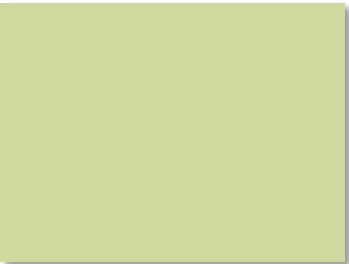
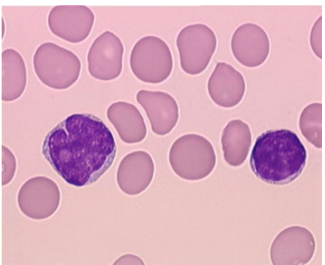
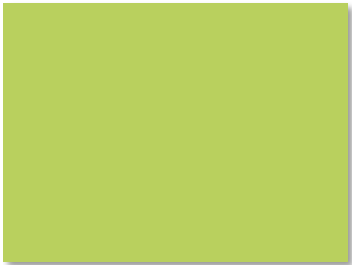


MANTLE CELL LYMPHOMA: CLINICAL CASE NO 1



Case report

Initial presentation - 2002

- **59 years, female**
- Stage IVa MCL
(nasopharynx, GI (gastric and colon),
bone marrow)

MC: First line– 2002

Optimal treatment

1. Bendamustine-Rituximab (BR)
2. R-CHOP
3. R-CHOP – autologous SCT
4. BR – autologous SCT
5. R-BAC

Case report

Initial presentation - 2002

- **59 years, female**

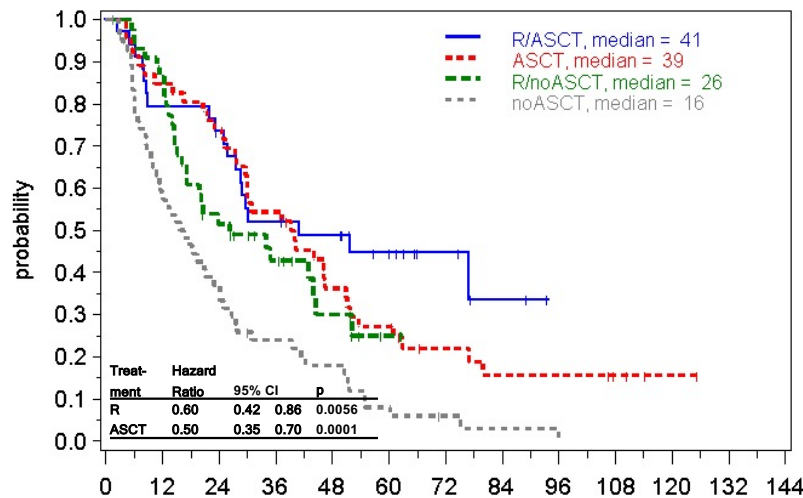
- Stage IVa MCL
(nasopharynx, GI (gastric and colon),
bone marrow)

- ➔ 6x R-CHOP - autologous transplantation

Metaanalysis : Autologous SCT and IFN

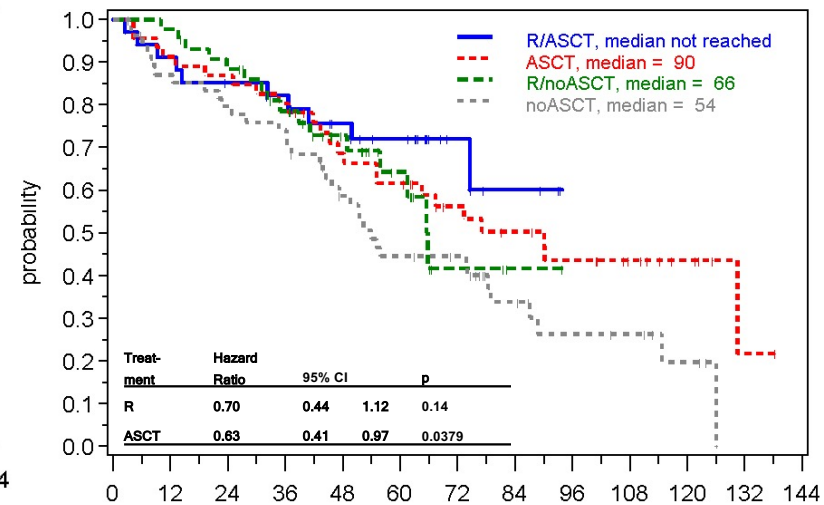
Survival rates

Remission duration



	numbers of patients at risk											
	months after end of induction											
R/ASCT	34	27	24	17	15	10	5	2	0			
ASCT	46	39	34	25	16	12	7	5	0	3	1	0
R/noASCT	44	38	21	14	7	2	0					
noASCT	56	31	20	12	9	4	2	1	0			

Overall survival



	numbers of patients at risk											
	months after end of induction											
R/ASCT	34	31	28	26	21	16	6	3	0			
ASCT	46	42	40	37	29	26	19	16	13	9	5	1
R/noASCT	44	43	38	31	20	11	3	1	0			
noASCT	56	47	43	40	29	22	20	11	7	6	3	0

Case report
First relapse - 2008

- **65 year, male**
- no B-symptoms
- leucocytes 11.000 /ml
- LDH elevated (255 U/l), Ki-67 20 - 30%
- stage IVa MCL
(nasopharynx, gastric and colon, abdominal bulk >5cm, bone marrow)

Risk profile ?

MC: First line– 2002

Risk profile (MIPI)

1. low
2. intermediate
3. high
4. n.a.

Case report
First relapse - 2008

- 65 year, male
- no B-symptoms
- leucocytes 11.000 /ml
- LDH elevated (255 U/l), Ki-67 20 - 30%

Table 7. Simplified prognostic index

Points	Age, y	ECOG	LDHULN	WBC, 10 ⁹ /L
0	<50	0-1	<0.67	< 6.700
1	50-59	—	0.67-0.99	6.700-9.999
2	60-69	2-4	1.000 -1.49	1.000-14.999
3	≥70	—	≥1.5000	≥15000

MC: First relapse – 2008

Optimal treatment

1. Cytarabine-Rituximab (R-HAD)
2. Bendamustine-Rituximab (BR)
3. Allogeneic transplantation
4. Bortezomib
5. Temsirolimus
6. other

young patient (≤ 65)

**elderly patient (>65)
First line treatment**

compromised patient

<p>dose-intensified immuno-chemotherapy (e.g. R-CHOP, high dose Ara-C) ⇒ Autologous SCT ⇒ Rituximab maintenance</p>	<p>conventional immuno-chemotherapy (e.g. R-CHOP, VR-CAP, BR) ↓ Rituximab maintenance</p>	<p>Best supportive care? R-Chlorambucil BR (dose-reduced) R-CVP</p>
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1. relapse

<p>immuno-chemotherapy (e.g. R-BAC, BR) or targeted approaches ↓ discuss: - allogeneic SCT</p>	<p>immuno-chemotherapy (e.g. BR, R-BAC) or targeted approaches ↓ discuss: - Rituximab maintenance - radioimmunotherapy</p>	<p>Immuno-chemotherapy (e.g. BR) or targeted approaches</p>
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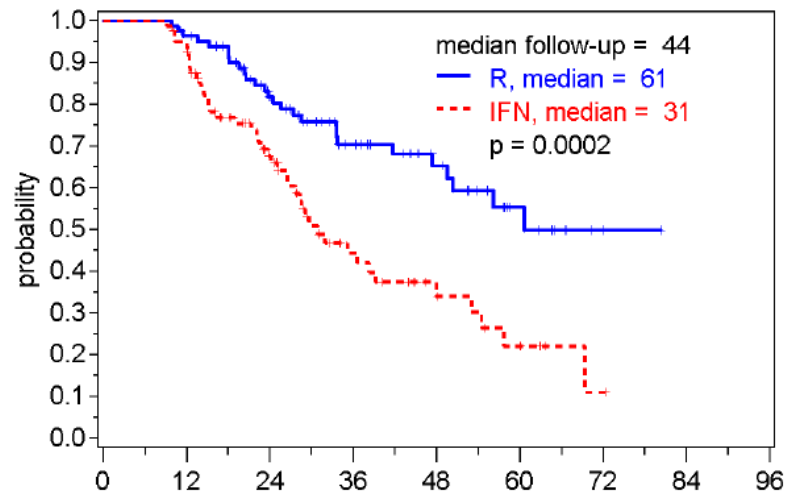
higher relapse

Targeted approaches: Ibrutinib, Lenalidomide, Temsirolimus, Bortezomib (preferable in combination)
Alternatively: repeat previous therapy (long remissions)

MCL Elderly

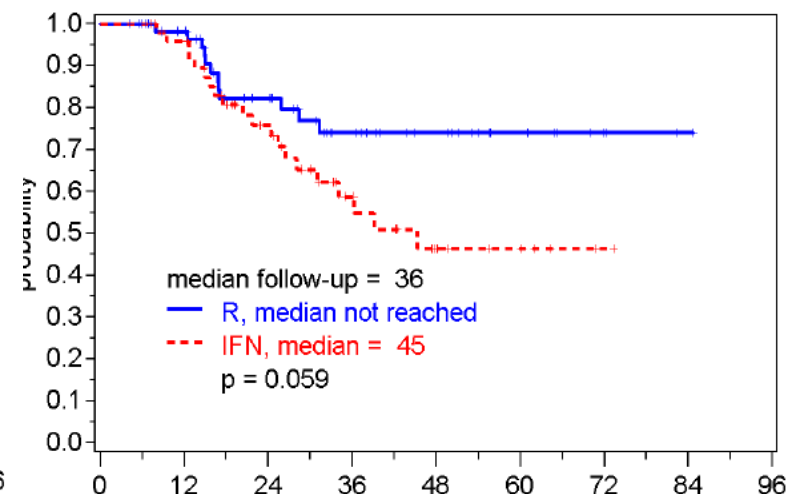
Response duration (death in remission censored)

After R-CHOP



	numbers at risk							
	0	12	24	36	48	60	72	84
R	82	78	56	36	23	10	1	0
IFN	81	75	41	19	10	4	1	0

After R-FC

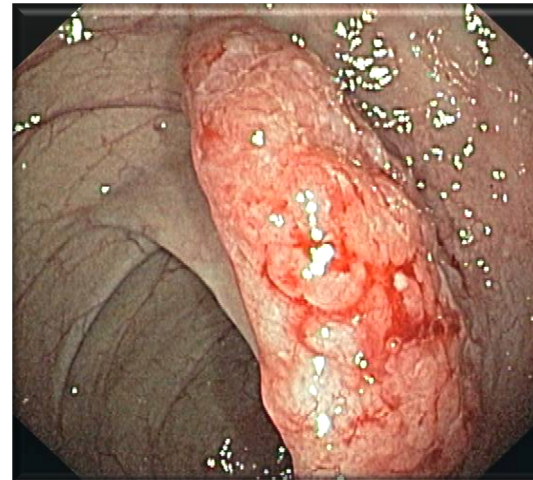


	numbers at risk									
	0	12	24	36	48	60	72	84	96	
R	61	53	35	22	15	8	3	1	0	
IFN	50	46	30	16	8	5	1	0	0	

Case report

after 3x R-FCM

- staging: partial remission
 - NMR head and neck
 - CT scan thorax/abdomen
 - gastroscopy
- but: progressive diarrhea!!!



coloscopy: MCL infiltration

Case report

Second relapse - 2009

- **67 years, female**
- no B-symptoms
- leucocytes 4.800 /ml
- LDH slightly elevated (355 U/l), Ki-67 30-40 %
- stage IVa MCL
(colon, abdominal lymph nodes, bone marrow)

Second relapse - 2009

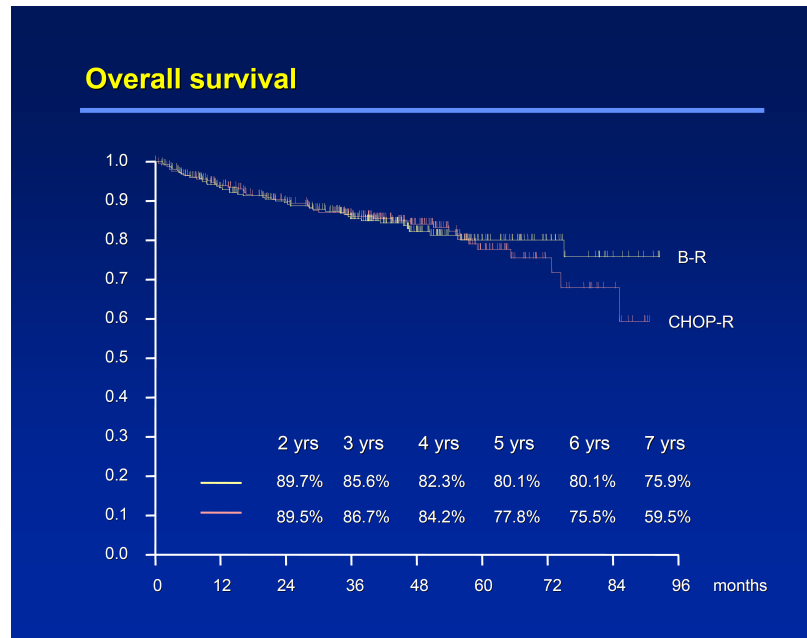
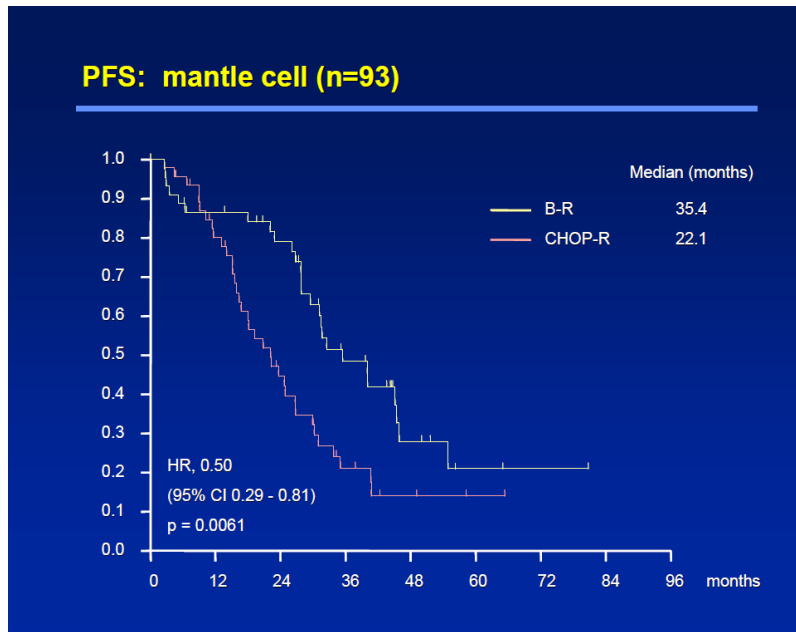
Optimal treatment



1. Gemcitabine-Oxaliplatin (GemOx)
2. Bendamustin-Rituximab (BR)
3. Bortezomib
4. Temsirolimus
5. Lenalidomide
6. Best supportive care

Immuno-chemotherapy in MCL

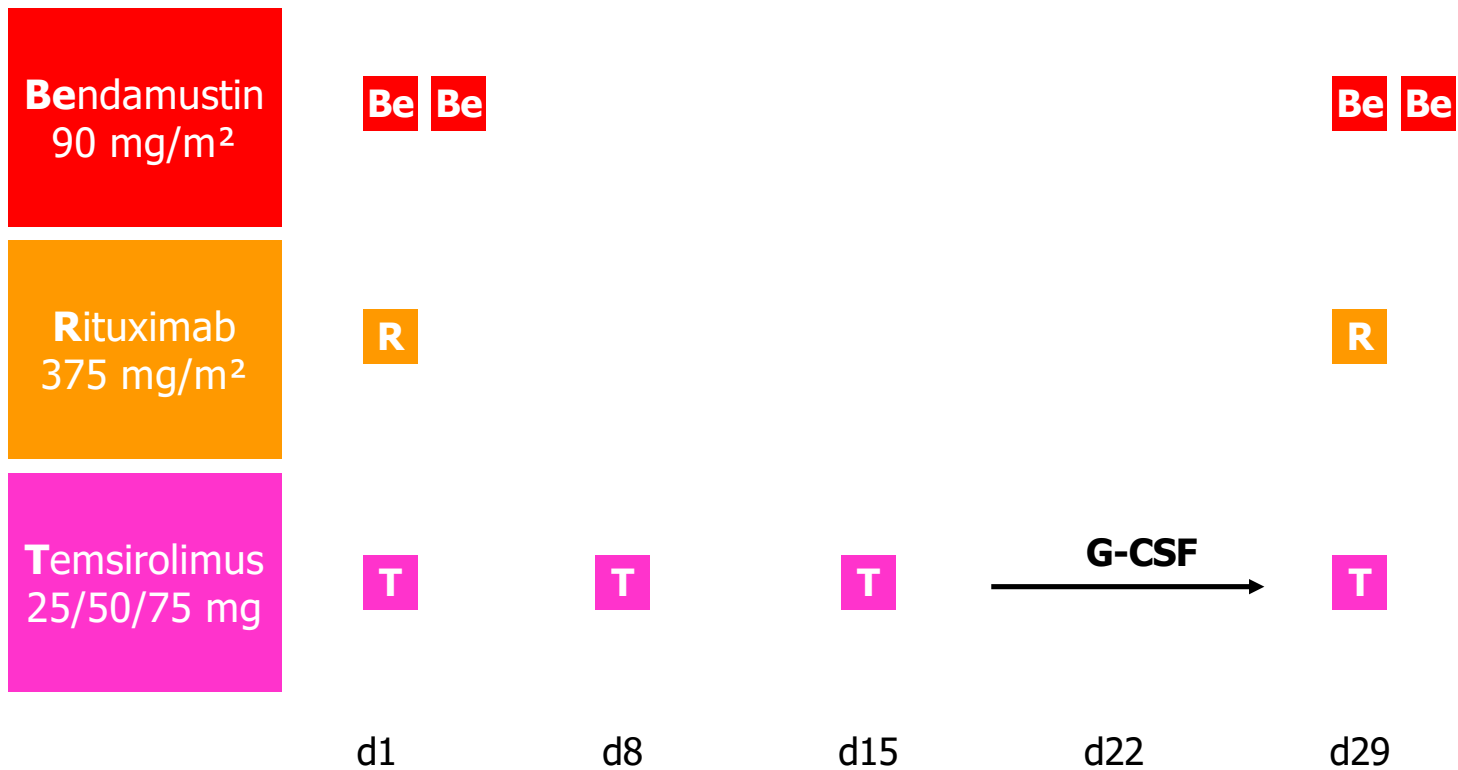
Progression-free survival



Rummel, Lancet 2013

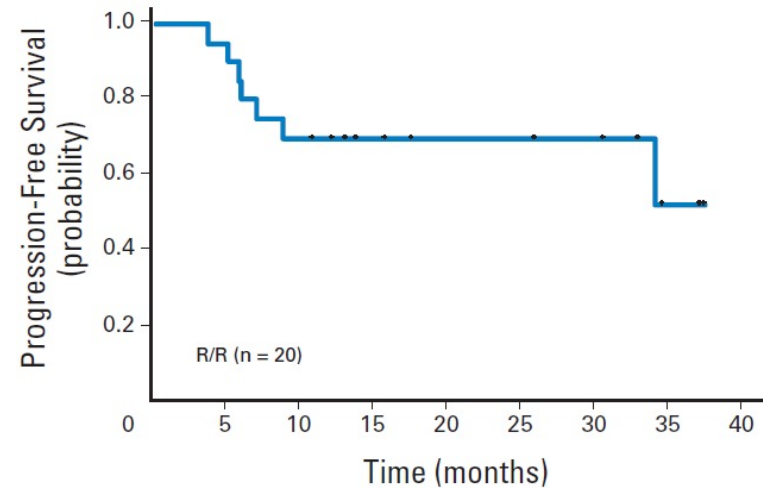
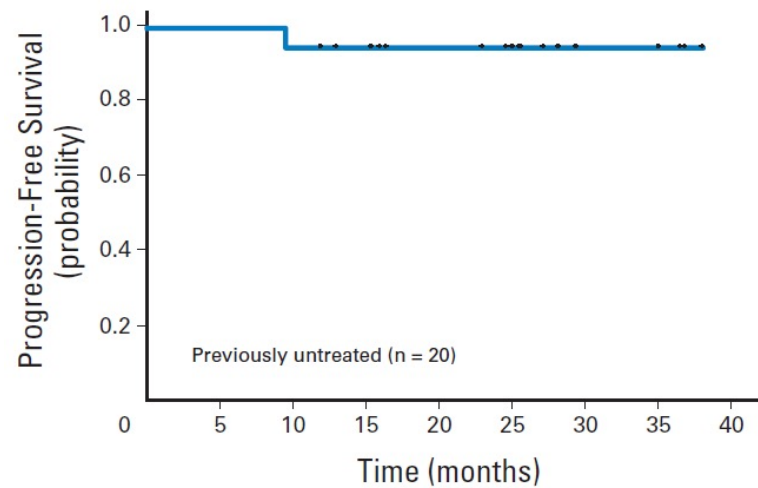


BeRT: Benda/Rituximab/Temsirolimus



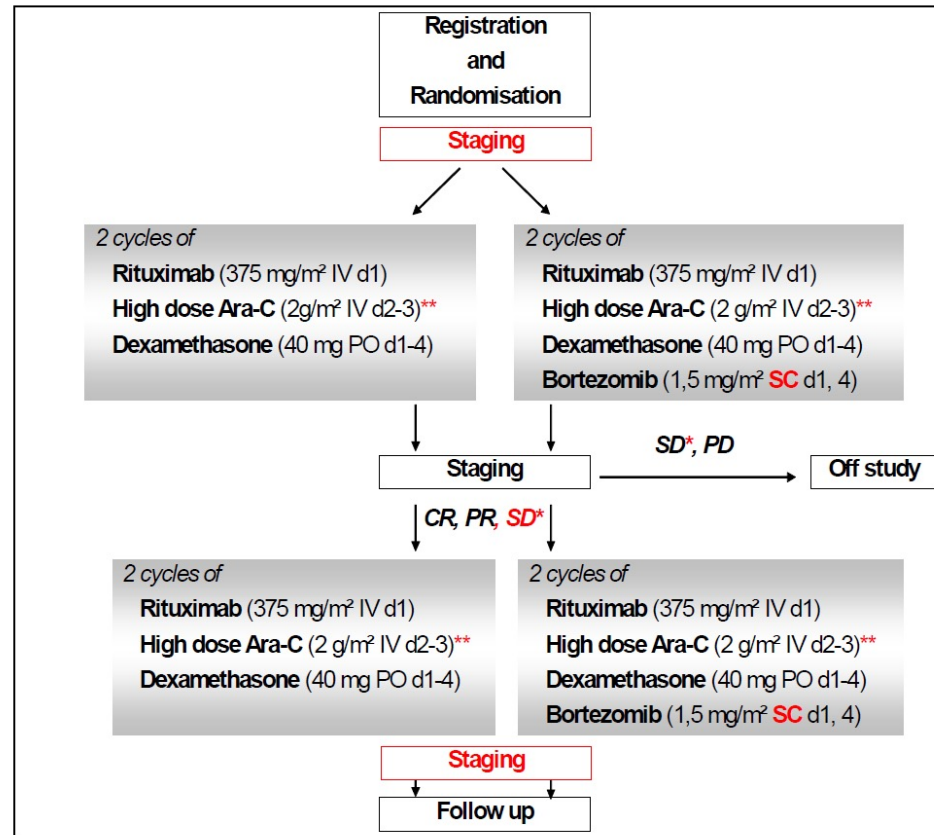
Mantle cell lymphoma R-BAC

Characteristic	All Patients (N = 40)		Previously Untreated Patients (n = 20)		R/R Patients (n = 20)	
	No.	%	No.	%	No.	%
Response rates						
OR	36	90	20	100	16	80
CR	33	83	19	95	14	70
PR	3	7	1	5	2	10
NR	3	7	0	0	3	15
PD	1	3	0	0	1	5



Visco, JCO 2013

R-HAD trial design



* In case of stable disease, patients may proceed with the treatment at the investigator's discretion.

** Patients >65 years or s/p myeloablative treatment: 1000 mg/m²

Case report

Third relapse - 2015

- **73 years, female**
- no B-symptoms
- leucocytes 3.800 /ml
- LDH slightly elevated (275 U/l), Ki-67 20 %
- stage IVa MCL
(colon, mediastinal lymph nodes)

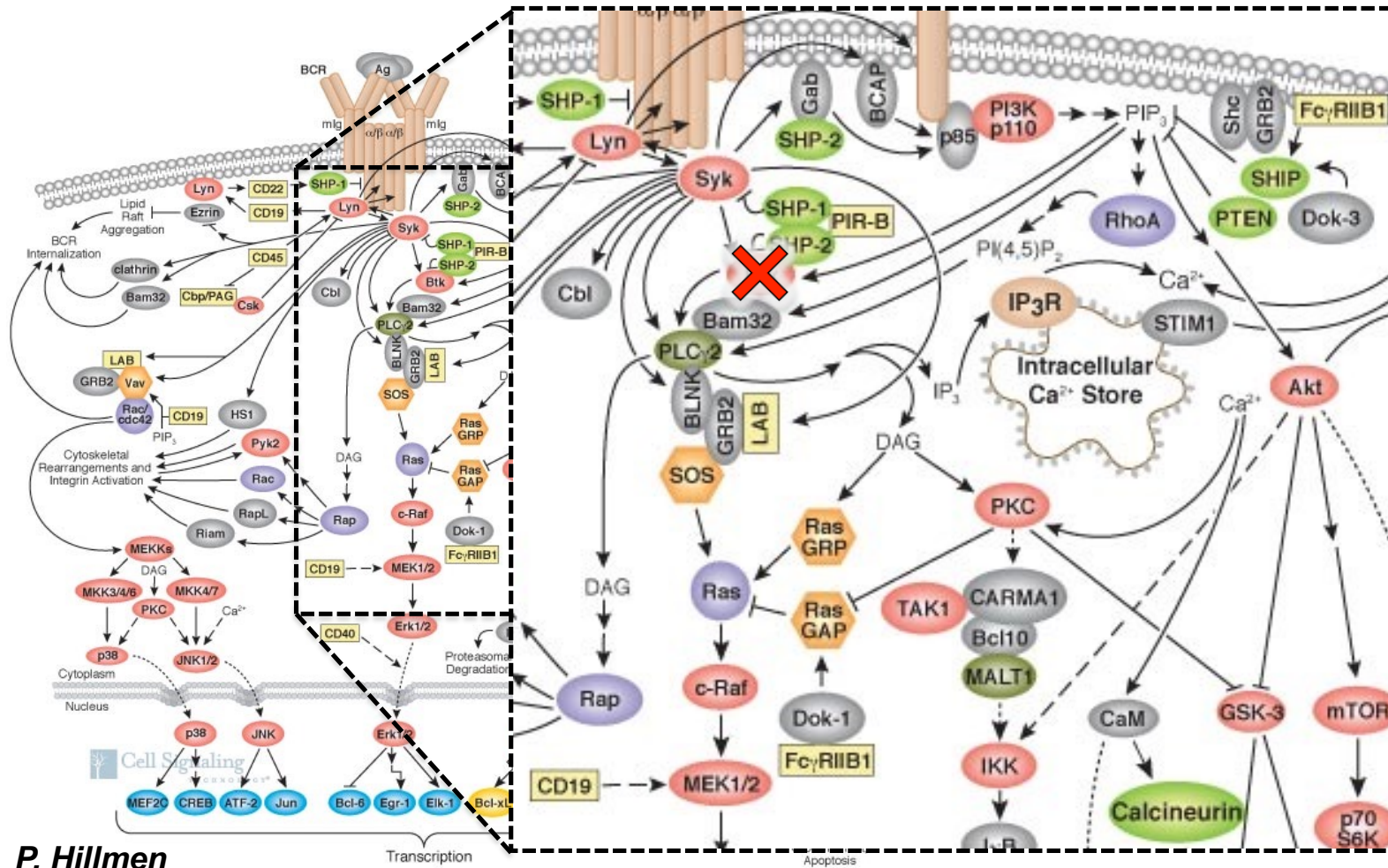
Third relapse - 2015

Optimal treatment



1. Bendamustin-Rituximab (BR)
2. Temsirolimus
3. Lenalidomide
4. Ibrutinib
5. Best supportive care

B cell receptor Targeting a critical pathway



Case report

Fourth relapse - 2020

- **78 years, female**
- no B-symptoms
- leucocytes 3.800 /ml
- LDH slightly elevated (275 U/l), Ki-67 20 %
- stage IVa MCL
(colon, mediastinal lymph nodes)

Fourth relapse - 2020

Optimal treatment



1. Bendamustin-Rituximab (BR)
2. Temsirolimus
3. Lenalidomide
4. Acalabrutinib
5. Best supportive care

Objective responses ABT-199 (Venetoclax)

