Not yet time to abandon the Deauville criteria in Diffuse Large B cell lymphoma

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Running title: Deauville criteria vs ΔSUVmax in DLBCL

We read the article by Rekowski and colleagues with interest, which reported improved response discrimination using ΔSUVmax compared to the Deauville Scale (DS) for interim PET (iPET) in Diffuse Large B-cell Lymphoma (DLBCL) but only assessed complete metabolic response (CMR) versus no-CMR considering binary cut offs of DS 1-3 vs. 4,5 and DS 1,2 vs. 3-5.

In a prospective blinded study in 189 DLBCL patients after 2 cycles of R-CHOP, we reported that DS-5 was associated with inferior progression free- (PFS) and overall survival (OS) compared with DS 1-4 whereas no-CMR (DS 4,5) was not (1). DS-5 was defined as maximum standardized uptake value (SUV_{max}) ≥three times the SUV_{max} in liver and/or new lesions. DS-5 and IPI were independent predictors in multivariable analysis, ΔSUVmax<66% was predictive in univariable analysis only. Eleven of 14 patients with ΔSUVmax<66% had DS-5, suggesting both identify increased risk of treatment failure. Comparable findings have been reported after one (2), and four cycles of R-CHOP (3) and in Hodgkin (4) and primary mediastinal B cell lymphomas (5) whereby only the proportion of patients with DS-5 had inferior PFS and OS.

We recently reported a comparative study of reading methods and timing of iPET in 1692 DLCBL patients (6). iPET post 2 and 4 R-CHOP significantly discriminated responders irrespective of reading method using DS 1-3, DS 1-4 or ΔSUVmax≥66% as good response with negative predictive values > 80%. This is relevant for clinical practice, where R-CHOP is standard treatment and early CMR using DS can be reassuring for patients and doctors. Multivariate HRs at cycle 2 were 4.91 for DS-5 vs. 2.93 for $ΔSUV_{max}$< 66% and at cycle 4 were 6.20 for DS-5 vs. 4.65 for $ΔSUV_{max}$< 70%. 2-year PFS for iPET2 positive patients was 36.7(95% CI: 26.3-51.5)% for DS-5 and 56.3(95% CI: 48.5-65.4) for ΔSUVmax<66% and for iPET4 positive patients was 33.3(95% CI: 18.9-58.7)% for DS-5 and 47.2(95% CI: 33.4-66.7)% for $ΔSUV_{max}$< 70%.

ΔSUV_{max} however identified a larger proportion of poor responders than DS-5, 12.7% vs. 5.6% of the population at cycle 2 and 10.2% vs. 5.0% at cycle 4.

Considering de-escalation in trials, all reading methods detect good response at cycle 2. Considering escalation, DS-5 identifies patients with the worse prognosis at cycles 2 and 4. Cycle 4 is the optimal timing for detection of poor response with more poor responders identified using $\Delta SUV_{max} < 70\%$, but which carries the disadvantage of later treatment escalation. Regardless of the method used, the positive predictive value is suboptimal and combining baseline metabolic tumor volume*(7)* and circulating tumor DNA*(8)* with early metabolic and molecular response appears promising.
It is premature to abandon the Deauville criteria in DLBCL.

DISCLOSURES

References

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