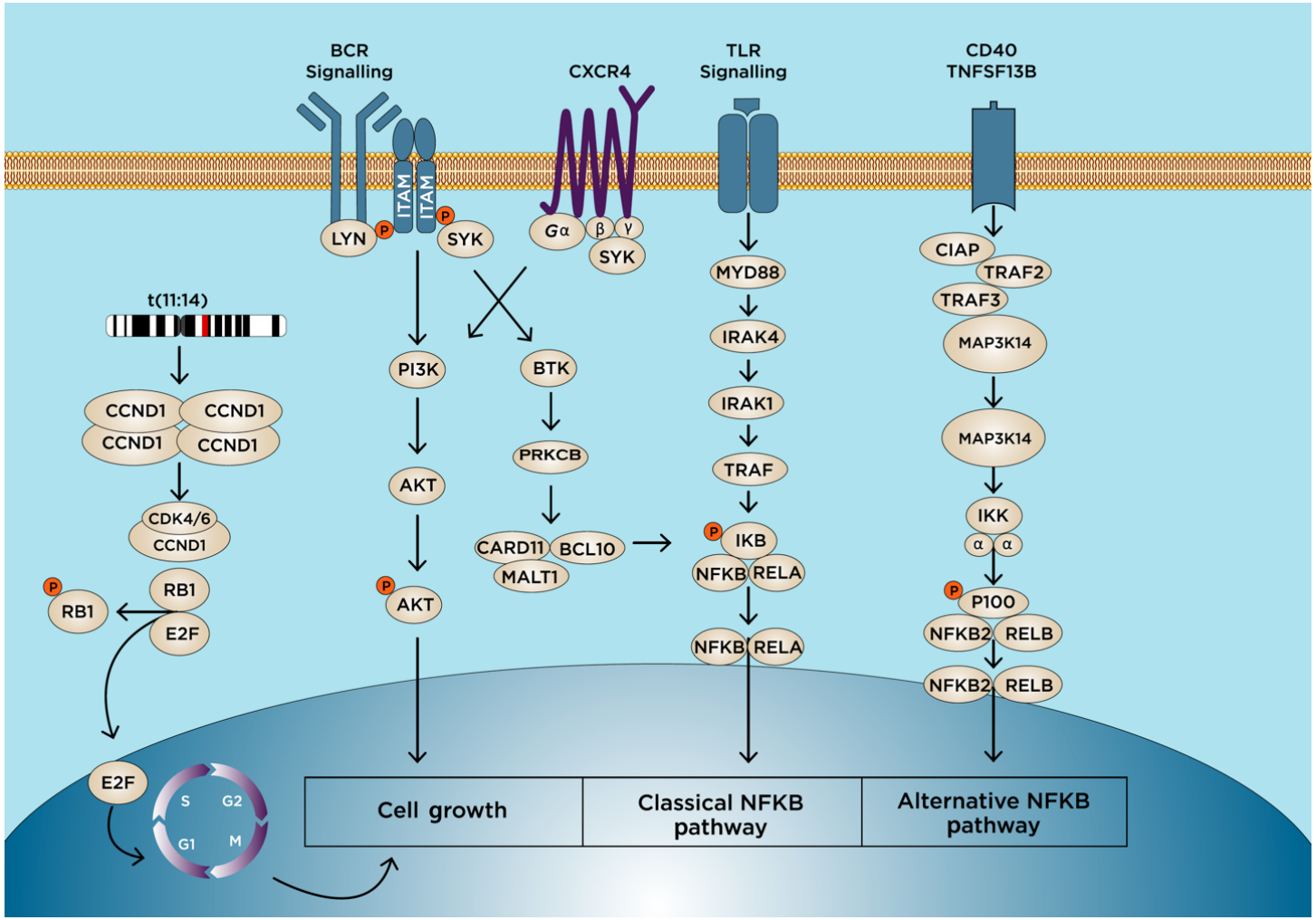
Mutational Analysis of Patients with Primary Resistance to Ibrutinib





Balasubramanian et al, ASH 2014

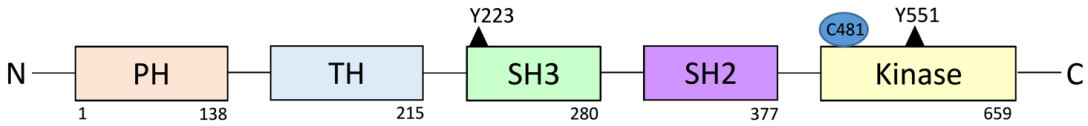
Mechanisms of primary Ibrutinib resistance



- sustained **distal BCR signaling** such as activation of PIK3 and protein kinase B (AKT) pathway,
- activation of the classical and alternative **NFkB pathways**,
- initiation of **cell cycle progression**

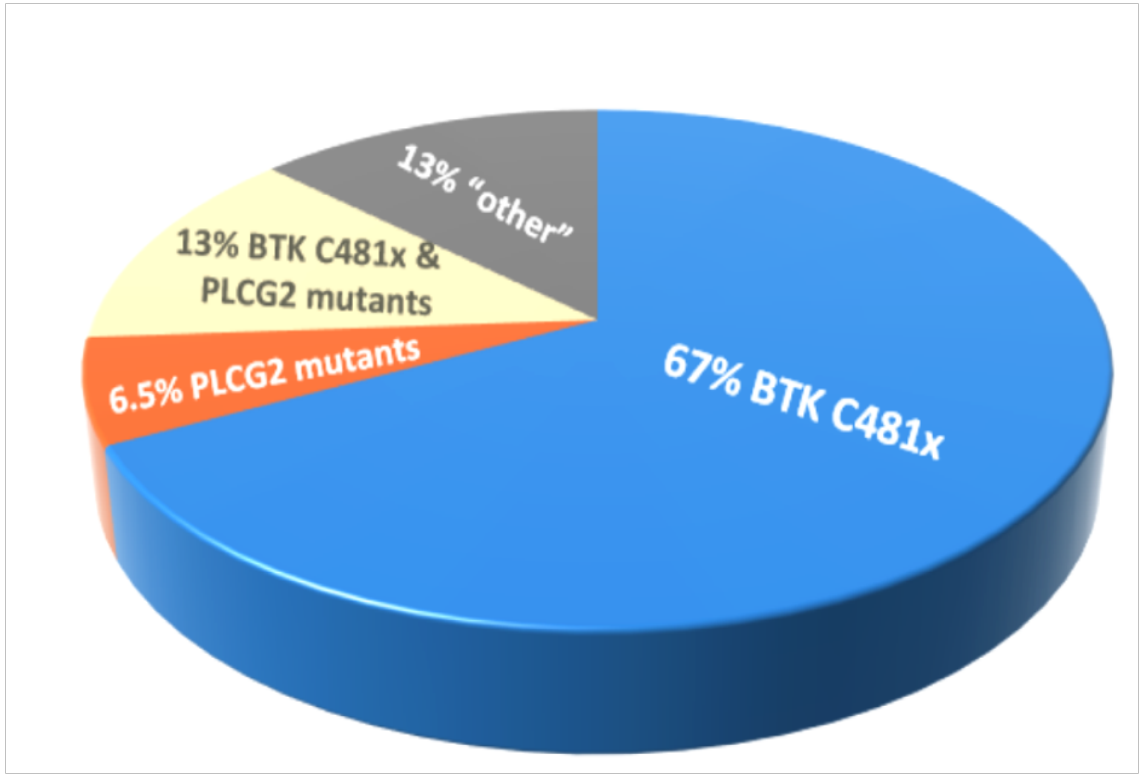
Hershkovitz-Rokah et al., BJH 2018

Mechanisms of acquired Ibrutinib resistance



Ineffective inhibition due to BTK mutation (10 – 30% of MCL patients)

Cysteine to Serine mutation of BTK binding site of Ibrutinib:



[1]Woyach et al. N Engl J Med. 2014; 370:2286–94, [2]Byrd et al. N Engl J Med. 2016; 374:323–32; [3]Woyach et al. J Clin Oncol. 2017; 35:1437–43; [4]Xu et al. Blood. 2017; 129:2519–25; [5]Hershkovitz-Rokah et al. Br J Haematol. 2018; 181:306–19

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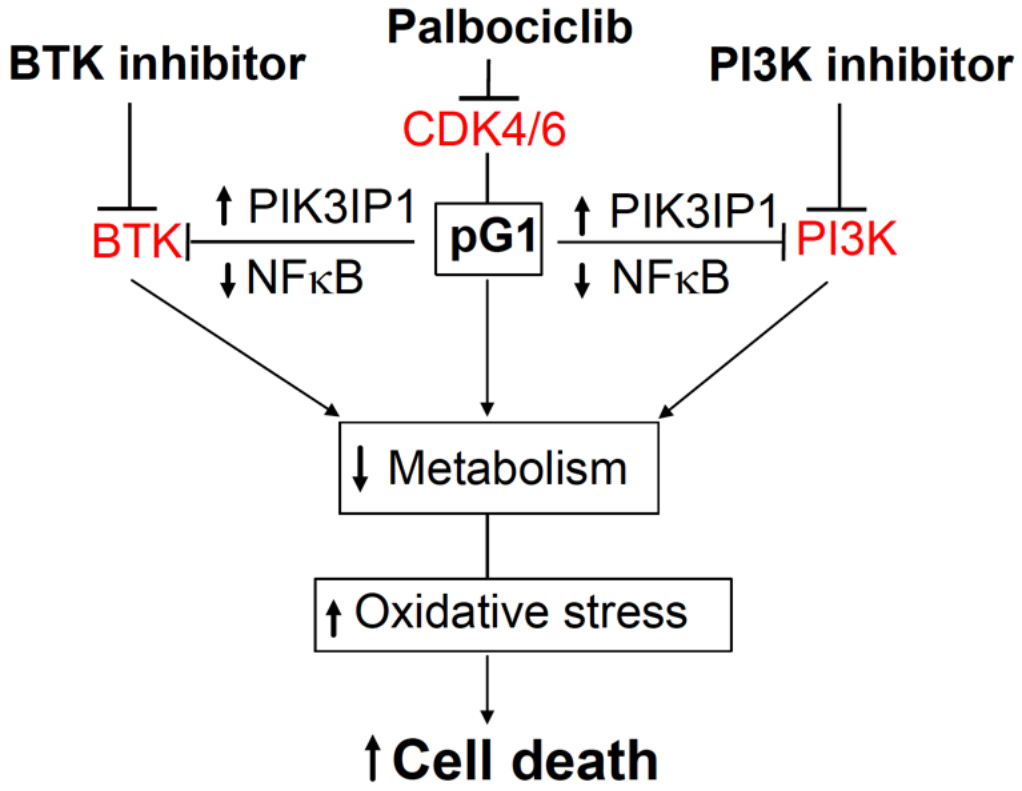
How to overcome Ibrutinib resistance ?

BTK inhibitor „combos” & „triplets”

Novel BTK inhibitors

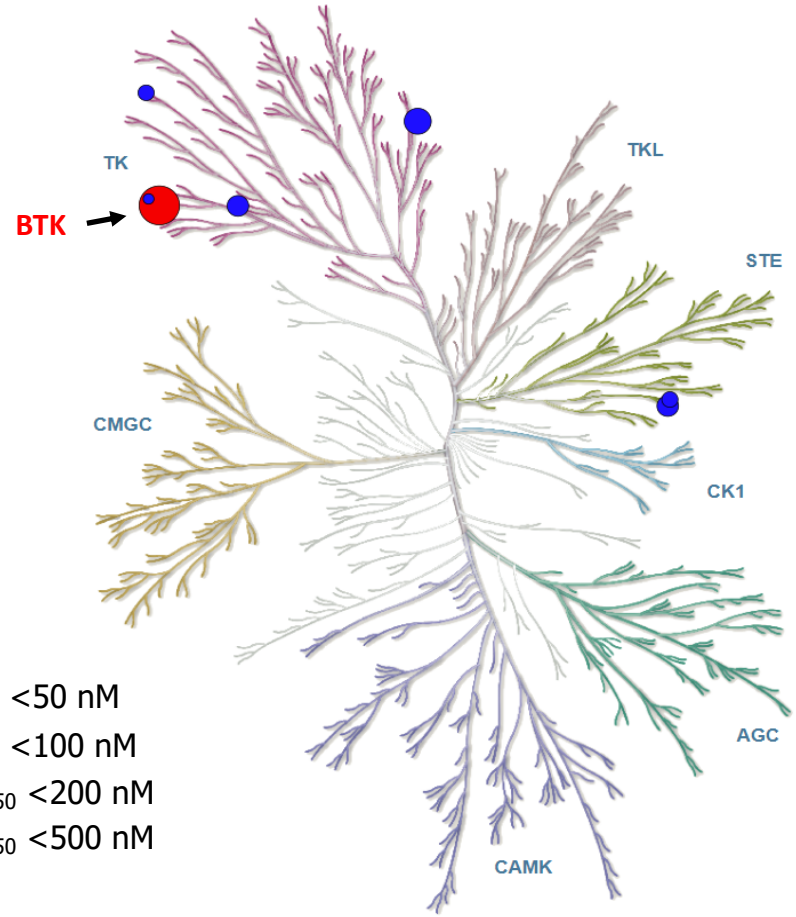
Loxo-305 – Loxo Oncology
ARQ 351 – ArQuele
Vecabrutinib – Sunesis
GDC583 - Genethech



IMIDS

Venetoclax

LOXO-305 potently and selectively inhibits BTK and BTK C481S

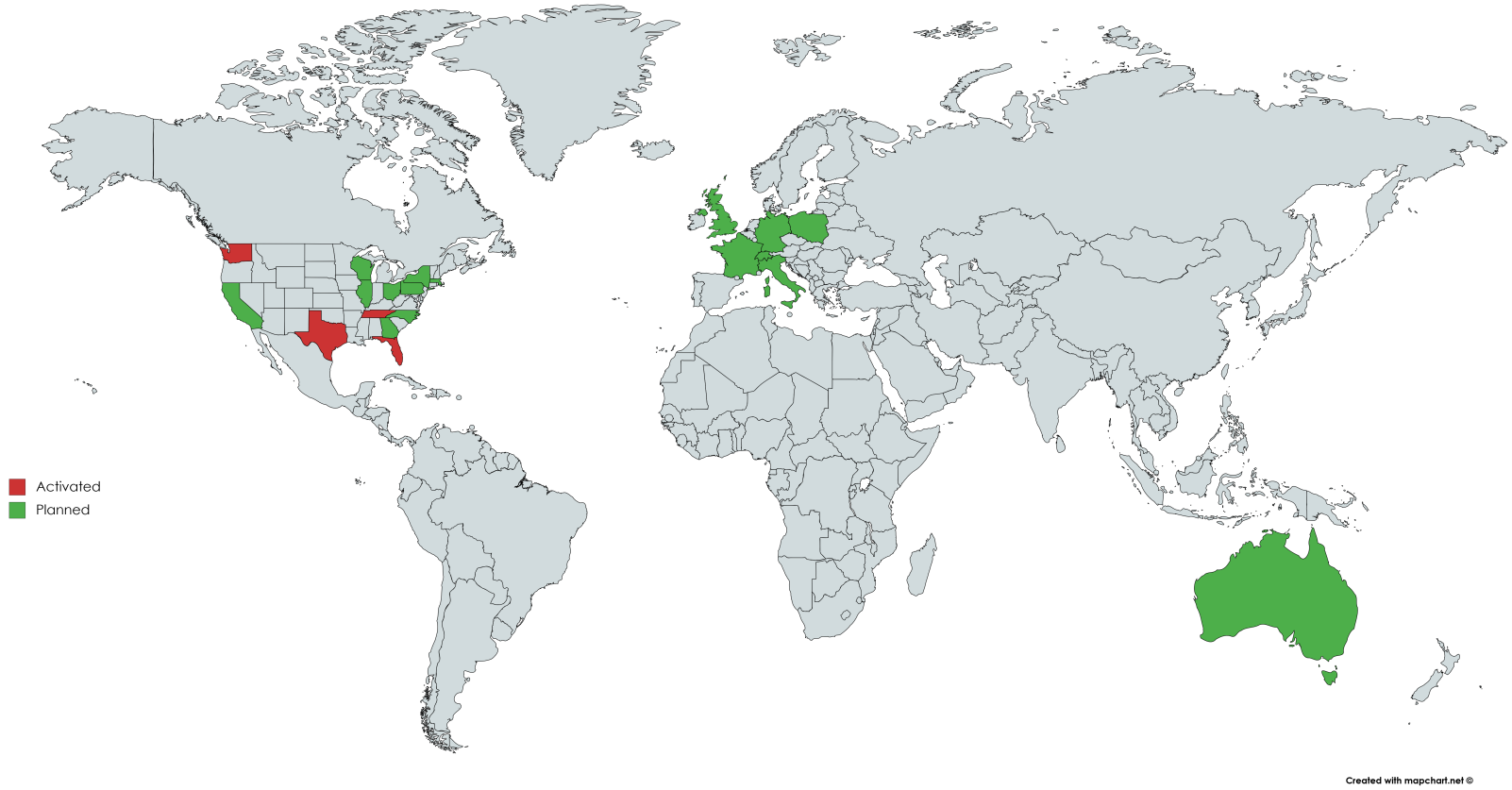


- IC_{50} <10 nM
- 10 nM < IC_{50} <50 nM
- 50 nM < IC_{50} <100 nM
- 100 nM < IC_{50} <200 nM
- 200 nM < IC_{50} <500 nM

LOXO-305 IC_{50}, [ATP] = K_M
BTK C481S = 1.42 nM
BTK = 3.15 nM

Kinase	Percent of control @1 µM LOXO-305, [ATP] = K_M (%)	IC_{50} [ATP] = K_M (nM)	Fold selectivity over BTK
BTK C481S	ND	1.42	0.5 X
BTK	1.8	3.15	1.0 X
ERBB4	2.6	13.3	4.2 X
BRK	10.3	54.3	17 X
MEK2	7.6	82.7	26 X
MEK1	12.2	147	47 X
YES1	38.6	157	50 X
TXK	19.6	209	66 X
BMX	70.2	1155	367 X
TEC	64.6	1234	392 X
BLK	72.8	4100	1302 X
EGFR	60.6	>1000	>317 X
ITK	103	>5000	>1587 X
SRC	90.5	>5000	>1587 X
JAK1	96.4	>30000	>9524 X
JAK2	94.5	ND	ND
JAK3	97	ND	ND

LOXO-BTK-18001 Phase 1/2 Study: current site selection



Targeted enrollment phase 1 and 2: ~190 patients

LOXO-BTK-18001 Study Key Eligibility Criteria

Key INCLUSION

- **CLL/SLL**, **iNHL** including **MCL and WM**
- Failed or intolerant to **≥ 2 prior lines** of therapy

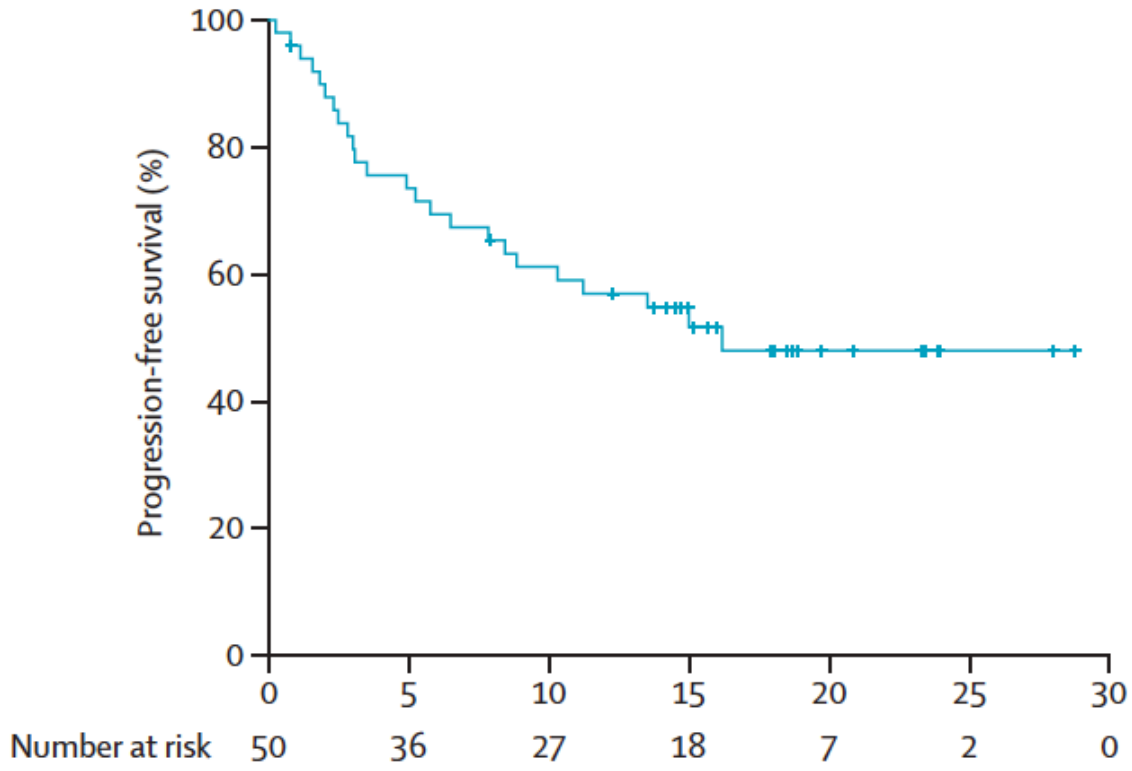
Key EXCLUSION

- Transformed lymphoma
- Anticoagulation therapy
- Allo/ Auto/ CAR-T therapy within 100 days of start
- CNS involvement
- HIV (+)

PHILEMON study in R/R MCL (N-50)
Ibrutynib + Lenalidomide + Rituximab *(≠)*

	All patients (n=50)
Age (years)	69 (45–85)
Sex	
Female	14 (28%)
Male	36 (72%)
ECOG performance status score 0–1	45 (90%)
MIPI score	
Low risk (<5·7)	8 (16%)
Intermediate risk (5·7–6·1)	15 (30%)
High risk (>6·2)	23 (46%)
Missing	4 (8%)
Ann Arbor stage IV disease	42 (84%)
Bone marrow involvement	34 (68%)
Refractory disease	8 (16%)
Number of previous therapies	2 (1–7)
Previous therapy	
Autologous stem-cell transplantation	21 (42%)
Allogeneic stem-cell transplantation	3 (6%)
Ibrutinib	4 (8%)
Lenalidomide	1 (2%)

Data are n (%) or median (range). ECOG=Eastern Cooperative Oncology Group. MIPI=Mantle Cell Lymphoma International Prognostic Index.



Jerkman et al., Lancet Haematol. 2018

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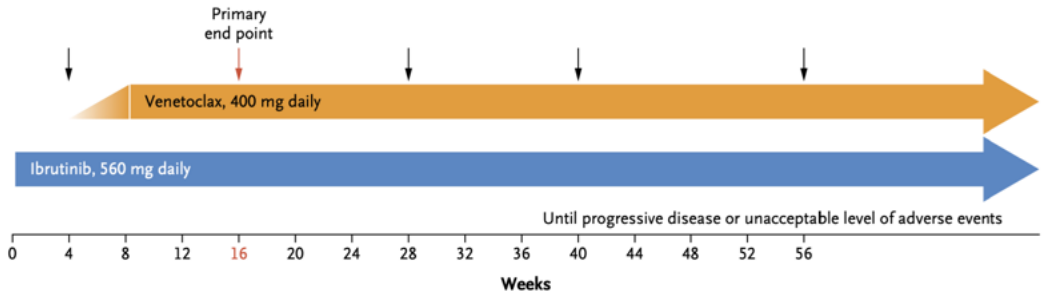
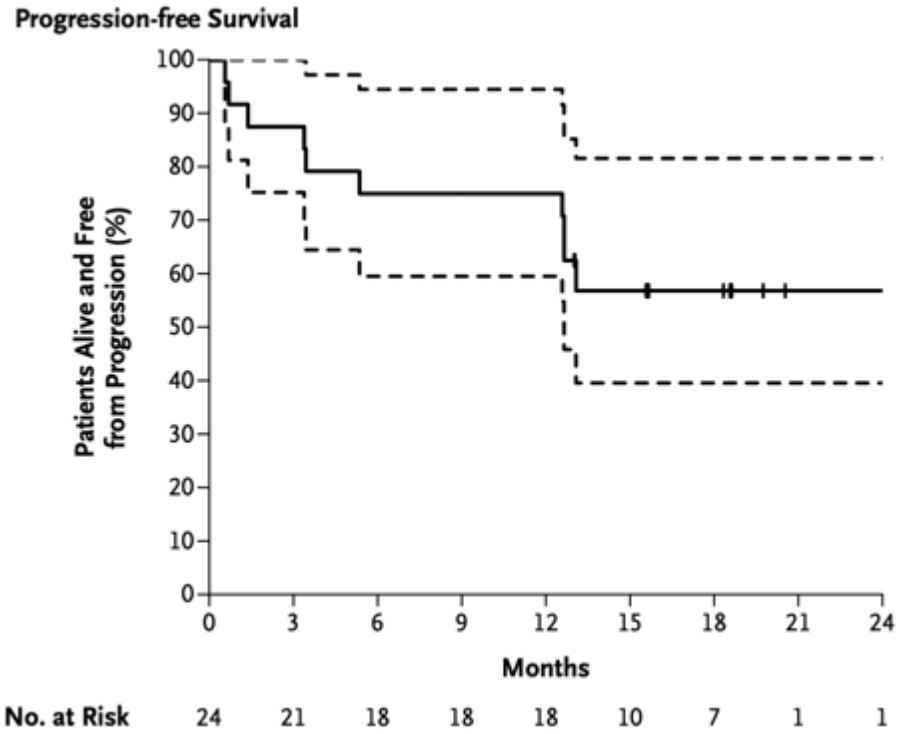
Ibrutinib + Venetoclax in R/R MCL *(≠)*

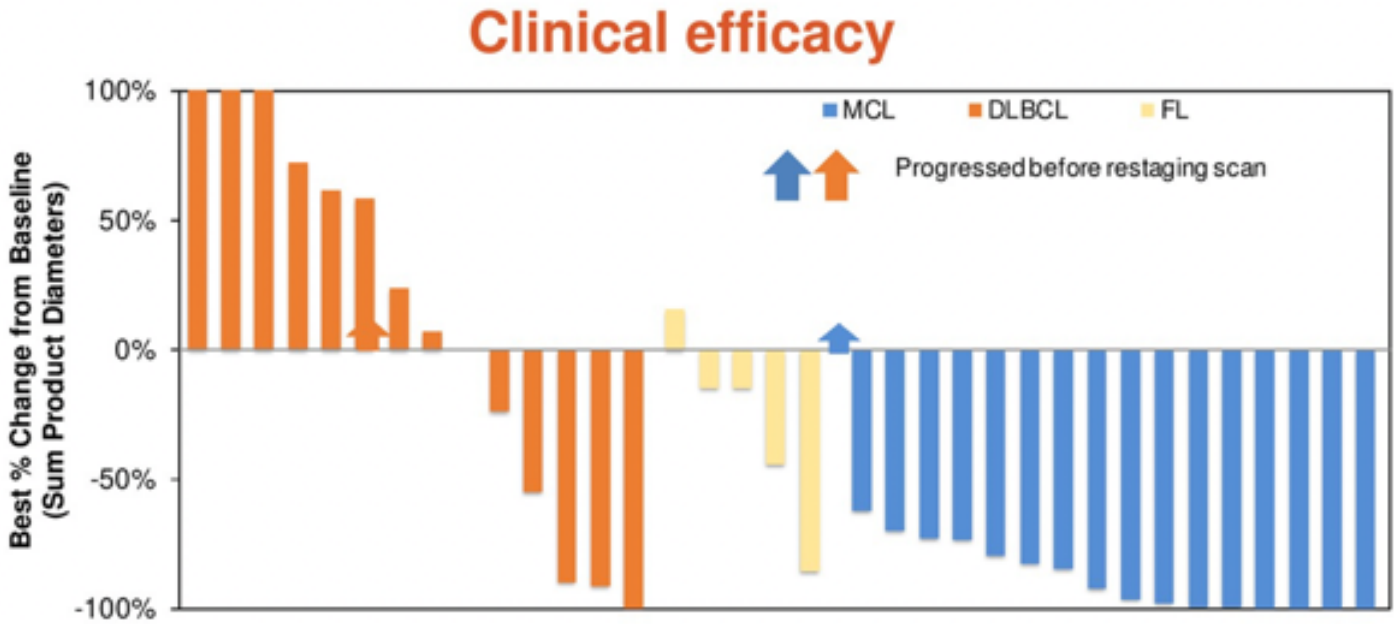


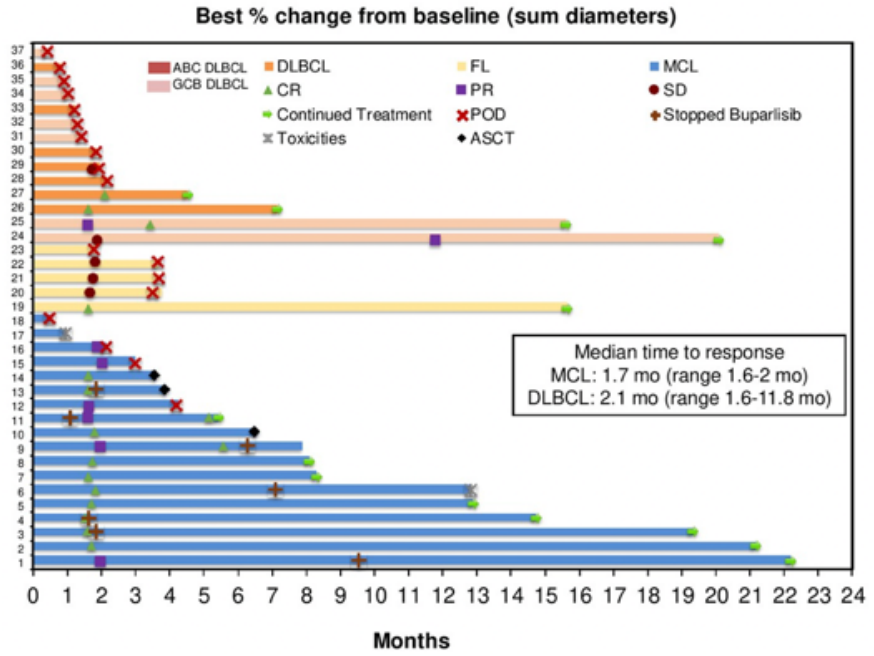
Ki-67 ≥30% — no./total no. (%)	9/21 (43)
TP53 status — no. (%)	
Mutated with deletion	4 (17)
Mutated without deletion	7 (29)
Deletion without mutation	1 (4)
NF-κB pathway mutations in *CARD11*, *BIRC3*, or *TRAF2* — no. (%)	6 (25)



Tam et al., NEJM 2018

Ibrutynib + Bupralisib in R/R B cel NHL *(≠)*



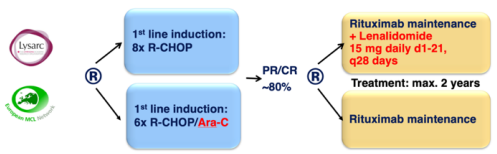


Batlevi et al., 2018

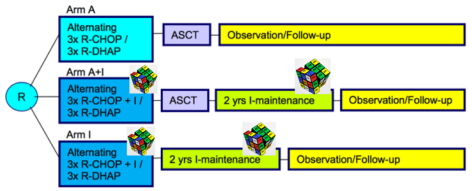
Badania kliniczne w Krakowie u chorych z MCL

Klinika Hematologii UJCM

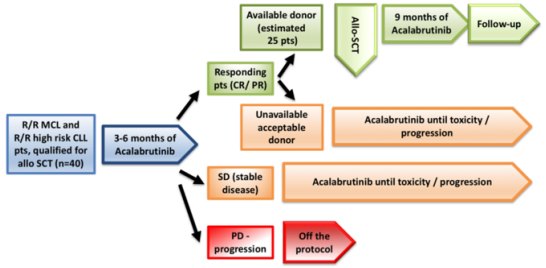
„Elderly study"



„Triangle" study



PLRG 12



Pratia-MCM

MCL

Rekrutacja otwarta

De novo		*Wznowa*	
ACERTA-106	Rituximab + ACP-196 + Venetoclax M.Majewska-Polak	**IMBRUVICA-1143**	Ibrutinib + Venetoclax / placebo A.Sawiec
ACERTA-308	ACP-196/placebo + Rituximab + Bendamustyna A.Macuda	**UNITY-205**	TGR-1202 / Ublituximab M.Gielarek
		CITADEL-205	tabletki INCB 50465-205 A.Macuda

Badanie z LOXO – w przygotowaniu

Polish Lymphoma Research Group

Podsumowanie

- Rokowanie chorych z MCL poprawia się
- Inhibitory kinazy Brutona, nieodwracalnie zmieniły standard leczenia MCL
- Optymalne skojarzenie inhibitorów BTK, leków immunomodulujących (IMID) i wenetoklaksu jest przdmiotem toczących się badań klinicznych.
- **Jedyną możliwością leczenia chorych z R/R MCL w sposób zgodny ze standardem, jest w Polsce, włączanie ich do toczących się badań klinicznych**

UNIWERSYTET JAGIELLOŃSKI
COLLEGIUM MEDICUM

MAŁOPOLSKA

Kraków

Szpital Uniwersytecki w Krakowie

VIII Myeloma and Lymphoma International Conference

(former „Complex treatment of plasma cell dyscrasia")

6-8 th September 2019, KRAKOW

VENUE: Jagiellonian University Medical College, Św. Anny 12 Str.