Patterns of Care in Medical Oncology

Follicular Lymphoma

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CASE 1: ***A 72-year-old man with multiple comorbidities including COPD/asthma presents with slowly progressive cervical adenopathy. Bone marrow biopsy is positive and the patient is diagnosed with Stage IV Grade I follicular lymphoma (FL) with a FLIPI score of 3 (nodal sites, age and stage).***

The patient receives weekly rituximab (R) x 4, achieves a complete response and subsequently receives R maintenance every 2 months for 4 cycles (SAKK regimen). Treatment is well tolerated.

Three years later, CT reveals new adenopathy in his chest, at which point he again receives rituximab weekly x 4, which results in a complete response. He then receives maintenance rituximab, again on the SAKK schedule.

— Jonathan W Friedberg, MD, MMSc
Rochester, New York

Of your patients with newly diagnosed FL, approximately what percent present with few or no symptoms? (Median)

Of your patients with FL for whom you recommend observation, approximately what percent have a difficult time accepting the approach? (Median)

	CI	PO
% of patients	20%	40%

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Which of the following statements applies to you as it relates to your approach to FL during the past 2 to 3 years?

	CI	PO
Recommend observation a lot less, R monotherapy more	4%	12%
Recommend observation somewhat less, R monotherapy more	25%	35%
No change	67%	45%
Recommend observation somewhat more, R monotherapy less	0%	1%
Recommend observation much more, R monotherapy less	4%	3%
I have not recommended R monotherapy	0%	4%

How would you compare your approach to initial induction therapy for FL today to your approach 2 to 3 years ago?

	CI	PO
Somewhat different	56%	44%
About the same	24%	46%
Very different	20%	10%

What is currently your usual preferred regimen for a patient with FL who requires initial treatment?

	58-year-old		75-year-old	
	CI	PO	CI	PO
R-CHOP	48%	32%	4%	5%
R-bendamustine	32%	36%	72%	34%
R-CVP	16%	26%	16%	32%
R-fludarabine	0%	3%	0%	4%
Rituximab monotherapy	0%	1%	4%	24%
Other	4%	2%	4%	1%

Efficacy data from the Phase III study comparing bendamustine/rituximab (BR) to R-CHOP in the front-line treatment of indolent lymphomas

	Overall response	Complete response	PFS (all patients)	PFS (patients with FL)
BR (n = 260 all patients, n = 143 FL only)	92.7%	39.6%	54.9 months	Not reached
R-CHOP (n = 253 all patients, n = 142 FL only)	91.3%	30.0%	34.8 months	46.7 months
Hazard ratio	—	—	0.57	0.63
p-value	Not reported	0.0262	0.00012	0.0281

Rummel MJ et al. *Proc ASH* 2009;Abstract 405.

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Safety data from the Phase III study comparing bendamustine/rituximab (BR) to R-CHOP in the front-line treatment of indolent lymphomas

Grade 3/4	Leuko-penia	Neutro-penia	G-CSF administration	Anemia	Thrombo-cytopenia
BR (n = 1,450) (% of cycles)	12.1%	10.7%	4.0%	1.4%	0.7%
R-CHOP (n = 1,408) (% of cycles)	38.2%	46.5%	20.0%	1.9%	1.2%
p-value	<0.0001	<0.0001	<0.0001	Not reported	Not reported

Rummel MJ et al. ASCO/ASH 2010 Joint Session.

How would you compare your approach to maintenance rituximab therapy after R/chemotherapy induction for FL today to your approach 2 to 3 years ago?

	CI	PO
More likely to use	68%	52%
About the same	28%	46%
Less likely to use	4%	2%

Do you currently use rituximab maintenance for patients receiving R/chemotherapy as front-line induction for FL?

	CI	PO
Yes, always or almost always	36%	53%
Yes, sometimes	36%	32%
Yes, rarely	20%	7%
No	8%	8%

Phase III PRIMA study: Efficacy results with rituximab maintenance after induction R/chemotherapy in previously untreated FL

	Observation (n = 513)	Rituximab maintenance (n = 505)	Hazard ratio	*p*-value
Two-year PFS	66%	82%	0.50	<0.0001

PFS = progression-free survival

Salles GA et al. *Proc ASCO* 2010;Abstract 8004.

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Which one of the following R maintenance regimens do you generally use?

	CI	PO
1 dose every 3 months for 2 years	39%	32%
1 dose every 8 weeks for 2 years	35%	16%
1 dose every 2 months for 4 cycles	13%	1%
4 weekly doses every 6 months for 2 years	9%	41%
1 dose every 3 months until disease progression	4%	10%

Which of the following best describes how long you generally recommend that R maintenance be administered?

	CI	PO
2 years	83%	74%
1 to <2 years	9%	13%
<1 year	4%	3%
Indefinitely (until disease progression)	4%	9%
Other	0%	1%

CASE 2: ***A 70-year-old man initially diagnosed in 2002 with FL achieves remission with R-CHOP x 6. One year later, he receives rituximab monotherapy for recurrent disease. Over the subsequent 6 years he experiences multiple relapses and receives immunotherapies and IMiD® therapies on and off protocol. Six months after receiving lenalidomide he experiences disease recurrence and receives ibritumomab tiuxetan.***

Radioimmunotherapy leads to a 1-year complete response. The patient then receives bendamustine with good partial remission.

— Mitchell R Smith, MD, PhD
Philadelphia, Pennsylvania

In your practice, is a nuclear medicine specialist or radiation oncologist with expertise in delivering radioimmunotherapy accessible to you for patient referral/consultation?

	CI	PO
Yes, a nuclear medicine specialist	76%	20%
Yes, a radiation oncologist	4%	32%
Yes, both	20%	15%
No	0%	33%

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In the past year, have you administered the following to your patients with NHL?

	% responding yes	
	CI	**PO**
Ibritumomab tiuxetan (Zevalin®)	**76%**	**43%**
I 131 tositumomab (Bexxar®)	**60%**	**17%**

Median number of patients

	CI*	PO*
Ibritumomab tiuxetan (Zevalin)	**2**	**2**
I 131 tositumomab (Bexxar)	**3**	**2**

*** Zevalin – CI n = 19; PO n = 43**
Bexxar – CI n = 15; PO n = 17

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If you do not use radioimmunotherapy in your practice, which of the following best describes your reason for not doing so?

	CI	PO
I am not confident in its current utility in the treatment algorithm	75%	31%
It is logistically impractical	25%	50%
Reimbursement issues	0%	6%
Other	0%	13%

CI n = 4; PO n = 52 participants who have not used radioimmunotherapy

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Randomized Phase III trial comparing R-CHOP to CHOP followed by tositumomab for the initial treatment of FL

Protocol ID: SWOG-SOO16

Target Accrual: 500

Eligibility

- Untreated FL
- Bulky Stage II or Stage III/IV
- Grade I to Grade III
- CD20-positive

R

- Rituximab[1] + CHOP x 6
- CHOP x 6 followed by tositumomab[2]

[1] A total of six doses of rituximab are administered.
[2] Two doses of tositumomab are administered after CHOP cycle 6.

www.clinicaltrials.gov. Identifier NCT00006721.

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In the past year, have you administered radioimmunotherapy as consolidation after R/chemotherapy with each of the following?

	% responding yes	
	CI	PO
Ibritumomab tiuxetan (Zevalin)	42%	58%
I 131 tositumomab (Bexxar)	47%	60%

Zevalin – CI n = 19, PO n = 40; Bexxar – CI n = 15, PO n = 15

Median number of patients

	CI*	PO*
Ibritumomab tiuxetan (Zevalin)	2	1
I 131 tositumomab (Bexxar)	2	1

* Zevalin – CI n = 8, PO n = 23; Bexxar – CI n = 7, PO n = 9

Are you aware of the consolidation data with ibritumomab tiuxetan?

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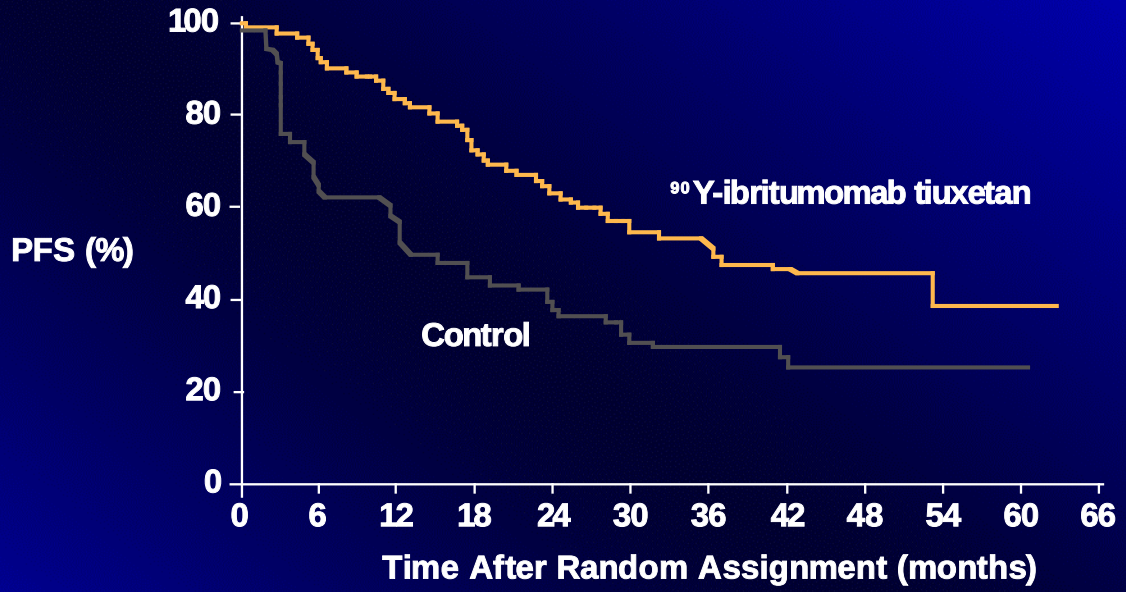
Phase III trial of consolidation therapy with yttrium-90-ibritumomab tiuxetan after first remission in advanced FL



	Ibritumomab tiuxetan (n = 208)	No additional therapy (n = 206)	Hazard ratio	*p*-value
Median PFS	36.5 months	13.3 months	0.465	<0.0001

Morschhauser F et al. **Phase III trial of consolidation therapy with yttrium-90–ibritumomab tiuxetan compared with no additional therapy after first remission in advanced follicular lymphoma.** *J Clin Oncol* 2008;26(32):5156-64**.** Reprinted with permission.

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When administering bendamustine either alone or with rituximab for the treatment of FL, what dose and schedule do you generally use?

	Patients age 65 or younger		Patients older than age 65	
	CI	PO	CI	PO
90 mg/m^2 IV on days 1 and 2 every 28 days	76%	24%	88%	45%
90 mg/m^2 IV on days 1 and 2 every 21 days	8%	21%	12%	26%
120 mg/m^2 IV on days 1 and 2 every 21 days	8%	26%	0%	11%
120 mg/m^2 IV on days 1 and 2 every 28 days	0%	19%	0%	8%
I have not administered bendamustine for patients with FL	8%	10%	0%	10%
	CI n = 25; PO n = 98		CI n = 25; PO n = 96	

When using bendamustine alone or with rituximab for FL, how many cycles do you generally administer?

	CI	PO
6 cycles	96%	77%
Until disease progression or development of unacceptable side effects	4%	4%
8 cycles	0%	19%

CI n = 25; PO n = 93

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How would you compare the efficacy and safety of R-bendamustine and R-CHOP in the front-line treatment of FL?

	CI	PO
R-bendamustine is less toxic and more efficacious	52%	19%
R-bendamustine is less toxic and equally efficacious	36%	55%
R-CHOP and R-bendamustine have comparable efficacy and toxicity	4%	16%
R-CHOP is more toxic and more efficacious	4%	10%
Other	4%	0%

What is your response when a patient being considered for R-bendamustine for FL asks, "What is the chance I will lose my hair?"

	CI	PO
Not at all likely	88%	61%
Somewhat likely	12%	34%
Very likely	0%	5%

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Do you perform biopsies on patients with FL at the time of relapse to rule out transformation?

	CI	PO
Yes, usually	80%	56%
Yes, occasionally	12%	31%
Yes, only if PET scan is suspicious for transformation	8%	11%
No	0%	2%

How often do you use PET scanning for patients with FL?

	CI	PO
Frequently	44%	56%
Occasionally	36%	34%
Rarely	20%	9%
Never	0%	1%

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Which of the following tests do you generally order for a patient starting a rituximab-containing regimen who has no history of hepatitis? (Check all that apply)

	CI	PO
HBsAg	96%	88%
Anti-HBc Ab	91%	60%
Anti-HBs Ab	74%	55%
Anti-HCV Ab	52%	52%

CI n = 23; PO n = 94

During the past year, have you administered any of the following to your patients with FL?

	% responding yes	
	CI	PO
Bendamustine + rituximab	100%	87%
Stem cell transplant	84%	46%
Lenalidomide	60%	38%
Bortezomib	36%	42%