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NCCN Guidelines Panel: B-Cell Lymphomas

I used to be an Associate Professor of Radiation Oncology on the Lymphoma Service at the MD Anderson Cancer Center in Houston, TX. Between 2010 and 2015, I served as a radiation oncologist on the Kidney and Testicular Cancer Panel Member for the NCCN. Since 2002, I have helped to write exam questions and served as an oral board examiner under the leukemia/lymphoma category for the American Board of Radiology (ABR). In an ABR teleconference yesterday, several radiation oncologists who write exam questions on non-Hodgkin lymphomas for the ABR expressed the hope that the NCCN will expand its Principles of Radiation Therapy recommendations for definitive radiation therapy for indolent B-cell lymphomas involving the orbit.

Orbital lymphoma patients have a low tumor burden and are more likely to experience complications from radiotherapy such as a dry eye,[1] particularly if they have Sjögren syndrome.[6] Stafford et al.[9] reported a 52% rate of acute complications, with doses ranging from 19 to 48 Gy in the treatment of lymphoma of the ocular adnexa. Kaushik et al.[10] investigated the risk of retinopathy in 67 patients with orbital non-Hodgkin lymphomas treated with conventional-dose radiation therapy to the entire orbit and found 12% of their patients developed radiation retinopathy. Only patients who received at least 20 Gy developed radiation retinopathy. These studies[9, 10] highlight cases of orbital toxicity that occurred with the use of doses as low as 19 Gy. It is also worth noting that a short course of low-dose radiotherapy offers greater patient convenience.[6]

On behalf of Oncology Analytics Inc, I respectfully request that the NCCN B-Cell Lymphomas Panel review the enclosed data for inclusion of "2 Gy x 2 fractions" as a definitive treatment option for orbital follicular lymphoma (FL), marginal zone lymphoma (MZL) and early-stage mantle cell lymphoma (MCL) under Principles of Radiation Therapy on page NHODG-D 3 of 4.

Specific Changes: Under "Definitive treatment (1.5-2.0 Gy daily fractions)," please include "2 Gy x 2 fractions" as an option for **orbital** FL, MZL and early-stage MCL. Currently, the NCCN Guidelines recommend definitive treatment with "24-30 Gy" for FL and MZL and "24-36 Gy" for early-stage MCL, with no anatomic site specified for the dose recommendations. The NCCN Guidelines only recommend the use of 2 Gy x 2 fractions for FL/MZL/MCL/SLL under "Palliative RT" on page NHODG-D 3 of 4.

FDA Clearance: Not applicable.

Rationale: Literature in the 1970s and 1980s suggested that radiation doses <20 Gy using conventional fractionation may be inadequate for primary orbital lymphoma. For example, Foster et al.[2] reported local recurrence in 5 of 33 orbital lymphoma patients who received doses < 12.6 Gy. In contrast, in a study by Mittal el al.,[3] all patients who received at least 20 Gy experienced local control.

However, literature from medical centers such as Stanford and MD Anderson that involves modern radiotherapy techniques supports the proposed 2 Gy x 2 fractions.[4-7] Two Gy × 2 fractions is effective in the definitive treatment of indolent non-Hodgkin lymphomas involving the orbit, with 85-100%

complete response rates, 0-14% partial response rates, 96-100% overall response rates and a 2-year freedom-from-regional relapse rate within the ipsilateral orbit of 96%.[4-7] Also, 2 Gy x 2 fractions is well-tolerated, with only mild (grade 1) acute side effects, i.e., dry eye, conjunctivitis or transient periorbital edema in 0-30% of treated sites, without any reports of long-term toxicity.[4-7] Patients who are initially treated with 2 Gy x 2 fractions can be re-irradiated with 2 Gy x 2 fractions in the unlikely event of a locoregional relapse in the orbit. Radiation therapy with higher dose-fractionation schemes, such as 2 Gy x 12 fractions, remains the standard-of-care for definitive treatment of indolent B-cell lymphomas involving non-orbital sites.[8]

References:

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Sincerely,

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