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# Learn more about the clinical trial design and primary endpoint of POLARIX

**Roche:** In the POLARIX trial, POLA-R-CHP showed a progression-free survival benefit for first-line DLBCL patients. The phase three trial compared the efficacy and safety of R-CHOP to a modified drug combination known as POLA-R-CHP. POLA-R-CHP omits vincristine, but includes polatuzumab vedotin, an antibody drug conjugate.
The trial was carried out in a broad patient population with previously untreated intermediate risk DLBCL. 879 patients were randomly assigned to receive either POLA-R-CHP or R-CHOP. 8 21-day cycles of treatments were planned. During the first six cycles, patients received either POLA-R-CHP or R-CHOP.
During cycle seven and eight, patients in both groups received rituximab as monotherapy.
The primary endpoint was investigator-assessed progression-free survival as calculated in a time to event analysis. A progression-free survival benefit was seen with POLA-R-CHP.
Professor Christopher Flowers puts the importance of this finding into perspective.

**Prof. Christopher Flowers (University of Texas, MD Anderson Cancer Center):** It's really been 20 years since we've had a positive study in front-line diffuse large B-cell lymphoma. Really, and if you think back to the true history of our management of this disease and going all the way back to the 1970s, that's when the CHOP regimen was first developed. And it was in the 1990s that we first found out in randomised trials that CHOP was really no different than any other aggressive chemotherapy regimen and served as the backbone. But it was the French group that led the first of several trials that showed the addition of rituximab to the CHOP regimen was a benefit for patients with front-line diffuse large B-cell lymphoma. And it was really that trial and the subsequent trials that led R-CHOP to be the standard of care. And over those last 20 years, it really wasn't that we weren't trying to do anything. We tried many different regimens to try and improve upon R-CHOP, but first, segmenting populations into the biologically poor risk groups like the activated B-cell, like or the non-GCB subtype and adding agents like lenalidomide or ibrutinib to that, or bortezomib, adding agents such as those to all patients with R-CHOP and intensifying their rituximab components to the chemotherapy, adding new anti-CD20 antibodies to the chemotherapy regimen or intensifying the therapy of the chemotherapy, like dose adjusted EPOCH and all of those approaches really did not improve upon the progression-free survival for patients with diffuse large B-cell lymphoma. And so this regimen, the R-CHP-POLA is the first real substitution of vincristine for polatuzumab vedotin. That's changed the outcomes that we've seen in terms of progression-free survival, and I think the 27% difference in progression-free survival that you see in this study really is a meaningful benefit for patients.

**Reference:**
1. Tilly H, et al. N Engl J Med. 2022;386:351-63.





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**Roche:** Which patient populations benefit? Professor Christopher Flowers provides his insight.

**Prof. Christopher Flowers:** Really, I think when you look at the major results of the POLARIX trial, what those show is that POLA-R-CHP in general benefits all patients who are eligible for the trial. And so I think that's the major population where we should think about the use of this regimen. The way that I interpret forest plots within the context of a clinical trial is this gives you a general sense of the trend, of the effect in certain subgroups, although this was not statistically designed to look at the subgroups from the standpoint of the design of the trial and gives you a general sense of the impact of the size of each subgroup on the overall trial results and essentially what this shows by all of these boxes or the vast majority of these boxes being to the left of the one which is the central line, showing whether one regimen or the other is better is that this favors the vast majority of the subgroups and the subgroup where this is a little bit less known are in some of the groups like the cell of origin being unclassified, or the double and triple hit lymphoma, where you can see from the box sizes that those were very small subgroups within the trial and that no clear conclusions can be drawn about those subgroups from this forest plot since both of those also have very wide confidence intervals across one.
But I see these results as showing that for the general population of patients who are eligible for the trial, that this regimen, POLA-R-CHP, benefits all patients that were eligible.

**Roche:** Dr Franck Morschhauser agrees that POLA-R-CHP offers a clinically meaningful benefit.

**Dr. Franck Morschhauser (MD PhD Professor of Hematology, University of Lille):** PFS benefit with POLA-R-CHP versus R-CHOP was statistically significant and clinically meaningful. You were told that exploratory analysis are ongoing with regard to various subgroups and other prognostic classification systems, but at this point we need to stick to the eligibility criteria.
That makes R-CHP-POLA broadly available. The safety profiles of R-CHP-POLA and R-CHOP were comparable, and clearly these results support the use of R-CHP-POLA in the initial management of patients with diffuse large B-cell lymphoma.

**Reference:**
1. Tilly H, et al. N Engl J Med. 2022;386:351-63.





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