LEUKEMIA2020-2021

April 26-27, 2021

Coordinator: A.M. Carella
AIL President: S. Amadori

ASSOCIAZIONE ITALIANA CONTRO LE LEUCEMIE-LINFOMI E MIELOMA ONLUS

The standard of care in CLL: new guidelines

Paolo Ghia

fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

GITMO
GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

SIE - Società Italiana di Ematologia

ASSOCIAZIONE ITALIANA
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LEUKEMIA2020

Rome, Hotel NH Collection - Vittorio Veneto
September 24 - 25, 2020

Disclosures of PAOLO GHIA

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
AbbVie	X		X			X	
Adaptive BeiGene			X			X	
ArQule/MSD			X			X	
AstraZeneca	X		X			X	
Celgene/Juno /BMS			X			X	
Janssen	X		X			X	
Loxo/Lilly			X			X	
Sunesis	X		X			X	

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up☆

B. Eichhorst[1], T. Robak[2], E. Montserrat[3], P. Ghia[4], C. U. Niemann[5], A. P. Kater[6], M. Gregor[7], F. Cymbalista[8], C. Buske[9], P. Hillmen[10], M. Hallek[1,11] & U. Mey[12], on behalf of the ESMO Guidelines Committee*

[1]Department I Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Dusseldorf, University of Cologne, Cologne, Germany; [2]Department of Hematology, Medical University of Lodz, Copernicus Memorial Hospital, Lodz, Poland; [3]Institute of Hematology and Oncology, Department of Hematology, Hospital Clinic, University of Barcelona, Barcelona, Spain; [4]Strategic Research Program on CLL, Division of Experimental Oncology, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy; [5]Department of Hematology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; [6]Department of Hematology, Cancer Center Amsterdam, Lymphoma and Myeloma Center Amsterdam, LYMMCARE, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands; [7]Hematology, Luzerner Kantonsspital, Luzern, Switzerland; [8]Hematology Biology, Hôpital Avicenne, Assistance Publique Hopitaux de Paris, UMR U978 INSERM, Bobigny, France; [9]Institute of Experimental Cancer Research, Comprehensive Cancer Center, University Hospital of Ulm, Ulm, Germany; [10]Leeds Institute of Medical Research, University of Leeds, St James's University Hospital, Leeds, UK; [11]Center of Excellence on Cellular Stress Responses in Aging-Associated Diseases, University of Cologne, Cologne, Germany; [12]Department of Oncology and Haematology, Kantonsspital Graubuenden, Chur, Switzerland

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Editorial

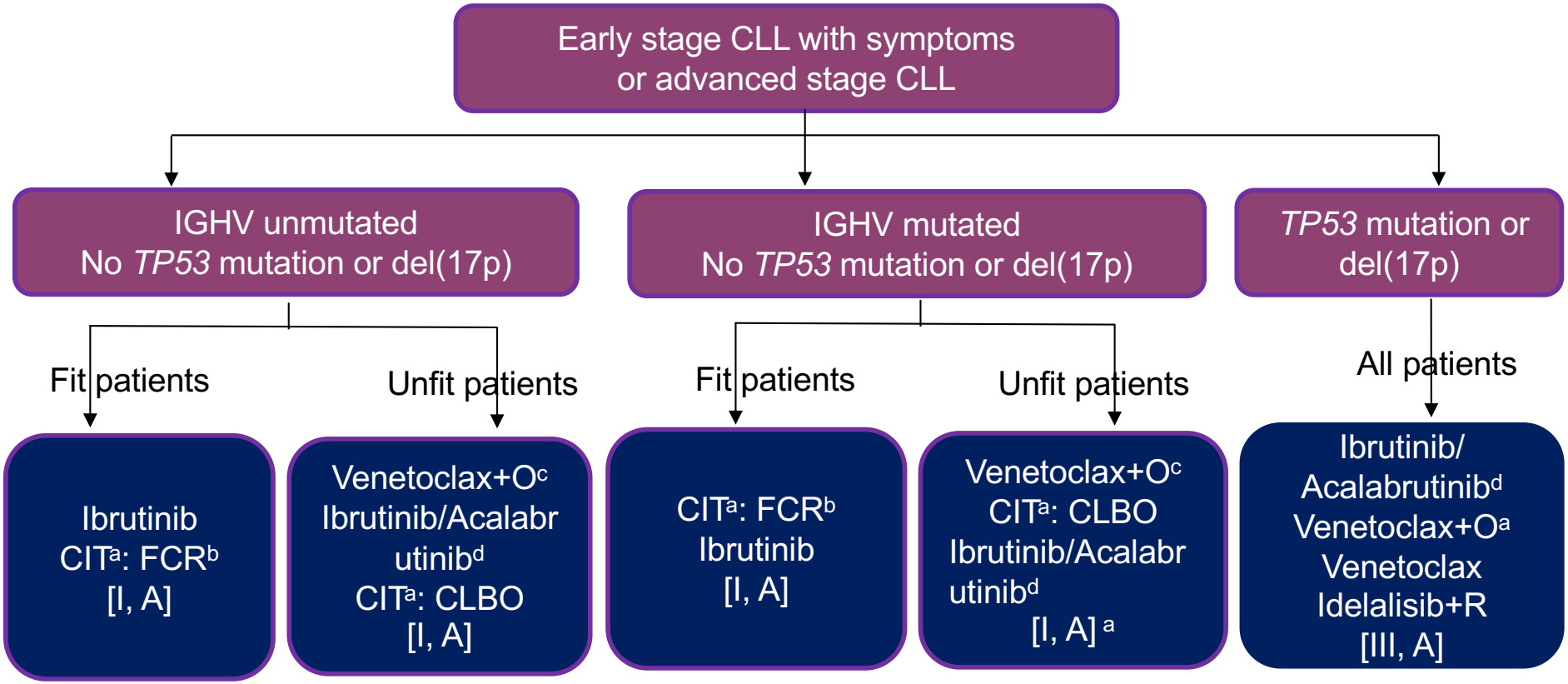
OPEN ACCESS

EHA Endorsement of ESMO Clinical Practice Guidelines for Diagnosis, Treatment, and Follow-up of Chronic Lymphocytic Leukemia

Barbara Eichhorst[1], Paolo Ghia[2,3], on behalf of the EHA Guidelines Committee

2021 ESMO guidelines for CLL treatment

1st Line Treatment



CIT: chemoimmunotherapy; Obin: obinutuzumab ; CLBO: Chlorambucil plus Obinutuzumab; R: rituximab; [a] Chemoimmunotherapy as alternative treatment only if no TP53 dysfunction and reasons against continuous treatment with ibrutinib or non-availability; [b] BR might be considered alternatively in patients above the age of 65 years; [c] If available; [d] if approved and available.

Eichhorst B et al, Ann Oncol 2021

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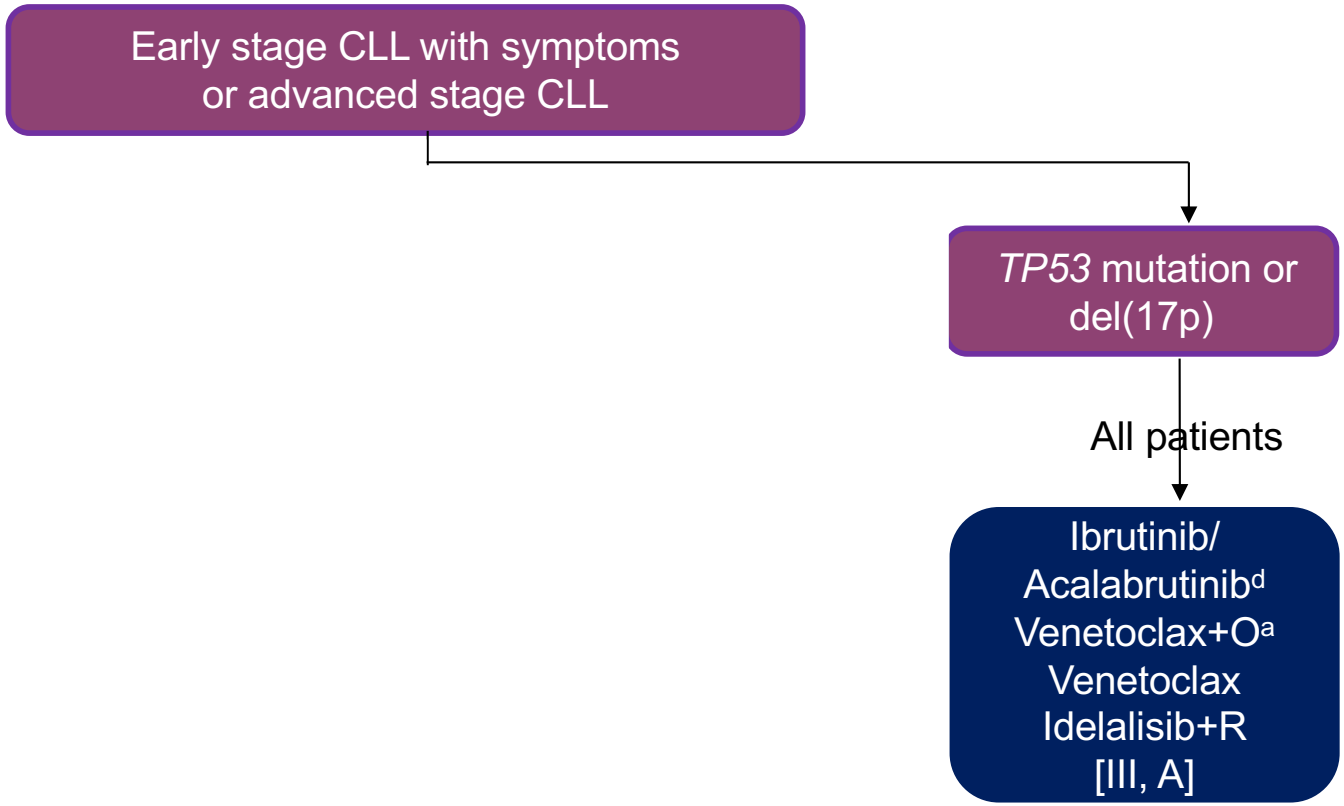

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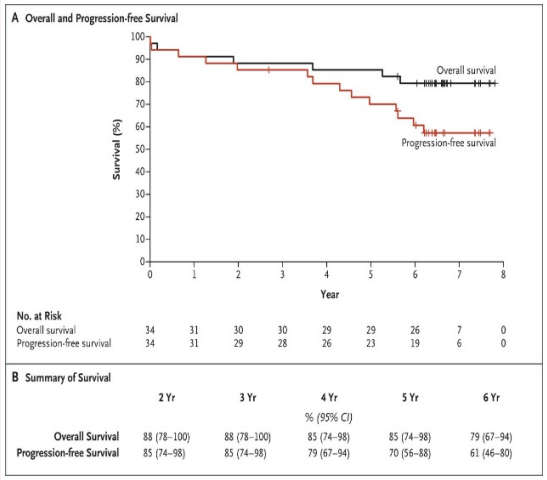
Eichhorst B et al, Ann Oncol 2021

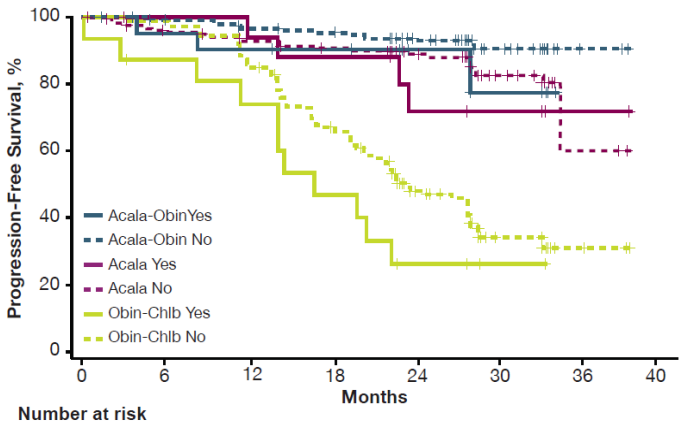
Novel therapies effective on CLL with *TP53* aberrations

PFS by *TP53* status

NIH Phase 2 study
Ibrutinib in *TP53*-aberrant patients



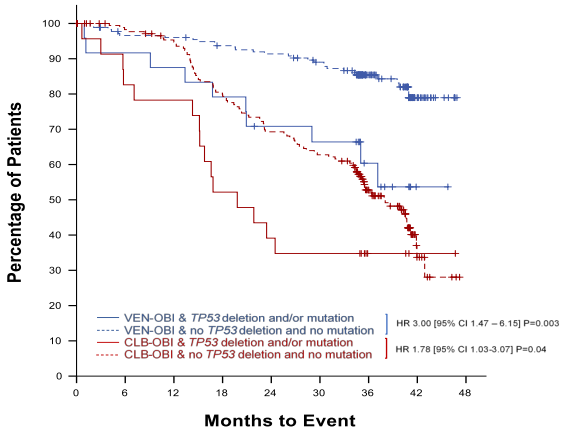
ELEVATE TN (IRC)
Acalabrutinib ± obinutuzumab versus chlorambucil + obinutuzumab



Number at risk

Yes	21	20	19	18	11	4	0
No	158	150	144	141	98	42	4
Yes	19	17	16	15	9	6	1
No	160	144	137	133	94	37	3
Yes	17	13	11	7	3	1	0
No	160	144	125	95	43	12	3

CLL14
Venetoclax + obinutuzumab versus chlorambucil + obinutuzumab



Ahn IE et al. N Engl J Med 2020; Sharman JP et al, Lancet 2020; Fischer et al., N Engl J Med 2019

TP53 Network

Testing for *TP53* aberrations is key to avoid using CIT in patients carrying *TP53* mutations or deletions

- **Eric promotes the adoption of appropriate diagnostic techniques to ensure reliable and comparable results by providing a service of**

Laboratory Certification

APPLY TODAY!

- **The process is for free**
- **Every lab is welcome to apply**
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ERIC
european research initiative on CLL

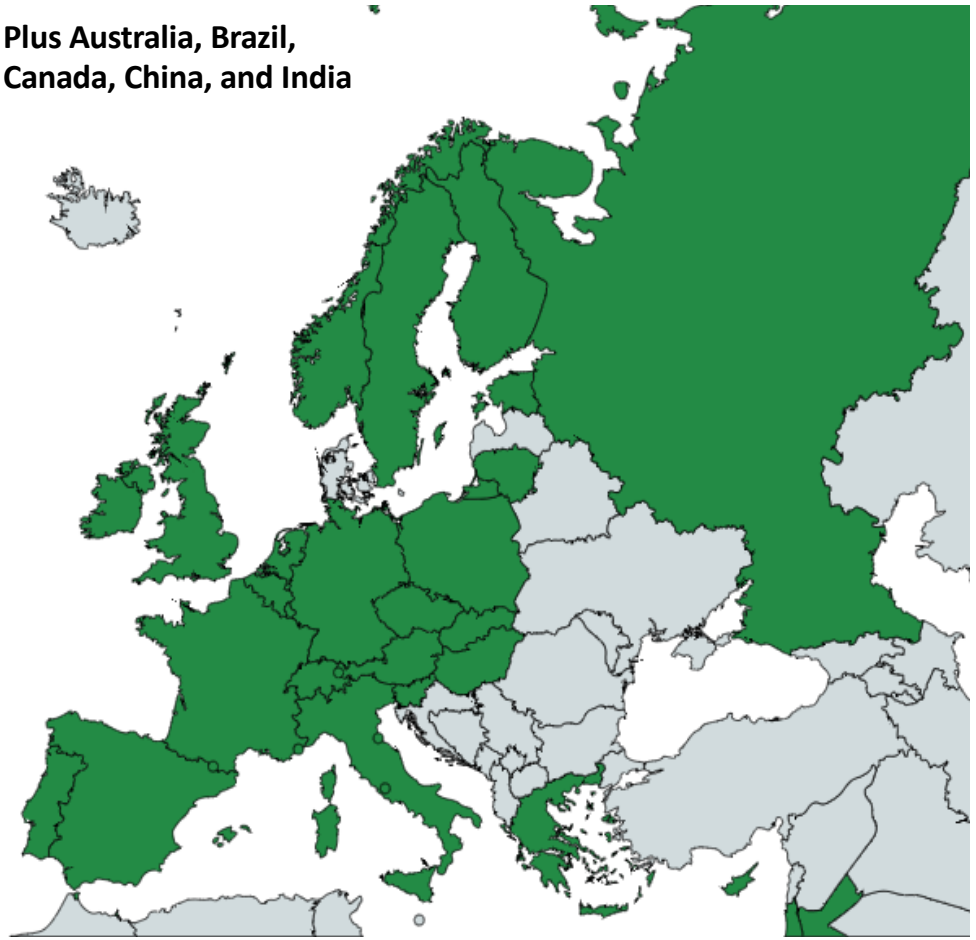
202 Certified Centres from 36 countries

11 Reference Centres

3 Certifying Centres

9 TP53 Certification Rounds completed

Plus Australia, Brazil, Canada, China, and India



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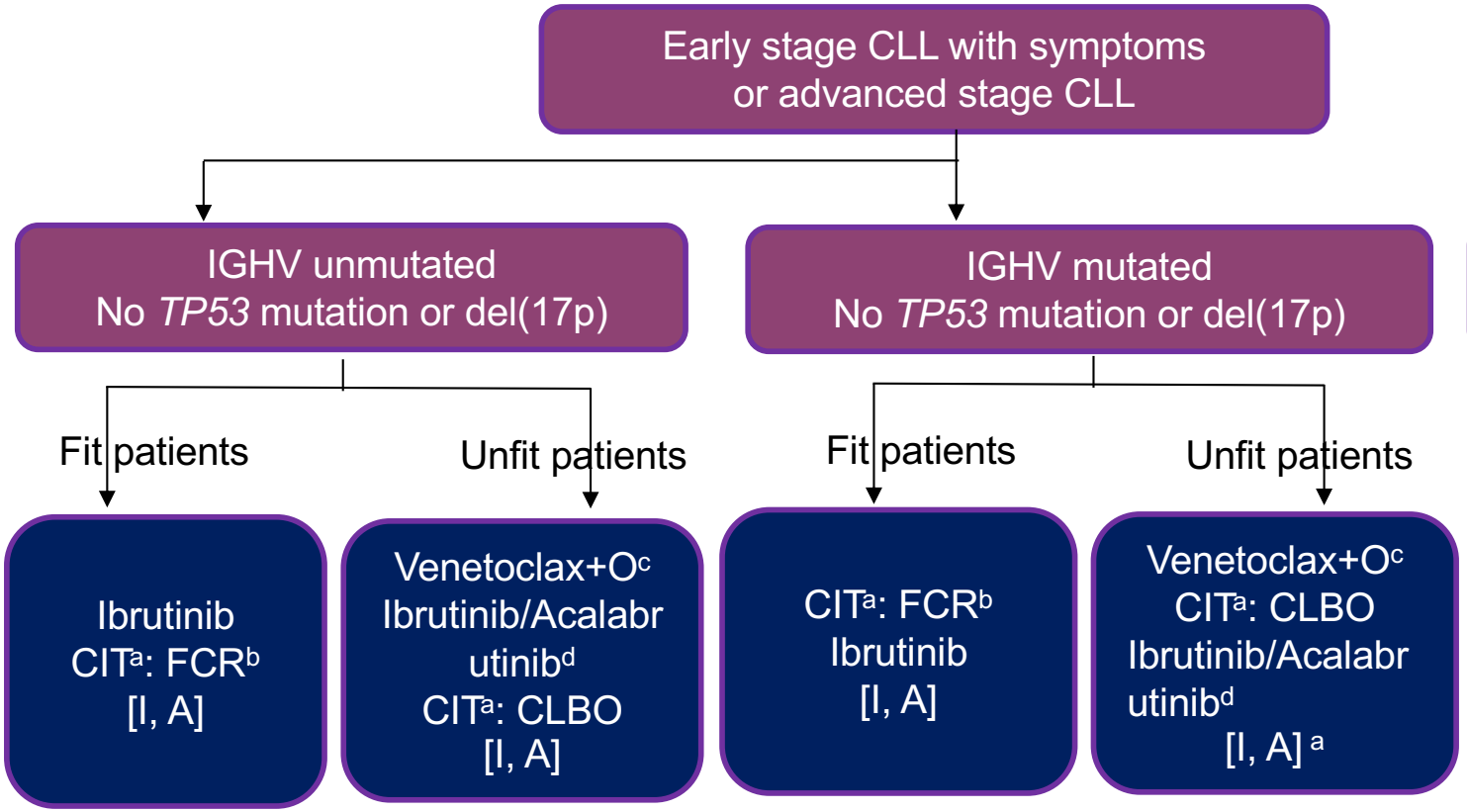

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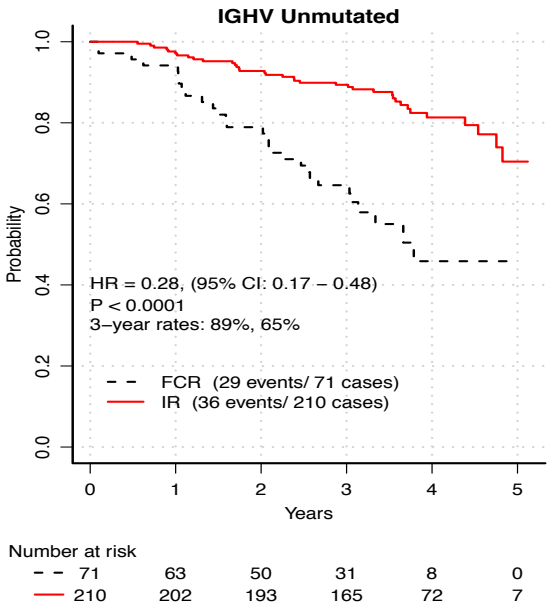
Eichhorst B et al, Ann Oncol 2021

Novel therapies effective on CLL with unmutated IGHV

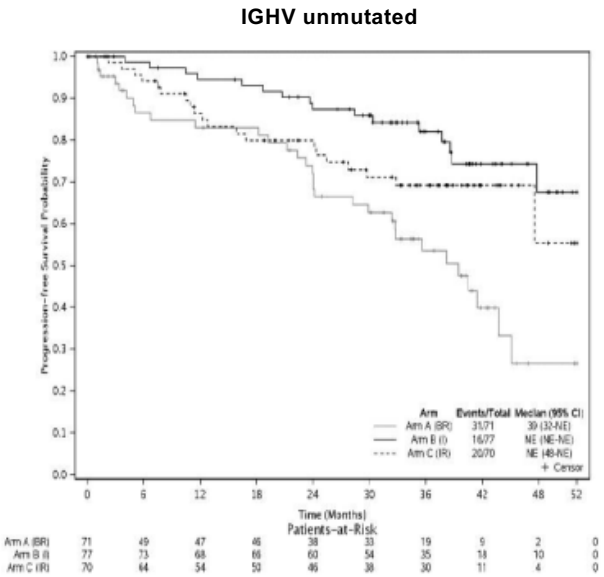
Fit and unfit patients

ECOG-1912:
Ibrutinib + rituximab versus
Fludarabine, Cyclophosphanide, Rituximab



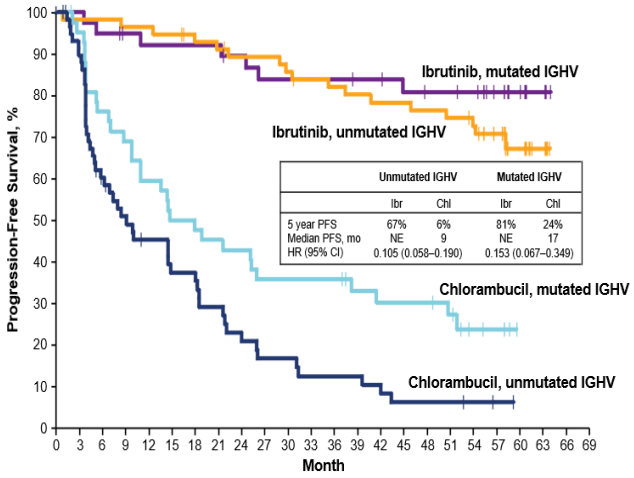
Shanafelt et al., NEJM 2019

Alliance 041202:
Ibrutinib +/- rituximab versus
Bendamustine + rituximab



Woyach et al., N Engl J Med 2018; 379:2517-2528

Resonate 2
Ibrutinib versus
chlorambucil



Burger J. et al, Leukemia 2020

Novel therapies effective on CLL with mutated IGHV

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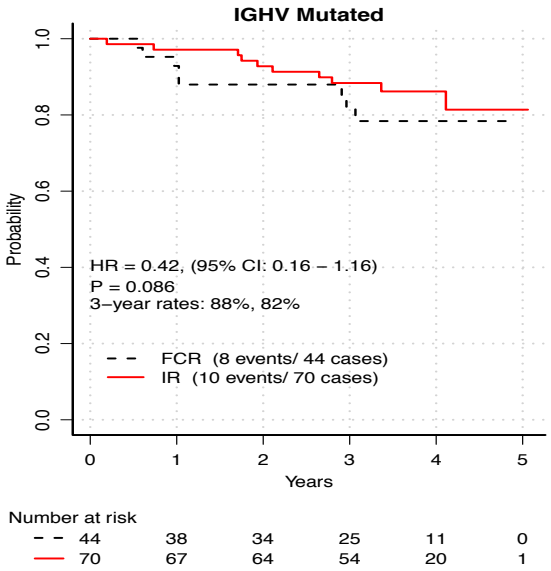

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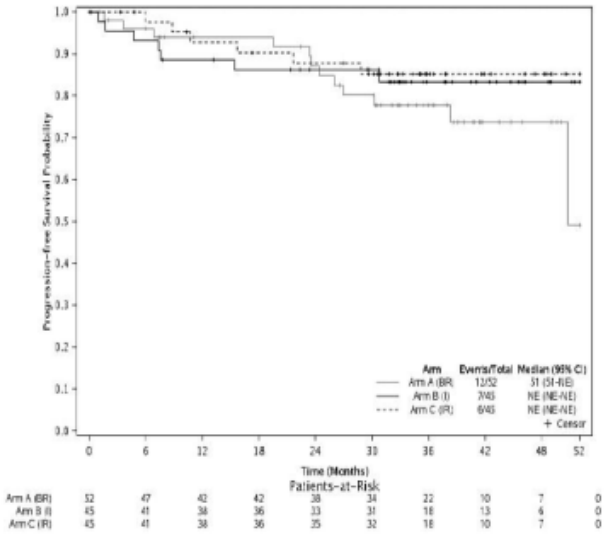

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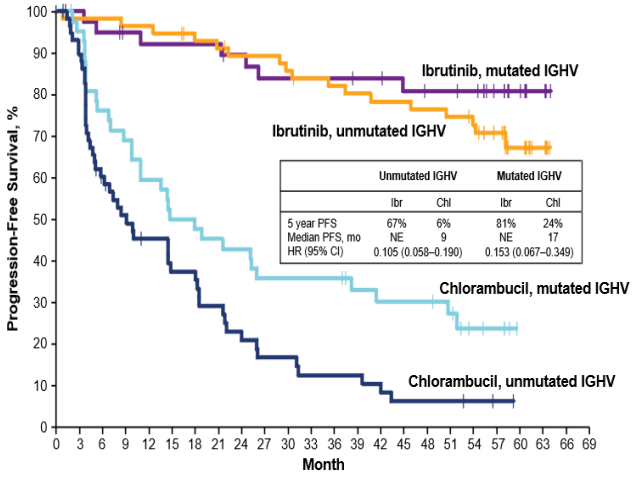
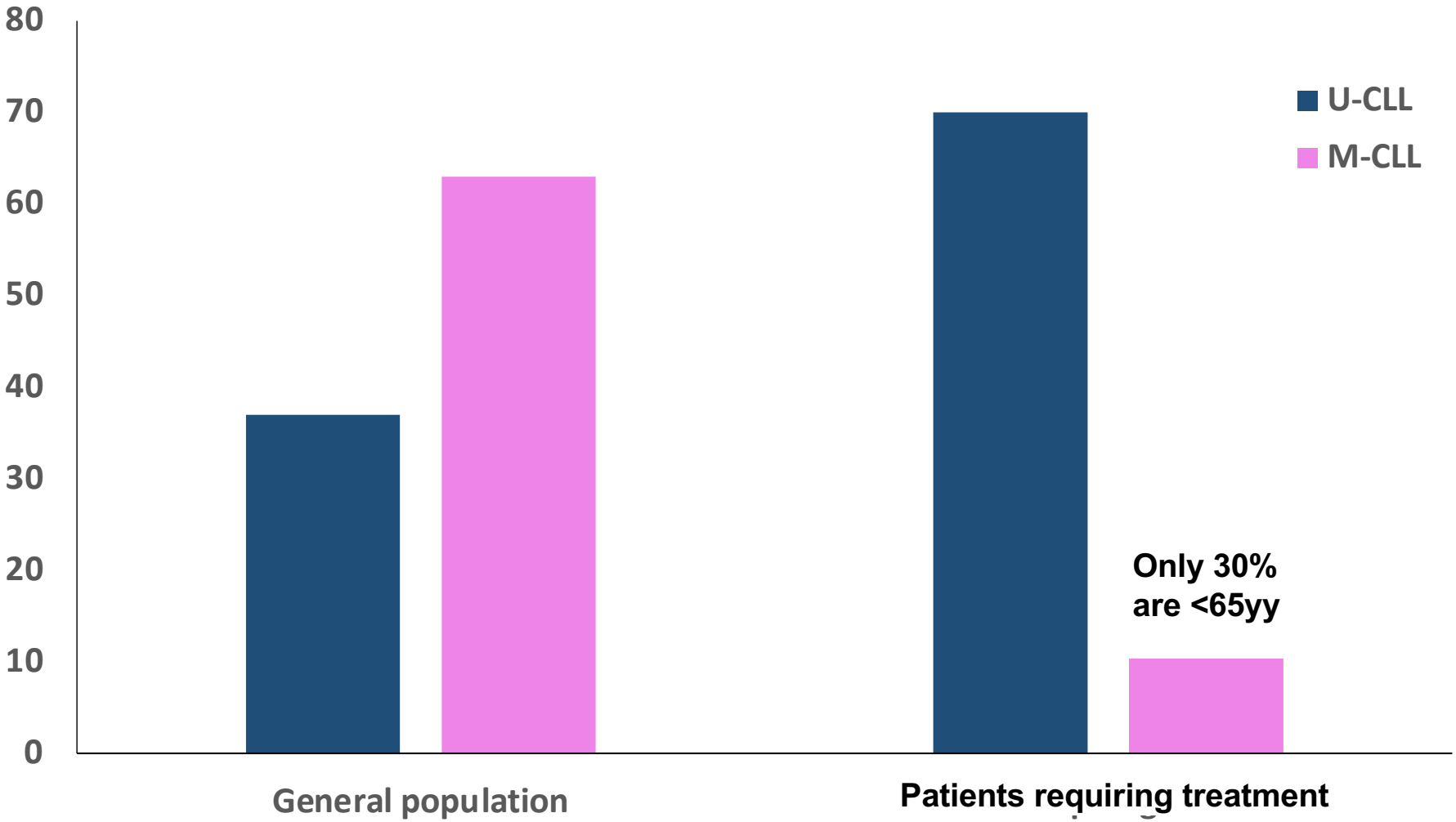


Burger J. et al, Leukemia 2020

Few IGHV mutated patients need treatment



K. Stamatopoulos, personal communication

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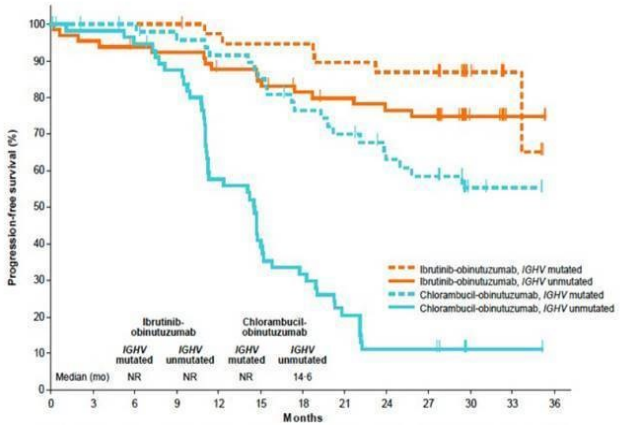
iLLUMINATE (IRC):
Ibrutinib + obinutuzumab versus chlorambucil + obinutuzumab



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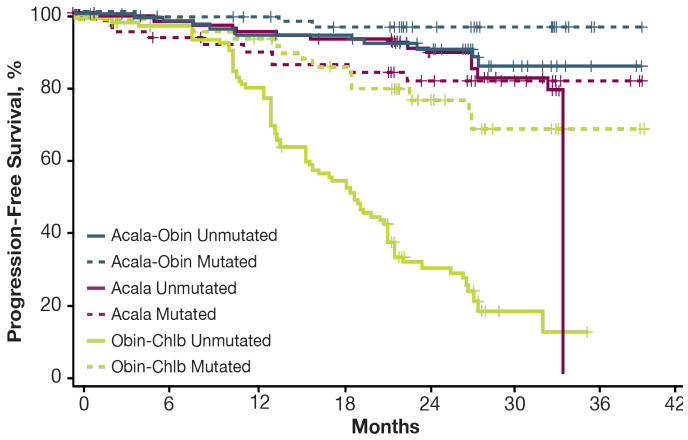

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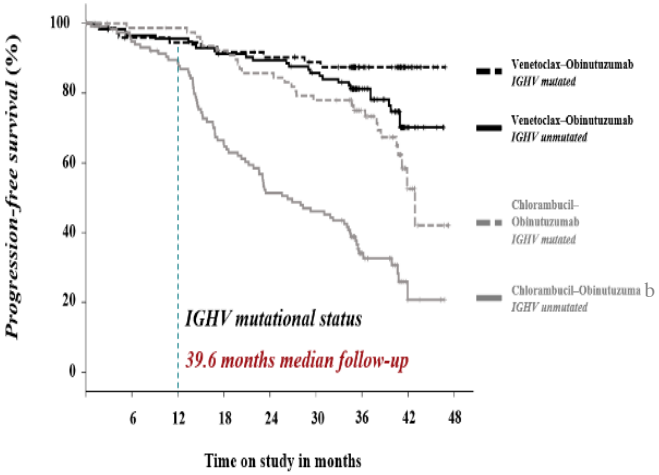

Moreno C et al, 2018 Lancet Oncol; Sharman JP et al, Lancet 2020; Fischer et al., N Engl J Med 2019

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116 Certified Centres from **30** countries

7 Reference Centres

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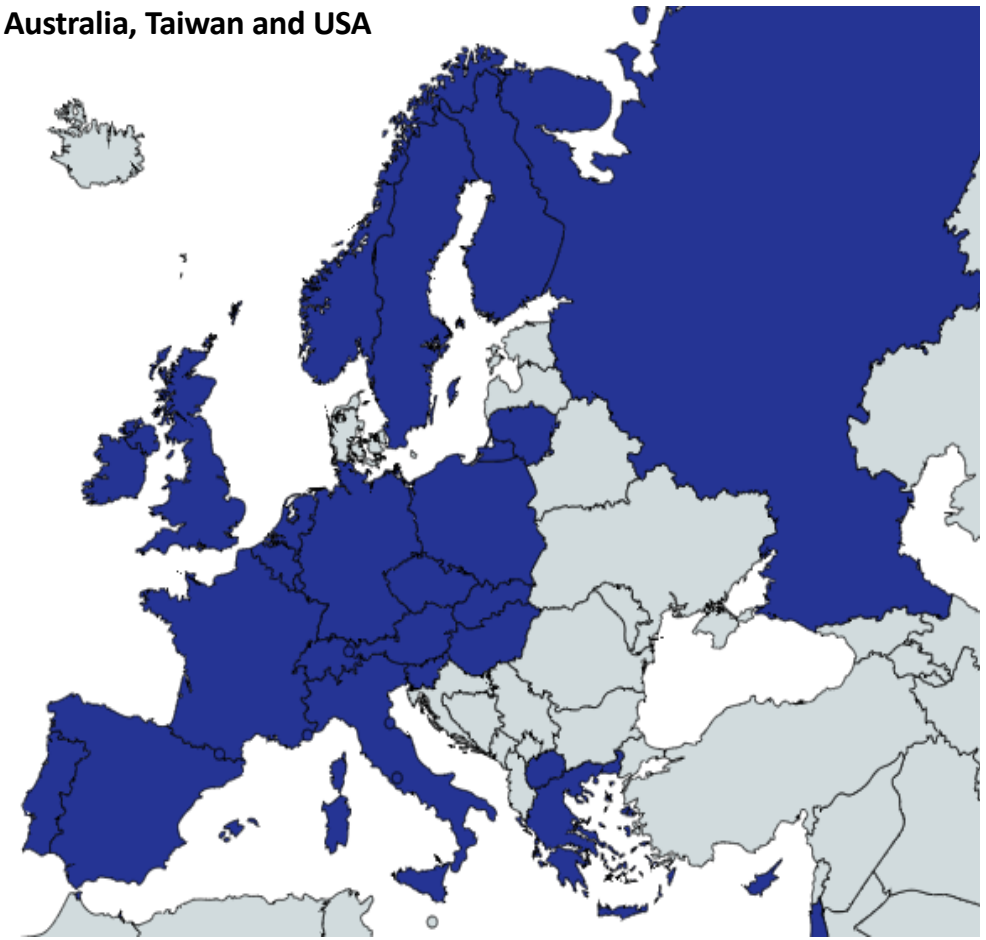
In Europe plus Argentina, Australia, Taiwan and USA



How can we choose the best therapy?

- **Treatment duration** (no termination versus fixed duration)
- **Administration** [oral (p.o) versus i.v.]
- **Compliance** (i.v. versus p.o.)
- **Evidence** (currently, longer follow-up with ibrutinib; lack of evidence in fit patients for VO)
- **Risk of complications** (in particular in the presence of specific comorbidities: bleeding and cardiac comorbidities with ibrutinib or other BTKis versus impaired renal function and neutropaenia with venetoclax)
- **Number and complexity of clinical controls** (two to four weeks for ibrutinib versus dose ramp up with three controls every week for five weeks to prevent TLS and potential hospitalisation in case of high TLS risk with venetoclax).

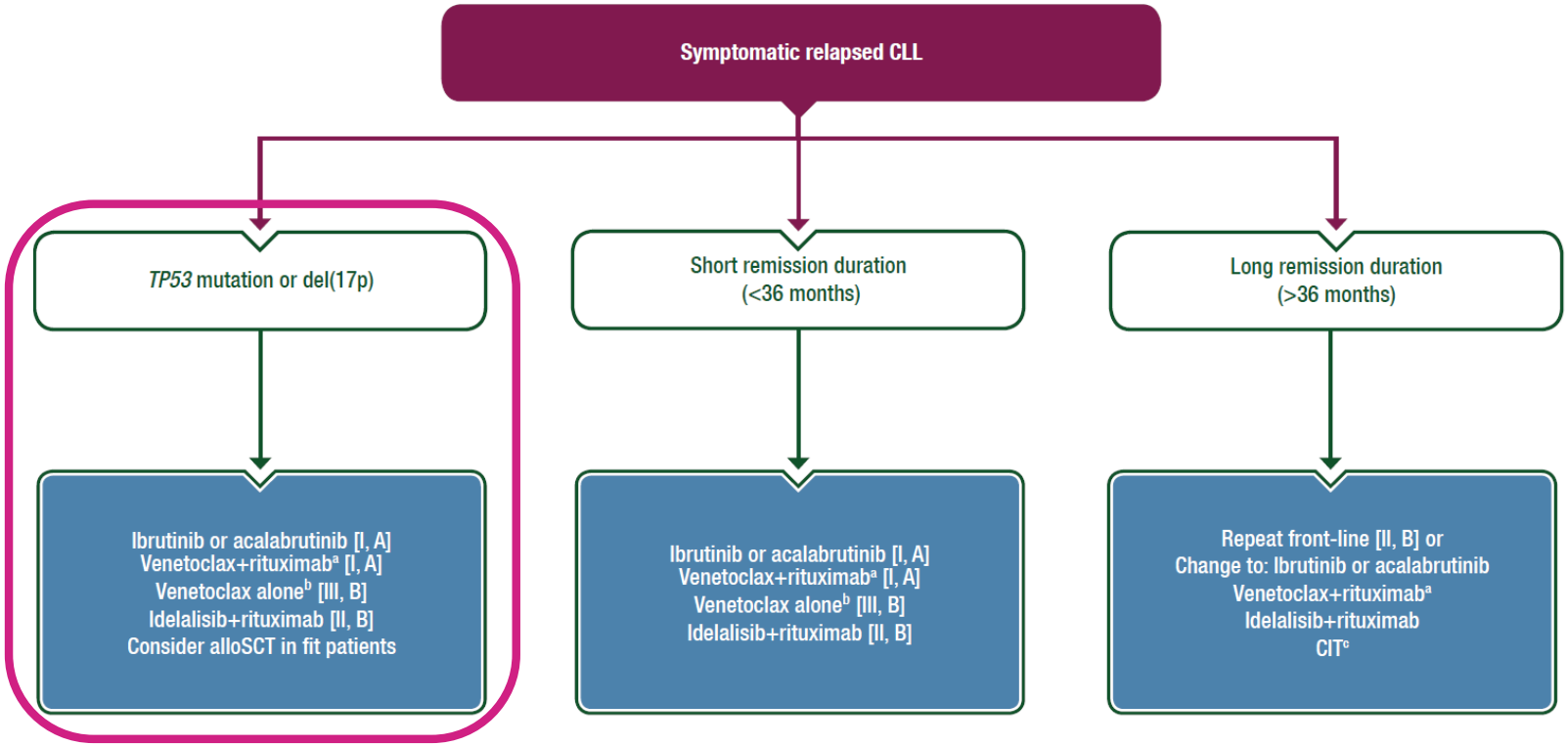
Eichhorst B et al, Ann Oncol 2021

Relevant factors for choice of **relapse therapy**

- Genetic evolution
- Prior treatment:
  - Response
  - Tolerability
- Comorbidity and Comedication
- Optimal sequence of therapy

2021 ESMO guidelines for CLL treatment

Relapsed/Refractory



Eichhorst B, Ghia P; Hemasphere. 2020

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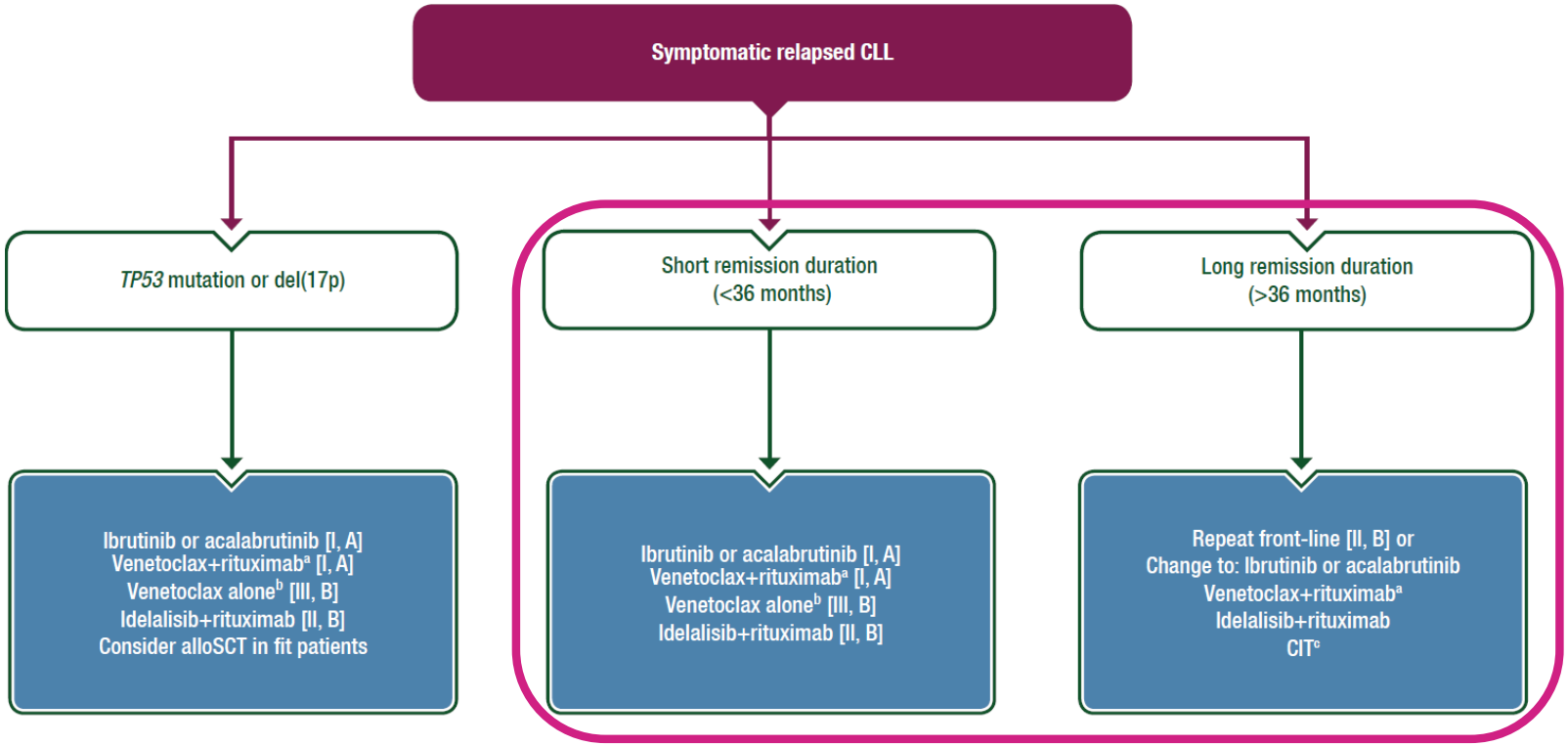
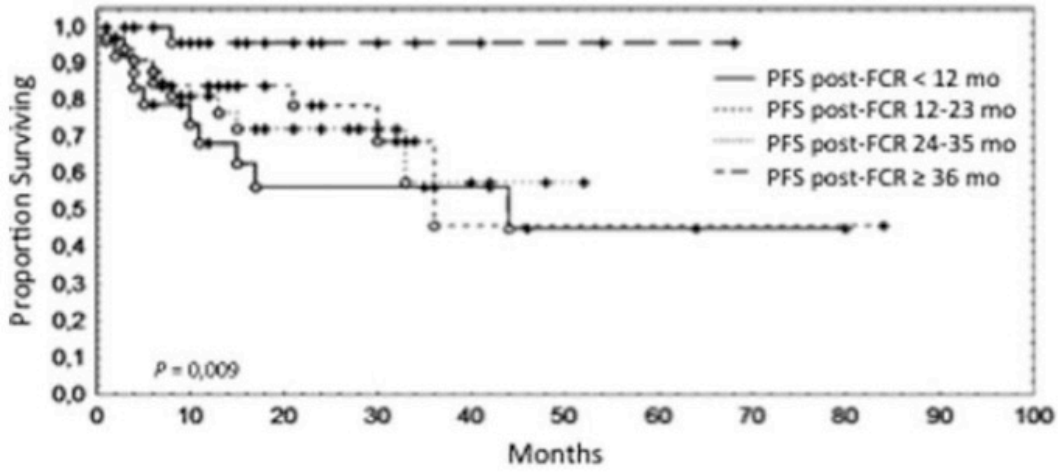


Eichhorst B, Ghia P; Hemasphere. 2020

Chemoimmuntherapy in R/R CLL:

Only after long remissions in firstline

	FCR Wierda et al., JCO 2005; 23(18): 4070	FCR Robak et al., JCO 2010; 28(10): 1765	BR Fischer et al., JCO 2011; 29(26): 3559	BR# Cuneo et al., Haematologica 2018; 103(7):1209
n patients	177	276	78	237
ORR	73%	70%	59%	82%
PFS med.	28.0 mo	30.6 mo	14.7 mo*	25 mo



Fornecker et al., Am J Hematol 2015

Phase III trials with targeted agents in relapse treatment

Treatment	Trial name	PFS HR (CI)	OS HR (CI)	Reference
Ibrutinib Ofatumumab	RESONATE 1	0.133 (0.099-0.178)	0.591 (0.378-0.926)	Byrd J. et al, Blood 2019; 133(19):2031
Ibrutinib + BR BR	HELIOS	0.206 (0.159–0.265)	0.652 (0.454–0.935)	Fraser et al., Leukemia 2019; 33:969
Acalabrutinib BR/Idelalisib + rituximab	ASCEND	0.31 (0.20-0.49)	0.84 (0.42-1.66)	Ghia P et al, EHA 2019; LBA 2606
Idelalisib + rituximab Placebo + rituximab	116	0.15 (0.08–0.28)	0.8 (0.5 - 1.1)	Sharman J et al., JCO 2019 37(16):1391
Duvelisib Ofatumumab	DUO	0.52 (0.39–0.70)	0.99 (0.65-1.50)	Flinn I et al Blood 2018, Vol 123,32: 2446
Venetoclax + rituximab BR	MURANO	0.13 (0.05-0.29)	0.48 (0.25-0.90)	Seymour J et al., NEJM 2018; 378(12):1107

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