Supplemental Table 1. Criterion categories in five DLBCL RCTs examining targeted therapy with R-CHOP in the control arm

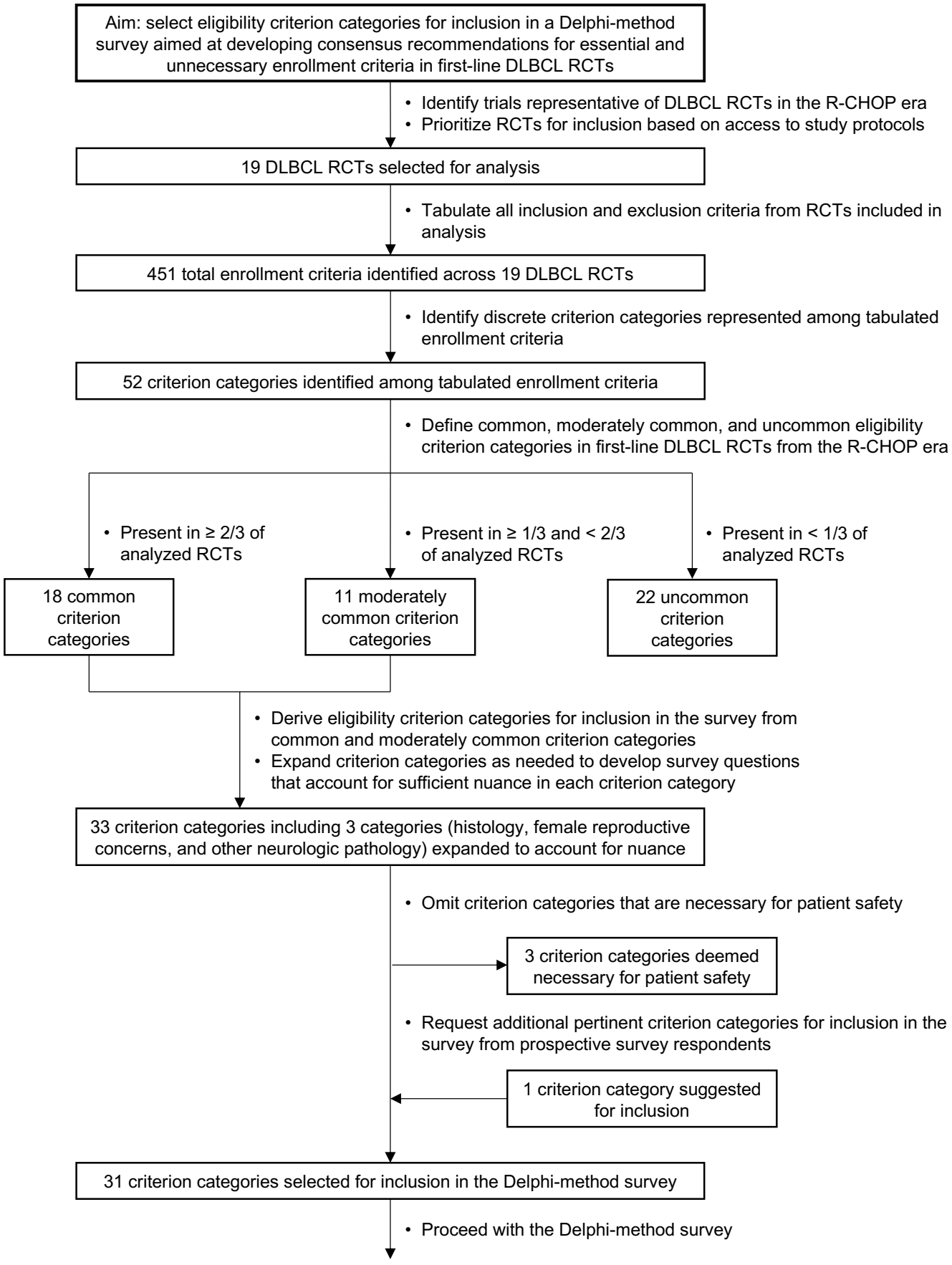
Number of studies with criterion category n (%)	Common criterion categories (present in > 66% of RCTs; n = 19 categories)	Number of studies with criterion category n (%)	Moderately Common criterion categories (present in 33%–66% of RCTs; n = 11 categories)	Number of studies with criterion category n (%)	Uncommon criterion categories (present in < 33% of RCTs; n = 10 categories)
5 (100)	Age (years)	3 (60)	Contraindicated therapies	1 (20)	History of PTLD
5 (100)	Cardiac function	3 (60)	Contraindications to study therapy	1 (20)	History of transformed lymphoma
5 (100)	Female reproductive concerns	3 (60)	Recent surgical history	1 (20)	HTLV-1 status
5 (100)	Histology	2 (40)	Ann Arbor stage	1 (20)	Minimum life expectancy
5 (100)	History of other malignancies	2 (40)	Coagulopathy	1 (20)	Organ transplant history
5 (100)	Imaging	2 (40)	HBV status	1 (20)	Patient compliance
5 (100)	Platelet count (platelets/μL)	2 (40)	HCV status	1 (20)	Pulmonary function
5 (100)	Prior DLBCL treatment	2 (40)	Hemoglobin (g/dL)	1 (20)	Sex
5 (100)	Renal function	2 (40)	Hypersensitivity to study drugs	1 (20)	Substance use
5 (100)	WBC count (cells/μL)	2 (40)	Participation in other study	1 (20)	Vaccination history
4 (80)	CNS involvement by lymphoma	2 (40)	Psychiatric history		
4 (80)	Hepatic function				
4 (80)	HIV status				
4 (80)	IPI score				
4 (80)	Male reproductive concerns				
4 (80)	Other infectious disease status				
4 (80)	Other neurologic pathology				
4 (80)	Other organ dysfunction				
4 (80)	Performance status				

Abbreviations: CNS, central nervous system; DLBCL, diffuse large B-cell lymphoma; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HTLV-1, human T-lymphotropic virus 1; IPI, International Prognostic Index; PTLD, post-transplant lymphoproliferative disorder; RCT, randomized controlled trial; WBC, white blood cell

Supplemental Table 2. Criterion categories in 21 DLBCL RCTs including REMoDL-B and GOYA

Number of studies with criterion category n (%)	Common criterion categories (present in > 66% of RCTs; n = 18 categories)	Number of studies with criterion category n (%)	Moderately Common criterion categories (present in 33%–66% of RCTs; n = 13 categories)	Number of studies with criterion category n (%)	Uncommon criterion categories (present in < 33% of RCTs; n = 25 categories)
21 (100)	Age (years)	13 (62)	HCV status	6 (29)	Sex
21 (100)	Histology	11 (52)	Hypersensitivity to study drugs	6 (29)	Patient compliance
21 (100)	History of other malignancies	11 (52)	Other infectious disease status	5 (24)	Coagulopathy
21 (100)	Prior DLBCL treatment	11 (52)	Participation in other study	5 (24)	Diabetes mellitus
21 (100)	Renal function	10 (48)	Imaging	4 (19)	Adult patient under tutelage
20 (95)	Hepatic function	10 (48)	Minimum life expectancy	4 (19)	Hemoglobin (g/dL)
20 (95)	HIV status	10 (48)	Other neurologic pathology	4 (19)	Uncontrolled hypertension
19 (90)	Cardiac function	8 (38)	History of transformed lymphoma	3 (14)	History of PTLD
18 (86)	CNS involvement by lymphoma	8 (38)	Psychiatric history	3 (14)	HTLV-1 status
18 (86)	Performance status	7 (33)	Contraindicated therapies	3 (14)	Organ transplant history
16 (76)	Contraindications to study therapy	7 (33)	Male reproductive concerns	2 (10)	Bone marrow infiltration
16 (76)	Female reproductive concerns	7 (33)	Pulmonary function	2 (10)	Gastrointestinal function
16 (76)	HBV status	7 (33)	Recent surgical history	2 (10)	Vaccination history
16 (76)	IPI score			1 (5)	CGA score
16 (76)	Other organ dysfunction			1 (5)	Corticosteroid use
16 (76)	Platelet count (platelets/μL)			1 (5)	Green tea consumption
16 (76)	WBC count (cells/μL)			1 (5)	History of multifocal leukoencephalopathy
14 (67)	Ann Arbor stage			1 (5)	LDH level
				1 (5)	Orthopedic history
				1 (5)	Physical exam findings
				1 (5)	Prior treatment with rituximab
				1 (5)	Recent monoclonal antibody treatment
				1 (5)	Rheumatologic disease
				1 (5)	Substance use
				1 (5)	Tumor invasion of major blood vessels

Abbreviations: CGA, Comprehensive Geriatric Assessment; CNS, central nervous system; DLBCL, diffuse large B-cell lymphoma; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HTLV-1, human T-lymphotropic virus 1; IPI, International Prognostic Index; LDH, lactate dehydrogenase; PTLD, post-transplant lymphoproliferative disorder; RCT, randomized controlled trial; WBC, white blood cell



Supplemental Figure 1. Criterion category selection process for eligibility criterion categories included in a Delphi-method survey aimed at developing consensus recommendations for essential and unnecessary eligibility criteria in first-line DLBCL RCTs.

DLBCL Eligibility Criteria - Delphi Questionnaire Round 1

Andrew Harkins, MD/MSCR Candidate
Christopher Flowers, MD, MS, FASCO
Emory University School of Medicine

Thank you for participating in a Delphi questionnaire conducted to modernize enrollment criteria for first-line clinical trials comparing R-CHOP with novel precision treatment in DLBCL.

* Required

1. Your name *

   Responses will be anonymized with respect to other Delphi questionnaire respondents. Names are requested for record-keeping only.

2. Today's date *

   Example: January 7, 2019

3. Number of years' experience as a hematologist/oncologist *

Round 1

Please assess the following eligibility criteria according to your estimation of their importance for use in future first-line DLBCL clinical trials comparing R-CHOP with novel precision treatment.
Scale: 1–9
1 = criterion is unnecessary for use in future DLBCL clinical trials
5 = uncertain whether criterion should be included in future DLBCL clinical trials
9 = criterion is essential for use in future DLBCL clinical trials

Please use the comments section provided for each criterion to explain your ranking choice. Comments are not required.

There will be an opportunity at the end of the survey to add any criteria not currently included that you feel should be considered by the group.

Thank you!

Demographic, clinical, and laboratory characteristics

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential;
A comments section is located beneath the Likert scale for each criterion. Comments are not required.

4. Criterion: Age *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

5. Criterion: Age

Explanation, elaboration, and/or context for ranking choice:

6. Criterion: Performance status *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

7. Criterion: Performance status

Explanation, elaboration, and/or context for ranking choice:

8. Criterion: Minimum life expectancy *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

9. Criterion: Minimum life expectancy

Explanation, elaboration, and/or context for ranking choice:

10. Criterion: Measurable disease on imaging *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

11. Criterion: Measurable disease on imaging

Explanation, elaboration, and/or context for ranking choice:

12. Criterion: IPI score *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

13. Criterion: IPI score

Explanation, elaboration, and/or context for ranking choice:

14. Criterion: Lymphoma stage *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

15. Criterion: Lymphoma stage

Explanation, elaboration, and/or context for ranking choice:

16. Criterion: Assessment of cardiac function *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

17. Criterion: Assessment of cardiac function

Explanation, elaboration, and/or context for ranking choice:

18. Criterion: Assessment of hepatic function *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

19. Criterion: Assessment of hepatic function

Explanation, elaboration, and/or context for ranking choice:

20. Criterion: Assessment of renal function *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

21. Criterion: Assessment of renal function

Explanation, elaboration, and/or context for ranking choice:

22. Criterion: CNS involvement by lymphoma *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

23. Criterion: CNS involvement by lymphoma

Explanation, elaboration, and/or context for ranking choice:

24. Criterion: Platelet count *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

25. Criterion: Platelet count

Explanation, elaboration, and/or context for ranking choice:

26. Criterion: White blood cell count *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

27. Criterion: White blood cell count

Explanation, elaboration, and/or context for ranking choice:

28. Criterion: CD20 positivity *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

29. Criterion: CD20 positivity

Explanation, elaboration, and/or context for ranking choice:

30. Criterion: Cell-of-origin subtype *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

31. Criterion: Cell-of-origin subtype

Explanation, elaboration, and/or context for ranking choice:

32. Criterion: Central pathology review prior to enrollment *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

33. Criterion: Central pathology review prior to enrollment

Explanation, elaboration, and/or context for ranking choice:

Cancer history

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential;
A comments section is located beneath the Likert scale for each criterion. Comments are not required.

34. Criterion: Prior DLBCL treatment *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

35. Criterion: Prior DLBCL treatment

Explanation, elaboration, and/or context for ranking choice:

36. Criterion: History of transformed lymphoma *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

37. Criterion: History of transformed lymphoma

Explanation, elaboration, and/or context for ranking choice:

38. Criterion: History of other malignancies *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

39. Criterion: History of other malignancies

Explanation, elaboration, and/or context for ranking choice:

40. Criterion: Participation in other study or treatment with other investigational drug *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

41. Criterion: Participation in other study or treatment with other investigational drug

Explanation, elaboration, and/or context for ranking choice:

Non-cancer medical history

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential;
A comments section is located beneath the Likert scale for each criterion. Comments are not required.

42. Criterion: History of stroke or intracranial hemorrhage *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

43. Criterion: History of stroke or intracranial hemorrhage

Explanation, elaboration, and/or context for ranking choice:

44. Criterion: Peripheral neuropathy *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

45. Criterion: Peripheral neuropathy

Explanation, elaboration, and/or context for ranking choice:

46. Criterion: Psychiatric illness *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

47. Criterion: Psychiatric illness

Explanation, elaboration, and/or context for ranking choice:

48. Criterion: Presence of other significant, uncontrolled, concomitant disease at investigator's discretion *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

49. Criterion: Presence of other significant, uncontrolled, concomitant disease at investigator's discretion

Explanation, elaboration, and/or context for ranking choice:

Infectious disease status

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential;
A comments section is located beneath the Likert scale for each criterion. Comments are not required.

50. Criterion: HBV status *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

51. Criterion: HBV status

Explanation, elaboration, and/or context for ranking choice:

52. Criterion: HCV status *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

53. Criterion: HCV status

Explanation, elaboration, and/or context for ranking choice:

54. Criterion: HIV status *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

55. Criterion: HIV status

Explanation, elaboration, and/or context for ranking choice:

56. Criterion: Active infection requiring systemic therapy *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

57. Criterion: Active infection requiring systemic therapy

Explanation, elaboration, and/or context for ranking choice:

Reproductive health

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential;
A comments section is located beneath the Likert scale for each criterion. Comments are not required.

58. Criterion: Female participants: effective contraception or abstinence from heterosexual intercourse if of childbearing potential *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

59. Criterion: Female participants: effective contraception or abstinence from heterosexual intercourse if of childbearing potential

Explanation, elaboration, and/or context for ranking choice:

60. Criterion: Female participants: pregnancy status *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

61. Criterion: Female participants: pregnancy status

Explanation, elaboration, and/or context for ranking choice:

62. Criterion: Female participants: breastfeeding status *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

63. Criterion: Female participants: breastfeeding status

Explanation, elaboration, and/or context for ranking choice:

64. Criterion: Male participants: effective contraception or abstinence from heterosexual intercourse *

Importance for use as an inclusion or exclusion criterion in future DLBCL clinical trials:

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

65. Criterion: Male participants: effective contraception or abstinence from heterosexual intercourse

Explanation, elaboration, and/or context for ranking choice:

Additional criteria (optional)

Please use this section to add any criteria not currently included that you feel should be considered by the group.
Additions are not required.

For any added criteria, please include your estimation of the importance of this criterion according to th 1–9 scale (1 = unnecessary, 5 = uncertain, 9 = essential) as well as an optional explanation for inclusion of this criterion.

66. Additional criteria

Thank you!

This completes the survey for Round 1.

When all participants have completed a survey for Round 1, each respondent will receive a personalized summary of Round 1 results including median values, personal responses, and anonymized sample comments from participants for each criterion.

Each respondent will then receive an invitation to participate in Round 2.

Thank you again for your time!

DLBCL Eligibility Criteria - Delphi Questionnaire Round 2 (Final Round)

Andrew Harkins, MD/MSCR Candidate
Christopher Flowers, MD, MS, FASCO
Emory University School of Medicine

Thank you again for participating in a Delphi questionnaire conducted to modernize enrollment criteria for first-line clinical trials comparing R-CHOP with novel precision treatment in DLBCL.

* Required

1. Your name *

Responses will be anonymized with respect to other Delphi questionnaire respondents. Names are requested for record-keeping only.

2. Today's date *

Example: January 7, 2019

Round 2

Round 2 will revisit criterion categories that were classified as Unresolved or showed Disagreement in Round 1. In-depth results from Round 1 are located in the personalized summaries of the Round 1 survey.

In addition, the Round 2 survey requests recommendations for numerical ranges for quantitative criterion categories that were designated as Consensus Essential, Unresolved, or showed Disagreement in Round 1.

Demographic, clinical, and laboratory characteristics

Please assess the following eligibility criteria according to your estimation of their importance for use in future first-line DLBCL clinical trials comparing R-CHOP with novel precision treatment.

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential

Round 1 median and IQR values are provided for each criterion.

Please use the comments section provided for each criterion to explain your ranking choice.
Comments are not required.

3. Criterion: Performance status - Unresolved *

Round 1 result: median = 6, IQR = 2

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

4. Criterion: Performance status

Explanation, elaboration, and/or context for ranking choice:

5. Criterion: Measurable disease on imaging - Disagreement *

Round 1 result: median = 5, IQR = 5

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

6. Criterion: Measurable disease on imaging

Explanation, elaboration, and/or context for ranking choice:

7. Criterion: Assessment of cardiac function - Unresolved *

Round 1 result: median = 6, IQR = 3

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

8. Criterion: Assessment of cardiac function

Explanation, elaboration, and/or context for ranking choice:

9. Criterion: Platelet count - Unresolved *

Round 1 result: median = 5, IQR = 3

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

10. Criterion: Platelet count

Explanation, elaboration, and/or context for ranking choice:

11. Criterion: White blood cell count - Unresolved *

Round 1 result: median = 5, IQR = 4

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

12. Criterion: White blood cell count

Explanation, elaboration, and/or context for ranking choice:

13. Criterion: Cell-of-origin subtype - Unresolved *

Round 1 result: median = 4, IQR = 4

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

14. Criterion: Cell-of-origin subtype

Explanation, elaboration, and/or context for ranking choice:

Cancer history

Please assess the following eligibility criteria according to your estimation of their importance for use in future first-line DLBCL clinical trials comparing R-CHOP with novel precision treatment.

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential

Round 1 median and IQR values are provided for each criterion.

Please use the comments section provided for each criterion to explain your ranking choice. Comments are not required.

15. Criterion: Prior DLBCL treatment - Unresolved *

Round 1 result: median = 6, IQR = 3

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

16. Criterion: Prior DLBCL treatment

Explanation, elaboration, and/or context for ranking choice:

17. Criterion: History of transformed lymphoma - Disagreement *

Round 1 result: median = 5, IQR = 5

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

18. Criterion: History of transformed lymphoma

Explanation, elaboration, and/or context for ranking choice:

Non-cancer medical history

Please assess the following eligibility criteria according to your estimation of their importance for use in future first-line DLBCL clinical trials comparing R-CHOP with novel precision treatment.

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential

Round 1 median and IQR values are provided for each criterion.

Please use the comments section provided for each criterion to explain your ranking choice. Comments are not required.

19. Criterion: Peripheral neuropathy - Unresolved *

Round 1 result: median = 4, IQR = 2

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

20. Criterion: Peripheral neuropathy

Explanation, elaboration, and/or context for ranking choice:

Infectious disease status

Please assess the following eligibility criteria according to your estimation of their importance for use i future first-line DLBCL clinical trials comparing R-CHOP with novel precision treatment.

Scale: 1 = unnecessary, 5 = uncertain, 9 = essential

Round 1 median and IQR values are provided for each criterion.

Please use the comments section provided for each criterion to explain your ranking choice. Comments are not required.

21. Criterion: Active infection requiring systemic therapy - Unresolved *

Round 1 result: median = 5, IQR = 4

Mark only one oval.

	1	2	3	4	5	6	7	8	9	
Unnecessary	◯	◯	◯	◯	◯	◯	◯	◯	◯	Essential

22. Criterion: Active infection requiring systemic therapy

Explanation, elaboration, and/or context for ranking choice:

Numerical ranges for quantitative criteria

In this section, please provide recommended numerical ranges for quantitative criterion categories for use in future first-line DLBCL clinical trials comparing R-CHOP with novel precision treatment.

Only quantitative criteria that were designated Consensus Essential, Unresolved, or showed Disagreement in Round 1 are included in this section.

When multiple choice options are provided, available options reflect ranges included in prior first-line DLBCL RCTs.

A comments section is included beneath each requested numerical range. Please use the comments section to provide context for your submitted response.

23. Criterion: Stage - Consensus Essential *

Please select all stages recommended for inclusion in future first-line trials for DLBCL; multiple responses allowed.

Check all that apply.

- [ ] I
- [ ] II
- [ ] III
- [ ] IV
- [ ] Stage should not be an eligibility criterion
- [ ] Uncertain/prefer not to answer

24. Criterion: Stage

Explanation, elaboration, and/or context for numerical range:

25. Criterion: Renal function - Consensus Essential *

Please select recommended eligibility criteria (available options based on ranges from prior trials); multiple responses allowed.

Check all that apply.

- [ ] Cr < 1.5 mg/dL
- [ ] Cr ≤ 1.7 mg/dL
- [ ] Cr ≤ 2.0 mg/dL
- [ ] Cr < 2.5 mg/dL
- [ ] Cr ≤ 2x ULN
- [ ] CrCl ≥ 60 mL/min
- [ ] CrCl ≥ 40 mL/min
- [ ] CrCl ≥ 30 mL/min
- [ ] CrCl ≥ 20 mL/min
- [ ] ...unless levels attributable to lymphoma
- [ ] No contraindicating renal dysfunction per investigator's discretion
- [ ] Renal function should not be an eligibility criterion
- [ ] Prefer an alternate range that is not included in the available options (please explain in comments section)
- [ ] Uncertain/prefer not to answer

26. Criterion: Renal function

Explanation, elaboration, and/or context for numerical range:

27. Criterion: Hepatic function - Consensus Essential *

Please select recommended eligibility criteria (available options based on ranges from prior trials); multiple responses allowed.

Check all that apply.

- [ ] Total bilirubin ≤ 1.75 mg/dL
- [ ] Total bilirubin ≤ 2.0 mg/dL
- [ ] Total bilirubin ≤ 3 mg/dL
- [ ] Total bilirubin ≤ 1.5x ULN
- [ ] Total bilirubin ≤ 2x ULN
- [ ] Transaminases < 2x ULN
- [ ] Transaminases ≤ 2.5x ULN
- [ ] Transaminases ≤ 3x ULN
- [ ] Alkaline phosphatase < 2x ULN
- [ ] Alkaline phosphatase ≤ 3x ULN
- [ ] ...unless levels attributable to lymphoma
- [ ] No contraindicating hepatic dysfunction per investigator's discretion
- [ ] Hepatic function should not be an eligibility criterion
- [ ] Prefer an alternate range that is not included in the available options (please explain in comments section)
- [ ] Uncertain/prefer not to answer

28. Criterion: Hepatic function

Explanation, elaboration, and/or context for numerical range:

29. Criterion: IPI - Consensus Essential *

Please select all IPI scores recommended for inclusion in future first-line trials for DLBCL; multiple responses allowed.

Check all that apply.

- [ ] 0
- [ ] 1
- [ ] 2
- [ ] 3
- [ ] 4
- [ ] 5
- [ ] IPI should not be an eligibility criterion
- [ ] Uncertain/prefer not to answer

30. Criterion: IPI

Explanation, elaboration, and/or context for numerical range:

31. Criterion: Age - Consensus Essential *

Please type recommended age range for use in future first-line DLBCL clinical trials comparing R-CHOP with novel precision treatment:

32. Criterion: Age

Explanation, elaboration, and/or context for numerical range:

33. Criterion: Performance status - Unresolved *

Please select all ECOG performance status levels recommended for inclusion in future first-line trials for DLBCL; multipl responses allowed.

Check all that apply.

- [ ] 0
- [ ] 1
- [ ] 2
- [ ] 3
- [ ] 4
- [ ] 5
- [ ] Performance status should not be an eligibility criterion
- [ ] Uncertain/prefer not to answer

34. Criterion: Performance status

Explanation, elaboration, and/or context for numerical range:

35. Criterion: Cardiac function - Unresolved *

Please select recommended eligibility criteria (available options based on ranges from prior trials); multiple responses allowed.

Check all that apply.

- [ ] No cardiac contraindication to an anthracycline
- [ ] No active heart disease in the past three months
- [ ] EF ≥ 45%
- [ ] EF ≥ 50%
- [ ] No non-compensated heart failure
- [ ] No heart failure with New York Heart Association classification > 2
- [ ] No unstable angina
- [ ] No angina with Canadian Cardiovascular Society grade > 2
- [ ] No dilated cardiomyopathy
- [ ] No unstable coronary artery disease
- [ ] No coronary artery disease with ST depression
- [ ] No recent MI (past 3 months)
- [ ] No recent MI (past 6 months)
- [ ] No clinically significant arrhythmia
- [ ] No contraindicating cardiac dysfunction per investigator's discretion
- [ ] Cardiac function should not be an eligibility criterion
- [ ] Prefer an alternate range that is not included in the available options (please explain in comments section)
- [ ] Uncertain/prefer not to answer

36. Criterion: Cardiac function

Explanation, elaboration, and/or context for numerical range:

37. Criterion: Platelet count - Unresolved *

Please select recommended eligibility criteria (available options based on ranges from prior trials); multiple responses allowed.

Check all that apply.

- [ ] ≥ 70,000 platelets/μL
- [ ] ≥ 75,000 platelets/μL
- [ ] ≥ 100,000 platelets/μL
- [ ] ...unless levels attributable to spleen involvement by DLBCL
- [ ] ...unless levels attributable to bone marrow infiltration
- [ ] ≥ 50,000 platelets/μL if bone marrow involvement
- [ ] Platelent count should not be an eligibility criterion
- [ ] Prefer an alternate range that is not included in the available options (please explain in comments section)
- [ ] Uncertain/prefer not to answer

38. Criterion: Platelet count

Explanation, elaboration, and/or context for numerical range:

39. Criterion: White blood cell count - Unresolved *

Please select recommended eligibility criteria (available options based on ranges from prior trials); multiple responses allowed.

Check all that apply.

- [ ] ANC ≥ 1,000 cells/μL
- [ ] ANC ≥ 1,500 cells/μL
- [ ] Granulocytes ≥ 1,500 cells/μL
- [ ] WBC ≥ 3,000 cells/μL
- [ ] ...unless levels attributable to spleen involvement by DLBCL
- [ ] ...unless levels attributable to bone marrow infiltration
- [ ] ANC ≥ 1,000 cells/μL if bone marrow involvement
- [ ] Leukocyte count should not be an eligibility criterion
- [ ] Prefer an alternate range that is not included in the available options (please explain in comments section)
- [ ] Uncertain/prefer not to answer

40. Criterion: White blood cell count

Explanation, elaboration, and/or context for numerical range:

41. Criterion: Measurable disease on imaging - Disagreement *

Please type recommended numerical range for use in future first-line DLBCL clinical trials comparing R-CHOP with nove precision treatment:

42. Criterion: Measurable disease on imaging

Explanation, elaboration, and/or context for numerical range:

Thank you!

This completes the survey for Round 2

Thank you again for your time!

DLBCL Eligibility Criteria - Preliminary Recommendations after Delphi-Method Survey

Andrew Harkins, MD, MS
Emory University School of Medicine

Christopher Flowers, MD, MS, FASCO
MD Anderson Cancer Center

Thank you again for participating in a questionnaire conducted to modernize enrollment criteria for first-lin clinical trials comparing R-CHOP with novel precision treatment in DLBCL.

The survey group has completed 2 out of 2 planned rounds for the Delphi-method survey. We have compiled preliminary recommendations for eligibility criteria based on quantitative and qualitative survey results.

The present questionnaire will ask survey respondents whether they agree or disagree with each preliminary recommendation.

Thank you in advance for your time in completing the present survey.

* Required

1. Your name *

Responses will be anonymized with respect to other survey respondents. Names are requested for record-keeping only.

2. Today's date *

Example: January 7, 2019

Regarding preliminary recommendations

Preliminary recommendations for each criterion include: 1) whether a criterion should be included in future eligibility criteria, and 2) the specific language, ranges, and parameters for any enrollment criteria that the survey group determined should be included in future studies.

The survey will ask participants whether they agree or disagree with each preliminary recommendation.

In addition, the current survey provides a comments section for each recommendation. Pleas use this space to provide context for your selection. When you do not agree with the preliminary recommendation for a given criterion, please suggest alternate recommendations in the comments section. Comments are not required.

Demographic, clinical, and laboratory characteristics

Preliminary recommendations are provided for each criterion based on prior survey results. Please provide a "yes/no" response regarding whether you agree with the preliminary recommendation for a given criterion.

Please use the comments section provided for each criterion to provide context for your selection. When you do not agree with the preliminary recommendation, please suggest alternate recommendations in the comments section. Comments are not required.

Criterion: Age

At baseline, patients with ages ≥ 18 years eligible for trial participation.

Determine final age range based on study intervention and target population, though studies investigating R-CHOP versus R-CHOP-X likely do not require additional age cutoffs beyond ages ≥ 18 years.

3. Criterion: Age *

Do you agree with the above recommendation?

Mark only one oval.

- ◯ Yes
- ◯ No

4. Criterion: Age

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Performance status

Include patients with PS of ECOG 0–2 and ECOG 3 if poor PS due to lymphoma.

5. Criterion: Performance status *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

6. Criterion: Performance status

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Minimum life expectancy

Do not include minimum life expectancy as an eligibility criterion.

7. Criterion: Minimum life expectancy *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

8. Criterion: Minimum life expectancy

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Measurable disease on imaging

If primary endpoint in trial is treatment response,
then patients with measurable disease on imaging ≥ 1.5 cm
in ≥ 1 diameter are eligible for enrollment.

Otherwise, do not include measurable disease on imaging as
an eligibility criterion. Any evidence of disease is sufficient for enrollment.

9. Criterion: Measurable disease on imaging *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

10. Criterion: Measurable disease on imaging

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: IPI

Recommend inclusion of IPI as an eligibility criterion.

No single IPI range recommended—determine range based on target population for a given study.

Alternately, consider using discrete elements of IPI as eligibility criteria rather than total IPI value.

11. Criterion: IPI *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

12. Criterion: IPI

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Stage

Ann Arbor stage II–IV required for enrollment.

13. Criterion: Stage *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

14. Criterion: Stage

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Cardiac function

Determine whether to include assessment of cardiac function as an eligibility criterion based on toxicity profile of study drugs.

If study includes an anthracycline, include assessment of cardiac function as an eligibility criterion using the following criteria:

- *No cardiac contraindication to an anthracycline*
- *No non-compensated heart failure*
- *No active heart disease in the past six months*
- *EF ≥ 45%*

15. Criterion: Cardiac function *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

16. Criterion: Cardiac function

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Hepatic function

Exclude patients based on selected threshold values for hepatic function unless hepatic dysfunction is attributable to lymphoma or Gilbert's syndrome.

Selection of threshold values should take into account specific therapies in trial.

Select thresholds from the following ranges based on the toxicity profile of study drugs:

- *Total bilirubin ≤ 1.5–2x ULN*
- *Total bilirubin ≤ 2–3 mg/dL*
- *Transaminases ≤ 2.5–5x ULN*
- *Alkaline phosphatase ≤ 3x ULN*

17. Criterion: Hepatic function *

Do you agree with the above recommendation?

Mark only one oval.

- ◯ Yes
- ◯ No

18. Criterion: Hepatic function

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Renal function

Exclude patients based on a selected threshold value for renal function unless renal dysfunction is attributable to lymphoma.

Selection of threshold value should take into account specific therapies in trial.

Allow for use of both a Cr threshold and a CrCl threshold from the following ranges:

- *Cr ≤ 1.5–2.0 mg/dL*
- *Cr ≤ 1.5–2.0x ULN*
- *CrCl ≥ 30 mL/min*

Consider a more liberal threshold value for older participants.

19. Criterion: Renal function *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

20. Criterion: Renal function

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: CNS involvement

No CNS involvement by lymphoma in frontline trials for R-CHOP versus R-CHOP-X.

21. Criterion: CNS involvement *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

22. Criterion: CNS involvement

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Platelet count

Patients with platelet count ≥ 75,000 platelets/μL are eligible for enrollment unless levels attributable to bone marrow infiltration or spleen involvement by DLBCL. If study drug is known to cause thrombocytopenia, consider higher threshold value.

If low platelets are due to lymphoma, patients with platelet count ≥ 50,000 platelets/μL are eligible for enrollment. If study drug is known to cause thrombocytopenia, consider higher threshold value.

23. Criterion: Platelet count *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

24. Criterion: Platelet count

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: White blood cell count

Patients with ANC ≥ 1,000 cells/μL are eligible for enrollment.
Exclude patients with ANC < 1,000 cells/μL unless low levels attributable to bone marrow infiltration or spleen involvement by DLBCL.

25. Criterion: White blood cell count *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

26. Criterion: White blood cell count

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: CD20 positivity

Assessment of CD20 positivity is standard for diagnosis but should not be included as an eligibility criterion for enrollment in first-line clinical trials unless the investigational drug requires CD20 positivity to be efficacious.

27. Criterion: CD20 positivity *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

28. Criterion: CD20 positivity

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Cell-of-origin subtype

Include COO subtype as an eligibility criterion if study is designed to target COO subtype using the investigational drug in question.

Otherwise, do not include COO subtype as an eligibility criterion.

29. Criterion: Cell-of-origin subtype *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

30. Criterion: Cell-of-origin subtype

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Central pathology review prior to enrollment

Do not include central pathology review prior to enrollment as an eligibility criterion.

31. Criterion: Central pathology review prior to enrollment *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

32. Criterion: Central pathology review prior to enrollment

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Cancer history

Preliminary recommendations are provided for each criterion based on prior survey results. Please provide a "yes/no" response regarding whether you agree with the preliminary recommendation for a given criterion.

Please use the comments section provided for each criterion to provide context for your selection. When yo do not agree with the preliminary recommendation, please suggest alternate recommendations in the comments section. Comments are not required.

Criterion: Prior DLBCL treatment

No prior DLBCL treatment except corticosteroids or one cycle of chemotherapy at investigator's discretion.

33. Criterion: Prior DLBCL treatment *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

34. Criterion: Prior DLBCL treatment

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: History of transformed lymphoma

No history of treated, indolent lymphoma.

Composite lymphoma does not preclude enrollment.

35. Criterion: History of transformed lymphoma *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

36. Criterion: History of transformed lymphoma

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: History of other malignancies

No other currently active malignancy, other malignancy requiring treatment that would preclude administration of study drugs, or other malignancy likely to be fatal during the trial evaluation window.

Otherwise, do not include history of other malignancies as an eligibility criterion.

37. Criterion: History of other malignancies *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

38. Criterion: History of other malignancies

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Participation in other study or treatment with other investigational drug

No concurrent treatment with any other investigational therapy.
No treatment within the last 30 days with any other investigational therapy.
Participation in nontherapeutic studies (e.g., subject registries) is permitted.

39. Criterion: Participation in other study or treatment with other investigational drug *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

40. Criterion: Participation in other study or treatment with other investigational drug

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Non-cancer medical history

Preliminary recommendations are provided for each criterion based on prior survey results. Please provide a "yes/no" response regarding whether you agree with the preliminary recommendation for a given criterion

Please use the comments section provided for each criterion to provide context for your selection. When you do not agree with the preliminary recommendation, please suggest alternate recommendations in the comments section. Comments are not required.

Criterion: History of stroke or intracranial hemorrhage

Do not include history of stroke or intracranial hemorrhage as an eligibility criterion unless experimental drug is known to increase risk for future CVA.

If experimental drug is known to increase risk for future CVA, no history of stroke or intracranial hemorrhage in the past six months.

41. Criterion: History of stroke or intracranial hemorrhage *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

42. Criterion: History of stroke or intracranial hemorrhage

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Peripheral neuropathy

If experimental drug is known to cause neuropathy, then exclude patients with neuropathy using a severity threshold based on the experimental drug's known toxicity profile.

Otherwise, exclude only patients with severe neuropathy, and include instructions for vincristine dose adjustment for patients with mild and moderate underlying peripheral neuropathy.

43. Criterion: Peripheral neuropathy *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

44. Criterion: Peripheral neuropathy

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Psychiatric illness

Do not include psychiatric illness as an eligibility criterion.

Inability to comply with study protocols, demonstrate decision-making capacity, or participate in informed consent precludes study enrollment, regardless of underlying reason (psychiatric illness or otherwise).

45. Criterion: Psychiatric illness *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

46. Criterion: Psychiatric illness

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Presence of other significant, uncontrolled, concomitant disease at investigator's discretion

No other significant, uncontrolled, concomitant disease at investigator's discretion.

47. Criterion: Presence of other significant, uncontrolled, concomitant disease at investigator's discretion *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

48. Criterion: Presence of other significant, uncontrolled, concomitant disease at investigator's discretion

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Infectious disease status

Preliminary recommendations are provided for each criterion based on prior survey results. Please provide a "yes/no" response regarding whether you agree with the preliminary recommendation for a given criterion.

Please use the comments section provided for each criterion to provide context for your selection. Wher you do not agree with the preliminary recommendation, please suggest alternate recommendations in the comments section. Comments are not required.

Criterion: HBV status

Do not include HBV status as an eligibility criterion.

49. Criterion: HBV status *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

50. Criterion: HBV status

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: HCV status

Do not include HCV status as an eligibility criterion.

51. Criterion: HCV status *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

52. Criterion: HCV status

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: HIV status

Do not include HIV status as an eligibility criterion.

53. Criterion: HIV status *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

54. Criterion: HIV status

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Active infection requiring systemic therapy

No serious, active infection at investigator's discretion.

If patient with active infection is enrolled, resolution of infection at investigator's discretion is required prior to initiation of study therapy.

55. Criterion: Active infection requiring systemic therapy *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

56. Criterion: Active infection requiring systemic therapy

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Reproductive health

Preliminary recommendations are provided for each criterion based on prior survey results. Please provide a "yes/no" response regarding whether you agree with the preliminary recommendation for a given criterion.

Please use the comments section provided for each criterion to provide context for your selection. When you do not agree with the preliminary recommendation, please suggest alternate recommendations in the comments section. Comments are not required.

Criterion: Female: contraception or abstinence

Effective contraception or abstinence from heterosexual intercourse required if of childbearing potential.

57. Criterion: Female: contraception or abstinence *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

58. Criterion: Female: contraception or abstinence

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Pregnancy status

Pregnant women excluded from enrollment.

59. Criterion: Pregnancy status *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

60. Criterion: Pregnancy status

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Breastfeeding status

Breastfeeding prohibited during trial participation.

61. Criterion: Breastfeeding status *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

62. Criterion: Breastfeeding status

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

Criterion: Male: contraception or abstinence

Effective contraception or abstinence from heterosexual intercourse required.

63. Criterion: Male: contraception or abstinence *

Do you agree with the above recommendation?

Mark only one oval.

- Yes
- No

64. Criterion: Male: contraception or abstinence

Comments section: if desired, please provide context for your selection here; if you do not agree with the preliminary recommendation, please provide alternate recommendations here. Comments are not required.

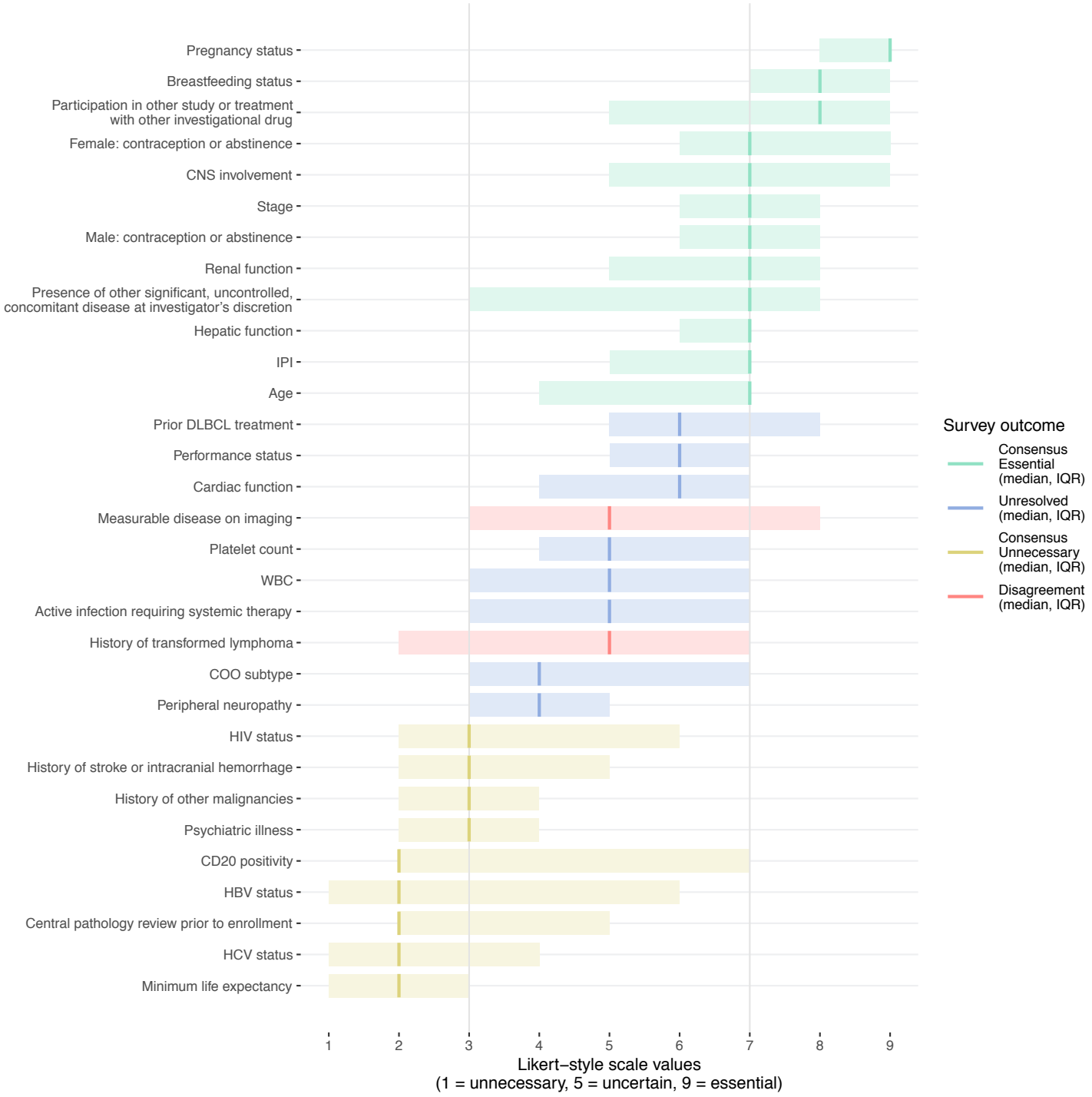
Thank you!

This completes the survey for preliminary recommendations

Thank you again for your time and participation!

DLBCL Eligibility Criteria – Delphi Questionnaire, Round 1 Results
Anonymized Summary

Anonymized summary figure:



Definitions for survey outcomes:

Outcome	Definition	n (% of 31 total criteria)
Consensus Essential	Median Likert-style scale value ≥ 7; no Disagreement	12 (39)
Unresolved	3 < median Likert-style scale value < 7; no Disagreement	8 (26)
Consensus Unnecessary	Median Likert-style scale value ≤ 3; no Disagreement	9 (29)
Disagreement	≥ 1/3 of respondents rate the criterion category ≤ 3 AND ≥ 1/3 of respondents rate the criterion category ≥ 7	2 (6)

Results

- Thank you for participating in a Delphi questionnaire conducted to modernize enrollment criteria for first-line clinical trials comparing R-CHOP with novel precision treatment in DLBCL.
- This document provides a personalized summary of Round 1 results.

Descriptive statistics of participants

- **Total number of respondents:** n = 17
- **Median number of years' experience as a hematologist/oncologist:** 17 (IQR = 12)

Results of survey: overall results

- **Consensus Essential:** n = 12 of 31 total criteria in survey (39%)

Criterion category	Median	IQR
Pregnancy status	9	1
Breastfeeding status	8	2
Participation in other study or treatment with other investigational drug	8	4
Female: contraception or abstinence	7	3
CNS involvement	7	4
Stage	7	2
Male: contraception or abstinence	7	2
Renal function	7	3
Presence of other significant, uncontrolled, concomitant disease at investigator's discretion	7	5
Hepatic function	7	1
IPI	7	2
Age	7	3

- **Unresolved:** n = 8 of 31 total criteria in survey (26%)

Criterion category	Median	IQR
Prior DLBCL treatment	6	3
Performance status	6	2
Cardiac function	6	3
Platelet count	5	3
WBC	5	4
Active infection requiring systemic therapy	5	4
COO subtype	4	4

Peripheral neuropathy	4	2

- **Consensus Unnecessary:** n = 9 of 31 total criteria in survey (29%)

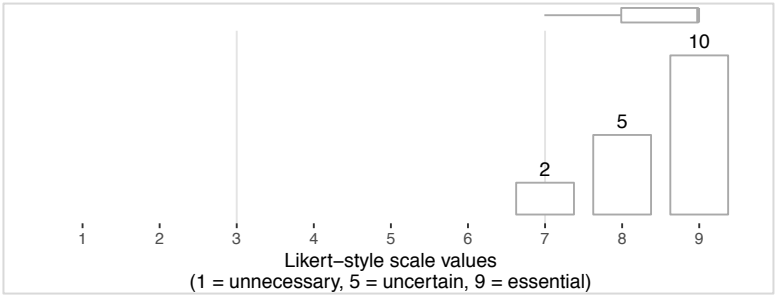
Criterion category	Median	IQR
HIV status	3	4
History of stroke or intracranial hemorrhage	3	3
History of other malignancies	3	2
Psychiatric illness	3	2
CD20 positivity	2	5
HBV status	2	5
Central pathology review prior to enrollment	2	3
HCV status	2	3
Minimum life expectancy	2	2

- **Disagreement:** n = 2 of 31 total criteria in survey (6%)

Criterion category	Median	IQR
Measurable disease on imaging	5	5
History of transformed lymphoma	5	5

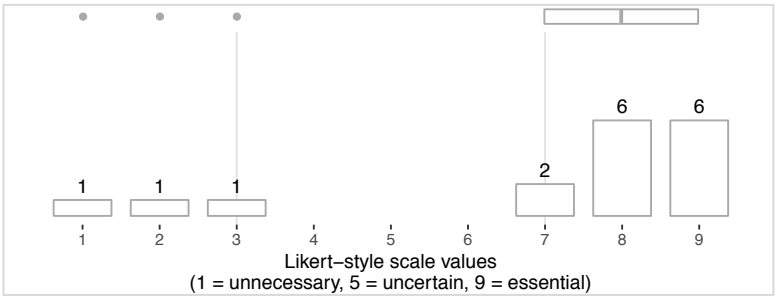
Results of survey: anonymized results by individual criterion category (ordered according to median value)

- **Pregnancy status: *Consensus Essential***



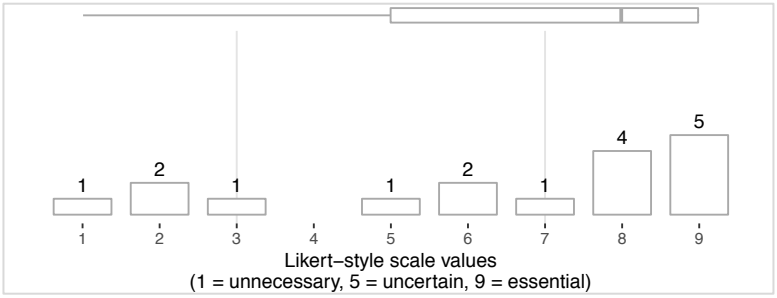
  - Median (IQR): 9 (1)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [9] *"would be better to know this in advance and avoid experimental drugs in pregnant patient who could receive chemo without experimental drugs."*
    - [7] *"Most novel agents will have pregnancy concerns/contraindications"*
    - [8] *"until fetal safety of novel agent is understood"*
    - [9] *"not to enroll"*

- **Breastfeeding status: *Consensus Essential***



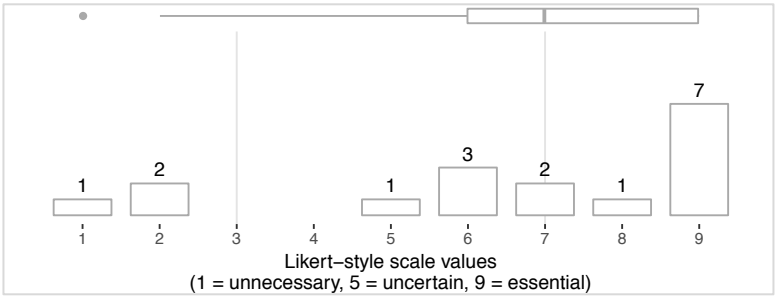
- Median (IQR): 8 (2)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [1] *"not necessary as eligibility. can simply prohibit breastfeeding during treatment if there is a concern."*
  - [7] *"Most novel agents will have pregnancy concerns/contraindications"*
  - [9] *"may not use medications given"*

- **Participation in other study or treatment with other investigational drug: *Consensus Essential***



- Median (IQR): 8 (4)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [8] *"can't be getting other anti-lymphoma treatment"*
  - [2] *"rarely an issue of confounding"*
  - [8] *"one experiment at a time"*
  - [9] *"If studying an investigational drug on the protocol. should not be exclusion for registry studies."*
  - [9] *"Active participation in a concurrent trial confounds results, prior participation after washout should not be a criterion."*
  - [1] *"not relevant as long as not therapeutic"*

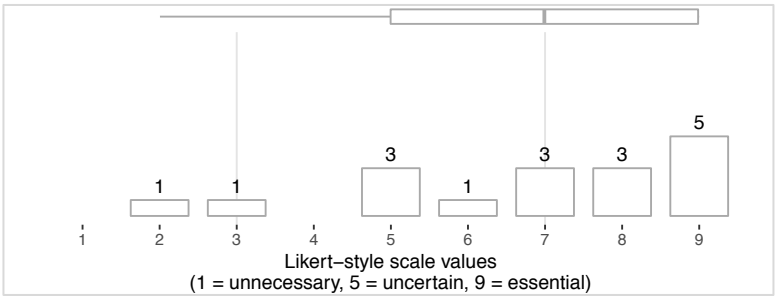
- **Female: contraception or abstinence: *Consensus Essential***



- Median (IQR): 7 (3)
- Anonymized comments from participants (format: [selected response] *"comment"*):

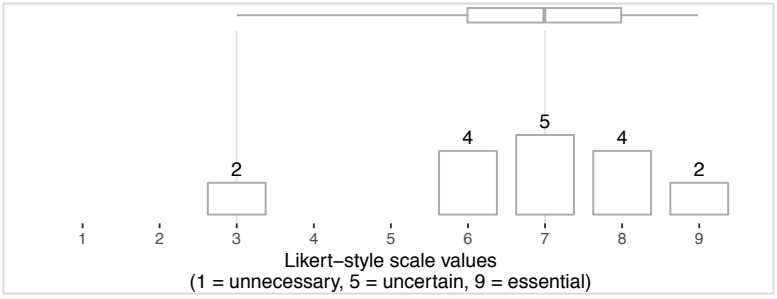
- [1] *"unnecessary as eligibility. can be required as part of trial."*
- [9] *"FDA required"*
- [7] *"During chemotherapy and beyond"*

- **CNS involvement: *Consensus Essential***



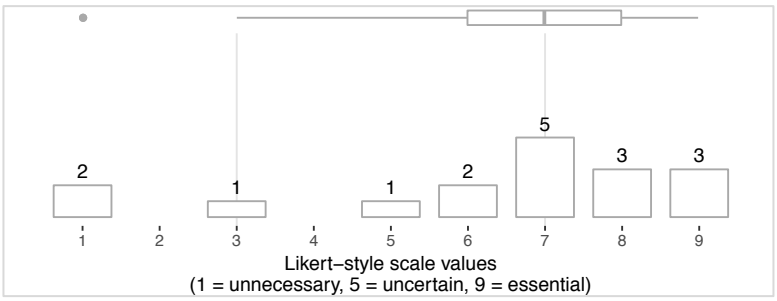
  - Median (IQR): 7 (4)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [9] *"requires completely different therapy"*
    - [8] *"Probably need to exclude such patients unless the therapy has a CNS directed component. "*
    - [7] *"to extent that regimen would be changed in CNS involved"*
    - [2] *"We should be including these patients on frontline trials"*
    - [5] *"If no symptoms or imaging concerns, it is rare to find occult involvement and many novel therapies enter the CSF."*
    - [9] *"therapy will need to be adjusted"*
    - [8] *"Should be treated differently"*

- **Stage: *Consensus Essential***



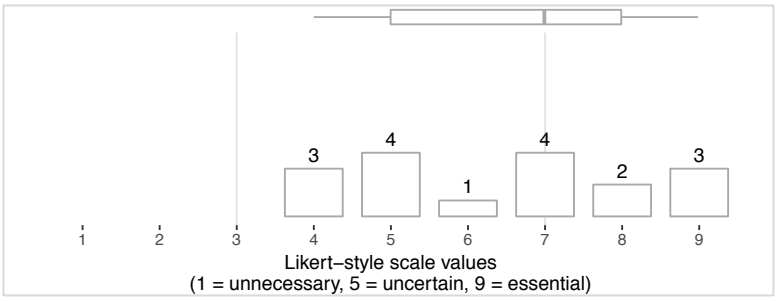
  - Median (IQR): 7 (2)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [8] *"I would consider including stage 2 along with 3 and 4 if stage 2 doesn't fit easily in one radiation port. Would probably avoid including stage 1/2 in single-arm studies."*
    - [7] *"May be reasonable to exclude stage I from certain trials."*
    - [6] *"In relation to number of cycles of therapy"*
    - [7] *"As with IPI, it is hard to find an unmet need to solve in stage I patients"*
    - [6] *"Criteria for immunochemotherapy, number of cycles"*
    - [7] *"Localized DLBCL appears to have a different biology than advanced stage."*
    - [9] *"PART of IPI"*
    - [3] *"Only as needed to calculate IPI"*

- **Male: contraception or abstinence: *Consensus Essential***



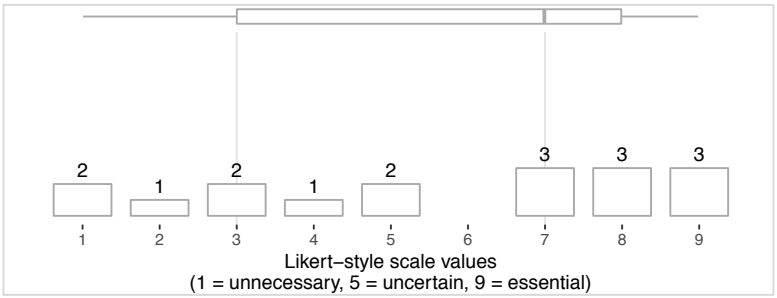
- Median (IQR): 7 (2)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [1] *"Non necessary as eligibility. Can require contraception as part of trial."*
  - [6] *"If drug is known teratogenic, then important, otherwise not."*
  - [9] *"to prevent pregnancy"*

- **Renal function: *Consensus Essential***



- Median (IQR): 7 (3)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [9] *"requires dose adjustments"*
  - [7] *"A Cr minimum is reasonable (unless elevation due to underlying lymphoma) to insure drug clearance."*
  - [4] *"depends on drugs being used"*
  - [8] *"should be more liberal for older pts and allow use of either the Cr or the CrCl."*
  - [5] *"Drug clearance"*
  - [4] *"Only to know that anthracyclines can be given"*
  - [7] *"but could rely on good standards of practice not requirements for trial entry"*

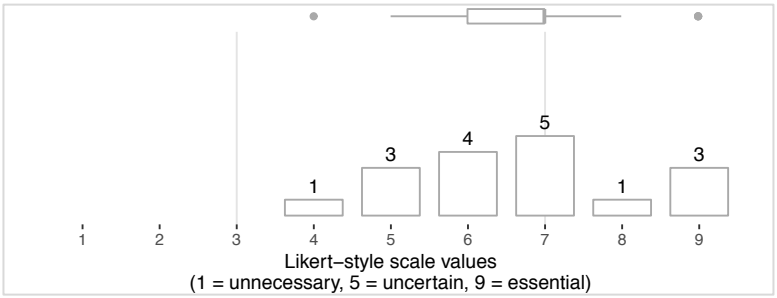
- **Presence of other significant, uncontrolled, concomitant disease at investigator's discretion: *Consensus Essential***



- Median (IQR): 7 (5)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [1] *"I like giving the investigator more discretion, but the patient clearly would't be enrolled if the investigator felt this way. it's not helpful"*

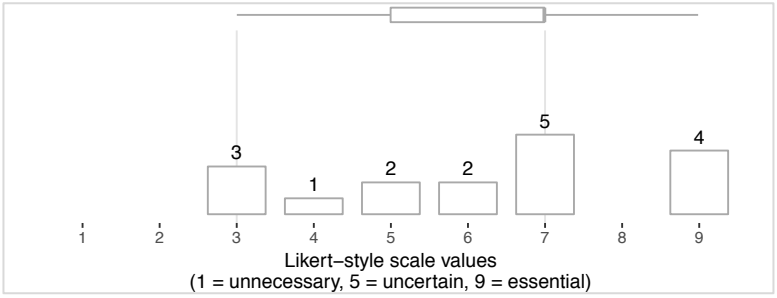
- [3] *“only exclude if R-CHOP can not be administered.”*
- [7] *“Good catch all”*
- [2] *“This is pretty much a meaningless statement.”*
- [7] *“If it has strong likelihood of limiting the ability to give the treatment on the protocol, then I can see excluding these patients.”*
- [1] *“that is what happens in real life”*
- [8] *“this can address many of the features above”*

- **Hepatic function: *Consensus Essential***



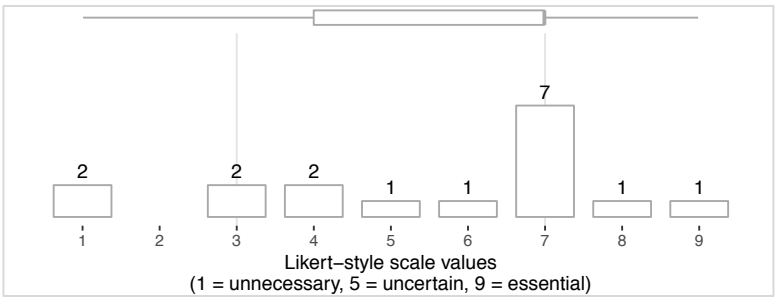
  - Median (IQR): 7 (1)
  - Anonymized comments from participants (format: [selected response] *“comment”*):
    - [9] *“Requires dose adjustments”*
    - [7] *“A bilirubin minimum is reasonable (unless elevation due to underlying lymphoma) to insure drug metabolism is ok”*
    - [6] *“in extreme in order to receive drugs in context of high bilirubin”*
    - [8] *“you can't use R-CHOP as control arm if hepatic function is inadequate”*
    - [5] *“Drug metabolism”*
    - [4] *“Only to know that anthracyclines can be given”*
    - [7] *“but could rely on good standards of practice not requirements for trial entry”*

- **IPI: *Consensus Essential***



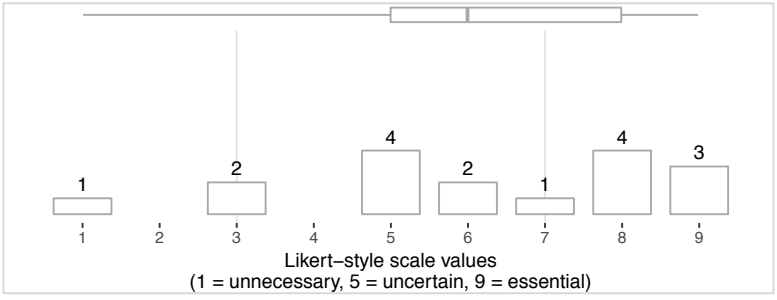
  - Median (IQR): 7 (2)
  - Anonymized comments from participants (format: [selected response] *“comment”*):
    - [4] *“In absence of biomarker this is best assessment of pre-treatment risk (i.e., need for better therapy vs. option for less therapy.)”*
    - [7] *“May be reasonable to exclude IPI 0-1 from certain trials due to low event rate.”*
    - [7] *“you won't find much benefit from any novel therapy for IPI 0 patients - they already do quite well with R-CHOP”*
    - [3] *“We can do better than IPI score”*
    - [5] *“The IPI is useful, but is obviously a surrogate for factors we aren't otherwise able to account for. As we improve our understanding of biology and therapy, the IPI will eventually be irrelevant.”*
    - [9] *“The best clinical prognostic factor”*
    - [9] *“As a stratification factor and to limit most trials to IPI >= 2; pts with IPI 0-1 do very well with standard therapy”*

- **Age: *Consensus Essential***



  - Median (IQR): 7 (3)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [6] *"age is important when targeting specific populations"*
    - [3] *"Generally not relevant, but maybe more important for trials specific to elderly patients"*
    - [7] *"Likely need a lower age limit (like 18) and an upper age limit (like 80)"*
    - [7] *"Depends on nature of intervention and tolerability. Most important at extremes (particularly very elderly)"*
    - [7] *"Depends upon the regimen; elderly patients may be appropriate for miniRCHOP questions; younger patients may be appropriate for CAR-T questions."*
    - [4] *"Not critical to exclude elderly patients, if they meet other I/E criteria."*
    - [7] *"I think there are approaches that are best suited for elderly patients and those for young patients, but many treatments of RCHOP+X do not need an upper age limit defined in the study"*
    - [4] *"you don't want to exclude per se on basis of age, but you should acknowledge that not all ages will have same risk/benefit ratio to a novel treatment #PHOENIX so you may need to stratify or at least carefully individualize the trial"*
    - [1] *"Frailty probably a better criteria for upper limit."*
    - [7] *"If trials include transplant, appropriate age ranges should be incorporated"*
    - [7] *"Age is a surrogate for ability to tolerate therapy, but it may also have implications for DLBCL subsets. However, I do not favor an arbitrary age cutoff as many elderly patients are fitter than their age suggests."*
    - [9] *"one of the best factors associated with outcome"*
    - [8] *"Prognostic factor"*
    - [3] *"Only to exclude children < 18 years"*

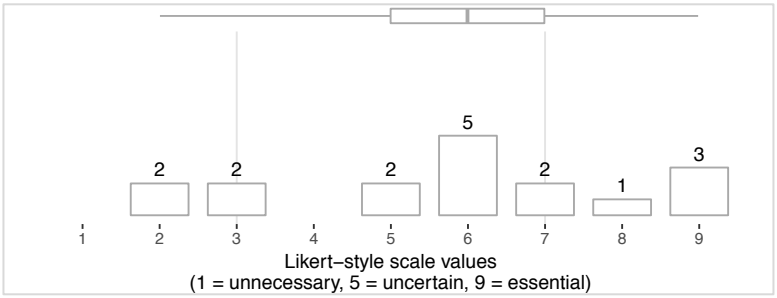
- **Prior DLBCL treatment: *Unresolved***



  - Median (IQR): 6 (3)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [5] *"Depends upon the trial.*
    - [5] *"depends on nature of intervention"*
    - [6] *"It can be very helpful to allow steroids or one cycle of chemo before enrollment, to ensure you can enroll patients who needed urgent therapy."*
    - [8] *"I may have misread - I thought this was for upfront trials comparing R-CHOP"*

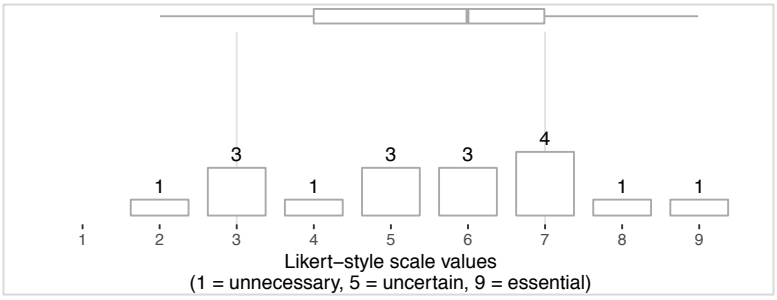
- [5] *"Depends on the prior treatment. short course of steroid or other bridge to starting chemotherapy should be allowed to discourage selection bias"*
- [3] *"If this mean number of prior lines, I don't think this is relevant for DLBCL patients as most patients either don't live to receive many lines if R/R or are serial responders."*
- [1] *"for first line should not be any"*

- **Performance status: *Unresolved***



- Median (IQR): 6 (2)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [6] *"performance status needs to be adequate"*
  - [2] *"In many instances the poor PS is due to the underlying lymphoma, which should not be exclusionary. A better way to phrase the PS eligibility would be to say "PS 0-2, unless PS 3-4 due to underlying lymphoma in which case patient is eligible"*
  - [5] *"not accurate"*
  - [8] *"ECOG 0-3"*
  - [3] *"Often performance status is limited by lymphoma or only truly observed in the context of the lymphoma by the provider, and therefore does not discriminate well"*
  - [3] *"Should never excluded pts with 0-2. 3 is "iffy" depending on treatment."*
  - *"As with age - we are probably past the point of having a novel agent fall in our lap that has similar risk/benefits across all performance statuses just as we are for all ages"*
  - [7] *"If disease related, poor PS is rapidly reversible in some patients. If comorbidity related, poor PS may compromise the evaluation of a good therapy."*
  - [9] *"part of the IPI- standard"*
  - [6] *"Only important if <2"*

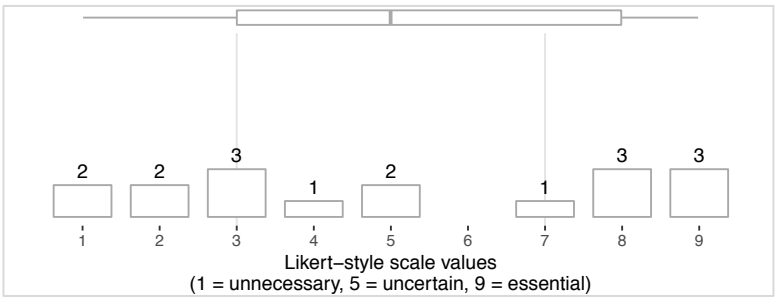
- **Cardiac function: *Unresolved***



- Median (IQR): 6 (3)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [5] *"hard to know how useful this is."*
  - [7] *"Probably need some minimum which would permit administration of anthracyclines."*
  - [6] *"anthracycline"*
  - [3] *"I think we do this way too much. This should be "as clinically indicated"."*
  - [7] *"criteria for immunochemotherapy"*
  - [7] *"Depends on the potential toxicity of the regimen"*

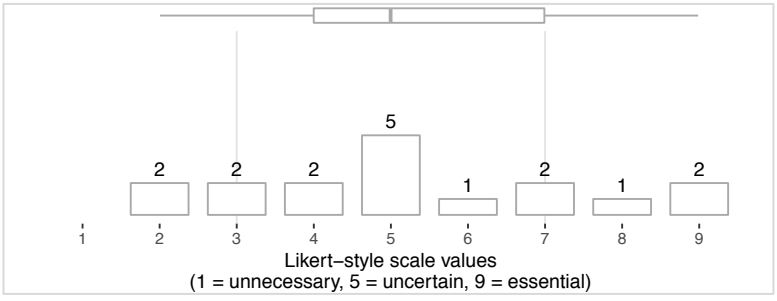
- [3] *"Unless the patient has symptomatic heart failure, testing of ejection fraction is not very useful clinically."*
- [3] *"Only to know that anthracyclines can be given"*
- [6] *"Depends on the treatment"*
- [4] *"Needed when an anthracycline is being included but could rely on good standards of practice not requirements for trial entry"*

- **Measurable disease on imaging: *Disagreement***



  - Median (IQR): 5 (5)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [1] *"with PET imaging this seems less important if there is marrow involvement for example"*
    - [2] *"CR, PFS, OS all depend on end of treatment assessment and FU, not pre-treatment assessment."*
    - [2] *"Not needed in the PET era."*
    - [3] *"Response rate not as important as PFS"*
    - [8] *"May depend somewhat on primary endpoint"*
    - [3] *"Frontline trials? Do measurements matter? Disease left after treatment and early relapse are what matters."*
    - [9] *"Without some measure of response, it is not possible to fully evaluate the effectiveness of therapy. If this could be replaced with MRD, then I would not feel strongly about measurable disease on imaging."*
    - [9] *"to assess response"*
    - [8] *"Need to ensure that response can be assessed"*

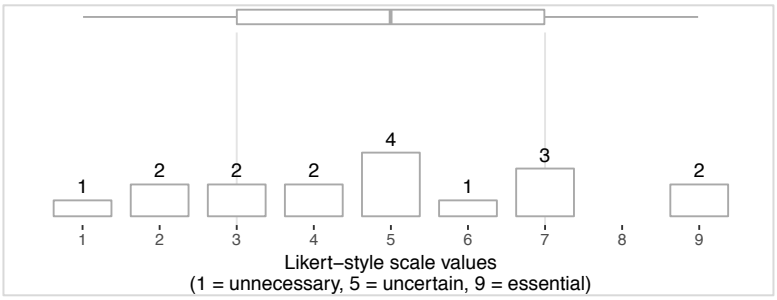
- **Platelet count: *Unresolved***



  - Median (IQR): 5 (3)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [6] *"if the reason is not related to lymphoma"*
    - [3] *"unimportant if lymphoma is cause of low platelets"*
    - [5] *"Depends upon the reason for the low plt count."*
    - [2] *"rarely an issue"*
    - [2] *"We can always transfuse plts."*
    - [4] *"only if study drug affects plts."*
    - [3] *"Many patients have borderline counts but do not routinely bleed."*
    - [4] *"not essential if due to BM involvement"*

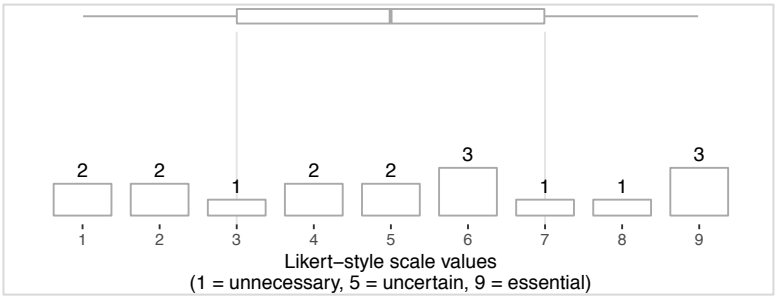
- [5] *"Only important when not due to disease but could rely on good standards of practice not requirements for trial entry"*

- **WBC: *Unresolved***



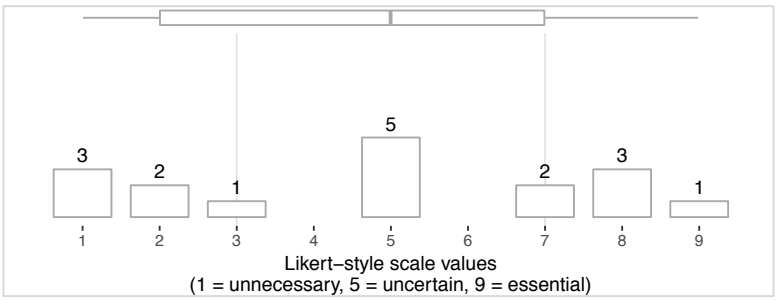
  - Median (IQR): 5 (4)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [6] *"if the reason is not related to lymphoma"*
    - [3] *"unimportant if lymphoma is cause of low WBC"*
    - [5] *"WBC does not matter. ANC does but again is depends upon the reason for the low ANC."*
    - [2] *"rarely an issue"*
    - [5] *"Only if the study drug affects WBC"*
    - [4] *"not essential if due to BM involvement"*

- **Active infection requiring systemic therapy: *Unresolved***



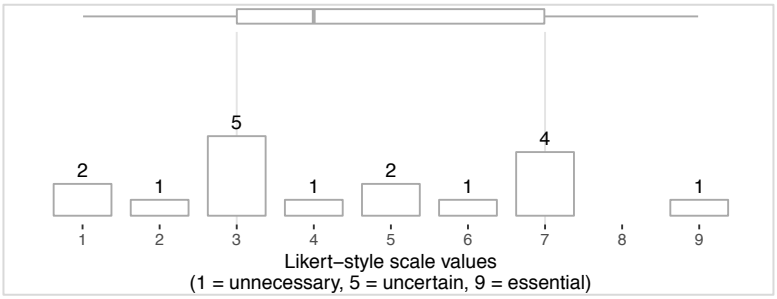
  - Median (IQR): 5 (4)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [4] *"too vague. no reason why a UTI that needs 3 days of abx should be exclusionary."*
    - [2] *"only exclude if R-CHOP can not be administered."*
    - [1] *"Should not be excluded. If it's severe, it will fall under the "other systemic illness, at the investigator's discretion.""*
    - [7] *"As immune suppression is common in protocols, active bacterial or fungal infections are risky"*
    - [9] *"not to enroll patient"*

- **History of transformed lymphoma: *Disagreement***



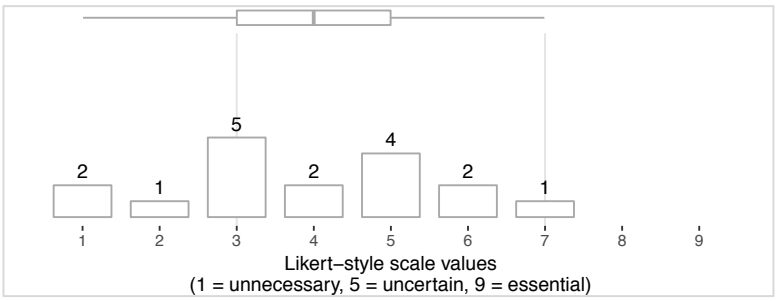
- Median (IQR): 5 (5)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [7] *"for front-line trial, would exclude prior therapy even if it was for different lymphoma"*
  - [5] *"If prior treatment for indolent lymphoma, then should be excluded. If no prior treatment for indolent lymphoma, then they should be allowed."*
  - [5] *"depends on nature of intervention"*
  - [1] *"Composites or presence of low-grade component at diagnosis should be included in frontline DLBCL studies. Transformation from previously diagnosed FL is a bit trickier. If candidate for R-CHOP then I think OK but should screen out double hits."*
  - [9] *"different disease"*

- **COO subtype: *Unresolved***



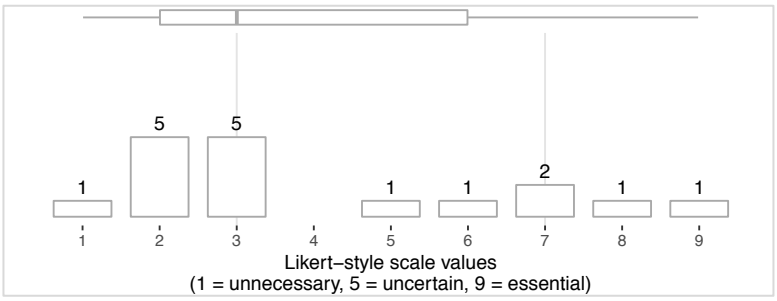
- Median (IQR): 4 (4)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [3] *"only relevant if presumed target is dependent on this. but we have been led astray by the relevance of this."*
  - [5] *"Depends upon the trial intervention."*
  - [5] *"depends on nature of intervention - also helps to characterize population"*
  - [6] *"May be needed rational on comparator arm."*
  - [3] *"I guess it depends on your novel targeted therapy"*
  - [1] *"Cell-of-origin based trials have been a bust"*
  - [7] *"The COO subtype needs to be further refined, but trying to target relevant subtypes will allow for greater confidence in the efficacy (or lack thereof) of therapies."*
  - [4] *"depends on the question asked in trial"*
  - [3] *"No strong evidence that any therapy has selective activity"*

- **Peripheral neuropathy: *Unresolved***



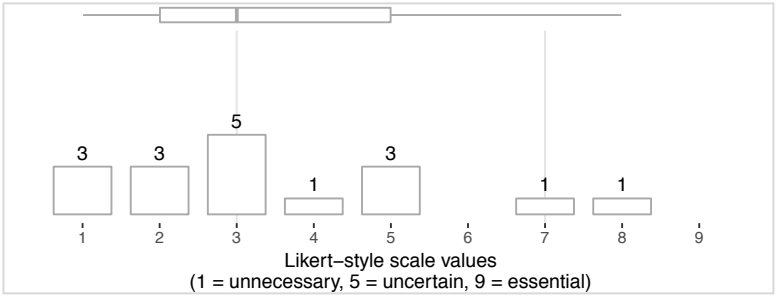
- Median (IQR): 4 (2)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [3] *"Only exclude if so severe they can not receive standard R-CHOP."*
  - [5] *"depends on nature of intervention"*
  - [6] *"Only exclude if severe."*
  - [3] *"In a fatal illness like DLBCL, mild/moderate neuropathy should not be a concern."*
  - [1] *"NA"*

- **HIV status: *Consensus Unnecessary***



- Median (IQR): 3 (4)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [2] *"can be managed"*
  - [5] *"depends on nature of intervention"*
  - [2] *"This is nearly always included but I don't think is relevant any longer with modern HIV therapy."*
  - [3] *"outcomes are similar with HAART"*

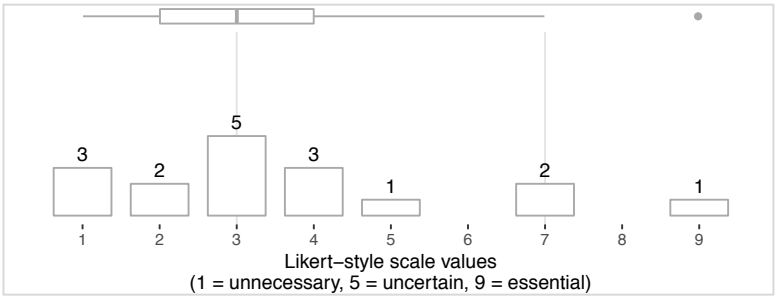
- **History of stroke or intracranial hemorrhage: *Consensus Unnecessary***



- Median (IQR): 3 (3)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [5] *"depends on nature of intervention"*
  - [7] *"Depends on toxicity of the investigational agent"*
  - [5] *"This is potentially relevant - if the patient has a risk of a second vascular event and the therapy exacerbates that risk."*

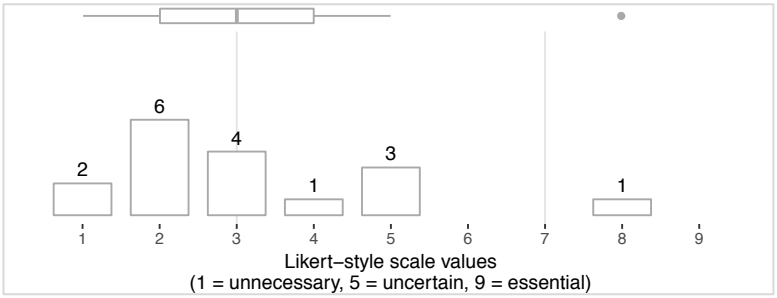
- [1] *"NA"*

- **History of other malignancies: *Consensus Unnecessary***



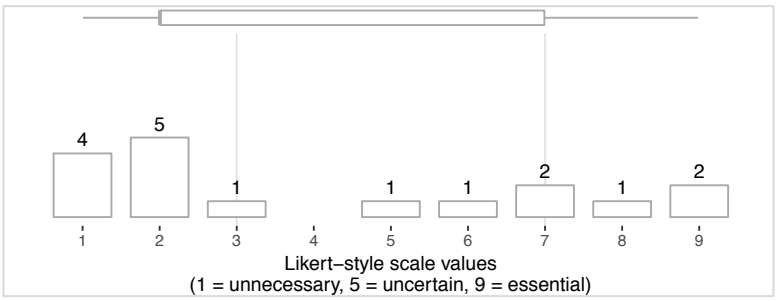
  - Median (IQR): 3 (2)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [4] *"probably not relevant unless currently active"*
    - [2] *"Only exclude if other malignancy is likely to be fatal in next 2 years or if requiring treatment that would preclude R-CHOP administration."*
    - [3] *"Only active or metastatic second cancers should be excluded."*
    - [7] *"not much point in studying novel agents in patients with impending death from other causes."*
    - [1] *"Unless actively receiving treatment."*
    - [3] *"Unless the other malignancy has a reasonable chance of causing death during the trial evaluation window, this is rarely relevant and excludes many patients who are otherwise good candidates."*
    - [3] *"only if currently active"*
    - [3] *"could rely on good standards of practice not requirements for trial entry"*

- **Psychiatric illness: *Consensus Unnecessary***



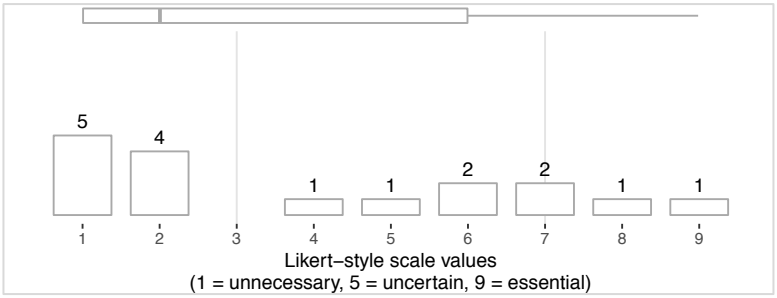
  - Median (IQR): 3 (2)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [1] *"as long as they possess capacity"*
    - [3] *"only exclude if they can not comply."*
    - [2] *"as long as subject can comply and that illness not expected to worsen"*
    - [3] *"Only exclude if it interferes with their ability to comply with the study treatment."*
    - [5] *"course of psychiatric illness is too highly variable. This should be encompassed in "other factors that may prevent patients from compliance""*
    - [4] *"ability for informed consent is key criteria here"*
    - [5] *"Adherence to therapy or risk of exacerbation of significant psychiatric illness"*
    - [1] *"unless wil prevent adherence to trial"*

- **CD20 positivity: *Consensus Unnecessary***



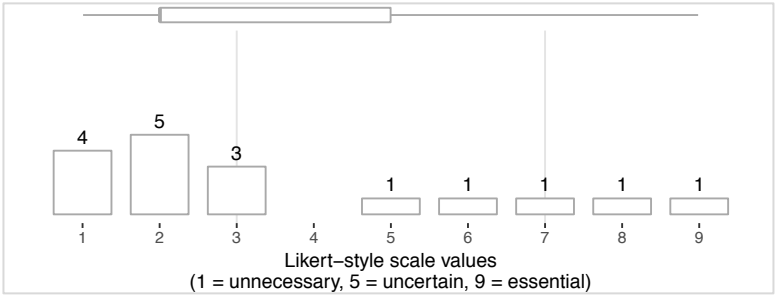
- Median (IQR): 2 (5)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [7] *"relevant to any patient, not just trials"*
  - [1] *"CD20 is rare and most people include Rituximab anyway"*
  - [5] *"is standard for diagnosis"*
  - [6] *"Depends on regimen"*
  - [9] *"you can't use R-CHOP as control arm if the patient isn't CD20+"*
  - [7] *"Depends on the mechanism of action of drug under investigation"*
  - [2] *"Rituximab is beneficial even in CD20 dim DLBCL."*
  - [2] *"most are positive"*
  - [2] *"O"*
  - [2] *"Nearly all DLBCL is"*

- **HBV status: *Consensus Unnecessary***



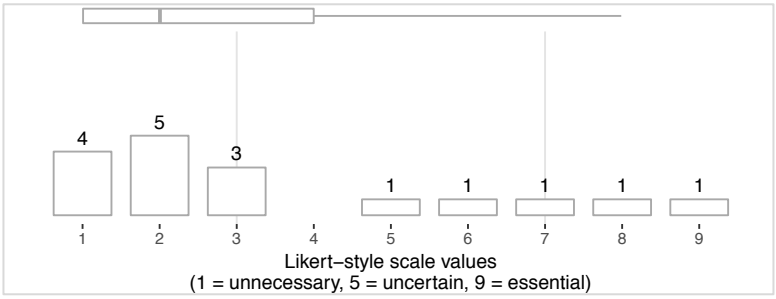
- Median (IQR): 2 (5)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [2] *"can be managed"*
  - [6] *"as long as controlled"*
  - [1] *"HBV needs to be tested and treated if positive, but it doesn't have to exclude patients from study."*
  - [2] *"Suppressive therapy works"*
  - [1] *"in practice we treat this patient ad provide prophylaxis"*

- **Central pathology review prior to enrollment: *Consensus Unnecessary***



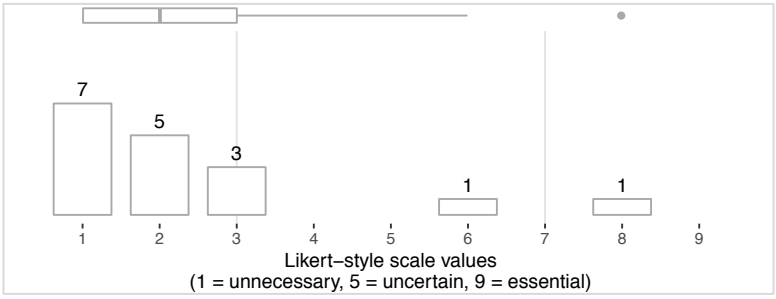
- Median (IQR): 2 (3)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [2] *"not practical. would prefer post-enrollment review and over-enrollment to account for error."*
  - [2] *"Central path review is important but does not need to be prior to enrollment."*
  - [3] *"can be done later"*
  - [2] *"We need to get away from this"*
  - [1] *"This introduces too much delay."*
  - [1] *"problematic - introduces too much bias and won't catch the neediest patients"*
  - [1] *"causes selection criteria. better to exclude after the fact"*
  - [3] *"This will limit enrollment"*
  - [2] *"Barrier to slow enrollment which selects for favorable patients who can wait."*
  - [6] *"more stringent study"*
  - [8] *"Often revised"*
  - [2] *"greatly slows enrollment"*

- **HCV status: *Consensus Unnecessary***



- Median (IQR): 2 (3)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [6] *"as long as controlled"*
  - [1] *"HCV needs to be tested and treated if positive, but it doesn't have to exclude patients from study."*
  - [2] *"Suppressive therapy works"*
  - [1] *"in real life we treat these patients"*

- **Minimum life expectancy: *Consensus Unnecessary***



- Median (IQR): 2 (2)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [1] *"for first line this seems to be somewhat unnecessary"*
  - [1] *"Other criteria should make this unnecessary"*
  - [1] *"A non sensical concept when someone has an aggressive but potentially curable cancer."*
  - [2] *"Very hard to tell life expectancy in lymphoma"*
  - [2] *"This criterion is too subjective."*
  - [3] *"It seems so highly dependent on the status of the lymphoma that it is hard to distinguish. Most studies exclude other comorbidities that limit life expectancy anyway."*
  - [8] *"not much point in studying novel agents in patients with impending death from other causes."*

- [2] *"Always struggled with this one. How defined?"*
- [1] *"This is a made up subjective trial criterion unless the patient is actively dying."*
- [3] *"to know patient is dying already"*
- [2] *"Difficult to estimate"*

- **Recommendations for additional eligibility criteria not addressed in the survey**
  - *"None"*
  - *"more liberal with steroids, allowance for a cycle of R-CHOP, if patient hospitalized, CTs with bone marrow biopsy adequate for enrollment"*
  - *"Eliminating prior malignancies and concomitant malignancies will go a long way."*

Next steps

Round 2 questionnaire: after reviewing the personalized summary, please begin the Round 2 (final round) questionnaire provided via email.

Round 2 will revisit criterion categories that were designated Unresolved or showed Disagreement in Round 1. In addition, Round 2 will seek recommendations regarding numerical ranges for quantitative criterion categories that were designated Consensus Essential, Unresolved, or showed Disagreement in Round 1.

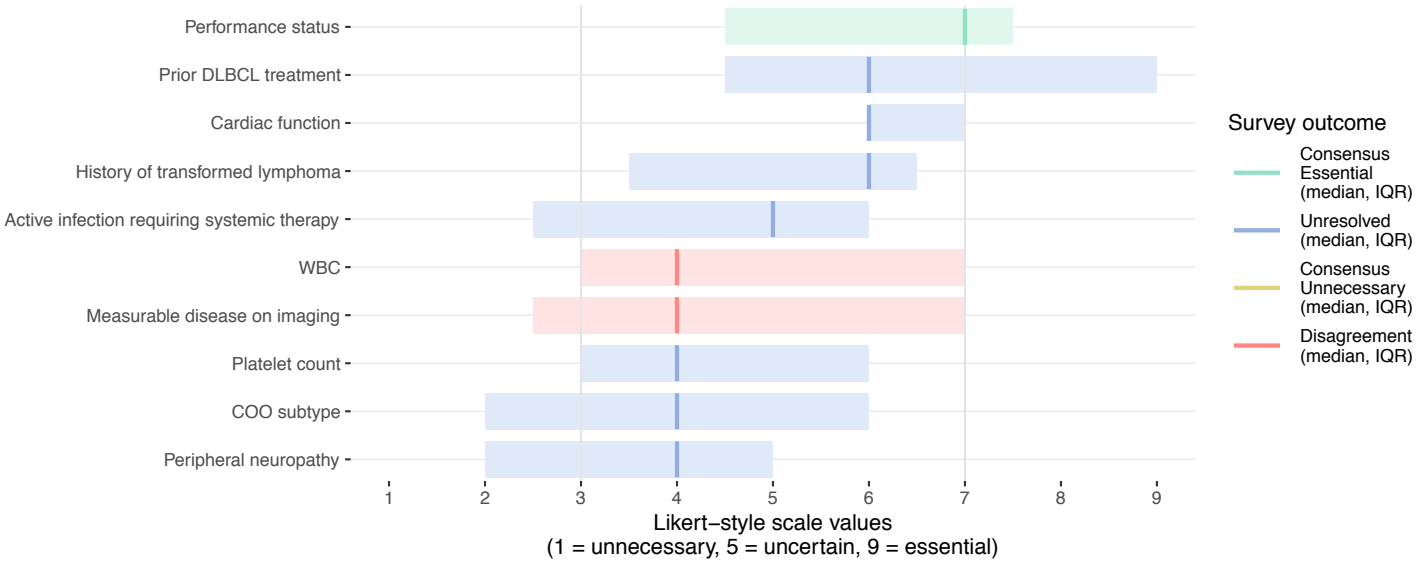
Thank you again for your participation!

Andrew Harkins, MD/MSCR Candidate
Chris Flowers, MD, MS, FASCO
Winship Cancer Institute
Emory University School of Medicine

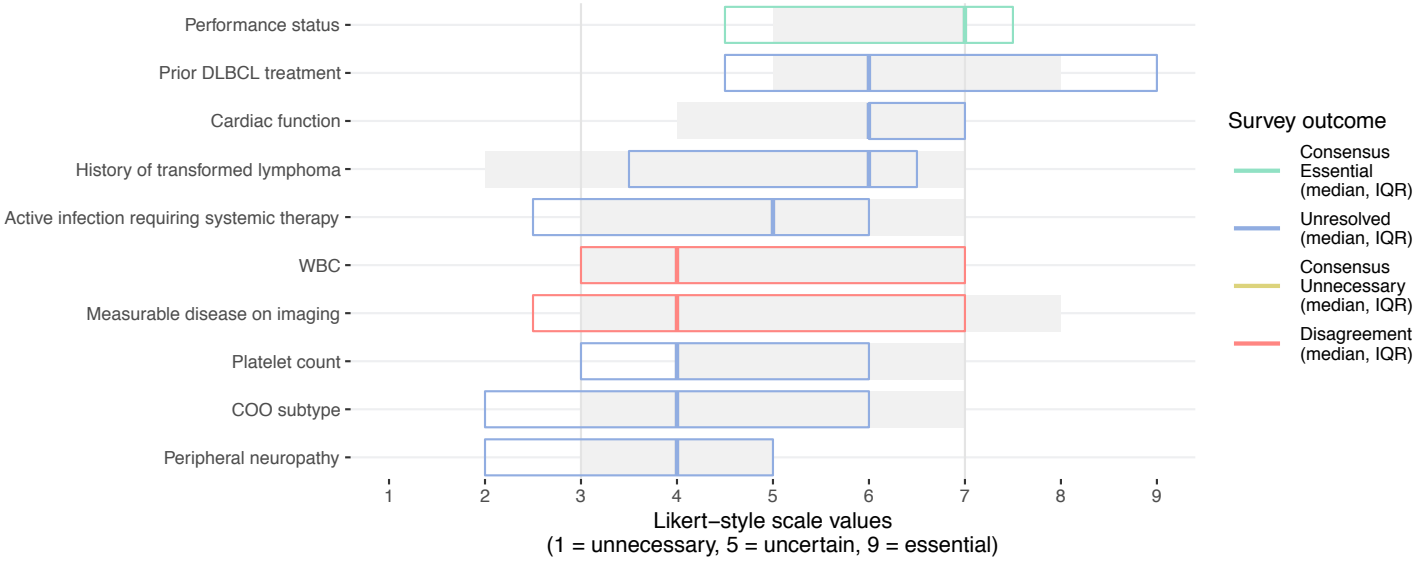
DLBCL Eligibility Criteria – Delphi Questionnaire, Round 2 Results
Anonymized Summary

Anonymized summary figures:

Round 2 results:



Round 2 results overlaid on Round 1 results for all criteria included in the Round 2 survey (grey indicates Round 1 IQR):



Definitions for survey outcomes:

Outcome	Definition	n (% of 10 total criteria)
Consensus Essential	Median Likert-style scale value ≥ 7; no Disagreement	1 (10)
Unresolved	3 < median Likert-style scale value < 7; no Disagreement	7 (70)
Consensus Unnecessary	Median Likert-style scale value ≤ 3; no Disagreement	0 (0)
Disagreement	≥ 1/3 of respondents rate the criterion category ≤ 3 AND ≥ 1/3 of respondents rate the criterion category ≥ 7	2 (20)

Results

Descriptive statistics of participants

- **Total number of prospective participants emailed:** n = 17 (i.e., all Round 1 participants)
- **Total number of respondents:** n = 15
- **Response rate:** 15/17 = 88.2%
- **Institutions represented:** n = 8
- **Median number of years' experience as a hematologist/oncologist:** 17 (IQR = 9.5)

Results of survey: overall results

- **Consensus Essential**: n = 1 of 10 total criteria in survey (10%)

Criterion category	Median	IQR
Performance status	7	3

- **Unresolved**: n = 7 of 10 total criteria in survey (70%)

Criterion category	Median	IQR
Prior DLBCL treatment	6	4.5
Cardiac function	6	1
History of transformed lymphoma	6	3
Active infection requiring systemic therapy	5	3.5
Platelet count	4	3
COO subtype	4	4
Peripheral neuropathy	4	3

- **Consensus Unnecessary:** n = 0 of 10 total criteria in survey (0%)

- **Disagreement:** n = 2 of 10 total criteria in survey (20%)

Criterion category	Median	IQR
WBC	4	4
Measurable disease on imaging	4	4.5

- **Results from Round 1 and Round 2 by criterion for all criteria included in the Round 2 survey:**

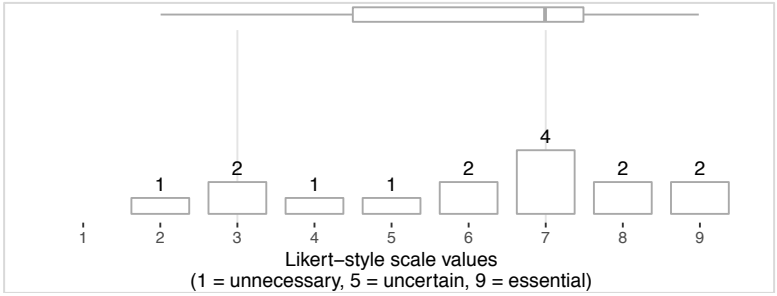
Criterion category	Round 1	Round 2
Performance status	**Unresolved**	**Consensus Essential**
Prior DLBCL treatment	Unresolved	Unresolved
Cardiac function	Unresolved	Unresolved
History of transformed lymphoma	**Disagreement**	**Unresolved**

Active infection requiring systemic therapy	Unresolved	Unresolved
WBC	**Unresolved**	**Disagreement**
Measurable disease on imaging	Disagreement	Disagreement
Platelet count	Unresolved	Unresolved
COO subtype	Unresolved	Unresolved
Peripheral neuropathy	Unresolved	Unresolved

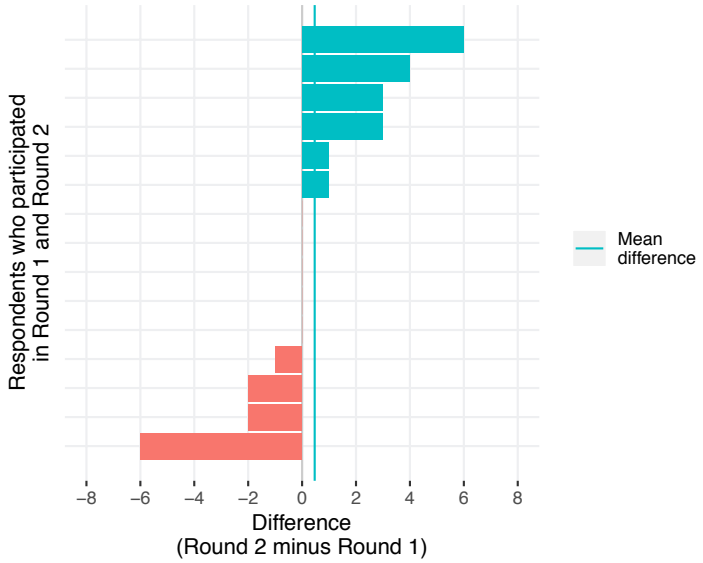
*Bold indicates result change from Round 1 to Round 2

Results of survey: anonymized results by individual criterion category (ordered according to median value)

- **Performance status: *Consensus Essential***

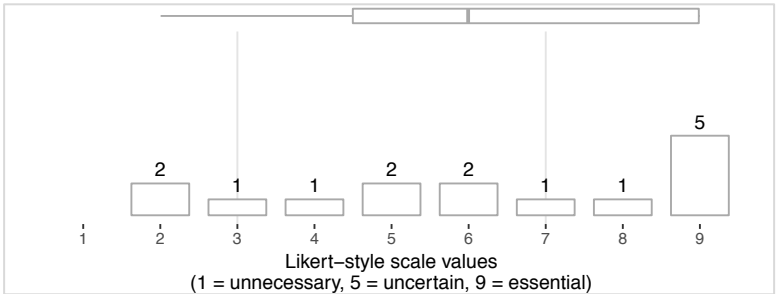


  - Median (IQR): 7 (3)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [3] *"If the poor PS is due to DLBCL, then the criterion is unnecessary. If the poor PS is due to co-morbidities, then it has some value if the PS is 3-4."*
    - [7] *"poor performance status patients may have excessive toxicity with new agents"*
    - [4] *"it is ideally desirable to include all performance status patients, unless identifying high risk patients requiring riskier experimental option."*
    - [9] *"One of the most important prognostic factors and also will determine how suitable the patient is for treatment"*
    - [7] *"I think this is a reasonable part of eligibility in theory, but I think that there is a reasonable chance that it is not reliably estimated when trial eligibility is being considered."*
    - [8] *"part of IPI"*
    - [7] *"MDs always exaggerate PS anyway so if you allow any PS corpses will go on study. I think "real" 4 should always be excluded and I am on the fence re 3..."*
    - [3] *"Correlates with outcome in studies but not reliably measured"*
    - [6] *"Experimental arm likely to be more toxic if poor PS patients included"*
    - [8] *"Needed to limit subject enrollment with poor PS unless due to disease"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

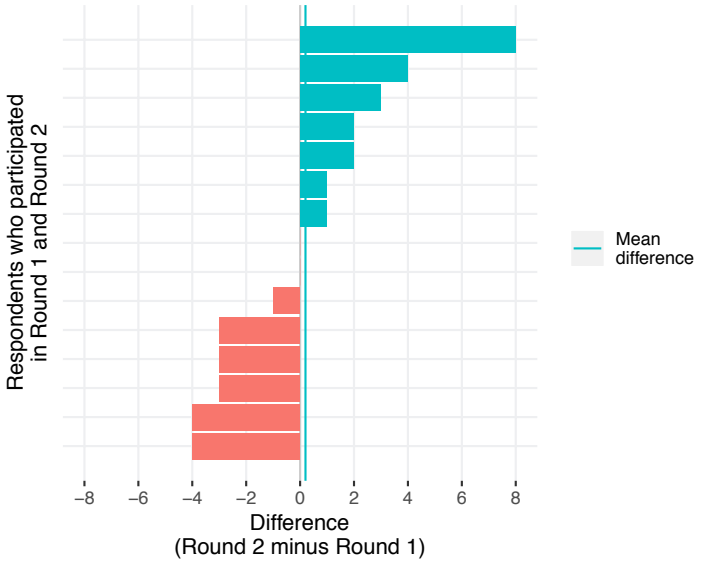


- Mean difference (SD): 0.47 (2.9)

- **Prior DLBCL treatment: *Unresolved***

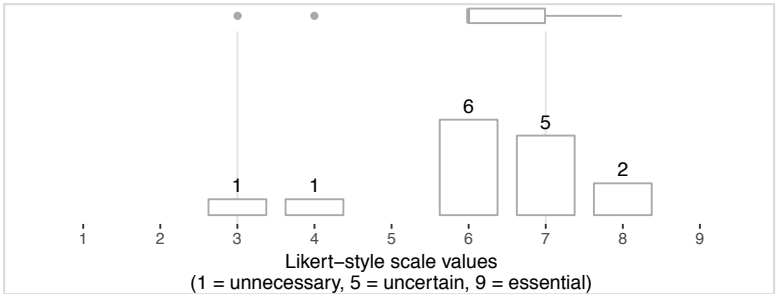


  - Median (IQR): 6 (4.5)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [6] *"depends upon trial and trial design."*
    - [9] *"Depends on goal of study, if adding to RCHOP then patient shouldn't have prior therapy"*
    - [9] *"maybe the question is confusing. If this is first-line trial it is essential to have LACK of prior DLBCL treatment as an eligibility criterion"*
    - [9] *"to know that the same medication is not used again and also to know how many lines received"*
    - [9] *"Maybe I don't understand this question. If it is first-line therapy for DLBCL then this is necessarily relevant."*
    - [5] *"Not sure what this means for upfront treatment"*
    - [9] *"confused...if you are testing first line RCHOP how can you allow pts with prior treatment for DLBCL...different pt population unless you mean one cycle of RCHOP. (which I am not really in favor of either....)"*
    - [2] *"good to allow a cycle of treatment if needed"*
    - [2] *"we need to allow for a dose of CHOP or R-CHOP for patients with urgent/emergent presentations"*
    - [8] *"This should be a criterion for a front-line study, but up to one cycle of chemo should be allowed before enrollment."*
    - [3] *"First-line?"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

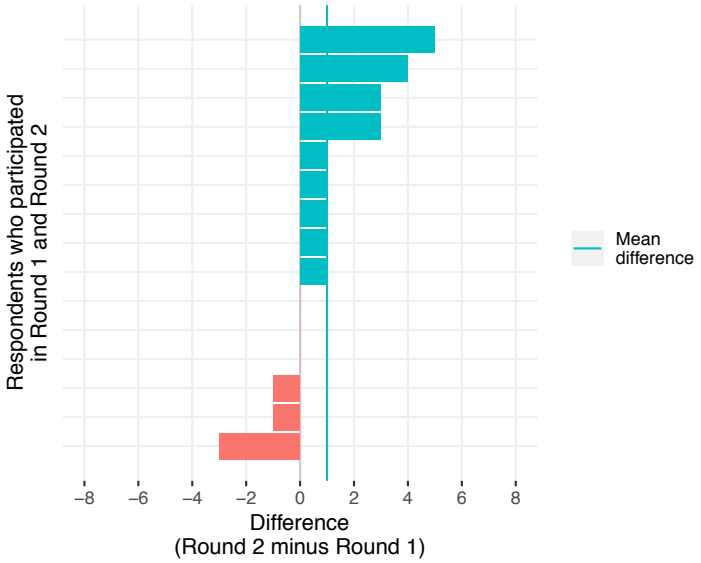


- Mean difference (SD): 0.20 (3.4)

- **Cardiac function: *Unresolved***

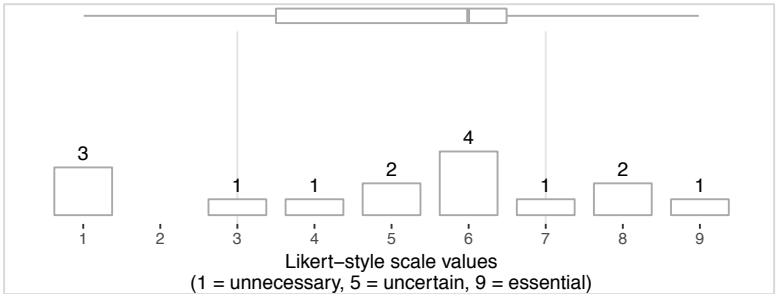


  - Median (IQR): 6 (1)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [4] *"Depends upon the treatment."*
    - [6] *"Depends on toxicity profile of the agents under study, if cardiac risk exists, this is essential"*
    - [6] *"this depends upon your choice of therapy. If proposed therapy in control or experimental arm requires bolus anthracycline, then cardiac function will need to be assessed."*
    - [3] *"Only if we use cardiotoxic regimens"*
    - [6] *"I suspect this delays enrollment and prevents high risk patients from being entered into clinical trials. Perhaps if it could be done before cycle 2 or something like that it would be better. Also, sometimes numbers are all over the place for no apparent reason and don't actually reflect true cardiac function."*
    - [7] *"Yes but could lower it to 40%. Many pts in that 45-50% range that are frustrating."*
    - [6] *"eligibility for anthracycline based therapy"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

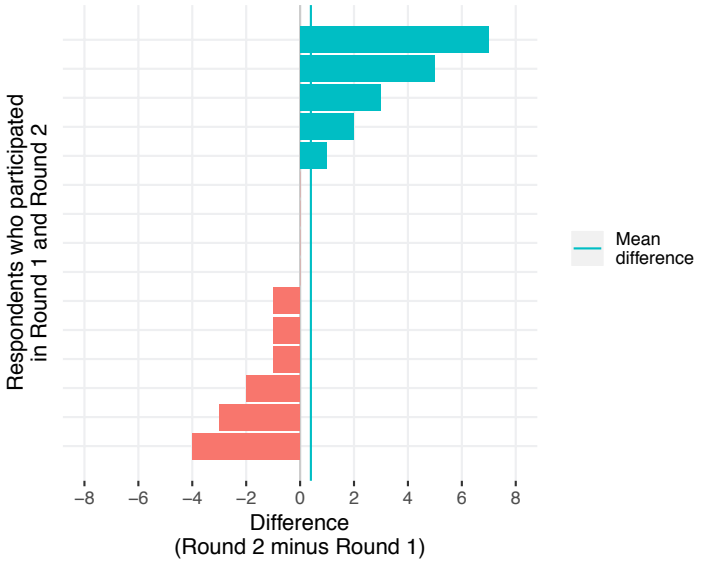


- Mean difference (SD): 1.0 (2.1)

- **History of transformed lymphoma: *Unresolved***

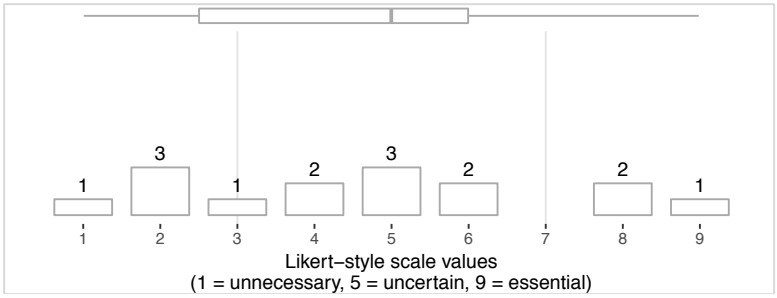


  - Median (IQR): 6 (3)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [6] *"depends upon trial design."*
    - [8] *"Depends on goal of study, if evaluating new agents in newly diagnosed DLBCL, then transformed pts should be excluded as their prognosis and outcomes are different"*
    - [9] *"Primary and transformed diseases are biologically different"*
    - [3] *"Probably depends on setting but my bias would be to include these cases in majority of trials as long as iNHL was not treated. For all we know, many of the DLBCLs are actually transformed from iNHL and we didn't really find the iNHL."*
    - [1] *"no prior treatment for underlying low grade NHL."*
    - [7] *"different diseas"*
    - [6] *"If prior history of FL with treatment, then I would exclude patients. If FL and DLBCL at diagnosis (composite/discordant) I would not exclude patients"*
    - [8] *"Transformed lymphoma should be allowed."*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

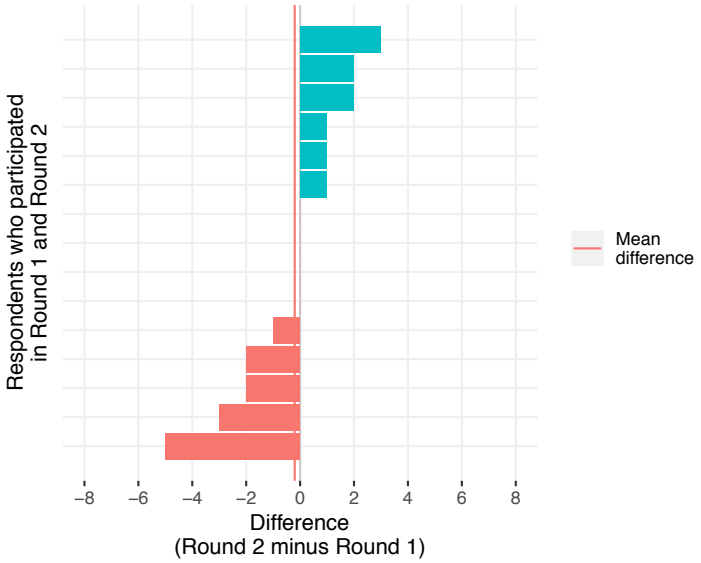


- Mean difference (SD): 0.40 (2.9)

- **Active infection requiring systemic therapy: *Unresolved***

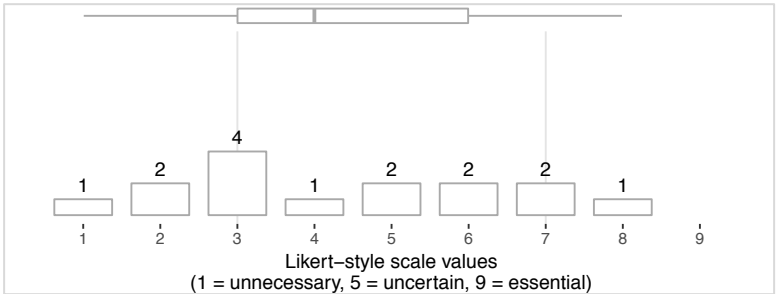


  - Median (IQR): 5 (3.5)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [4] *"depends upon infection and status of infection"*
    - [8] *"Generally pts with active infection should be excluded due to higher risk of worsened toxicity"*
    - [9] *"may lead to complications and complicate analysis of the data"*
    - [5] *"depends. shouldn't necessarily be a barrier to enrollment but should probably be resolved before initiation of therapy."*
    - [2] *"how do you define unresolved? UTI needed oral cipro - how long do you have to wait to start treatment. Some of them say no active infection in 14 days and that is unnecessary but pneumonia on IV antibiotics???"*
    - [3] *"rarely relevant"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

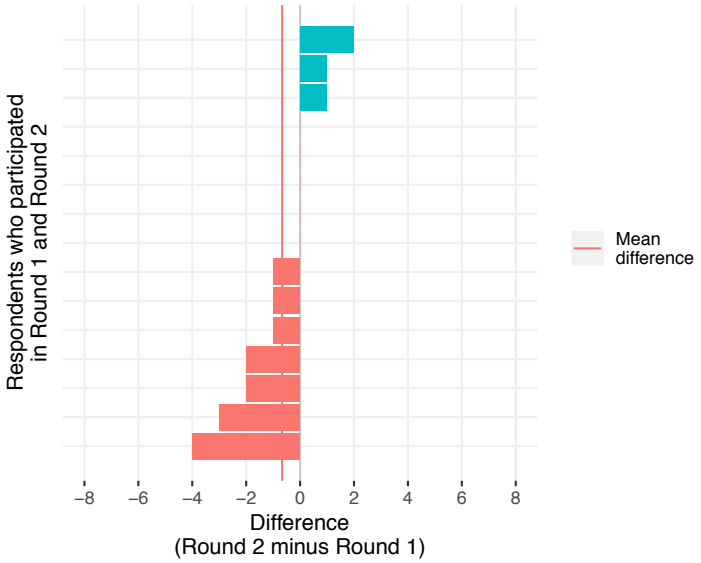


- Mean difference (SD): -0.20 (2.11)

- **Platelet count: *Unresolved***

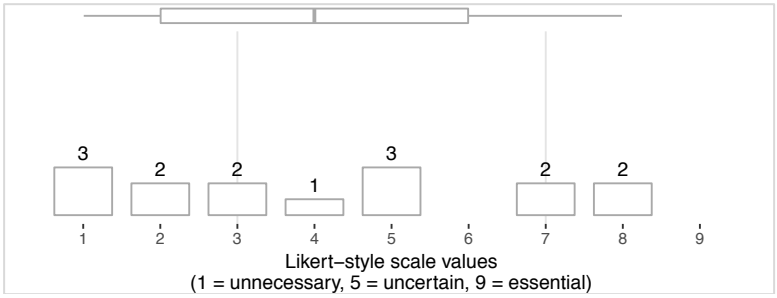


  - Median (IQR): 4 (3)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [3] *"Depends of plts are low due to disease or due to some co-morbid condition."*
    - [7] *"depends again on toxicity profile of agents under study, if known to cause thrombocytopenia, this is essential"*
    - [2] *"Rarely would platelet count contraindicate therapy."*
    - [4] *"the patient will need therapy irrespective of that so less important"*
    - [3] *"If platelets are low due to DLBCL and there is not a really significant risk of bleeding from the experimental drug (i.e., drug doesn't have anticoagulant effect) then pts should be eligible."*
    - [3] *"RCHOP does not really affect plts so could have a very liberal lower limit. Would also need to be disease related if <50.....but above that I would be OK with it no matter what the etiology."*
    - [3] *"uncommon issue"*
    - [7] *"unless due to underlying lymphoma"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

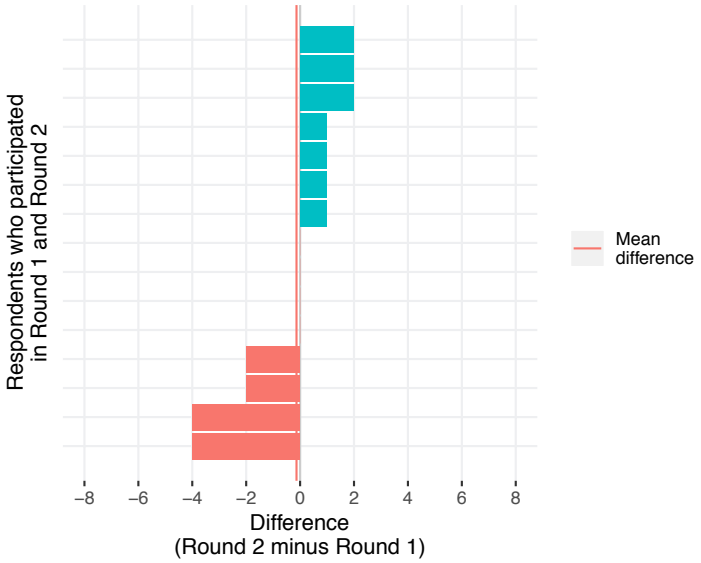


- Mean difference (SD): -0.67 (1.6)

- **COO subtype: *Unresolved***

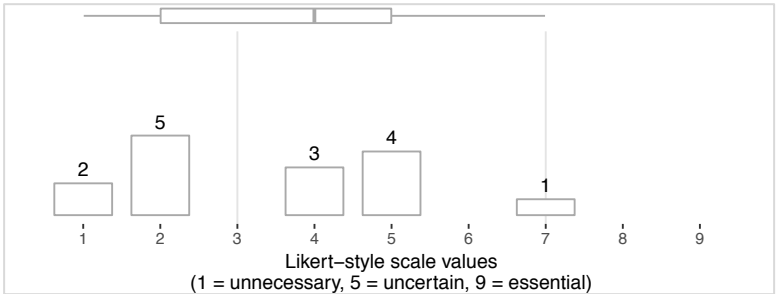


  - Median (IQR): 4 (4)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [8] *"Depends on drugs under evaluation, if believed to have more activity in particular DLBCL subgroup, this is essential"*
    - [5] *"this answer depends on whether your experimental agent is thought to have selective effect on different cell of origin. There is no correct "yes/no" global answer"*
    - [4] *"for most cases will not be important unless really is directed to specific mechanism in specific subtype with PPV of >90%"*
    - [1] *"Entirely dependent on experimental therapy, and even then apparently we get it wrong."*
    - [8] *"Still important for WHO"*
    - [5] *"depends on drug/intervention"*
    - [5] *"depending on the type of study"*
    - [1] *"useful for stratification, but unnecessary at enrollment"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

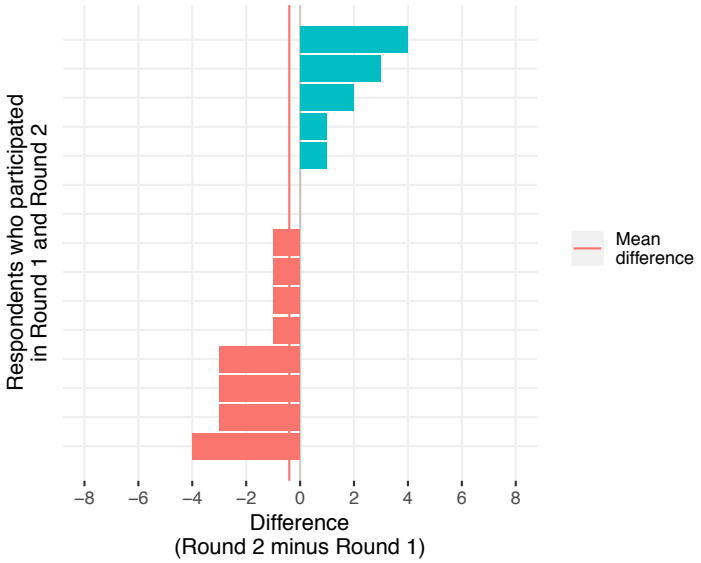


- Mean difference (SD): -0.13 (2.0)

- **Peripheral neuropathy: *Unresolved***

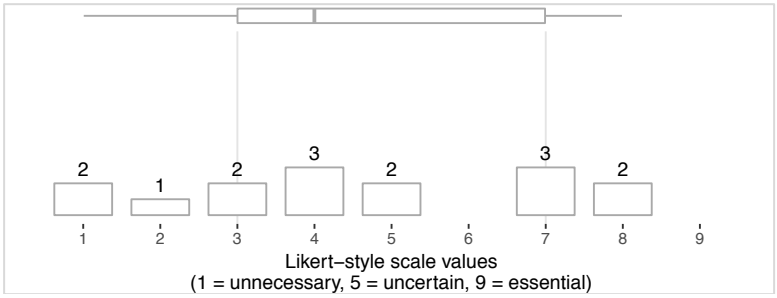


  - Median (IQR): 4 (3)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [5] *"depends upon treatment"*
    - [7] *"depends again on toxicity profile of agents under study, if known to cause neuropathy, this is essential"*
    - [5] *"see answer on cardiac assessment"*
    - [1] *"not important in most cases unless contraindication fro specific medication"*
    - [2] *"I would include this if it precluded patient from getting experimental therapy, but not otherwise. Trial can provide instructions on how to adjust vincristine for neuropathy."*
    - [2] *"Depends upon agents being studied"*
    - [2] *"rarely relevant"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

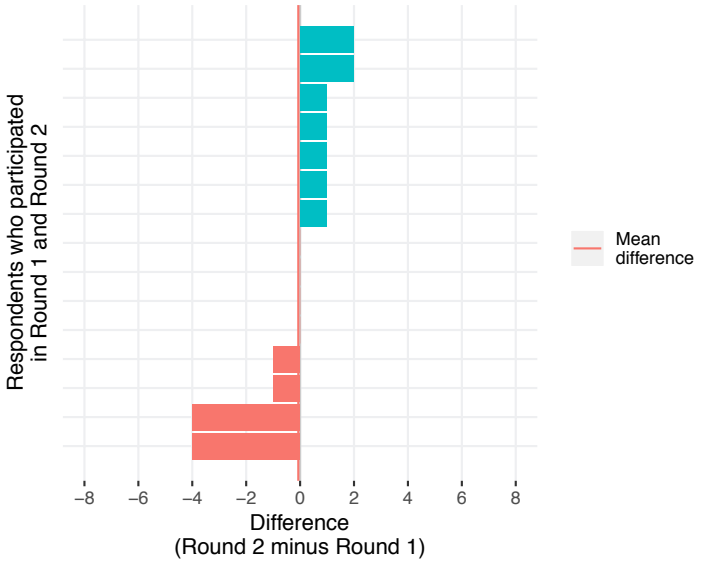


- Mean difference (SD): -0.40 (2.3)

- **WBC: *Disagreement***

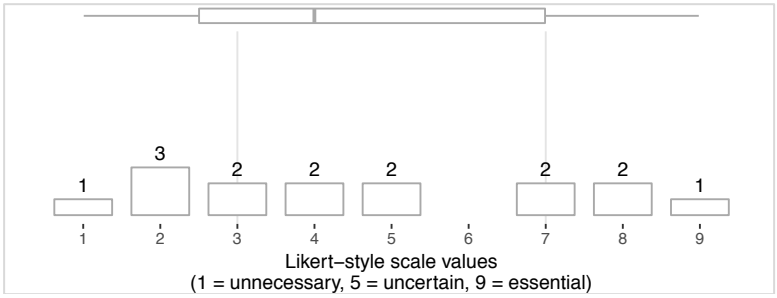


  - Median (IQR): 4 (4)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [8] *"depends again on toxicity profile of agents under study, if known to cause thrombocytopenia, this is essential"*
    - [4] *"as above especially if disease attributed"*
    - [4] *"I just don't think there are many cases where ANC has justifiably prevented patients from enrolling on a trial."*
    - [7] *"If disease related could allow but if chronic neutropenia how are you going to dose the pt with low anc at every cycle?"*
    - [3] *"uncommon issue"*
    - [7] *"unless due to underlying lymphoma"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:

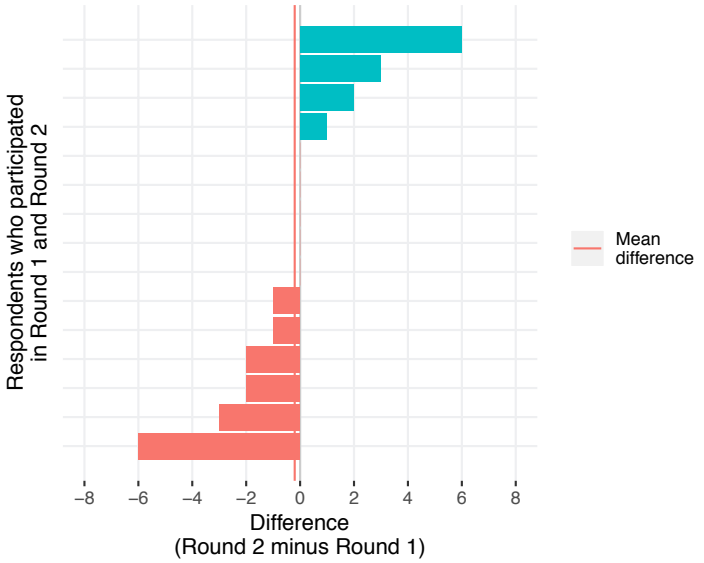


- Mean difference (SD): -0.067 (1.8)

- **Measurable disease on imaging: *Disagreement***



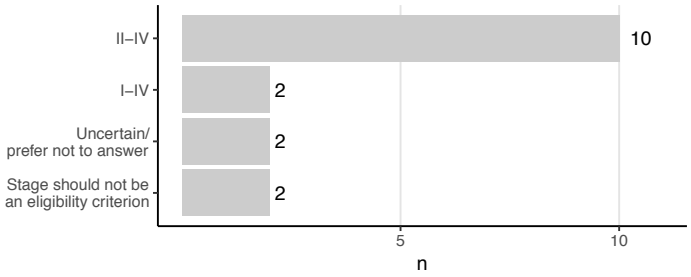
  - Median (IQR): 4 (4.5)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [3] *"Only need measurable disease if the primary endpoint is ORR. Otherwise not needed."*
    - [4] *"Evaluable disease by PET/CT is sufficient"*
    - [1] *"optimal endpoint should be progression free survival, and not radiologic response to measurable disease. If disease can only be assessed by blood or marrow (and not on imaging), those patients should be enrolled and assessed as appropriate."*
    - [9] *"need to know from what we start to kn0w what we achieve"*
    - [2] *"DLBCL is a fatal illness, and the goal of treatment is complete response with no detectable disease anywhere. If disease can be detected at baseline, that is sufficient for me provided that the criteria for complete response include lack of evidence of lymphoma that was present at baseline. Additionally, the primary objective of most DLBCL trials is either OS or PFS, which should not be significantly impacted by measurable disease at baseline."*
    - [2] *"If Phase 3 study and PFS or OS are endpoint then this seems unnecessary. If Phase 2 where primary endpoint is response then need to be able to visualize something. 1 cm should be adequate though. Why do they require 1.5 cm. Now that we have PET even subcm would be measurable. "*
    - [5] *"needed for response rate but not duration metrics"*
    - [7] *"i think that it is important, but in the PET era, perhaps we need to change this definition especially with bony lesions"*
    - [8] *"Needed to determine response"*
  - Change from Round 1 by respondents who participated in Round 1 and Round 2:



- Mean difference (SD): -0.20 (2.7)

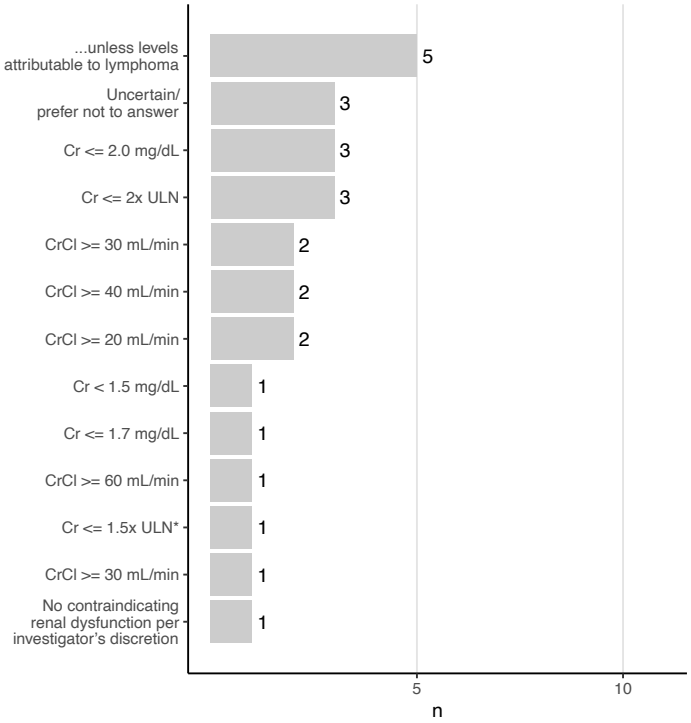
Results of survey: recommended numerical ranges for quantitative criteria that were Consensus Essential, Unresolved, or in Disagreement after Round 1

- **Stage**



  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [Uncertain/prefer not to answer] *"Depends on goal of study and what patient population you are evaluating - is it all pts, pts with only higher risk/advanced stage disease or low stage pts getting limited number of cycles."*
    - [I–IV] *"I think that stage I should probably be separated from 2+"*

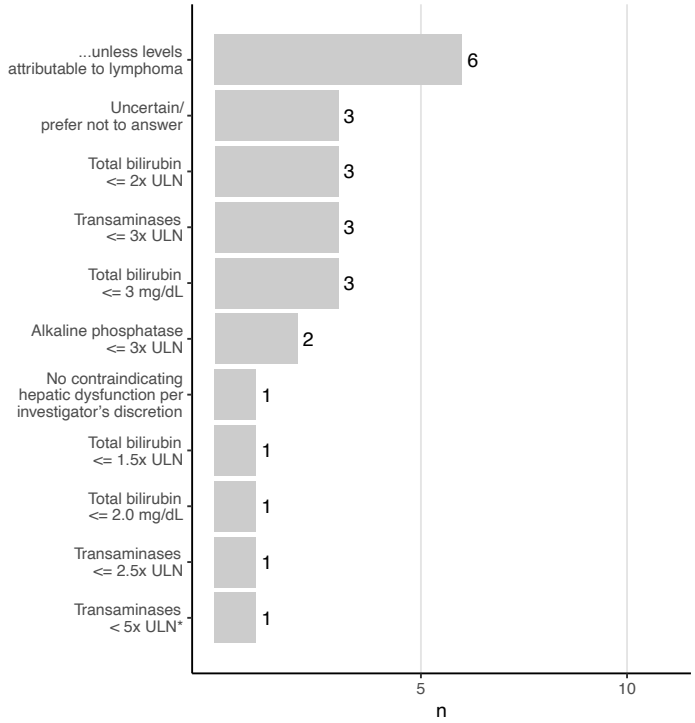
- **Renal function**



***** indicates alternate response provided by respondent in lieu of or in addition to available responses present in the survey

- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [Uncertain/prefer not to answer] *"this depends upon your choice of therapy. If proposed therapy in control or experimental arm requires bolus anthracycline, then renal function will need to be assessed."*
  - [CrCl ≥ 20 mL/min] *"most RCHOP drugs not impacted by renal dysfunction. If experimental drug is impacted then that should drive eligibility."*
  - [CrCl ≥ 30 mL/min unless levels attributable to lymphoma] *"depends on drugs included on trial"*
  - [Uncertain/prefer not to answer] *"This should be based on the safety of the novel treatment and is less relevant to RCHOP itself"*

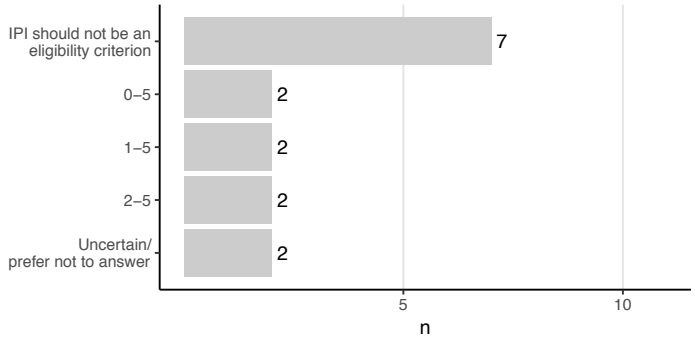
- **Hepatic function**



***** indicates alternate response provided by respondent in lieu of or in addition to available responses present in the survey

- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [Total bilirubin ≤ 2.0 mg/dL] *"depends again on toxicity profile of agents under study and how they are cleared, if cleared hepatically this is essential"*
  - [Uncertain/prefer not to answer] *"this depends upon your choice of therapy. If proposed therapy in control or experimental arm requires bolus anthracycline, then hepatic function will need to be assessed."*
  - [Total bilirubin ≤ 2x ULN] *"Gilbert's should not preclude eligibility. If due to lymphoma relatively low levels should improve quickly with steroids. as long as doxorubicin dose isn't impacted should be ok."*
  - [Uncertain/prefer not to answer] *"This should be based on the safety of the novel treatment and whether the abnormal hepatic function is due to lymphoma"*

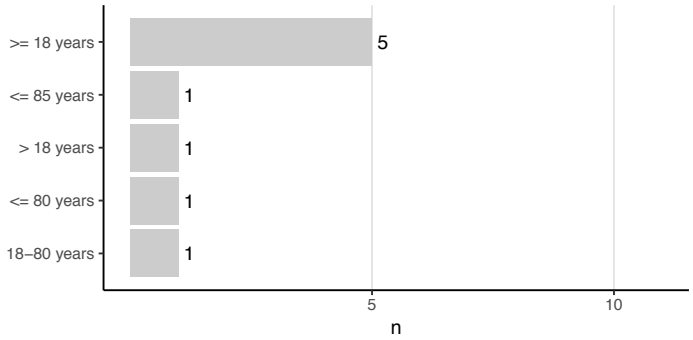
- **IPI**



- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [Uncertain/prefer not to answer] *"Depends on goal of study and what patient population you are looking to study"*

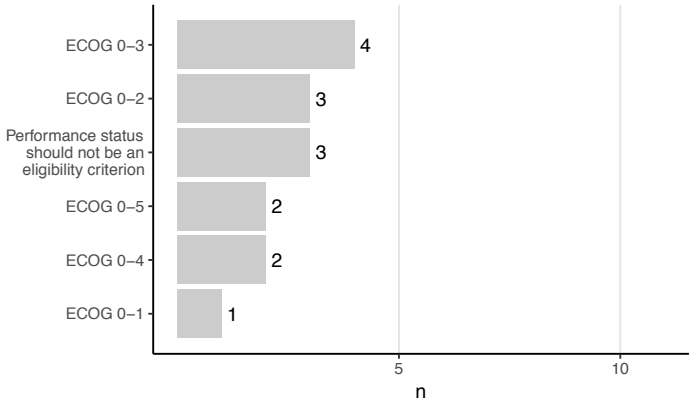
- [0–5] *"age is the most important factor for OS since in elderly events may occur related to age and not disease or treatment"*
- [IPI should not be an eligibility criterion] *"would only be important if trial targets very high risk or very low risk pts."*
- [0–5] *"depends on scenario"*
- [IPI should not be an eligibility criterion] *"Depends on the trial, probably best to craft around elements of IPI (stage, age, etc)"*
- [Uncertain/prefer not to answer] *"This depends on the risk fo the therapy honestly. The study would have to be larger if including lower IPI"*

- **Age**



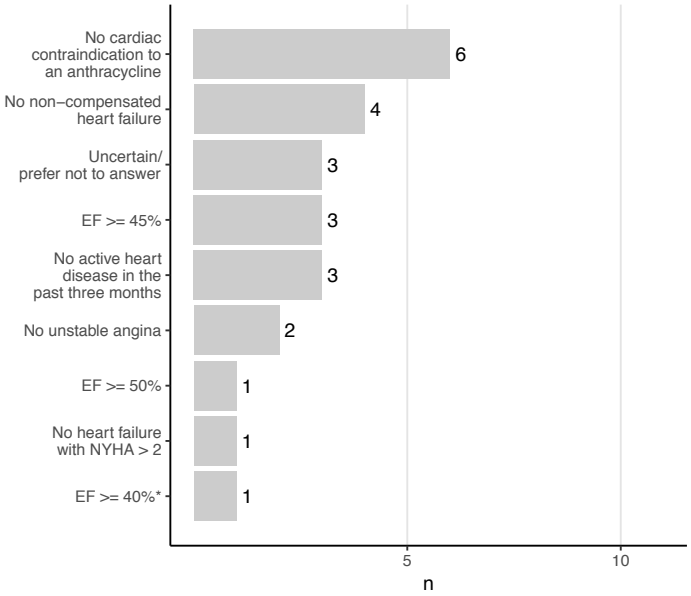
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [no quantitative response provided] *"Wouldn't recommend a cut-off. LEss likely to be essential, particularly if PS or functional status is assessed"*
  - [no quantitative response provided] *"this depends on the toxicity of the proposed therapy."*
  - [no quantitative response provided] *"varies based on design"*
  - [≤ 80 years] *"Above age 80 I would be less inclined to give full dose CHOP."*
  - [no quantitative response provided] *"depends upon what is being studied"*
  - [no quantitative response provided] *"depends on scenario; depends on nature of study"*
  - [≥ 18 years] *"probably better using frailty measures than age at the top end of range"*
  - [≥ 18 years] *"ideally the very elderly should have studies designed especially for them, but i would propose no age range"*
  - [no quantitative response provided] *"I think any age where you think RCHOP is appropriate should be eligible"*
  - [≥ 18 years] *"No age limit provided patient meets the other entry criteria"*
  - [≥ 18 years] *"limiting age makes trials less applicable"*

- **Performance status**



- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [ECOG 0–3] *"Unless related to disease burden"*
  - [ECOG 0–4] *"Provided lymphoma is cause of poor performance status, otherwise 2"*
  - [ECOG 0–2] *"+/- 3....if all due to disease then I could include 3. already answered this."*
  - [ECOG 0–3] *"3 if disease related"*
  - [ECOG 0–3] *"3 if due to lymphoma"*
  - [ECOG 0–3] *"3 allowed if due to lymphoma and expected reversible with therapy"*

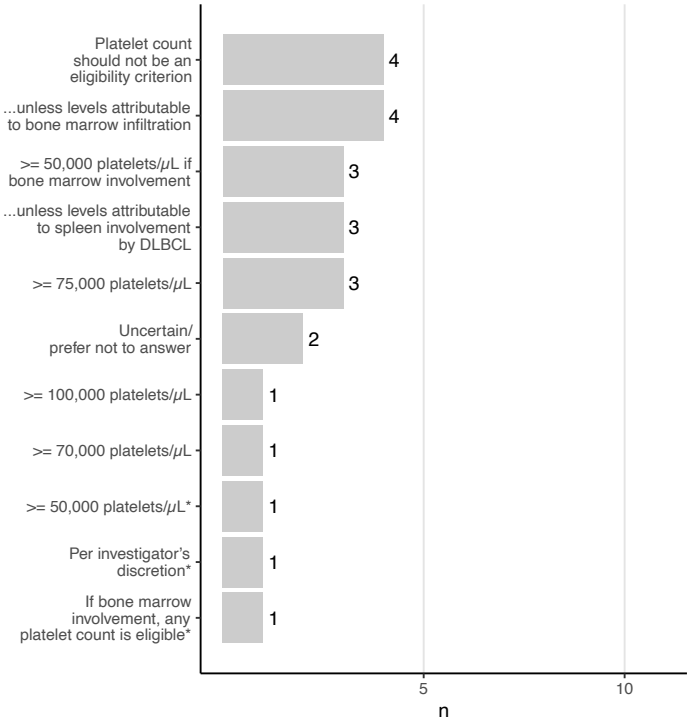
- Cardiac function



***** indicates alternate response provided by respondent in lieu of or in addition to available responses present in the survey

- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [Uncertain/prefer not to answer] *"Again, depends on toxicity of agents under study. If its agents being added to RCHOP then due to anthracycline use the EF has to be > 50%, would recommend no recent MI in last 6 months, no active cardiac disease"*
  - [Uncertain/prefer not to answer] *"this depends upon your choice of therapy. If proposed therapy in control or experimental arm requires bolus anthracycline, then cardiac function will need to be assessed."*
  - [No active heart disease in the past three months] *"I like this answer. It covers recent MI, it covers CHF."*

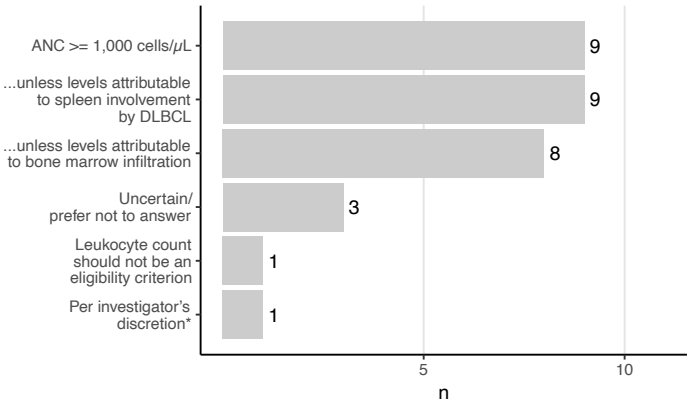
- Platelet count



***** indicates alternate response provided by respondent in lieu of or in addition to available responses present in the survey

- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [≥ 75,000 platelets/μL] *"Usually sufficient to continue RCHOP, but would adjust higher if new agent causes significant thrombocytopenia"*
  - [Uncertain/prefer not to answer] *"Rarely would platelet count contraindicate therapy.."*
  - [...unless levels attributable to bone marrow infiltration] *"or splenomegaly"*

- WBC count

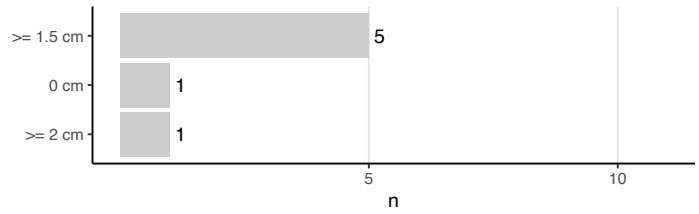


***** indicates alternate response provided by respondent in lieu of or in addition to available responses present in the survey

- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [ANC ≥ 1,000 cells/μL unless levels attributable to spleen involvement by DLBCL or unless levels attributable to bone marrow infiltration] *"Sufficient to give RCHOP, but if disease related cytopenias, then its fine to proceed on study"*
  - [Uncertain/prefer not to answer] *"addressed earlier"*

- [ANC ≥ 1,000 cells/μL unless levels attributable to spleen involvement by DLBCL or unless levels attributable to bone marrow infiltration] *“none - use the anc”*

- **Measurable disease on imaging**



  - Anonymized comments from participants (format: [selected response] *“comment”*):
    - [no quantitative response provided] *“Would not require measurable disease but rather PET assessable disease - for example if has extensive osseous lesions assessable by PET, these pts can be enrolled”*
    - [no quantitative response provided] *“optimal endpoint should be progression free survival, and not radiologic response to measurable disease. If disease can only be assessed by blood or marrow (and not on imaging), those patients should be enrolled and assessed as appropriate.”*
    - [no quantitative response provided] *“not clear; needed to determine extent of response”*
    - [no quantitative response provided] *“no; no limit. it's there or it's not.”*
    - [no quantitative response provided] *“If Phase 3 study and PFS or OS are endpoint then this seems unnecessary. If Phase 2 where primary endpoint is response then need to be able to visualize something. 1 cm should be adequate though. Why do they require 1.5 cm. Now that we have PET even subcm would be measurable.”*
    - [≥ 1.5 cm] *“needs measureable disease for response assessment”*
    - [no quantitative response provided] *“?”*
    - [≥ 1.5 cm] *“again should accommodate for patients with bony disease as you can measure response with Deauville”*
    - [no quantitative response provided] *“measureable disease not required”*
    - [no quantitative response provided] *“Measurable disease based on imaging is less pertinent in frontline DLBCl studies”*

DLBCL Eligibility Criteria – Preliminary Recommendations Survey
Anonymized Summary

Results

Descriptive statistics of participants

- **Total number of prospective participants emailed:** n = 17 (i.e., all Round 1 participants)
- **Total number of respondents:** n = 12
- **Response rate:** 12/17 = 70.6%
- **Institutions represented:** n = 7
- **Median number of years' experience as a hematologist/oncologist:** 18 (IQR = 8.25)

Results of survey: overall results

- **Demographic, clinical, and laboratory characteristics**: n = 15 criterion categories out of 31 total (48%)

Criterion category	Agree with recommendation	Percent in agreement
Age	11	92
Performance status	11	92
Minimum life expectancy	11	92
Measurable disease on imaging	10	83
IPI	12	100
Stage	7	58
Cardiac function	9	75
Hepatic function	11	92
Renal function	10	83
CNS involvement	11	92
Platelet count	9	75
White blood cell count	11	92
CD20 positivity	11	92
Cell-of-origin subtype	12	100
Central pathology review prior to enrollment	12	100

- **Cancer history:** n = 4 criterion categories out of 31 total (13%)

Criterion category	Agree with recommendation	Percent in agreement
Prior DLBCL treatment	11	92
History of transformed lymphoma	9	75
History of other malignancies	11	92

Participation in other study or treatment with other study drug	12	100

- **Non-cancer medical history:** n = 4 criterion categories out of 31 total (13%)

Criterion category	Agree with recommendation	Percent in agreement
History of stroke or intracranial hemorrhage	12	100
Peripheral neuropathy	12	100
Psychiatric illness	11	92
Presence of other significant, uncontrolled, concomitant disease at investigator's discretion	11	92

- **Infectious disease status:** n = 4 criterion categories out of 31 total (13%)

Criterion category	Agree with recommendation	Percent in agreement
HBV status	10	83
HCV status	11	92
HIV status	10	83
Active infection requiring systemic therapy	12	100

- **Reproductive health:** n = 4 criterion categories out of 31 total (13%)

Criterion category	Agree with recommendation	Percent in agreement
Female: contraception or abstinence	11	92
Pregnancy status	12	100
Breastfeeding status	12	100
Male: contraception or abstinence	11	92

Results of survey: anonymized results by individual criterion category (ordered according to median value)

- **Age at diagnosis**

  - Participants in agreement with preliminary recommendation: 11/12 (92%)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [No] *"In a theme that will likely be consistent throughout the survey, it will still be appropriate in some cases to tailor eligibility criteria to the hypothesis being tested. If the X in R-CHOP +X has the potential for increased toxicity and the expectation is that CHOP should be delivered at full doses, it may well be appropriate to put an upper age limit on eligibility. Although I do not wish to be labeled an ageist, nor do I wish to be naive to the increasing risk of therapy to patients with advanced age. I do not believe we can identify through surrogate eligibility criteria which 85 yo's can tolerate full dose R-CHOP."*
    - [Yes] *"Primary mediastinal should include less than 18"*

- **Performance status**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"I would probably include all ECOG 3, though my comments about age could be applied here as well if the proposed therapy were felt to be potentially toxic enough to be intolerable to PS 3."*

- **Minimum life expectancy**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"I don't think this is necessary. Other criteria (e.g., PS, labs, should suffice)"*

- **Measurable disease on imaging**

    - Participants in agreement with preliminary recommendation: 10/12 (83%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"why does it have to be 1.5 cm . A 1 cm PET+ node is easy to measure and follow."*
        - [Yes] *"I agree with the spirit. It could be stronger - perhaps no trial in 1L DLBCL should have ORR or CR as a primary endpoint"*
        - [Yes] *"I agree with this; should we also comment on evaluable disease?"*
        - [Yes] *"Primary endpoint for frontline DLBCL should not be response."*
        - [No] *"I think they should be eligible if eligible based on the response criteria used (e.g. Lugano 2014)"*

- **IPI score**

    - Participants in agreement with preliminary recommendation: 12/12 (100%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [Yes] *"IPI is easy, but it would be preferable to use individual components for eligibility."*

- **Ann Arbor stage**

    - Participants in agreement with preliminary recommendation: 7/12 (58%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [Yes] *"once concern is what to do with bulky patients as they typically are excluded from all studies"*
        - [No] *"what is difference between a pt with DLBCL with a 2 cm mesenteric and 2 cm R iliac node (stage 2) and a 10 cm mesenteric node (stage I). Why exclude stage I if including stage 2??"*
        - [No] *"As above, this depends upon the hypothesis being tested. There remains plenty of recently published literature that raises the question of late peril to those with stage I DLBCL. This entity in appropriate designs still deserves appropriate research."*
        - [No] *"very few stage II patients get RT. Depending on the trial design/situation, it may be reasonable to include stage II patients. Admittedly 4 cycles (rather than 6) may be used in some setting but would be flexible"*
        - [Yes] *"Favor these eligibility criteria, unless the trial is focused on patients with stage I disease. Most patients with stage I DLBCL have very favorable outcomes with standard therapy."*
        - [No] *"I think this depends on the study and type of therapy (escalation therapy? Deescalation therapy? elderly studies)"*
        - [No] *"depedms on the study question- in some studies need to analyze stage I"*

- **Cardiac function**

    - Participants in agreement with preliminary recommendation: 9/12 (75%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"too vague..."no active heart disease in the last 6 mo"...a pt in afib always has active heart disease....could say the same about someone with compensated CHF...they still have active heart disease...that sentence needs to go."*
        - [No] *"the criteria listed above - with the exception of EF - are not very precise and would be open to substantial variation in interpretation. (e.g. what are the cardiac contraindications to anthracycline use?)"*
        - [Yes] *"Active heart disease is very vague. I like "no cardiac contraindication" as this is a very subjective issue and depends on context"*
        - [Yes] *"I agree with this. I do not believe it is always standard or necessary to check EF prior to protocol enrollment. We do it in the US, but it is not a worldwide standard."*
        - [No] *"I think "no active heart disease" should fall under no cardiac contraindication to anthracycline"*

- **Hepatic function**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"I like the part that says to select thresholds based upon the specific therapies in the trial, but in some cases that might include even more liberal thresholds than proposed. Of course your thresholds are reasonable for CHOP-based regimens, but this survey seems to be bigger than just CHOP-based eligibility criteria - yes?"*
        - [Yes] *"To some degree this has to be defined by the study drug. None of these would exclude someone from RCHOP. So go with the higher level and then bring it down if the study drug requires."*
        - [Yes] *"The less than equal sign needs to be flipped to exclude patients with values greater than or equal to the values listed"*

- **Renal function**

    - Participants in agreement with preliminary recommendation: 10/12 (83%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"see answer for hepatic function"*
        - [Yes] *"Same answer as above. Recommend the most liberal threshold and then adjust based on the study drug."*
        - [Yes] *"R-CHOP is not really a problem with impaired renal function so any requirements depend on context/drugs involved"*
        - [Yes] *"Liberalizing the threshold for older participants is important."*
        - [Yes] *"CrCl is a more precise threshold. Cr <1.5-2 is too strict, unless the specific therapy requires excellent renal funcion."*
        - [Yes] *"The less than equal sign needs to be flipped to exclude patients with values greater than or equal to the values listed"*

- **CNS involvement by lymphoma**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [Yes] *"what if drug X is hypothesized to be magical for CNS disease? Although I see your point if you are saying R_CHOP should not be a control arm with known CNS disease."*
        - [No] *"I think this needs to be a bit more vague. E.g., no known CNS involvement. Otherwise we will be obliged to do extra testing on everyone with a risk factor."*
        - [Yes] *"We should not require scanning if the patient is not symptomatic."*

        - [Yes] *"No documented CNS involvement by lymphoma. However, testing for CNS lymphoma is not required for enrollment and should be performed only when based on clinical suspicion."*

- **Platelet count**

    - Participants in agreement with preliminary recommendation: 9/12 (75%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"If platelets are due to lymphoma infiltration in the marrow or spleen, I don't care what the platelet count is. "Treat em - and support em" If you're afraid to play hardball with the disease (not the patient - the disease) take your glove and go home"*
        - [No] *"This one should really be drug dependent and study phase dependent. Phase 1 will have to be more conservative. Phase 2 can be more liberal. Depends on cause of thrombocytopenia."*
        - [No] *"If low platelets are due to lymphoma, there should be no threshold count"*

- **White blood cell count**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"see answer regarding platelets."*

- **CD20 positivity**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"CD20 positivity should also be required if one of the non-investigational drugs is targeting CD20."*

- **Cell-of-origin subtype**

    - Participants in agreement with preliminary recommendation: 12/12 (100%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [Yes] *"As this is now part of the WHO lymphoma classification, I would expect at some point COO to be assessed in all trial participants."*

- **Central pathology review prior to enrollment**

    - Participants in agreement with preliminary recommendation: 12/12 (100%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [Yes] *"Should be done afterward"*

- **Prior DLBCL treatment**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [Yes] *"in spirit but needs more detail"*
        - [Yes] *"It's very helpful to enrollment to allow one previous cycle of chemotherapy."*
        - [Yes] *"Allowing 1 prior cycle of chemotherapy may be included or excluding at the investigator's discretion depending on the goals and target population of the protocol."*

        - [No] *"depending on the study, you could consider allowing one cycle of CHOP based therapy and starting study therapy at cycle 2 (to help facilitate referrals to academic sites and provide trials for patients admitted with lymphoma to OSH)"*

- **History of transformed lymphoma**

    - Participants in agreement with preliminary recommendation: 9/12 (75%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"would include discordant lymphoma, and patients with transformed lymphoma who had no previously been treated"*
        - [No] *"What is composite lymphoma. - that term is not really used very often...implies DLBCL nad FL (ex) in the same node)...that does not need to be specified. If pts with transformed lymphoma are eligible than that includes pts with composite lymphoma...this statement will just confuse people (especially CRAs)."*
        - [Yes] *"What about untreated indolent lymphoma (that is under observation)? Most of these patients should be included. Generally 6 month timeline used to differentiate between composite lymphoma."*

- **History of other malignancies**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"Pts with active prostate cancer under observation should be eligible. Also pts with active skin cancer!"*

- **Participation in other study or treatment with other investigational drug**

    - Participants in agreement with preliminary recommendation: 12/12 (100%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No comments provided by respondents]

- **History of stroke or intracranial hemorrhage**

    - Participants in agreement with preliminary recommendation: 12/12 (100%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No comments provided by respondents]

- **Peripheral neuropathy**

    - Participants in agreement with preliminary recommendation: 12/12 (100%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [Yes] *"may need to list grade. E.g., grade 1 allowed or something like that."*

- **Psychiatric illness**

    - Participants in agreement with preliminary recommendation: 11/12 (92%)
    - Anonymized comments from participants (format: [selected response] *"comment"*):
        - [No] *"Inability to comply with study protocols should be exclusion criterion, but not inability to participate in informed consent. Given the potential benefit of the study treatment, people with*

impaired decision making capacity should be allowed to enroll if a legally authorized representative consents on their behalf."

- **Presence of other significant, uncontrolled, concomitant disease at investigator's discretion**

  - Participants in agreement with preliminary recommendation: 11/12 (92%)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [No] *"Generally this is unnecessary. If I think someone can't do the study, then I don't screen them."*

- **HBV status**

  - Participants in agreement with preliminary recommendation: 10/12 (83%)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [No] *"it depends upon the therapy being tested"*
    - [Yes] *"May want to expect that it is controlled if present (e.g. on therapy)"*
    - [Yes] *"HBV testing should be performed prior to the administration of certain agents and part of standard of practice"*
    - [No] *"I think if the experimental therapy has risk of HBV reactivation, that should be considered in the eligibility criteria (or mandate entecavir)"*

- **HCV status**

  - Participants in agreement with preliminary recommendation: 11/12 (92%)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [Yes] *"May want to expect that it is controlled if present (e.g. on therapy)"*
    - [No] *"I think if the experimental therapy has risk of HBV reactivation, that should be considered in the eligibility criteria"*

- **HIV status**

  - Participants in agreement with preliminary recommendation: 10/12 (83%)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [No] *"uncontrolled HIV disease is still a dangerous disease to give R-CHOP to. Uncontrolled HIV deserves special attention in decision to be eligible or not depending - again on the therapeutic drugs being studied."*
    - [Yes] *"May want to expect that it is controlled if present (e.g. on therapy)"*
    - [Yes] *"If patients are on anti-retroviral therapy for HIV, there are many potential drug interactions which need to be considered."*
    - [Yes] *"HIV testing may need be performed as a part of lymphoma evaluation as a part of a standard of practice"*

- **Active infection requiring systemic therapy**

  - Participants in agreement with preliminary recommendation: 12/12 (100%)
  - Anonymized comments from participants (format: [selected response] *"comment"*):
    - [No comments provided by respondents]

- **Female: contraception or abstinence**

- Participants in agreement with preliminary recommendation: 11/12 (92%)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [No] *"This seems silly for eligibility always but should be discussed like we discuss concomitant medications. It seems there should always be an "alternative option" for contraception"*

- Pregnancy status

- Participants in agreement with preliminary recommendation: 12/12 (100%)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [No comments provided by respondents]

- Breastfeeding status

- Participants in agreement with preliminary recommendation: 12/12 (100%)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [Yes] *"May depend on study. E.g., device study would be ok."*

- Male: contraception or abstinence

- Participants in agreement with preliminary recommendation: 11/12 (92%)
- Anonymized comments from participants (format: [selected response] *"comment"*):
  - [No] *"This seems silly for eligibility always but should be discussed like we discuss concomitant medications. It seems there should always be an "alternative option" for contraception"*
