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How progression-free survival (PFS) is a surrogate for overall survival (OS)

Roche: Overall survival has been viewed as the gold standard when it comes to tevaluating the efficacy of DLBCL treatment. However, it requires prolonged follow up. Professor Christopher Flowers gives us his view on using progression-free survival as a surrogate for overall survival.

Prof. Christopher Flowers (University of Texas, MD, Anderson Cancer Center): PFS clearly is a significant endpoint for diffuse large B-cell lymphoma, and I was a part of this international initiative, the SEAL protocol that put together randomised controlled trials in front-line diffuse large B-cell lymphoma, where we clearly established that progression-free survival as a surrogate endpoint is an established surrogate for overall survival.

Roche: How was the validity of PFS as a surrogate for overall survival determined? Professor Christopher Flowers explains.

Prof. Christopher Flowers: We set a preselected criteria for surrogacy, analysed the individual patient level data and the trial level data for those trials, and found that PFS clearly is a surrogate for overall survival, and PFS should be a valid and regulatory endpoint for front-line clinical trials in diffuse large B-cell lymphoma, so I think for that reason PFS alone is important. I think overall survival has become a more challenging endpoint in front-line DLBCL. I think for many reasons that Hervé alluded to, perhaps going back to the history books and comparing kind of our last positive trial in diffuse large B-cell lymphoma. Those trials that compared CHOP to R-CHOP, where we did see early on in overall survival advantage, at least in the French trial, and that was in part because the things that we had as options for those patients who were early relapsers with diffuse large B-cell lymphoma were relatively few and far between we had autologous stem cell transplant as an option, but really no potentially curative options for patients who relapsed beyond that. And so I think many of those patients who progressed early on in that study did ultimately die, and so there was a clear benefit in terms of overall survival for those who were progression-free.

Reference:
1. Shi Q, et al. J Clin Oncol. 2018;36:2593-602.

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Now, in the modern era, we have multiple lines of therapies for patients with diffuse large B-cell lymphoma that can potentially produce curative options like autologous transplant and CAR T-cell therapy, but also many other therapies that can prolong life so that with the early follow up that we've seen on this trial, we may not see an early overall survival advantage, and so I think that we'll need a much longer follow up before we might see that in a trial like this, but because of those potentially curative options in the second line setting, we may not see overall survival advantages for trials in the future that look at front-line DLBCL.

Reference:
1. Shi Q, et al. J Clin Oncol. 2018;36:2593-602.