

HemeCaRe Follicular Lymphoma Study

Biostatistics 699 Project #2

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Background

Follicular Lymphoma

- ▶ Type of non-Hodgkin's lymphoma that affects B-lymphocyte white blood cells, which are responsible for secreting antibodies
- ▶ Not known to be curable, but progresses slowly
- ▶ Can transform to Diffuse Large B-cell Lymphoma (DLBCL)

Overview of Dataset

- ▶ 418 individuals with Follicular Lymphoma (FL)
- ▶ Many variables to consider:
 - ▶ Demographics
 - ▶ Key dates (birth, death, diagnosis, last contact, etc.)
 - ▶ Additional diagnosis/disease specifics (e.g. stage of disease)
 - ▶ Lab measurements upon entering treatment at Michigan
 - ▶ Treatment information on up to 10 treatment regimens

Aims

1. Compare the overall survival (OS) and progression free survival (PFS) of patients with FL.
 - ▶ Specifically: Compare OS and PFS between patients treated with Bendamustine + Rituximab and those with other treatments.
2. What is the incidence of Transformation of FL to Diffuse Large B-cell Lymphoma (DLBCL)?
 - ▶ Specifically: Does treatment play a role in progression to DLBCL?

Aim #1

Defining Overall and Progression Free Survival

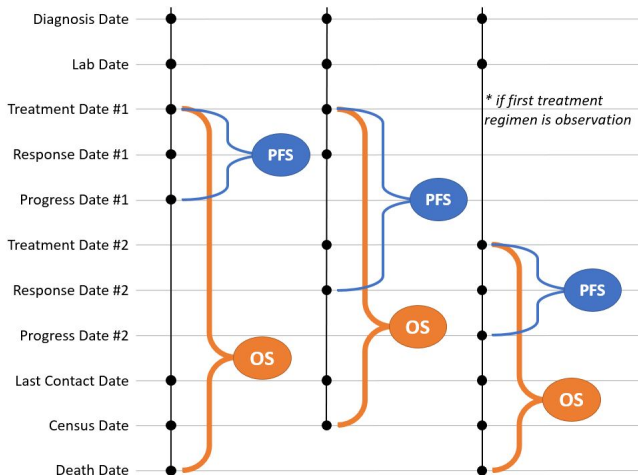
Overall Survival

- ▶ Time Zero defined as date of **first official treatment**
- ▶ Observation does not count as an official treatment
- ▶ Survival time defined as time until **death** or censoring
- ▶ Date of censoring is the later of the **censor date** and **last contact date**

Progression Free Survival

- ▶ Time Zero defined the same way as OS
- ▶ Survival time defined as time until **first progression** or censoring
- ▶ Date of censoring is the last available **response date**

Defining OS and PFS Continued



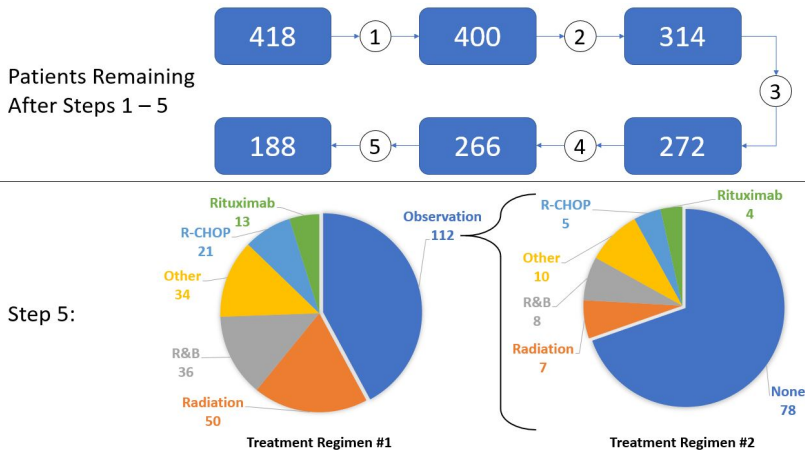
Patients to Exclude from Analysis

1. Those who transformed to DLBCL before treatment at Michigan
 - ▶ no information about pre-transformative state
 - ▶ 18 patients excluded
2. Those who were diagnosed away from Michigan and did not start treatment at Michigan soon after
 - ▶ an effort to deal with **left truncation**
 - ▶ only look at patients whose lab date is within 6 months of diagnosis date
 - ▶ 86 patients excluded

Patients to Exclude from Analysis

3. Those who did not receive a treatment and/or did not have a treatment date
 - ▶ without a date to use as time zero, there's not much we can do
 - ▶ 42 patients excluded
4. Those who had a treatment date, but no treatment specified
 - ▶ 6 patients excluded
5. Those under observation during the first regimen, but did not receive a treatment after
 - ▶ as useful as the people without a treatment at all
 - ▶ 78 patients excluded

Patients to Exclude from Analysis



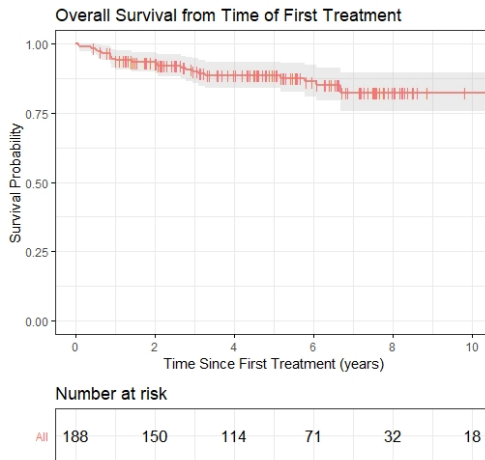
Patients to Exclude from Analysis

21 additional patients had to be excluded for the PFS analysis:

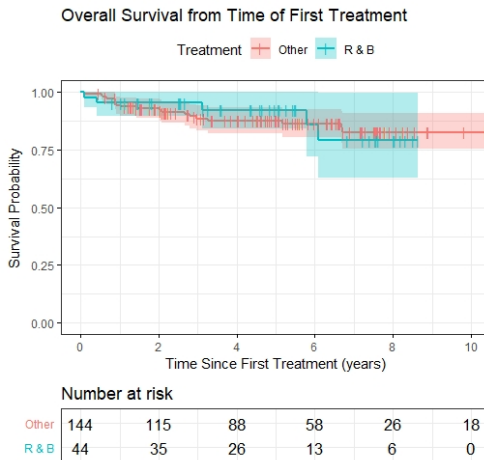
6. Those who somehow responded to treatment before actually receiving treatment
 - ▶ 2 patients excluded
7. Those who did not progress, but also did not have any response dates
 - ▶ without a date to use for time until censoring, there's not much we can do
 - ▶ 19 patients excluded

New total of 167 patients for the PFS analysis

5-year survival: 0.887 (0.840, 0.949)



No Apparent Difference Between Treatments



No Apparent Difference Between Treatments

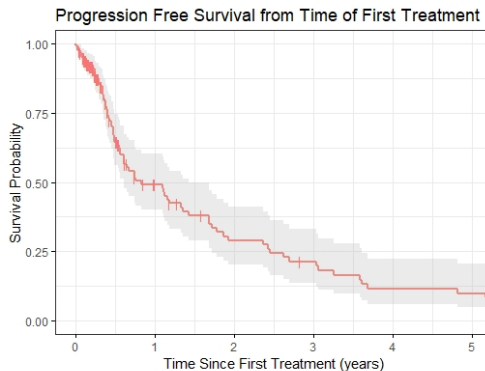
Fit a Cox model to estimate treatment effect (unadjusted)

- ▶ Those who received the Rituximab & Bendamustine treatment have a 10% reduction in hazard of death compared to those receiving other treatments.
- ▶ Hazard Ratio: 0.897
- ▶ 95% CI: (0.335, 2.404)

Fit a second Cox model that adjusts for age and gender

- ▶ Reached nearly the same conclusion
- ▶ Hazard Ratio: 0.916
- ▶ 95% CI: (0.339, 2.470)

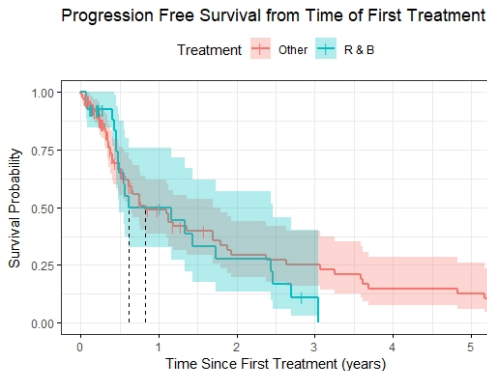
Median survival: 0.83 years (approx. 10 months)



Number at risk

	0	1	2	3	4	5
All	167	37	19	13	7	6

No Apparent Difference Between Treatments



Number at risk

Other	127	27	14	12	7	6
R & B	40	10	5	1	0	0

No Apparent Difference Between Treatments

Fit a Cox model to estimate treatment effect (unadjusted)

- ▶ Those who received the Rituximab & Bendamustine treatment have a 20% increase in hazard of progression compared to those receiving other treatments.
- ▶ Hazard Ratio: 1.195
- ▶ 95% CI: (0.714, 2.001)

Fit a second Cox model that adjusts for age and gender

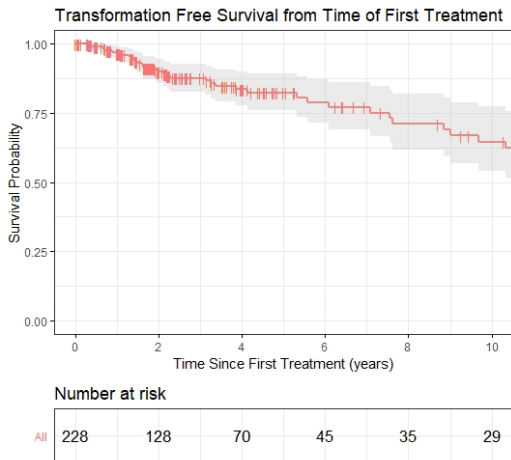
- ▶ Reached nearly the same conclusion
- ▶ Hazard Ratio: 1.187
- ▶ 95% CI: (0.707, 1.994)

Aim #2

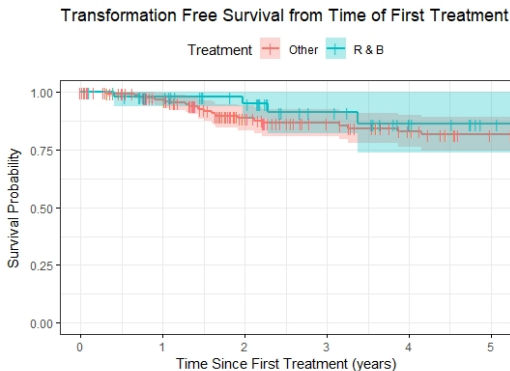
Defining Transformation Free Survival

- ▶ Time Zero defined as date of **first official treatment**
- ▶ Survival time defined as time until date of **last contact** for *both* those who transform to DLBCL ($\delta = 1$) and those who do not, and are thus censored ($\delta = 0$)
- ▶ Relaxed exclusion criteria (step 2 addressing left truncation) to include more events (increasing from 27 to 47 transformations)

5-year survival: 0.824 (0.761, 0.892)



No Apparent Difference Between Treatments



Number at risk

Other	178	145	95	75	60	47
R & B	50	42	33	20	10	4

No Apparent Difference Between Treatments

Fit a Cox model to estimate treatment effect (unadjusted)

- ▶ Those who received the Rituximab & Bendamustine treatment have a 2% increase in hazard of transformation compared to those receiving other treatments.
- ▶ Hazard Ratio: 1.02
- ▶ 95% CI: (0.41, 2.53)

Fit a second Cox model that adjusts for age and gender

- ▶ Reached nearly the same conclusion
- ▶ Hazard Ratio: 0.98
- ▶ 95% CI: (0.39, 2.44)

Summary

- ▶ There was no apparent difference between being treated with Rituximab & Bendamustine and other treatments in any of the analyses
- ▶ Limitations:
 - ▶ Proportionality assumption violated
 - ▶ Not enough events to answer the given research questions

Open for questions. . .