FORESIGHT DIAGNOSTICS

Allogene THERAPEUTICS

The ALPHA3 Trial

Harnessing the Potential of Combining Next-Generation Allogeneic Investigational CAR T with Advanced MRD Testing to Improve Outcomes in First Line LBCL

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Disclosures

- Scientific co-founder, Foresight Diagnostics
- Consultancy: CiberMed, Foresight Diagnostics, Pharmacyclics, FortySeven, Roche, Gilead, ADC Therapeutics, Adaptive Biosciences
- Research Funding: Bristol Myers Squibb
- Equity: CARGO Therapeutics

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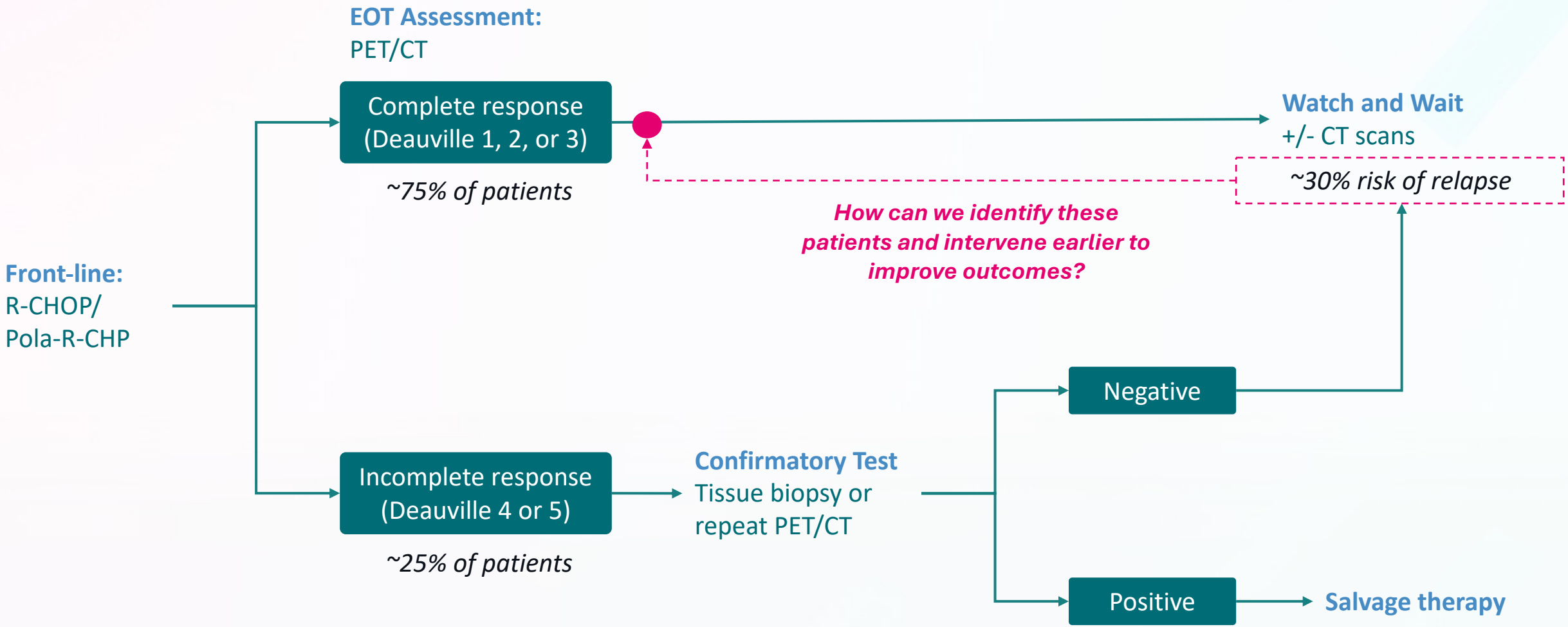
Current practice in lymphoma generally has remained unchanged in 20 years



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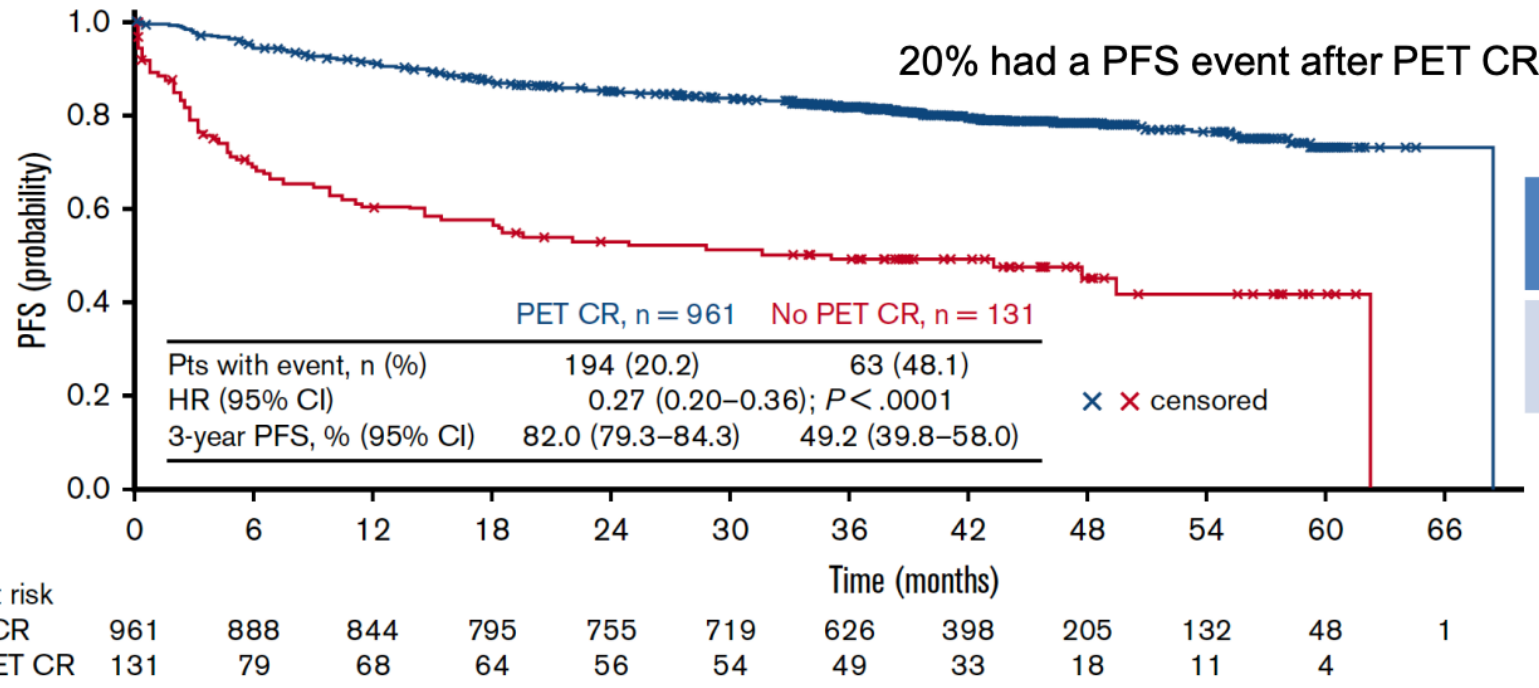
Adapted from NCCN guidelines 2024; Coiffier, et al, 2010.

End-of-treatment PET scans lack the specificity needed to guide risk-adapted treatment decisions in 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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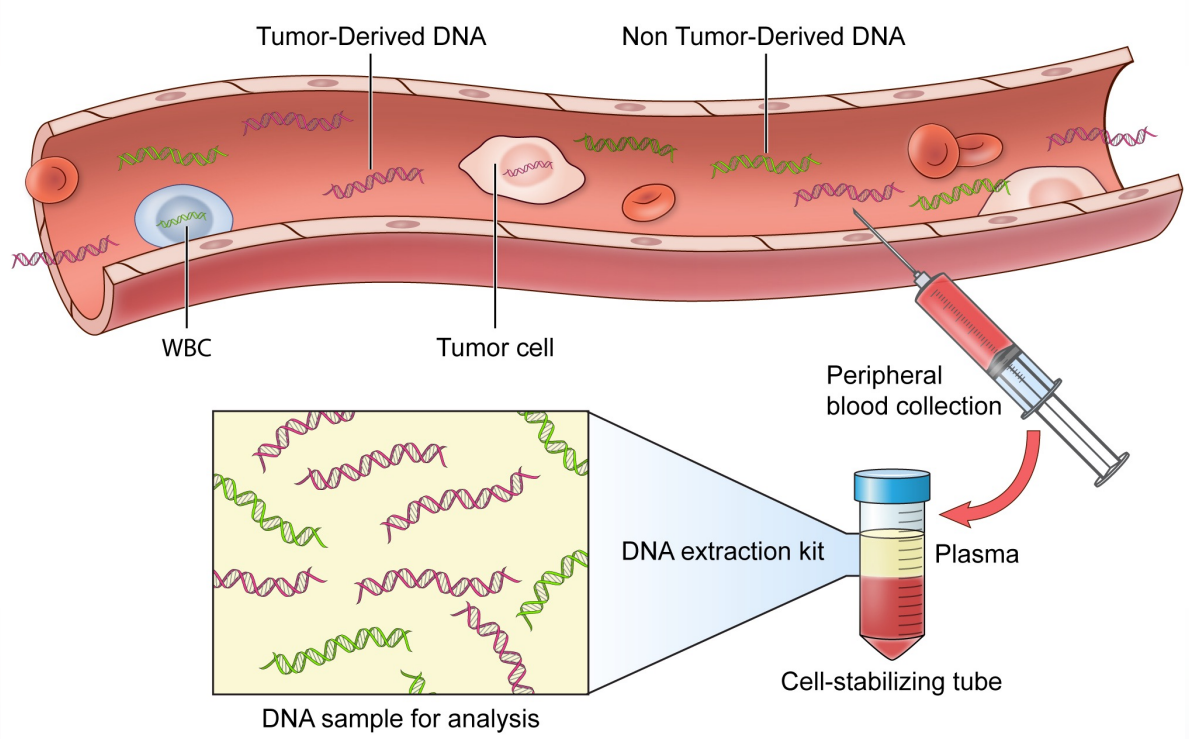
Figure: Kostakoglu et al. *Blood Adv* 2021;5(5):1283-1290; Data analysis from Roschewski, et al. ASH 2023

ctDNA and MRD detection address many imaging and biopsy limitations



Sensitive *and* specific

LOD's range from parts per thousand to parts per million; near-universal specificity

Non-invasive

Allows for serial testing with minimal risk/toxicity

Quantitative and dynamic

Correlates with tumor burden over time

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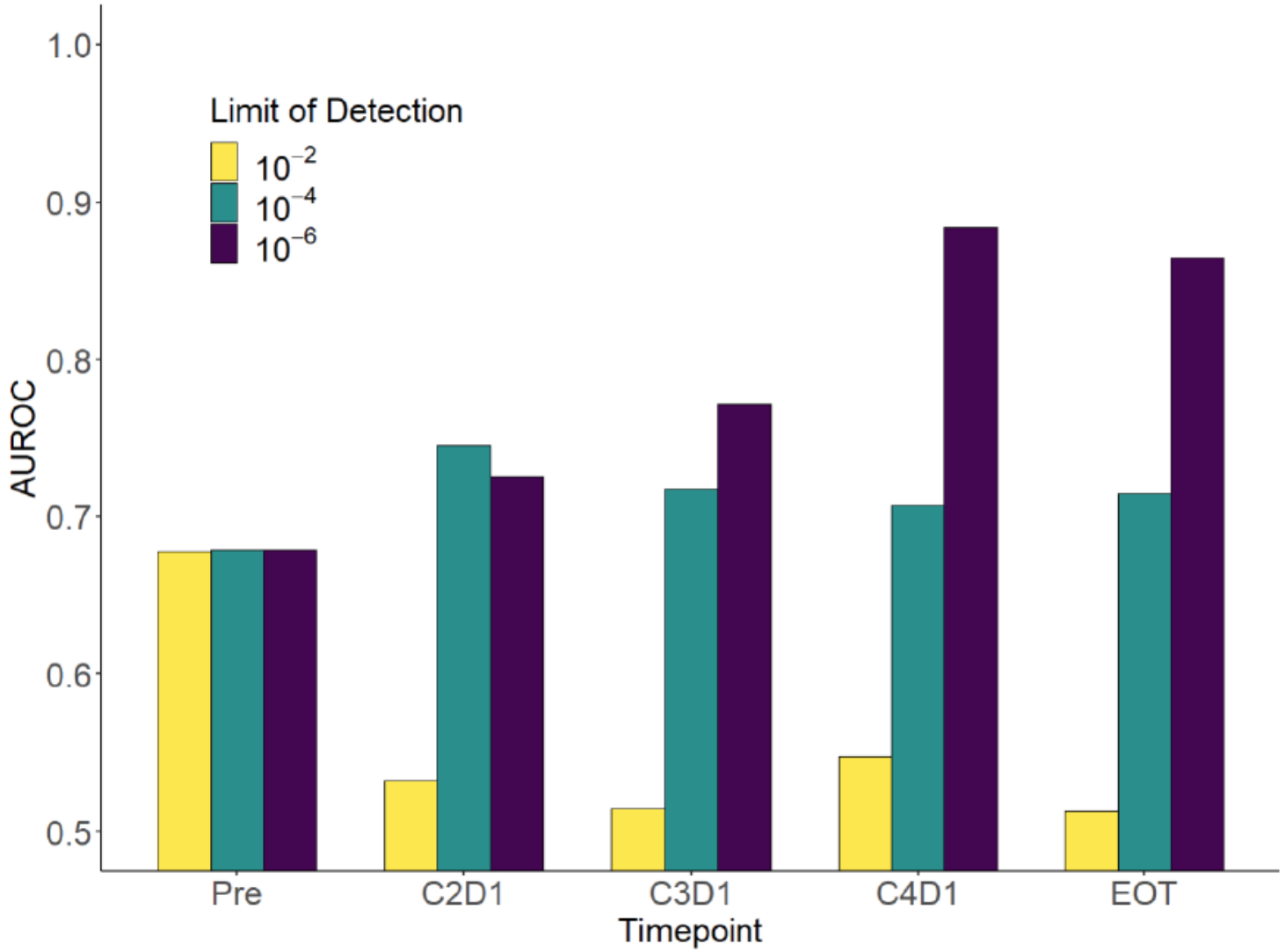
Roschewski et al. Blood Cancer Discov 2022 Jan;3(1):5-15; Presented at Advancing Precision Medicine (Nov 24)

Ultra-sensitivity ctDNA assays critical for MRD detection at end of therapy



AUROC is the predictive ability for PFS by MRD at a given LOD

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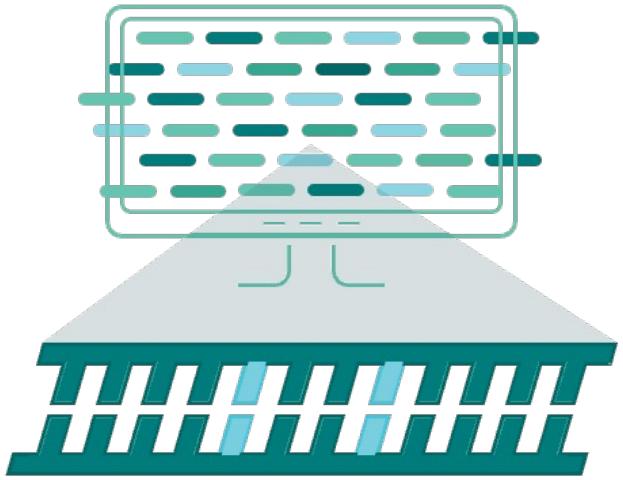
Goldstein et al., ASH 2023

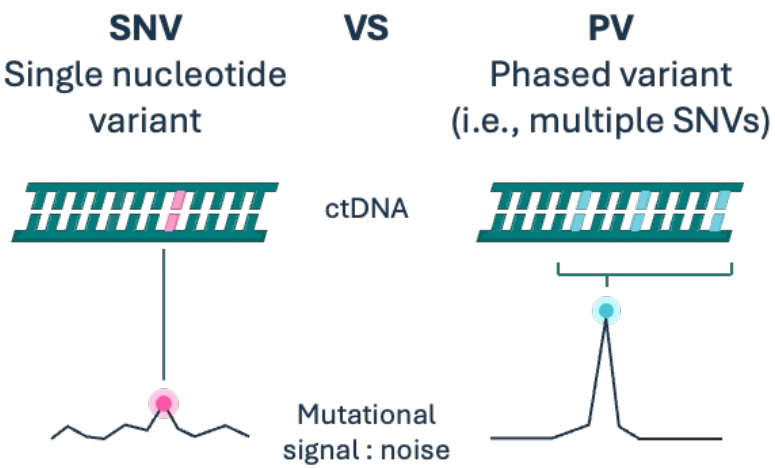
Foresight CLARITY™ IUO MRD delivers high level of sensitivity by leveraging phased variants technology

Phased Variant **E**nrichment and **D**etection **Seq**uencing (PhasED-Seq™)



Phased variants (PVs) are **two or more single nucleotide variants (SNVs)** that occur on the same DNA molecule.

Foresight CLARITY identifies **patient-specific PVs** by comparing variants present in tumor but absent in germline.



Leveraging PVs to detect ctDNA **substantially reduces the background error rate** compared to traditional SNV-based approaches.

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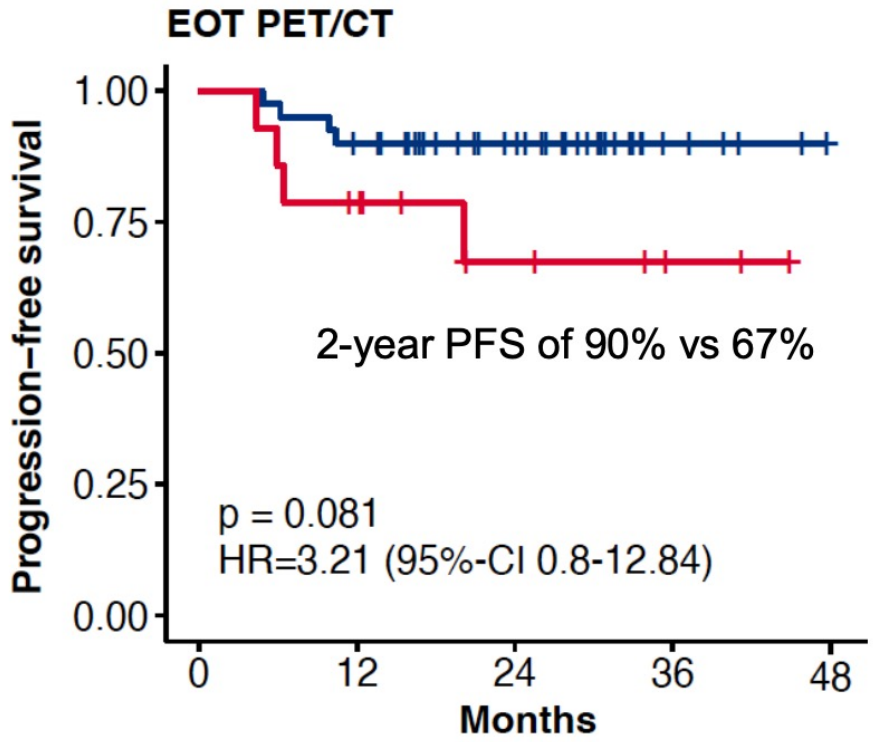
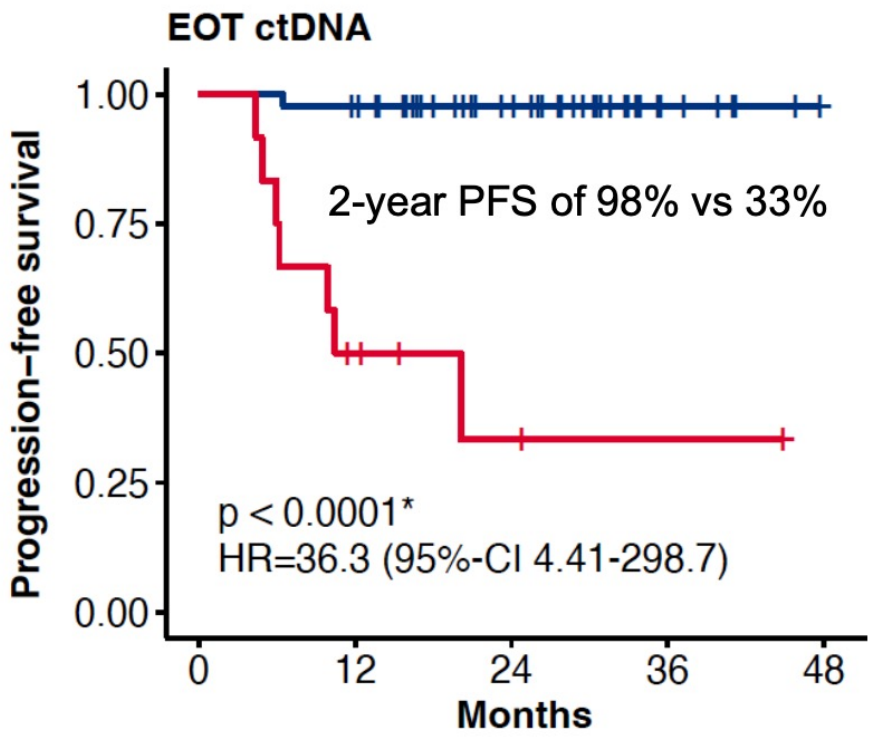
ctDNA-MRD status by Foresight CLARITY™ outperformed PET for response assessment at end of therapy in exploratory studies





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

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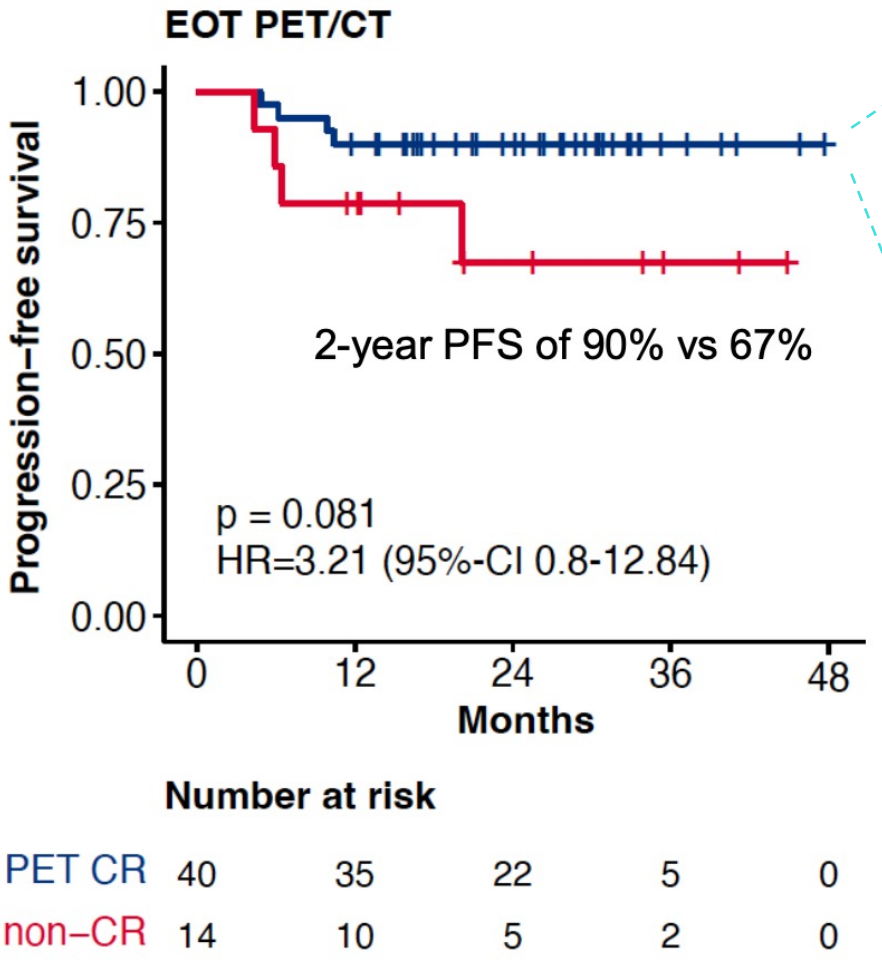
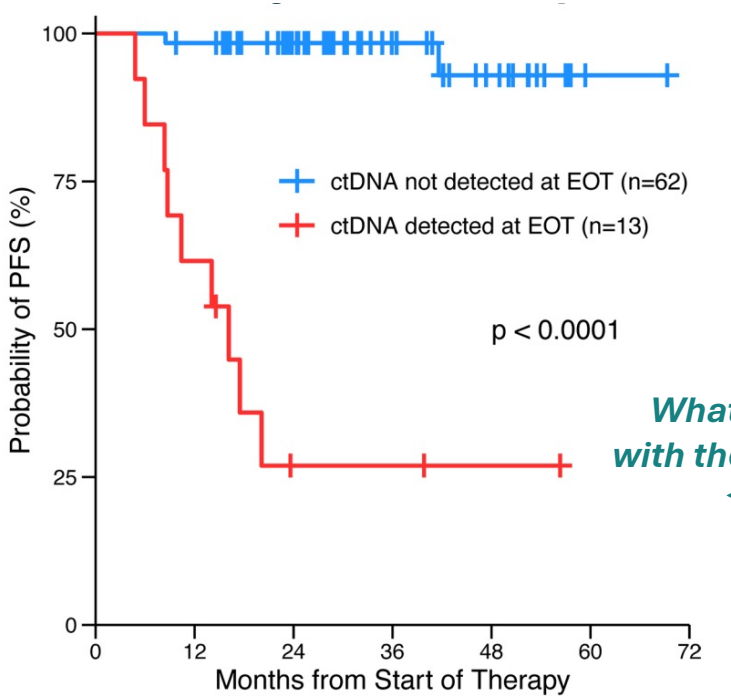
Roschewski et al. Hematological Oncology 41(S2):177-179, ICML 2023

MRD positivity at end of therapy **may increase risk of relapse** in PET negative patients



MRD Status at End of Therapy (EOT) Further Stratifies Outcomes Among Patients with PET/CT Remissions



What can we do with these patients?

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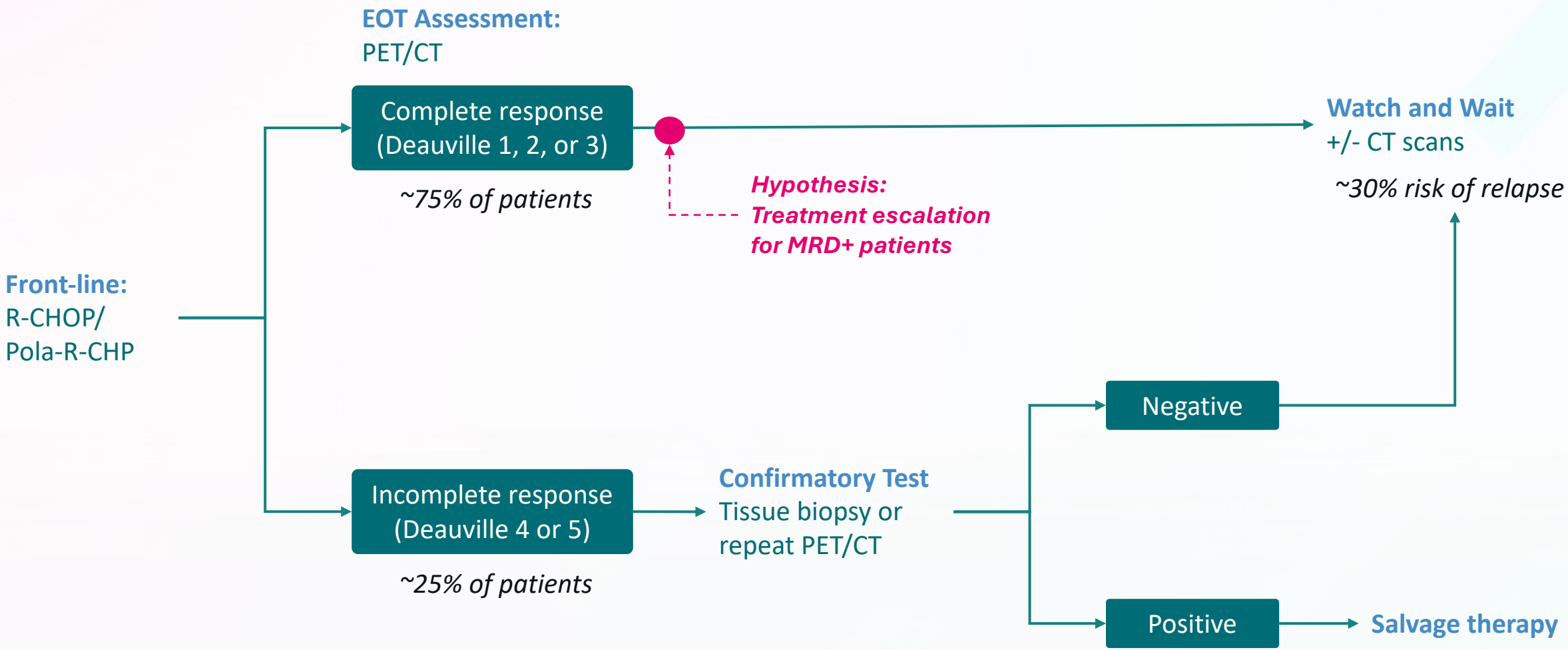
Roschewski et al. Hematological Oncology 41(S2):177-179, ICML 2023

Current practice in lymphoma generally has remained unchanged in 20 years



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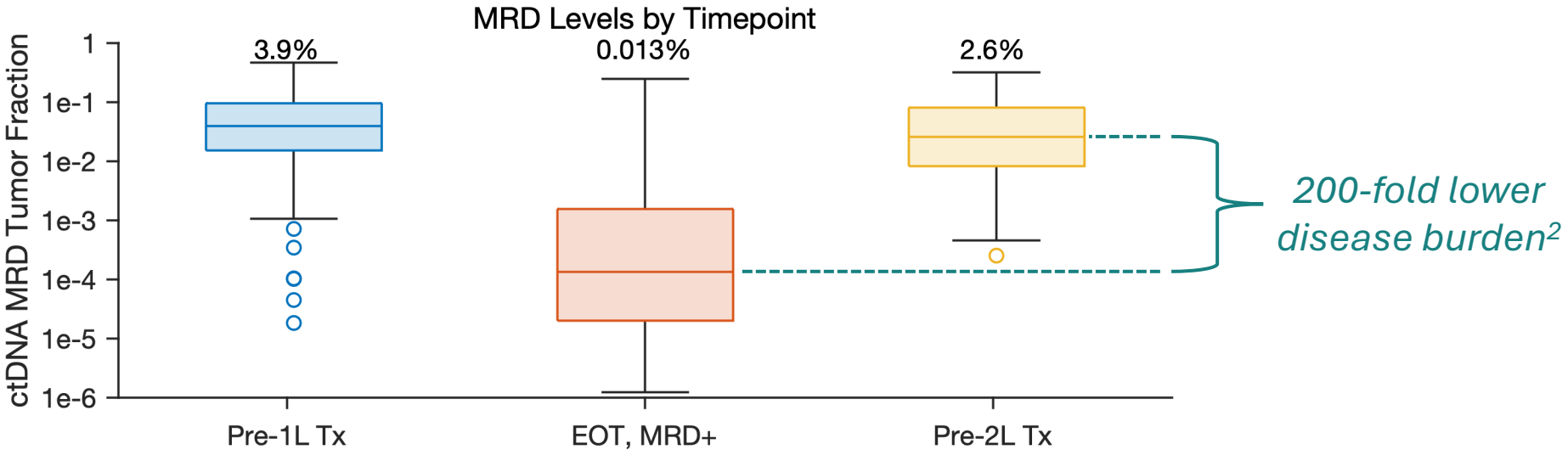
Adapted from NCCN guidelines 2024; Coiffier, et al, 2010.

Identifying patients with residual disease using CLARITY enables initiation of CAR-T treatment when disease burden is ~200-fold lower compared to imaging

- CAR T-cell treatment is most **effective & safest, when disease-burden is low**[1]
- Median disease-burden is ~200-fold lower in MRD+ patients at the end of 1L treatment than in patients who clinically relapse and require second-line therapy[2]
  - Many patients may not be eligible for CAR therapy at the time of 2L therapy due to comorbidities, symptom burden, or other issues
  - **The end of 1L therapy – if MRD+ – is potentially the optimal time for treatment with CAR T-cells**[3]



1 Locke Blood 2022
2 Kurtz JCO 2018; Alig JCO 2021
3 Preliminary analysis; unpublished data on file
ctDNA levels are highly correlated with metabolic tumor volume

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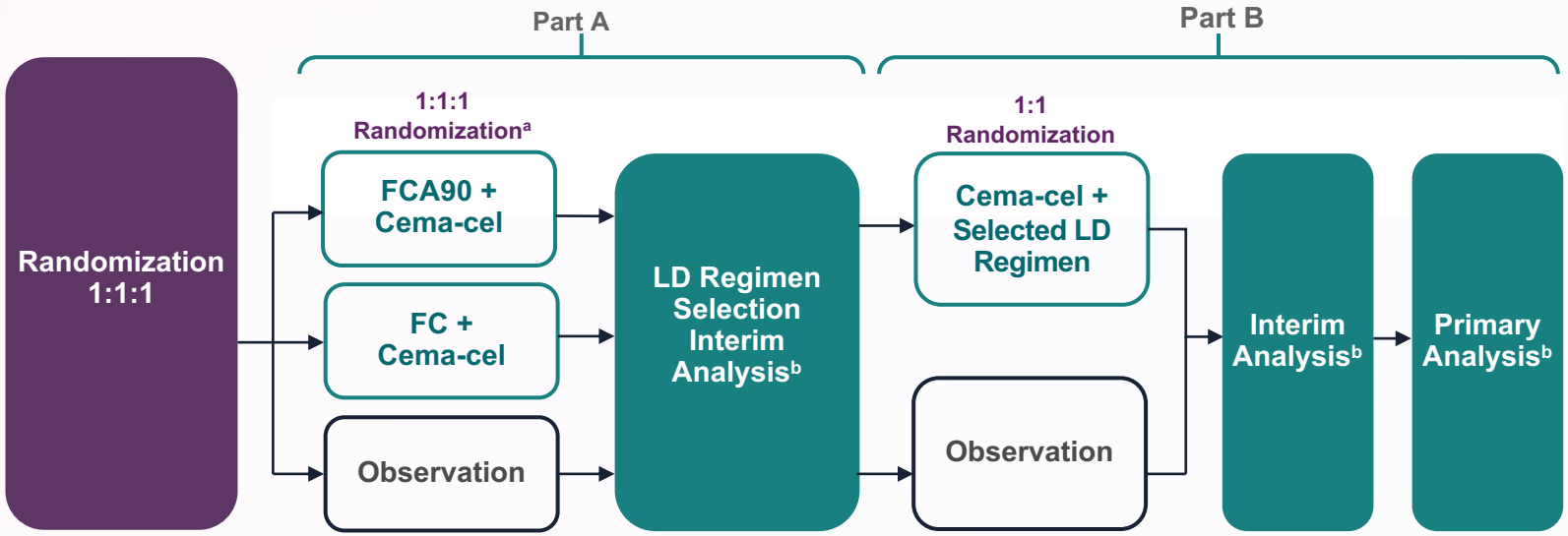
ALPHA3 pivotal design is seamless and efficient, utilizing MRD status by Foresight CLARITY IUO for patient enrollment



[a] Randomization ratio may be adjusted after the safety interim analysis. [b] Safety and interim efficacy analyses will occur and culminate in LD regimen selection. Patients treated with the selected regimen or followed in observation during Part A will be included in inferential testing in Part B.
AE, adverse event; AESI, adverse event of special interest; cema-cel, cemacabtagene ansegedleucel; EFS, event free survival; FC, fludarabine and cyclophosphamide; FCA90, fludarabine and cyclophosphamide and ALLO-647 (90 mg); IRC, independent review committee; LD, lymphodepletion, MRD, minimal residual disease; OS, overall survival; PFS, progression free survival; PR, partial response; SAE, serious adverse event; TRAE, treatment-related adverse event.

Primary Endpoint[d]

EFS per IRC assessment

Secondary Endpoints

PFS per IRC assessment

Overall survival

Rate of conversion to MRD-

EFS and PFS per investigator assessment

Incidence and severity of AEs,TRAEs, SAEs, AESI & laboratory toxicities

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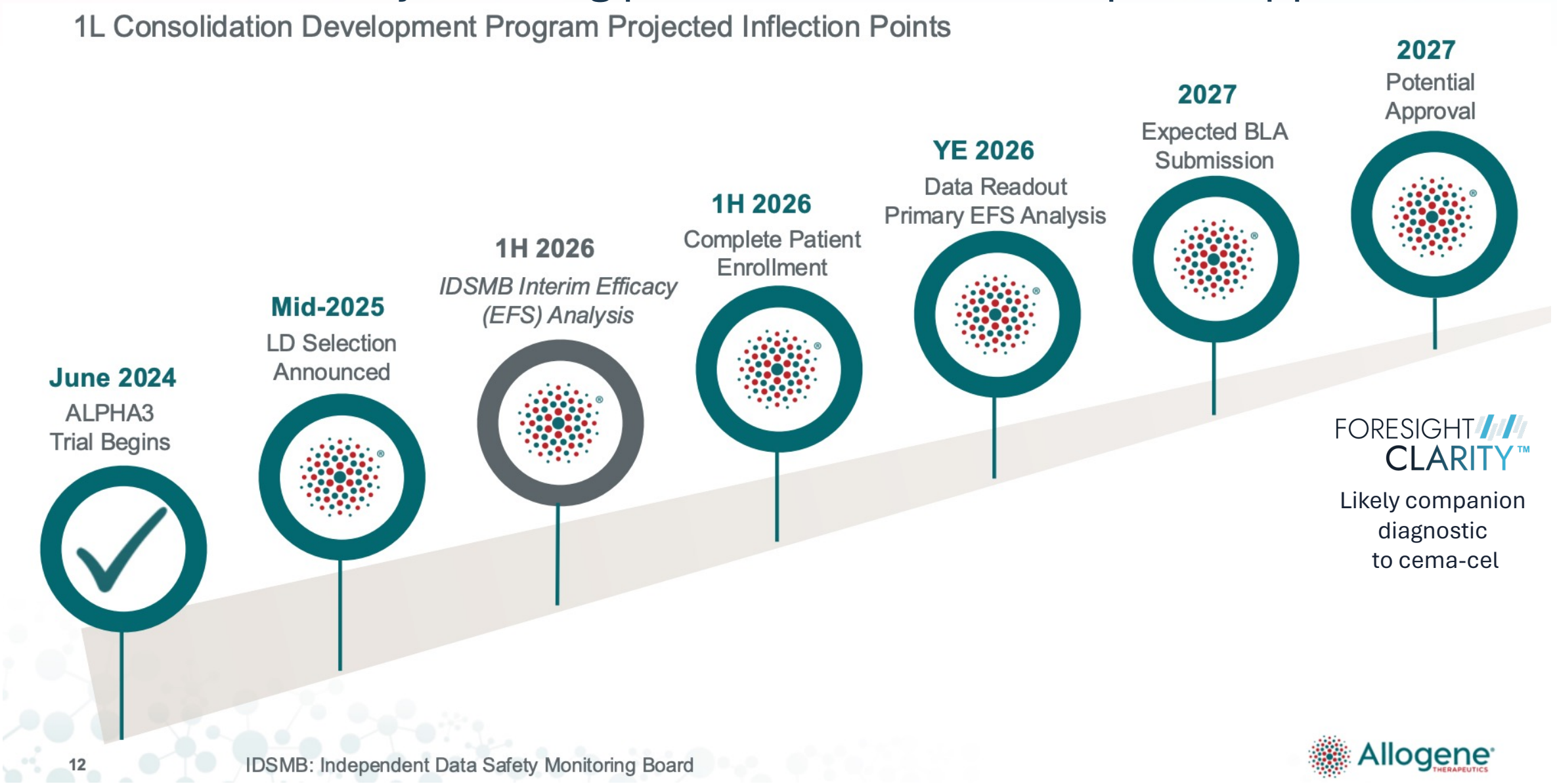
ALPHA3 is currently enrolling patients for 2027 anticipated approval



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Note: as presented at ASH 2024. Visit www.Allogene.com for most up-to-date information

Summary

MARRYING TWO NOVEL TECHNOLOGIES WITH THE AIM TO IMPROVE CURE RATES IN 1L SETTING AND IMPROVE PATIENT ACCESS TO CARE

- PET-CT is poorly prognostic in LBCL, forcing a "watch-and-wait" approach to relapse monitoring.
- Despite a ~30% disease recurrence rate in LBCL, current practice does not enable accurate relapse risk assessment.
- Foresight CLARITY™ IUO ultra-sensitive MRD gives us the potential ability to detect disease when imaging does not, which can lead to tailored escalation of care, focusing on just those patients more likely to relapse.
- ALPHA3 is the first and only trial[1] to evaluate an off-the-shelf allogeneic CAR T product candidate, cema-cel, in patients who are in remission by PET-CT but are MRD positive at the end of therapy.
- Allogenic CAR T combined with a blood-based MRD test may improve access to novel, effective therapies in community cancer centers, where ~80% of lymphoma patients are managed.

1 At time of presentation (December 2024)

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Thank you

Lean more about the ALPHA3 trial:
www.Allogene.com/alpha3

Lean more about Foresight CLARITY™:
www.Foresight-Dx.com