2025 ASCO ANNUAL MEETING

Prospective Validation of End-of-Treatment ctDNA-MRD by PhasED-Seq in 1L DLBCL Patients from a National Cohort

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Key Takeaway Points

1

This prospective study confirms that ctDNA-MRD after curative-intent 1L treatment is prognostic in DLBCL.

2

ctDNA-MRD provides independent evidence of residual disease beyond PET-CT.

3

ctDNA-MRD should be integrated as a standard component of response evaluation in 1L DLBCL patients.

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Background

Circulating Tumor DNA – based Measurable Residual Disease (ctDNA-MRD) in 1L DLBCL Patients

- Current DLBCL response evaluation relies on PET-CT, but these scans suffer from suboptimal sensitivity and specificity.
- PhasED-Seq is an ultrasensitive sequencing method for detecting ctDNA-based MRD.
- Prior DLBCL studies* using ctDNA suggest prognostic value, but are limited by heterogeneity in treatment regimens, patient populations, and sampling.
- A prospective, independent validation in a large, uniformly treated 1L DLBCL cohort is essential for clinical translation.

*Roschewski et al. ICML 2023. Sworder et al. ASH 2023.

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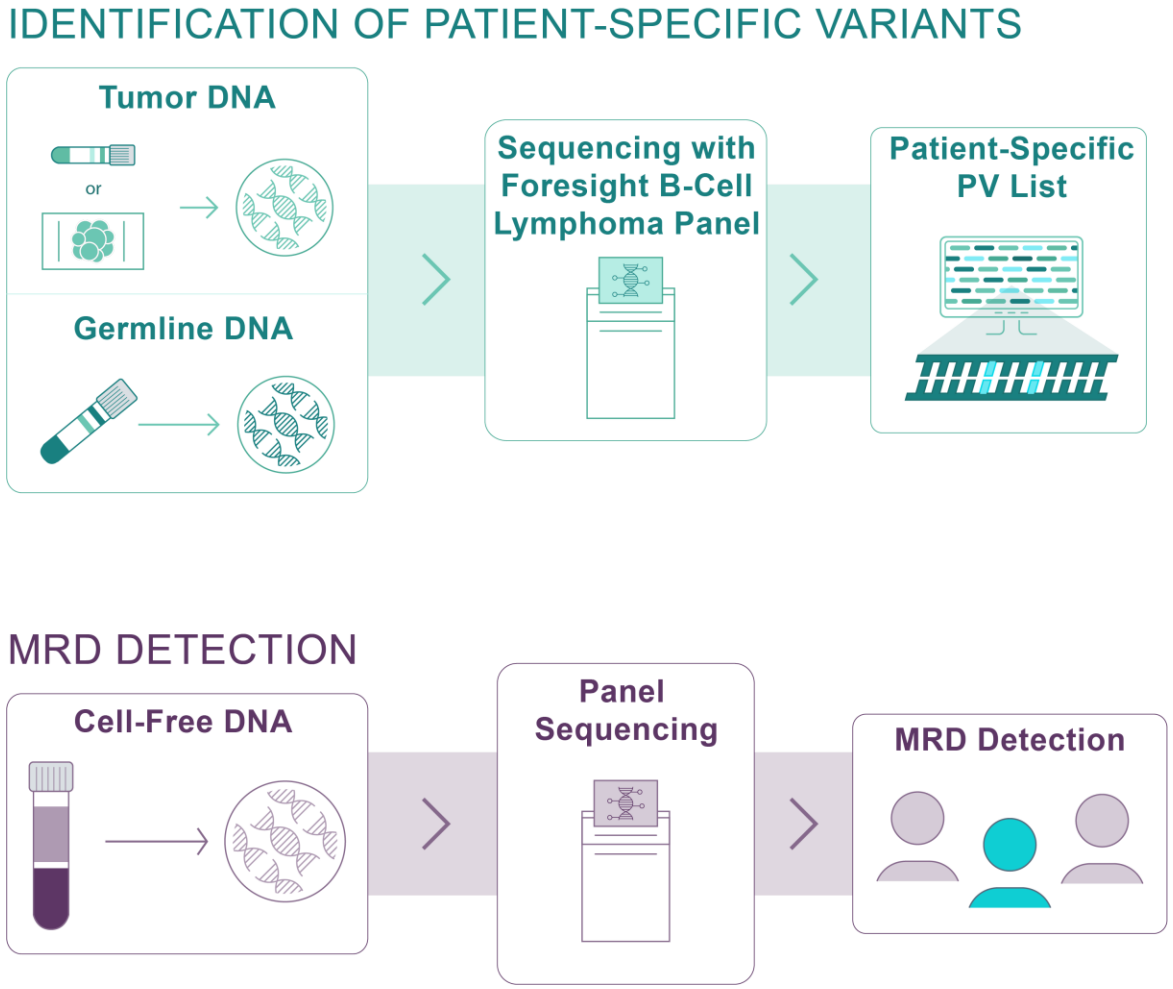
Methods
Ultrasensitive ctDNA-MRD by PhasED-seq



- PVs were identified in baseline samples:
  - FFPE (58%) or pretreatment plasma (42%) (median: 3.5 mL)
- MRD detection in EOT samples:
  - Plasma (median: 5.2 mL)
  - Analytical LOD95*: 0.7 parts per million

Klimova N et al. Oncotarget 2025.
Kurtz DM et al. Nat Biotechnol 2021.

*The sensitivity for disease detection in any given sample depends on both the analytical LOD95 of the assay as well as the amount of available DNA input.

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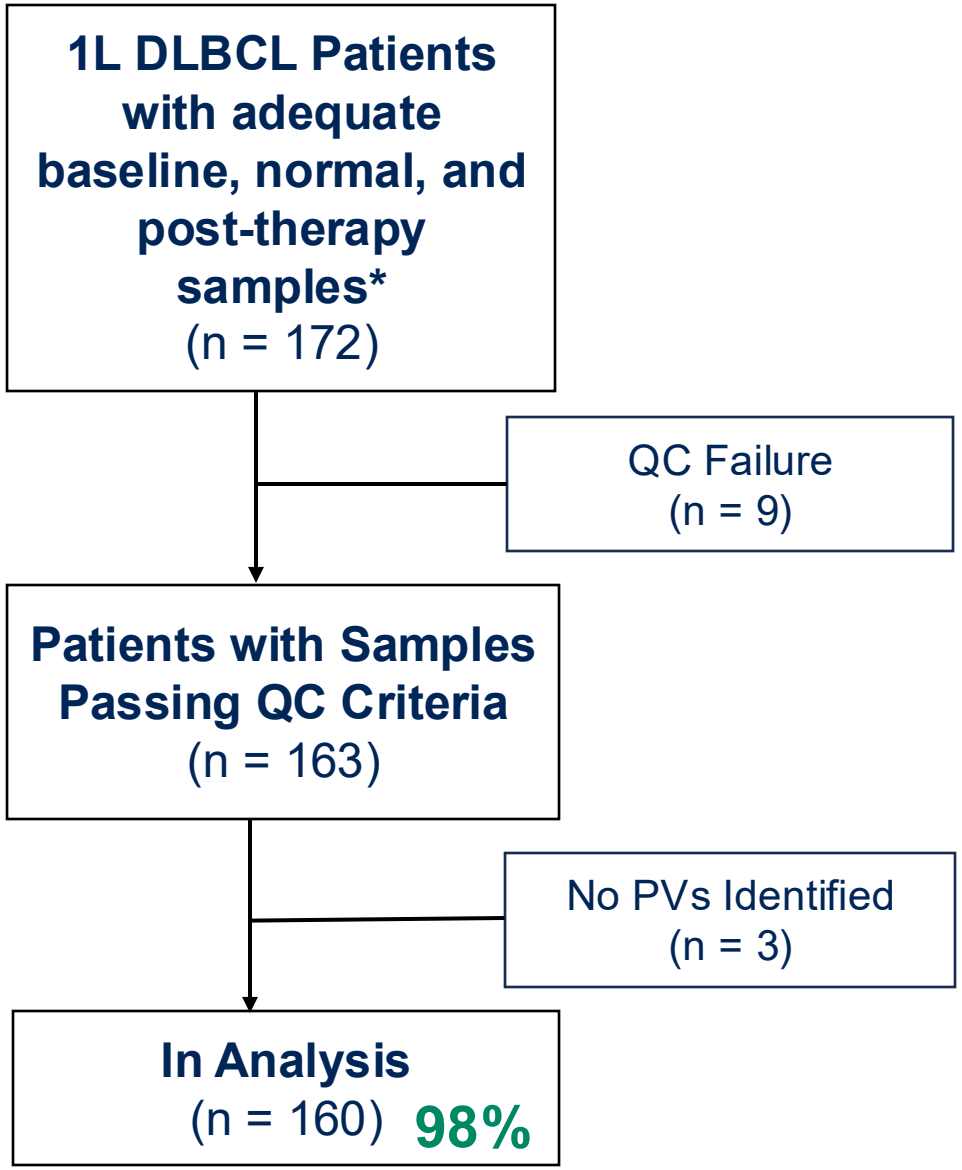
Methods
1L DLBCL* from a National Cohort

- Newly diagnosed prospective real-world cohort of 1L DLBCL patients
- > 50 centers in the Netherlands & Belgium
- Curative-intent 1L therapy
  - R-CHOP or DA-EPOCH-R



*Including LBCLs: HGBL, Transformed iNHL, PMBCL and IVLBCL

*Patients receiving consolidative Rx after EOT blood sampling were excluded

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Methods

1L DLBCL* from a National Cohort & Patient Characteristics

- Newly diagnosed prospective real-world cohort of 1L DLBCL patients
- > 50 centers in the Netherlands & Belgium
- Curative-intent 1L therapy
  - R-CHOP or DA-EPOCH-R

Characteristic	Number (n = 160)	Percentage (%)
Median age, years	67 (18-88)	
Male	103	64%
Female	57	36%
Diagnosis		
DLBCL	144	89%
HGBL-DH/TH	14	9%
PMBCL/IVLBCL	2	2%
Stage		
I-II	34	21%
III-IV	126	79%
IPI		
0-2	83	52%
3-5	77	48%
1L Therapy Regimen		
R-CHOP	146	91%
DA-EPOCH-R	14	9%
Cycles of Treatment		
6 cycles	144	90%

*Including LBCLs: HGBL, Transformed iNHL, PMBCL and IVLBCL

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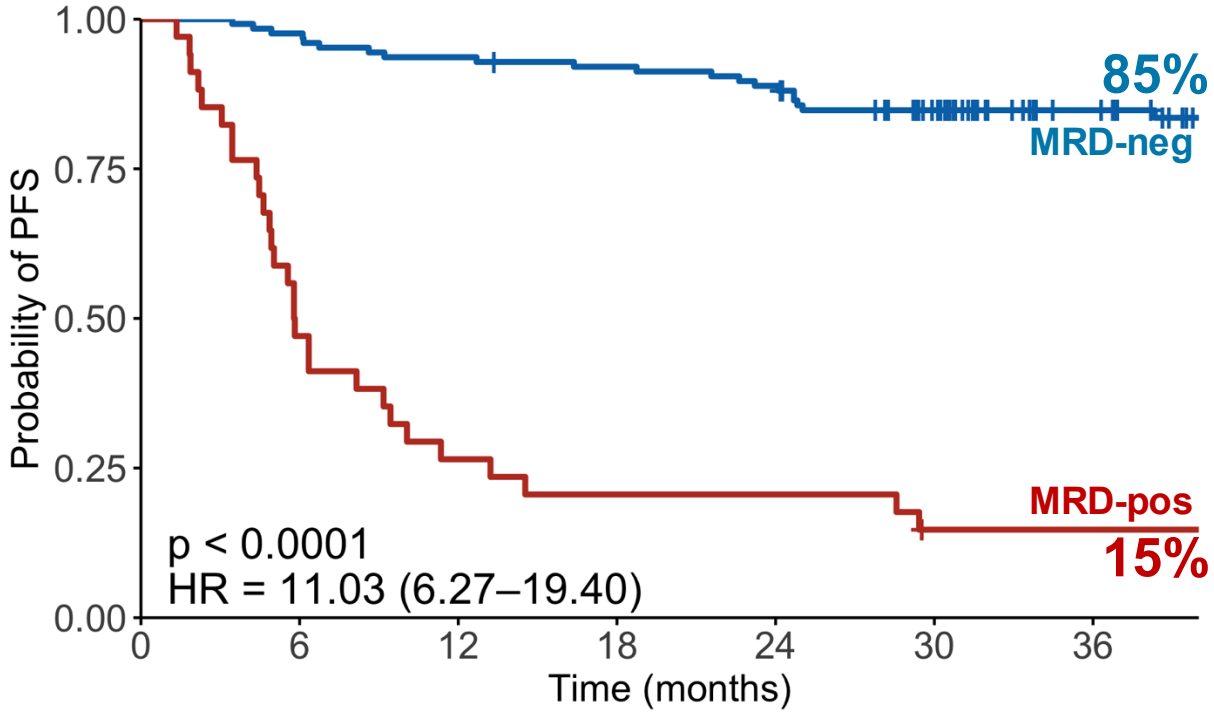
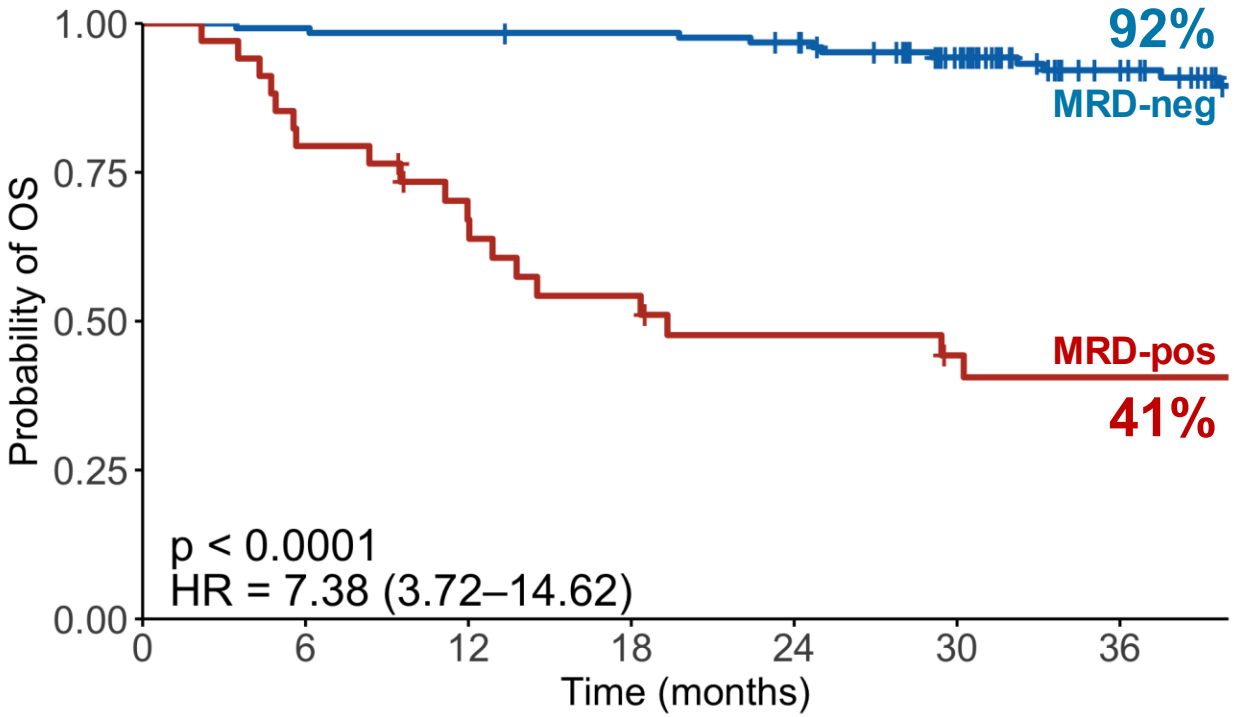
Results

EOT ctDNA MRD is Strongly Prognostic for PFS and OS



Number at risk

MRD-	126	123	118	115	111	96	74
MRD+	34	16	9	7	7	4	4



Number at risk

MRD-	126	125	124	123	120	104	79
MRD+	34	27	21	17	14	12	11

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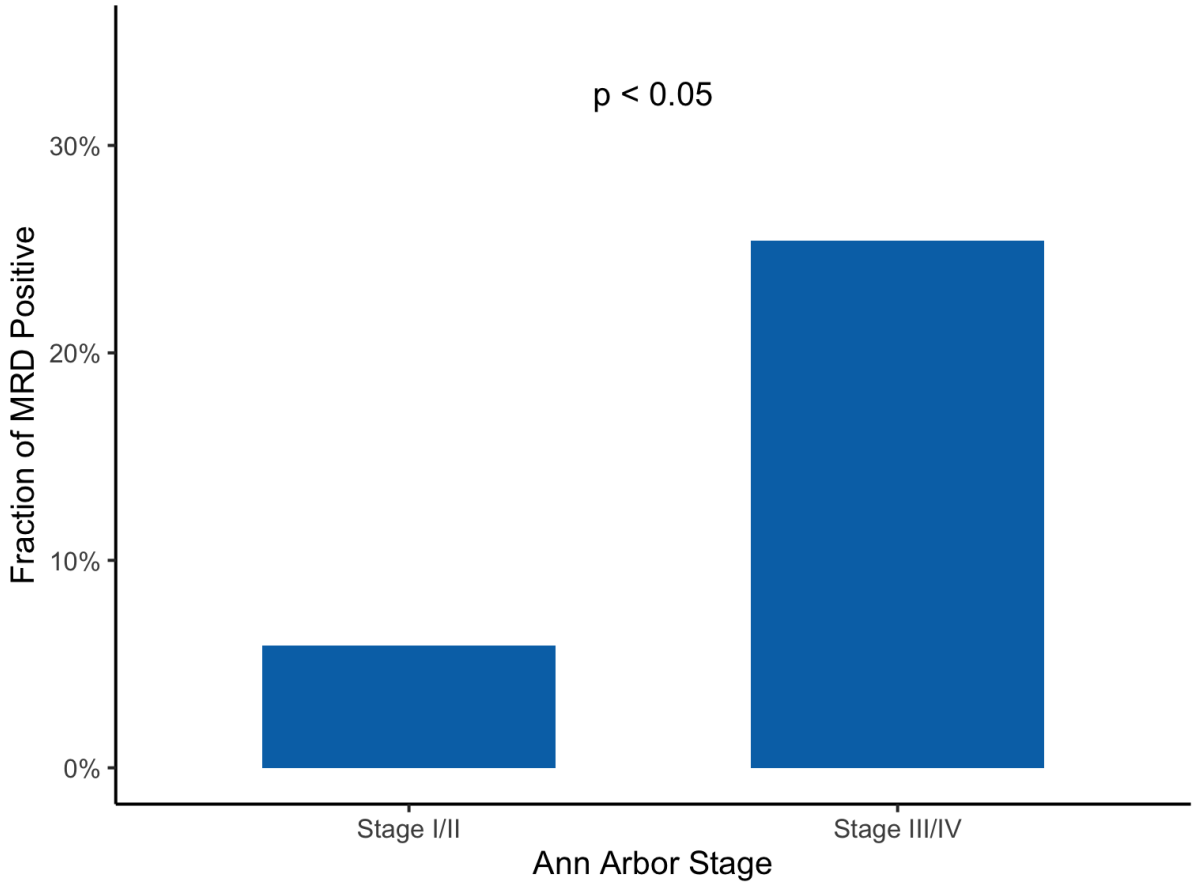
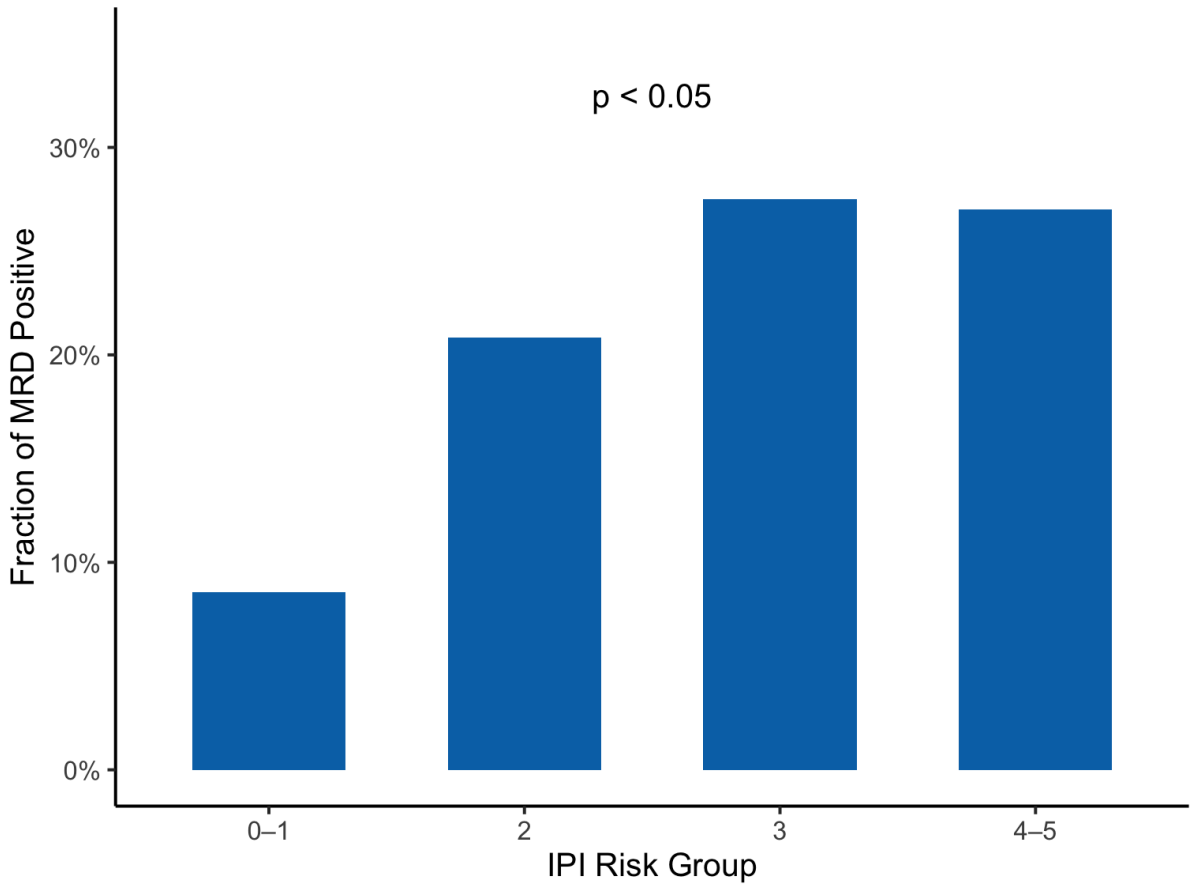
Results

Higher Stage/IPI are Correlated with MRD-positivity





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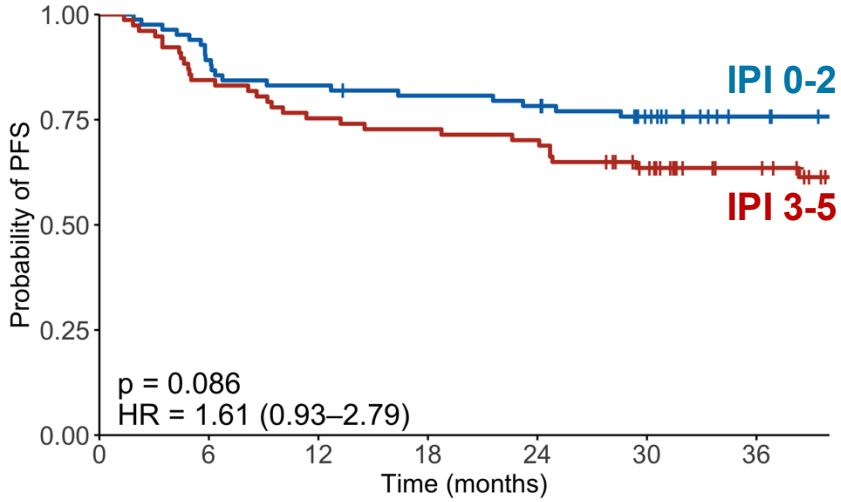
Results

EOT ctDNA-MRD is Most Prognostic for PFS

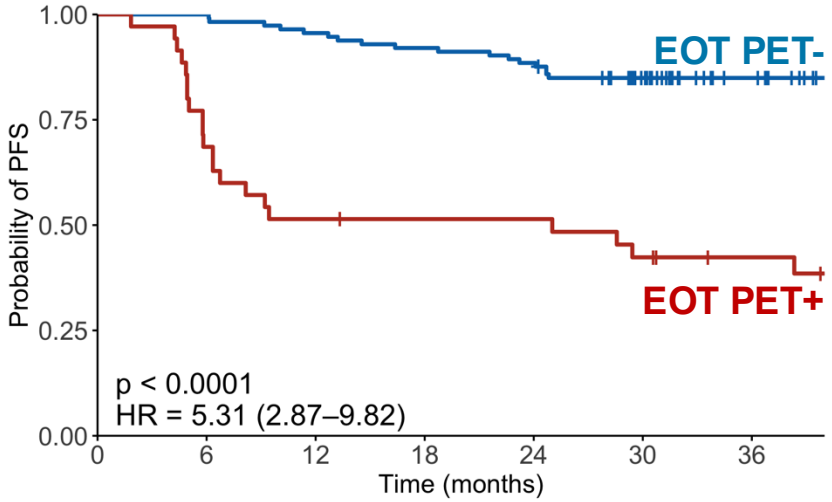
IPI



Number at risk

IPI 0-2	83	74	69	66	64	56	46
IPI 3-5	77	65	58	56	54	44	32

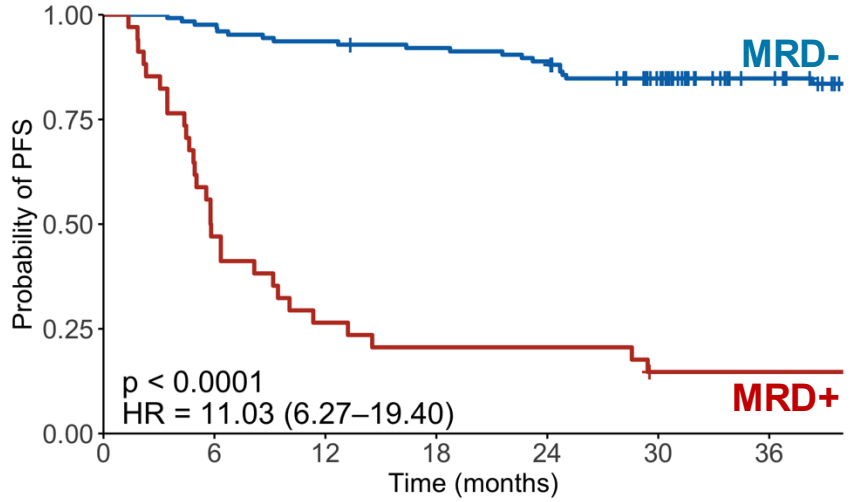
EOT PET-CT



Number at risk

CMR	113	113	108	104	100	86	67
No-CMR	35	24	18	17	17	14	11

ctDNA-MRD



Number at risk

MRD-	126	123	118	115	111	96	74
MRD+	34	16	9	7	7	4	4

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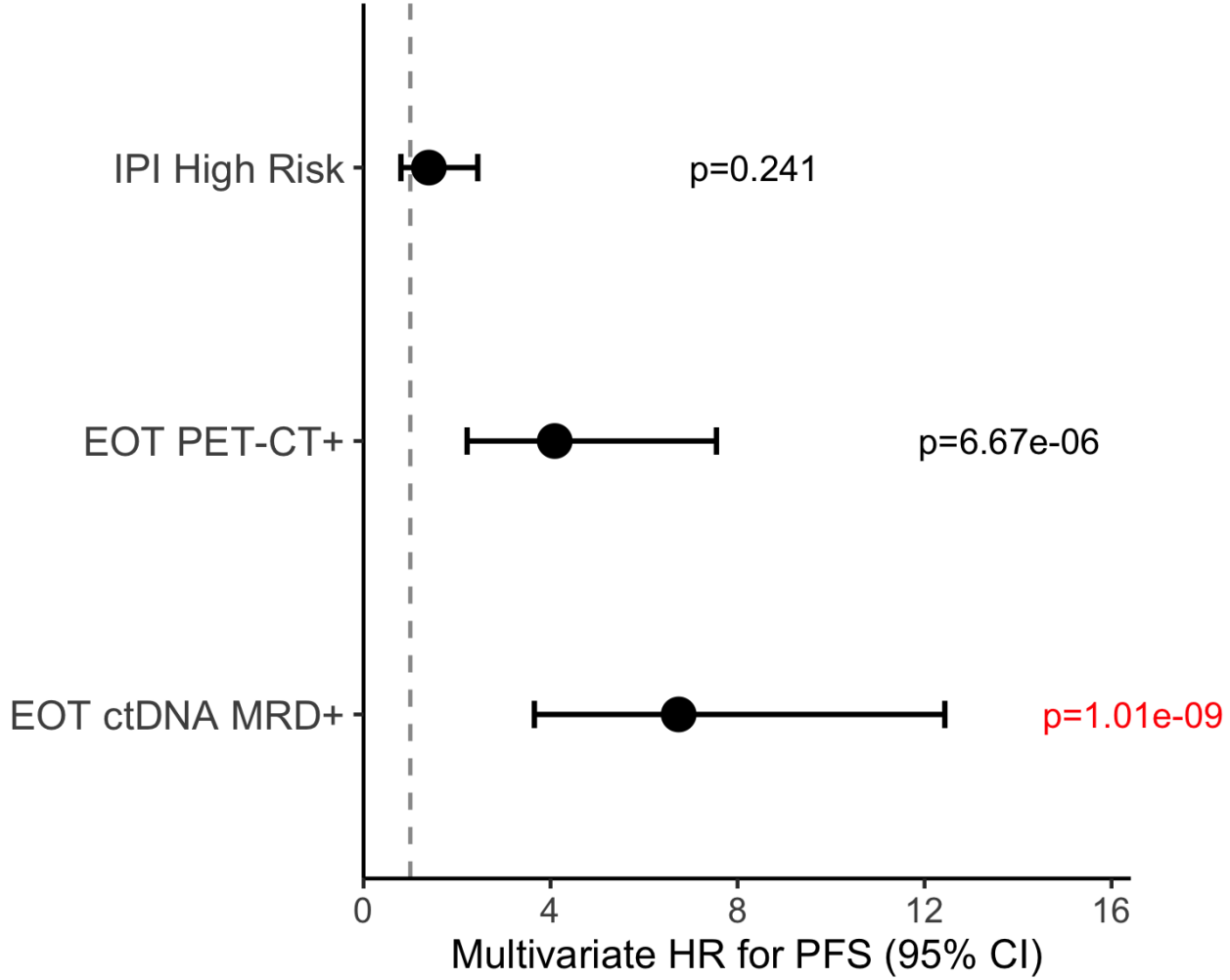
Results
ctDNA MRD is Independently Prognostic for PFS



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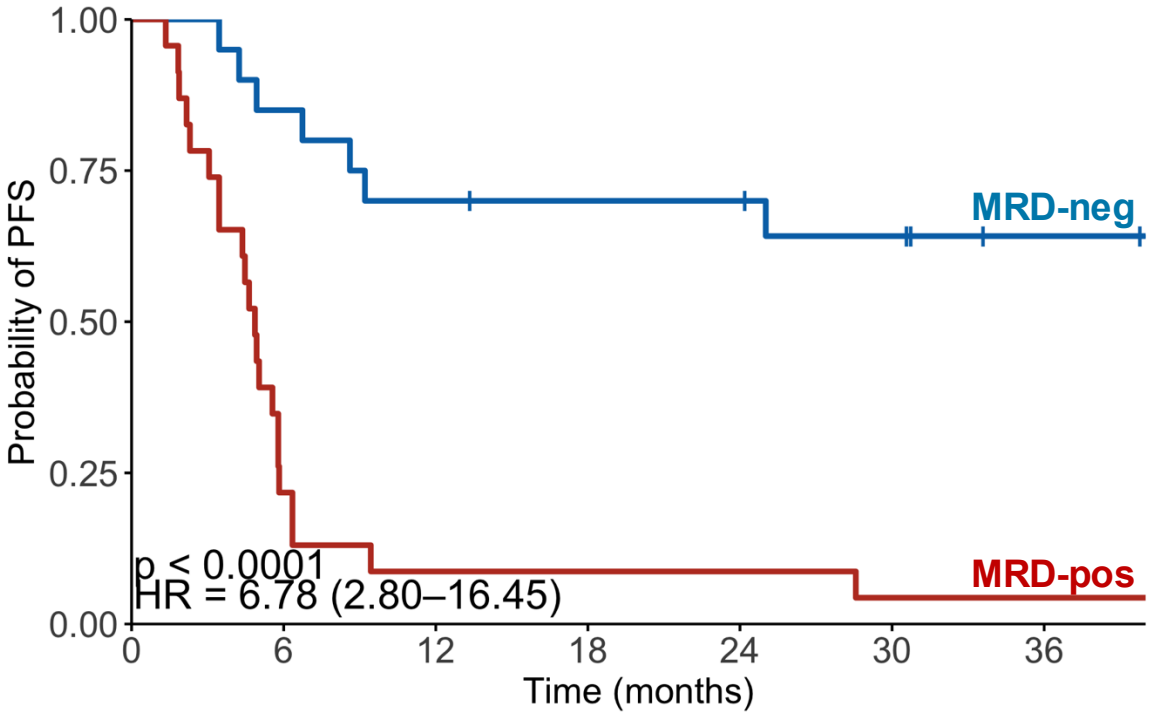
Results

EOT ctDNA MRD+ in Patients Without Complete Response Have Especially Poor Outcomes



Number at risk

MRD-	20	17	14	13	13	11	8
MRD+	23	5	2	2	2	1	1

- **In patients without CMR by PET†:**
  - **ctDNA MRD-pos: 3-year PFS: 4%**
  - **ctDNA MRD-neg: 3-year PFS: 64%***

*2/7 PFS events due to death unrelated to lymphoma

† CMR defined as either a negative EOT PET or a positive EOT PET adjudicated as negative based on follow-up PET or biopsy.

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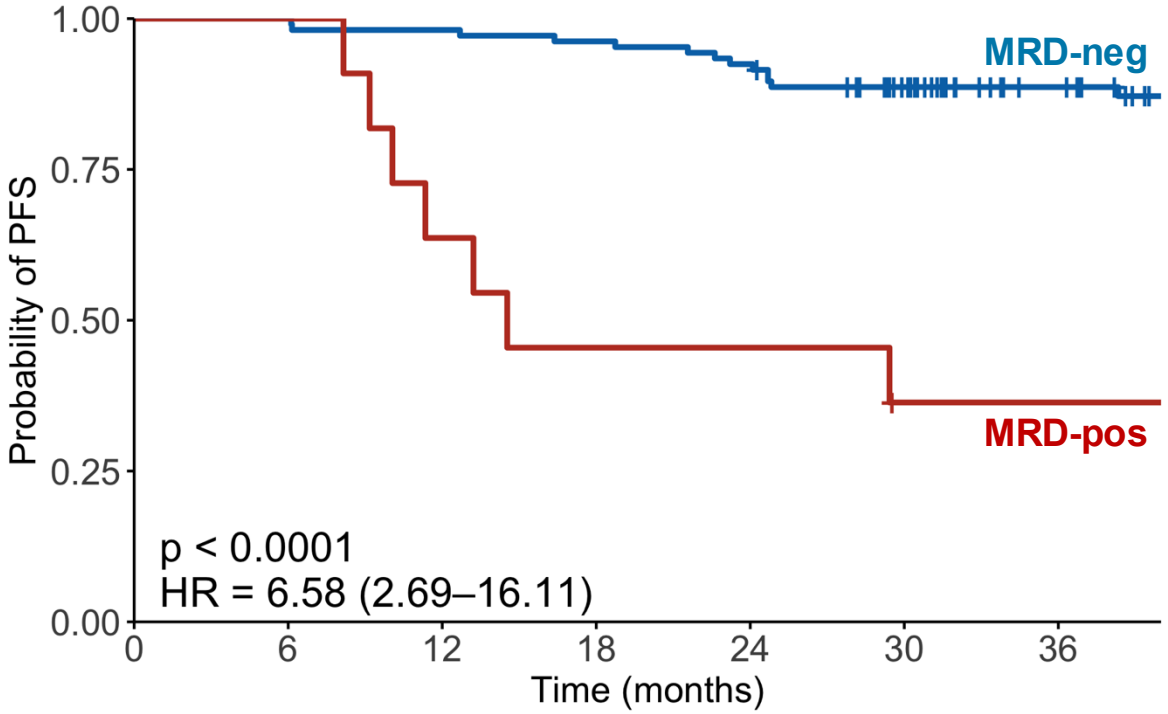
Results

EOT ctDNA MRD+ Patients With Complete Response Also Have Poor Outcomes



Number at risk

MRD-	106	106	104	102	98	85	66
MRD+	11	11	7	5	5	3	3

- **In patients with CMR by PET scan†:**
  - **ctDNA MRD-neg: 3 -year PFS 89%**
  - **ctDNA MRD-pos: 3 -year PFS 36%**

† CMR defined as either a negative EOT PET or a positive EOT PET adjudicated as negative based on follow-up PET or biopsy.

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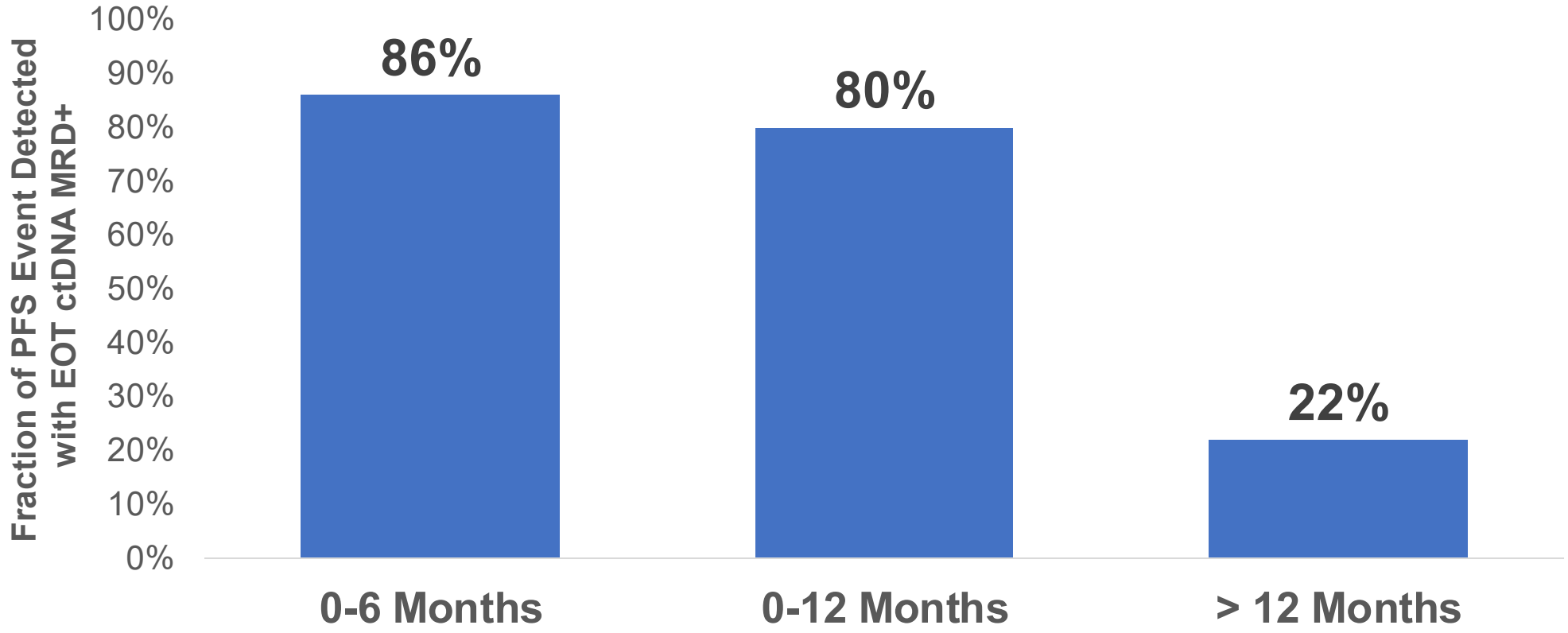
Results

EOT ctDNA MRD is Highly Sensitive to Predict Early Relapse



- EOT ctDNA MRD predicts both PFS events within 6- and 12-months window.
- Continued longitudinal monitoring is likely required to capture late relapses.

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Limitations

- EOT PET-CT scans were not centrally reviewed.
- Timing of EOT sample collection varied following completion of 1L therapy.

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Thank you to all patients and their families for their invaluable contributions to advancing lymphoma research.

HOVON

KNL Netherlands comprehensive cancer organisation

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Avinash Dinmohamed, PhD
All Principal Investigators

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Visit these posters on 6/1 to learn more about ctDNA MRD:

- Poster #272a
- Poster #267a
- Poster #229
- Poster #223

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Lay Summary

- This work showed that a blood test measuring tiny traces of cancer DNA after treatment can help predict which lymphoma patients are most likely to stay in remission and which ones might relapse.
- This work is important for patients who have been diagnosed with DLBCL for the first time planning to receive curative treatment. It also helps doctors to provide cancer care.
- This work supports the adoption of this blood test in routine care, it brings us closer to using personalized, non-invasive tests to guide follow-up care and decide who might need more or less treatment after chemotherapy in the future.

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