Rearrangements of MYC gene facilitate risk stratification in diffuse large B-cell lymphoma patients treated with rituximab-CHOP.

In order to address the debatable prognostic role of MYC rearrangements in diffuse large B-cell lymphoma patients treated with rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone, we evaluated MYC rearrangements by fluorescence in situ hybridization in 563 cases using break-apart probes and IGH/MYC dual-fusion probes. Concurrent BCL2 and BCL6 aberrations were also assessed. Data were correlated with clinicopathological variables and prognostic parameters. MYC rearrangements were observed in 39/432 evaluable cases (9%), including 4 rearrangements detectable only with the dual-fusion probes, 15 detectable only with the break-apart probes and 20 detectable with both dual-fusion probes and break-apart probes. MYC rearrangements correlated with germinal center B-cell origin (P=0.02), MYC protein expression (P=0.032), and larger tumor mass size (P=0.003). Patients with MYC rearrangements were more likely to be treatment resistant (P<0.0001). All types of MYC
rearrangements were associated with poorer disease-specific survival, that is, 20/39 dead, median
disease-specific survival 42 months, compared with 98/393 dead among the non-rearranged cases,
median disease-specific survival not reached (P=0.0002). Cases with MYC rearrangements that
overexpressed MYC protein were at risk with respect to disease-specific survival independent of the
International Prognostic Index (P=0.046 and P<0.001, respectively). Presence of concurrent BCL2
aberrations but not of BCL6 aberrations was prognostically additive. Radiotherapy seemed to diminish
the prognostic effects of MYC rearrangements in diffuse large B-cell lymphoma patients since only
2/10 irradiated patients with MYC rearrangements died of/with disease, compared with 16/28
non-irradiated patients with MYC rearrangements. We conclude that MYC rearrangements add
prognostic information for individual risk estimation and such cases might represent a distinct,
biologically determined disease subgroup.