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CO16

LIMITED IMPACT OF MYC, BCL2 AND BCL6 BREAKS IN THERAPEUTIC DECISIONS FOR DIFFUSE LARGE B CELL LYMPHOMAS (DLBCL) IN A REAL WORLD SETTING

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Diagnosis of DLBCL with *MYC, BCL2* and/or *BCL6* breaks (double hit, DH) is rare but relevant given the poor outcome with conventional treatment and possible treatment-escalation benefits suggested by retrospective studies.

In order to characterize the impact of *MYC*, *BCL2* and *BCL6* breaks in treatment decisions in DLBCL patients (pts) all DLBCL biopsies tested by FISH for *MYC*, *BCL2* and *BCL6* breaks between 2010-2017 in a single center, and patient characteristics, were reviewed. Cell-of-origin was defined according to Hans algorithm. Positivity cut-offs for MYC and BCL2 were ≥40% and ≥50%, respectively. FISH was done in pre-selected immunophenotypically-defined germinal center (GC) cases and in additional pts with unusual morphological and/or clinical features. The impact of FISH was assessed as the number of pts needed to screen (NNS) to intensify treatment in one (calculated using prevalence of DH and number of treatment changes informed by FISH) and NNS to avoid one progression/death (based on published data comparing PFS with aggressive treatments versus RCHOP calculated as stated in Rembold 1998).

76 biopsies underwent FISH. The sample (49% male, median age 57, 66% stage III/IV, 39% IH/H risk IPI) included 43% pts ≥60yo, 30% with significant comorbidities and 16% transformed lymphomas. 85% were GC, 16% double MYC/BCL2 expressors. 16% had DH (6 *MYC/BCL2*, 5 *MYC/BCL6* and 1 *MYC/BCL2/BCL6).* Overall 12% pts were escalated from RCHOP to aggressive regimens based on clinical factors (8 pts) and FISH (1 pt). 9/12 (75%) DH pts were not escalated due to age, comorbidities and prior anthracyclines. Overall, only 35/76 tested pts were fit for aggressive regimens. Assuming a 16% DH prevalence in our tested pts and a selection of fit pts for FISH testing so that half treatment changes are due to FISH results, the NNS for one therapeutic change decreases from 76 to 13. For a median 12-month PFS with RCHOP, a 26% reduction in the risk of PFS events with aggressive regimens (Howlett et al 2015) a 16% prevalence of DH and 8% therapeutic changes, 836 pts need testing to avoid one progression/death in 1 year. If only fit pts undergo FISH this decreases to 140.

The results suggest that for treatment purposes FISH testing in DLBCL can be restricted using clinical information added to cell-of-origin and/or protein expression. This impacts on costs/feasibility of testing while new therapies with acceptable toxicity for a predominantly elderly/comorbid population are unavailable.