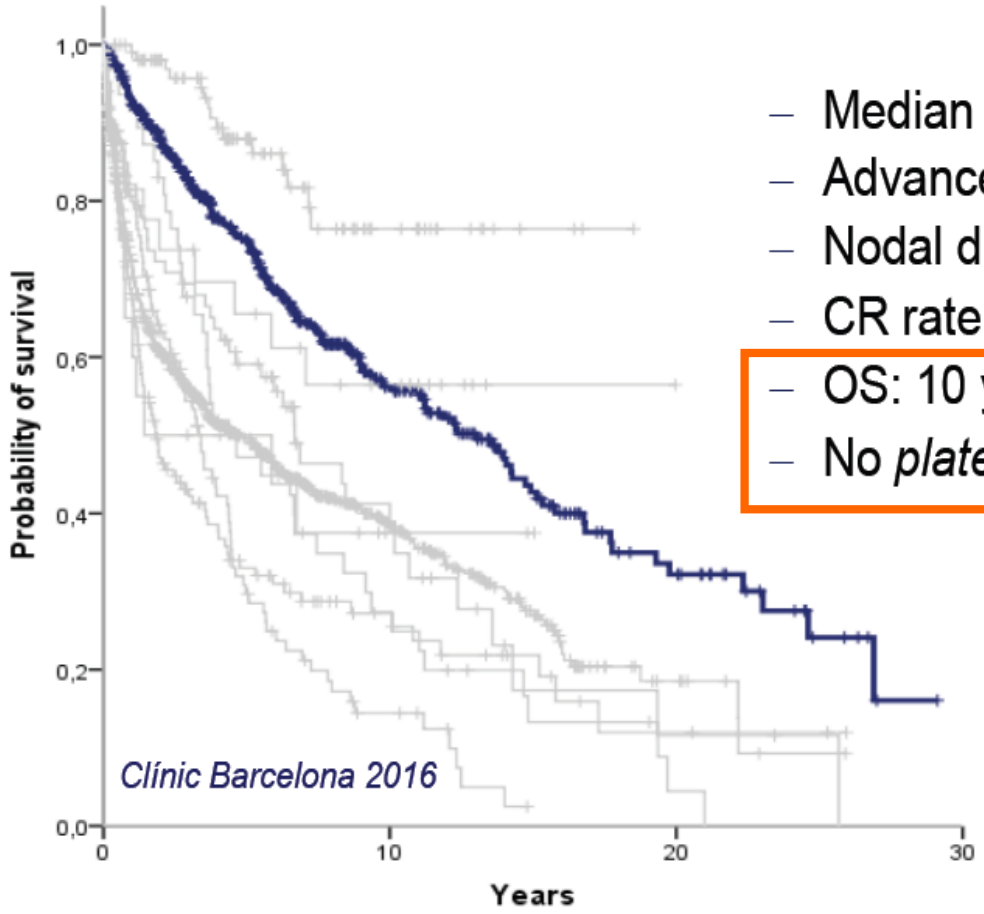
TERAPIA DEL LINFOMA FOLLICOLARE ALLA RICADUTA

dott.ssa Monica Tani

U.O.C Ematologia Ravenna

Follicular lymphoma



- Median age: 60 years
- Advanced stage: 80%
- Nodal disease; BM+
- CR rate: 10-80%
- OS: 10 years (↑)
- No *plateau* in PFS or OS curves

1st step: diagnosis
Is mandatory a new biopsy?

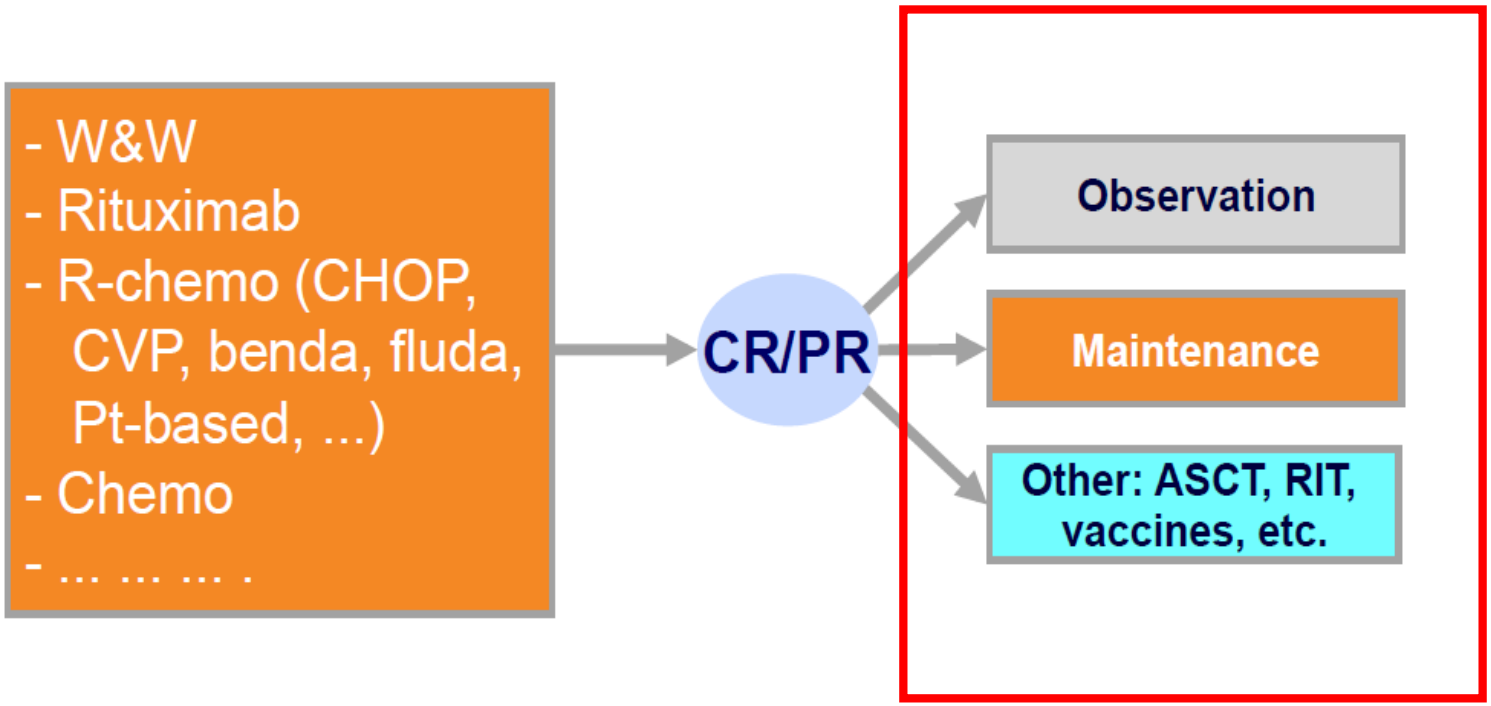
- YES – everybody agrees on that[1]
  - "It is strongly recommended to obtain a new biopsy in order to exclude transformation"
  - "It may be useful to target the biopsy based on PET"
- However in real life:
  - In the GELTAMO series[2] (1734 patients consecutively diagnosed with FL (grades 1, 2 or 3a) in 18 Spanish centers between 2002 and 2012) a new biopsy was performed in only 41% of the cases showing lymphoma progression

1. Dreyling M, Ann Oncol 2016 (suppl 5):v83-90
2. Alonso S, Br J Haematol 2017

Relevant factors to decide treatment at 1st relapse/progression

- Prior (front line) treatment
- Duration of response
- Symptomatic or asymptomatic
- Risk factors at relapse (age, PS, stage, FLIPI, biology?…)
- Histologic transformation

Follicular lymphoma: treatment at relapse



FL at 1st relapse/progression

Something else after induction?

- Maintenance with Rituximab?
  - Yes, if not received R in 1st line (I, A)
  - After maintenance in 1st line? Probably not if relapsed during maintenance (IV, D)
- ASCT?
  - "Should be considered in patients who experience short-lived first remissions (<2-3 years) after rituximab-containing regimens" (I, B)
  - However, the general role of ASCT has to be re-defined in the rituximab era
  - Rituximab maintenance after ASCT may achieve some improvement in PFS (II, B)

Dreyling M, Ann Oncol 2016 (suppl 5):v83-90

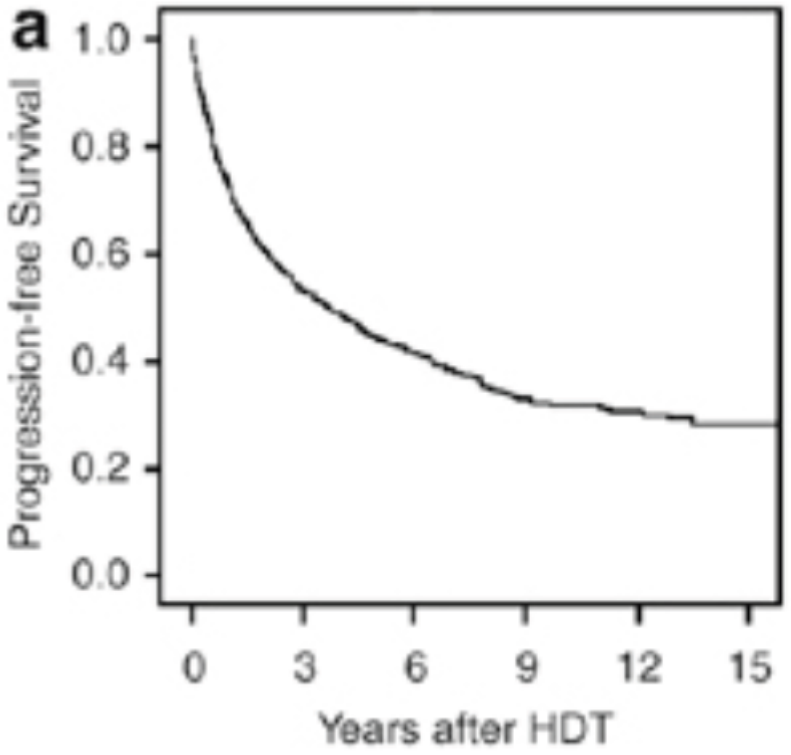
ROLE FOR ASCT IN FL AT RELAPSE

- Support comes from several retrospective analyses and a single randomized trial (CUP trial) performed prior Rituximab era
- Retrospective analyses have tried to compare outcomes following ASCT or chemoimmunotherapy in Rituximab era: **mixed result**
  1) Sebban C JCO 2008: 254 patients with relapsed FL treated with high dose therapy followed by ASCT had higher rates of 5-year EFS e OS when compared with patients who did not receive ASCT. However, when this analysis was limited to patients who received rituximab as part of their salvage regimen the benefit lost its statistical significance for both EFS and OS. 2) Casulo C Biol Blood marrow Transpl 2018: 349 patients who progressed within two years or did not response to initial rituximab-based cht: OS similar whether or not HCT was performed in the whole population. Subset analysis: 123 patients receiving ASCT within one year of treatment failure had superior OS at 5-years. So early ASCT may benefit high-risk population

FL at 1st relapse/progression

Role for ASCT

- Rituximab mig … of ASCT in the treatmer
- In the rituxima … ted by at least two trials
- Data in USA a … of ASCT in FL is decreasi
- Still it may hav … ort previous respc
- Rituximab doe … f ASCT[6]
- A plateau in the PFS curve?[7]
- R Maintenance after ASCT[8]



1) Sebban, JCO 2008;26:3614; 2) Le Gouill, Haematologica 2011;96:1128; 3) Link Clin Oncol 2011;29(#8049); 4) van Oers, JCO 2010;28:2853; 5) Montoto, Haematologica 2013;98:1014; 6) El Najar ASH 2011(#502); 7) Montoto, Leukemia 2007;21:2324; 8) Pettengell, JCO 2013;31:1624

EBMT Lymphoma Working Party

Consensus project on hemopoietic transplant in FL

- HDT-ASCR is not an appropriate treatment option to consolidate first remission in patients with FL responding to immunochemotherapy, outside the setting of clinical trials
- In patients in first relapse with chemo-sensitive disease HDT-ASCR is an appropriate treatment option to consolidate remission
- Allogeneic transplantation should be considered in patients with relapse after HDT-ASCR
- Reduced-intensity/ non-myeloablative conditioning regimens are generally more appropriate in patients receiving an allogeneic transplant.

Montoto S, Haematologica 2013;98:1014-21

FL at 1st relapse/progression

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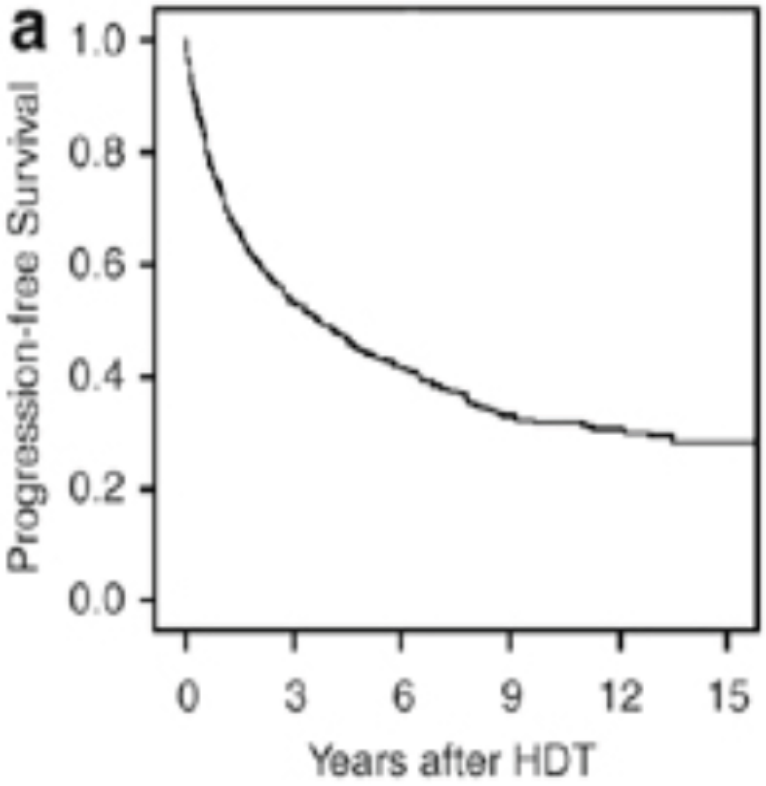

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ROLE MAINTENANCE RITUXIMAB POST ASCT

- Maintenance Rituximab appears to improve PFS rates
- Toxicities are increased
- Effect on OS is not clear

- For relapsed/refractory FL in at least partial response prior to ASCT maintenance rituximab is suggested rather than observation
- However maintenence rituximab is associated with higher rate of late neutropenia, infections, reactivation of viral infections and blunted responsiveness to vaccination

- Pettengel R, et al. J Clin Oncol 2013; 31: 1624.

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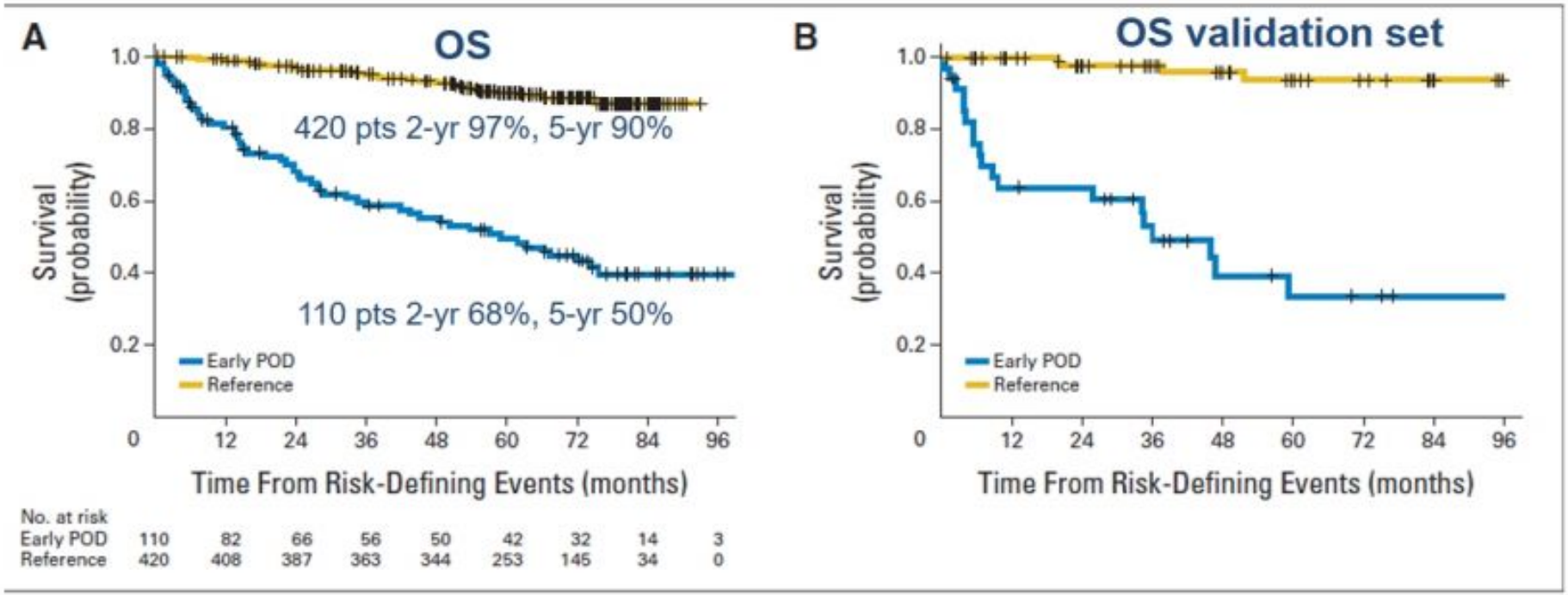
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Early Relapse of Follicular Lymphoma After Rituximab Plus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone Defines Patients at High Risk for Death: An Analysis From the National LymphoCare Study



Casulo C et al, JCO 2015

Management Challenges in R/R FL

1 of 5 patients have ER and/or have refractory disease

- No way to identify these patients before frontline therapy

ER usually means aggressive disease with poor outcomes

- Likely to cycle through available therapies quickly
- Analyze first-line treatment to guide choice of subsequent therapies

Casulo C, et al. *J Clin Oncol.* 2015;33:2516-2522.

Strategies for Selecting Therapy for R/R FL

Determine whether it is early or late relapse

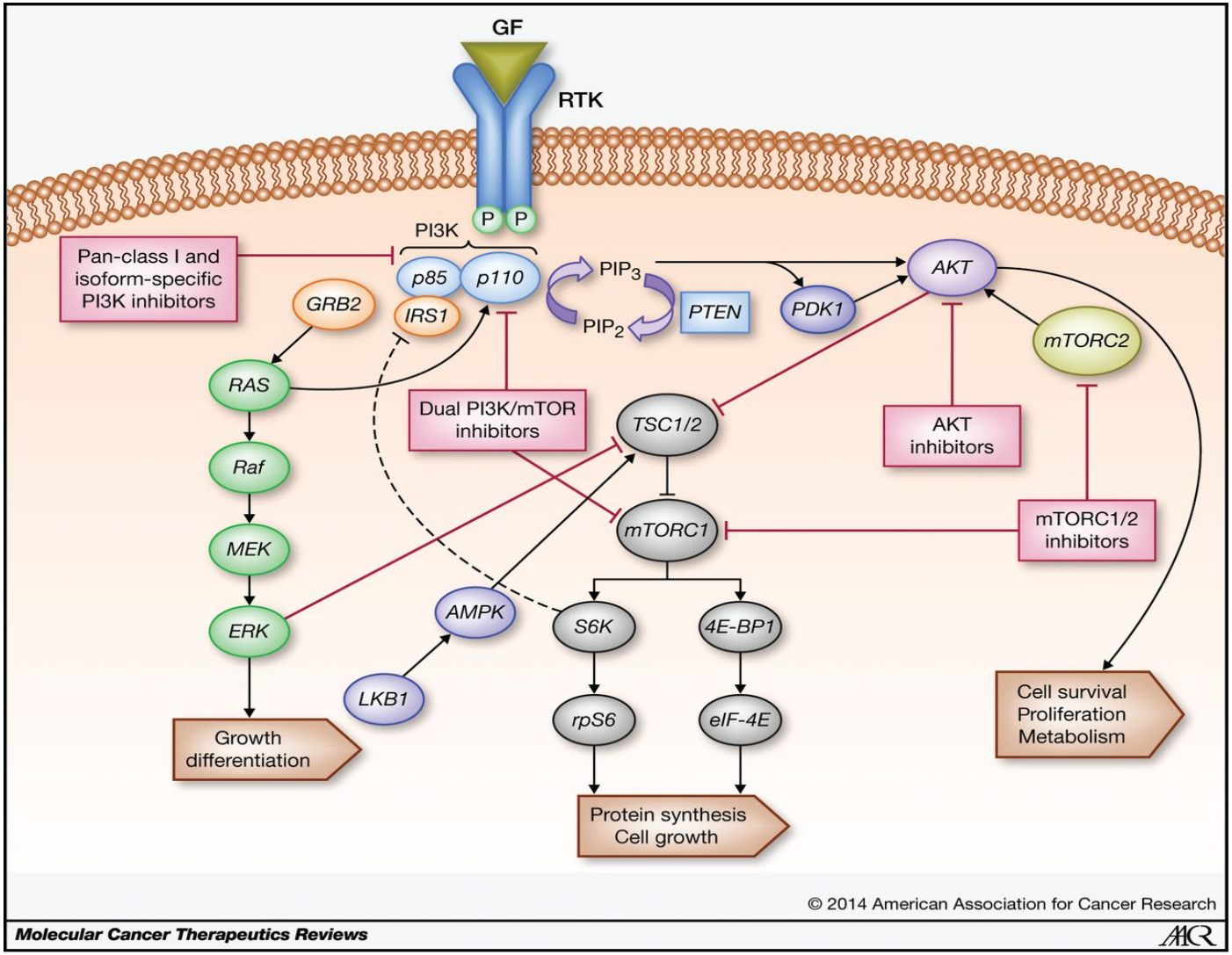
- ER: consider transplant if suitable, consider novel/emerging therapies
- Late relapse: more flexibility, more options, less time pressure

Consider patient characteristics

Consider comorbidities

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas. Version 3.208. Updated April 13, 2018. https://www.nccn.org.

PI3K INHIBITORS



Idelalisib

Idelalisib is a potent, small-molecule PI3K inhibitor that is highly selective for the δ isoform

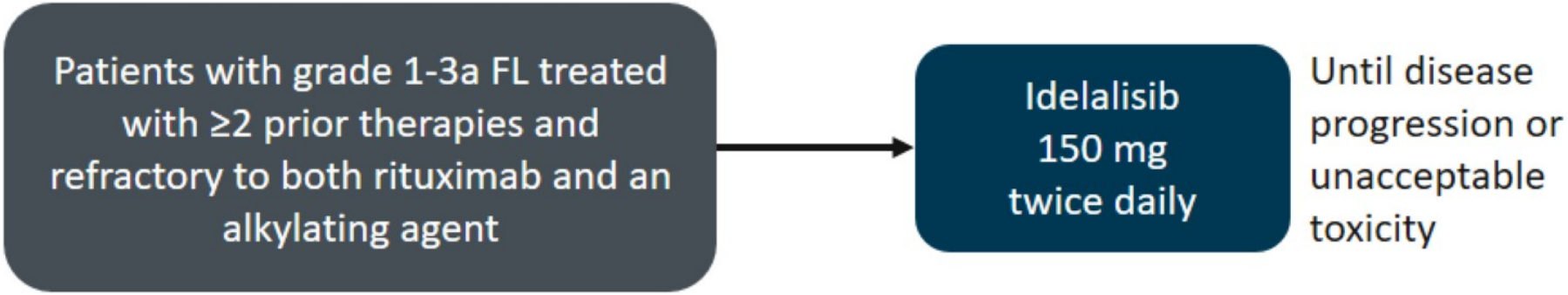
Indications*

- Relapsed CLL, in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other comorbidities
- Relapsed FL in patients who have received ≥2 prior systemic therapies
- Relapsed SLL, in patients who have received ≥2 prior systemic therapies

*Accelerated approval was granted for FL and SLL based on ORR. Improvement in patient survival or disease-related symptoms has not been established. Continued approval for these indications may be contingent on verification of clinical benefit in confirmatory trials.
Zydelig® PI 2018.

Phase 2 Trial of Idelalisib Monotherapy in R/R FL

Design and Efficacy



Parameter	Results (N = 72)
ORR (95% CI)	55.6 (43.4, 67.3)
CR, %	13.9
PR, %	41.7
Median DoR, mo (range)	10.8 (0-26.9)
Median PFS, mo (95% CI)	11.0 (8.0, 14.0)
2-y OS (at 24 mo), %	69.8

Salles G, et al. *Haematologica.* 2017;102:e156-e159.

Phase 2 Trial of Idelalisib Monotherapy in R/R FL
Safety

AEs, n (%)[a]	Any Grade	Grade ≥3
Diarrhea	37 (51.4)	10 (13.9)
Upper respiratory tract infection	11 (15.3)	0 (0)
Pneumonia	8 (11.1)	5 (6.9)
Neutropenia	37 (51.4)	16 (22.2)
ALT/AST elevated	–	10 (13.9)

- Steroids can be considered in some cases of idelalisib-associated diarrhea[b]
- ALT/AST elevation can sometimes resolve by temporary withholding of treatment[c]

a. Salles G, et al. *Haematologica*. 2017;102:e156-e159.
b. Coutré SE, et al. *Leuk Lymphoma*. 2015;56:2779-2786.
c. Gopal AK, et al. *N Engl J Med*. 2014;370:1008-1018.

Copanlisib

- Targeted inhibition of PI3K is a therapeutic strategy for patients with R/R indolent B-cell lymphoma
- Copanlisib is an IV pan-class I PI3K inhibitor with predominant and potent activity against the PI3Kα and PI3Kδ isoforms
- FDA granted accelerated approval to copanlisib for the treatment of adult patients with relapsed FL who have received ≥2 prior systemic therapies

Dreyling M, et al. *J Clin Oncol*. 2017;35:3898-3905.

CHRONOS-1 Trial of Copanlisib
Methods

- 142 patients, of whom 141 had indolent B-cell lymphoma (FL grades 1-3a, MZL, SLL, LPL/WM)
- Eligibility: R/R to ≥2 prior lines of treatment
  - Previous treatment had to include rituximab and an alkylating agent
- Copanlisib was administered at a fixed dosage of 60 mg via 1-h IV infusion on days 1, 8, and 15 of a 28-d cycle
  - Treatment continued until progression or unacceptable toxicity
- Primary efficacy endpoint was ORR
- Secondary efficacy endpoints included DoR, PFS, and OS

Dreyling M, et al. *Blood*. 2017;31:2777.

CHRONOS-1 Trial of Copanlisib
Efficacy

Response	% (N = 142)
CR	12.0
PR	47.2
SD	29.6
PD	2.1
ORR (95% CI)	59.2 (50.6, 67.3)
DCR (95% CI)	85.9 (79.1, 91.2)

Median PFS = 11.3 mo (95% CI: 8.1, 24.2)
Median DoR = 12.2 mo

Dreyling M, et al. *Blood.* 2017;31:2777.

CHRONOS-1 Trial of Copanlisib
Safety

- Low rates of severe elevation of hepatic transaminases, diarrhea, or pneumonitis
- 49.3% of patients had transient hyperglycemia
- 29.6% had transient hypertension
- 33.8% had diarrhea (all-grade)
- Serious AEs included:
  - Pneumonitis (1.4%, grade 3)
  - Colitis (0.7%, grade 4)
- Low rates of opportunistic or fatal infections or other fatal TEAEs

Dreyling M, et al. *Blood.* 2017;31:2777.

Duvelisib

Duvelisib, an oral drug, is a dual inhibitor of PI3Kδ and γ[a]

Follicular Lymphoma (FL)*

[redacted] is indicated for the treatment of adult patients with relapsed or refractory FL after at least two prior systemic therapies.

**This indication is approved under accelerated approval based on overall response rate (ORR). 24/09/2018*

DYNAMO trial[a]

- Duvelisib (25 mg twice daily) 28-d treatment cycle until disease progression or unacceptable toxicity
- 129 patients with FL, SLL, or MZL whose disease was DR to rituximab (monotherapy/combination) and to chemotherapy or radioimmunotherapy

a. Zinzani PL, et al. *Hematol Oncol.* 2017;35(suppl 2):69-70.
b. Verastem press release, April 9, 2018. http://investor.verastem.com

DYNAMO TRIAL

- • DYNAMO, a Phase 2 single-arm study, evaluated the efficacy and safety of duvelisib (25 mg twice daily) as a monotherapy in 129 patients whose disease has progressed and who are refractory to rituximab and to either chemotherapy or radioimmunotherapy.
- – Follicular Lymphoma (n = 83)
- – Small Lymphocytic Lymphoma (n = 28)
- – Marginal Zone Lymphoma (n = 18)
- • The study met its primary endpoint of overall response rate (ORR) as assessed by an independent review committee.

	FL (N=83)	SLL (N=28)	MZL (N=18)	Overall (N=129)
ORR, N(%)	34 (41)	19 (68)	18 (33)	59 (46)

- **High level safety:**
- • Majority of side effects were reversible and clinically manageable.
- • Most common ≥ Grade 3 side effects that occurred in at least 10 percent of patients in the study were:
- – neutropenia (28%)
- – diarrhea (15%)
- – thrombocytopenia (13%)
- – anemia (12%)
- • Twenty percent (20%) of patients experienced ≥ Grade 3 infection.
- • These data showed that duvelisib has a positive benefit/risk profile in this difficult to treat patient population.

DYNAMO Trial of Duvelisib

- Primary endpoint: ORR = 41% (all were PRs)
  - SD as best response = 36%
  - PD as best response = 17%
- Median time to response: 1.9 mo (range, 1.6–11.7)
- 80% of patients with FL exhibited reduction in nodal target lesions after treatment
- Among 34 patients with FL who responded, median DoR = 9.2 mo
- Median PFS for all patients with FL = 8.3 mo
- Median OS = 11.1 mo
- Similar AE profile to idelalisib

Zinzani PL, et al. *Hematol Oncol*. 2017;35(suppl 2):69-70.

New PI3K inhibitor

Phase 1/2 study of INCB050465 in patients with relapsed or refractory B-cell malignancies

INCB050465: highly selective and highly potent PI3Kδ inhibitor, designed to avoid hepatotoxicity and to have favourable PK exposure; 20 mg oral QD for 9ws, then 20 mg QW

Characteristic	Total: 72 pts
Median (range) age, y	66 (30-80)
≥ 65 y, n (%)	37 (51)
≥ 3 prior therapies, n (%)	43 (60)
Prior ASCT, n (%)	21 (29)
DLBCL n (%)	23 (32)
FL n (%)	14 (19)

Forero-Torres A et al, abs 410

New PI3K inhibitor

INCB050465: safety

Nonhematologic TEAEs Occurring in ≥20% of Patients

Total (N=72)	Any Grade, n (%)	Grade 3 or 4, n (%)
Any TEAE	68 (94)	41 (57)
Diarrhea/Colitis*	26 (36)	7 (10)
Nausea	26 (36)	0
Fatigue	22 (31)	0
Rash*	22 (31)	4 (6)
Cough	17 (24)	0
Vomiting	17 (24)	0

Median time to onset:
colitis 4.4 ms, rash 2.9 ms.
Transaminitis: 25%, Grade 1 in all cases

Forero-Torres A et al, abs 410

New PI3K inhibitor

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New or Worsening Hematologic TEAEs

Total (N=72)	Any Grade, n (%)	Grade 3, n (%)	Grade 4, n (%)
Neutropenia	32 (44)	10 (14)	4 (6)
Thrombocytopenia	24 (33)	3 (4)	4 (6)
Anemia	20 (28)	5 (7)	0 (0)

Median time to onset:
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Forero-Torres A et al, abs 410

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Anemia	20 (28)	5 (7)	0 (0)

Dose Modifications Due to Any Grade TEAE

Event, n (%)	Total (N=72)
Interruption	30 (42)
Reduction	4 (6)
Discontinuation	14 (19)

Forero-Torres A et al, abs 410

New PI3K inhibitor

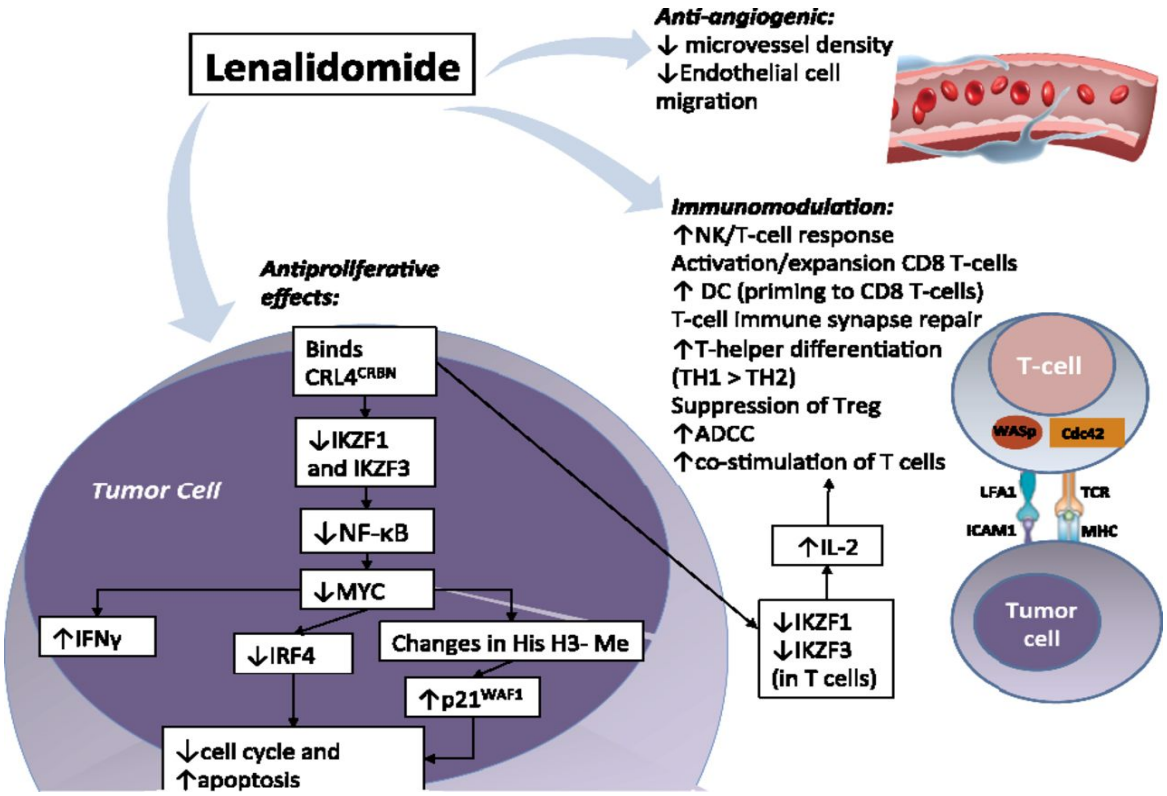
INCB050465: efficacy

Patients	N	ORR, n (%)
DLBCL*	23	7 (30)
GCB	19	6 (32)
ABC	2	1 (50)
FL	14	10 (71)

Median time to response: 2 months

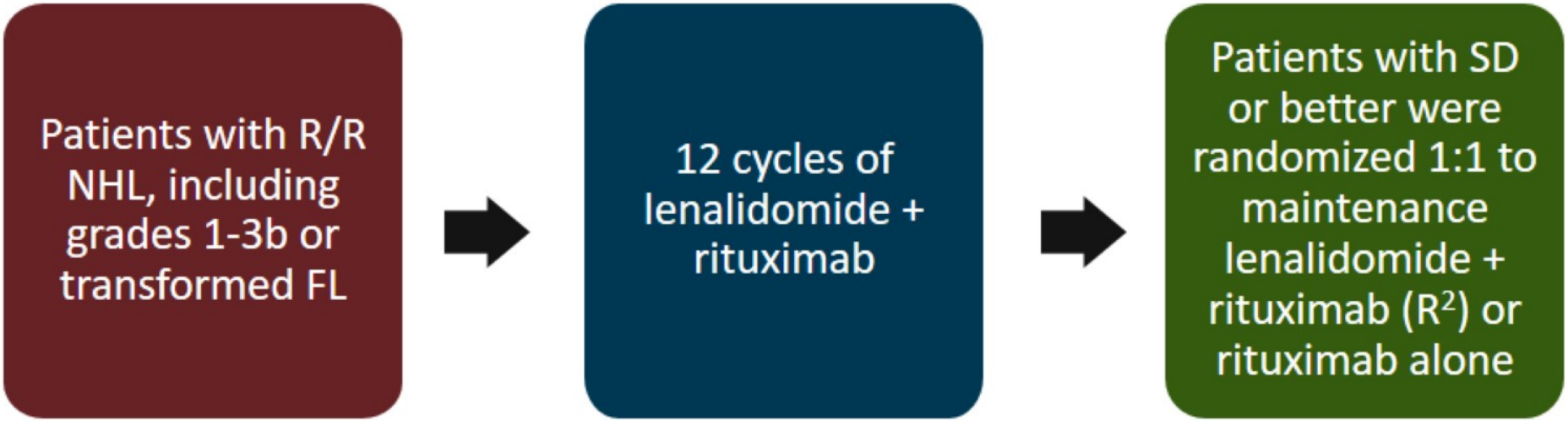
Forero-Torres A et al, abs 410

LENALIDOMIDE



MAGNIFY Trial of Rituximab + Lenalidomide
Design

Multicenter, Open-Label Phase 3 Trial



Andorsky DJ, et al. ASCO 2017.

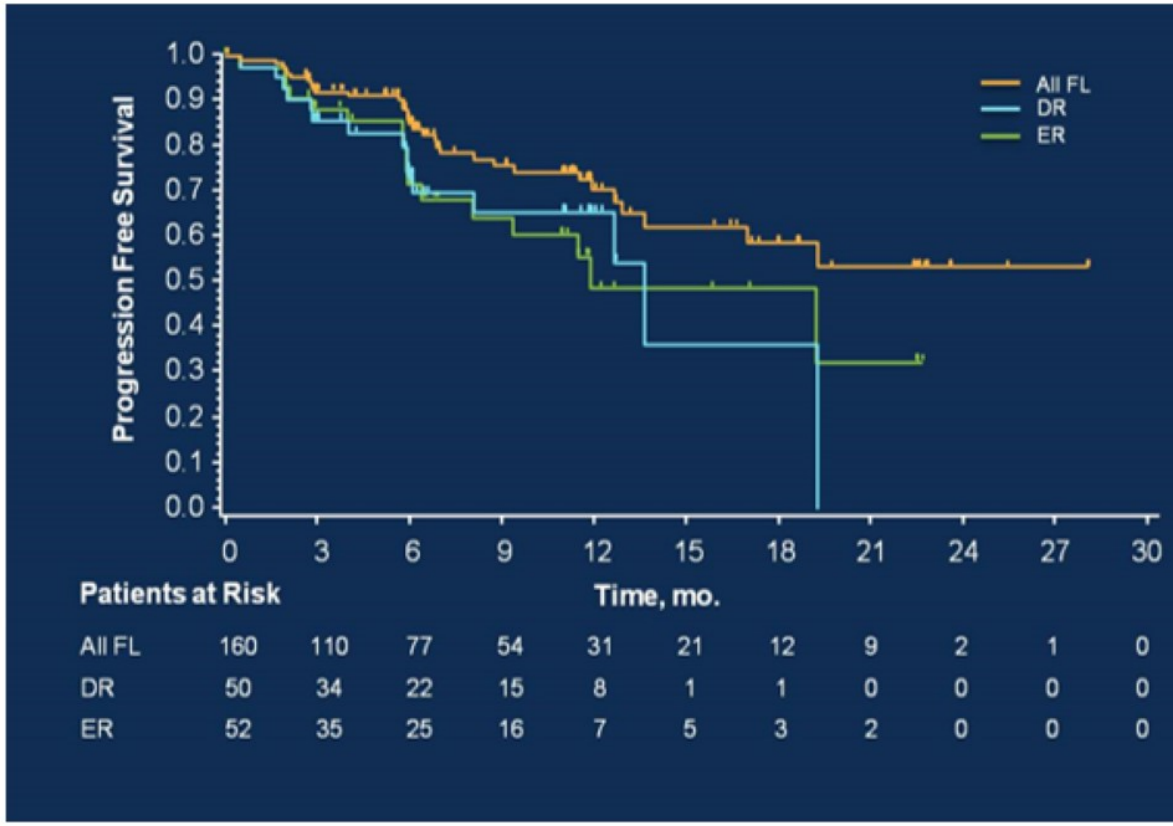
MAGNIFY Trial
Response

- Subgroup analysis
- DR: patients with DR FL -- both rituximab (as monotherapy or combination) and an alkylating agent
- ER: patients with ER -- disease progressed/relapsed within 2 y of initial diagnosis

Best Response, n (%)	All FL (n=128)	DR (n=42)	ER (n=43)
ORR (CR + Cru + PR)	85 (66)	19 (45)	20 (47)
CR/CRu	49 (38)	9 (21)	9 (21)
PR	36 (28)	10 (24)	11 (26)
SD	31 (24)	15 (36)	17 (40)
PD*	12 (9)	8 (19)	6 (14)

*Includes patients with PD and/death before completion of the response evaluation.
Andorsky DJ, et al. ASCO 2017.

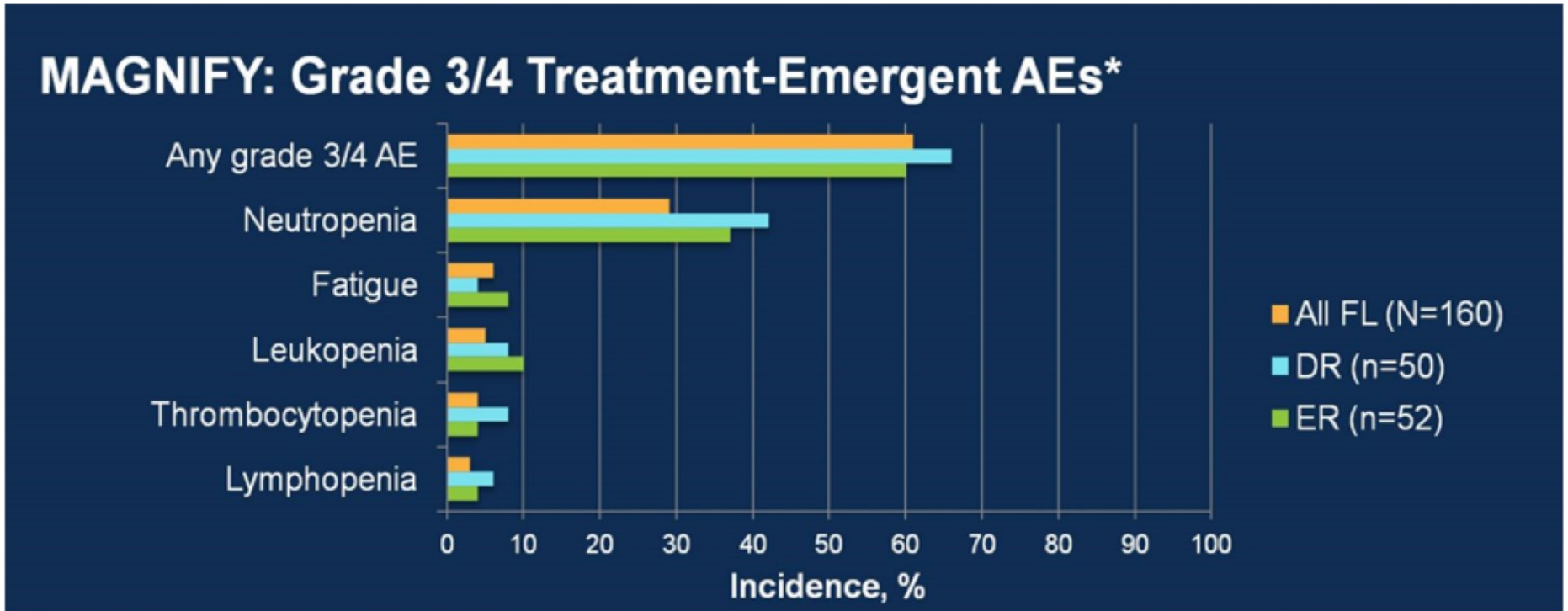
MAGNIFY Trial
PFS



- 1-year PFS
  - FL (N=160): 70%
  - DR (n=50): 65%
  - ER (n=52): 49%
- 1-year PFS was similar in the subgroups of ER patients treated with
  - First-line R-chemotherapy (n=39, 52%)
  - First-line non-R-chemotherapy (n=13, 44%)

With permission of author David Jacob Andorsky.

MAGNIFY Trial
Safety



- Most common grade 3/4 TEAEs for DR and ER patients were neutropenia (42%; 37%), leukopenia (8%; 10%), thrombocytopenia (8%; 4%), and lymphopenia (6%; 4%)
- Other Grade 3/4 AEs for DR and ER patients included febrile neutropenia (4%, 4%) and thrombosis (2%, 0%), with no such events of tumor lysis syndrome, tumor flare reaction, or hepatic disorders

With permission of author David Jacob Andorsky.

AUGMENT Trial

Rituximab + Lenalidomide for R/R FL and MZL

- Ongoing, double-blind randomized phase 3 trial: NCT01938001
- To evaluate the efficacy and safety of lenalidomide in combination with rituximab in patients with R/R FL or MZL
- Patients will be randomly assigned to receive either lenalidomide or placebo for twelve 28-d cycles in combination with rituximab for a 1-y period

ClinicalTrials.gov. NCT01938001.

Additional Trials of R + Lenalidomide

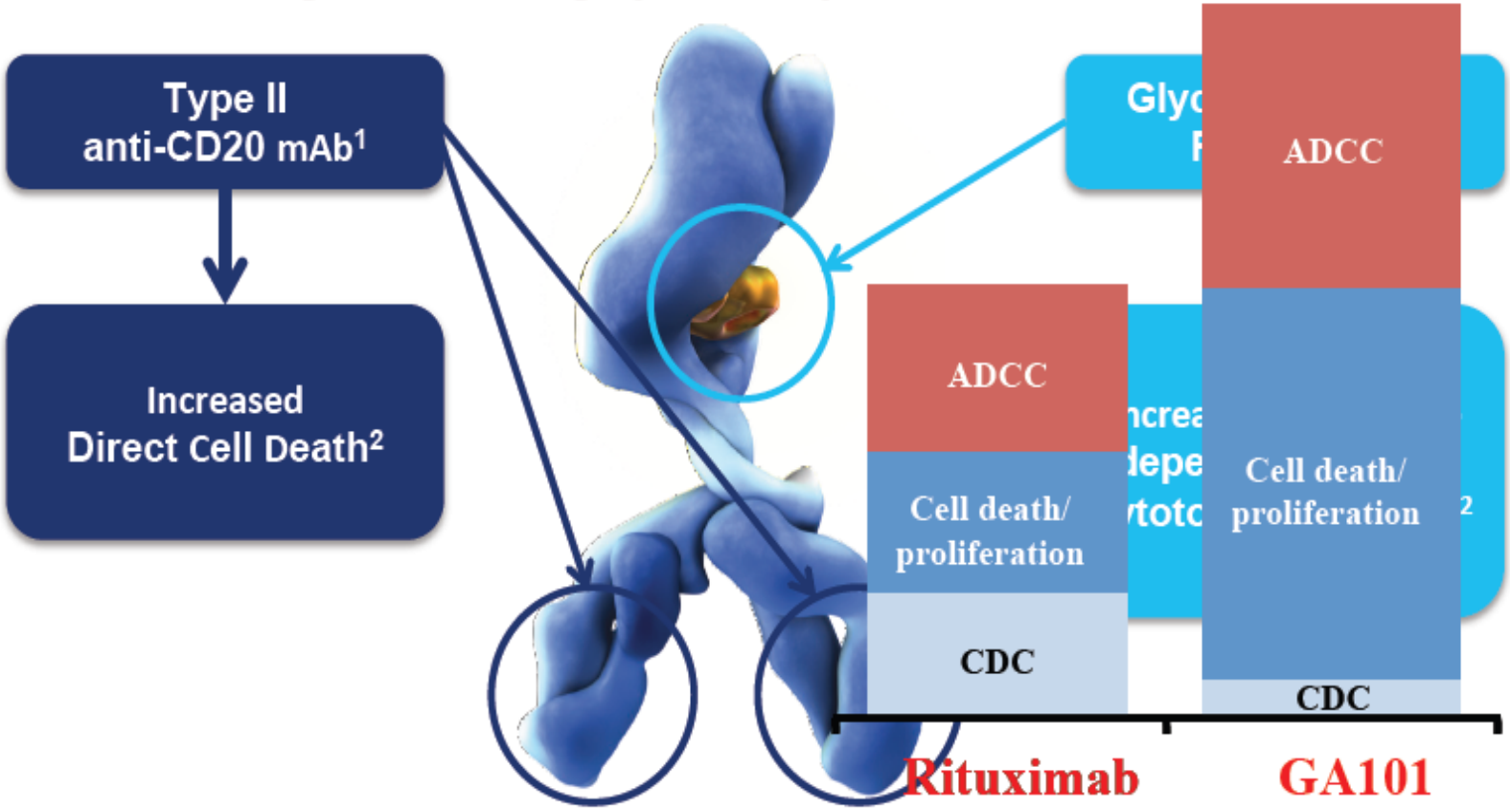
AUGMENT[a] -- ongoing randomized, double-blind, phase 3 trial

We are pleased to share the initial results that Lenalidomide plus rituximab achieved a highly statistically significant improvement in the primary endpoint of progression-free survival (PFS), compared to rituximab plus placebo.
In addition to achieving the primary endpoint of the study, a favorable trend was observed for overall survival (OS) during this analysis and follow-up will continue for the mature OS results.
The safety profile of R2 was consistent with the known safety profiles of the individual medicines, and no new safety signals were identified with the combination.

a. ClinicalTrials.gov. NCT01938001.
b. ClinicalTrials.gov. NCT01650701.

LINFOMA FOLLICOLARE

GA101: Designed for increased antibody-dependent cellular cytotoxicity (ADCC) and Direct Cell Death



Extensive clinical development program to evaluate the superiority of GA101 over rituximab in multiple head-to-head trials

1. Niederfellner G, *et al. Blood* 2011; 118:358–367. 2. Mössner E, *et al. Blood* 2010; 115:4393–4402.

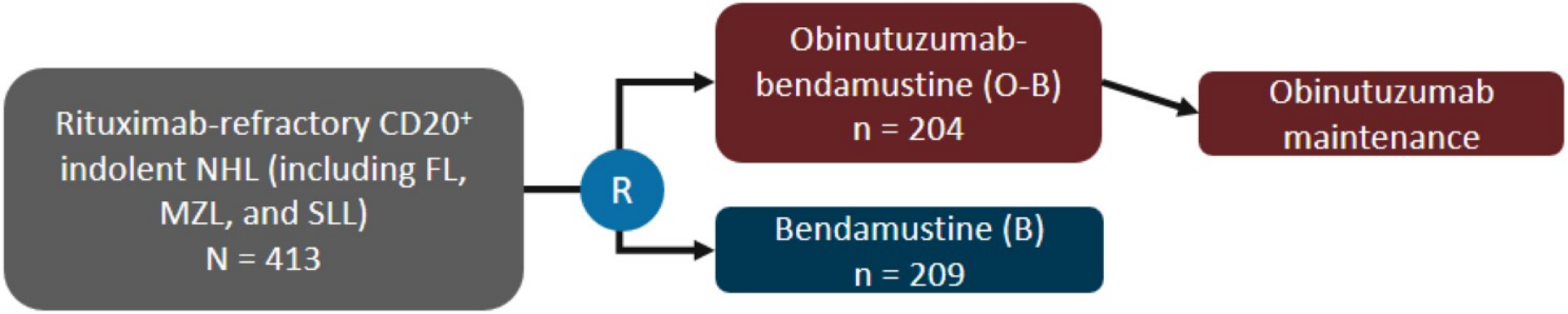
Obinutuzumab

CD20-directed cytolytic antibody

Indications:

- In combination with chlorambucil, for the treatment of patients with previously untreated CLL
- In combination with bendamustine followed by obinutuzumab monotherapy, for the treatment of patients with FL who relapsed after, or are refractory to, a rituximab-containing regimen
- In combination with chemotherapy followed by obinutuzumab monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III, or IV FL

GADOLIN Trial
Design



- Phase 3 trial
- O-B (O 1000 mg IV on days 1, 8, and 15 of cycle 1 and day 1 of cycles 2 to 6, B 90 mg/m^2/d IV on days 1 and 2 of cycles 1 to 6)
- B alone (120 mg/m^2/d IV on days 1 and 2 of each cycle for up to 6 cycles)
- Each cycle was 28 d
- Patients in the O-B arm without evidence of progression after induction received O maintenance 1000 mg IV every 2 mo for 2 y or until disease progression

Cheson BD, et al. *J Clin Oncol*. 2018. [Epub ahead of print]. doi:10.1200/JCO.2017.76.3656

GADOLIN Trial
Efficacy

Median Follow-Up of 31.8 mo

Parameter	O-B n = 204	B n = 209	HR (95% CI)
Median PFS, mo	25.8	14.1	0.57 (0.44, 0.73) *P* <.001

Cheson BD, et al. *J Clin Oncol.* 2018. [Epub ahead of print]. doi:10.1200/JCO.2017.76.3656

GADOLIN Trial
Safety

AEs grades ≥3 (O-B vs B): 72.5% vs 65.5%

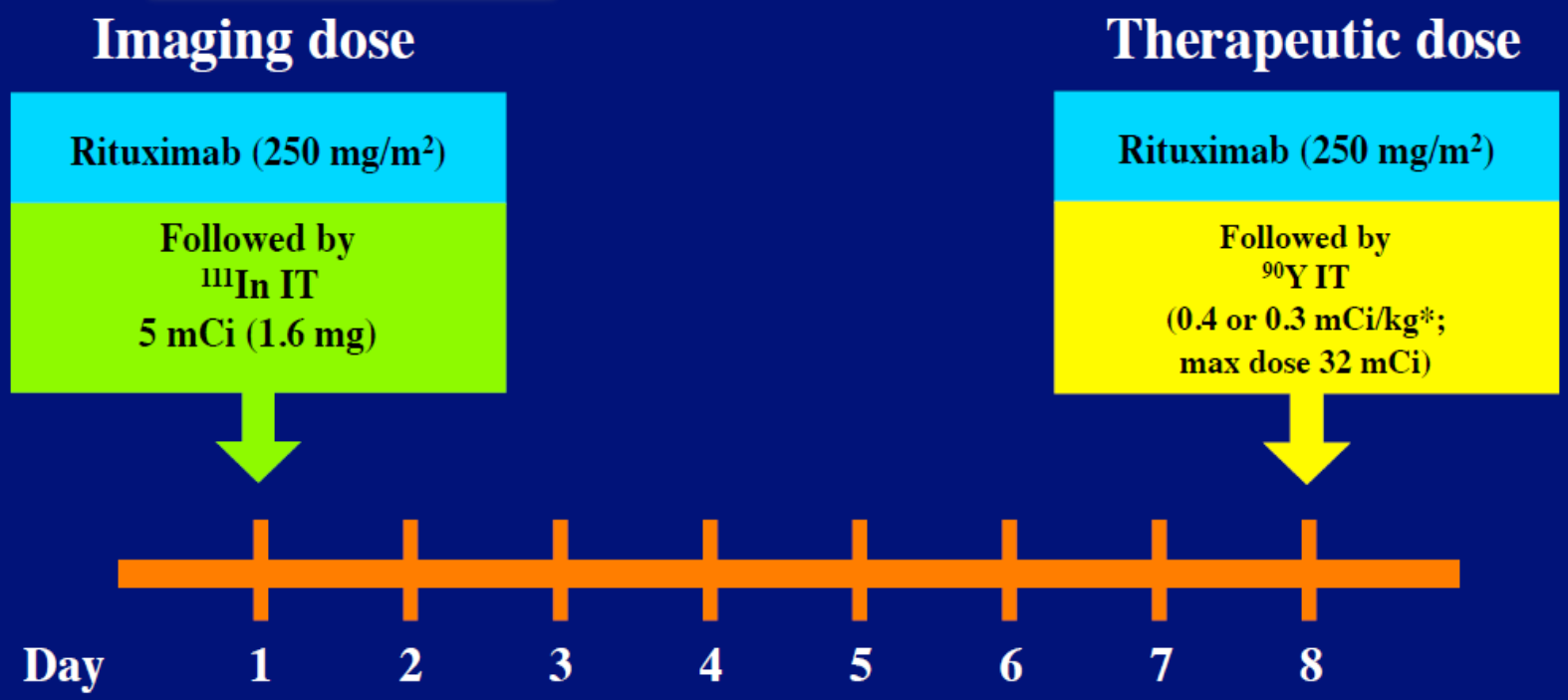
Grade ≥3 AEs (O-B vs B)

- Neutropenia (34.8% vs 27.1%)
- Thrombocytopenia (10.8% vs 15.8%)
- Anemia (7.4% vs 10.8%)
- Infusion-related reactions (9.3% vs 3.4%)

Serious AEs (O-B vs B): 43.6% vs 36.9%

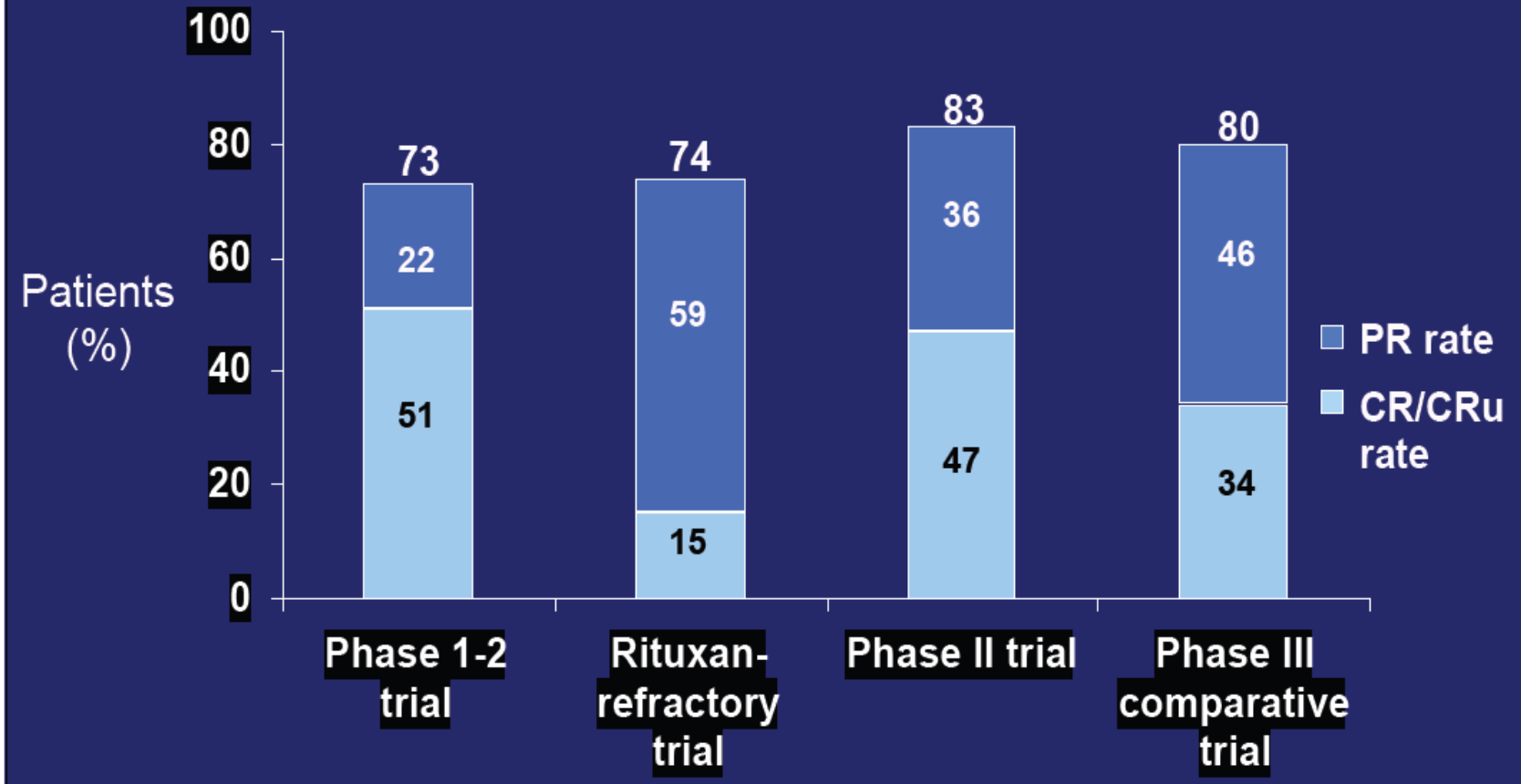
Cheson BD, et al. *J Clin Oncol.* 2018. [Epub ahead of print]. doi:10.1200/JCO.2017.76.3656

Y90 Ibritumomab Tiuxetan [redacted] Treatment Schema



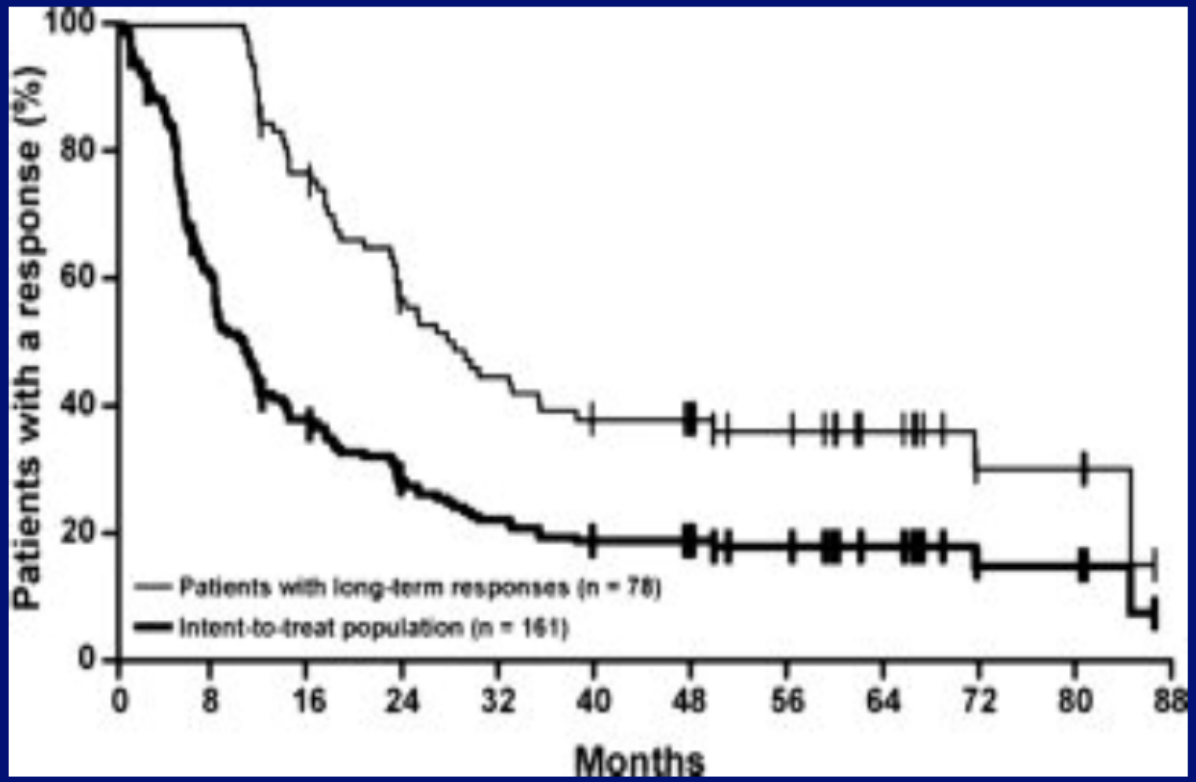
*0.4 mCi/kg in patients with a platelet count ≥150,000/μL or 0.3 mCi/kg with a platelet count 100,000–149,000/μL.

Overview of Y-90 Ibritumomab Tiuxetan Experience in Relapsed/Refractory B-Cell NHL



Gordon et al. *Blood*. 2004;103:4429–4431. Witzig et al. J Clin Oncol. 20:3262–3269. Wiseman et al. *Blood*. 2002;99:4336–4342. Witzig et al. J Clin Oncol. 2002;20:2453–2463.

Long-term responses in patients with recurring or refractory B-cell NHL treated with yttrium 90 ibritumomab tiuxetan



Witzig et al, Cancer 109, I 1804-,2007

Ibrutinib in R/R FL

- The DAWN trial was an open-label, multicenter, single-arm, phase 2 study of ibrutinib (560 mg) in patients with chemoimmunotherapy-refractory FL (N = 110)
  - Eligible patients had ≥ 2 prior lines of therapy with documented progressive disease within 12 mo after last dose of chemotherapy in a chemoimmunotherapy regimen comprising an anti-CD20 monoclonal antibody
- Median follow-up was 27.7 mo
- ORR by IRC was 20.9%, and CR rate was 10.9%, with a median DoR of 19.4 mo
  - ORR was 24.7% in patients with nonbulky disease (longest diameter ≤ 6 cm)
    - 24-mo OS was 63% (95% CI: 0.53, 0.72)
- DCR (CR + PR + stable disease for ≥ 6 mo) was 56.3%
- 7 patients had IRC-confirmed response when allowed to remain on therapy
- Median TTNT on ibrutinib was 16 mo compared with 10 mo on the last line of treatment before enrollment
- Median PFS was 4.6 mo
- Serious adverse effects were reported in 48.2% of patients, with major hemorrhage and atrial fibrillation occurring in 3.6% and 9.1%, respectively

Gopal AK, et al. ASH 2016. Abstract 1217.

Venetoclax
Bcl-2 Inhibitor

- Active in patients with R/R NHL, according to a phase 1 study (MCL = 28; FL = 29; DLBCL = 34, DLBCL-RT = 7; WM = 4; MZL = 3)
  - Doses received were ≤ 400 mg in 22 patients, 600 to 900 mg in 33 patients, and 1200 mg in 51 patients
- Further study of this agent, including in combination therapy to augment response rates and durability, is ongoing

Results (N = 106)	Patients with FL (n=29)
ORR,% (44% for all histological types)	38
PFS, mo (6 mo for all histological types)	11

AEs in all histologies:
- Grade 3 to 4 AE occurred in 56%, with the most common being anemia (15%), neutropenia (11%), and thrombocytopenia (9%)
- Serious AEs occurred in 25%

Davids MS, et al. *J Clin Oncol.* 2017;35:826-833.

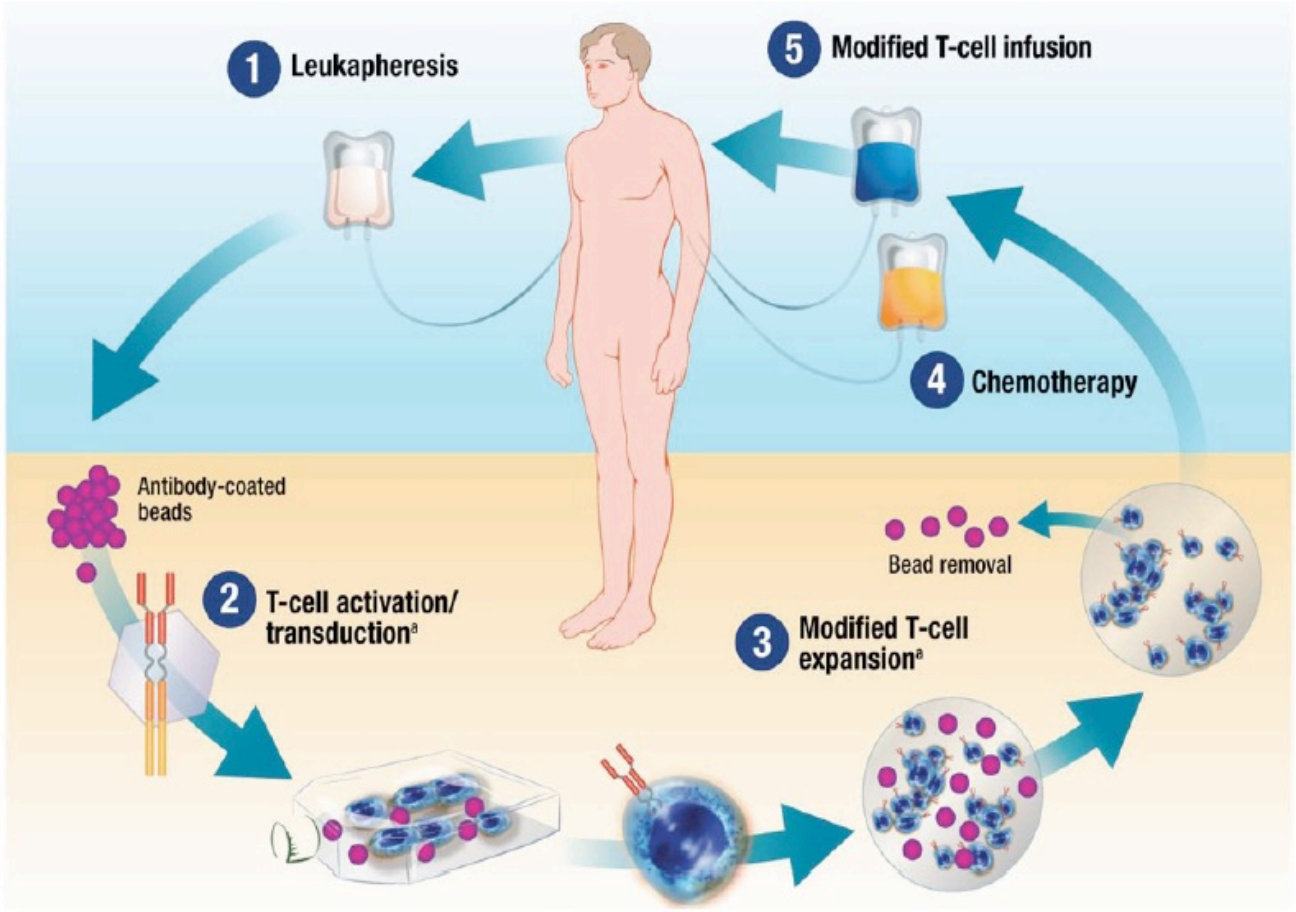
Checkpoint Inhibitors for FL

- 2 main pathways, the CTLA-4 and PD-1, have emerged as key targets of checkpoint blockade therapy, showing unprecedented activity in heavily pretreated R/R HL and some forms of NHL
  - Modest response rates in low-grade lymphomas
  - Need for further studies to look at combination with IMIDs or monoclonal antibodies

Agent	Disease Type, (n)	Response, %
Ipilimumab[a] (CTLA-4)	R/R NHL: FL (14), DLBCL (3), MCL (1)	ORR 11 CR 5.6 PR 5.6
Pidilizumab (PD-1) + rituximab[b]	R/R FL (32)	ORR 66 CR 52 PFS 18.8 mo
Nivolumab[c]	R/R B-NHL (31)	ORR 36 to 40

a. Ansell SM, et al. *Clin Can Res*. 2009;15:6446-6453; b. Westin JR, et al. *Lancet Oncol*. 2014;15:69-77;
c. Lesokhin AM, et al. *J Clin Oncol*. 2016; 34:2698-2704.

Overview of CTL019 Therapy



T cells transduced ex vivo with a lentivirus encoding anti-CD19 scFv linked to 4-1BB and CD3-ζ signaling domains

CAR-T IN R/R FL

	Kochendefer JN (Blood 2012) NCI group	**FHCRC study Turtle CJ Sci Transl Med 2016**	**Phase II CTCL019 CAR University of Pennsylvania**
Conditioning regimen	Cyclophosphamide/ Fludarabine	CD4/CD8 ratio 1:1	Bendamustine Cyclophosphamide RT+ Cyclophosphamide Fluda/Cyclophosphamide
N° patients **Patient characteristics** **Prior therapies**	4	6 (5 evaluable)	14 Refractory Median 5 lines Post autologousHCT 21% Post allogenicHCT 1
Response to therapy	75% PR	ORR 80% (2/5) CR 40%	ORR 79% (3-month) CR 50% PFS not reached FU 28.6 months 70% disease free

Grazie per l'attenzione!