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Original Research

Diversity of brain metastases screening and management in non-small cell lung cancer in Europe: Results of the European Organisation for Research and Treatment of Cancer Lung Cancer Group survey☆

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Abstract ***Background:*** Brain metastases (BM) are frequent in non-small cell lung cancer (NSCLC) patients, but there is a lack of evidence-based management of this patient group. We aimed to capture a snapshot of routine BM management in Europe to identify relevant research questions for future clinical trials.

Methods: An EORTC Lung Cancer Group (LCG) online survey containing questions on NSCLC BM screening and treatment was distributed between 16/02/17 and 15/06/17 to worldwide EORTC LCG members, and through several European scientific societies in the thoracic oncology field.

Results: A total of 462 European physician responses (394 institutions) were analysed (radiation oncologist: 53% [n = 247], pulmonologist: 26% [n = 119], medical oncologist: 18% [n = 84]; 84% with >5 years' experience in NSCLC). Italy (18%, n = 85), Netherlands (15%, n = 68), UK (14%, n = 66), and France (12%, n = 55) contributed most. 393 physicians (85%) screened neurologically asymptomatic patients for BM at diagnosis (52% using magnetic resonance imaging). Most often screened patients were those with a driver mutation (MUT+; 51%, n = 234), stage III (63%, n = 289), and IV (43%, n = 199). 158 physicians (34%) used a prognostic classification to guide initial treatment decisions, and in 50%, lowest prognostic-score threshold to receive treatment differed between MUT+ and non-driver mutation (MUT−) patients. MUT+ patients with >4 BM were more likely to receive stereotactic radiosurgery (SRS) compared with MUT− (27% versus. 21%; $p < 0.01$). Most physicians (90%) had access to SRS. After single BM surgery, 50% systematically prescribed SRS or WBRT, and 45% only in case of incomplete resection. The preferred treatment in neurologically asymptomatic treatment-naive patients diagnosed with >5 BM was systemic treatment (79%). Of all, 45%/49% physicians stated that all tyrosine kinase inhibitors and immune checkpoint blockers were discontinued (timing varied) during SRS/WBRT, respectively. Drugs most often continued during SRS/WBRT were erlotinib (44%/40%), gefitinib (39%/34%), afatinib (29%/25%), crizotinib (33%/26%) and anti-PD-(L)-1 (28%/22%).

Conclusion: BM management is highly variable in Europe: screening is not uniform, prognostic classifications are not often used and MUT+ NSCLC patients generally receive more intensive local treatment. Prospective assessment of BM management in MUT+ NSCLC patients is required.

1. Introduction

Brain metastases (BM) are associated with a detrimental outcome and a negative impact on quality of life (QoL). Approximately 40% of non-small cell lung cancer (NSCLC) patients will present with or develop BM during their disease. This rate can increase to up to 80% in molecularly selected groups, such as anaplastic lymphoma kinase (*ALK*) positive NSCLC patients [1]. This incidence of BM is anticipated to increase over time due to advances in diagnosis (mainly brain magnetic resonance imaging [MRI]) and due to the extended overall survival reported in patients with BM as a result of better systemic treatment options [2]. Radiation therapy (SRS: stereotactic radiosurgery) and surgery are standard local treatments for the management of patients with a limited number of BM [3]. Whole brain radiotherapy (WBRT) alone was until recently the preferred option for patients who are not candidates for surgery or SRS, but its role has been challenged by recent randomised phase III trials [4–6]. Despite the limited penetration of drugs through the blood–brain barrier (BBB), chemotherapy or tyrosine kinase inhibitors (TKI) can be used upfront in neurologically asymptomatic NSCLC patients without (MUT−) and with an oncogenic driver mutation (MUT+), respectively [7–11]. Furthermore, newer TKI generations with superior central nervous system (CNS) penetration rates are already available (e.g. osimertinib for epidermal growth factor receptor [*EGFR*] mutated patients, and ceritinib or alectinib for *ALK*) or in late-stage development (e.g. brigatinib and lorlatinib [*ALK*]) [1,12–14]. Immune checkpoint blockers (ICBs) have recently become available for NSCLC