PMBCL, may be still safely adopted. Further studies on toxicity and economic costs are needed.

Keywords: Aggressive B-cell non-Hodgkin lymphoma

No conflicts of interest pertinent to the abstract.

AGGRESSIVE NHL

166 | HIGH ADIPOSE TISSUE DENSITY IS A NEGATIVE PROGNOSTIC FACTOR IN DLBCL PATIENTS TREATED BY R-CHOP, INDEPENDENT FROM TMTV AND PS –FROM THE REMARC STUDY

J.-F. Deux[1], M. Meignan[2], L. Chartier[3], A. Judet[4], L. Vercellino[5], O. Casasnovas[6], V. Baud[7], H. Tilly[8], A.-S. Cottereau[9], C. Thieblemont[4]
[1]APHP, Hopital Henri Mondor, Radiologie, Creteil, France, [2]LYSA-IM, Hopital Henri Mondor, LYSA-IM, Paris, France, [3]LYSARC, Statistique, Pierre-Benite, France, [4]APHP, Saint-Louis Hospital, Hemato-oncology, Paris, France, [5]APHP, Hopital Saint-Louis, Medecine Nucleaire, Paris, France, [6]CHU le Bocage, Hematologie, Dijon, France, [7]Université de Paris, NF-KappaB, différenciaation et Cancer, Paris, France, [8]Centre Henri Becquerel, INSERM U1245, Rouen, France, [9]APHP, Hopital Cochin, Medecine Nucleaire, Paris, France

Background: Body mass composition (BMC) including body mass index (BMI), muscle and adipocyte tissue structure has been reported to be associated with survival in oncological patients (pts). The aim was to analyze the prognostic impact of the BMC in elderly pts with diffuse large B-cell lymphoma treated with R-CHOP in first line.

Patients and Methods: Pts included in the REMARC study (NCT01122472), (DLBCL >60 to 80 years old, responder to R-CHOP randomized between lenalidomide or placebo). BMC parameters were measured at the level of L3 with an Artificial Intelligence software on the CT part of the baseline PET/CT performed before treatment: lumbar skeletal muscle index (LSMI, cm^2/m^2) and density (LSMD, Hounsfield Unit (HU)), lumbar psoas muscle index (LPMI) and density (LPMD), lumbar subcutaneous adipose index (LSAI) and density (LSAD), and lumbar visceral adipose index (LVAI) and density
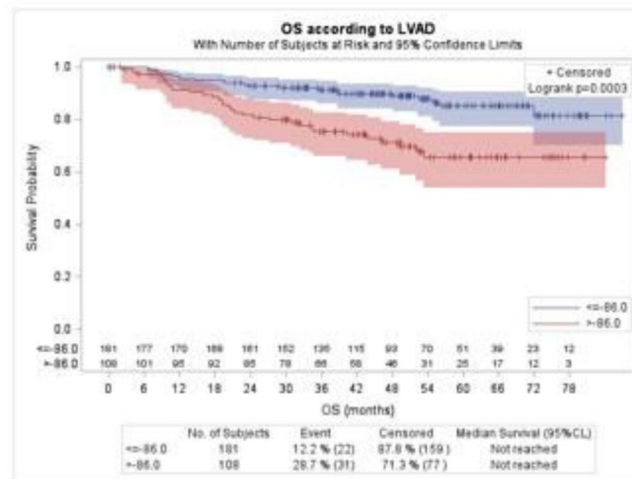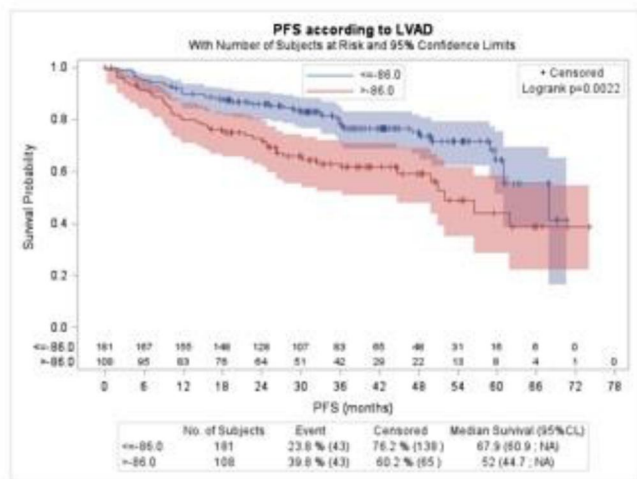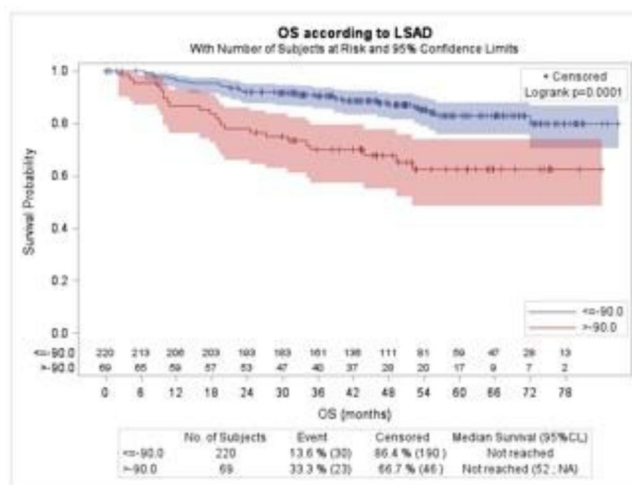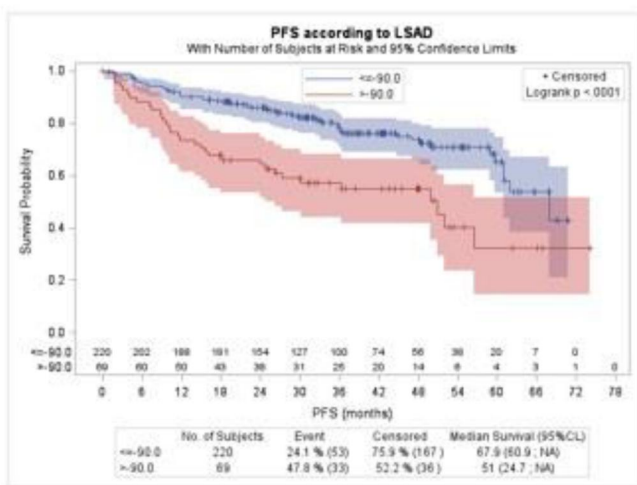
(LVAD). The optimal body parameters cut-offs for PFS and OS were determined by X-tile analyses and confirmed by a training validation method.

Results: 289 pts were analyzed, including 171 males (59.2%) and 113 (39.1%) pts≥70. In male, BMC showed significant higher BMI LSMI LPMI, and LVAI. In pts ≥70, BMC showed significant lower LSMI and higher LVAI than in pts < 70. In univariate analysis, only adipose densities (LSAD and LVAD) were prognostic of outcome.

Pts with high LSAD (>-90 HU, n = 69, 24%) had a 3-year PFS of 57.1% vs 77.8% (HR = 2.39 (95%CI = 1.5-3.7)) and OS of 70.0% vs 90.4% (HR = 2.77 (95%CI = 1.6; 4.8)) for the low LSAD pts (≤-90HU). They had lower weight, BMI, worse ECOG PS (≥2, 26.1% vs 12.3%, p = 0.012), more extranodal sites (≥2, 75.4% vs 45%, p < 10^{-3}), higher TMTV (median of 327 cm^3 vs 211 cm^3, p = 0.009), and higher IPI (IPI 3-5, 85.5% vs 66.4%, p = 0.002) and NCCN-IPI (high/high-intermediate, 84.1 vs 63.7%, p = 0.010), but no difference in age (p = 0.24) or sex (p = 0.26).

Pts with high LVAD (>-86 HU, n = 108, 37.4%) had a 3-year PFS of 63.1% vs 78.5% (HR = 1.92 (95%CI = 1.3; 2.9)) and OS of 75.4% vs 91.4% (HR = 2.66 (95%CI = 1.5;4.6)), lower weight, BMI, more extranodal sites (≥2, 61.1% vs 47%, p = 0.021), more bone marrow involved (25.9% vs 13,3%, p = 0.026), higher TMTV (median of 306 cm^3 vs 207 cm^3, p = 0.017), and higher NCCN-IPI (high/high inter-mediate, 79.6% vs 61.9%, p = 0.010), and no difference in age (p = 0.19) or sex (p = 0.27).

Mutivariable analysis including densities, TMTV and ECOG showed that LSAD(>-90) and TMTV (>220cm^3) were independent predictors of PFS and OS and LVAD TMTV (>220cm3) and ECOG (≥2) were independent predictors of PFS and OS .

Conclusions: This is the first report showing that adipose tissue alteration is a strong prognosticator of outcome in DLBCL. The key question remains if this adipose tissue alteration should be considered as an inherent pt's frailty or would be a consequence of metabolic changes induced by the tumor. Metabolomic analysis of the baseline plasma is ongoing and might give us new insights into this question.

Keywords: Diagnostic and Prognostic Biomarkers

167 | LYMFOREST-25: PERSONALLY-TAILORED SURVIVAL PREDICTION OF PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA USING CLINICO-GENOMIC PROGNOSTIC MODELS

A. Mosquera Orgueira[1], M. Cid López[1], A. Peleteiro Raindo[1], J. Án. Díaz Arias[1], M. S. González Pérez[1], B. Antelo Rodríguez[1], L. Bao Pérez[1], R. Ferreiro Ferro[1], C. Aliste Santos[1], M. M. Pérez Encinas[1], M. F. Fraga Rodríguez[1], Z. Xu-Monette[2], C. Visco[3], K. Young[2], J. L. Bello López[1]

[1]University Hospital of Santiago de Compostela, Hematology, SANTIAGO DE COMPOSTELA, Spain, [2]Duke University Medical Center, Pathology, Durham, USA, [3]University of Verona, Medicine, Verona, Italy

Diffuse Large B-cell Lymphoma (DLBCL) is the most frequent type of lymphoma. Despite its high cure rate, 30–40% of cases exhibit relapsed or refractory disease which frequently precludes a dismal prognosis. For this reason, new therapies are being actively investigated for the treatment of DLBCL, such as polatuzumab vedotin and CAR-T therapies. As new drugs are developed, it becomes increasingly important to provide patients with an optimal prediction about the expected outcome of treatment with R-CHOP. Today, clinical risk stratification of DLBCL is still based on the International Prognostic Index (IPI) and its variants. Recently, we demonstrated the feasibility of applying machine learning on gene expression and clinical data to make individual predictions about DLBCL patient outcome.

Our objective was to reproduce the clinico-genomic survival model developed by our team and to refine its predictive capacity by including new clinical and biochemical variables. For this purpose, we used data from the International DLBCL Rituximab-CHOP Consortium Program Study. Gene expression was data was rank-normalized, and the database was randomly split in a training (80%) and validation (20%) group. Afterwards, we created random forests models of survival using the same set of variables that we reported in our previous report, reaching C-indexes >0.66 in all cases, which indicate good discrimination capacity.

In a second step, we included the following data in order to refine the precision of the model: IPI score, ECOG, high LDH, age at diagnosis, Ann-Arbor stage, number of extranodal sites affected, bulky disease, cell-of-origin (COO) status and the percentage of cells positive for CD10, BCL6, FOXP1, GCET and MUM1. We created random forests with and without resampling and with 10 different values of the nsplit variable, and variables with low importance were iteratively removed. The best model was selected for variable optimization and further reduction, reaching c-indexes of 0.762 and 0.731 in the training and validation sets. This model included 25 variables, including 19 transcripts, and was named LymForest-25. Importantly, the model excluded COO status from the classification. A graphical representation of LymForest-25 survival predictions and real patient outcomes clearly indicates the capacity of this tool to stratify patient risk (Figure 1). Furthermore, LymForest-25 outperformed the predictive capacity of the IPI score, all individual IPI variables, Bulky disease and COO status.

In comparison with other tools, LymForest-25 has the advantage of making individualized predictions that do not reside in pre-established clinical and molecular subgroups, overcoming the limitations of imperfect patient subgrouping scores. Such an approach could drive the development of new first-line therapeutic interventions for selected high-risk patients based on personalized predictions.