AJR Accepted Manuscript

Role of FDG PET/CT in Patients With Lymphoma Treated With CAR T-Cell Therapy: Current Concepts

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https://doi.org/10.2214/AJR.23.30301
Accepted: November 22, 2023
Article Type: Review
Article Section: Nuclear Medicine

The complete title page, as provided by the authors, is available at the end of this article.

Abstract

Chimeric antigen receptor (CAR) T-cell therapy is a cellular therapy in which the patient's T cells are enhanced to recognize and bind to specific tumor antigens. CAR T-cell therapy was initially developed for the treatment of leukemia, but its current main indication is the treatment of relapsed or refractory non-Hodgkin lymphoma. FDG PET/CT plays a fundamental role in the diagnosis, staging, therapy response assessment, and recurrence evaluation of patients with metabolically active lymphoma. Consistent with the examination's role in lymphoma management, FDG PET/CT is also the imaging modality of choice to evaluate patients before and after CAR T-cell therapy, and evidence supporting its utility in this setting continues to accumulate. In this article, we review current concepts in CAR T-cell therapy in patients with lymphoma, emphasizing the critical role of FDG PET/CT before and after therapy. A framework is presented that entails obtaining FDG PET/CT at four time points over the course of CAR T-cell therapy: two pre-therapy time points (at baseline at the time of decision to administer CAR T-cell therapy and after any bridging therapies) and two post-therapy time points (1 month and 3 months after infusion). PET parameters assessed at these time points predict various patient outcomes.

Recommended citation:
Murad V, Kohan A, Ortega C, Prica A, Veit-Haibach P, Metser U. Role of FDG PET/CT in Patients With Lymphoma Treated With CAR T-Cell Therapy: Current Concepts. *AJR* 2023 Dec 6 [published online]. Accepted manuscript. doi:10.2214/AJR.23.30301

Highlights

- FDG PET/CT is the imaging modality of choice for assessment before and after CAR-T cell therapy in patients with metabolically active lymphoma.
- High disease metabolic activity and high tumor burden on baseline FDG PET/CT predict worse patient outcomes.
- Unfavorable imaging parameters on the first post-therapy FDG PET/CT examination, performed 1 month after infusion, strongly predict short overall survival.

Introduction

Chimeric antigen receptor (CAR) T-cell therapy is an innovative cellular therapy based on the genetic modification of patient-derived T cells, initially developed for the treatment of refractory hematologic malignancies, but currently available for different types of cancers. To perform CAR T-cell therapy, the patient's T cells are extracted and enhanced in the laboratory by adding CARs, which are synthetic functional receptors artificially created from monoclonal antibodies targeting CD19 in non-Hodgkin lymphoma (NHL), CD30 in Hodgkin lymphoma (HL), or CD33 in acute myeloid leukemia (AML). The CARs are transfected into the patient's harvested T cells using viral vectors and function primarily to allow the T cells to recognize and bind to specific tumor antigens, even if those antigens are not presented by the major histocompatibility complex, thereby activating host immune cascades to attack tumor cells (Fig. 1) [1,2]. The complete manufacturing process for CAR T cells typically requires 9 to 14 days [3].

After the enhanced T cells are re-infused into the patient, the patient's CAR T-cell levels immediately begin to increase. The CAR T cells show local amplification between days 8-10 after infusion and redistribution to peripheral blood and other organs between days 10–21. As CAR T cells infiltrate the tumor, they produce swelling and edema within the tumor. These

effects become most pronounced between days 3-6, after which time responding patients begin to show tumor regression. Concurrent activation of the inflammatory cascade is characterized by significant increases in Interleukin (IL) levels (predominantly IL-2, IL-6 and IL-8), with peaks occurring around day 8 and day 12. Bone marrow function is initially decreased due to programmed depletion before the infusion, and recovery typically starts at days 10-12, with significant improvement by day 21 [1]. Accounting for all these changes, the risk for organ dysfunction from cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), or, rarely, macrophage activation syndrome (MAS), is greatest during the first week after infusion and decreases considerably beyond 15 days after infusion.

CAR T-cell therapy was initially developed for the treatment of leukemia [acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL)] [4,5]. In 2017, CAR T-cell therapy was approved for the treatment of relapsed or refractory (R/R) NHL in patients who had completed two or more lines of therapy, and R/R NHL is currently the therapy's main indication. This indication encompasses aggressive B-cell NHL, diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), transformed follicular lymphoma (FL), and mantle cell lymphoma [6]. Four different types of CAR T-cell therapies targeting CD19 antigen are currently approved in the United States [7], and two new CAR T-cell therapies for treatment of R/R multiple myeloma (MM) were approved in 2021 and 2022 [8] (**Table 1**). The use of CAR T-cell therapies continues to expand to an array of additional solid tumor types, based on emerging data supporting wider indications [9].

FDG PET/CT plays a fundamental role in the diagnosis, staging, therapy response assessment, and recurrence evaluation of patients with metabolically active lymphoma. Consistent with this role of FDG PET/CT in the management of patients with lymphoma, FDG PET/CT is the imaging test of choice for the evaluation and follow-up of patients undergoing CAR T-cell therapy, and evidence supporting its utility in this setting continues to accumulate. At

present, standard guidelines or practice parameters that clearly define the timing to perform FDG PET/CT before and after CAR-T cell therapy are lacking. Nonetheless, available data support a recommendation to perform FDG PET/CT at four specific time points during the course of CAR-T cell therapy, including two pre-therapy and two post-therapy time points (**Fig. 2**).

In this article, we review current concepts in CAR T-cell therapy in patients with lymphoma, emphasizing the critical role of FDG PET/CT before and after therapy.

Role of Pre-Therapy FDG PET/CT

Two FDG PET/CT examinations should be obtained before CAR T-cell infusion, one at the time of the decision to administer CAR T-cell therapy (providing a new baseline study) and the other after completion of bridging therapy (i.e., any treatments, including steroids, systemic therapy, or radiotherapy, administered between T-cell harvesting and CAR T-cell infusion). Biopsy is also often performed at the time of the decision, to confirm that the patient still harbors aggressive lymphoma as had been diagnosed before earlier therapies. In some institutions, CD19 status is also assessed at the time of the decision, although this assessment is not a requirement to determinate eligibility for CAR T-cell therapy. The baseline FDG PET/CT examination at the time of the decision has important roles in predicting patient outcomes, identifying patients who will most strongly benefit from CAR T-cell therapy, and selecting patients for aggressive bridging therapy.

Studies indicate that the presence of disease with high metabolic activity on baseline FDG PET/CT examination is an independent risk factor for shorter overall survival (OS), that a higher tumor burden predicts early relapse, and that lower tumor burden predicts longer OS and progression-free survival (PFS) [7,10-14]. For example, in a sample of 48 patients, Cohen et al.

[10] reported that an SUV_{max} > 17.1 at the time of decision and an SUV_{max} > 12.1 before CAR T-cell infusion were both associated with shorter OS (P < .05). In addition, in a sample of 96 patients with DLBLC treated with CAR T-cell therapy, Dean et al. [11] found that patients with lower metabolic tumor volume (MTV; i.e., the volume of hypermetabolic tissue having an SUV greater than a defined threshold) had significantly better OS (HR, 0.25; 95% CI) and PFS (HR, 0.40; 95% CI). Vercellino et al. observed similar results in a sample of 48 patients, again showing that high MTV was associated with early relapse [12]. Moreover, in a sample of 56 patients with large B-cell lymphoma evaluated before CAR T-cell infusion, Marchal et al. [13] found that MTV was an independent prognostic factor for PFS (p < .001). Those investigators additionally found that the distance separating the two farthest lesions on FDG PET/CT (standardized by the patient's body surface area, described as D_{max}) was an independent prognostic factor for OS (p = .008). Finally, in 59 patients who underwent CAR T-cell therapy for large B-cell lymphoma, Ababneh et al. [14] reported that a low total lesion glycolysis (TLG) at baseline predicted a better overall response after therapy (OR = 9.5, p = .03), and that high pre-therapy TLG was associated with cytokine release syndrome (OR = 3.25, p = .04).

Baseline FDG PET/CT parameters obtained at the time of decision have also shown a role in predicting the development of treatment-related complications. In a sample of 41 patients treated with CAR T-cell therapy for R/R NHL, Hong et al. [15] found that baseline SUV average (SUV_{avg}) and baseline TLG were independent risk factors for the development of CRS (OR: 1.481, p = .034), and that patients with higher baseline MTV, TLG, and SUV_{avg} experienced higher-grade CRS (p < .001). Likewise, in 19 patients with NHL, Wang et al. [16] found that higher baseline tumor burden as defined by MTV and TLG was associated with more severe CRS (P = .008 for MTV; P = .011 for TLG). Finally, in 10 patients treated with CAR T-cell therapy for R/R DLBCL, Derlin et al. [17], reported that higher baseline SUV_{max} was associated with increased risk of developing neurotoxicity (P = .0489),

The second FDG PET/CT examination, performed between bridging therapy and CAR T-cell infusion, is important because the achievement of adequate disease control before CAR T-cell infusion is associated with longer PFS [18]. Bridging therapy seeks to reduce tumor burden before infusion in order to improve clinical outcomes. The decision to proceed with bridging therapy is individualized for each patient and considers baseline tumor burden, number, and types of prior lines of therapy, and the expected time to CAR T-cell infusion. A complete or partial response to bridging therapy is reported to confer a 42% reduction in risk of progression or death after CD19 CAR T-cell therapy [19]. In a sample of 72 patients, Sesques et al. [20], observed a mean PFS of 6.8 months in patients with low tumor burden after bridging therapy, as measured by MTV and TLG, in comparison with a mean PFS of 2.7 months in patients with high tumor burden. In our experience, the FDG PET/CT examination performed after bridging therapy may also help to identify organ-threatening complications that could be of concern during CAR T-cell therapy, such as impending renal or bowel obstruction and possible development of leptomeningeal disease. To our knowledge, strict criteria are lacking to exclude patients from receiving CAR T-cell infusion after bridging therapy, since trials and real-world evidence have demonstrated that even patients with progressive disease at this time point can benefit from CAR T-cell therapy. Nonetheless, certain findings of organ compromise (e.g., bowel invasion with high risk for perforation; new active CNS involvement) may exclude individual patients from CAR T-cell infusion.

Role of Post-Therapy FDG PET/CT

The two post-therapy FDG PET/CT examinations should be obtained at 1 month and 3 months after CAR T-cell infusion. The initial post-therapy FDG PET/CT examination is used to classify patients as showing response (decrease in lesions size and/or FDG uptake); non-response (lack of complete metabolic response, observed in up to 40% of patients); and failure

(progression or relapse). Treatment failure is classified as early or late depending on if the failure is observed within or after the first 90 days after treatment [21, 22]. Imaging parameters that are most commonly used in this setting to guide FDG PET/CT interpretation include SUV_{max} and the Deauville score (DS), assigned on a 1-5 scale. To determine a lesion's DS, the lesion's degree of FDG uptake is visually compared with uptake in the mediastinal blood pool (MBP) and in the liver **(Table 2)**. Once a DS is assigned, this score is compared with the highest DS on the prior examination, to classify the type of response based on the Lugano classification **(Table 3)** [23]. A reduction in SUV_{max} of less than 66%, or persistent lesion FDG uptake greater than that of the liver (i.e., DS 4 or 5), are considered to represent an unfavorable response [24, 25]. Image acquisition and processing parameters should be standardized to improve measurements' reproducibility. Additionally, when using new-generation PET/CT scanners, which have high sensitivity and improved detection of small-volume lesions, the number of new lesions may be more predictive than changes in existing lesions' SUV [26].

Multiple studies have demonstrated the impact of performing the first follow-up FDG PET/CT examination at 1 month after infusion, supporting 1 month as the preferable time point for initial response assessment that may prompt an early therapeutic intervention [7,27-31]. In one study, the presence of unfavorable parameters on FDG PET/CT performed 1 month after infusion was the strongest predictor of short OS [10]. In a study of 170 patients, Kuhn et al. [27] found that patients achieving early metabolic complete response (DS 1or 2) had excellent long-term outcomes, whereas patients with persistent lesions having DS 4 had a 31% risk for early relapse. In addition, an SUV_{max} threshold of 10 may help predict partial response and stable disease rather than progressive disease [27]. A further study of 69 patients who underwent FDG PET/CT 1 month after CAR T-cell infusion included a sub analysis of 28 patients in whom the 1-month follow-up examination showed stable disease or partial response [28]. Twelve of these 28 patients subsequently progressed. Among the 28 patients, progressive disease was observed in

86% of those in whom the 1-month FDG PET/CT showed residual lesions with SUV_{max} > 10, versus in 36% of those in whom the 1-month FDG PET/CT showed lesions with SUV_{max} ≤10. In a study of 204 patients with large B-cell lymphoma, Al Zaki et al. [29] found that a low SUV_{max} on the 1-month FDG PET/CT predicted conversion of partial response or stable disease to complete response ($p < .001$), and that all patients with SUV_{max} ≥ 10 at 1 month progressed. Also, a study of 7 patients suggested that only patients without residual MTV on the 1-month FDG PET/CT continued to show complete metabolic response for more than 2 years after treatment [30]. Finally, in a study of 75 patients receiving CAR T-cell therapy for large B-cell lymphoma, Lutfi et al. [31] demonstrated that both a lower SUV_{max} and a lower TMV at 1 month predicted favorable PFS and OS.

The 3-month follow-up FDG PET/CT is used mainly to determine early therapeutic efficacy by assessing for stability in patients with complete response at 1 month, as well as for improved response over time in the absence of additional therapies in patients with a partial response at 1 month. In a study of 275 patients [32], Nastoupil et al. found that 32% of 93 patients with a partial response at 1 month achieved a complete response at 3 months without further treatment. In a study of 10 patients with aggressive B-cell lymphoma [33], all four patients with a favorable response at 1 month and who underwent further follow-up evaluation without additional treatment showed complete response at 3 months.

The 3-month FDG PET/CT examination is also useful to identify possible therapy-related complications. Complications at this time point are most commonly infectious, occurring in approximately 17% and 11% of patients with prolonged cytopenia and neutropenia, respectively [34]. Approximately 42% and 33% of patients experience at least one infection during the first 3 months and 6 months after therapy, respectively, with such infections being most commonly respiratory in nature (1) (Fig. 3).

Response Patterns and Pseudoprogression

Typical metabolic response patterns after CAR T-cell infusion include complete response (Fig. 4), partial response (Fig. 5), stable disease, and disease progression (Fig. 6). Sanmamet et al. [35] evaluated the relationship between serum IL-8 levels and response on 1-month FDG PET/CT after CAR T-cell therapy, finding an association between high IL-8 levels and true early progression. In that study, 14 of 56 patients showed an unfavorable response on FDG PET/CT performed 7-10 days after the infusion. Of those 14 patients, 11 showed definitive progression on day 30, whereas 3 showed complete response; IL-8 levels remained high throughout the follow-up period in all patients with true early progression, but began to decline after day 14 in responders.

In addition to the typical metabolic response patterns, the pseudoprogression phenomenon, defined by an initial increase in tumor volume with or without new lesions, followed by a definitive decrease in tumor burden [36], has also been described [38-40]. This phenomenon has been previously recognized in association with other therapies, mainly immune checkpoint inhibitors, and causes challenges in image interpretation that require close follow-up imaging in order to distinguish tumor sites, inflammation, and real disease progression [37]. Although the cause of pseudoprogression remains incompletely understood, it is believed to represent a sudden potentiated immune response with infiltration of both tumor lesions and other organs.

The few case reports to date of pseudoprogression after CAR T-cell therapy all occurred during the first 7-9 days after therapy and were associated with a complete response on the 1-month follow-up examination [38, 39, 40]. These observations highlight the importance of understanding CAR T-cell biology to optimize the timing of follow-up FDG PET/CT examinations and further support obtaining the first follow-up examination 1 month after infusion.

Conclusion

FDG PET/CT is the imaging modality of choice for assessment before and after CAR T-cell therapy in patients with metabolically active lymphoma. High disease metabolic activity and high tumor burden on baseline FDG PET/CT are predictors of worse patient outcomes. The preferable time point to initially assess therapy response and determine the need for additional therapeutic intervention is 1 month after infusion; use of this time point helps to avoid misinterpretation of apparent metabolic progression that may result from a potentiated immune response as instead representing true disease progression.

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Table 1. Different types of CAR T-cell therapies with regulatory approval in the United States and Europe.

Agent	**Month of Regulatory Approval**	**Associated Malignancy**
Tisagenlecleucel (Kymriah)	August 2017	Adult R/R large B-cell lymphoma; pediatric and young adult R/R B-cell precursor acute lymphocytic leukemia
Axicabtagene ciloleucel (Yescarta)	October 2017	Adult R/R large B-cell lymphoma; adult R/R follicular lymphoma
Brexucabtagene autoleucel (Tecartus)	July 2020	Adult R/R B-cell precursor acute lymphocytic leukemia; adult R/R mantle cell lymphoma
Lisocabtagene maraleucel (Breyanzi)	February 2021	Adult R/R large B-cell lymphoma
Idecabtagene vicleucel (Abecma)	March 2021	Adult R/R multiple myeloma
Ciltacabtegene autoleucel (Carvykti)	February 2022	Adult R/R multiple myeloma

CAR = chimeric antigen receptor; R/R = relapse/recurrent

Table 2. Détermination of Deauville score on FDG PET/CT

Deauville score	Definition
1	No uptake or no residual uptake
2	Slight uptake, but equal to or below blood pool uptake
3	Uptake above mediastinal uptake, but below or equal to uptake in the liver
4	Uptake slightly to moderately higher than uptake in the liver
5	Markedly increased uptake or any new lesion

Table 3. Response assessment in lymphoma based on Deauville score (DS; assessed on 5-point scale).

Type of Response	Definition
mCR	DS 1, 2 or 3, regardless of persistent lesions on CT, in the absence of FDG-avid bone marrow lesions.
mPR	DS 4 or 5 but uptake decreased compared with baseline and no morphologic progression.
mST	DS 4 or 5 without significant change in FDG uptake from baseline and no morphologic progression.
mPD	DS 4 or 5 with: increasing intensity compared to baseline or interim scan and/or any new FDG-avid malignant lesion.

mCR = metabolic complete response; mPR = metabolic partial response; mSD = stable disease; mPD = metabolic progressive disease.

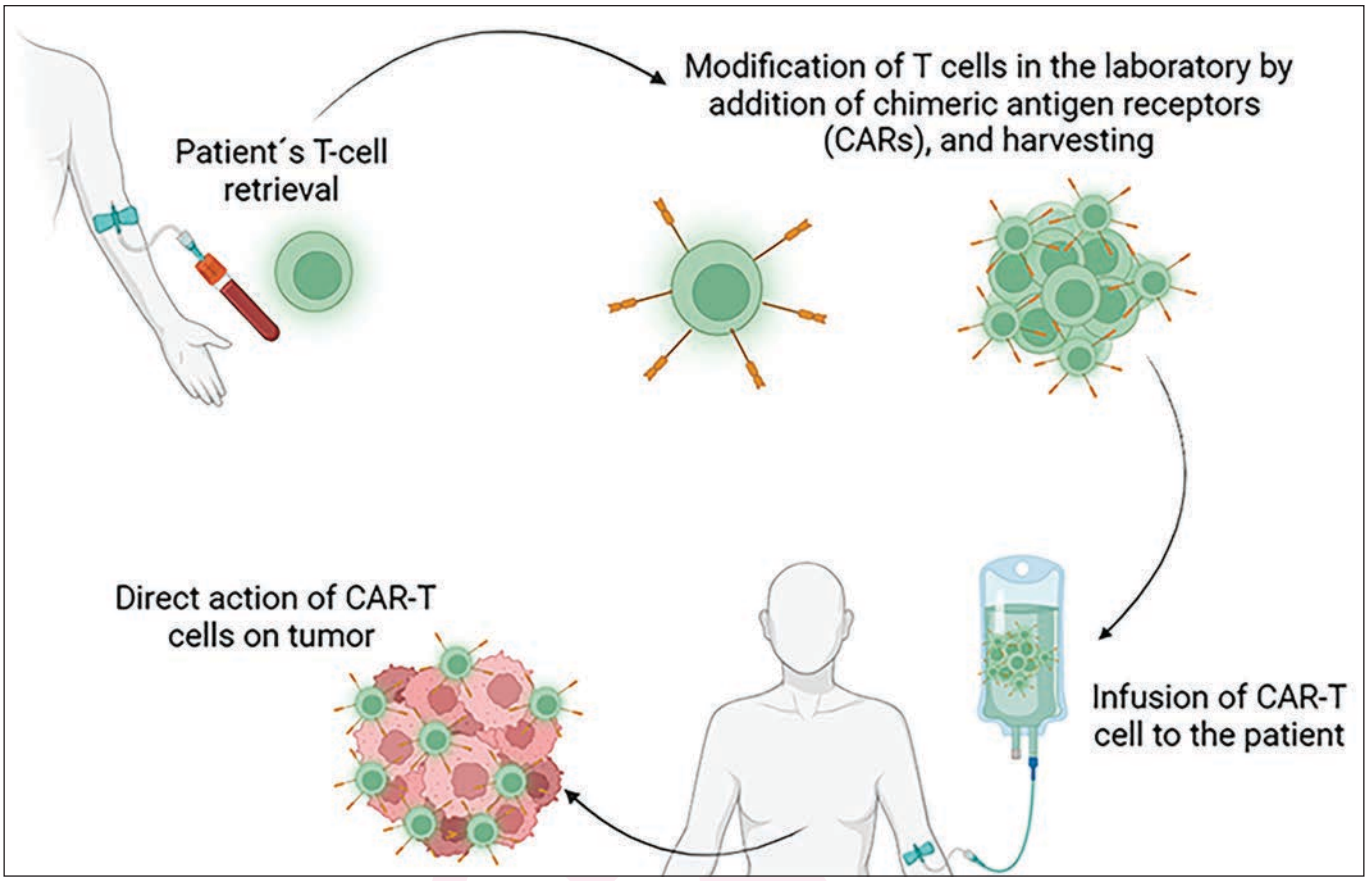


Figure 1. Basic principle of chimeric antigen receptor (CAR) T-cell therapy. T cells are retrieved from patient and modified in laboratory by adding CARs. Once harvested, enhanced T cells are re-infused to patient. These cells activate host immune cascades to attack tumor cells by recognizing and binding directly to specific tumor antigens.

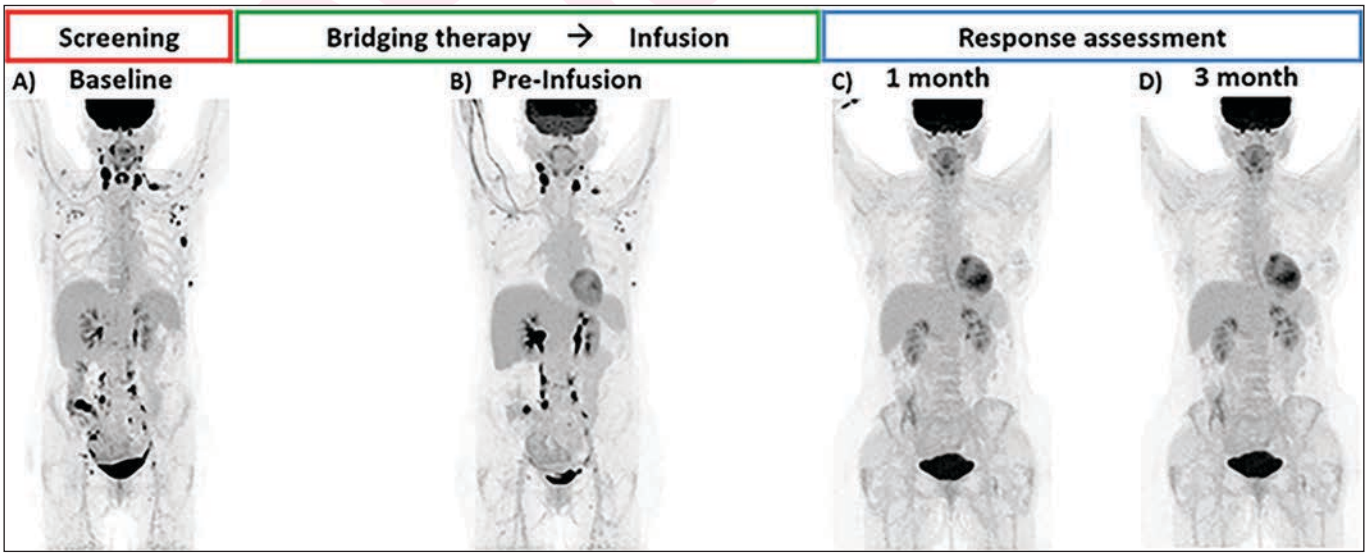
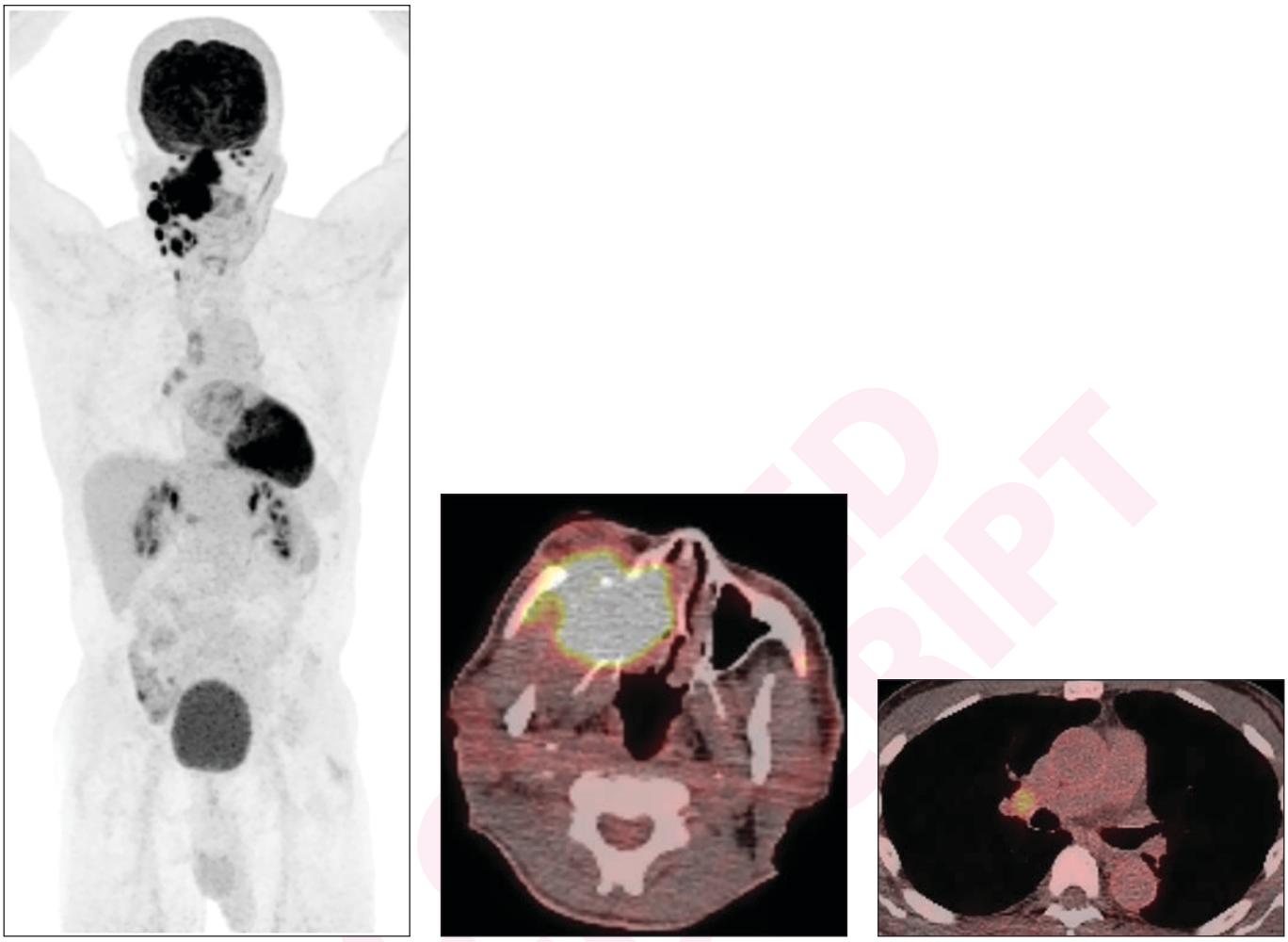


Figure 2. Recommendations for timing of FDG PET/CT examinations over course of chimeric antigen receptor (CAR) T-cell therapy. FDG PET/CT is currently recommended at four specific time points: two before therapy [at baseline at the time of decision to administer CAR T-cell therapy (A) and after bridging therapy (B)] and two after therapy [at 1 month (C) and 3 months (D) after infusion].



A B C

Figure 3. 48-year-old patient with relapsed diffuse large B-cell lymphoma. (A-C) Baseline FDG PET/CT examination at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A), axial fused image at level of mid face (B), and axial fused image at level of mid chest (C). Images show large mass with intense metabolic activity mass involving right orbit and paranasal cavities, as well as several metabolically active right neck lymph nodes (Deauville score 5). Also present are few right paratracheal and right hilar lymph nodes with mild metabolic activity, initially suggestive of different disease process. (D-F) FDG PET/CT examination, performed 1 month after CAR T-cell infusion. Coronal MIP PET image (D), axial fused image at level of mid face (E), and axial fused image at level of mid chest on soft tissue window (F). Images show evidence of interval complete metabolic response with significant morphologic response of lymphomatous involvement in right orbit, paranasal cavities, and neck lymph nodes (Deauville score 2). However, images also show multiple new metabolically active lymph nodes above and below diaphragm. Diagnostic considerations at this time point included infectious process (e.g., sarcoidosis, tuberculosis) versus disease progression. Patient underwent endobronchial ultrasound-guided biopsy, indicating diagnosis of sarcoidosis. (G-I) FDG PET/CT examination, performed 3 months after CAR T-cell infusion. Coronal MIP PET image (G), axial fused images at level of mid face (H), as well as axial fused image at level of mid chest on soft tissue window (I). Images show evidence of sustained complete metabolic response of lymphomatous involvement, with persistent infectious or inflammatory lymphadenopathy, despite treatment.

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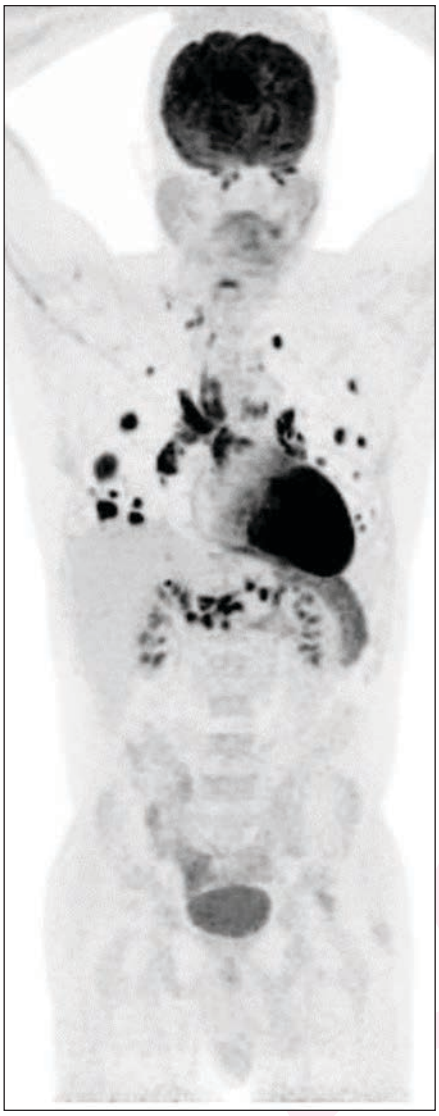

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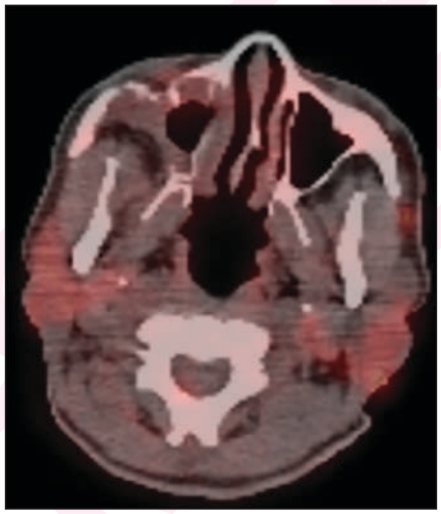

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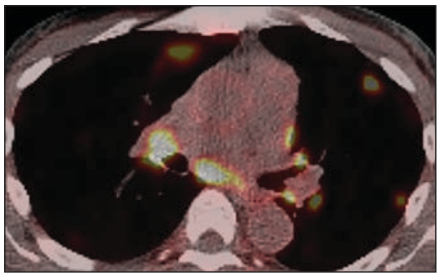

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Figure 3 (continued). 48-year-old patient with relapsed diffuse large B-cell lymphoma. (A-C) Baseline FDG PET/CT examination at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A), axial fused image at level of mid face (B), and axial fused image at level of mid chest (C). Images show large mass with intense metabolic activity mass involving right orbit and paranasal cavities, as well as several metabolically active right neck lymph nodes (Deauville score 5). Also present are few right paratracheal and right hilar lymph nodes with mild metabolic activity, initially suggestive of different disease process. (D-F) FDG PET/CT examination, performed 1 month after CAR T-cell infusion. Coronal MIP PET image (D), axial fused image at level of mid face (E), and axial fused image at level of mid chest on soft tissue window (F). Images show evidence of interval complete metabolic response with significant morphologic response of lymphomatous involvement in right orbit, paranasal cavities, and neck lymph nodes (Deauville score 2). However, images also show multiple new metabolically active lymph nodes above and below diaphragm. Diagnostic considerations at this time point included infectious process (e.g., sarcoidosis, tuberculosis) versus disease progression. Patient underwent endobronchial ultrasound-guided biopsy, indicating diagnosis of sarcoidosis. (G-I) FDG PET/CT examination, performed 3 months after CAR T-cell infusion. Coronal MIP PET image (G), axial fused images at level of mid face (H), as well as axial fused image at level of mid chest on soft tissue window (I). Images show evidence of sustained complete metabolic response of lymphomatous involvement, with persistent infectious or inflammatory lymphadenopathy, despite treatment.

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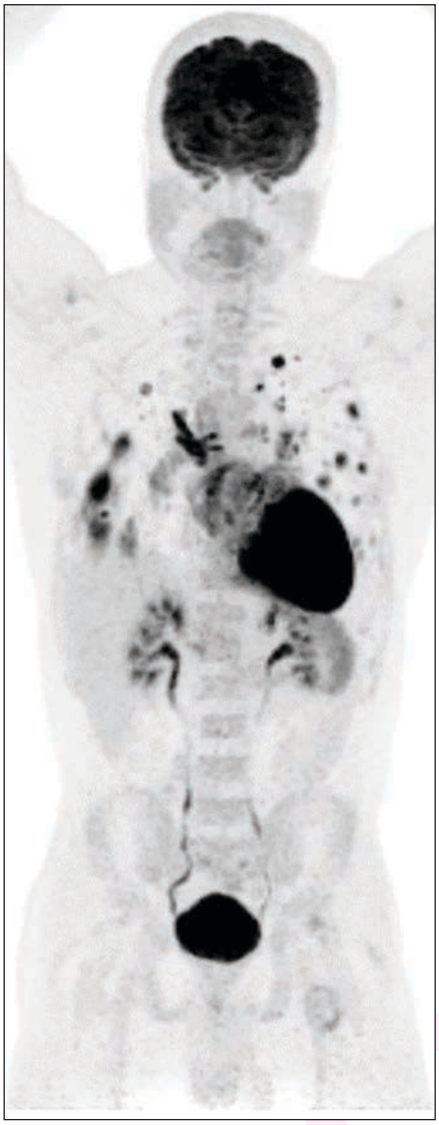

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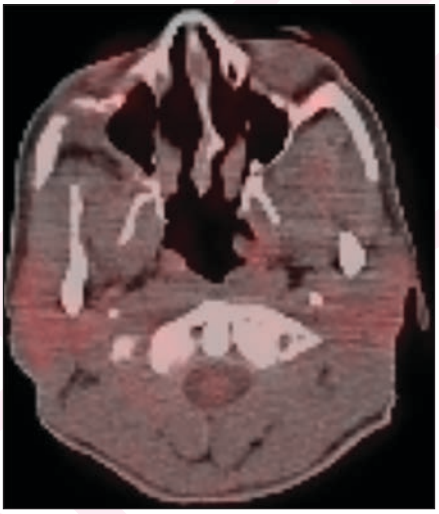

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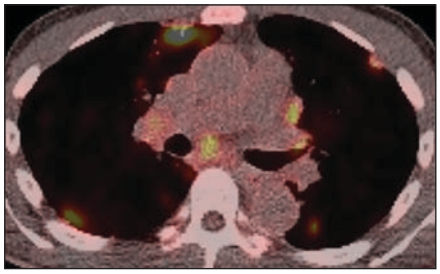
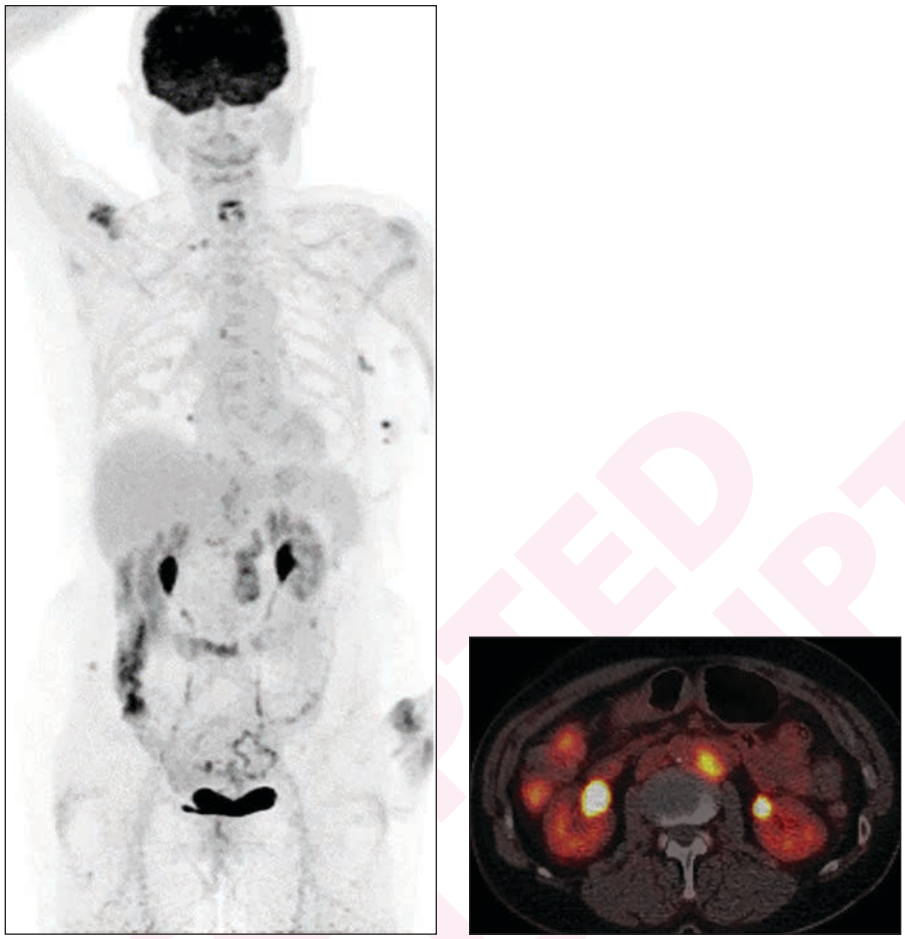


I

Figure 3 (continued). 48-year-old patient with relapsed diffuse large B-cell lymphoma. (A-C) Baseline FDG PET/CT examination at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A), axial fused image at level of mid face (B), and axial fused image at level of mid chest (C). Images show large mass with intense metabolic activity mass involving right orbit and paranasal cavities, as well as several metabolically active right neck lymph nodes (Deauville score 5). Also present are few right paratracheal and right hilar lymph nodes with mild metabolic activity, initially suggestive of different disease process. (D-F) FDG PET/CT examination, performed 1 month after CAR T-cell infusion. Coronal MIP PET image (D), axial fused image at level of mid face (E), and axial fused image at level of mid chest on soft tissue window (F). Images show evidence of interval complete metabolic response with significant morphologic response of lymphomatous involvement in right orbit, paranasal cavities, and neck lymph nodes (Deauville score 2). However, images also show multiple new metabolically active lymph nodes above and below diaphragm. Diagnostic considerations at this time point included infectious process (e.g., sarcoidosis, tuberculosis) versus disease progression. Patient underwent endobronchial ultrasound-guided biopsy, indicating diagnosis of sarcoidosis. (G-I) FDG PET/CT examination, performed 3 months after CAR T-cell infusion. Coronal MIP PET image (G), axial fused images at level of mid face (H), as well as axial fused image at level of mid chest on soft tissue window (I). Images show evidence of sustained complete metabolic response of lymphomatous involvement, with persistent infectious or inflammatory lymphadenopathy, despite treatment.



A B

Figure 4. 69-year-old woman with refractory diffuse large B-cell lymphoma. (A,B) Baseline FDG PET/CT examination performed at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A) and axial fused image (B). Images show several metabolically active lymph nodes above and below diaphragm, including right supraclavicular, right internal mammary, cardiophrenic, upper abdominal, and retroperitoneal lymph nodes (which are most FDG-avid nodes). Examination was assessed as Deauville score 4. (C,D). FDG PET/CT examination performed 1 month after infusion. Coronal MIP PET image (C) and axial fused image (D). Images show evidence of complete metabolic resolution at all nodal sites of disease (Deauville score 2).

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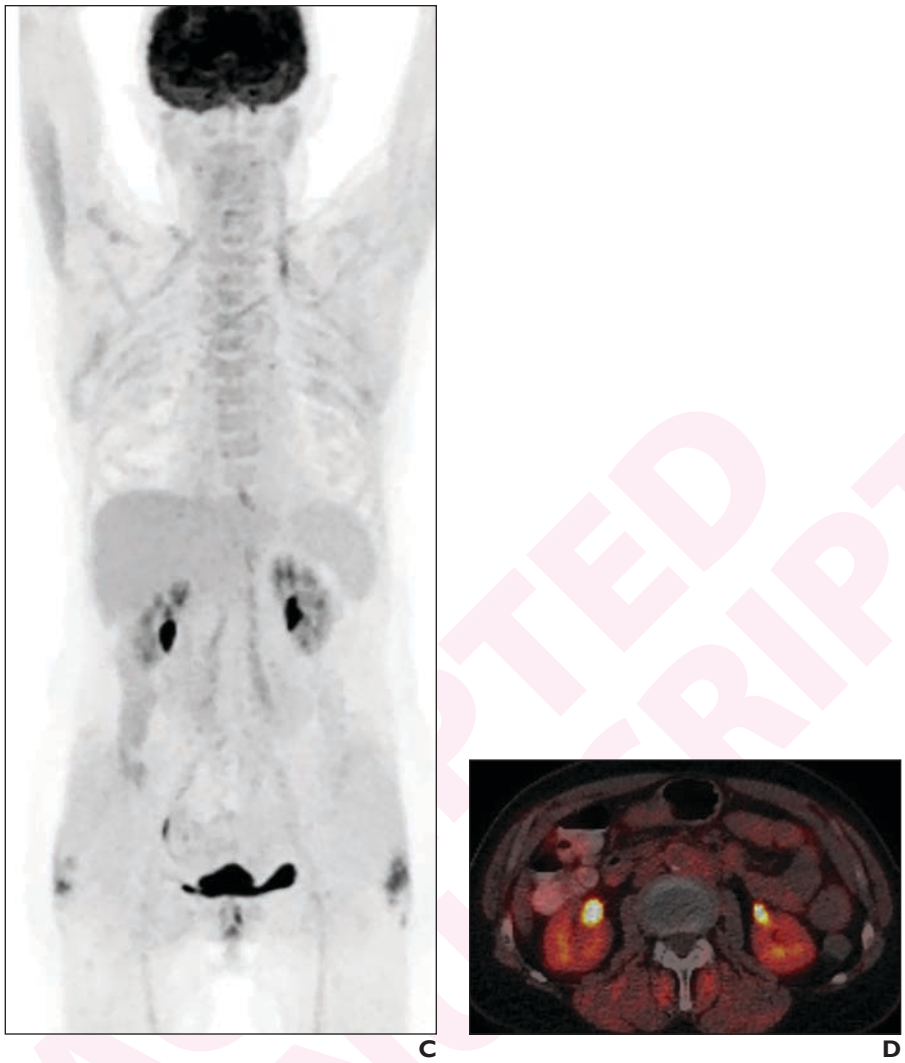
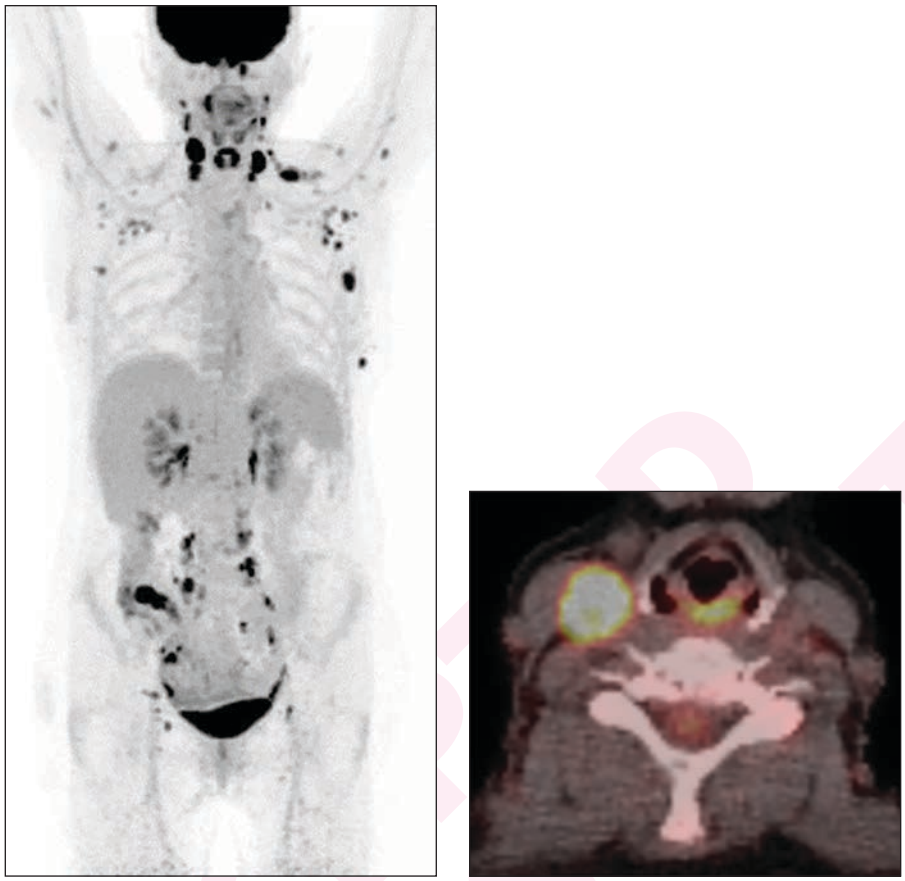


C D

Figure 4 (continued). 69-year-old woman with refractory diffuse large B-cell lymphoma. (A,B) Baseline FDG PET/CT examination performed at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A) and axial fused image (B). Images show several metabolically active lymph nodes above and below diaphragm, including right supraclavicular, right internal mammary, cardiophrenic, upper abdominal, and retroperitoneal lymph nodes (which are most FDG-avid nodes). Examination was assessed as Deauville score 4. (C,D). FDG PET/CT examination performed 1 month after infusion. Coronal MIP PET image (C) and axial fused image (D). Images show evidence of complete metabolic resolution at all nodal sites of disease (Deauville score 2).



A B

Figure 5. 60-year-old patient with relapsed diffuse large B-cell lymphoma. (A,B) Baseline FDG PET/CT examination performed at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A) and axial fused image (B) at level of neck, showing multiple metabolically active lymph nodes above and below diaphragm involving neck, supraclavicular fossae, axillae, retroperitoneum, both iliac chains, and both inguinal regions (Deauville score 5). Distal ileum also showed focal increased FDG uptake, without definitive CT correlate. (C,D) FDG PET/CT examination performed 3 weeks after completing bridging therapy. Coronal MIP PET image (C) and axial fused image at level of neck (D) show interval partial metabolic response, with persistent metabolically active nodal involvement on both sides of diaphragm and in distal ileum (Deauville score 5). (E,F) FDG PET/CT examination performed 1 month after CAR-T cell infusion. Coronal MIP PET image (E) and axial fused image at level of neck (F) show further metabolic partial response with interval resolution of most of sites of disease, although with few persistent metabolically active lymph nodes in right neck (Deauville score 4). Images also show interval development of focal FDG uptake at tip of peripherally inserted central catheter, which was confirmed to correspond to partial thrombosis. (G,H) FDG PET/CT examination performed 3 months after CAR-T cell infusion. Coronal MIP PET image (G) and axial fused image at level of neck (H) show interval complete metabolic response of residual lymph nodes in neck (Deauville score 2).

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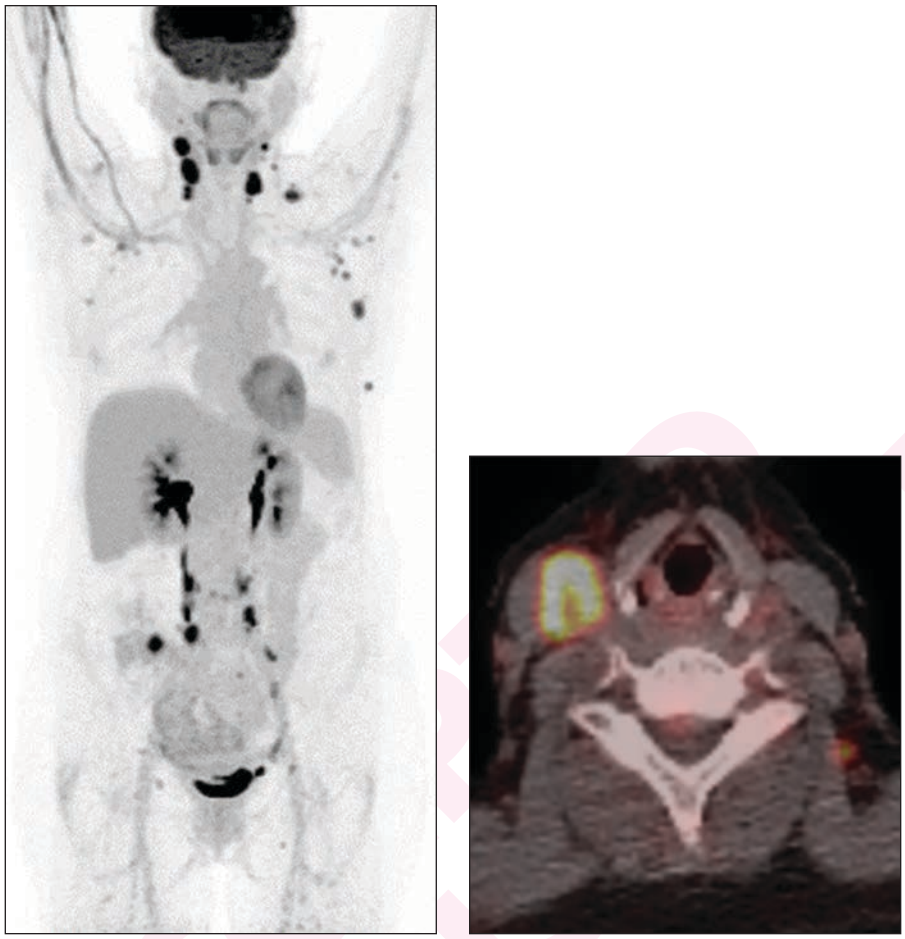

C D

Figure 5 (continued). 60-year-old patient with relapsed diffuse large B-cell lymphoma. (A,B) Baseline FDG PET/CT examination performed at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A) and axial fused image (B) at level of neck, showing multiple metabolically active lymph nodes above and below diaphragm involving neck, supraclavicular fossae, axillae, retroperitoneum, both iliac chains, and both inguinal regions (Deauville score 5). Distal ileum also showed focal increased FDG uptake, without definitive CT correlate. (C,D) FDG PET/CT examination performed 3 weeks after completing bridging therapy. Coronal MIP PET image (C) and axial fused image at level of neck (D) show interval partial metabolic response, with persistent metabolically active nodal involvement on both sides of diaphragm and in distal ileum (Deauville score 5). (E,F) FDG PET/CT examination performed 1 month after CAR-T cell infusion. Coronal MIP PET image (E) and axial fused image at level of neck (F) show further metabolic partial response with interval resolution of most of sites of disease, although with few persistent metabolically active lymph nodes in right neck (Deauville score 4). Images also show interval development of focal FDG uptake at tip of peripherally inserted central catheter, which was confirmed to correspond to partial thrombosis. (G,H) FDG PET/CT examination performed 3 months after CAR-T cell infusion. Coronal MIP PET image (G) and axial fused image at level of neck (H) show interval complete metabolic response of residual lymph nodes in neck (Deauville score 2).

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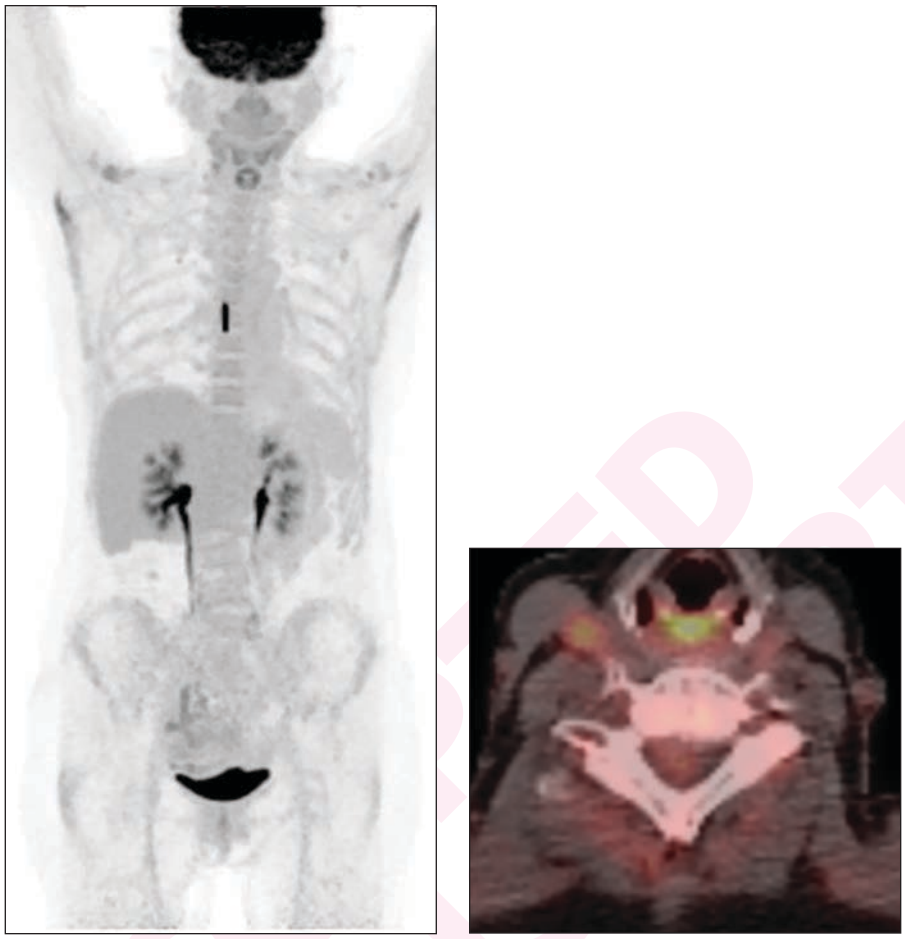

E F

Figure 5 (continued). 60-year-old patient with relapsed diffuse large B-cell lymphoma. (A,B) Baseline FDG PET/CT examination performed at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A) and axial fused image (B) at level of neck, showing multiple metabolically active lymph nodes above and below diaphragm involving neck, supraclavicular fossae, axillae, retroperitoneum, both iliac chains, and both inguinal regions (Deauville score 5). Distal ileum also showed focal increased FDG uptake, without definitive CT correlate. (C,D) FDG PET/CT examination performed 3 weeks after completing bridging therapy. Coronal MIP PET image (C) and axial fused image at level of neck (D) show interval partial metabolic response, with persistent metabolically active nodal involvement on both sides of diaphragm and in distal ileum (Deauville score 5). (E,F) FDG PET/CT examination performed 1 month after CAR-T cell infusion. Coronal MIP PET image (E) and axial fused image at level of neck (F) show further metabolic partial response with interval resolution of most of sites of disease, although with few persistent metabolically active lymph nodes in right neck (Deauville score 4). Images also show interval development of focal FDG uptake at tip of peripherally inserted central catheter, which was confirmed to correspond to partial thrombosis. (G,H) FDG PET/CT examination performed 3 months after CAR-T cell infusion. Coronal MIP PET image (G) and axial fused image at level of neck (H) show interval complete metabolic response of residual lymph nodes in neck (Deauville score 2).

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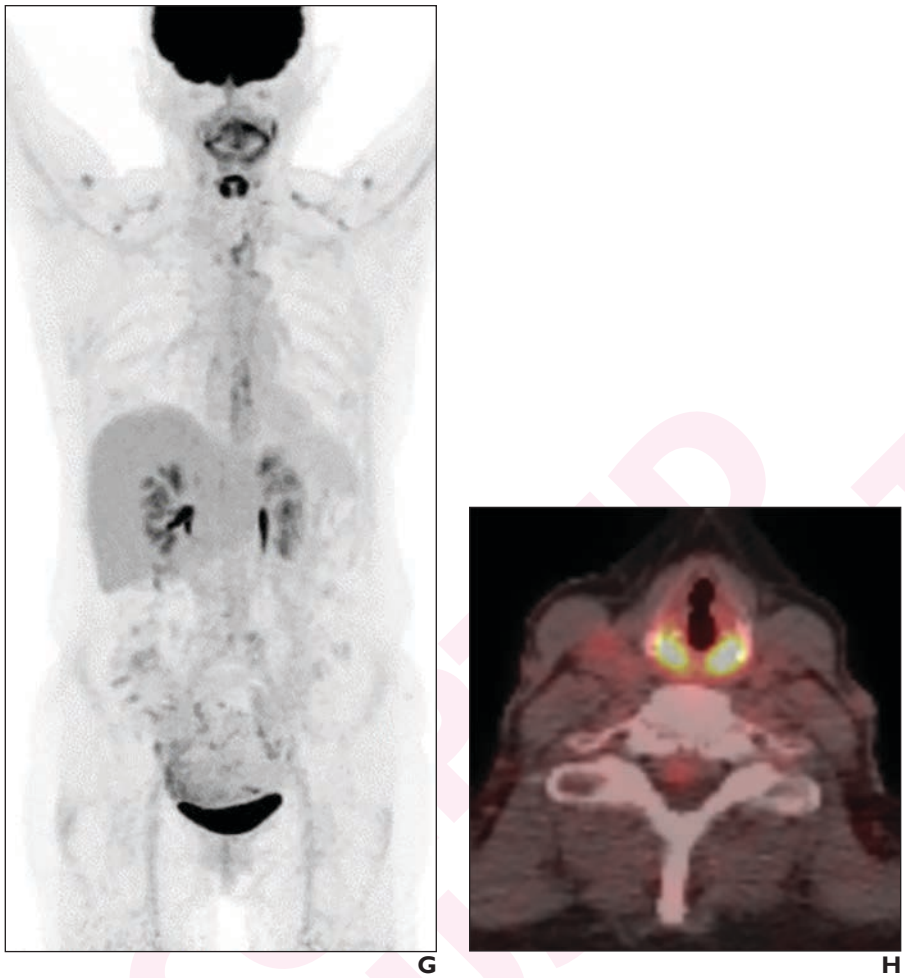

G H

Figure 5 (continued). 60-year-old patient with relapsed diffuse large B-cell lymphoma. (A,B) Baseline FDG PET/CT examination performed at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Coronal maximum intensity projection (MIP) PET image (A) and axial fused image (B) at level of neck, showing multiple metabolically active lymph nodes above and below diaphragm involving neck, supraclavicular fossae, axillae, retroperitoneum, both iliac chains, and both inguinal regions (Deauville score 5). Distal ileum also showed focal increased FDG uptake, without definitive CT correlate. (C,D) FDG PET/CT examination performed 3 weeks after completing bridging therapy. Coronal MIP PET image (C) and axial fused image at level of neck (D) show interval partial metabolic response, with persistent metabolically active nodal involvement on both sides of diaphragm and in distal ileum (Deauville score 5). (E,F) FDG PET/CT examination performed 1 month after CAR-T cell infusion. Coronal MIP PET image (E) and axial fused image at level of neck (F) show further metabolic partial response with interval resolution of most of sites of disease, although with few persistent metabolically active lymph nodes in right neck (Deauville score 4). Images also show interval development of focal FDG uptake at tip of peripherally inserted central catheter, which was confirmed to correspond to partial thrombosis. (G,H) FDG PET/CT examination performed 3 months after CAR-T cell infusion. Coronal MIP PET image (G) and axial fused image at level of neck (H) show interval complete metabolic response of residual lymph nodes in neck (Deauville score 2).

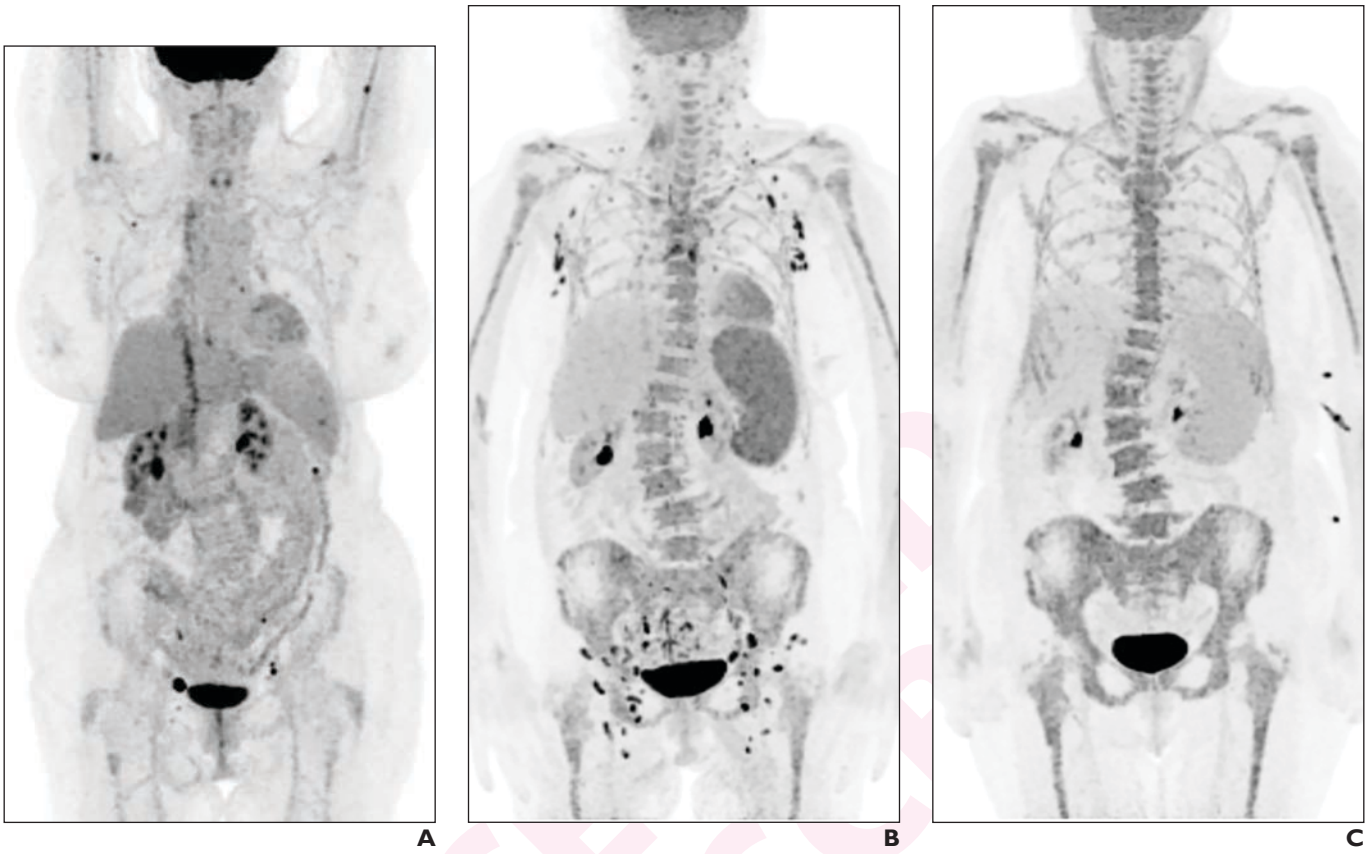

Figure 6. 77-year-old patient with history of refractory diffuse large B-cell lymphoma. (A) Coronal maximum intensity projection (MIP) PET image from baseline FDG PET/CT examination, performed at time of decision to administer chimeric antigen receptor (CAR) T-cell therapy. Image shows several metabolically active, small-volume lymph nodes in axillae and pelvis, as well as couple of peritoneal nodules in left upper quadrant and couple of skeletal deposits in proximal humeri (Deauville score 5). (B) Coronal MIP PET image from FDG PET/CT examination performed 1 month after CAR-T cell infusion. Image shows interval disease progression with development of multiple metabolically active lymph nodes on both sides of diaphragm, as well as new splenic involvement (Deauville score 5). However, image also shows interval resolution of peritoneal and skeletal deposits. Treatment was subsequently modified by adding Bendamustine and Rituximab. (C) Coronal MIP PET image from FDG PET/CT examination performed 1 month after treatment modification shows interval complete metabolic response at all sites of disease (Deauville score 2).

AJR

Role of FDG PET/CT in Patients With Lymphoma Treated With CAR T-Cell Therapy: Current Concepts

Review article.

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Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Conflict of interests: The authors declare no relevant financial or non-financial interests relevant for this manuscript.