CXCR4-directed PET/CT in 100 patients with Marginal Zone Lymphoma – Superior diagnostic performance, Predictive Potential and Eligibility for CXCR4-directed Endoradiotherapy

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Journal of Nuclear Medicine June 2023, 64 (supplement 1) P23;

Abstract

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Introduction: We aimed to determine the diagnostic performance of CXCR4-directed PET/CT when compared to guideline-compatible work-up in patients with marginal zone lymphoma (MZL; including gastrointestinal endoscopy [GIE], bone marrow-derived biopsy [BMB] and CT-based Ann Arbor classification). We also assessed predictive potential of CXCR4 PET signal and evaluated the portion of patients eligible for CXCR4-directed endoradiotherapy (ERT) in a theranostic approach.

Methods: 100 MZL patients underwent CXCR4-directed PET/CT. A visual and quantitative assessment was conducted (total number of volume of interests, 686), including mean/maximum/peak standardized uptake values [$SUV_{mean/max/peak}$], tumor volume (TV) CXCR4 fractional tumor activity (CXCR4-FTA, defined as TV x SUV_{mean}). We then evaluated the diagnostic performance of CXCR4-directed imaging relative to guideline-compatible work-up and evaluated the prognostic performance of CXCR4-PET for progression-free survival (PFS). We also determined the rate of patients which would be eligible for a CXCR4-directed ERT (based on intensity and widespread disease).

Results: On a patient-based level, CXCR4-directed PET was positive in 78/100 (78%). Quantitative results were as follows: SUV_{mean}, 5.20 (range 0.68-22.09); SUV_{max}, 9.35 (2.53-44.90); SUV_{peak}, 5.07 (1.32-26.31); TV, 23.22 (0.60-934.0) and FTA, 142.2 (1.74-7522.0). Relative to CT, CXCR4-directed imaging led to an upstaging in 48/100 (48%, with Ann Arbor re-classification from I/II to III/IV in 14/48 [29%]), no change in 51/100 (51%) and downstaging in the remaining subject (1/100 [1%]). Moreover, in 59 cases in whom GIE was available, CXCR4 PET/CT yielded concordant findings (59/63 [94%]; discordant, 4/63 [6%]). Comparable results were recorded for comparing PET/CT with 60 available BMB (concordant, 46/60 [77%]; discordant, 14/60 [23%]). In CXCR4 PET/CT positive patients, increased CXCR4-FTA (median 165.6 ml) was linked to decreased PFS (716 days vs. median PFS not reached; HR of progress = 2.25 [95%CI = 0.96–5.30]; P= 0.07). CXCR4-directed ERT would have been feasible in 15/100 (15%).

Conclusions: Relative to CT, CXCR4-directed PET/CT led to an upstaging in 48%, in particular for the clinically relevant re-classification from Ann Arbor I/II to III/IV, thereby potentially triggering change in therapeutic management. Increased PET-derived FTA may also be linked to shorter PFS. In a theranostic approach, 15% of patients would have been eligible for CXCR4-directed ERT.