

FAIR Data, Clear Insights: Enhanced PRO Analysis

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Agenda

- Introduction to Data Mart
- Patient Reported Outcomes (PROs) data
- Use Case: PRO scales for DLBCL Patients
- Future Work: PRO for TPP development
- Conclusion
- Q & A



Introduction to Data Mart

FAIR Principles

EDIS data mart



Findable
"I know where data is"



Accessible
"I can access data I need"



Interoperable
"I use consistent standards & terms"



Reusable
"I use existing data to answer new questions"

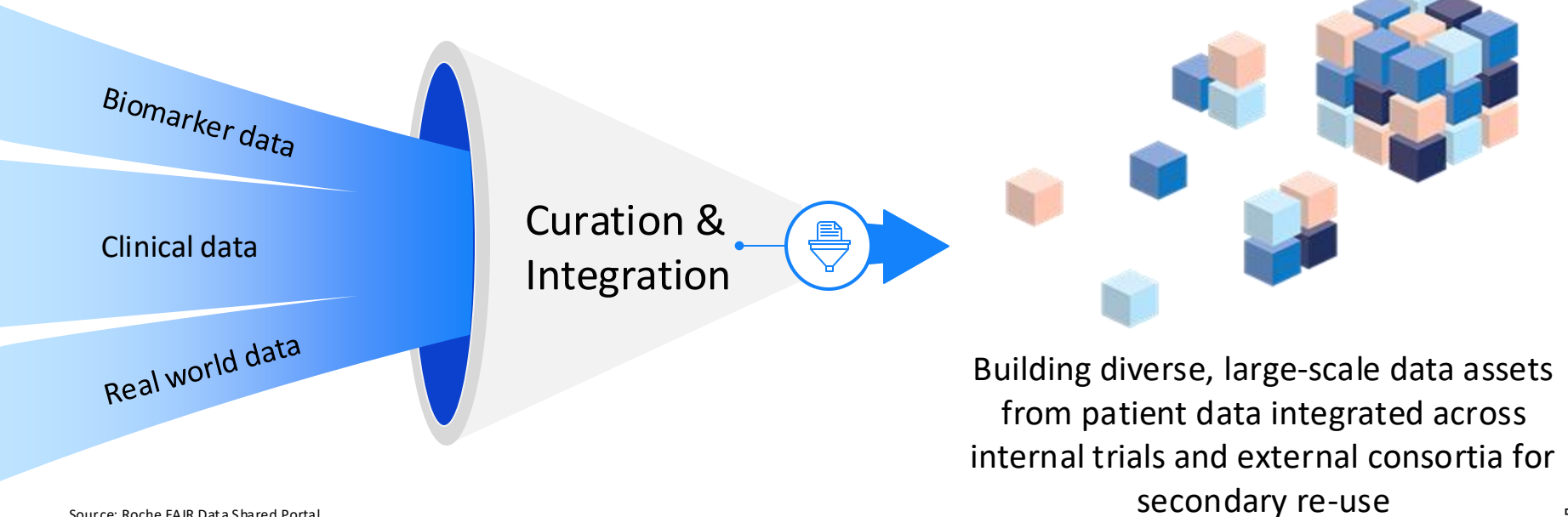
EDIS intends to make our data FAIR and Shared to accelerate generation of meaningful insights



**Enhanced Data & Insights Sharing
(EDIS)**

Data Marts

A data mart is a collection of harmonized data modalities from multiple studies and/or external data sources that are available in a single place and can be analyzed by scientists throughout the company.



Data Mart Portfolio



EDIS NHL Data Mart

VISION

Using EDIS to deepen our understanding of NHL disease biology will be a critical support for making portfolio decisions and increasing PTS of our trials

GOALS

A Generate Datamart

Create a F.A.I.R NHL data mart of our legacy clinical trials in a way that will be easily analyzable

Capacity building with historical studies and **genomic data**

B Identify prognostic subgroup(s)

Find ≥ 1 subgroup of patients diagnosed with FL or DLBCL who have High Unmet Medical Need (UMN) with available therapies

C Inform pipeline + disease biology

Test the hypotheses brought forward by molecule teams that will inform strategic or trial design decisions

D Patient reported outcomes

To conduct analyses on the data from multiple NHL studies that will be curated and integrated with the clinical data to inform future studies

E Safety

Correlation of safety outcomes with baseline factors, patient characteristics, and efficacy.

*Patient-centric approach with potential to incorporate **genomic data**?*

Identify actionable patient subset(s)

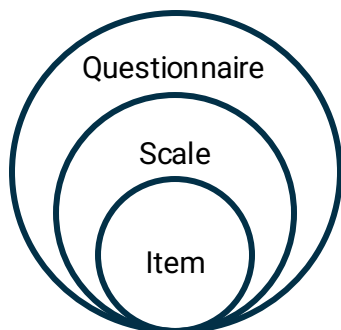
EDIS NHL 2024 Workstreams & Goals (Impact)

	Curation/Integration	Moonshots	2L CART Eligible segment	Treatment sequencing	Single agent contribution	ctDNA in 1L DLBCL	PROs	CRS
Data generation to support market uptake/asset positioning	✓	✓		✓	✓		Using PRO data inform PRO endpoint selection	
Increasing disease biology knowledge	✓	✓	✓	✓	✓	✓		✓
Support portfolio strategy decisions	✓	✓	✓	✓	✓			✓
Informing Study design/support TPP development	✓					✓	Using PRO data inform PRO endpoint selection	✓

Patient Reported Outcomes (PROs) data

Patient Reported Outcome Data

Definition: PROs include any health outcome that comes directly from the patient's experience, with no interpretation by a clinician or another intermediary.



	Scale	Number of items	Item range*	Version 3.0 Item numbers	Function scales
Global health status / QoL					
Global health status/QoL. (revised) [†]	QL2	2	6	29, 30	
Functional scales					
Physical functioning (revised) [†]	PF2	5	3	1 to 5	F
Role functioning (revised) [†]	RF2	2	3	6, 7	F
Emotional functioning	EF	4	3	21 to 24	F
Cognitive functioning	CF	2	3	20, 25	F
Social functioning	SF	2	3	26, 27	F
Symptom scales / items					
Fatigue	FA	3	3	10, 12, 18	
Nausea and vomiting	NV	2	3	14, 15	
Pain	PA	2	3	9, 19	
Dyspnoea	DY	1	3	8	
Insomnia	SL	1	3	11	
Appetite loss	AP	1	3	13	
Constipation	CO	1	3	16	
Diarrhoea	DI	1	3	17	
Financial difficulties	FI	1	3	28	

EORTC QLQ-C30 and FACT-Lym

During the past week:

Item

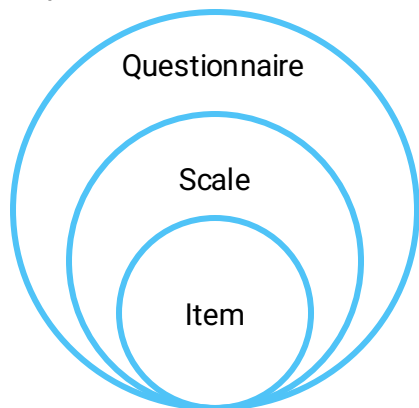
17. Have you had diarrhea?

18. Were you tired?

19. Did pain interfere with your daily activities?

Not at All	A Little	Quite a Bit	Very Much
1	2	3	4
1	2	3	4
1	2	3	4

Each scale is derived into a single number (or score) calculated from answers to a single item or a group of items; represents the health-related quality of life specific to what the scale is describing



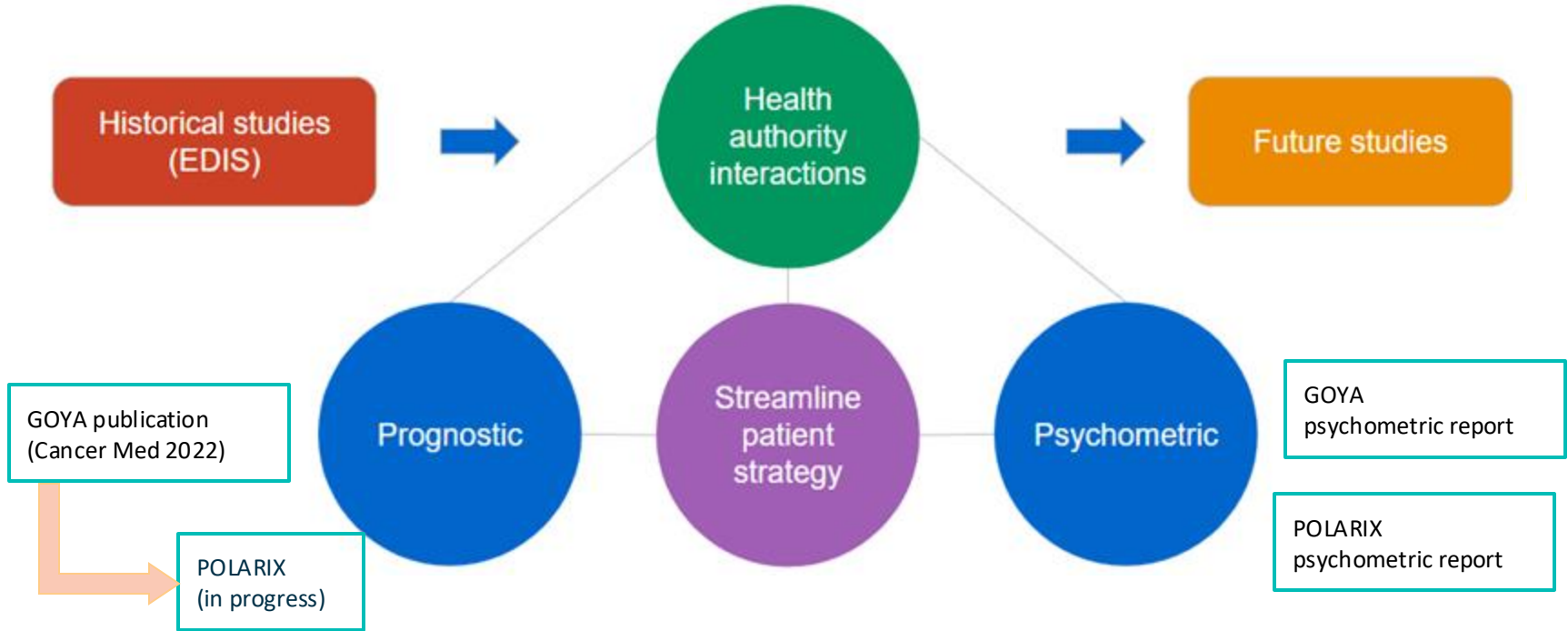
Scale

Questionnaire

FACT-LYM Scales	EORTC QLQ C30 Scales
Lymphoma (LYMS) Additional Concerns	Overall QoL - Global Health Status Functional Scales - Physical Functioning - Role Functioning - Emotional Functioning - Cognitive Functioning - Social Functioning Symptomatic Scales - Fatigue - Nausea & Vomiting - Pain - Dyspnoea - Insomnia - Appetite Loss - Constipation - Diarrhoea - Financial Difficulties

Objectives

To inform future studies

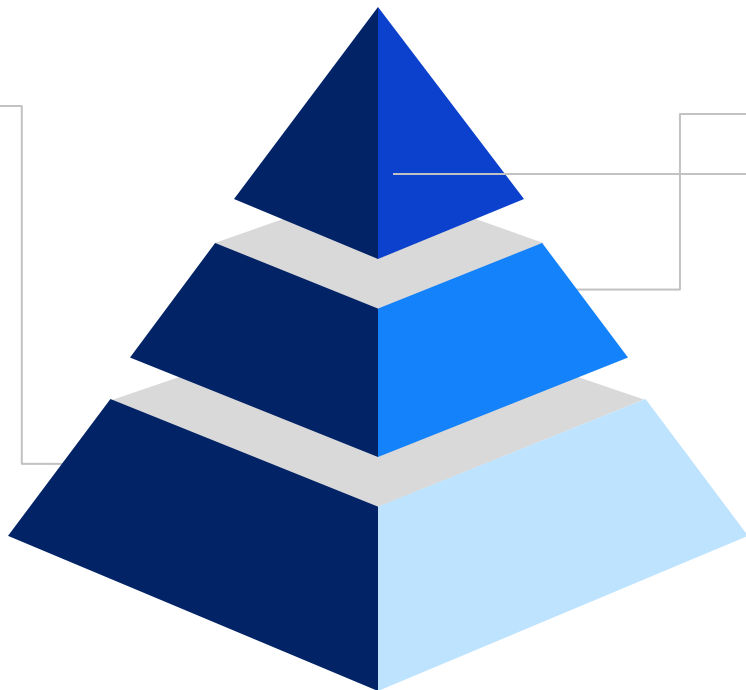


PRO workflow

Harnessing the EDIS NHL datamart

Assess collected PRO data

- Identify questionnaires 1
- Assess feasibility
- Calculate PRO scales
- Understand study properties
 - Phase
 - Treatment type
 - Dose
 - SOA



Focus on PROs of high value

- Narrow down from the many (~tens) PRO scales collected
- Develop criteria of selection
 - Data availability
 - Prognostic value
 - Physcometric value
 - Clinical relevance
 - Regulatory PTS
 - Prior experience

Assess endpoint value

- Change from baseline
- Time to deterioration

Use Case: PRO scales for DLBCL Patients

Background¹

Diffuse large B-cell lymphoma (**DLBCL**) is an aggressive non-Hodgkin lymphoma (**NHL**).

Identifying high-risk patients in untreated (1L) DLBCL is crucial for advancing treatment strategies.

The International Prognostic Index (**IPI**) is a frequently-used estimator of prognostic outcomes in 1L DLBCL patients.²

GOYA (NCT01287741) is a phase III study examining the efficacy of obinutuzumab + CHOP versus rituximab + CHOP in previously untreated CD20+ DLBCL patients.³

The prognostic value of patient-reported health-related quality of life (**HRQoL**) in DLBCL remains underexplored.

We aim to evaluate whether pre-treatment HRQoL adds prognostic value beyond IPI in identifying high-risk 1L DLBCL patients.

Overview

EDIS NHL - Baseline PRO in 1L DLBCL

Goal: Find > 1 subgroup of patients diagnosed with Diffuse large B cell lymphoma (DLBCL) who have High Unmet Medical Need with available therapies

Prior work on PRO prognostic value

- Select PRO scales with high prognostic value to potentially address unmet needs.
- Reduce patient burden by collecting less data on low-value PRO scales.

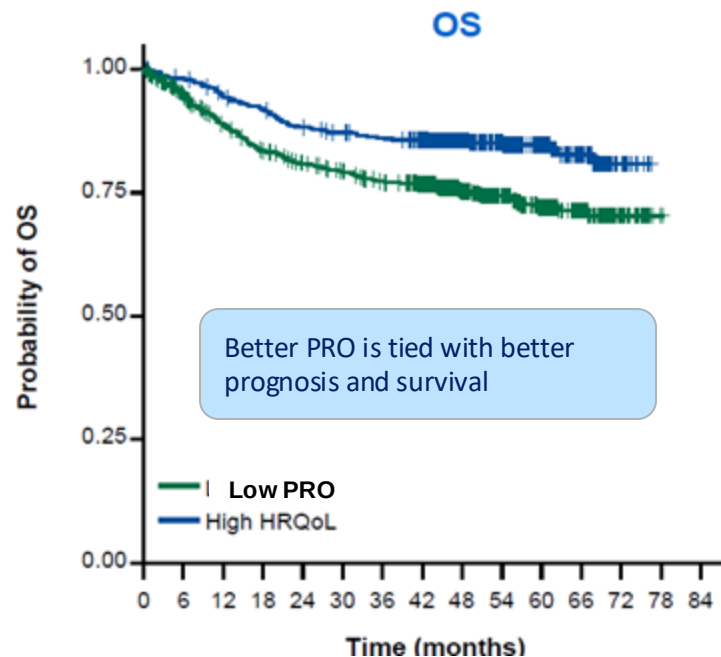
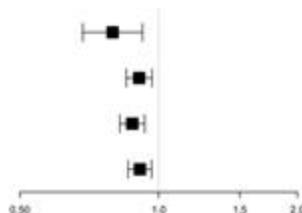
Result¹

Pre-treatment Health Related Quality of Life (HRQoL) provides prognostic value for survival

Multivariable Cox Model OS ~ IPI + PRO + COO + BCL2 + TMTV

PRO subscales

	HR (95% CI)
FACT-LYM: Lymphoma subscale (LYMS)	0.79 (0.68 , 0.92)
EORTC QLQ-C30: Global health status/QoL	0.91 (0.85 , 0.97)
EORTC QLQ-C30: Physical functioning	0.88 (0.82 , 0.93)
EORTC QLQ-C30: Fatigue	0.91 (0.86 , 0.97)



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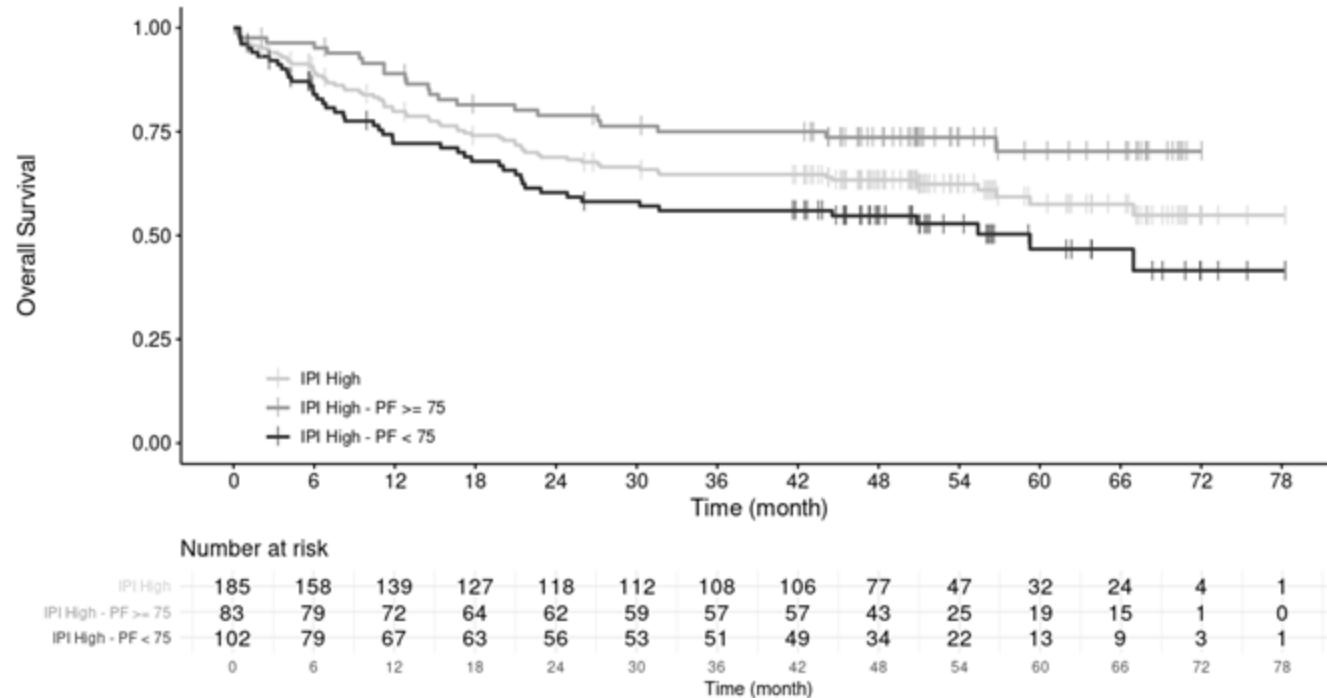
Prior work on PRO prognostic value

Finding optimal PRO cutoff

- Select PRO scales with high prognostic value to potentially address unmet needs.
- Reduce patient burden by collecting less data on low-value PRO scales.
- Facilitate the clinical use/interpretation of PRO by translating ordinal scale to binary scale

Result¹

Patients identified as high risk by IPI can be further separated in terms of risk (OS) by the binary Physical Functioning scale



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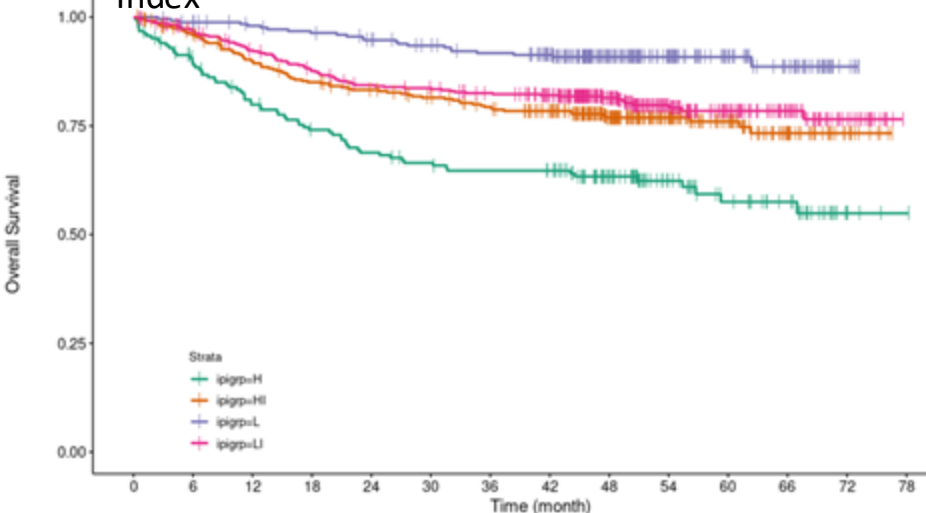
Develop new risk index

- Incorporate PRO scales with a well-established NHL prognosis prediction index (IPI) to develop a new risk index
- Find > 1 subgroup of patients who have High Unmet Medical Need

Result¹

Adding PRO to IPI (well-established index in predicting the prognosis of patients with aggressive NHL) potentially redefines patient risk

Old Index

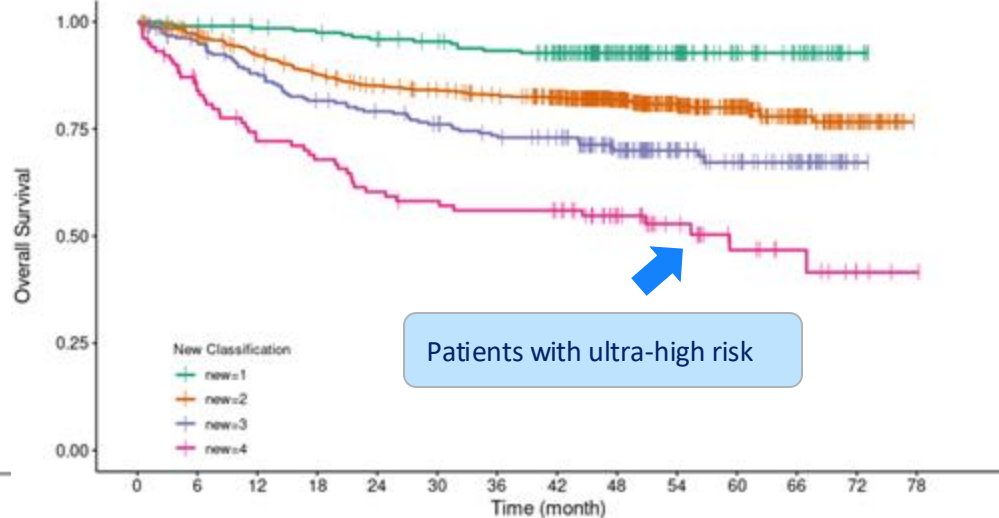


Number at risk

Strata	0	6	12	18	24	30	36	42	48	54	60	66	72	78
ipigrp=H	185	158	139	127	118	112	108	106	77	47	32	24	4	1
ipigrp=HI	360	335	310	292	281	270	258	242	176	108	68	36	11	0
ipigrp=L	253	247	240	235	228	220	213	199	130	85	52	34	5	0
ipigrp=LI	456	431	406	383	366	361	350	330	220	127	85	50	21	0

Time (month)

New Index



Number at risk

New Classification	0	6	12	18	24	30	36	42	48	54	60	66	72	78
new=1	201	198	193	190	186	181	175	164	106	67	41	27	4	0
new=2	735	695	655	619	593	579	561	528	362	220	140	80	32	0
new=3	216	199	180	165	158	150	142	136	101	58	43	28	2	0
new=4	102	79	67	63	56	53	51	49	34	22	13	9	3	1

Time (month)

Future Work: PRO for TPP Development

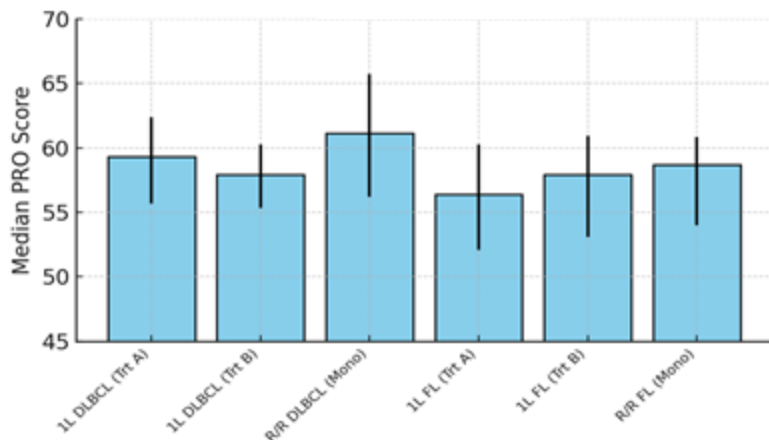
PRO data availability

Certain questionnaires are more commonly collected vs. others

Questionnaire	NHL				Bispecifics		InHarmony	CLL
	Study A	Study B	Study C	Study D	Study E	Study F	Study G	Study H
EORTC QLQ-C30 V3.0	☒		☒		☒	☒		☒
FACT-LYM V4	☒	☒		☒	☒	☒		
EQ-5D-3L	☒	☒		☒				
KATZ ADL		☒		☒				
IADL		☒		☒				
FACT-G V4			☒					
EORTC QLQ-CLL16								☒
PRO-CTCAE V1						☒		
EQ-5D-5L					☒			
TINAS							☒	

Endpoint: Baseline median PRO scales

Consistent baseline PROs provides robust basis for TPP development



PRO scale	Description
Global health status	Overall health and quality of life
Physical functioning	Difficulty in performing routine activities
Fatigue	Needing to rest, feeling tired/weak
Role functioning	Limited in work/other daily/leisure activities
Pain	Level of pain and its interference with daily activities
LYMS	Disease-specific measure of lymphoma symptoms deemed important by patients

- Baseline median PRO scales consistent across different indications and lines of therapy.
- Robust PRO baseline measures means that our in house trial PRO data may be sufficient in establishing a solid basis for estimating TPPs

Looking ahead to 2025



PRO endpoint selection - additional endpoints to be completed:

- Time to deterioration of a PRO scale
- Max % change from baseline
- Change from baseline at specific follow up



Set up the PRO book of knowledge for NHL for TPP development and endpoints selection

Conclusion

Conclusion

FAIR Data, Clear Insights: Enhanced PRO Analysis

EDIS NHL data mart makes our data **FAIR** and Shared to accelerate generation of meaningful insights



Incorporating PRO into risk stratification improves risk assessment in DLBCL patients, identifies subgroups with high unmet needs, enhances a patient-centered approach, and informs future PRO data collection and assessment.

Further development can help set up the PRO book of knowledge for NHL for TPP development and endpoints selection



Q&A

Doing now what patients need next

Reference

1. Huang, H., Datye, A., Fan, M., Knapp, A., Nielsen, T., Bottos, A., Paulson, J. N., Trask, P. C., & Efficace, F. (2022). Patient-reported outcomes provide prognostic information for survival in patients with diffuse large b-cell lymphoma: Analysis of 1239 patients from the goya study. *Cancer Medicine*, 11(17), 3312–3322. <https://doi.org/10.1002/cam4.4692>
2. Maurer, M. J. (2023). The international prognostic index in aggressive B-cell lymphoma. *Haematologica*, 108(11), 2874–2879. <https://doi.org/10.3324/haematol.2023.284070>
3. Vitolo, U., Trněný, M., Belada, D., Burke, J. M., Carella, A. M., Chua, N., Abrisqueta, P., Demeter, J., Flinn, I., Hong, X., Kim, W. S., Pinto, A., Shi, Y. K., Tatsumi, Y., Oestergaard, M. Z., Wenger, M., Fingerle-Rowson, G., Catalani, O., Nielsen, T., Martelli, M., & Sehn, L. H. (2017). Obinutuzumab or rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone in previously untreated diffuse large B-cell lymphoma. *Journal of Clinical Oncology*, 35(31), 3529–3537. <https://doi.org/10.1200/JCO.2017.73.3402>

Backup slide

Method for Use case

- Finding PRO cut-off from GOYA study
 - Combined data from both treatment arms
 - Performed cox regression hazard models on selected PROs
 - Evaluated different metrics on univariate cox with PRO dichotomized by all possible cut-off values (cordance index, AIC, log rank statistics and HR)
 - Selected the cutoff value with the overall highest ranking in all metrics
- Validation on POLARIX study
 - Combined data from both treatment arms
 - Adjusting for IPI and other prognostic values
 - Added prognostic value of PRO in stratifying high risk patient with the proposed PRO