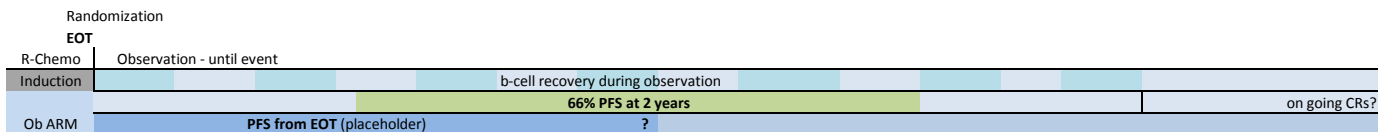
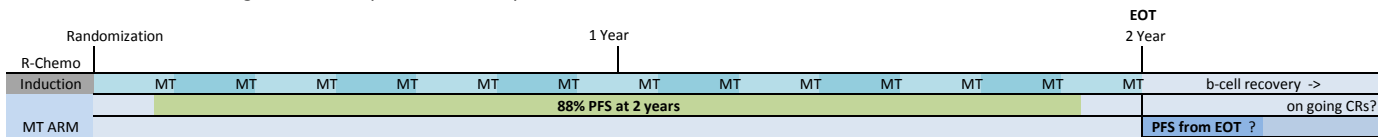


PRIMA Questions

PFS -- Progression Free Survival, measured from randomization to event - Progression or death from any cause
 EOT -- End of last Treatment

Sponsor reports **88% PFS at 2 years for MT vs 66% for observation**

MT - Rituxan 375 mg/m² i.v. every 8 weeks for 2 years.



Discussion and Questions:

Our perception of the meaning of clinical data depends on what is measured and how - and also by what is reported or left out.

When you compare an active drug (responses expected in ~50%) to observation, shouldn't we expect a longer PFS measured from the end of induction therapy?

Is the clinical significance of PFS (the benefit to patients) in part determined by the starting point from which it's measured, specifically: from randomization versus from end of treatment (EOT)?

We ask also that the sponsor provide the CR rate and number of ongoing CRs to see if this data suggests that MT improves the quality of the induction response, or if we are just trading side effects for symptoms. Noting that FL patients can be asymptomatic at relapse, so delaying relapse does not necessarily improve quality of life.

QUESTIONS:

- * What is the median **PFS from End of Therapy (EOT)**?
- * Is MT improving the quality of the remission and providing meaningful clinical benefit?
 ... to evaluate this, do we need also to compare:

PFS from EOT,
 CR (complete response) rate, and
 Ongoing CRs?

OTHER QUESTIONS:

- * How many participants in MT arm would have done as well anyway - were possibly exposed to MT risks unnecessarily?
- * What is the potential clinical impact of long term b-cell depletion in MT arm (such as the need for IV IG)?
- * What is the impact of MT on response to subsequent therapy with Rituxan-based protocols?
- * Might the risks in the general population be different? Noting that for the study population Median age is ~ 10 years less than median age for FL at diagnosis.

COMMENT: Since MT is already commonly prescribed, is there an urgent need to judge the data at this point? We submit that longer follow up could be needed to evaluate this data - particularly if a comparison of **PFS from EOT** and **CR data** does not favor MT.

~ Karl Schwartz, Patients Against Lymphoma