A patient with asymptomatic, Stage III, Grade 2, FLIPI high-risk follicular lymphoma

An otherwise healthy 60-year-old patient is diagnosed with low tumor burden Stage III, Grade II, FLIPI high-risk FL and is asymptomatic. Which induction treatment, if any, would you most likely recommend?

- Watch and wait: 38%
- Rituximab (R) monotherapy: 12%
- Bendamustine/R: 19%
- R-CHOP: 29%
- R-CVP: 2%

DR KAHL: Watch and wait
DR WILLIAMS: R monotherapy

EDITOR’S COMMENTS

Dr Kahl notes that a variety of evidence-based options are available for a patient with low tumor burden by GELF criteria, and his preference is to “watch and wait,” although he acknowledges that rituximab monotherapy or rituximab/chemotherapy are also considerations given the high FLIPI score. Both faculty members were co-chairs of the landmark RESORT study, which demonstrated prolonged responses with 4 courses of weekly rituximab monotherapy in most patients with low tumor-burden disease, and although the trial did not reveal a survival benefit with prolonging rituximab indefinitely, Dr Williams and many other oncologists now frequently turn to rituximab monotherapy for these patients with the hope of delaying disease progression and the need for chemotherapy.

SELECT REFERENCES WITH LINKS


A patient with mildly symptomatic, Stage III, Grade 2, FLIPI high-risk follicular lymphoma

An otherwise healthy 60-year-old patient is diagnosed with low tumor burden Stage III, Grade II, FLIPI high-risk FL and is mildly symptomatic with night sweats but no weight loss. Which induction treatment, if any, would you most likely recommend?

**EDITOR’S COMMENTS**

This case differs slightly from the first in that the patient is symptomatic and requires treatment, and in this instance Dr Kahl generally recommends rituximab monotherapy with the idea of adding chemotherapy if the response is not adequate. Most of the survey respondents (MO) who use up-front chemotherapy with rituximab opt for bendamustine/rituximab (BR), but 28% use R-CHOP, a choice Dr Kahl believes is a reasonable alternative, particularly in view of the fact that as patients age the ability to tolerate anthracycline toxicity diminishes.

**SELECT REFERENCES WITH LINKS**


Hiddemann W et al. Frontline therapy with rituximab added to the combination of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) significantly improves the outcome for patients with advanced-stage follicular lymphoma compared with therapy with CHOP alone: Results of a prospective randomized study of the German Low-Grade Lymphoma Study Group. *Blood* 2005;106(12):3725-32. [Abstract](#)

A patient with mildly symptomatic, Stage III, Grade 2, FLIPI high-risk follicular lymphoma in partial remission after rituximab/chemotherapy

An otherwise healthy 60-year-old patient is diagnosed with low tumor burden Stage III, Grade II, FLIPI high-risk FL and is mildly symptomatic with night sweats but no weight loss.

If the patient received R/chemotherapy and achieved a partial response or better with resolution of symptoms, would you administer R maintenance?

<table>
<thead>
<tr>
<th></th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR KAHL: Yes</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>DR WILLIAMS: Yes</td>
<td>18%</td>
<td></td>
</tr>
</tbody>
</table>

If you would recommend R maintenance, for what duration?

<table>
<thead>
<tr>
<th>Duration</th>
<th>% of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1 year</td>
<td>3%</td>
</tr>
<tr>
<td>2 years</td>
<td>87%</td>
</tr>
<tr>
<td>Indefinitely (until disease progression)</td>
<td>10%</td>
</tr>
</tbody>
</table>

**EDITOR’S COMMENTS**

Dr Williams points out that 2 years of rituximab maintenance has become standard after induction rituximab/chemotherapy, and these results confirm that. However, he also notes that a survival benefit has not yet been documented, and therefore he does not hesitate to stop treatment in patients having difficulty tolerating rituximab maintenance.

**SELECT REFERENCES WITH LINKS**


Both faculty members and the majority of MO surveyed use rituximab monotherapy, although another common choice was BR. Dr Kahl notes that when BR is used in elderly patients consideration should be given to reducing the dose of bendamustine to, for example, 70 milligrams per square meter.

An older (80) patient with mildly symptomatic, Stage III, Grade 2, FLIPI high-risk follicular lymphoma

An otherwise healthy 80-year-old patient is diagnosed with low tumor burden Stage III, Grade II, FLIPI high-risk FL and is mildly symptomatic. What induction treatment, if any, would you most likely recommend?

Watch and wait: 12%
Rituximab monotherapy: 41%
R-CHOP: 5%
R-CVP: 10%
Bendamustine/R: 30%
Chlorambucil/R: 2%

DR KAHL: R monotherapy
DR WILLIAMS: R monotherapy

EDITOR’S COMMENTS

Both faculty members and the majority of MO surveyed use rituximab monotherapy, although another common choice was BR. Dr Kahl notes that when BR is used in elderly patients consideration should be given to reducing the dose of bendamustine to, for example, 70 milligrams per square meter.

SELECT REFERENCES WITH LINKS


In discussing this clinical situation, Dr Kahl points out that single-agent rituximab is less effective in high tumor-burden disease, and for that reason he often chooses BR. That said, he feels that R-CHOP — which is Dr Williams’s choice based on his desire to quickly palliate symptoms and concern about transformation — is a valid alternative. Both faculty use 2 years of rituximab maintenance in this situation.

A patient with bulky Stage III, Grade 2, FLIPI high-risk follicular lymphoma with night sweats and weight loss

An otherwise healthy 60-year-old patient who presents with night sweats and a recent 20-lb weight loss is diagnosed with bulky, Stage III, Grade II, FLIPI high-risk FL. Which induction treatment, if any, would you most likely recommend?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watch and wait</td>
<td>0%</td>
</tr>
<tr>
<td>Rituximab monotherapy</td>
<td>4%</td>
</tr>
<tr>
<td>Bendamustine/R</td>
<td>53%</td>
</tr>
<tr>
<td>R-CHOP</td>
<td>40%</td>
</tr>
<tr>
<td>R-CVP</td>
<td>3%</td>
</tr>
</tbody>
</table>

**DR KAHL:** Bendamustine/R or R-CHOP  
**DR WILLIAMS:** R-CHOP

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**EDITOR’S COMMENTS**

In discussing this clinical situation, Dr Kahl points out that single-agent rituximab is less effective in high tumor-burden disease, and for that reason he often chooses BR. That said, he feels that R-CHOP — which is Dr Williams’s choice based on his desire to quickly palliate symptoms and concern about transformation — is a valid alternative. Both faculty use 2 years of rituximab maintenance in this situation.

**SELECT REFERENCES WITH LINKS**


Because the results will not change his treatment approach, Dr Williams does not test these patients unless they are experiencing recurrent infections. Dr Kahl on the other hand evaluates patients annually, noting that symptomatology such as infections take an extended time to develop. He also points out that many patients with lymphoma have low baseline immunoglobulin levels but do not develop recurrent infections, and therefore he only takes action if a low level is accompanied by repeated infections.

**SELECT REFERENCES WITH LINKS**


A patient has been receiving maintenance R for 1 year, and the disease is in remission but the patient has begun developing recurrent infections (sinusitis, etc). Immunoglobulin G levels are 250 mg/dL. What would you generally do?

- Discontinue maintenance R, initiate treatment with IV immunoglobulin: 40%
- Discontinue maintenance R until recovery, then reinitiate treatment with R: 11%
- Discontinue maintenance R until recovery, then reinitiate treatment with R plus IV immunoglobulin: 9%
- Continue maintenance R with IV immunoglobulin: 39%
- Discontinue R: 1%

**DR KAHL:** Discontinue, then initiate with IV immunoglobulin

**DR WILLIAMS:** Discontinue, then initiate treatment with IV immunoglobulin

**EDITOR’S COMMENTS**

Although more than a third of MO would administer gamma globulin and continue rituximab maintenance in this situation, the faculty and a majority of MO would discontinue treatment. This approach is based primarily on the fact that rituximab maintenance has not been shown to increase overall survival and recurrent infections can cause a major detriment to quality of life.

**SELECT REFERENCES WITH LINKS**


A patient receiving maintenance R while the disease is in remission develops neutropenia (ANC <1,000 cells/uL). What would you generally do?

- Discontinue maintenance R: 42%
- Discontinue maintenance R until recovery, then reinitiate treatment: 56%
- Other: 2%

**DR KAHL:** Discontinue maintenance R, investigate cause of neutropenia, reinitiate treatment after recovery

**DR WILLIAMS:** Discontinue maintenance R

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**EDITOR’S COMMENTS**

While most of the MO would hold treatment and restart when the counts recover, the faculty members generally stop therapy. Dr Kahl will also consider the selective use of pegfilgrastim and will then reinitiate treatment if counts increase sufficiently.

**SELECT REFERENCES WITH LINKS**


Routine surveillance imaging is receiving considerable attention in all corners of oncology because of concerns regarding costs, but both faculty and most of the MO surveyed do use this modality. Dr Kahl’s rationale is that he wants to avoid the expense and toxicity of treatment in patients with asymptomatic disease progression who are not benefitting from it.

Dr Kahl: Every 6 months
Dr Williams: Every 12 months


A patient with bulky Stage III, Grade 3A, FLIPI high-risk follicular lymphoma with night sweats and weight loss

An otherwise healthy 60-year-old patient who presents with night sweats and a recent 20-lb weight loss is diagnosed with bulky, Stage III, Grade IIIa, FLIPI high-risk FL. What induction treatment, if any, would you most likely recommend?

- **Rituximab monotherapy**: 0%
- **Bendamustine/R**: 35%
- **R-CHOP**: 57%
- **R-CVP**: 4%
- **Dose-adjusted EPOCH-R**: 3%
- **Other**: 1%

**DR KAHLE**: R-CHOP
**DR WILLIAMS**: R-CHOP

**EDITOR’S COMMENTS**

Dr Kahl confesses that clinical decision-making is particularly challenging for Grade 3A disease, but he, Dr Williams and a majority of the MO surveyed use R-CHOP. Dr Williams points out that several major clinical studies suggest the possibility of a “tail on the curve” in this subset and that perhaps 40% or so of patients receiving R-CHOP may indeed have durable responses and might even be “cured” akin to what is observed in diffuse large B-cell lymphoma.

**SELECT REFERENCES WITH LINKS**

