

Novel Therapeutics for Waldenström Macroglobulinemia February 26

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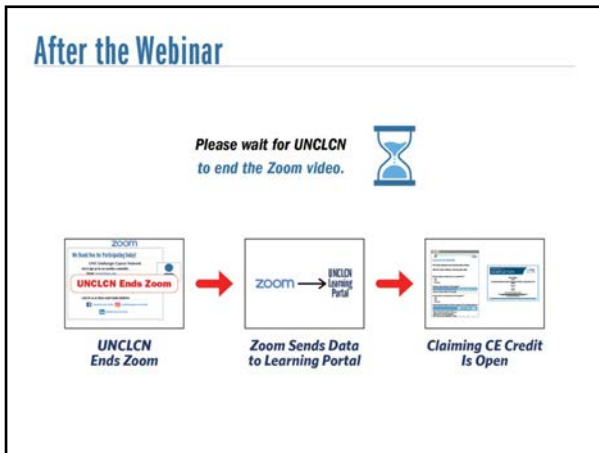
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Our Presenter



Christopher Dittus, DO, MPH

Christopher Dittus, DO, MPH, specializes in the diagnosis and management of all types of lymphoma, but he is particularly interested in rare lymphomas such as Waldenström macroglobulinemia, primary central nervous system lymphoma, and virus-associated lymphomas. Dr. Dittus is a clinical researcher and specializes in investigator-initiated clinical trials aimed at rare lymphomas and underserved populations. Dr. Dittus is currently active in the Waldenström research community and is listed in the International Waldenström's Macroglobulinemia Foundation Directory of Physicians, participated in the 12th International Workshop on Waldenström's Macroglobulinemia, and is active in the Waldenström's Macroglobulinemia clinical trials network. He also served as the AIDS Malignancy consortium UNC site PI for over 5 years.

Dr. Dittus completed medical school at the New York College of Osteopathic Medicine. He trained in internal medicine at Lenox Hill Hospital in New York City, where he also served as Chief Resident. Following his internal medicine training, Dr. Dittus completed a fellowship in hematology and oncology at Boston University Medical Center, where he served as Chief Fellow. After completing his training, he moved to North Carolina to take his current faculty position at the University of North Carolina at Chapel Hill. He is currently an Associate Professor of Medicine in his 9th year as faculty.

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Sample Poll Everywhere Question

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Disclosures

ACCME:
This activity has been planned and implemented under the sole supervision of the Course Director, Stephanie Wheeler, PhD, MPH, in association with the UNC Office of Continuing Professional Development (CPD). The course director received research support from AstraZeneca (ended June 2023) and Pfizer Medical Foundation (ended December 2023). These financial relationships have been mitigated. CPD staff have no relevant financial relationships with ineligible companies as defined by the ACCME.

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Waldenström's macroglobulinemia (WM) is an uncommon blood cell cancer that originates from malignant B-cells.

True 0%



False 0%

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Novel Therapeutics for Waldenström Macroglobulinemia



Christopher Dittus, DO, MPH
Associate Professor of Medicine
February 26, 2025
Chris_dittus@med.unc.edu

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Overview

- Case Presentation
- Background
- Diagnosis and Workup
- Treatment



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Case Presentation



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WM Case



- 53y M p/w headache, weight loss, and cervical LAD
- ECOG: 0
- Lab could not obtain a value for his CBC. Lab noted plasma was thick and smear showed diffuse rouleaux formation
- Primary oncologist was c/f hyperviscosity and transferred to UNC



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WM Case Continued

- At UNC, a serum viscosity returned at 5
- An IgM level was obtained and was >8g
- CBC showed WBC 5.6; Hg 7.3; and platelets 348
- Transfusion medicine consulted for Plasma Exchange (PLEX)



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Background





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WM Background

- Indolent B-Cell NHL with IgM Paraprotein
- Primary site is the bone marrow
- MC in older, white males
- Rare: ~2000 cases/year in US



McMaster, Sem Hematol, 2023
Treon. NEJM 2012



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WM Incidence

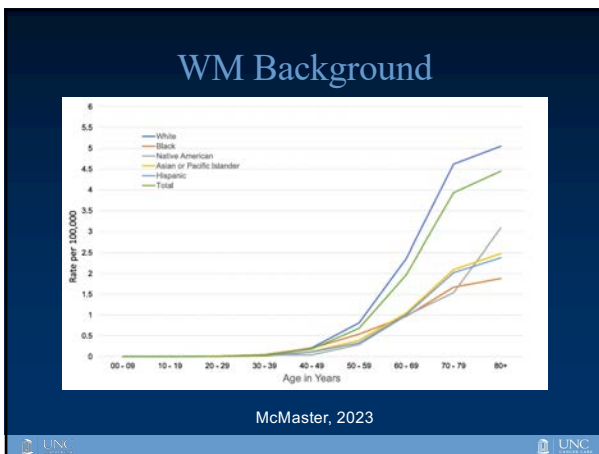
SUBTYPE*	ICD-O-3 CODES	INCIDENCE RATE*, 2011-2012	ESTIMATED NEW CASES, 2016
25a) 2.1. Chronic/Small/Polymorphocytic/Mantle B-cell non-Hodgkin lymphoma		5.9	24,420
25a) 2.1.1. Chronic lymphocytic leukemia/small lymphocytic lymphoma	9670, 9623	5.1	20,980
25a) 2.1.2. Polymorphocytic leukemia, B-cell	963201, 9633	<0.1	120
25a) 2.1.3. Mantle cell lymphoma	9673	0.8	3,320
25a) 2.2. Lymphoplasmacytic lymphoma, including Waldenström macroglobulinemia	9671, 9761	0.6	2,330
25a) 2.2.1. Lymphoplasmacytic lymphoma	9671	0.3	1,060
25a) 2.2.2. Waldenström macroglobulinemia	9761	0.3	1,270
25a) 2.5. Marginal zone lymphoma		1.8	7,460
25a) 2.5.1. Splenic marginal zone lymphoma	9689	0.2	640
25a) 2.5.2. Extranodal marginal zone lymphoma	9699 (excluding C77.0-77.9)	1.1	4,450
25a) 2.5.3. Nodal marginal zone lymphoma	9699 (C77.0-77.9)	0.6	2,370
25a) 2.6. Follicular lymphoma		3.4	13,960
25a) 2.6.1. Primary cutaneous follicle center lymphoma	9597, 9690 (C44.0-44.9)	0.1	430
25a) 2.6.2. Follicular lymphoma NOS	9691, 9695, 9698	3.3	13,530

Teras, Cancer Journal, 2016

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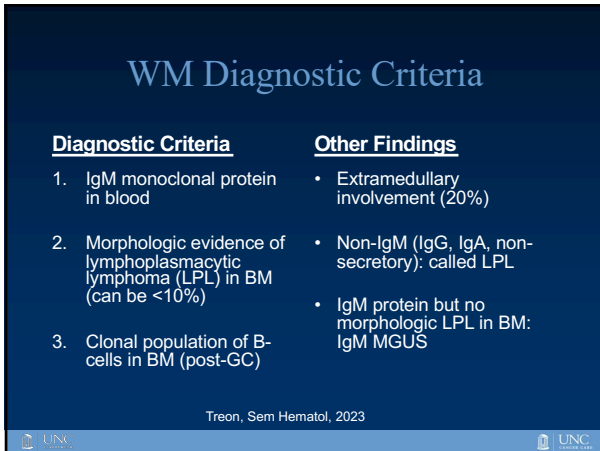
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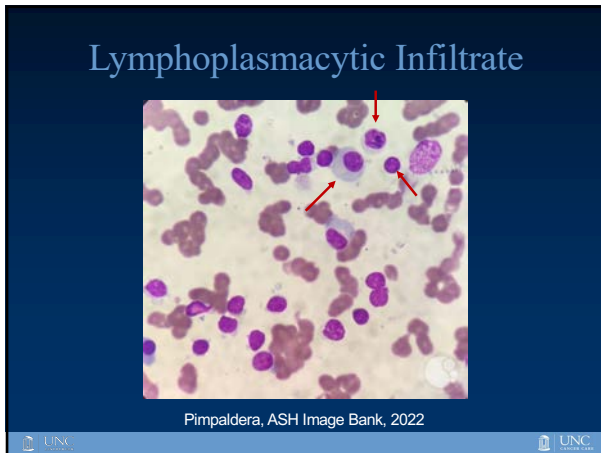
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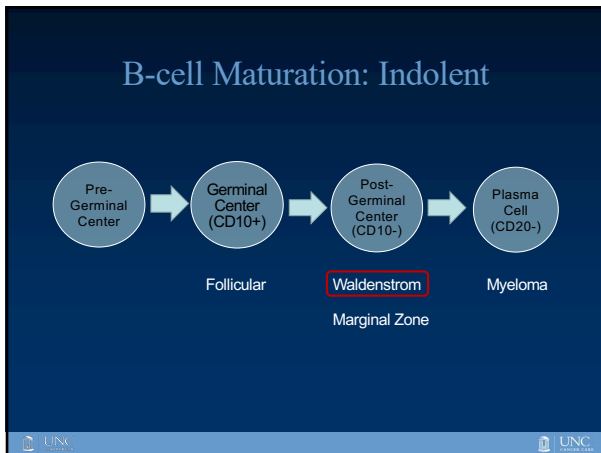
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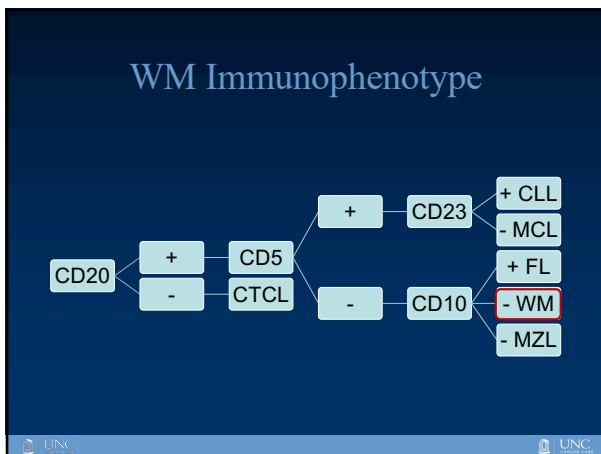
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Molecular Testing

- *MYD88*^{L256P} mutation via PCR
 - Present in 96% of WM (other 4% is a different *MYD88* mutation)
 - Present in about 90% of IgM MGUS
 - Rare in myeloma and other NHL (except immune-privilege sites)
- *CXCR4* mutation
 - Found in 30-40% of WM
 - a/w symptomatic hyperviscosity and shorter time to first tx
 - a/w response to ibrutinib (wild type=better response)
- *TP53* mutation
 - Prognostic importance
 - Possible impact on treatment



Garcia-Sanz, Sem Hematol, 2023

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WM Case Continued

- Pt had further workup completed while arranging for PLEX treatment:
 - SPEP/IFE: IgM Kappa; M-spike: 6g
 - Kappa FLC: 3.3; K/L FLC was 4.29
 - CT Imaging showed cervical, axillary and mediastinal LAD
 - BM Biopsy: 50% LPL by morphology; flow+ for clonal B-cells; MYD88+

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The patient meets the following WM diagnostic criteria:

IgM paraprotein	0%
LPL on bone marrow morphology	0%
Clonal B-cell population in bone marrow	0%
All of the above	0%

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WM Workup: Specific Situations

- **Hyperviscosity:**
 - Urgent/Emergent indication for treatment
 - Neurologic evaluation w/ Brain MRI, Refinal Exam
 - Serum Viscosity
- **Neuropathy:**
 - Neurologic evaluation with EMG testing
 - MAG and Ganglioside Ab testing
- **Renal failure:**
 - Nephrology evaluation
 - Renal biopsy
- Cold agglutinins (hemolysis) and Cryoglobulins
- Amyloid workup if clinically indicated

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Ann Arbor/Lugano Staging

Revised staging system for primary nodal lymphomas (Lugano classification)

Stage	Involvement	Extranodal (E) status
Limited		
I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky*	II as above with "bulky" disease	Not applicable
Advanced		
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

Extent of disease is determined by positron emission tomograph/computed tomography (PET/CT) for avid lymphomas and CT for nonavid histologies. Testis, Waldeyer's ring, and spleen are considered nodal tissue.

* Whether stage II bulky disease is treated as limited or advanced disease may be determined by histology and a number of prognostic factors.

Cheson et al, JCO, 2014

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Prognosis: rIPSSWM

Table 2 Assignment of points for the formulation of the revised staging system

Point
Age < 65
Age 66-75
Age > 75
β2-microglobulin > 4 mg/L
LDH > 250 IU/L
Serum albumin < 3.5 g/dL

Table 3 Revised ISSWM categories, patient disposition, and outcomes per stage in the derivation cohort

Stage	Score	% of patients	3-year WM related mortality	3-year OS	10-year OS
Very low	0	33%	0%	95%	84%
Low	1	33.5%	30%	86%	59%
Intermediate	2	25.5%	14%	78%	37%
High	3	16%	38%	47%	19%
Very high	4-5	12%	48%	36%	9%

Category	6	9	12	15	18	21
Very Low	64	62	60	24	14	7
Low	165	150	101	62	15	9
Intermediate	226	181	56	28	12	3
High	79	50	29	15	5	0
Very High	58	24	12	5	5	0

Kastritis, Leukemia, 2019

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Front-Line Therapy

Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial

Mathias J Rummel, Norbert Niederle, Georg Maschmeyer, G Andre Bonat, Ulrich von Ginneken, Christoph Lorenz, Dorothea Kijak-Krause

Phase III
N=514
BR x6
RCHOPx6

Rummel et al, Lancet, 2013

49

Table 1: Histology

	B-R (n=261)	CHOP-R (n=253)
Age (years)		
<60	64 (24.5%)	63 (24.9%)
61-70	107 (41.0%)	105 (41.5%)
>70	90 (34.5%)	85 (33.6%)
Stage		
II	9 (3.4%)	9 (3.5%)
III	50 (19.2%)	47 (18.6%)
IV	202 (77.4%)	197 (77.9%)
Histology		
Follicular	139 (53.3%)	140 (55.3%)
Mantle cell	46 (17.6%)	48 (18.9%)
Marginal zone	37 (14.2%)	30 (11.8%)
Lymphoplasmacytic*	22 (8.4%)	19 (7.5%)
Small lymphocytic	10 (3.8%)	11 (4.3%)
Low grade, unclassifiable	7 (2.7%)	5 (2.0%)

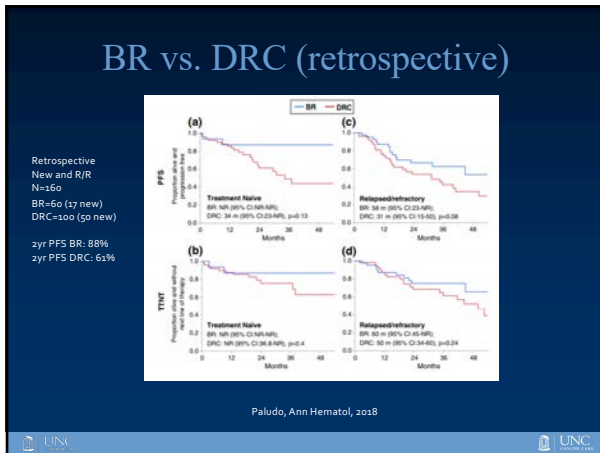
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BR vs. R-CHOP

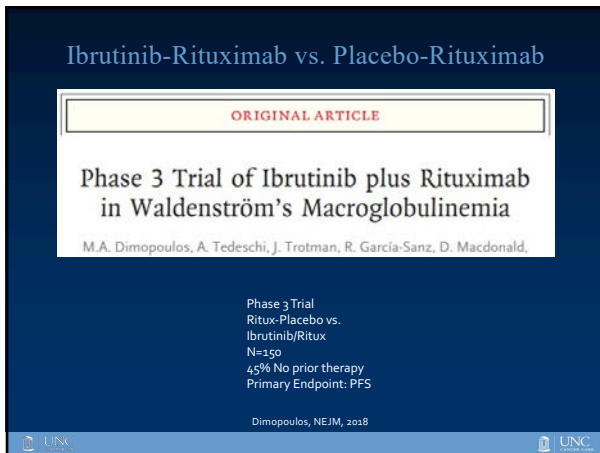
N=31 with LPL/WM

Rummel et al, Lancet, 2013

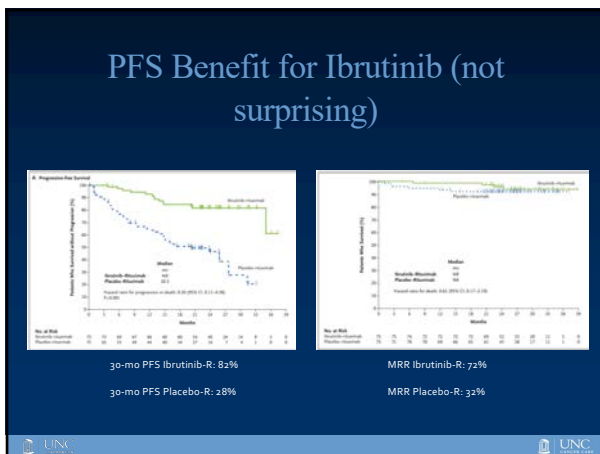
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CLINICAL TRIALS AND OBSERVATIONS

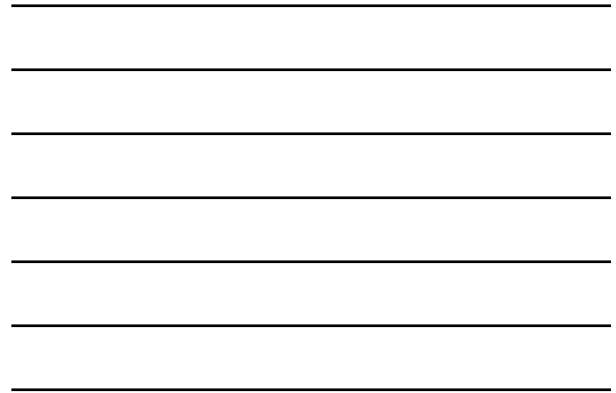
A randomized phase 3 trial of zanubrutinib vs ibrutinib in symptomatic Waldenström macroglobulinemia: the ASPEN study

Constantine S. Tam,^{1*} Stephen Cpat,^{1,2} Shirley D'Sa,³ Wojciech Jurczak,⁴ Hui-Peng Lee,⁵ Gavin Cull,^{6,7,8} Roger G. Owen,^{9,10} Paula Marlow,^{11,12}

- Randomized, Phase III
- N=201
- MYD88 mutated
- ≥1 prior tx (~80%) or tx naive but not eligible for chemo
- Primary Endpoint: CR or VGPR
- Excluded: prior BTK, CNS, transformed.

Tam, Blood, 2021

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Response Rates

Table 2. OR-assessed efficacy outcomes

	IBR		ZAN		Overall	
	Response (n = 81)	Response (n = 120)	Response (n = 120)	Response (n = 120)	Response (n = 199)	Response (n = 102)
Best overall response, n (%)						
CR	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
VGPR	14 (17)	24 (20)	3 (2)	5 (4)	19 (10)	29 (28)
PR	49 (61)	41 (34)	9 (8)	9 (8)	58 (29)	50 (49)
MR	11 (14)	13 (11)	4 (3)	4 (3)	19 (10)	17 (17)
SD	2 (3)	3 (2)	1 (1)	0 (0)	3 (2)	3 (3)
PD	2 (3)	1 (1)	0 (0)	1 (1)	2 (1)	2 (2)
Not evaluable ^a	1 (1)	1 (1)	1 (1)	0 (0)	2 (1)	1 (1)
Response rates, % (95% CI)						
VGPR or CR	14 (17)	24 (20)	3 (2)	5 (4)	19 (10)	29 (28)
CR	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
PR	49 (61)	41 (34)	9 (8)	9 (8)	58 (29)	50 (49)
MR	11 (14)	13 (11)	4 (3)	4 (3)	19 (10)	17 (17)
SD	2 (3)	3 (2)	1 (1)	0 (0)	3 (2)	3 (3)
PD	2 (3)	1 (1)	0 (0)	1 (1)	2 (1)	2 (2)
Not evaluable ^a	1 (1)	1 (1)	1 (1)	0 (0)	2 (1)	1 (1)
Duration of CR/VGPR, mo						
Median (range)	82 (15-108)	78 (68-87)	47 (31-67)	74 (68-81)	78 (68-86)	77 (68-85)
CR	94 (96-98)	84 (87-90)	89 (83-95)	95 (94-100)	93 (88-97)	94 (88-98)
Duration of major response, months						
Median (range)	86 (51-281)	86 (51-281)	86 (51-281)	86 (51-281)	86 (51-281)	86 (51-281)
18 Mo overall rate, % (95% CI)	84 (79-89)	80 (75-85)	86 (81-91)	86 (81-91)	84 (79-89)	80 (75-85)
PFS						
Median (range), mo	86 (51-281)	86 (51-281)	86 (51-281)	86 (51-281)	86 (51-281)	86 (51-281)
18 Mo overall rate, % (95% CI)	82 (77-87)	84 (79-89)	84 (79-89)	84 (79-89)	84 (79-89)	80 (75-85)

Tam, Blood, 2021

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CR/VGPR:
Ibr-19%
Zanu-28%
P=0.09

At 18mo
PFS:
84 and
85%



Zanubrutinib vs Ibrutinib

A

HR (95% CI)	0.846 (0.425, 1.759)
Likelihood ratio test P-value	.6874

Tam, Blood, 2021

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WM Case Continued

- The patient was treated with bendamustine alone and discharged to clinic for further treatment.
- He received 2 cycles of bendamustine before his IgM decreased <4g.
- At this point, rituximab was added to bendamustine for the remaining 4 cycles

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End of Treatment Workup

- Serum IgM decreased from 8g to 1.8g (78% reduction)
- SPEP still positive for IgM kappa clone
- BM Bx shows 20% LPL involvement (down from 50%)
- PET is negative for LAD

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Based on the patient's end-of-treatment workup, he achieved a:

Complete Response (CR)	0%
Very Good Partial Response (VGPR)	0%
Partial Response (PR)	0%
Progressive Disease (PD)	0%

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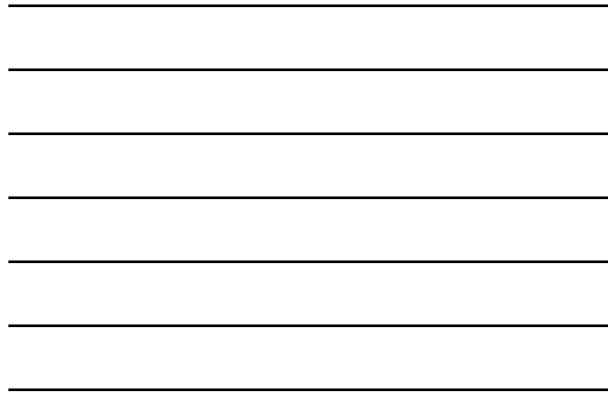
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Regimens for Relapsed LPL/WM

- **Chemotherapy (if not previously used):**
 - BR, DRC
- **Covalent BTK Inhibition (if not previously used):**
 - Zanubrutinib or ibrutinib
- **Noncovalent (Reversible) BTK Inhibition:**
 - Pirtobrutinib (can be used if prior BTK)
- **Proteasome Inhibition:**
 - CaRD (carfilzomib): ORR: 87%; CR/VGPR: 36%
 - IDR (ixazomib): ORR 96%, MRR 77%, 18-mo PFS 90%
 - BDR (bortezomib)
- **BCL2 Inhibition:**
 - Venetoclax

Trean, Blood, 2014;
Castillo, Blood Adv, 2020

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Pirtobrutinib in relapsed or refractory B-cell malignancies (BRUIN): a phase 1/2 study

Mato, Lancet, 2021

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	Number of Sites	Number of Patients	Treated Patients	ORR (%)	Response rate
Chronic lymphocytic leukemia and small lymphocytic lymphoma					
All patients	3 (3-10)	176	139	88	83% (52-79)
Multiple myeloma					
All patients	4 (3-10)	146	139	75	67% (53-77)
With at least 1 prior BTKi	5 (4-7)	57	48	35	31% (21-38)
With at least 2 prior BTKi	4 (3-6)	36	30	48	34% (21-51)
With at least 3 prior BTKi	5 (4-7)	54	45	79	64% (49-78)
With at least 4 prior BTKi	4 (3-6)	33	28	43	37% (24-54)
With at least 5 prior BTKi	5 (4-7)	48	39	27	19% (12-28)
With at least 6 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 7 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 8 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 9 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 10 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 11 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 12 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 13 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
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With at least 15 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 16 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
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With at least 18 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 19 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 20 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 21 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 22 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 23 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 24 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 25 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 26 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 27 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 28 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 29 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 30 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 31 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 32 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 33 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 34 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 35 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 36 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 37 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 38 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 39 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 40 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 41 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 42 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 43 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 44 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 45 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 46 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 47 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 48 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 49 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 50 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 51 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 52 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 53 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 54 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 55 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 56 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 57 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 58 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 59 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 60 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 61 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 62 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 63 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 64 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 65 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 66 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 67 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 68 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 69 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 70 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 71 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 72 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 73 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 74 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 75 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
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With at least 85 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 86 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 87 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 88 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 89 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 90 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 91 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 92 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 93 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 94 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 95 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 96 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 97 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 98 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 99 prior BTKi	4 (3-6)	34	27	7	2% (0-16)
With at least 100 prior BTKi	4 (3-6)	34	27	7	2% (0-16)

Mato, Lancet, 2021

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Efficacy of Pirtobrutinib, a Highly Selective, Non-Covalent (Reversible) BTK Inhibitor in Relapsed / Refractory Waldenström Macroglobulinemia: Results from the Phase 1/2 BRUIN Study

M.Lia Palomba, Manish R. Patel, Toby A. Eyre, Wojciech Jurczak, David John Lewis, Thomas Gastinne, Shuo Ma, Jonathon B. Cohen

- N=78 (72 evaluable); 78% prior BTKi
- Major Response Rate: 68%
 - 17 VGPR (24%), 32 PR (44%)
- MRR (prior BTKi) was 64% (13 VGPR, 28 PR)
- Toxicity: fatigue, diarrhea

Palomba, Blood, 2022

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Venetoclax in Previously Treated Waldenström Macroglobulinemia

- Phase II trial
- N=32; 16 w/ prior BTKi
- Venetoclax 200mg→800mg (up to 2 yrs)
- All MYD88 mutated

Castillo, JCO, 2021

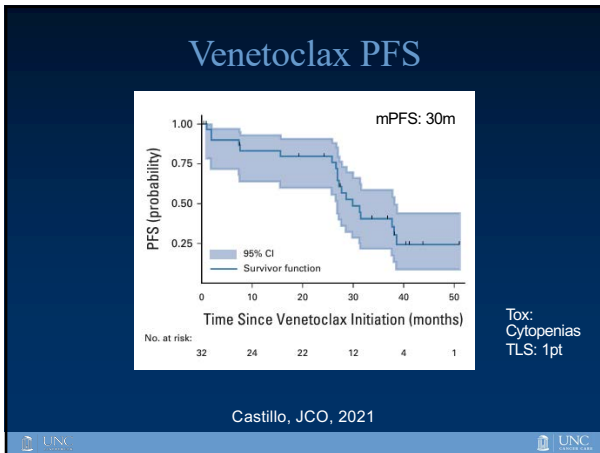
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Venetoclax Response Rates

ORR: 84%
MRR: 80%
VGPR: 19%

Castillo, JCO, 2021

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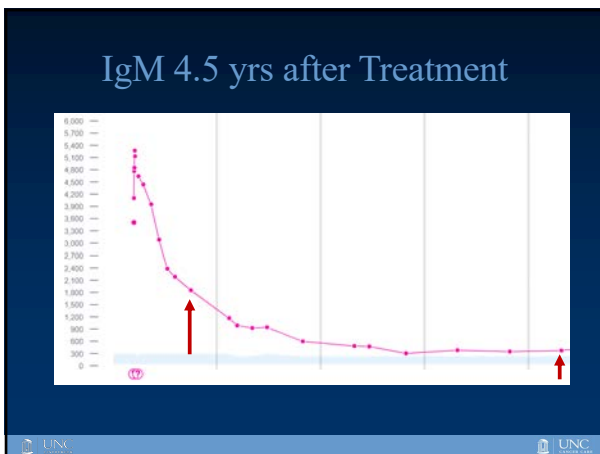


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WM Case Continued

- Patient is now 4.5 years out from completing treatment.
- His CBC is normal, and he is asymptomatic
- His IgM is down to 370, improving his response to a VGPR

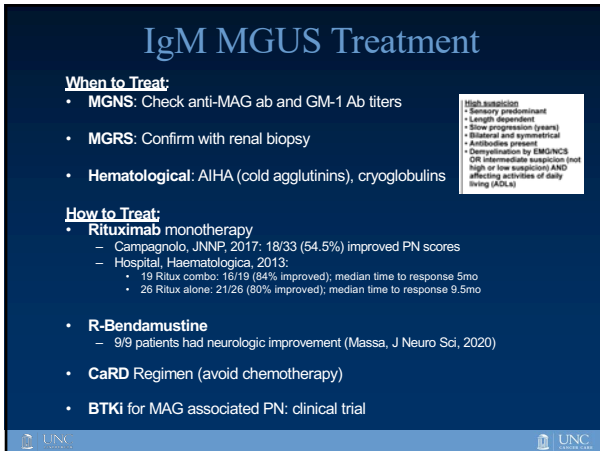
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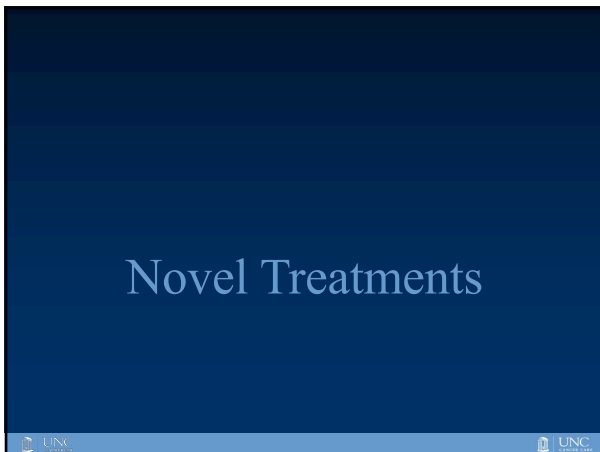
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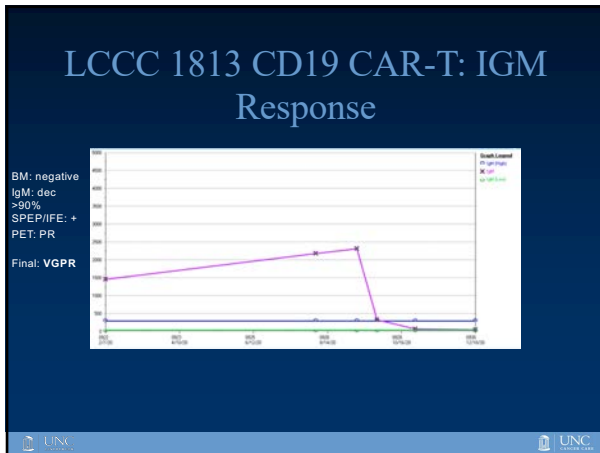
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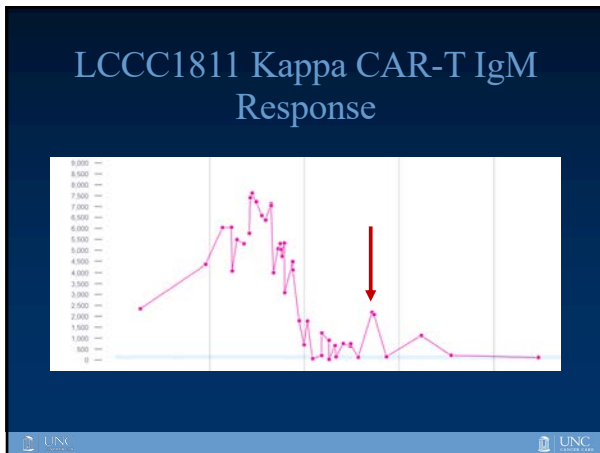
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WM IIT: Bispecific Antibody



- A Phase 2 Trial Investigating Epcoritamab (CD20+CD3) in Patients with Previously Treated Waldenstrom Macroglobulinemia (WM) (NCT06510491)
- Primary Site: BIDMC
- PI: Gottfried von Keudell
- Opening at UNC 3/2025

UNC

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BTK Degraders



- NX-5948 studied in 30 pts w/ CLL:
 - ORR 76.7%
 - Shah, ASH, 2024
- NX-5948 reported in 9 pts w/ WM:
 - 7 of 9 had objective responses
 - More data needed



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Clinical Trials



- BTK Degradar study for WM specifically
- Loncastuximab for WM (open at DFCI)
- Bispecific antibodies (opening at UNC)
- CAR-T (2 studies open at UNC)



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WM Treatment Summary

- Consider Clinical Trial for any pt requiring treatment
- Frontline: BR vs Zanubrutinib vs Surveillance
- 2nd Line: Zanubrutinib vs BR
- 3rd Line: Pirtobrutinib vs Venetoclax



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WM Research and Advocacy Groups

- WM-NET Clinical Trial Group
- 12th International Workshop on Waldenström's Macroglobulinemia (IWWM)
- International Waldenström's Macroglobulinemia Foundation (IWWMF)




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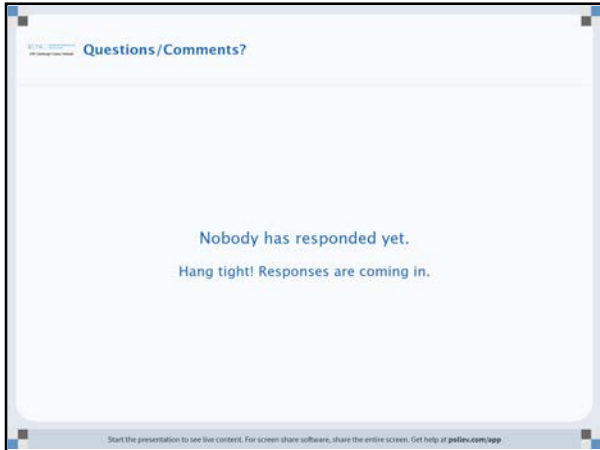
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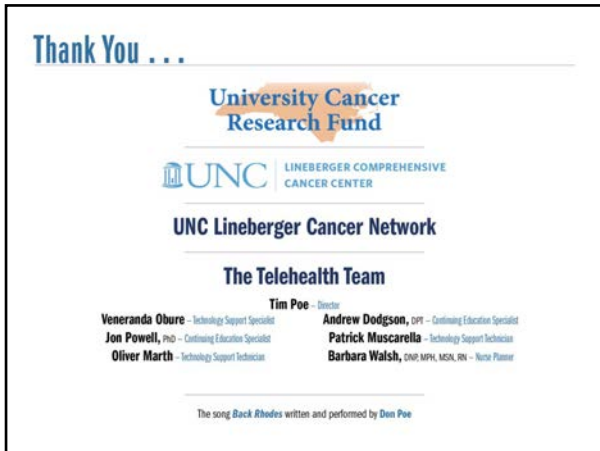
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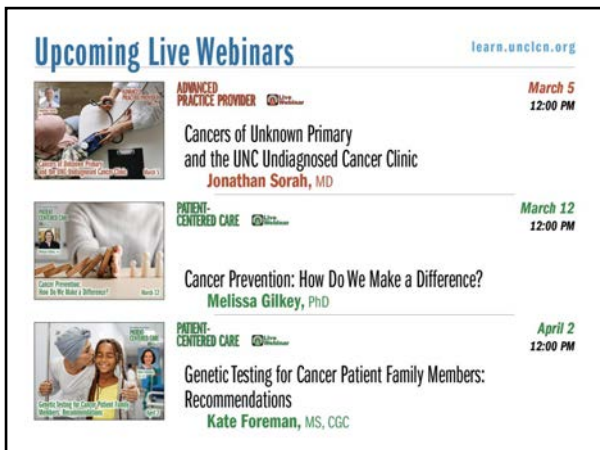

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