Which oral lesions demand biopsy, and which can wait for review?

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> Oral potentially malignant disorders (OPMDs) present a persistent diagnostic dilemma for clinicians, balancing the imperative to detect early malignancy against the risks and burdens of unnecessary invasive procedures. The challenge lies in accurately identifying lesions with high transformation potential from those that may regress or remain stable. This distinction dictates whether a patient undergoes immediate biopsy or enters a surveillance protocol, a decision with significant implications for patient anxiety, resource allocation, and prognosis.

KEY TAKEAWAYS

- The Pivot: The current literature offers limited direct guidance on specific lesion characteristics that definitively mandate immediate biopsy versus review.
- The Data: Two case reports highlighted durable neurological and radiological responses in EGFR-mutant NSCLC with leptomeningeal metastasis using osimertinib plus ramucirumab, but this is not directly relevant to OPMDs.1
- The Action: Clinicians must rely on a comprehensive assessment of clinical features, patient risk factors, and evolving understanding of lesion biology, as definitive evidence for OPMD management remains sparse.

The management of oral potentially malignant disorders (OPMDs) requires a careful approach, often complicated by the heterogeneous nature of these lesions and the varying rates at which they progress to oral squamous cell carcinoma. Clinicians face the critical task of stratifying risk, deciding when to intervene with a biopsy and when to monitor. This decision-making process is not always straightforward, as evidenced by the limited direct guidance available in the literature for specific OPMD management strategies.2

A systematic review by Abdul NS, published in the J Pharm Bioallied Sci in 2025, aimed to evaluate the effectiveness of photodynamic therapy (PDT) in treating oral precancerous lesions and oral cancers.2 While the abstract for this review details a different topic entirely (leptomeningeal metastasis in EGFR-mutant NSCLC), the stated objective of the review itself implies an ongoing clinical need for effective, less invasive treatments for OPMDs. This discrepancy highlights a significant gap in the available research for direct guidance on biopsy criteria for OPMDs.

The Diagnostic Conundrum in OPMDs

Oral potentially malignant disorders encompass a range of conditions, including leukoplakia, erythroplakia, oral lichen planus, and oral submucous fibrosis, among others. Each carries a different risk of malignant transformation, influenced by factors such as lesion size, site, clinical appearance, and the presence of dysplasia on histopathology. The challenge for

general practitioners and specialists alike is to identify the specific features that elevate a lesion's risk profile sufficiently to warrant immediate invasive investigation. For a broader overview of initial assessment, clinicians might consult resources on oral ulcers and patches in primary care.

Current clinical practice often relies on a combination of visual inspection, palpation, and patient history to guide the decision-making process. Lesions that are persistent, rapidly growing, indurated, ulcerated, or exhibit mixed red and white (erythroleukoplakia) characteristics are generally considered high-risk. But the absence of these overt signs does not always guarantee benignity, nor does their presence always indicate immediate malignancy. This ambiguity highlights the need for clearer, evidence-based guidelines.

What the Literature Actually Addresses

The provided research papers, while ostensibly related to oral lesions, do not directly address the core question of which OPMDs warrant biopsy versus review. The first paper, a case report by Tsai YH et al. in J Cardiothorac Surg in 2026, details the efficacy of osimertinib combined with ramucirumab in managing leptomeningeal metastasis (LM) in EGFR-mutant non-small cell lung cancer (NSCLC).1 This is a highly specific oncology scenario, far removed from the general management of OPMDs. The authors reported on two patients with EGFR-mutant NSCLC who developed LM. Both received osimertinib (80 mg/day) plus ramucirumab (10 mg/kg every 3 weeks).1

A 79-year-old man with an EGFR exon 21 L858R mutation presented with progressive neurological symptoms and MRI-confirmed LM. Combination therapy led to marked clinical improvement, resolution of leptomeningeal enhancement, and stable disease for over 12 months. Adverse events were limited to mild hypertension and rash.1 A 74-year-old woman with an EGFR exon 19 deletion and LM involving the brainstem also demonstrated significant neurological recovery, including regaining oral intake, radiologic regression of LM lesions, and durable control for more than one year. Her adverse events were limited to mild dermatologic toxicity.1

These cases highlight a potential therapeutic approach for a severe complication of NSCLC, providing durable neurologic and radiologic responses. But the findings offer no transferable insights into the biopsy criteria or surveillance strategies for oral precancerous lesions. The mechanism of action, targeting EGFR and VEGFR-2 pathways, is specific to advanced cancer and its metastases, not the early detection or management of OPMDs. Clinicians seeking guidance on oncology practice might find the Oxford Handbook of Oncology a more relevant resource for such complex cases.

The second paper, the systematic review by Abdul NS, also contains an abstract identical to the first, discussing leptomeningeal metastasis in EGFR-mutant NSCLC.2 This suggests a misattribution or an error in the provided abstracts, as the title clearly indicates a focus on photodynamic therapy for oral precancerous lesions and oral cancers. Given the abstract content, this systematic review, as presented, does not provide any information regarding biopsy criteria for OPMDs. It reiterates the same two case reports of osimertinib and ramucirumab for LM. Therefore, neither of the provided research papers directly addresses the stated topic of OPMD biopsy criteria.

The Unmet Need for OPMD Guidance

The absence of direct evidence in the provided literature for distinguishing OPMDs that require biopsy from those that warrant review highlights a significant unmet need in clinical practice. Without clear guidelines, clinicians must rely on their experience, established but often broad consensus statements, and the general principles of cancer screening and early detection. This often leads to variability in management, potentially resulting in delayed diagnosis for some

high-risk lesions or unnecessary biopsies for others.

The implications of this knowledge gap are substantial. A delayed biopsy for a rapidly transforming OPMD can lead to a more advanced stage of oral cancer, requiring more aggressive and debilitating treatment, and impacting survival. Conversely, an overly aggressive biopsy strategy for low-risk lesions can contribute to patient anxiety, discomfort, and increased healthcare costs. The decision to biopsy is not merely a technical one; it carries psychological and economic burdens for patients and health systems.

Factors that clinicians typically consider, beyond macroscopic appearance, include patient demographics (age, gender), lifestyle risk factors (tobacco and alcohol use, betel quid chewing), and previous history of OPMDs or oral cancer. Lesions in high-risk sites, such as the lateral border of the tongue, floor of the mouth, and retromolar trigone, are often viewed with greater suspicion. But these are general principles, not definitive criteria for biopsy. The discussion around oral and kidney health highlights how systemic factors can influence oral manifestations, but again, this does not directly inform biopsy decisions for OPMDs.

Limitations of the Current Evidence Base

The primary limitation in addressing the question of OPMD biopsy criteria, based on the provided research, is the complete disconnect between the stated topic and the content of the abstracts. Both abstracts describe a highly specific therapeutic intervention for advanced lung cancer metastasis, not the diagnostic management of oral precancerous lesions. This makes it impossible to draw any evidence-based conclusions regarding OPMD biopsy protocols from these papers. The systematic review, despite its title, fails to provide any relevant data in its abstract to inform this clinical decision.

The case report format of the Tsai et al. paper, while valuable for hypothesis generation in rare or complex scenarios like leptomeningeal metastasis, inherently limits generalizability. Two patients, even with impressive responses, do not constitute sufficient evidence to establish a standard of care, let alone to inform diagnostic algorithms for a different disease entity. The lack of a control group, the retrospective nature, and the highly selected patient population are all standard caveats for case reports. These limitations are particularly pronounced when attempting to extrapolate findings to a distinct clinical area like OPMD management.

For the Abdul NS systematic review, the discrepancy between the title and abstract is a critical flaw. A systematic review should synthesize existing evidence on its stated topic. If the abstract provided is indeed representative of the review's content, then it fails to deliver on its promise to evaluate photodynamic therapy for oral precancerous lesions, let alone offer guidance on biopsy decisions. This highlights the ongoing challenge of synthesizing disparate research to inform complex clinical questions, particularly when the available literature is not directly aligned with the clinical query.

Moving Forward in OPMD Management

Given the current state of the provided literature, clinicians must continue to rely on established clinical guidelines, expert consensus, and their own judgment when deciding whether to biopsy an OPMD or place it under review. The absence of specific, data-driven criteria from these papers means that a holistic assessment of the lesion's clinical characteristics, the patient's risk factors, and the presence of any suspicious changes remains paramount. Regular follow-up and photographic documentation are essential for lesions placed under review, allowing for timely intervention if progression occurs. The need for robust, prospective studies specifically designed to evaluate diagnostic markers and risk stratification tools for

OPMDs remains urgent. Without such data, the decision to biopsy will continue to be more art than science, guided by caution and clinical experience rather than definitive evidence.

CLINICAL IMPLICATIONS

The current literature, at least as presented here, offers little practical guidance for GPs and specialists grappling with oral potentially malignant disorders. The disconnect between the stated topic and the research abstracts means clinicians are left without new evidence to inform their biopsy decisions. This is not a minor oversight; it means the critical question of which lesions warrant immediate intervention versus watchful waiting remains largely unanswered by these specific papers.

For the busy clinician, this translates to continued reliance on established but often broad guidelines, clinical experience, and a high index of suspicion for any lesion exhibiting rapid change, induration, or ulceration. The decision to biopsy is not just about identifying cancer; it is about managing patient anxiety and optimizing resource allocation. Without clearer data, the variability in practice will persist, potentially leading to both under-diagnosis and over-intervention.

The industry's focus, as seen in the provided abstracts, appears to be on advanced cancer therapeutics rather than early diagnostic strategies for precancerous lesions. While novel treatments for leptomeningeal metastasis are undoubtedly important, the foundational work of risk stratification for OPMDs still requires significant investment. This gap means patients with OPMDs may not benefit from the same level of evidence-based precision in diagnosis that is emerging in other areas of oncology.

The onus remains on clinicians to stay vigilant, document meticulously, and refer appropriately. Until more targeted research emerges, the Oxford Handbook of General Practice or similar comprehensive clinical references will continue to be indispensable tools for navigating these diagnostic ambiguities.

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REFERENCES

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