ABSTRACT #192, American Society of Hematology, December 9, 2023

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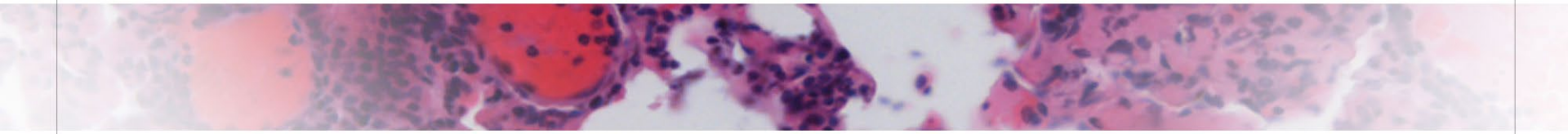


End of Treatment Response Assessment After Frontline Therapy for Aggressive B-cell Lymphoma: Landmark Comparison of a Singular PET/CT scan vs Ultrasensitive Circulating Tumor DNA

Mark Roschewski, Liza Lindenberg, Esther Mena, Rahul Lakhotia, Christopher Melani, Seth Steinberg, Andre Schultz, Gregory Hogan, Jacob Chabon, Sandra Close, Maximilian Diehn, Brian J. Sworder, David M. Kurtz, Ash A. Alizadeh, and Wyndham H. Wilson

Presented at ASH 2023

Conflicts of interest for Mark Roschewski

None		

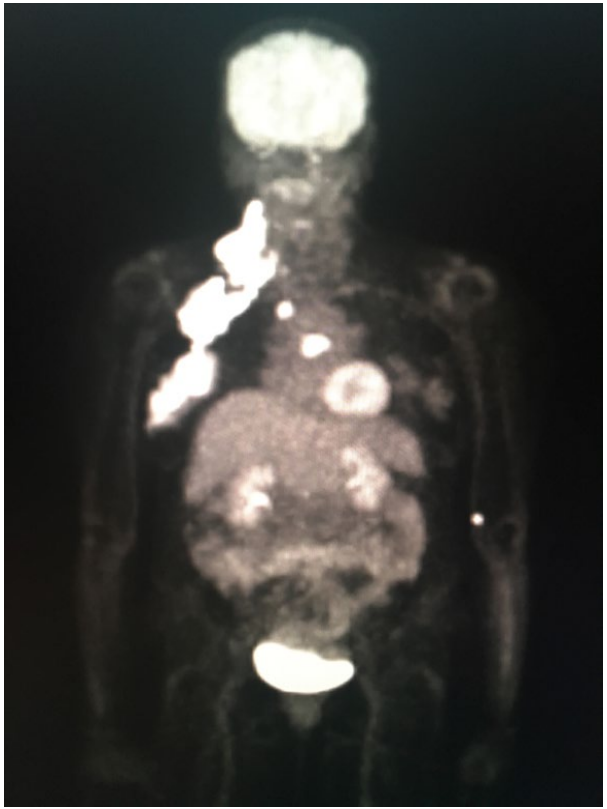
Response Assessment in Lymphoma Reliant on PET/CT

Current standard (FDG-PET scans):

- *Baseline staging*
- *End of therapy (EOT) response assessment*

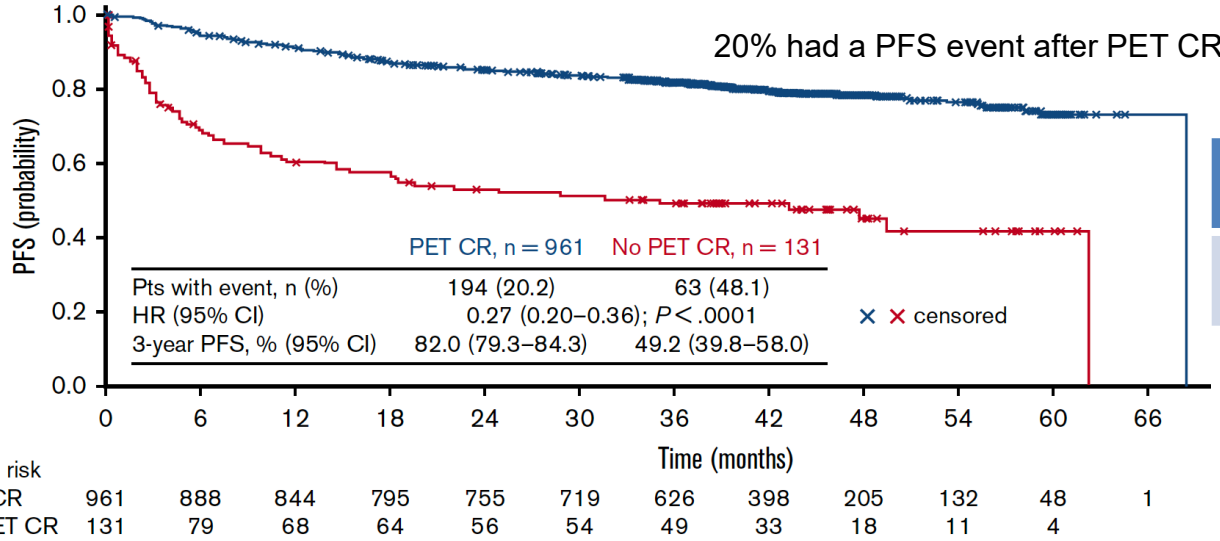
Fundamental limitations:

- *Cannot detect measurable residual disease*
- *Lack of specificity for lymphoma*
- *Radiation exposure*



PET Scans at EOT are Prognostic But Not Specific for Lymphoma

Application of the Lugano 2014 response criteria (GOYA)



PPV at 2.5 years	48.8%
NPV at 2.5 years	83.5%

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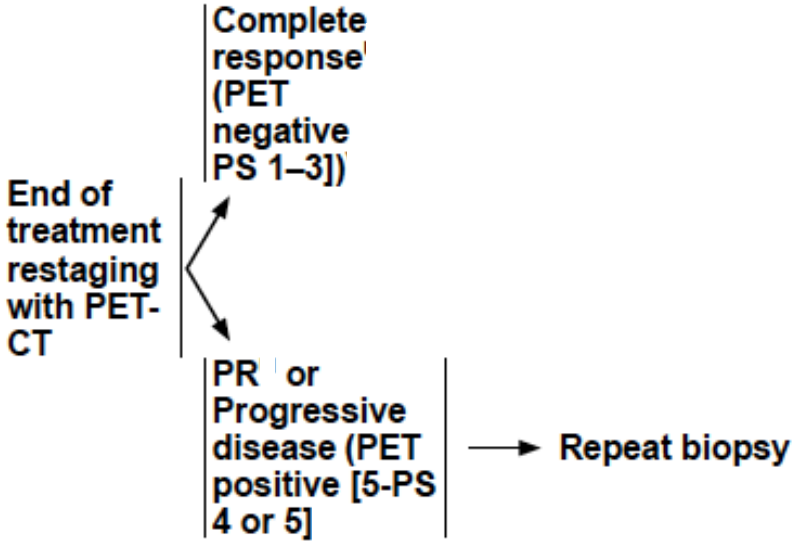
Kostakoglu et al. *Blood Adv* 2021;5(5):1283-1290

Additional Procedures Are Required Prior to Salvage Therapy

"If further treatment based on residual metabolically active disease on PET-CT is being considered, either biopsy or follow-up scan is advised."

Cheson et al. *J Clin Oncol.* 2014 Sep 20;32(27):3059-68



NCCN Guidelines 12/4/2023

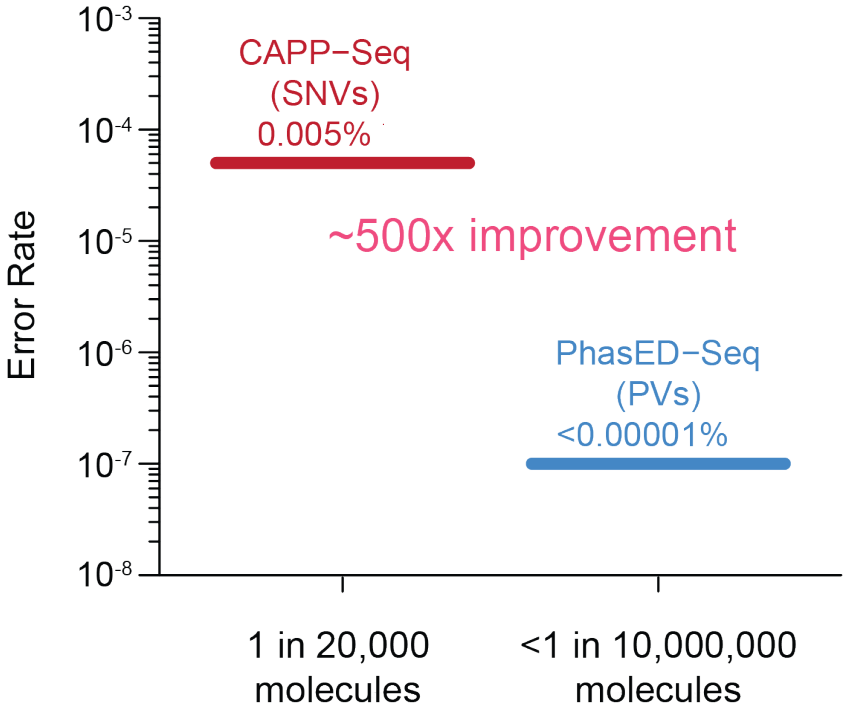
"Repeat biopsy should be strongly considered if PET-positive prior to additional therapy. If biopsy negative, follow PET-negative pathway."

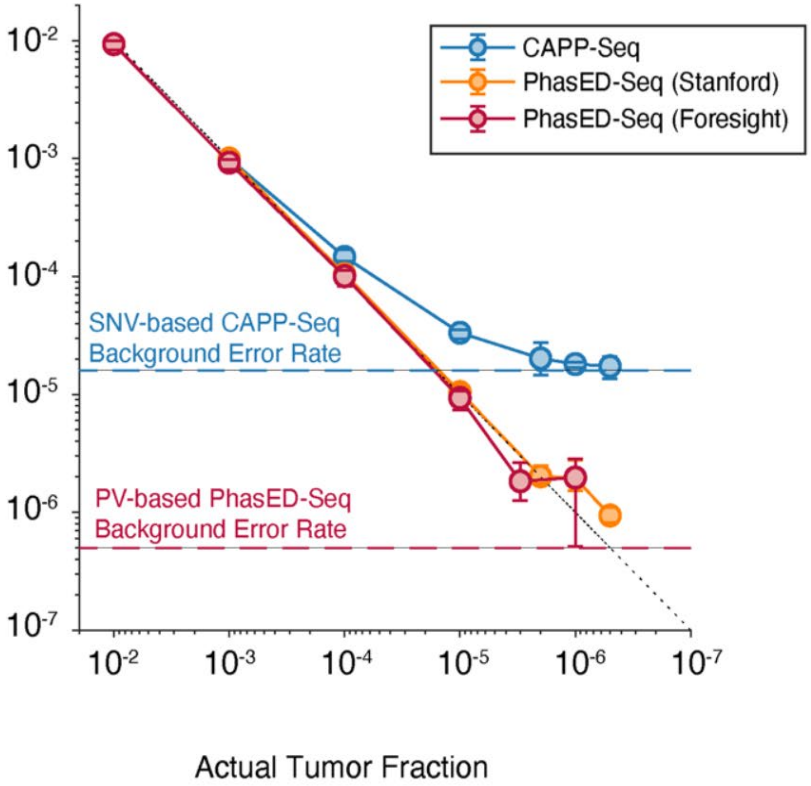
Open questions:

1. Frequency of additional procedures?
2. Proportion of patients who receive salvage therapy without biopsy-proven disease?

Ultrasensitive ctDNA Detection by PhasED-Seq

Analytical Sensitivity (~1x10^{-6})





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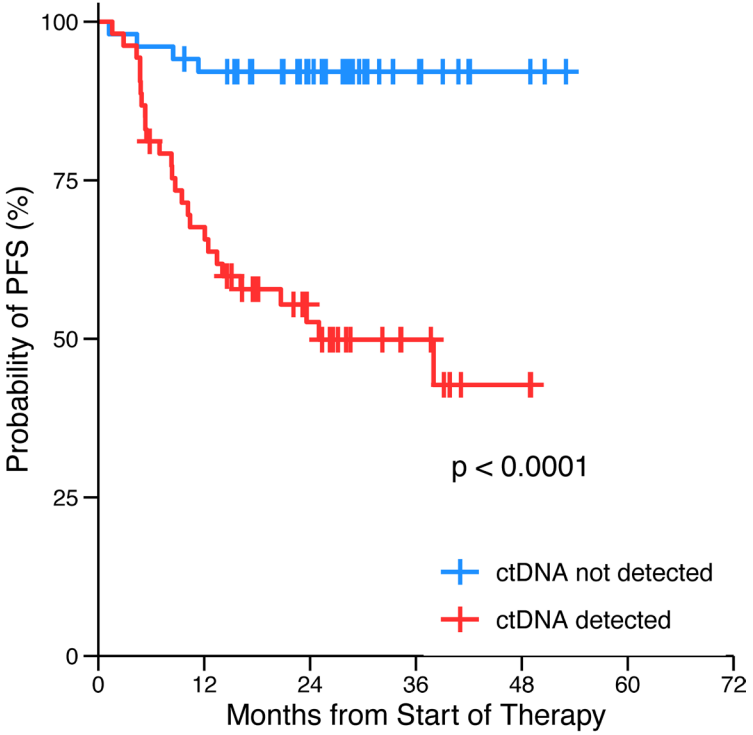
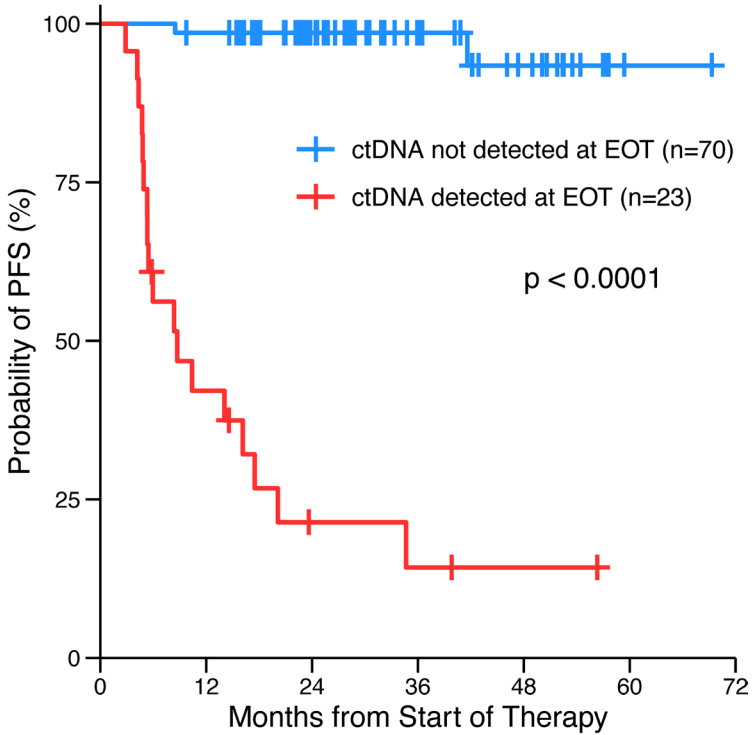
Kurtz et al. *Nat Biotechnol* 2021 Dec;39(12):1537-1547

PhasED-Seq MRD Is Prognostic After 2 Cycles and EOT

ctDNA MRD after 2 Cycles



ctDNA MRD at End of Therapy



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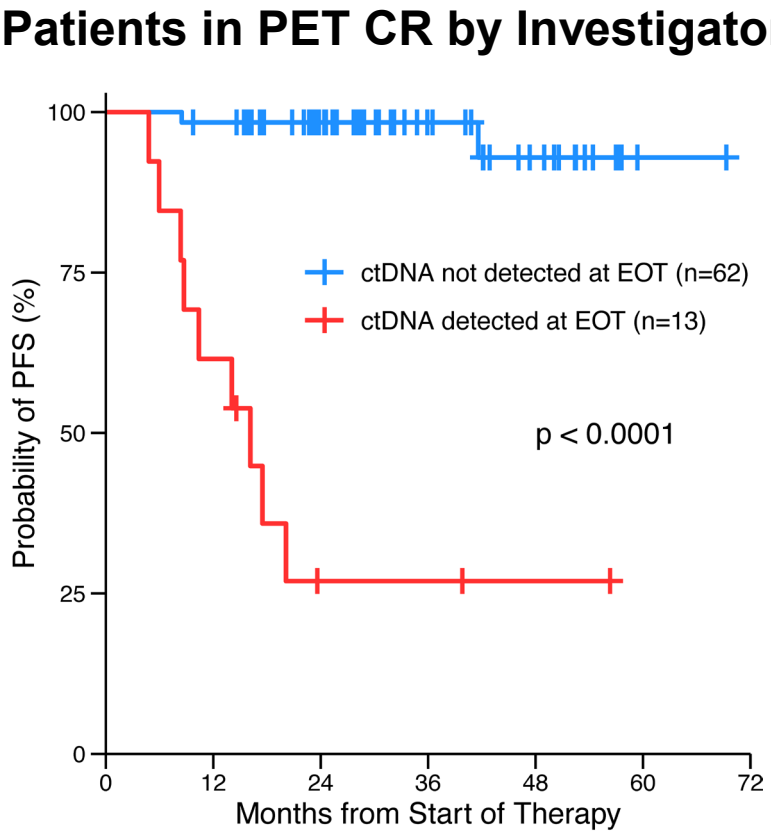
Roschewski et al. *Hematological Oncology* 41(S2):177-179, ICML 2023

PhasED-Seq MRD at EOT Stratifies PET CR



Presented at ASH 2023

Roschewski et al. *Hematological Oncology* 41(S2):177-179, ICML 2023

Hypotheses

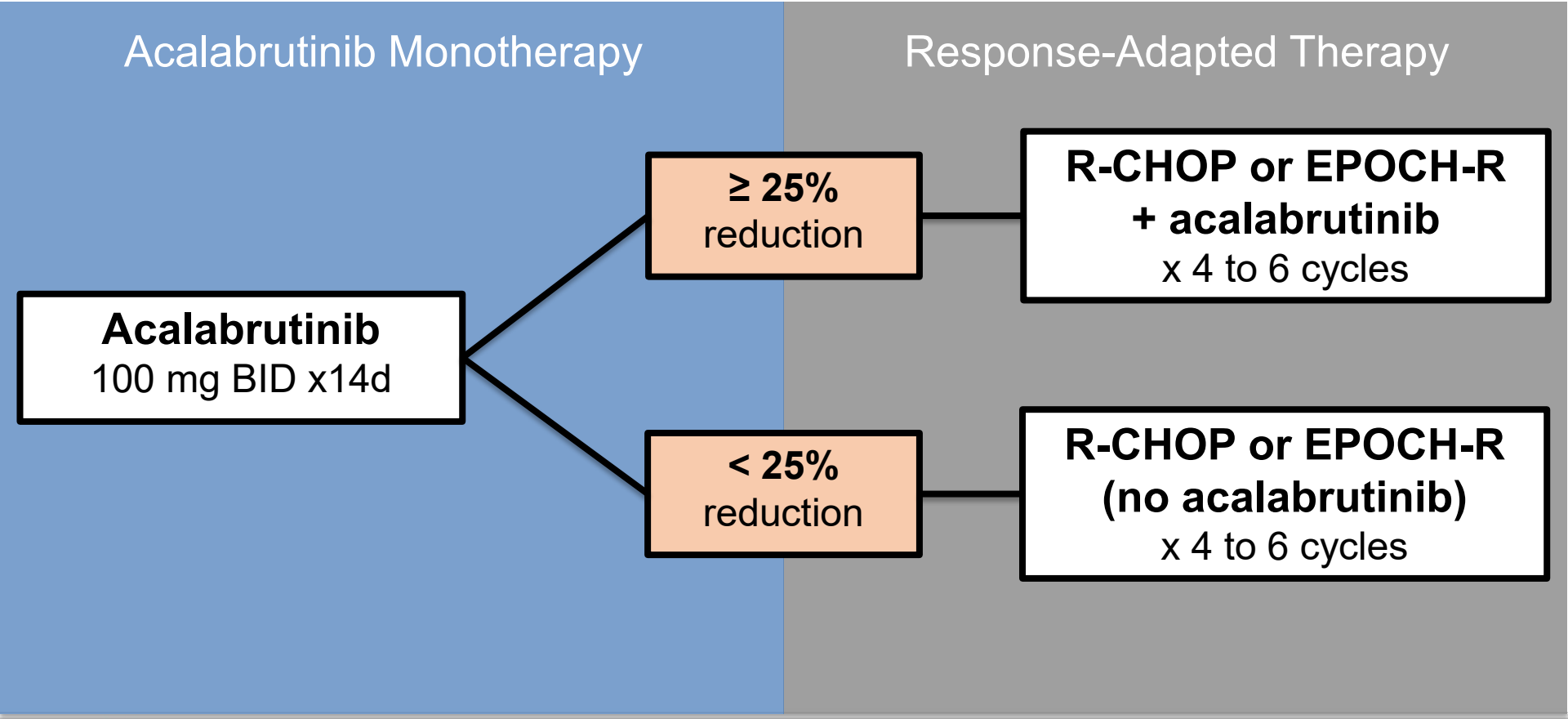
Hypothesis 1: most pts with a singular positive EOT PET/CT scan (Deauville 4 or 5) do not have active lymphoma and will not progress.

Hypothesis 2: PhasED-Seq can outperform a singular PET/CT at the landmark timepoint of EOT to detect active lymphoma

Methods

- Pts ongoing trial testing chemotherapy +/- acalabrutinib as frontline therapy for LBCL
  - Pts with available PET/CT and plasma at EOT were included
- EOT PET/CT scans were interpreted by 2 nuclear medicine radiologists blinded to clinical outcomes using the 5-point Deauville Score (DS)
- Plasma samples after C2 and EOT were centrally analyzed by PhasED-Seq blinded to clinical outcomes with an analytical threshold of $1x10^{-6}$
- Unplanned PET/CT scans and tissue biopsies after EOT were recorded
- We compared the prognostic utility of PhasED-Seq MRD to PET/CT scans at EOT

Clinical Trial: Acalabrutinib Window Study



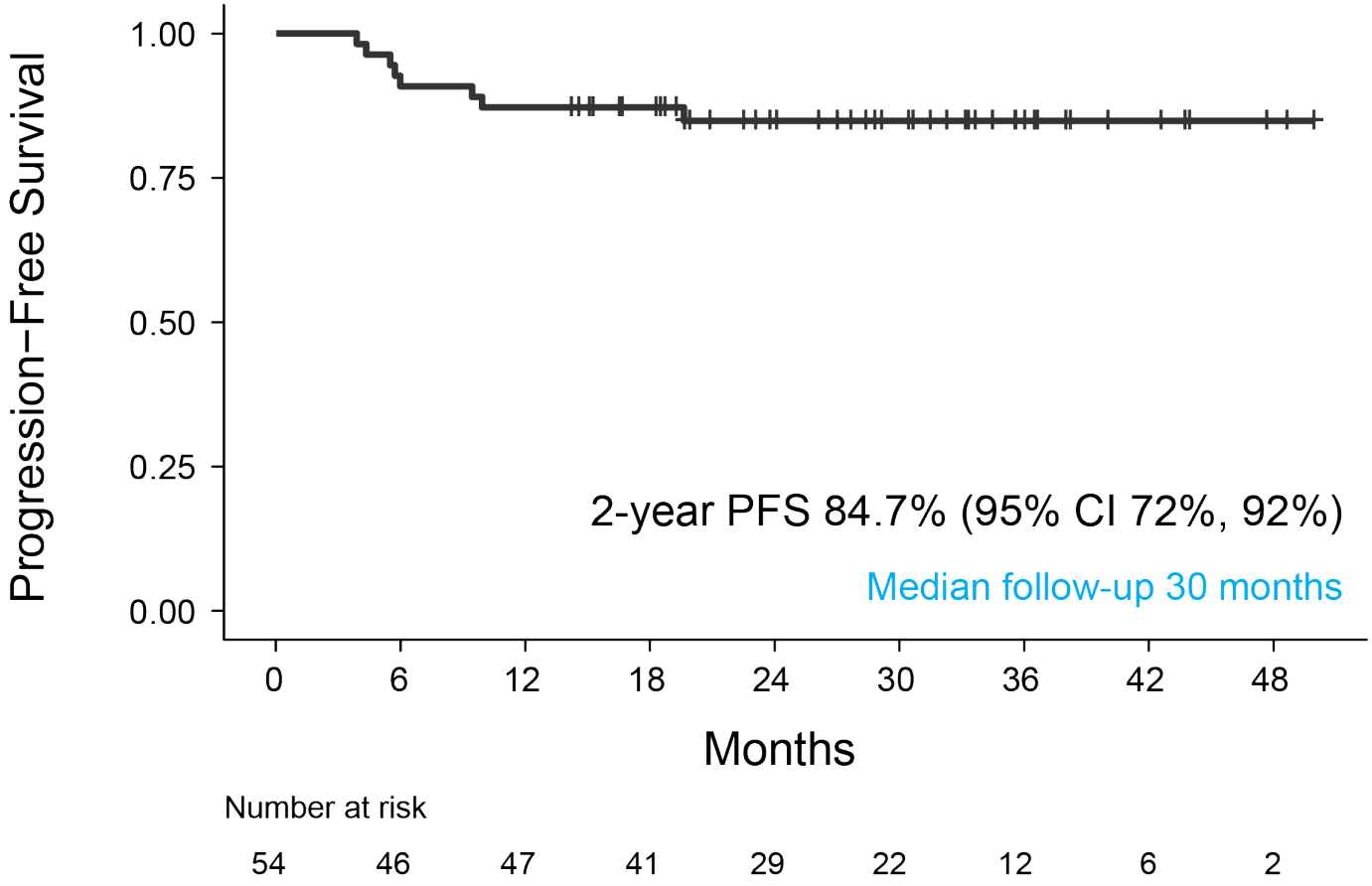
Characteristics of the Study Population

55 pts had a PET/CT and plasma at EOT
54 (98%) were successfully genotyped

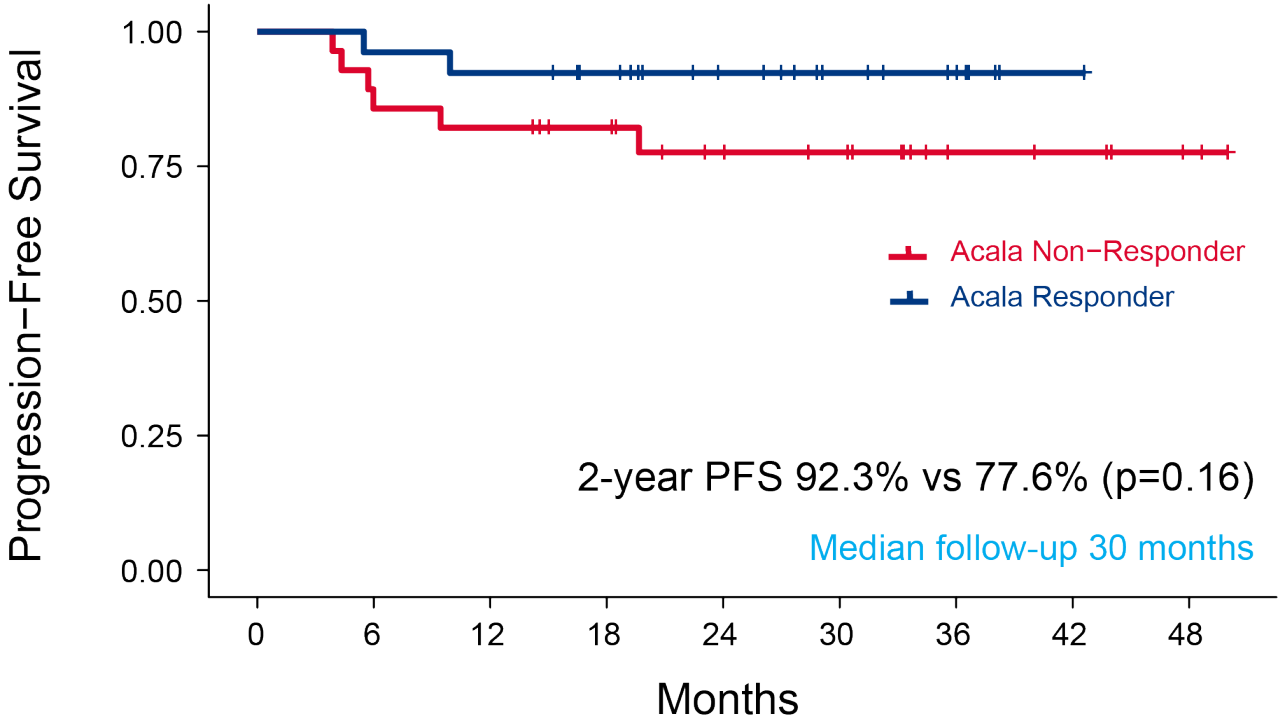
Table 1. Characteristics of the Patients

Characteristic	N (%)
Number of patients	54
Female sex	22 (41%)
Age	
Median (range) - yr	62 (26-85)
< 60 years	22 (41%)
60-69 years	22 (41%)
≥ 70 years	10 (18%)
International Prognostic Index	
0-1 (low-risk)	13 (24%)
2 (low-intermediate risk)	15 (28%)
3 (high-intermediate risk)	18 (33%)
4-5 (high risk)	8 (15%)
DLBCL:NOS subtype (Hans)	46 (85%)
Non-GCB	21 (39%)
GCB	24 (44%)
T-cell/histocyte rich	1 (2%)
HGBL with MYC and/or BCL2 or BCL6	8 (15%)

Progression Free Survival All Patients



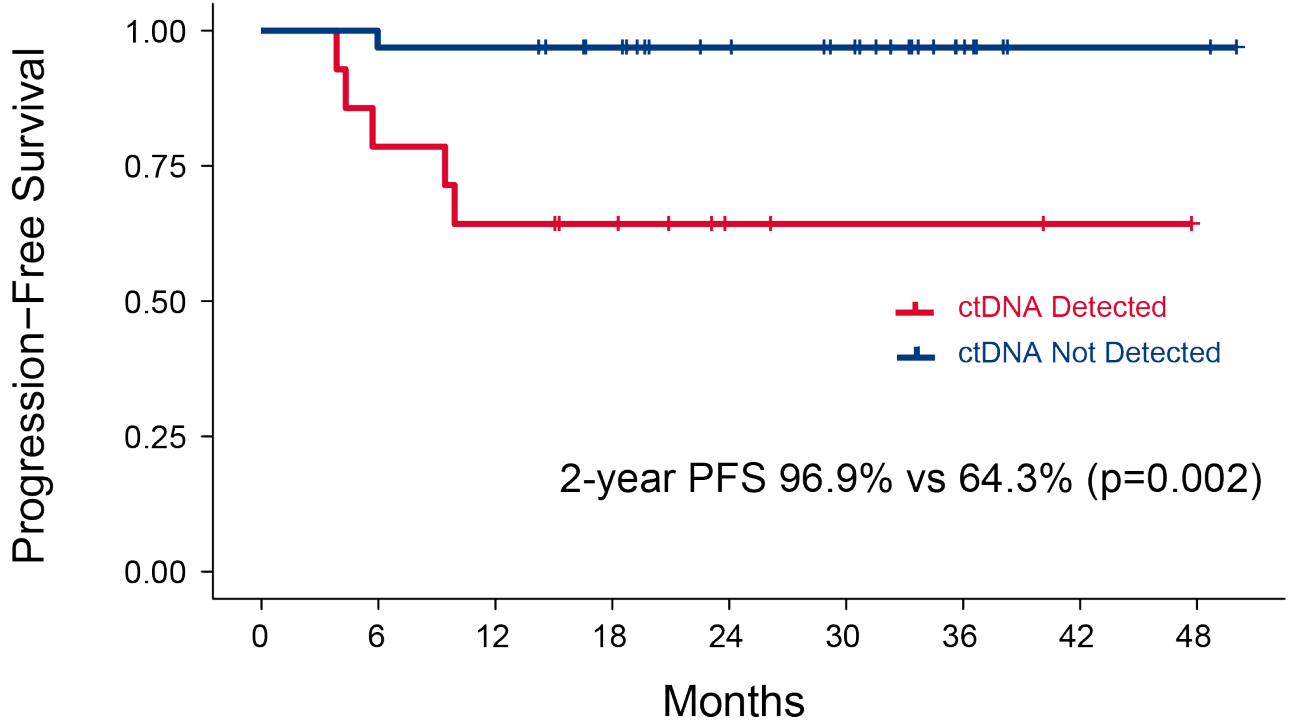
Progression Free Survival By Response to Acalabrutinib



Number at risk

Acala Non−Responder	28	24	23	20	15	13	6	5	2
Acala Responder	26	25	24	21	14	9	6	1	0

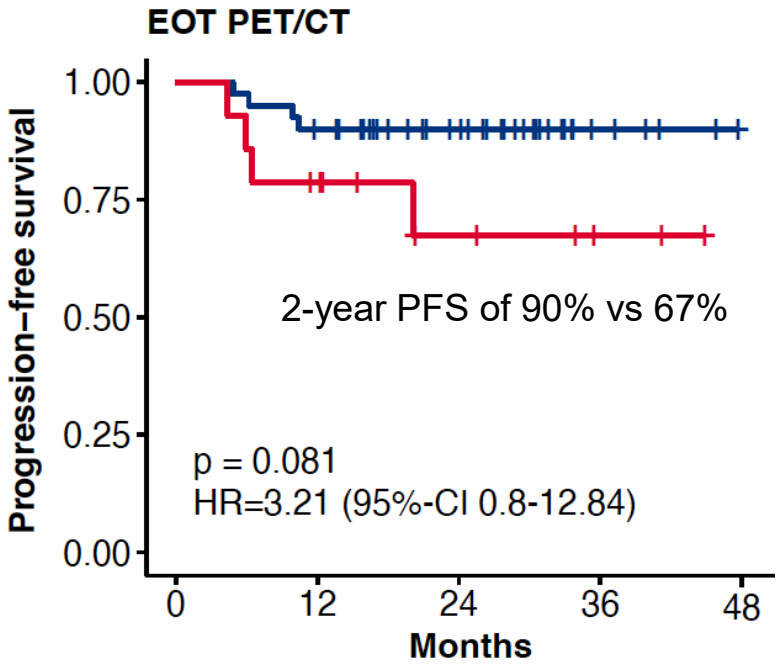
Progression Free Survival By MRD Status after 2 Cycles

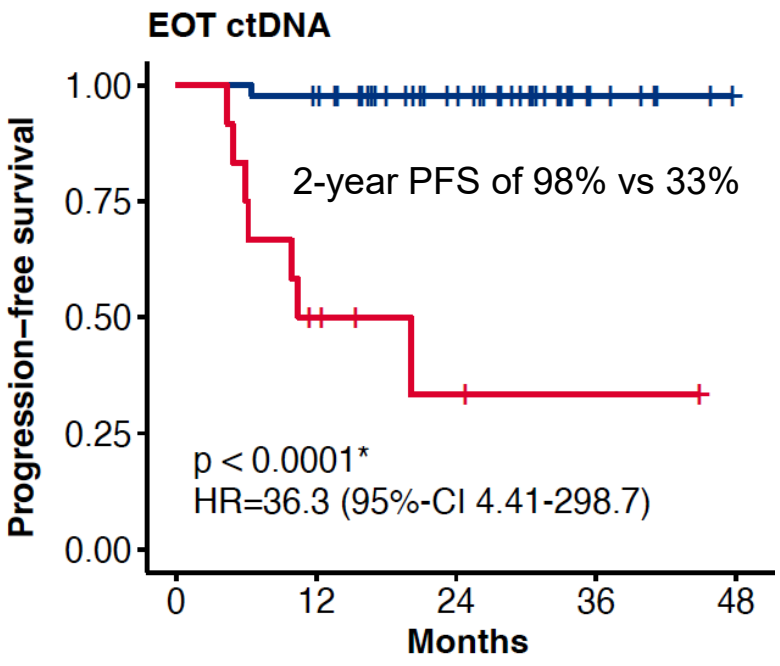


Number at risk

ctDNA Detected	14	11	9	7	3	2	2	1	0
ctDNA Not Detected	32	31	31	27	20	17	7	2	2

Progression Free Survival By PET/CT and ctDNA at EOT





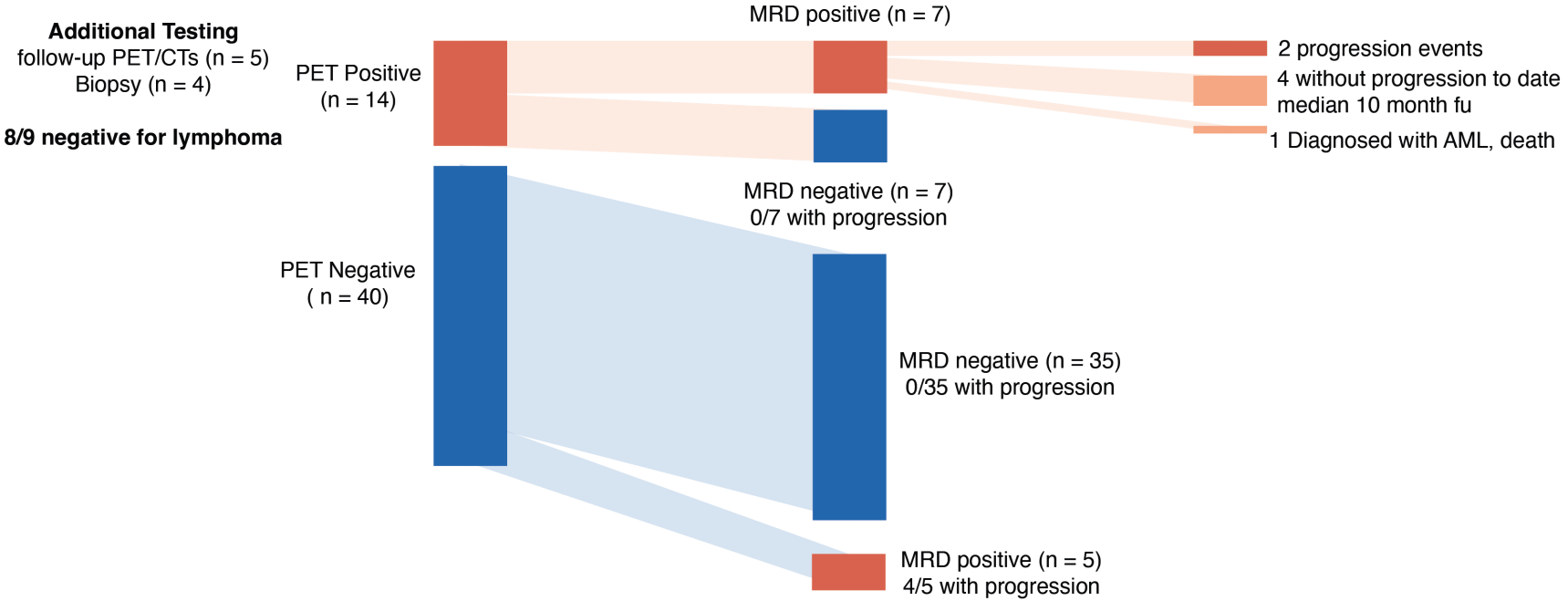
Number at risk

PET CR	40	35	22	5	0
PET non–CR	14	10	5	2	0

Number at risk

ctDNA Undetected	42	40	25	6	0
ctDNA Detected	12	5	2	1	0

Additional Procedures at EOT to Determine Remission



Only 2 of 14 (14%) pts with positive EOT PET/CT by progressed

8 of 9 (89%) pts who underwent additional procedures were without active lymphoma

No patient with undetectable MRD at EOT progressed

Conclusions

- ctDNA by PhasED-Seq is prognostic both after 2 cycles and at EOT
- Undetectable ctDNA by PhasED-Seq at EOT predicts a very low likelihood of progression with greater predictive value than PET/CT
- Additional procedures (biopsy, repeat PET/CT scans) are often required to adjudicate EOT PET/CT scans; most do not have active lymphoma
- Salvage therapy should not be delivered based on a singular EOT PET/CT

Wyndham H. Wilson

Thank you to all patients and their families

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