The impact of FLIPI on outcome of frontline treatment with single-agent I-131 tositumomab for follicular lymphoma (FL)

**Presenter:** M.S. Kaminski  
**Presenter’s Affiliation:** University of Michigan Comprehensive Cancer Center, Ann Arbor, MI  
**Type of Session:** Scientific

**Background**
- Follicular lymphoma is an indolent Non-Hodgkin’s lymphoma that usually presents in an advanced stage.
- Follicular lymphomas usually express CD20, a B-cell marker.
- An antibody to CD20, rituximab, has been widely used in the treatment of Non-Hodgkin’s lymphomas including follicular lymphomas.
- The addition of rituximab to chemotherapy has been shown to improve progression free survival in follicular lymphoma patients.
- Radioimmunotherapy combines the technology of monoclonal antibodies and radiation therapy.
- I-131 tositumomab (Bexaar) links radioactive iodine to an anti-CD20 antibody and could potentially be more active than an antibody alone.
- Studies using radioactive antibodies either alone or in consolidation after chemotherapy have yielded promising results.
- The FLIPI (Follicular Lymphoma International Prognostic Index) has been shown to be a good predictor of outcomes in follicular lymphoma patients.
- The FLIPI categorizes patients into low, intermediate, and high risk groups based on 5 prognostic indicators (age, stage, LDH, hemoglobin, # of extranodal sites).
- FLIPI scores in individual trials may be helpful in comparing the results of the various clinical trials performed to date.

**Materials and Methods**
- This study re-analyzed data from a study of Bexaar as frontline treatment for follicular lymphoma published by Kaminsky et al. in the New England Journal of Medicine in 2005.
- An additional analysis of the FLIPI scores from that trial was performed in order to compare their results with other studies that used either unlabeled or radiolabeled antibodies as part of the treatment regimen.
- The initial trial was a single arm phase II trial run at the University of Michigan which evaluated the safety and efficacy of a single course of Bexaar in previously untreated patients with advanced stage follicular lymphoma.
- 76 patients were enrolled and the median follow-up is 5.1 years.
- FLIPI scores were available for 74 of the 76 patients in this study.

**Results**
- The overall response rate was 95% and the complete response rate was 75%.
- The 5 year progression free survival (PFS) was 59% and the median PFS was 6.1 years.
- Complete responders had improved PFS compared to partial responders.
- The most common treatment related toxicity was neutropenia (34% grade 3 or 4).
- The presence of bone marrow involvement was the only factor that significantly influenced outcomes on multivariate analysis.
- The breakdown of patients by FLIPI was: 15% low risk, 50% intermediate risk, 35% high risk.
- There was no significant difference seen in PFS or overall survival when comparing patients by FLIPI score.
- If high risk patients were compared to low risk and intermediate risk patients grouped together, a significant difference in overall survival was seen (p=0.028).
8 other recent trials utilizing antibody therapy with chemotherapy were compared to this trial (3 using radiolabeled antibody and 5 using unlabeled antibody).

The rates of low risk, intermediate risk, and high risk FLIPI scores in this trial were similar to the other 8 trials.

The 5 year PFS rate in this study for high risk patients (52%) is the same as the PFS rate seen in the SWOG 9911 trial of CHOP + Bexaar (52%).

Author's Conclusions

- Even high risk FLIPI groups have excellent results with single agent Bexaar.
- Single agent Bexaar overcomes the negative prognosis of high FLIPI for PFS.
- Results compare favorably to those obtained from combination treatments (chemotherapy + radiolabeled/unlabeled antibody).
- The necessity of pretreatment with chemotherapy is unclear.
- Randomized trials evaluating single agent Bexaar versus combination treatment should be considered.

Clinical/Scientific Implications

The authors performed a retrospective analysis of data gathered from a single institution phase II trial. This weakens the strength of any conclusions that can be drawn from this presentation. The claim that FLIPI score did not predict for outcome is not consistent with other studies of follicular lymphoma. Also, there are numerous statistical problems comparing two completely separate clinical trials. However, this analysis is certainly thought provoking. The most important piece of information that can be gathered from this analysis is that the patients in this study of single agent Bexaar were not in a lower risk group than patients from other trials; and thus the excellent results that were obtained in the initial study cannot be explained away with the criticism that the patients were lower risk than other studies. The authors' last conclusion, that a randomized trial is needed to compare single agent Bexaar to combination treatments, is certainly valid.