Feasibility of Using Positron Emission Tomography–Computed Tomography (PET-CT) Scans from Real-World Medical Record Data to Support Lymphoma Treatment Response Assessment

CO201

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INTRODUCTION

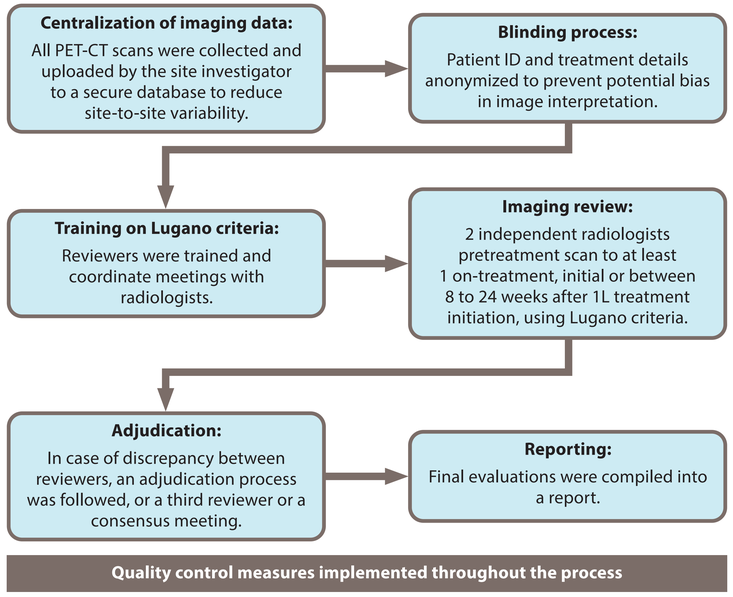
- Clinical outcome assessment criteria, such as RECIST v1.1 and Lugano 2014,[1] provide a standardized approach to assess treatment efficacy in clinical trials.
- Similar standardized methodologies for outcome classification may be applied to real-world clinical data.
- Blinded independent central review (BICR) is well-established and has been used in DLBCL clinical research and is critical to these assessment methodologies.[2]
- Radiologic assessments of patients with cancer performed outside the clinical trial setting are rarely reported using RECIST/Lugano criteria and do not undergo BICR.
- Real-world data (RWD) sources lack the required elements (e.g., BICR) for RECIST/Lugano response assessment, therefore surrogate effectiveness measures typically preclude direct comparisons between real-world evidence (RWE) and findings from clinical trials.[3]
- We explored the feasibility of performing BICR on positron emission tomography–computed tomography (PET-CT) scans in a retrospective RWD-cohort of patients with diffuse large B-cell lymphoma (DLBCL).

METHODS

Study Design

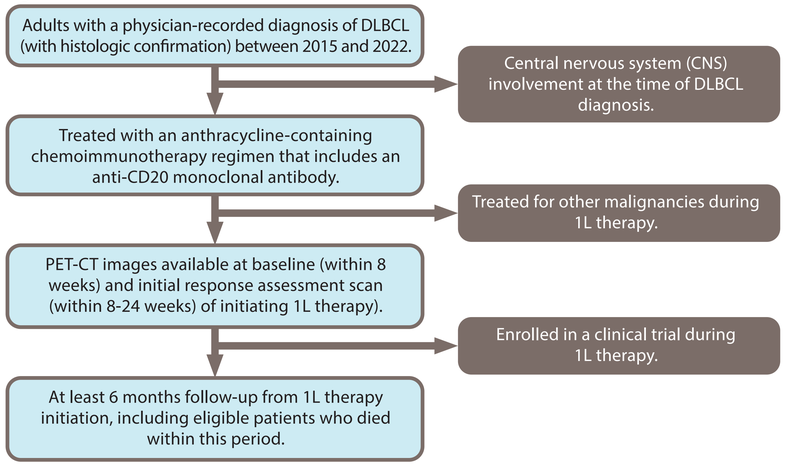
- A multicenter, retrospective chart review study conducted at 6 sites within the Cardinal Health Oncology Practice Research Network (PRN), a consortium of US-based community oncologists and hematologists.
- The study included patients ≥18 years old with physician-diagnosed, histologically confirmed, diffuse large B-cell lymphoma (DLBCL) treated with chemoimmunotherapy as first-line (1L) therapy.
- Each participating PRN site selected consecutive patients, starting with the earliest eligible, at each practice.
  - Data could be entered for up to 40 eligible patients from each site.
  - Deidentified data, including histopathology, were extracted from patient electronic medical records (EMRs), and captured via an electronic case report form (eCRF).
  - Digital PET-CT scans (1 baseline and 1 follow-up performed between 8 and 24 weeks following initiation of 1L therapy) were deidentified upon upload to a secure platform.
- All study materials were reviewed by a central Institutional Review Board.
- Study endpoints
  - CR (primary endpoint) – complete response
  - PR – partial response
  - SD – stable disease
  - PD – progressive disease
  - ORR – overall response rate

Figure 1. BICR Procedures



METHODS

Figure 2. Inclusion and Exclusion Criteria



Statistical Analysis

- Participating PRN sites abstracted clinical data derived from medical records, PET-CT reports, and digital images at treatment initiation and first response assessment.
- Deidentified images were uploaded for direct digital image evaluation via BICR adjudicated by 2 lymphoma radiologists using Lugano 2014 criteria to classify treatment response.
- A generalized linear mixed model (GLMM) with a logit link estimated the odds ratio (OR) of CR comparing physician-charted response to BICR, adjusting baseline characteristics such as provider ID, disease characteristics, stage at diagnosis, anemia, and heart disease.

RESULTS

- We identified 185 eligible patients with DLBCL across 7 PRN sites. PET-CT reports were readily available in every patient's medical record (N=185, 100%).
- Obtaining digital PET-CT images posed significant logistical challenges including submitting a request, frequently on a paper form, and waiting 1 to 2 weeks for scans to be sent.
  - We obtained baseline and follow-up scans for 178 (94%) patients, including 105 (59%) male and 73 (41%) female patients with mean age of 66 years as treatment initiation (**Table 1**)
  - 6 PRN sites participated in the study
- For initial response, physician-charted assignment of CR was 63.5%, compared to 83.1% CR assessed via BICR.
- A statistically significant difference was evident between physician-charted and BICR-assessed CR.
  - Compared to BICR, physician-charted responses had lower CR estimation (OR=0.23; 95% CI:0.12-0.43).

Table 1. Baseline patient demographic and clinical characteristics (N=178)

Participant characteristics	N=178
Age at first line treatment initiation (years), mean (SD)	66.5 (12.8)
Sex, n (%)	
Male	105 (59.0)
Female	73 (41.0)
Race, n (%)	
American Indian or Alaska Native	0 (0)
Asian	5 (2.8)
Black or African American	18 (10.1)
Native Hawaiian or Other Pacific Islander	0 (0)
White	137 (77.0)
Unknown	18 (10.1)
Ethnicity, n (%)	
Hispanic or Latino	13 (7.3)
Not Hispanic or Latino	143 (80.3)
Uknown	22 (12.4)
Duration of follow-up from 1L therapy initiation (months), median (P25-P75)	25.6 (16.8-43.8)
Ann Arbor stage at 1L therapy initiation among patients with known stage, n (%)	154 (86.5)
Stage I	24 (15.6)
Stage II	42 (27.3)
Stage III	38 (24.7)
Stage IV	50 (32.5)

RESULTS (CONTINUED)

- BICR classification of initial response per Lugano was concordant for CR for 155 (87%; k=0.67, 95%CI 0.53-0.79) scans and for 150 (84%) scans across all response categories CR/PR/SD/PD/Indeterminate) (**Tables 3 and 4**).
- All charts achieved concordance after adjudication with a 3rd party.

Table 3. BICR Agreement Between Radiologist 1 and Radiologist 2 for All Response Categories

Agreement between Radiologist 1 and Radiologist 2	Radiologist 2				
Radiologist 1	**CR**	**PR**	**SD/NR**	**PD**	**Indetermined**
CR	122	3	1	1	9
PR	6	20	1	1	1
SD/NR	1	1	2	0	0
PD	3	1	0	3	0
Indeterminate	0	0	0	0	3
Overall percent agreement (total concordance/total sample)	84.27%				

Table 4. ICR Agreement Between Radiologist 1 and Radiologist 2 for CR

Agreement between Radiologist 1 and Radiologist 2	Radiologist 2	
Radiologist 1	**CR**	**Non-CR**
CR	122	14
Non-CR	9	33

	Kappa/Percentage	95% CI-Lower Limit	95% CI-Upper Limit
Overall percent agreement (total concordance/total sample)	87.08%		
Kappa	0.656	0.527	0.785

CONCLUSIONS

- This study demonstrated that pairing manual chart abstraction with de-identified digital image transfer for BICR is challenging, yet feasible.
- Physician-charted manual assessment tended to underestimate the initial assessment of CR compared to BICR, demonstrating the importance of BICR research in the real-world setting.
- Such approaches may reduce outcome misclassification and increase comparability between RWD and clinical trial data.

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ACKNOWLEDGEMENTS

This project was supported by the Oncology Center of Excellence, Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) contract number **75F40121C00134** totaling $749,362 with 100 percent funded by FDA/HHS. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA/HHS, or the U.S. Government.

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Presented at ISPOR 2024 - The Professional Society for Health Economics and Outcomes Research
May 5-8, 2024
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