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DIPARTIMENTO DI
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POLICLINICO DI
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Aggressive
Lymphoma
Workshop

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MECHANISM-BASED THERAPY OF DLBCL

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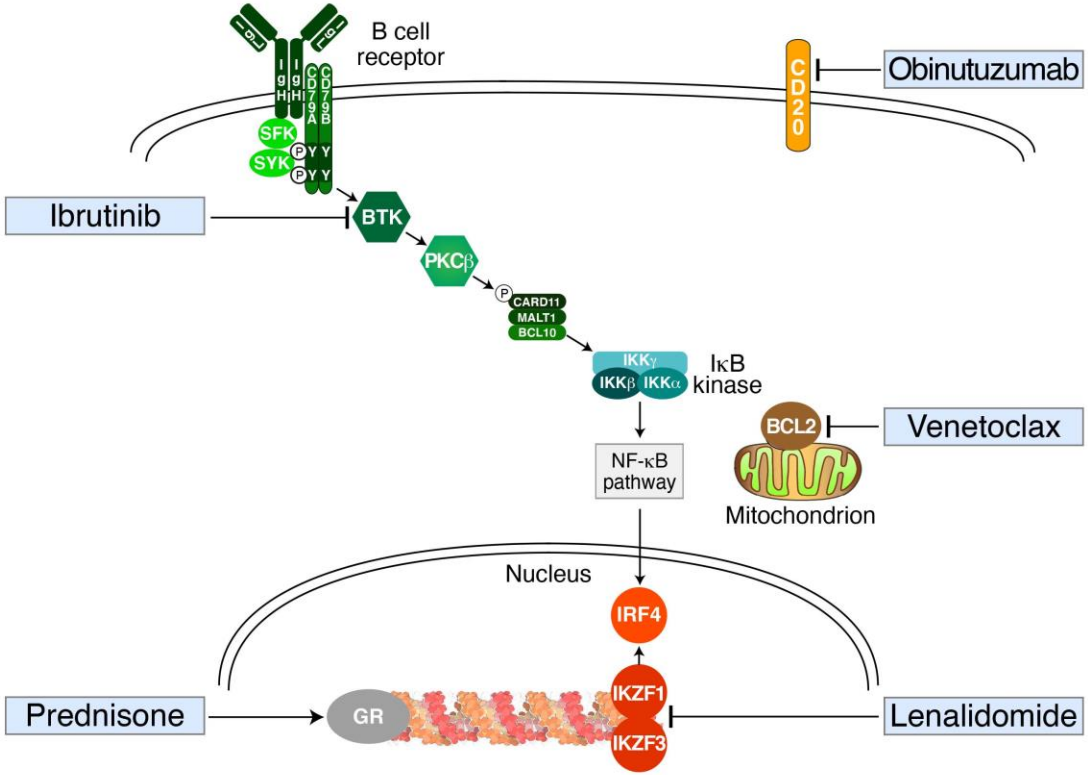
Disclosures

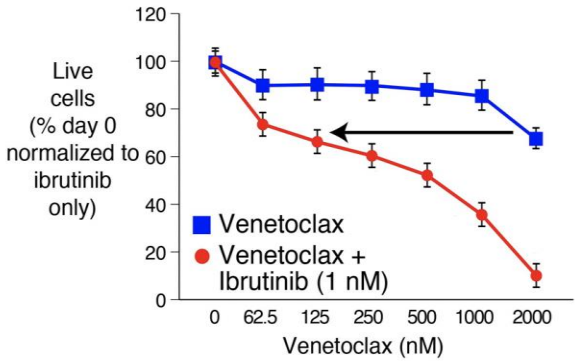
Disclosures of Mark Roschewski

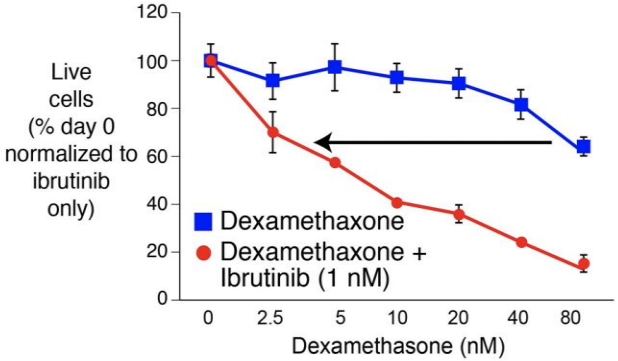
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
	None	None	None	None	None	None	None

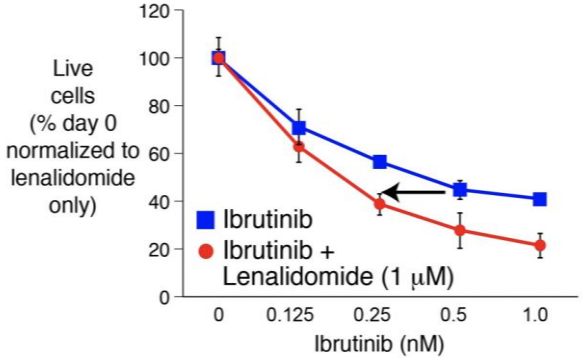
ViPOR: A Mechanism-based Combination of Synergistic Drugs to Treat Lymphoma



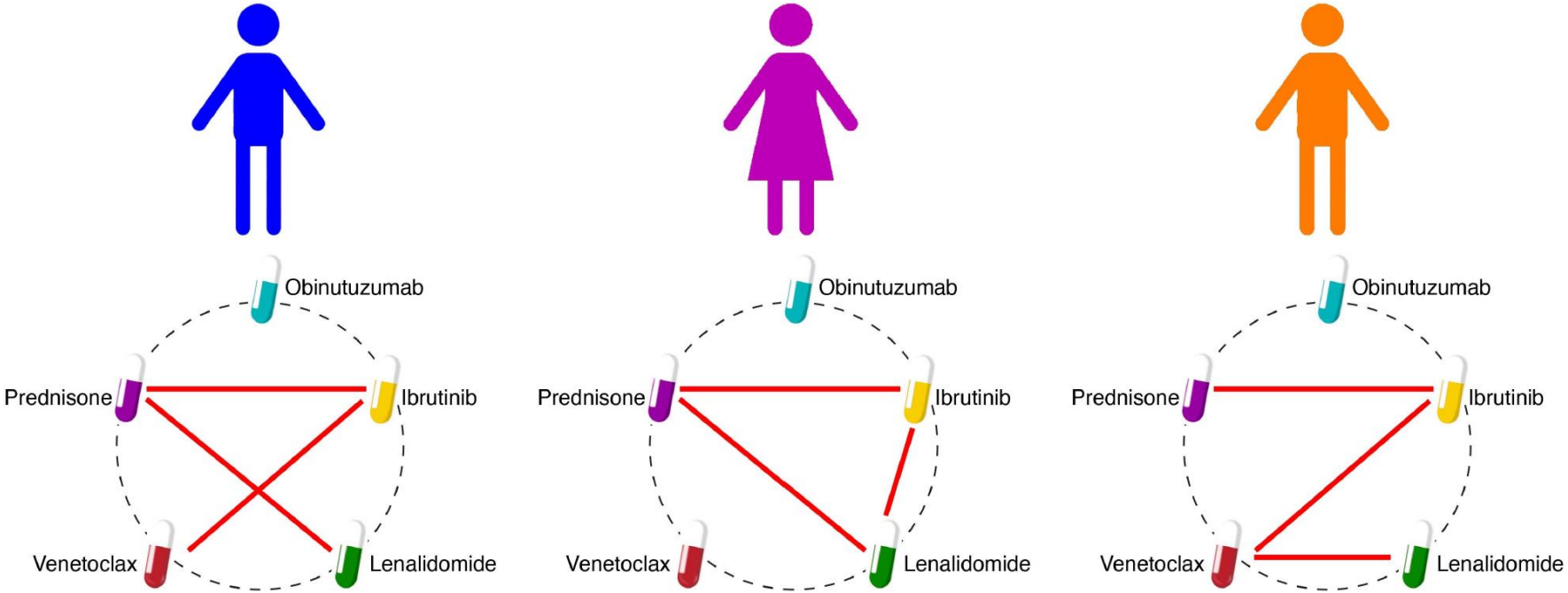
Pre-Clinical Evidence of Synergy in DLBCL cell lines



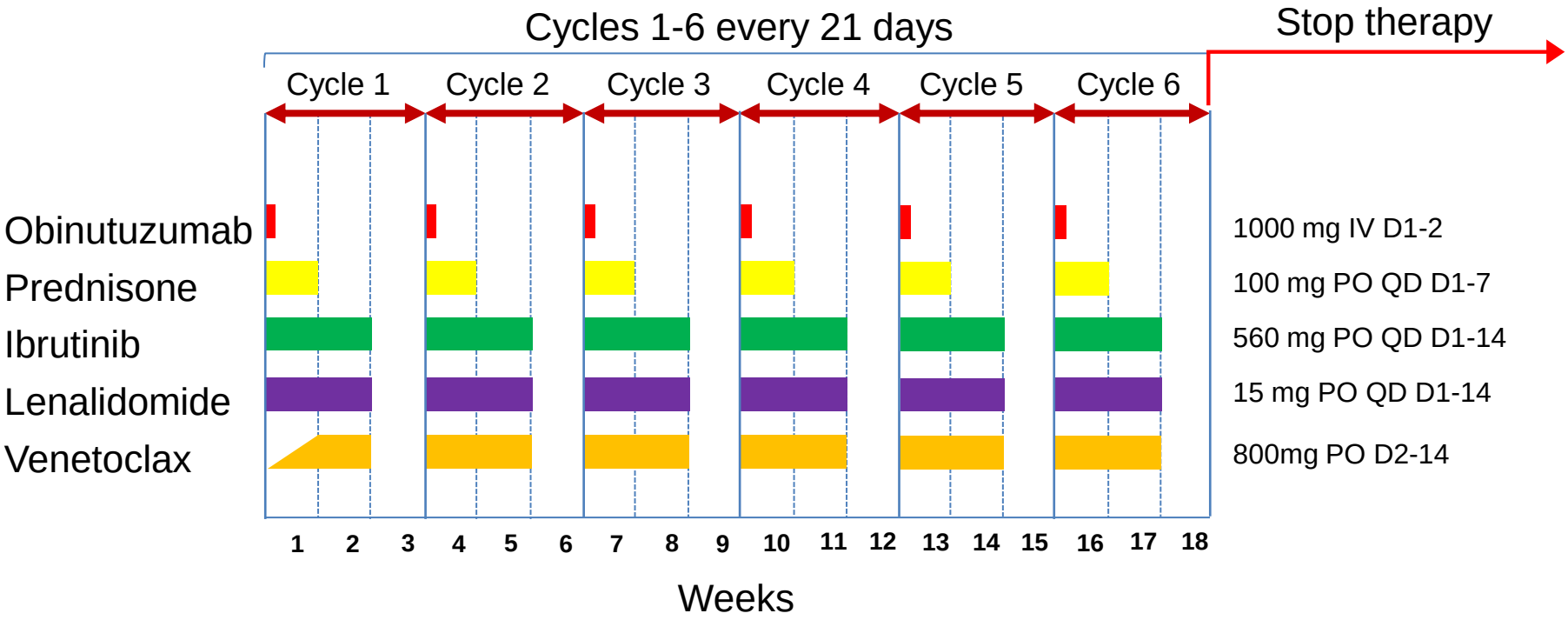




Synergistic Combinations Address Genetic Heterogeneity



ViPOR is Administered for Six Cycles Only



Characteristics of DLBCL Patients

	(N=50)
Age - median (range) yr.	61 (29-77)
Disease histology – no. (%) Diffuse large B-cell lymphoma: NOS High grade B-cell lymphoma-DH T-cell histiocyte rich DLBCL	 25 (50%) 20 (40%) 5 (10%)
Intermediate-High/High-risk IPI	34 (68%)
Refractory to most recent therapy	28 (56%)
Prior therapies - median (range)	3 (1-9)
Prior CAR-T therapy Prior ibrutinib, lenalidomide, or venetoclax Prior auto transplant Prior allogeneic transplant	20 (40%) 18 (36%) 5 (10%) 1 (2%)

Grade 3 or Higher Adverse Events

Hematologic (per cycle, N=251):

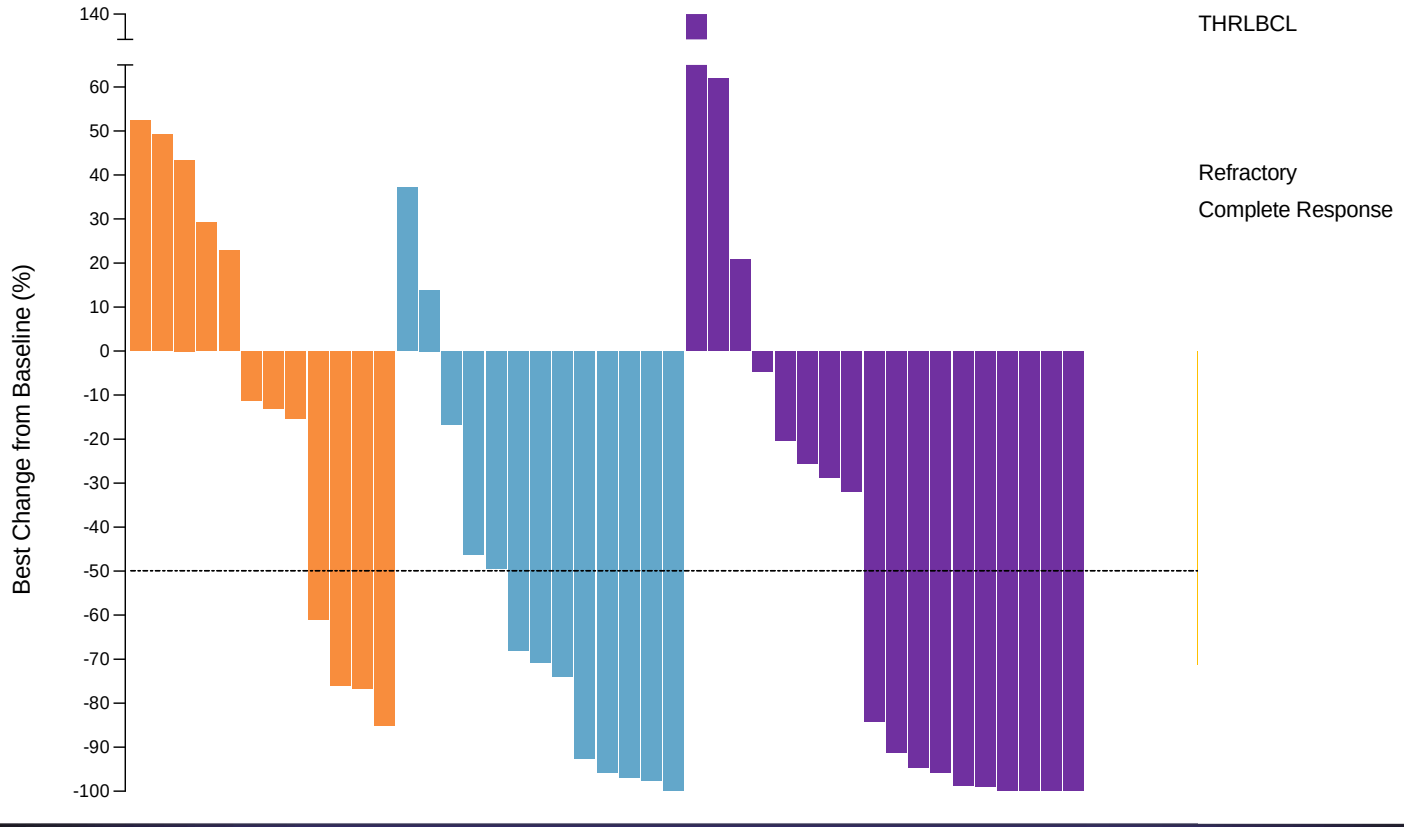
Adverse Event	≥Grade 3 N (%)
Neutropenia	60 (24%)
Thrombocytopenia	57 (23%)
Anemia	16 (6%)
Febrile neutropenia	3 (1%)

All patients receive G-CSF support

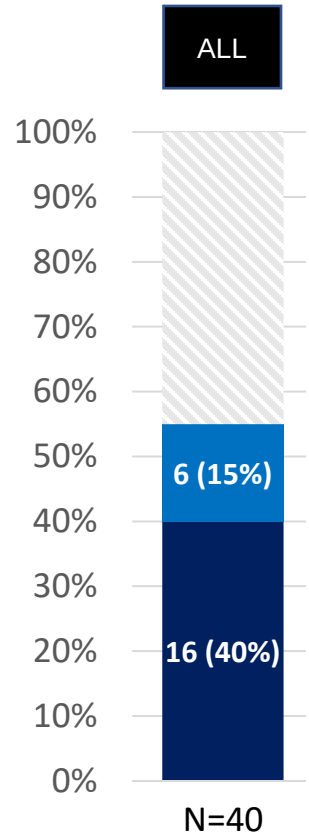
Dose Reductions: 6% of cycles

Dose Delays: 10% of cycles

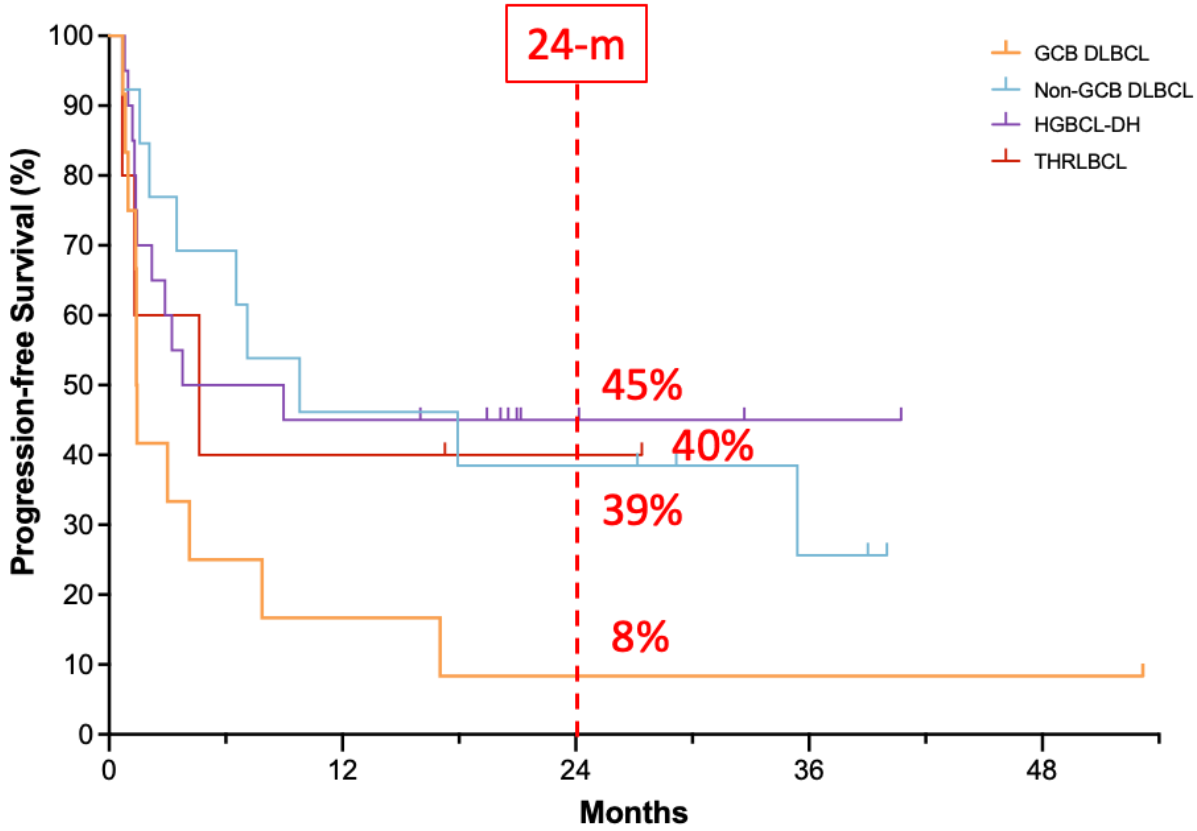
Response by DLBCL Subtype



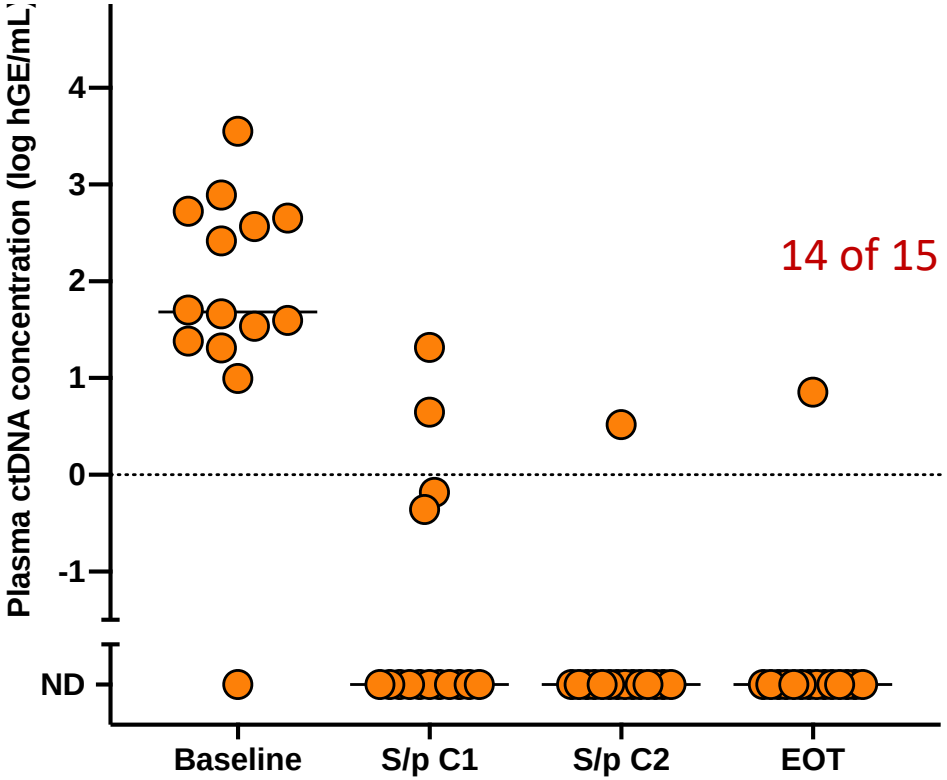
ViPOR Response Rate by DLBCL Subtype



2-year PFS Landmark by DLBCL Subtype

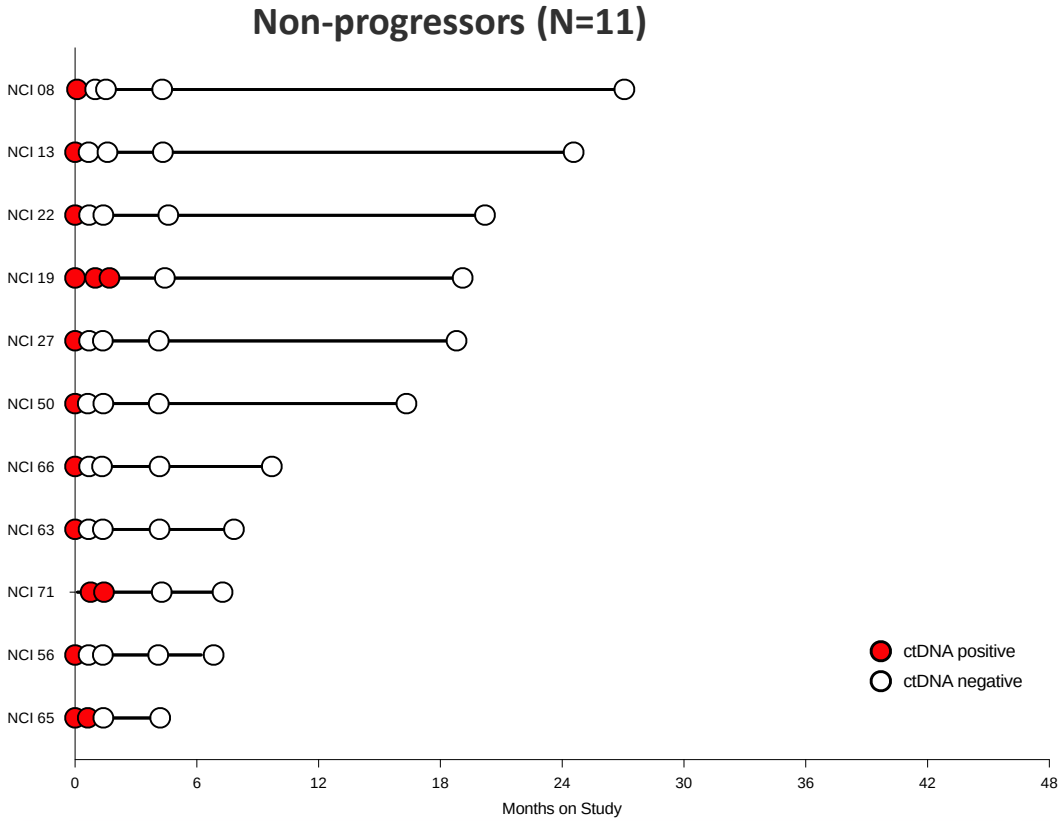


Circulating Tumor DNA at End of Therapy

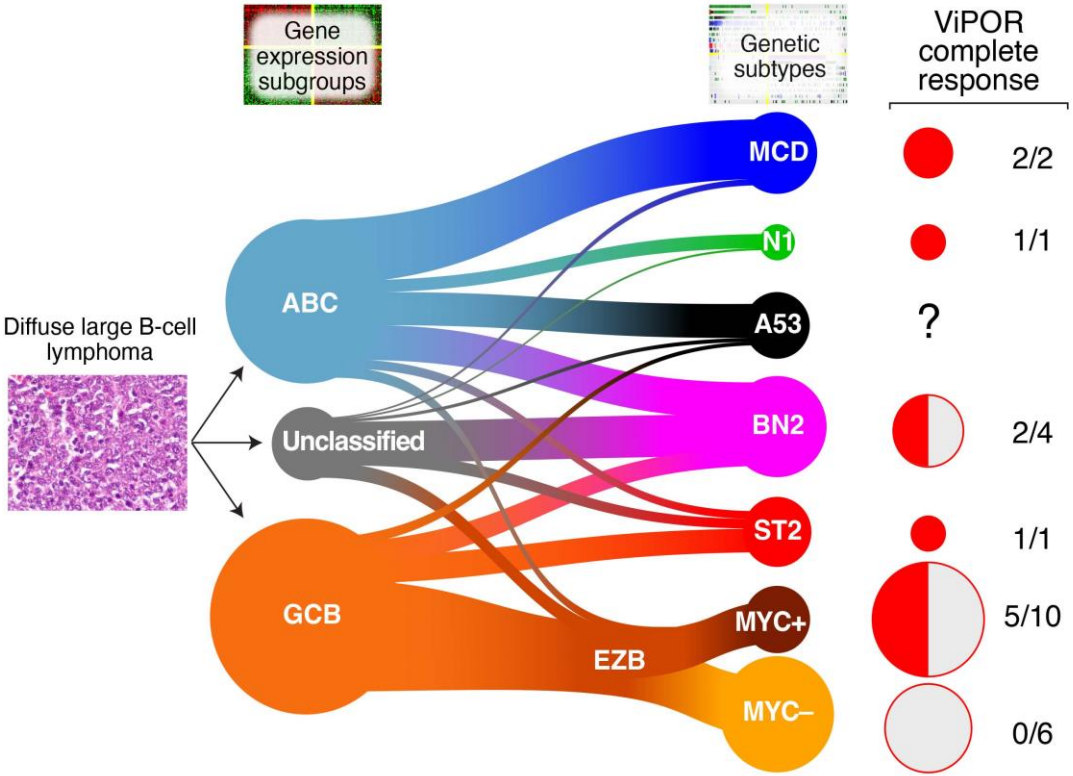


14 of 15 (93%) undetectable

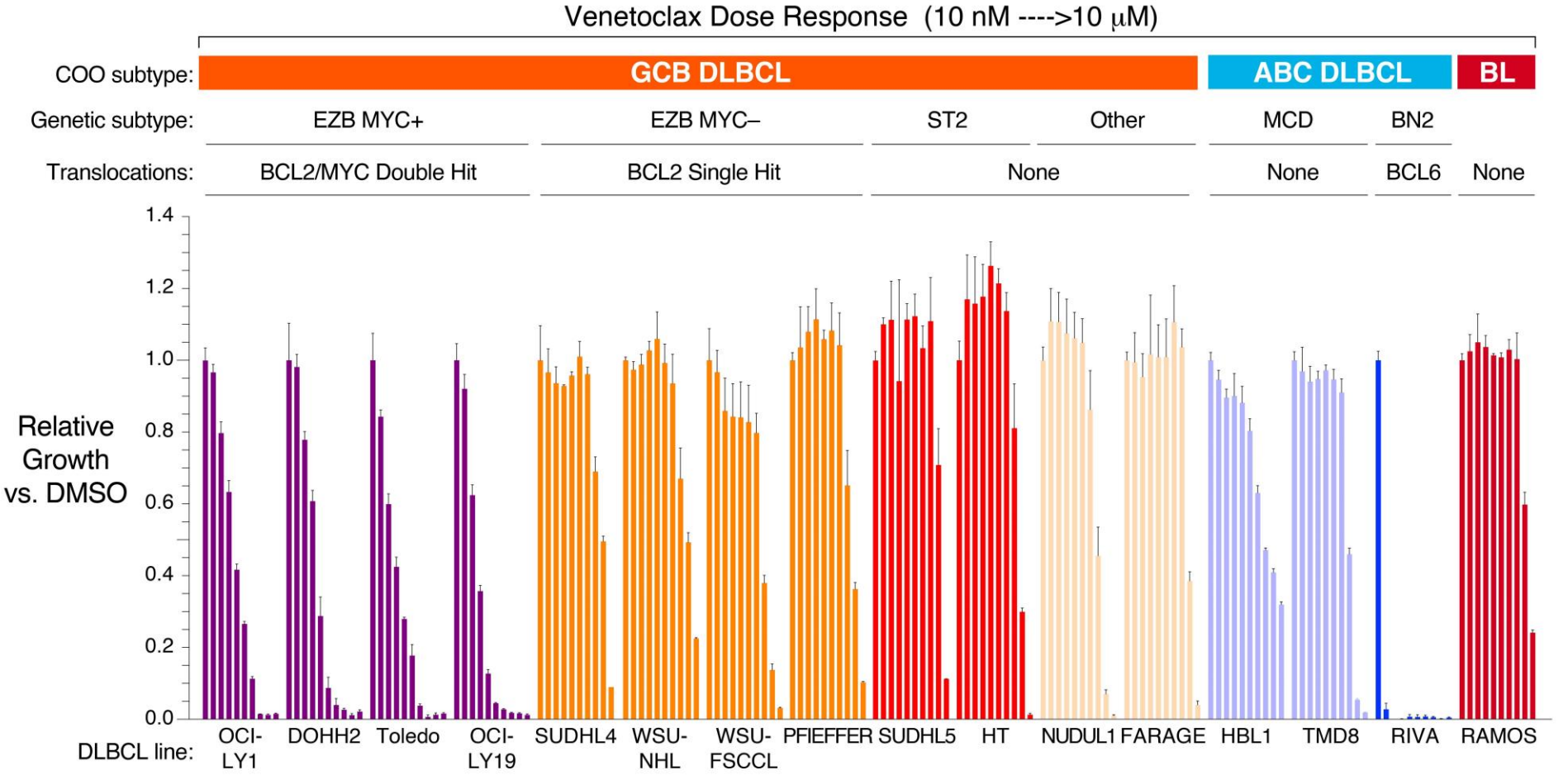
ctDNA Remains Undetectable in Non-Progressors



ViPOR Complete Responses By LymphGen Genetic Subtype

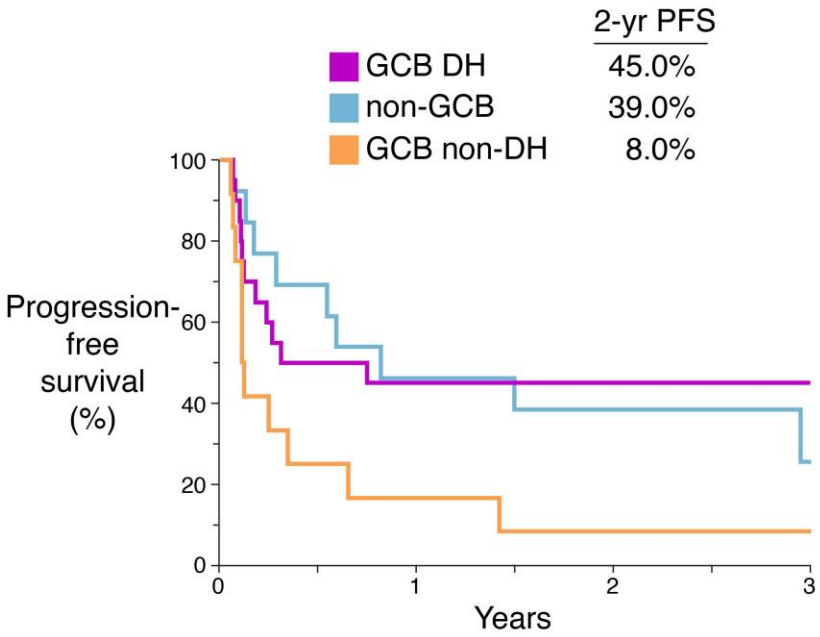


Venetoclax is Preferentially Toxic for GCB MYC+ DLBCL (Double Hit)



ViPOR Compares Favorably with CAR-T in Relapsed/refractory DLBCL

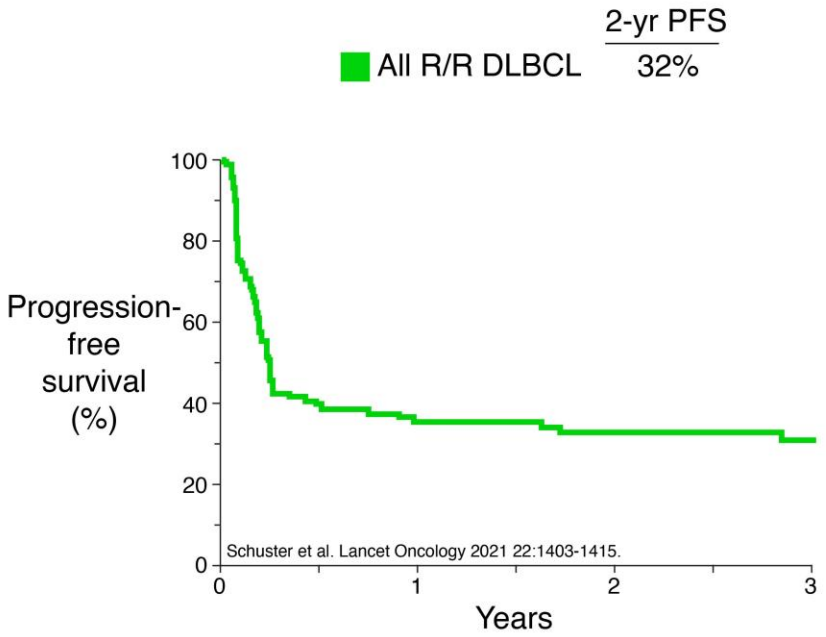
ViPOR



Patients treated: 100%
Patients refractory to last Rx: 56%

CAR-T

JULIET Trial (Tisagenlecleucel)



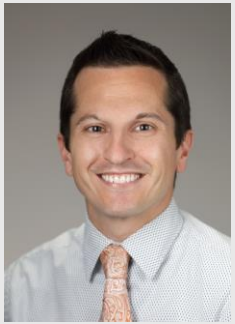
Patients treated: 67%
Patients refractory to last Rx: 55%

Cost of Targeted Therapy for DLBCL

Regimen	Duration	Cost
ViPOR	5 months	$169,498
Lenalidomide + Rituximab	12 to 18 months	$199,139
Lenalidomide + Obinutuzumab	24 months	$351,584
Rituximab + Ibrutinib + Lenalidomide	12 months	$321,414
CAR-T cells	1 to 3 months	$440,000
Mosutenuzumab	12 months	$171,867

Conclusions

- Targeted combination therapy for fixed cycles induces durable remissions in genetic subtypes of DLBCL
- ViPOR regimen has a favorable safety profile and can be delivered to all ages
- ViPOR is an effective platform to add rational targeted agents or immunotherapy



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