Supplementary Material

Molecular Surveillance of Aggressive Large B-cell Lymphoma using Circulating Tumor DNA Duplexes

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Running head: Circulating tumor DNA monitoring in B-cell lymphomas

Key words: Circulating tumor DNA, duplex sequencing, measurable residual disease, B-cell lymphoma, surveillance, relapse, longitudinal

Supplementary Table Legends

Table S1. List of resources and reagents used in the study.

Table S2. Confusion matrixes of the MRD test results and clinical end points with related statistics in the measured time-points on-therapy.

Table S3. Cox regression univariable models according to on-therapy ctDNA risk factors.

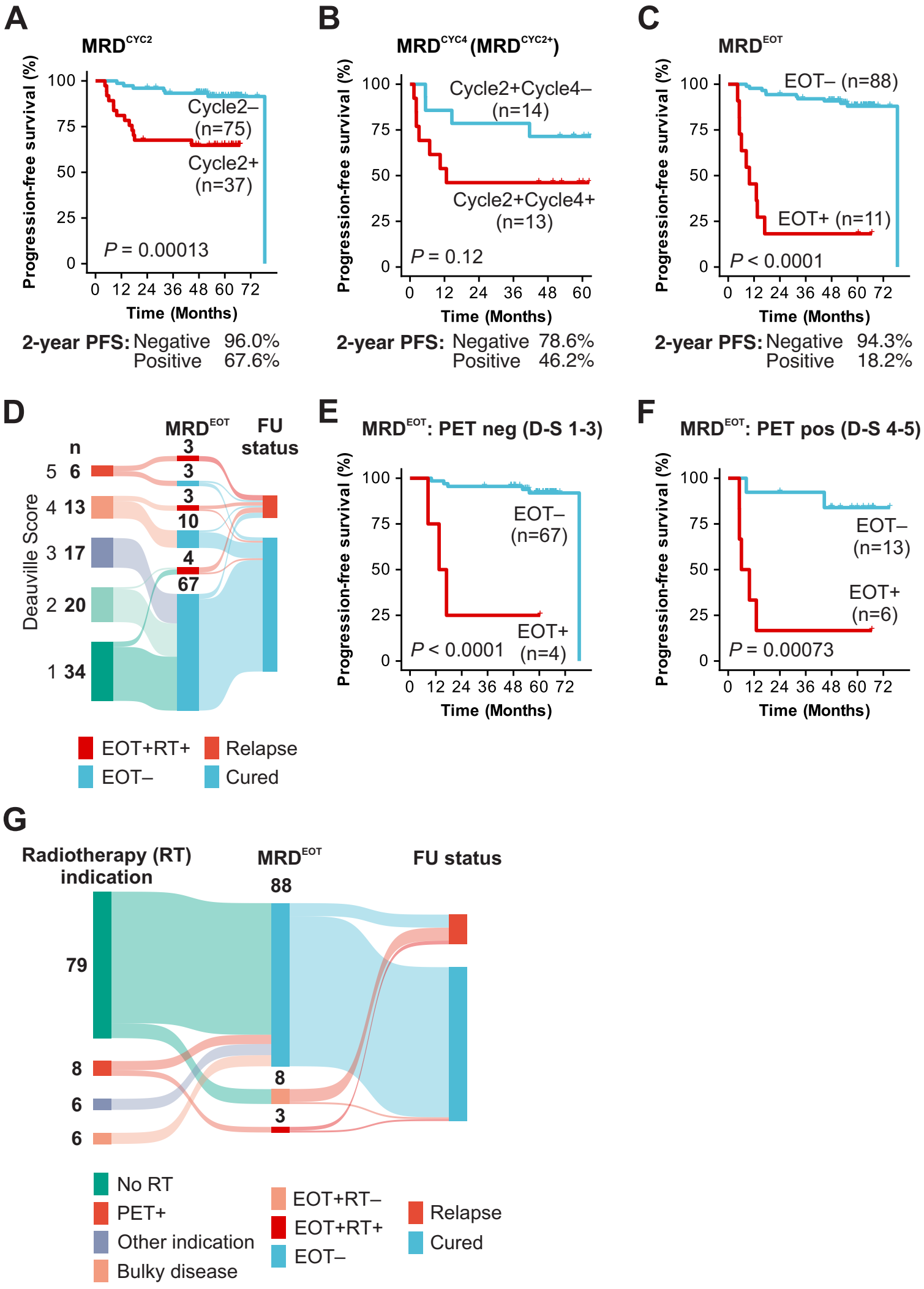
Table S4A-B. Sequencing metrics and measurable residual disease assessments of the study samples.

Supplementary Figure Legends and Figures

Figure S1. Prognostic significance of circulating tumor DNA (ctDNA) detection in serial samples collected during chemoimmunotherapy.

A) Kaplan-Meier (KM) survival estimates for progression-free survival (PFS) according to presence of measurable residual disease (MRD) after two cycles of therapy.
B) KM survival estimates for PFS among evaluable MRD^{CYC2+} patients according to MRD after four cycles (n=27)
C) KM survival estimates for PFS according to EOT MRD.
D) Sankey plot of study patients at EOT according to Deauville scores, MRD^{EOT} and relapse status on follow-up (FU). Numbers in bold indicate the number of patients per group.
E) KM survival estimates for PFS according to EOT MRD among the patients with complete metabolic response (Deauville score [D-S] 1-3).
F) KM survival estimates for PFS according to EOT MRD among the patients with incomplete metabolic response (D-S 4-5).
G) Sankey plot of the study patients at EOT according to radiotherapy (RT) administration status, RT indications, MRD^{EOT} and relapse status on FU. Numbers in bold indicate the number of patients per group.

Figure S1.


A
MRD^CYC2
Progression-free survival (%)
Cycle2– (n=75)
Cycle2+ (n=37)
P = 0.00013
Time (Months)
2-year PFS: Negative 96.0%
Positive 67.6%
B
MRD^CYC4 (MRD^CYC2+)
Cycle2+Cycle4– (n=14)
Cycle2+Cycle4+ (n=13)
P = 0.12
Time (Months)
2-year PFS: Negative 78.6%
Positive 46.2%
C
MRD^EOT
EOT– (n=88)
EOT+ (n=11)
P < 0.0001
Time (Months)
2-year PFS: Negative 94.3%
Positive 18.2%
D
MRD^EOT
FU status
n
Deauville Score
5 6
4 13
3 17
2 20
1 34
3
3
3
10
4
67
EOT+RT+
EOT–
Relapse
Cured
E
MRD^EOT: PET neg (D-S 1-3)
EOT– (n=67)
EOT+ (n=4)
P < 0.0001
Time (Months)
F
MRD^EOT: PET pos (D-S 4-5)
EOT– (n=13)
EOT+ (n=6)
P = 0.00073
Time (Months)
G
Radiotherapy (RT) indication
MRD^EOT
FU status
79
8
6
6
88
8
3
No RT
PET+
Other indication
Bulky disease
EOT+RT–
EOT+RT+
EOT–
Relapse
Cured