Abstract: S218

Title: CORRELATION BETWEEN PROGRESSION-FREE AND OVERALL SURVIVAL IN PATIENTS WITH CLASSICAL HODGKIN LYMPHOMA: A COMPREHENSIVE ANALYSIS OF INDIVIDUAL PATIENT DATA FROM RANDOMIZED GHSG TRIALS

Abstract Type: Oral Presentation

Session Title: Hodgkin Lymphoma - Clinical

Background:

Progression-free survival (PFS) and overall survival (OS) are predominant measures of treatment efficacy in classical Hodgkin lymphoma (HL). Despite preference for OS from many regulatory authorities, PFS is most relevant to patients and frequently serves as primary endpoint in clinical trials. The relationship between PFS and OS in HL is of immediate interest but remains unknown to date.

Aims:

We aimed to evaluate the correlation of PFS with OS after first-line treatment of HL and its potential to serve as a surrogate parameter.

Methods:

We analyzed individual patient data obtained during and after polychemotherapy based treatment in nine randomized phase III GHSG first line trials (HD7-HD15) between 01/93 - 08/18. PFS was defined as time from randomization until progression, relapse, or death; OS was defined as time from randomization until death. Effects of 16 experimental treatments on PFS and OS on trial level were evaluated by estimation of the treatment effects with Cox proportional hazards (PH) regression and a linear weighted least squares (WLS) regression. On the patient level, marginal Cox PH models for multiple endpoints were applied according to the Wei-Lin-Weissfeld method (WLW). Additionally, we correlated risk factor effects with marginal Cox PH models at the patient level (WLW) and applied copula models to correlate PFS and OS directly at patient level.

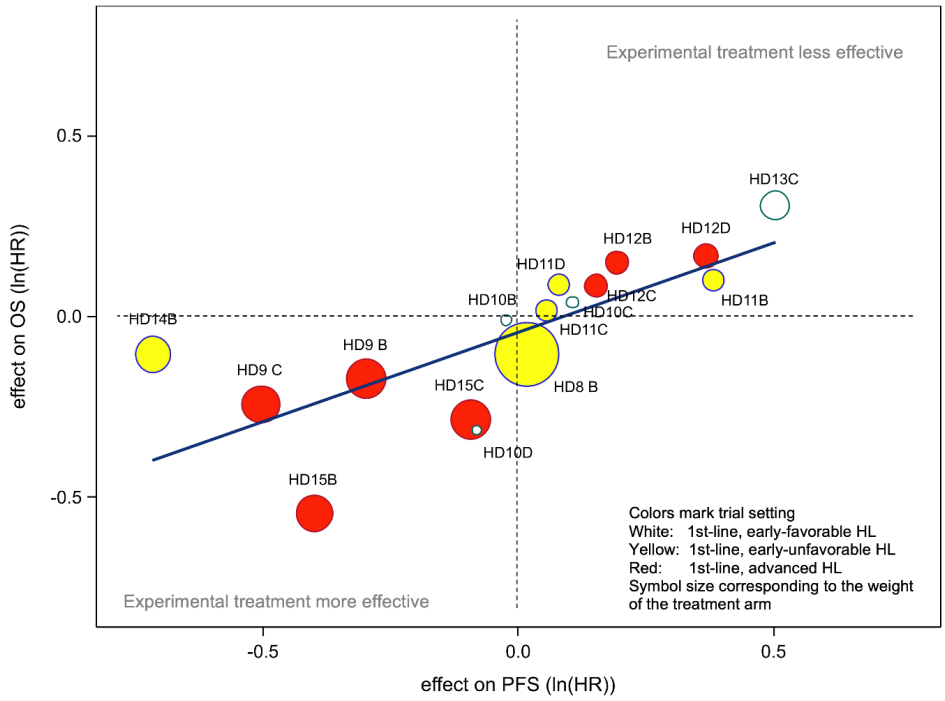
Results:

At least one PFS and OS event was recorded in 1,682 and 1,064 of 10,605 HL patients, respectively. The statistical analysis at the trial level revealed a high and significant correlation of treatment effects on PFS and OS ($r= 0.72$, $r^2= 0.54$, $P< 0.001$, Figure 1). A multiple regression model accounting for different effectiveness of experimental treatments and historical progress over trial generations reached almost perfect fit ($r^2= 0.93$). The statistical analysis at patient level confirmed a high correlation of treatment effects on PFS and OS. Within the trials, Pearson r was ranging between 0.61 and 0.85 (each $P< 0.001$) and with two exceptions all correlations were $r > 0.70$. In total, Pearson r was 0.74, r being higher in advanced stages of HL ($r= 0.78$) than in limited stages ($r= 0.72$). At patient level, we found similar high correlations between effects of risk factors on PFS and OS (Pearson $r= 0.74$-0.85, each $P< 0.001$, WLW analysis) and when correlating PFS and OS with copula (Pearson $r= 0.72$-0.83, each $P< 0.001$).

Summary/Conclusion:

In first-line trials of HL, PFS and OS as well as treatment effects and prognostic effects of risk factors on PFS and OS are highly correlated. PFS thereby predicts treatment effects on OS to a high degree and many years before OS can be reliably evaluated.

Figure 1. Sixteen separately estimated treatment effects on PFS and OS at Trial Level and Resulting Linear Regression Line with r= 0.721 (95%CI= 0.350-0.896)



Keywords: Long-term follow-up, treatment-free remission, Hodgkin's lymphoma, Prognostic