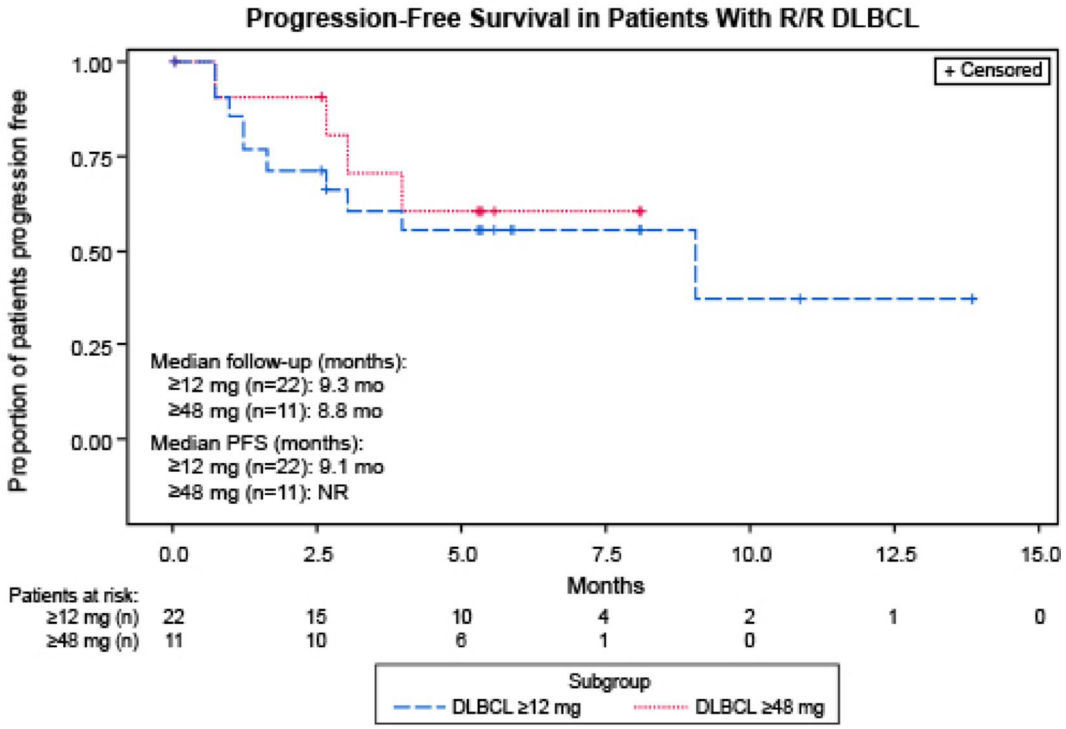

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SESSION 2: LYMPHOMA IMAGING

017 | DEFINING ULTRA-HIGH-RISK DLBCL PATIENTS PRIOR TO INITIAL TREATMENT BASED ON AN INTEGRATIVE HOST AND DISEASE PROGNOSTIC SCORE (FROM REMARC STUDY)

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Background: The risk stratification of patients (pts) with diffuse large B-cell lymphoma (DLBCL) is based on the widely used IPI. Three of the IPI variables (LDH, stage and number of EN sites) may be refined in two metabolic measures obtained by 18FDG-PET, the total metabolic tumor volume (TMTV) and the

		PFS			OS		
	Parameter estimate for score	HR	95%CI	p-value	HR	95%CI	p-value
ECOG>=2,	0.57	1.77	1.0-3.0	0.0359	1.95	1.0-3.6	0.0349
DMAX>32m^{-1}	0.76	2.13	1.3-3.4	0.0013	1.57	0.88-2.8	0.13
LSAD>−90HU	0.70	2.01	1.3-3.2	0.0033	2.06	1.2-3.7	0.0152
TMTV>220cm^3	0.59	1.81	1.1-3.0	0.0171	2.72	1.4-5.4	0.0042

TABLE 1 Hazard ratio (HR) and p-value considering ECOG PS and TMTV, SDmax, LSAD for PFS and OS

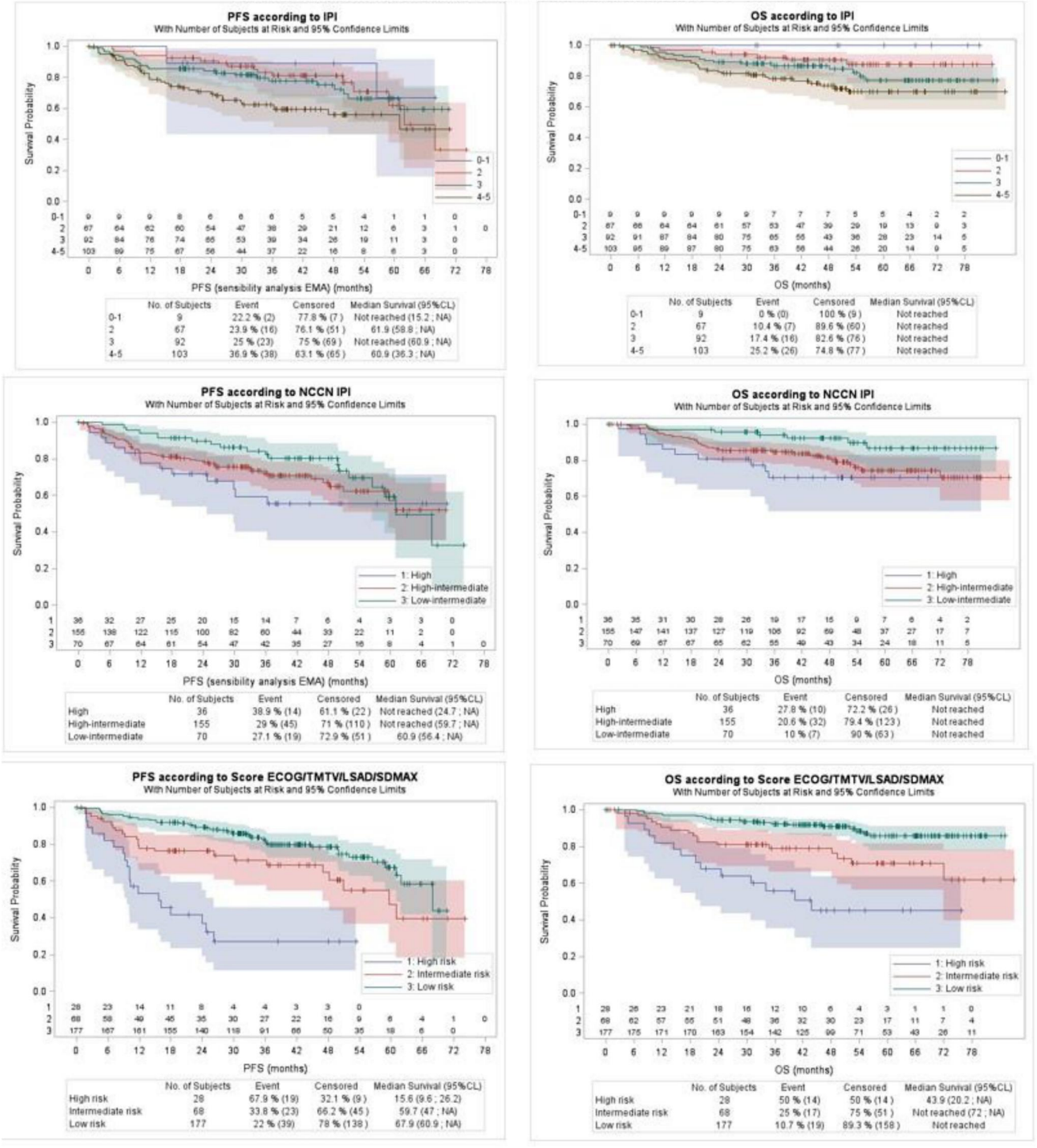

FIGURE 1 Progreesion-free survival and overall survival according to the IPI, the NCCN IPI and the MVED^2 score

distance between 2 lesions (SDmax). We recently demonstrated that the adipose tissue alteration measured by the lumbar subcutaneous adipose density (LSAD) (i.e an increased density) is an independent prognostic parameter in DLBCL. The aim was to analyze if these combined parameters characterizing the host (ECOG PS) and the disease (TMTV, SDmax, LSAD) could help to better identify patients at high risk of relapse, prior to initial treatment.

Patients and Methods: Pts were included in the REMARC study (NCT01122472), (DLBCL >60 to 80 years old, responder to R-CHOP randomized between lenalidomide or placebo). TMTV, SDmax, LSAD were measured on the baseline PET/CT performed before treatment. Statistical methods included multiple Cox regression for developing the MVE2D score.

Results: 273 pts were analyzed. 195 (71%) pts were scored high-risk (3-5) IPI, and 155 (57%) high-intermediate-risk NCCN IPI and 36 (13%) high-risk NCCN IPI. ECOG PS and TMTV, SDmax, LSAD were identified as the 4 independent prognostic factors for PFS and OS (Table 1).

Accordingly, a score Metabolic Volume ECOG Distance Density ($MVED^2$) was calculated as 0.57 (if ECOG PS ≥2) + 0.76 (if SDMAX > 32) + 0.70 (if LSAD > −90) + 0.59 (if TMTV>220).

According to the $MVED^2$ score, pts were classified into low risk (65% of pts, median PFS and OS of 68 months and not reached, respectively), intermediate risk (25% of pts, median PFS and OS of 60 months and not reached, respectively) and high risk (10% of pts, median PFS and OS of 16 and 44 months, respectively) (Fig 1). The $MVED^2$ score has a significant impact on PFS ($p < 0.001$) and OS ($p < 0.001$) (Figure 1). More extra-nodal sites (89.3% >1 vs 47.3%, $p < 0.001$), more high-IPI 3-5 (96.4% vs 68.6%, $p = 0.001$), more high-NCCN IPI (35.7% vs 10.6%, $p < 0.001$), more ABC profile (46.4% vs 20.8%, $p = 0.033$), more involved bone marrow biopsy (42.9% vs 14.7%, $p < 0.001$) and male sex (78.6% vs 58%, $p = 0.041$) were observed in high risk patients than in the low- and intermediate-risk patients.

Conclusions: The $MVED^2$ is the first prognostic index based on new metrics measured on 18FDG-PET and ECOG PS that may help to discriminate ultra high-risk DLBCL pts, even responder to R-CHOP.

Keywords: Diagnostic and Prognostic Biomarkers

Conflicts of interests pertinent to the abstract

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018 | INTEGRATION OF BASELINE METABOLIC PARAMETERS AND MUTATIONAL PROFILE PREDICTS OUTCOME IN DLBCL PATIENTS. A *POST HOC* ANALYSIS OF SAKK38/07 STUDY

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Background: Metabolic tumor volume (MTV), metabolic heterogeneity (MH) and other functional parameters from baseline (18)F-fluorodeoxyglucose positron emission tomography (PET)/computed tomography (CT), combined with gene expression and mutational profiles could be useful to predict the risk of treatment failure in diffuse large B-cell lymphoma (DLBCL). Nevertheless, so far, prognostic algorithms integrating measurable PET/CT parameters and genetic information have not been proposed.

Methods: In the clinical study SAKK38/07 (NCT00544219) of the Swiss Group for Clinical Cancer Research (SAKK), 141 DLBCL patients received R-CHOP14 immunochemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone every 2 weeks). Targeted high-throughput sequencing on tumor genomic DNA was performed on either all exons or hotspots of 68 genes frequently mutated in B-cell lymphomas. The measurement of baseline MTV and MH PET/CT was combined with the mutational profiles in order to explore whether this may allow a better prognostication.

Results: Mutational profiles were available for 72 (51%) patients. The presence of mutations of *SOCS1*, without mutations in *CREBBP* and *EP300*, defined a group of patients with favorable prognosis with a 5-year progression-free survival (PFS) rate of 100%, while patients harboring mutations in *CREBBP* or *EP300* or with *SOCS1* wild-type had a 5-year PFS of 69% ($p = 0.025$).

Using an unsupervised recursive partitioning approach, we generated a decision-tree algorithm, stratifying patients at each step according to the characteristic with the greater capability to predict PFS (Figure 1A). MTV with a cut-off at 9311mL was the factor with the highest correlation with PFS. Among patients with high MTV, the presence of MH higher than 0.43 AUC-CSH defined a high risk group ($N = 21$; 15%). Among patients with low MTV, the presence of