predicted higher EFS in patients with age >60, male sex, IPI 3-5 and stage II-IV (Figure 1D).

Conclusion: New treatment modalities like CARTs, resulted in renewed interest in iPET adaptive frontline trial design strategies. Our results support the prognostic impact of iPET/CT in a prospective clinical trial setting and helps design and interpretation of ongoing and future clinical trials evaluating iPET/CT adaptive frontline trials.

Keywords: PET-CT, Aggressive B-cell non-Hodgkin lymphoma, Combination Therapies

No conflicts of interest pertinent to the abstract.

172 | BONE MARROW INFILTRATION ASSESSMENT BY FDG^{18}-PET: CAN THIS IMAGING TEST REPLACE BONE MARROW TREPHINE BIOPSY IN DIFFUSE LARGE B CELL LYMPHOMA STAGING?

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Introduction: Bone marrow assessment (BMI) is an important part of disease staging in lymphoma, and includes FDG^{18}-PET and BM trephine biopsy (BMB), which is the gold-standard for detecting BM infiltration. Nevertheless, studies indicate that PET accurately detects BMI in aggressive lymphomas.

We aimed to assess the accuracy of PET in detecting BMI in diffuse large B-cell lymphoma (DLBCL).

Methods: Single centre retrospective analysis of 335 patients (pts) diagnosed with DLBCL from 2010 to 2019. BMB and PET data at diagnosis was available in 144 pts. Agreement between PET and BMB findings was assessed by Cohen's *k* computation. For survival analysis, Cox regression model was used.

Results: A total of 144 pts underwent PET and BMB, 57% males, median age 63 years (22-89). Positive BMB (BMB+) was observed in 22 (15%) pts (19 with BMI by DLBCL and 3 by discordant low-grade lymphoma). Positive PET (PET+) was observed in 36 (25%) pts (diffuse BMI pattern in 18 pts, focal in 16 and both in 2 pts). At diagnosis, 92% of all PET+ pts presented with advanced stage disease due to extra-medullary organ involvement (AdS). Concordant detection of BMI by PET and BMB was observed in 14 pts. Twenty-two pts with PET+ (out of 36) were missed by BMB (BMB-), 12 of these with focal BMI pattern. BMI was not detected by PET in 8/22 BMB+ pts (2/8 with low-grade lymphoma in BMB). Only 8/108 (7%) pts with PET- had BMB+ and 22/122 (18%) pts with BMB- showed PET+. We observed a moderate agreement between PET and BMB ($k = 0.36$; $p < 0.001$).

Considering BMB as the gold standard for BMI, the sensitivity and specificity of PET for BMI assessment were 64% (95%CI: 41-82%) and 82% (95%CI: 74-88%), respectively. PPV (positive predictive value) was 39% (95%CI: 24-56%) and NPV (negative predictive value) was 93% (95%CI: 85-97%).

In our cohort, the progression free survival (PFS) at 5 years (yrs) was 58%. Median PFS for BMB- and BMB+ was NR (not reached) and 25 months, respectively (HR 1.68; $p = 0.097$). For BMI by PET, PFS was NR and 15.8 months for PET- and PET+, respectively, significantly higher in PET- group (HR 2.49; $p = 0.001$). The negative impact of PET positivity in PFS became not significant after multivariate analysis for different prognostic variables.

Total overall survival (OS) at 5 yrs was 67%. Median OS was NR for both BMB- and BMB+ (HR 1.61; $p = 0.181$; 70% and 53% at 5 yrs) and NR for both PET- and PET+ (HR 1.70; $p = 0.084$; 72% and 51% at 5 yrs).

Conclusions: We showed a higher specificity of FDG^{18}-PET over BMB in BMI assessment in DLBCL. In fact, a higher number of pts presented BMI by PET compared with BMB, which may have failed to detect focal BMI. However, although we showed that BMI by PET had a negative impact on global PFS, further studies are necessary to clarify if BMI adds a negative impact on survival of DLBCL pts with AdS already in PET staging. Contrastingly, PET sensitivity in detecting BMI was lower which may be related to its low avidity for low tumour burden and low volume disease.

Keywords: Diagnostic and Prognostic Biomarkers, PET-CT, Aggressive B-cell non-Hodgkin lymphoma

No conflicts of interest pertinent to the abstract.

173 | THE ELDERLY PROGNOSTIC INDEX (EPI) PREDICTS EARLY MORTALITY IN OLDER PATIENTS WITH DLBCL. A SUBSTUDY OF THE ELDERLY PROJECT BY THE FONDAZIONE ITALIANA LINFOMI (FIL)

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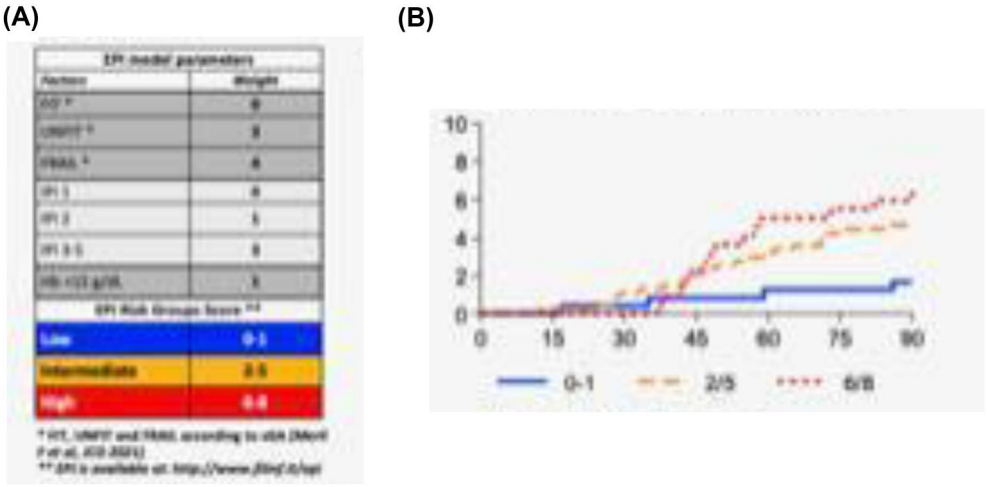
Introduction: The Elderly Prognostic Index (EPI) is based on the integration of a simplified geriatric assessment (sGA), haemoglobin levels, and International Prognostic Index (IPI) and has been validated to predict overall survival in older patients with Diffuse Large B-cell lymphoma (DLBCL) *(Merli et al, JCO 2021)*. In this study we evaluated the ability of EPI to predict the risk of early mortality in older DLBCL patients.

Methods: This analysis was conducted starting from the same dataset of the prospective observational Elderly Project (EP) that has been used to define the EPI. The main endpoint of this analysis was early mortality rate defined as death occurring within 90 days from the date of diagnosis. Starting from EP we only excluded alive patients with a follow-up shorter than 90 days. Clinical features, treatment details, and causes of death were retrieved from the EP dataset. Treatment was classified in three groups: Full Dose (FD; > 70% of theoretical dose of anthracycline), Reduced Dose (RD; < 70%), and Palliative therapy (PT; No anthracyclines). EPI was calculated as originally reported *(Merli et al. JCO 2021)* (Figure 1A).

Results: This study was conducted on 1150 out of 1163 patients retrieved from the EP who were evaluable for the type of therapy and follow-up. Median age was 76 years (65 to 94). Thirty-one percent were older than 80 years; 55%, 28% and 17% were FIT, UNFIT , and FRAIL based on sGA. EPI score was 0-1 (low), 2-5 (intermediate), and 6-8 (high) in 24%, 48% and 28%, respectively. Time to Therapy (TTT) was shorter than 15 days in 24%. A pre-phase therapy was administered in 14% of patients but details were lacking. Overall, 69 early deaths were observed being 19% of all reported deaths. The cumulative incidence of early death at 90 days was 6.0%. Comparing the causes of the deaths occurring earlier or later than 90 days we observed lower frequency of deaths due to lymphoma progression for early events (42% vs 75%) and higher frequency of deaths due to toxicity and to infections (32% vs 4% and 22% vs 3%, respectively). In univariable analysis factors associated with higher risk of early deaths were age >80 years, sGA, anemia, high risk IPI, TTT < 15 days, bulky disease, EPI (intermediate and high risk) and the use of PT. We conducted a multivariable analysis on 931 patients excluding PT and confirmed an independent prognostic role to predict Early death for high risk EPI (OR 3.45; 95% CI 1.07–11.2) (Figure 1B) and for bulky disease (OR 2.09; 95% CI 1.09 – 3.98)

Conclusions: The cumulative incidence of early death for older patients with DLBCL is not negligible (6%), is mainly associated with non-lymphoma related events and suggests the adoption of adequate preventive measures. For patients treated with an anthracycline



containing regimen, high risk EPI and bulky disease are independent factors to predict the risk of dying early during treatment.

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Keywords: Diagnostic and Prognostic Biomarkers, Aggressive B-cell non-Hodgkin lymphoma, Therapeutics and Clinical Trials in Lymphoma - Other

No conflicts of interest pertinent to the abstract.

174 | POLATUZUMAB VEDOTIN WITH BENDAMUSTINE AND RITUXIMAB FOR RELAPSED/REFRACTORY HIGH-GRADE B-CELL LYMPHOMA: THE UK EXPERIENCE

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Introduction: For patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) ineligible for stem cell transplantation (SCT) the addition of polatuzumab vedotin to bendamustine and rituximab (Pola-BR) has been shown to improve progression-free survival (PFS) and overall survival (OS). The combination is also increasingly used as bridging to CAR T-cell therapy (CAR-T) and after CAR-T failure. We aimed to assess its efficacy when used for these indications via 2 UK early access schemes.

Methods: This retrospective study included patients treated with Pola-BR via the Early Access to Medicines Scheme (EAMS) for re-induction therapy and Cancer Drugs Fund (CDF) for CAR-T bridging at 28 UK hospitals between July 2019-October 2020. Responses were investigator-assessed. Time to event was measured from the first day of Pola-BR treatment.

Results: 133 patients were included: 65.4% male; median age 72 (18-88); 30.1% performance status (PS) 2-4; 21.8% bulky disease (>7.5cm); 64.7% ≥ 2 prior treatments and 68.4% refractory to the last treatment. The median number of cycles completed was 4 for all patients and 1 for CAR-T bridging. Bendamustine was dose reduced for 36.8% and omitted for 7.5% in at least 1 cycle. The overall response rate (ORR) was 57.0% (complete response (CR) 32.8%), median follow-up was 7.7 months, median PFS 4.8 months and median OS 8.2 months.

Seventy-eight patients received Pola-BR with no planned SCT/CAR-T. Of these 78.2% were SCT ineligible due to age, co-morbidity or PS. The ORR was 65.8% (CR 40.8%), median PFS 5.4 months and median OS 10.2 months. Significant factors for shortened PFS by univariate analysis were bulk disease >7.5cm (HR 2.32 (95% CI 1.23-4.38) p = 0.009), ≥2 prior treatments (HR 2.17 (95% CI 1.19-3.95) p = 0.01) and refractoriness to last treatment (HR 3.48 (95% CI 1.79-6.76) p < 0.001). Significance was maintained in a multivariate model of these 3 variables.

Forty patients received Pola-BR as bridging to CAR-T. The ORR was 42.1% (CR 18.4%, partial response 23.7%, stable disease 15.8%, PD 42.1%) and 31/40 (77.5%) proceeded to CAR-T infusion (N = 5 died due to PD; N = 1 died due infection during bridging; N = 2 infusion pending; N = 1 unavailable).

Sixteen patients received Pola-BR after CAR-T failure. The ORR was 43.8% (CR 18.8%) and 3/16 were successfully bridged to allogeneic SCT.

Conclusions: The data from this real-world cohort of support the use of Pola-BR use as an efficacious treatment for SCT ineligible patients with R/R DLBCL and suggest that bulk disease, number of prior treatments and response to prior treatment are predictors of PFS. These data also provide new insights into the use of Pola-BR as