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# The relevance of progression-free survival (PFS) data for predicting long-term patient outcomes

**Roche:** Through the POLARIX trial, POLA-R-CHP brings meaningful improvement over the current standard of care, R-CHOP. However, the short follow-up period, disease characteristics as well as the availability of subsequent therapies make it difficult to analyze the effect on overall survival. Therefore, the primary efficacy endpoint in the POLARIX trial was investigator-assessed progression-free survival.

This endpoint was met and showed a 27% reduction in the risk of progression, relapse, or death compared to R-CHOP. At two years, there were six and a half percent more patients living progression-free on POLA-R-CHP compared to those on R-CHOP.
Dr Laurie Sehn gives her thoughts on this data.

**Dr Laurie H. Sehn (MD, MPH, Clinical Assistant Professor with the BC Cancer Agency and University of British Columbia):** The median follow up at this point is about two years, and I think that is pretty mature for progression-free survival. But when you talk about overall survival, you know these patients do have numerous options that some of them can potentially offer a second chance of cure, or some of them can help to palliate and control disease now for longer periods of time, especially with some of the novel drugs. So I think that the data on overall survival is still somewhat immature and I'd like to see longer follow up on that and I think this slide here really serves to document that the patients who were receiving the R-CHOP only did have a higher likelihood of needing to go onto these secondary therapies, and that's probably at this point in time, impacting our ability to appreciate whether or not there'll be an overall survival benefit.

**Roche:** How is the connection between progression-free survival and overall survival evolving with today's treatment options for patients with DLBCL? More from Dr Laurie Sehn.

**Dr Laurie H. Sehn:** So we used to expect a close connection between PFS and OS in the past because if you progressed, you really didn't have much in the way of any options that allowed you to keep the patient alive for very long and I think it's very different now.

**Reference:**
1. Tilly H, et al. N Engl J Med. 2022;386:351-63
2. US FDA. Clinical Trial Endpoint for the Approval of Cancer Drugs and Biologics. Guidance for INdustry. 2018.
3. Shi Q, et al. J Clin Oncol. 2018;36:2593-602.





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So we've got a lot more options in the second line setting. Some of them are aimed to try and cure patients with a second go around, but I think you could still argue whether or not we're talking about stem cell transplant or CAR T-cell therapy. The majority of patients still will have their disease relapse after those, even though we may be curing more patients second line, we're doing better, I think with novel agents that trying to keep patients alive longer and all of that is going to push out the survival curve for sure.

But what you can see here is that more patients in the R-CHOP arm had to go on to these second line therapies and as we said, if we could avoid them and cure our patients with front-line, that would be everybody's preference for sure.

**Roche:** With the availability of more second-line therapies for DLBCL, overall survival is going to become an increasingly difficult endpoint to assess. Dr Laurie Sehn explains why.

**Dr Laurie H. Sehn:** Preventing relapse with front-line therapy is really my primary goal. I think we're entering an era where there's going to be a disconnect between progression-free survival and overall survival because of the secondary therapies that can provide longer term durable benefit.

But I still think, you know, the real goal is to cure patients up front. So, I think PFS will become probably the acceptable, relevant endpoint moving forward, particularly as it becomes harder and harder to expect an overall survival difference.

**Reference:**
1. Tilly H, et al. N Engl J Med. 2022;386:351-63
2. US FDA. Clinical Trial Endpoint for the Approval of Cancer Drugs and Biologics. Guidance for INdustry. 2018.
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