XIX CONGRESSO NAZIONALE SIES 2026

VALUTAZIONE COMPARATIVA DEI PANNELLI NGS TARGETED E DEGLI ALGORITMI PER UNA STRATIFICAZIONE MOLECOLARE OTTIMALE DEI DLBCL NELLA PRATICA CLINICA

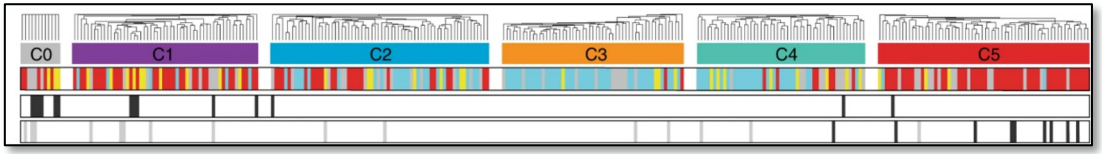
D. Gallucci, M. C. Vegliante, G. Gargano, A. Ferri, L. Pasini, S. Lonardi, G. Mandelli, D. Medicina, P. Balzarini, V. Pellegrini, W. Vermi, C. Re, P. Bossini, A. Sanzogni, E. Albertini, A. Tucci, A. Re, M. Pizzi, A. Di Napoli, F. Cordero, L. Lorenzi, S. Ciavarella.

Firenze | 4-6 marzo 2026
Palazzo degli Affari

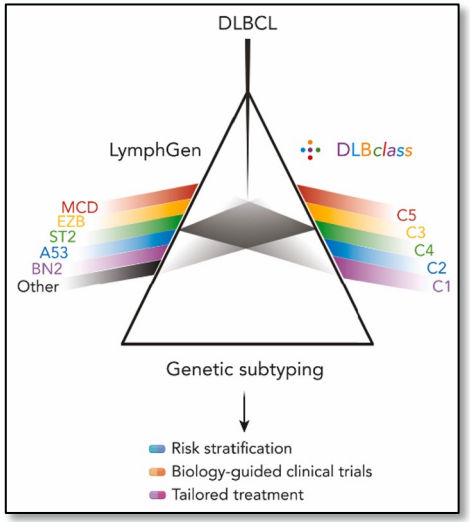
Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

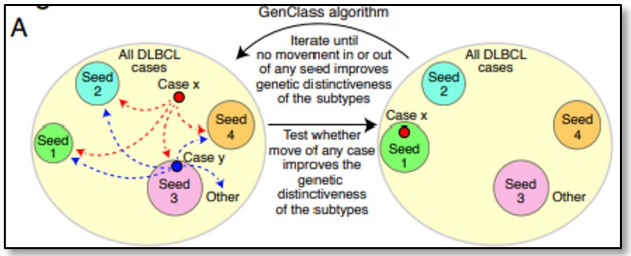
Predictive value of targeted NGS in molecular classification of DLBCL



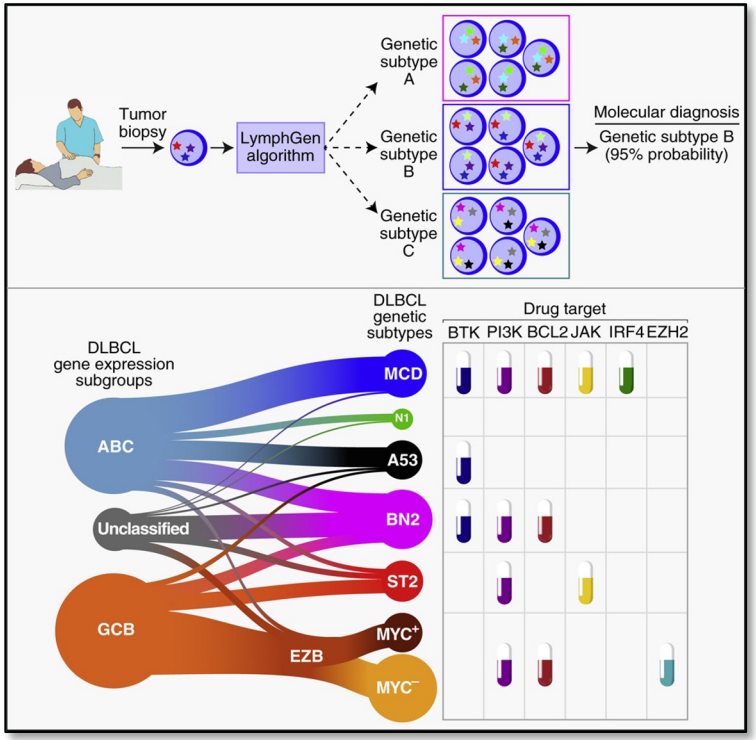
Chapuy B. et al. Nature 2018



Chapuy B. et al. Blood 2025



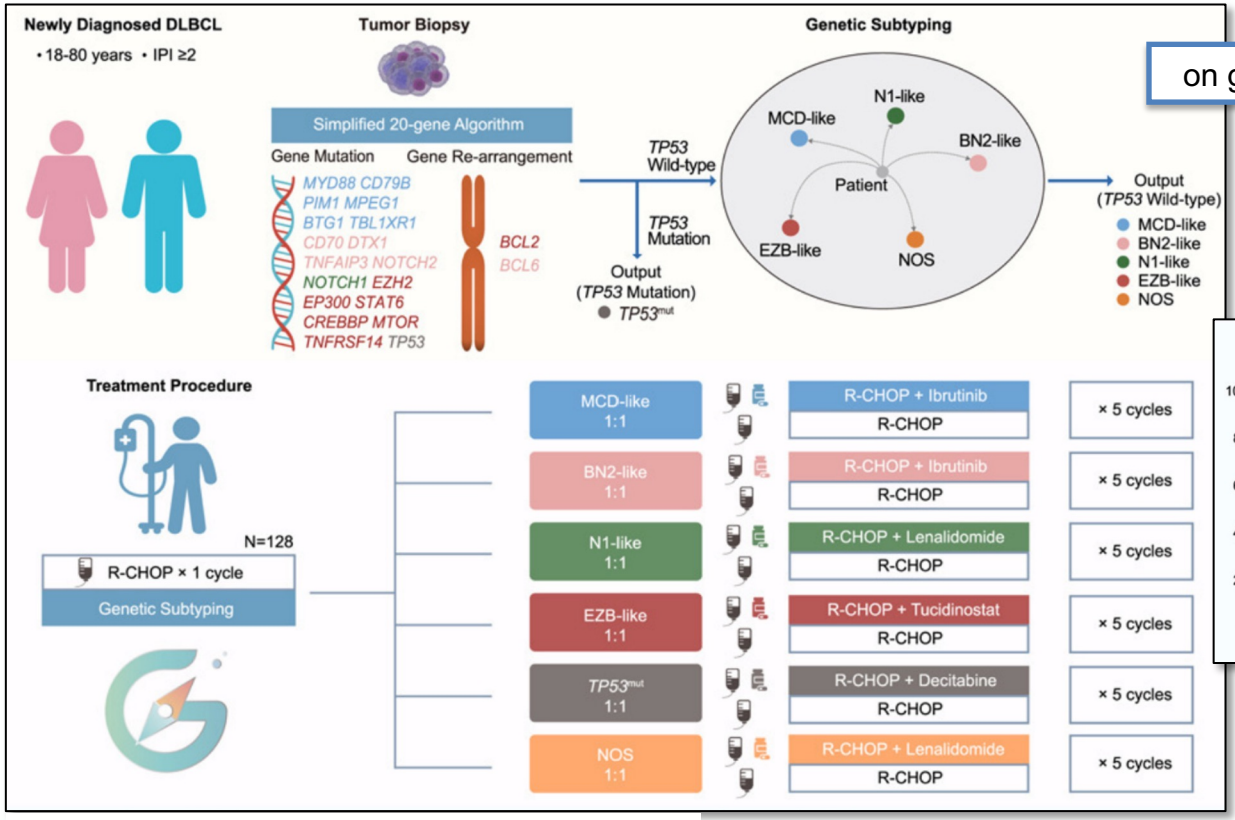
Schmitz R. et al. NEJM 2018



Wright G. et al. Cancer Cell 2020

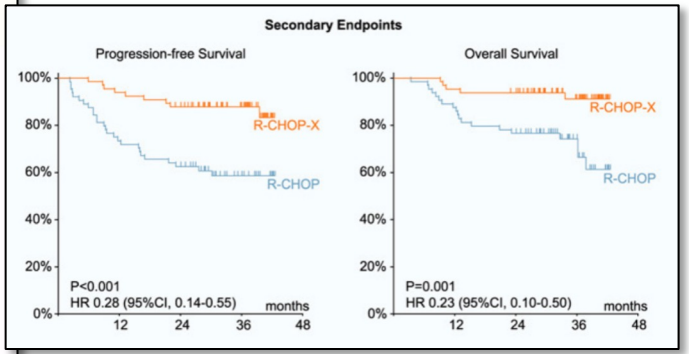
Algorithms are based on WES, that is not feasible in clinical practice

Predictive value of targeted NGS in molecular classification of DLBCL



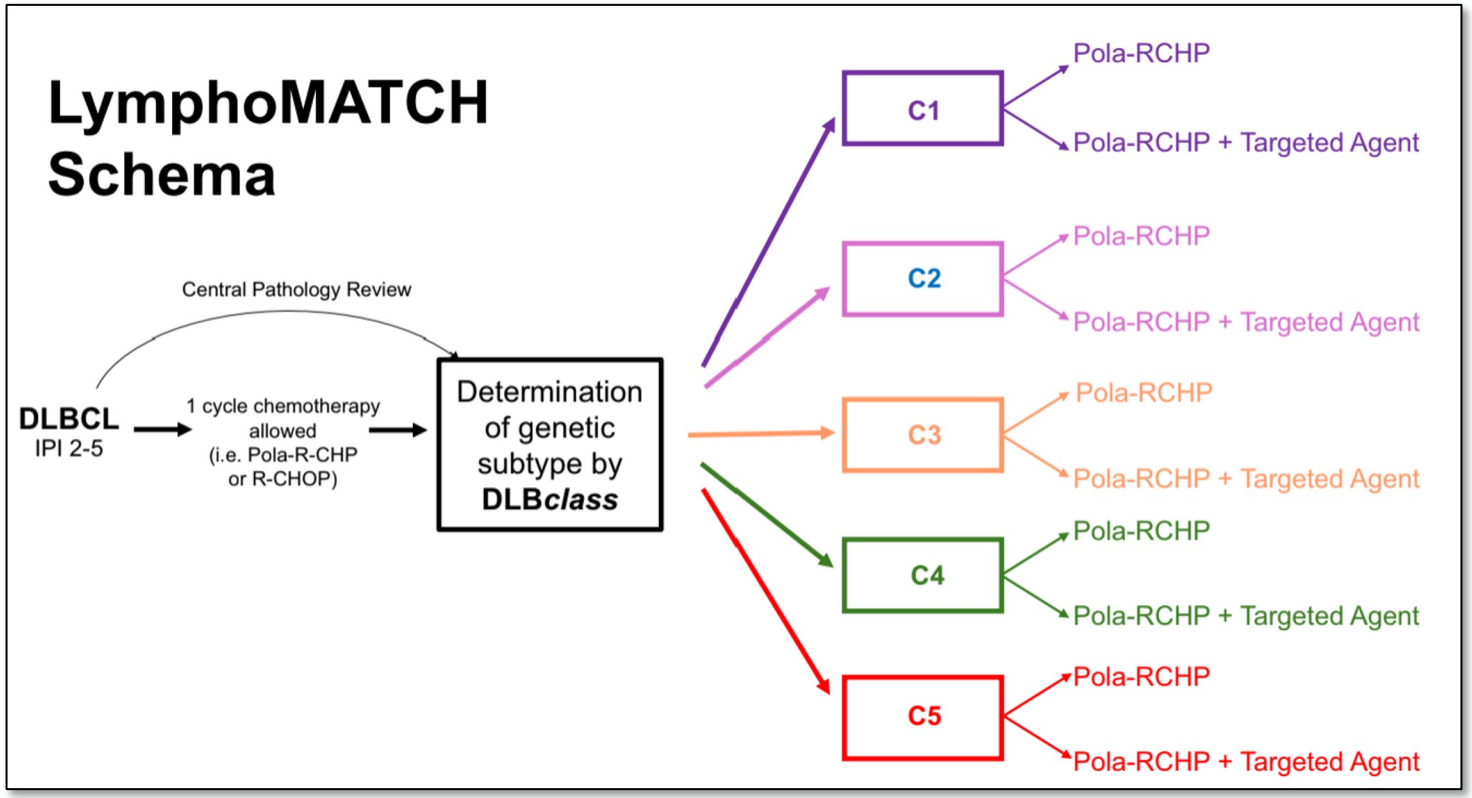
on going..

GUIDANCE-02
(NCT05351346)
OT05- multi-center, randomized, phase 3 study
*(**Lymphplex alghoritm**)*
Zhao W. Hematol Oncol 2025



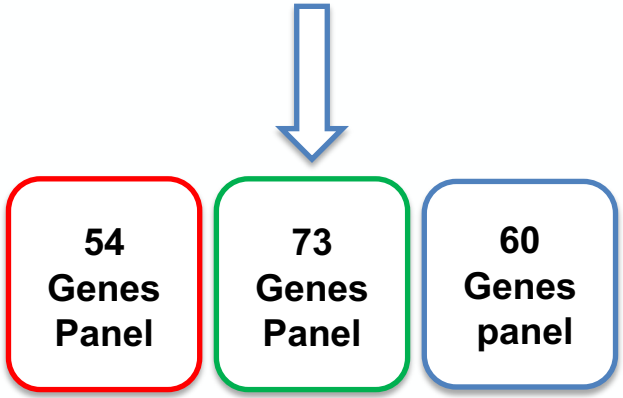
Therapeutic choices based on genetic subtyping improve PFS and OS

Zhang M.C. et al. Cancer Cell 2023



Rutherford S. et al. ASH 2025

Can we apply NGS targeted panels to routinary classify DLBCL?



Methodological workflow

Cohort A
n= 574 pz
Lymphgen

Cohort B
n= 664 pz
Lymphplex

Cohort C
n= 128 pz
GUIDANCE-sa

Cohort D
n= 119 pz
DLBClass

Coverage overlap

54 genes panel

73 genes panel

60 genes panel

Cohort A | Cohort B | Cohort C | Cohort D

Cohort A | Cohort B | Cohort C | Cohort D

Cohort A | Cohort B | Cohort C | Cohort D

LymphGen 2.0

LymphPlex 1.0

GUIDANCE-sa

DLBclass

Bioinformatic analysis

I. Cohen's Kappa
II. Confusion matrices
III. Sensitivity/ Specificity

Do the targeted panels agree with the 'gold standard'?

K < 0.04

Poor Agreement vs LymphGen

PANEL	COHEN'S KAPPA	SENSITIVITY
54-GENES PANEL	0.035	EZB≈20% N1≈5%
73-GENES PANEL	0.035	EZB≈20% N1≈5%
60-GENES PANEL	0.012	EZB≈20% N1≈5%

LymphGen 2.0

Do the targeted panels agree with the 'gold standard'?

0.66 < K < 0.75

Substantial Concordance vs Lymphplex

PANEL	COHEN'S KAPPA	SENSITIVITY
54-GENES PANEL	0.66	TP53≈100% ST2≈0%
73-GENES PANEL	0.74	TP53≈100% ST2≈25%
60-GENES PANEL	0.75	TP53≈100% BN2≈33%

LymphPlex 1.0

Do the targeted panels agree with the 'gold standard'?

0.63 < K < 0.75

Substantial Concordance vs GUIDANCE-sa

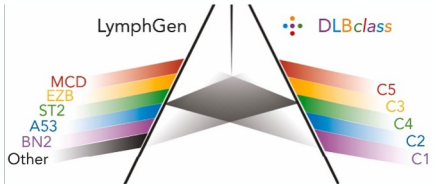
PANEL	COHEN'S KAPPA	SENSITIVITY
54-GENES PANEL	0.63	TP53≈100% BN2≈0%
73-GENES PANEL	0.64	TP53≈100% BN2≈0%
60-GENES PANEL	0.75	TP53≈100% BN2≈0%

GUIDANCE-sa

Do the targeted panels agree with the ‘gold standard’?

0.43 < K < 0.51

Moderate concordance vs DLBClass



PANEL	COHEN’S KAPPA	SENSITIVITY
54-GENES PANEL	0.43	C3 (EZB)≈100% C2 (BN2)≈0%
73-GENES PANEL	0.47	C3 (EZB)≈100% C2 (BN2)≈0%
60-GENES PANEL	0.51	C3 (EZB)≈100% C4 (BN2)≈0%

DLBclass

Conclusion and future directions

- NGS targeted panels (54/73/60 genes) struggle to perform with WES-based algorithms (i.e Lymphgen).
- Targeted panels perform poorly in specific categories (e.g : BN2 or ST2 subtypes).
- NGS targeted panels (54/73/60 genes) perform better with targeted-based algorithms (i.e Lymphplex, Guidance-SA, DLBclass).
- Refinements of NGS targeted panels is needed to improve DLBCLs molecular subtyping in clinical practice.

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