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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

treatment (e.g. pembrolizumab, nivolumab) and are also under investigation in NSCLC patients with BM [15].

BM management becomes increasingly important, but there are still numerous variations in their management. Local practices and used guidelines may differ [3,7,16–18] (Table S1). There is heterogeneity in the access to modern management across countries, including equipment (brain MRI, SRS facilities), and access to newer systemic treatments [19–21]. Indications for SRS (maximum and number of eligible BM, but also used prognostic indicators) are likewise not well defined [22]. The paucity of evidence and the lack of large ongoing trials, regarding the routine management of this patient group in Europe led to the development of this European survey. We aimed to capture a snapshot of BM screening and management in NSCLC patients and to identify relevant research questions for future clinical trials.

2. Methods

2.1. Study design and population

An online (Google® form) survey developed by the Young Investigators (YI) European Organisation for Research and Treatment of Cancer (EORTC) Lung Cancer Group (LCG) was distributed on 16/02/17 to all EORTC LCG and radiation oncology group (ROG) worldwide members. National cancer societies in Europe (medical oncology, pulmonology, neurology, radiation oncology) were also contacted with the question to forward the survey to their members. Responses were collected until 15/06/2017.

2.2. Description of the survey

The survey was strictly confidential and anonymous. The questionnaire was divided into six sections: physician demographic data, screening, initial treatment decision, surgery, radiotherapy, and systemic treatments questions. The questionnaire consisted of 27 questions, of which 6 were 'tick boxes' type questions. The survey was reviewed by all EORTC LCG board members (N = 12), and all EORTC LCG YI (N = 32). The questionnaire was designed to be completed in approximately 10 min. A copy of the full survey is available in the Supporting Information.

2.3. Statistical analysis

As the aim of the survey was to have a snapshot of BM management in Europe, and therefore only answers from European physicians were selected for the analysis. The Chi-squared or Fisher exact tests were used for dichotomous variables comparison (type of speciality: radiation oncologists versus medical oncologists/pulmonologists and type of institution: cancer centre/university hospitals versus private/general hospitals). Paired comparisons of similar questions were performed using the Bhapkar test. A two-sided P-value <0.05 was considered significant. All analyses were performed using software SPSS version 19.0 (SPSS Inc., Chicago, Illinois).

3. Results

3.1. Physician demographical data

A total of 485 worldwide responses were collected, and 462 European responses from 394 institutions were analysed (exclusion of 23 responses [5%] from outside Europe). Italy (n = 85; 18.3%), the Netherlands (n = 68; 14.7%), UK (n = 66; 14.3%), and France (n = 55; 11.9%) contributed most (Fig. 1; Table S2). Physicians specialities were: radiation oncologist: 53.4% (n = 247), pulmonologist: 25.6% (n = 119), medical oncologist: 18.2% (n = 84), and others: 3% (n = 12). Most (84.4%; n = 390) physicians had >5 years of experience in NSCLC treatments, and 94% (n = 436) had completed their postgraduate education. Hospital types were: university hospital (43%; n = 198), general public hospital (29%; n = 132), cancer centre (20%; n = 92), private centre (7%; n = 33) and others (n = 7).

3.2. Initial treatment decision

Of all, 85% physicians (n = 393) declared to screen neurologically asymptomatic patients for BM at diagnosis. Of these, 52.2% used MRI; private/general institutions used more MRI than university/cancer centres: 59% versus 48%, p = 0.03 (there was no difference in MRI use according to the doctors' speciality [p = 0.2]). Hundred and twenty-five (27%) physicians stated that they screened all NSCLC patients. Most physicians screened patients with stage III (63%), and MUT+ (51%). 4343% screened stage IV, and 39 screened stage I–II before treatment (Fig. 2; Table S3).

A prognostic classification to guide initial treatment decisions was used by 34.2% (n = 158/462; Fig. S1). Prognostic classification to guide initial treatment decisions were more often used by radiation oncologists than medical oncologists/pulmonologists (46.6% versus 19.6%, p < 0.001; there was no difference according to the type of institution [p = 0.3]). Recursive partitioning analysis (RPA) was the most often used prognostic classification (117/158; 74%). Graded prognostic assessment (GPA), and ds (diagnosis-specific)-GPA classifications were used by 68/158 (43%) and 30/158 (19%) of the physicians, respectively (total is >100% given that some physicians used more than one score; Fig. 2; Table S3). The median lowest prognostic-score thresholds to receive treatment were 2 (range: 1–3),

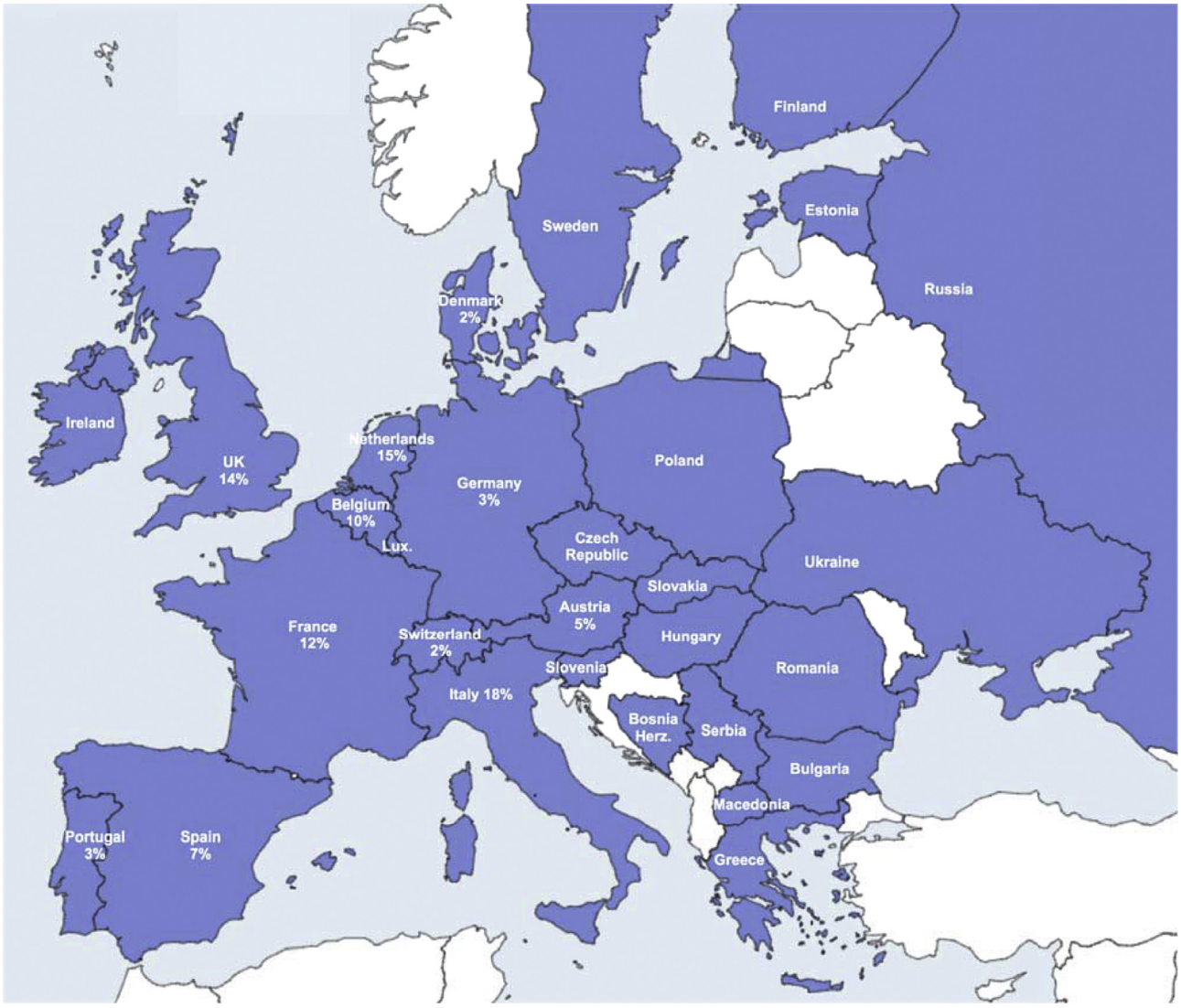

Fig. 1. **Participating countries.** Indicated numbers only if > 5 responses/country. Abbreviations: Herz.: Herzegovina; Lux: Luxembourg.

1.5 (range: 0–2.5), and 2 (range: 0–3) for RPA, GPA, and ds-GPA, respectively. In 50%, lowest prognostic-score threshold to receive treatment differed between MUT+ and non-driver (MUT−) patients (no further question on the actual difference in score). Ten physicians did not use a prognostic score but used performance status (Karnofsky score or World Health Organisation [WHO]) only.

3.3. Local treatments

SRS was accessible for the majority (90%; n = 415, including 97 physicians that did not have direct access to SRS but could easily refer patients; Table 1). No data were provided regarding SRS delivery delay in "referred patients". There was no difference in SRS accessibility according to the type of institution (p = 0.05). BM surgery was most often considered when patients had a single BM (when symptomatic: 84% [n = 390/462]; when asymptomatic: 61% [n = 284/462]), when decompression was necessary (77%; n = 357/462) and for histological diagnosis when no other biopsy for diagnostic purposes were possible (71%; n = 329/462; Table 1). Patients with >1 BM were less frequently considered for surgery (when symptomatic: 29% [n = 135/462]; when asymptomatic: 14% [n = 65/462]). After single BM surgery, 50.4% routinely prescribed SRS (n = 136/462; 29.4%) or WBRT (n = 97/462; 21%), and 45% only in case of incomplete resection (SRS: 32% [n = 148]; WBRT: 13% [n = 60]). Twenty-one (4.5%) never applied post-operative radiotherapy. There was no difference in postoperative radiotherapy strategy according to the type of institution (p = 0.6) or the speciality (p = 0.08).

Physicians most often considered 3 BM as maximum 'cut-off number' for SRS eligibility (MUT-: n = 220 [48%]; MUT+: 197 [43%]). Patients with >4 BM were more likely to receive SRS if MUT+ compared with

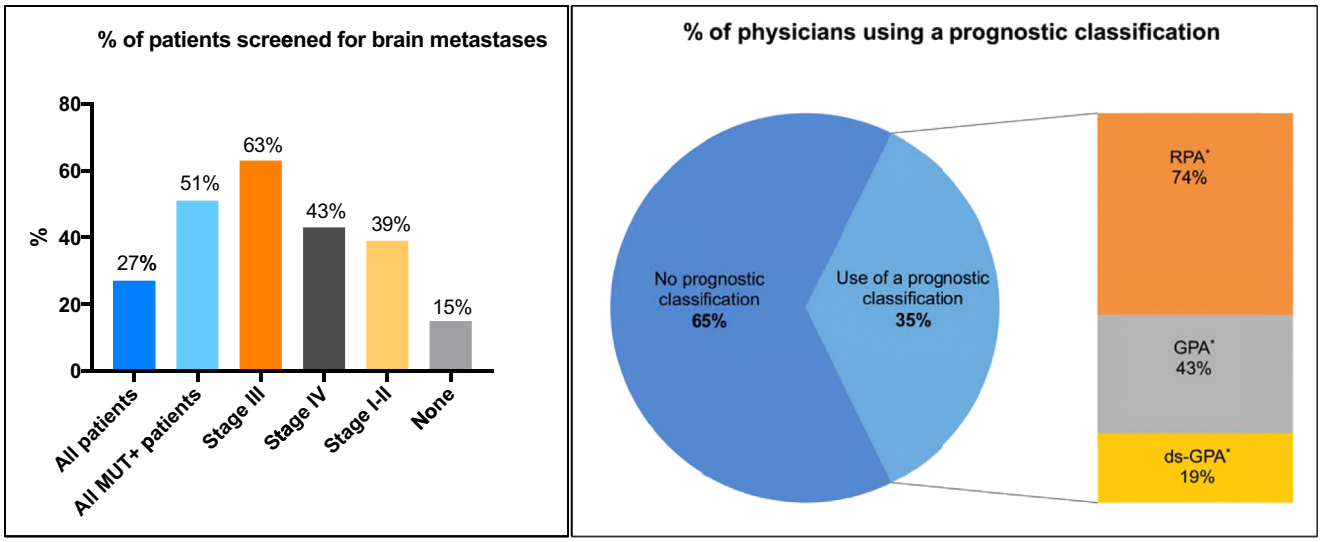

Fig. 2. **Initial treatment decision.** *Results among 158/462 physicians using a prognostic classification to guide initial treatment decision; some physicians used >1 classification therefore % is >100%. Abbreviations: MUT+, oncogenic driver mutation; BM, brain metastases; RPA, recursive partitioning analysis; GPA, graded prognostic assessment; ds-GPA, diagnosis-specific GPA.

MUT-patients (27% [n = 123] versus 21% [n = 98]; $p < 0.01$; Tables 2 and 3). The decision to give SRS was based on tumour volume (and not a specific threshold number of BM) for 11% (n = 53 MUT−) and 13% (n = 59 MUT+). There was no difference in the routinely used BM "cut-off number" for SRS eligibility according to the speciality (radiation oncologists versus medical oncologists/pulmonologists; MUT−: p = 0.9; MUT+: p = 0.9) or the type of institution (cancer centre/university hospital versus private/general hospital; MUT−: p = 0.8; MUT+: p = 0.9). The maximum BM size to consider a patient eligible for SRS was 3 cm for 61% (n = 284) of physicians (2 cm: 11%; 4 cm: 20%; 5 cm: 8%). Radiation oncologists considered larger BM size for SRS eligibility than medical oncologists/pulmonologists (≥4 cm: 32% versus 22%, respectively, p = 0.03).

The regimens used to deliver WBRT were 30 Gy in 10 fractions (n = 234; 51%), 20 Gy in 5 fractions (n = 142; 31%), both (n = 55; 12%) or others (n = 31; 7%). One hundred eight (23%) physicians offered neuroprotective WBRT outside of a clinical trial (hippocampal sparing: n = 102; neuroprotective agent [memantine or donepezil]: n = 6).

Three hundred fifty-four (77%) physicians were aware of the QUARTZ trial publication [4]. QUARTZ trial results influenced the decision to give WBRT in 39.1% of physicians (n = 181) who now use less WBRT in poor prognosis patients. Among those physicians, groups of patients not considered anymore for WBRT were those with poor PS (175/181; 97%), uncontrolled extracranial disease (114/181; 63%), and those suitable for systemic treatments (53/181; 29%). One hundred seventeen of 281 physicians who did not modify their WBRT prescription based on the QUARTZ trial results also did not use a prognostic score to select treatment options.

In a growing lesion after SRS that could be either progressive disease (PD) or radionecrosis, 434 physicians (94%) had access to dynamic MRI and 162 (35%) to brain biopsy as a diagnostic tool. Forty-nine (11%) used specifically bevacizumab as a therapeutic tool.

3.4. Systemic treatments questions

The preferred treatment in neurologically asymptomatic treatment-naive patients diagnosed with >5 BM was (Table 3) systemic treatment (n = 364; 78.8%) if MUT- and molecularly targeted therapies (e.g. TKI; n = 391 [85%]) if MUT+. If BM progressed in a MUT+ patient, the preferred treatment options were second-line TKI (324; 70%) in case of extracranial progression, and local treatment with TKI continuation (355; 76.8%) in those cases with no extracranial progression. There was no difference according to the type of institution in the previously described systemic treatment strategy. Medical oncologists/pulmonologists stated in a higher proportion that second-line TKI was their preferred treatment in neurologically asymptomatic treatment-naive patients diagnosed with >5 BM (93% versus 80% for radiation oncologists; $p < 0.001$). If BM progressed in a MUT+ patient with extracranial progression, radiation oncologists favoured local treatment with TKI continuation (21%) more than medical oncologists/pulmonologists (10%; $p < 0.001$).

44.6% (n = 206)/49.4% (n = 228) physicians stated that all TKI and ICBs were discontinued during SRS/WBRT, respectively. Radiation oncologists discontinued TKI-ICB during brain irradiation more often than medical oncologists/pulmonologists (SRS: 51% versus 37%, respectively, p = 0.004; WBRT: 55% versus 42%, respectively, p = 0.008; no difference according to the type of institution). Drugs most

Table 1
Local treatments.

	n (%)			
Surgery indications				
Single BM				
Symptomatic	390 (84)			
Asymptomatic	284 (61)			
Multiple BM				
Symptomatic	135 (29)			
Asymptomatic	65 (14)			
Decompression	357 (77)			
Possible access to SRS				
Yes	318 (69)			
No but I can easily refer patient	97 (21)			
No	47 (10)			
Adjuvant radiotherapy indication after a single BM resection				
Always SRS	136 (29.4)			
Always WBRT	97 (21)			
Incomplete resection				
SRS	148 (32)			
WBRT	60 (13)			
Never	21 (4.5)			
Maximum BM number for SRS eligibility				
	MUT−		MUT+	
1	13	(3)	12	(3)
Up to 3	220	(48)	197	(43)
Up to 4	78	(17)	71	(15)
Up to 5	73	(16)	87	(19)
Up to 10	18	(4)	28	(6)
Decision based on total tumour volume only	53	(11)	59	(13)
No maximum	7	(2)	8	(2)
Maximum BM size for SRS eligibility				
2 cm	50 (11)			
3 cm	284 (61)			
4 cm	91 (20)			
5 cm	37 (8)			
Neuroprotective WBRT outside of a clinical trial				
No	354 (77)			
Hippocampal sparing	102 (22)			
Neuroprotective agent	6 (1)			
Less WBRT prescription in poor prognosis patients based on QUARTZ trial results				
Yes	181 (39)			
No	173 (38)			
Not aware of the publication	108 (23)			
Strategy in a growing lesion after SRS that could be either PD or radionecrosis				
Dynamic MRI as a diagnostic tool	434 (94)			
Brain biopsy as a diagnostic tool	162 (35)			
Bevacizumab as a therapeutic tool	49 (11)			

Abbreviations: BM: brain metastases; RPA: Recursive partitioning analysis; GPA: Graded prognostic assessment; ds-GPA: diagnosis-specific GPA: SRS: radiosurgery; WBRT: Whole brain radiotherapy.

Table 2
Systemic treatments questions.

	n (%)			
Preferred treatment in neurologically asymptomatic treatment-naive patients diagnosed with >5 BM				
	MUT−		MUT+	
Bevacizumab containing regimen	34	(7)	14	(3)
Driver mutation specific treatment (e.g. TKI)	6	(1)	391	(85)
Other	43	(9)	27	(6)
PD-(L)1 inhibitors	15	(3)	5	(1)
Platinum-based doublet	364	(79)	25	(5)
Preferred treatment if BM progressed in a MUT+ patient				
	with extracranial PD		without extracranial PD	
Local treatment and continue TKI	88	(19)	355	(77)
Second line TKI	324	(70)	73	(16)
Other	50	(11)	34	(7)
Drugs continued during brain RT				
	SRS		WBRT	
None	206	(44.6)	228	(49.4)
Erlotinib	203	(44)	185	(40)
Gefinitib	180	(39)	157	(34)
Crizotinib	152	(33)	120	(26)
Anti-PD-(L)-1	129	(28)	102	(22)
Duration of discontinuation during brain RT				
	SRS		WBRT	
1 day before until 1 day after RT	49	(11)	30	(6)
3 days before, until 3 days after RT	117	(25)	128	(28)
3× T1/2, until 3× T1/2 after RT	48	(10)	52	(11)
5× T1/2 before, until 5× T1/2 after RT	31	(7)	36	(8)
During cranial radiotherapy	61	(13)	58	(13)
Other	44	(10)	43	(9)
NA	112	(24)	115	(25)
Reasons for continuing the targeted agent during cranial radiotherapy				
Absence of perceived safety issues	217 (47)			
Risk of systemic flare	176 (38)			
Possible radiosensitising effects	134 (29)			

Abbreviations: BM: brain metastases; RT: radiotherapy; SRS: radiosurgery; WBRT: Whole brain radiotherapy; T1/2: halftime of the drug; PD: progressive disease; MUT: oncogenic driver mutation; TKI: tyrosine-kinase inhibitor; PD-L1: programmed-death ligand 1; NA: no answer.

continued during cranial radiotherapy (SRS-WBRT) were erlotinib (44–40%), gefitinib (39–34%), afatinib (29–25%), crizotinib (33–26%) and anti-PD-(L)-1 (28-22%). Timing varied, but the most frequent duration of discontinuation was 3 days before and 3 days after RT (25–28%). The reasons mentioned by physicians for continuing the targeted therapy during cranial radiotherapy were the absence of perceived safety issues (47%) and/or risk of systemic flare (38%), or the possible radiosensitising effects (29%). A proportion of 44.8% (n = 207) physicians stated that they used WBRT to increase the systemic treatment efficacy through BBB disruption.

4. Discussion

To the best of our knowledge, this is the first BM European survey collecting data on screening, treatment decisions, radiation and systemic therapy practice specifically in NSCLC patients, including data on patients with driver mutations. Other surveys (range of number

Table 3
Management variations according to the presence of an oncogenic driver mutation (eg. EGFR, ALK).

	Overall n (%)	MUT− n (%)	MUT+ n (%)	p
Screening at any stage	125 (27)		234 (51)	–
Different p-score threshold in MUT+	–	–	79 (50)[a]	–
Maximum n of BM for SRS eligibility				
≤4	–	311 (67)	280 (61)	<0.01[b]
>4	–	98 (21)	123 (27)	
Decision based on total tumour volume		53 (11)	59 (13)	
No maximum		7 (2)	8 (2)	

Abbreviations: MUT: oncogenic driver mutation; p: prognostic; BM: brain metastases; SRS: radiosurgery.
[a] Total = 158 physicians using a prognostic classification to guide initial treatment decision.
[b] Bhapkar test.

of respondents between 59 and 711) on the management of patients with BM were not specific to lung cancer, and predominantly included radiation oncologists from the USA and Australia (Table S4) [23–29].

Our results highlight the current heterogeneous practice patterns and decision-making processes. BM screening practice varied widely: 63% screened all stage III, 43% screened all stage IV patients, and only half used MRI for screening purposes. According to ESMO (European Society for Medical Oncology) guidelines, brain imaging (preferably contrast-enhanced MRI): i) might be useful in early and locally advanced patients considered for curative therapy [30], ii) should be performed in all patients planned for curative stage III NSCLC treatment [30], and iii) is most relevant in stage IV patients with neurological symptoms or signs, although screening all stage IV patients should be considered [7]. Possibly, the low use of MRI in our survey can be explained by limited access to MRI in a timely fashion, as described in another survey [29]. According to the Organisation for Economic Co-operation and Development, the median number of MRI equipment per 1,000,000 inhabitants is three time higher in the USA as compared with the European union (36.7 versus 12.3 [range, 3.6–33.6], respectively) [21]. Prognostic scores were used by only 34% of physicians (and mainly by radiation oncologists), despite being considered key information in decision-making in this group of patients [31–33]. The ESMO guideline on metastatic NSCLC recommends that the RPA classification is used, and that radiotherapy in poor prognosis patients (RPA class III) should not be offered [7].

Regarding local treatments, most physicians considered 3 BM as maximum for SRS eligibility (MUT−: n = 220 [48%]; MUT+: 197 [43%]) and/or 3 cm as a maximum BM size (61%). It should be noted that SRS using a unique fraction versus a hypo-fractionated procedure was not individualised in the survey. Few respondents (10%) now use total volume rather than number of BM to make SRS decision. Yamamoto *et al.* [33] have recently showed that SRS without WBRT was feasible as the initial treatment for patients with five to ten BMs, if the cumulative volume of all BMs is ≤ 15 mL. Sandler *et al.* have performed a survey of 711 practicing radiation oncologists, and it was found that the optimal BM 'cut-off number' for SRS was significantly higher for high-volume CNS centres (≥10 patients/month) than for either low-volume CNS centres (5–9 patients/month) or high-volume, non-CNS specialists (number of BM: 8.1 versus 5.6 and 5.1, respectively; $p < 0.001$) [26]. In our study, there was no difference in the optimal 'cut-off number' according to the institution type. Results on the ongoing randomised trials comparing SRS and WBRT for patients with four to ten BMs (NCT02353000, primary endpoint QoL 3 months after radiotherapy) will hopefully better define the role of SRS in this setting.

The preferred treatment in neurologically asymptomatic treatment-naive patients diagnosed with >5 BM was systemic chemotherapy (78.8%) in MUT- and TKI (85%) in MUT+ patients. In accordance with ESMO guidelines [7], physicians surveyed stated that systemic treatments should be initiated in non-symptomatic patients with multiple BM. Intracranial response rates slightly below extracranial response rates have been observed with first-line chemotherapy or first-line TKI in MUT+ patients, with the possibility to delay or withhold WBRT [8–11,34]. However, a recent retrospective report showed that EGFR-TKI, and deferral of radiotherapy, was associated with inferior outcomes in patients with *EGFR*-mutant NSCLC [35]. To the best of our knowledge, there are no completed trials comparing upfront cranial radiotherapy followed by a TKI to upfront TKI in MUT+ patients with BM. Such trial investigating gefitinib in *EGFR*-mutant NSCLC (NCT01363557) was prematurely closed due to poor accrual. However, based on the heterogeneous management of BM in MUT+ patients, trials evaluating the sequencing of cranial radiotherapy and targeted therapies mentioned above are warranted. Another strategy is the evaluation upfront newer generation TKIs in patients with BM and driver mutations. Recently, it was shown that first-line alectinib (*ALK*+ patients) and osimertinib (*EGFR*-mutated patients) provided superior intracranial control compared with standard of care [1,36]. This survey shows that, in the routine setting, MUT+ NSCLC patients generally received more aggressive local treatment. This group was more frequently screened for BM, in all stages of disease (234; 51%), and in 50%, the lowest prognostic-score threshold to receive treatment differed between driver MUT+ and MUT− patients. MUT+ patients with >4 BM were also more likely to receive SRS than MUT- NSCLC patients ($p < 0.01$; Table 3).

More than half of physicians did not discontinue TKI and ICB during SRS (55.4%)/WBRT (50.6%). Drugs most often continued (SRS-WBRT) were TKI (29%–44% – 25–40%) and the main reasons for continuing the targeted agent during cranial radiotherapy were the absence of perceived safety issues (47%). A phase II study demonstrated that erlotinib is well tolerated in combination with WBRT [37]. However those results may not be extrapolated to other TKI and ICB delivered concurrently with brain irradiation, even if most retrospective data are reassuring [38–42]. Ideally, safety and efficacy should be evaluated within the context of a clinical trial.

Limitations of this survey include the fact that number of questions was restricted and therefore cannot provide a full picture of BM practice, particularly in rare subgroups of patients (e.g. ROS1), and the absence of a known response rate, as we do not know the total number of physicians who received the survey because of the forwarding by the national societies. We adopted a pragmatic approach, as it is known that the number of respondents decreases when the number of questions and time to survey completion increases. Selection bias is probable as interested oncologists were more likely to respond to the survey. This may have impacted on the results (e.g. high rate of access to SRS of 90%). However, half of the respondents worked in general and private hospitals. Furthermore, the respondents represent a specific population. Indeed most respondents came from Western Europe (Fig. 1), and the networks used to send the questionnaire generally targeted a specific population (physician were the members of scientific society or an organisation that include patients in trials, with a consequence of relatively few physicians from private practice [7%]).

5. Conclusion

BM management differed widely within European centres. Some of the main findings of the survey are that screening was not uniform and prognostic classifications were not often used, despite robust evidence in the literature supporting these strategies. Half of respondents declared that they routinely deliver adjuvant radiotherapy, which is demonstrated to decrease the risk of local recurrence, even if complete resection has been performed [43–45]. Cancer societies' teachings may focus on already existing studies and decision-making tools such as prognostic scores to optimise NSCLC BM management. MUT + NSCLC patients generally received more aggressive local treatment. Specific BM guidelines for MUT + NSCLC patients should be written to help physicians in the management of this patients group. Prospective assessment of BM treatment strategies in MUT + NSCLC patients is also required. More attention should as well be paid to BM in MUT– patients on conferences and webinars as the majority of NSCLC BM patients is MUT–. Finally, there is a lack of data on safety and sequencing of most targeted therapies/ICB combined with radiotherapy, although trials are ongoing. Efforts in harmonisation throughout Europe in terms of management and screening of BM should be pursued [3,7] through clinical trials conducted by oncology societies.

Conflict of interest statement

None declared.

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France: SNRO (Radiotherapy and Oncology National Union), CORP (Radiotherapy and Oncology Parisian Club), SPLF (French Language Pneumology Society). Spain: SEOR (Spanish Association of Radiotherapy and Oncology), SEOM (Spanish Society of Medical Oncology). Austria: SANO (Austrian Society of Neuro-Oncology), OGRO (Austrian Society for Radiation Oncology), OeGHO (Austrian Society of Haematology and Medical Oncology). Denmark: DSKO (Danish Society of Clinical Oncology). Netherlands: NVALT (Dutch Association of Physicians for Pulmonary Diseases and Tuberculosis), section oncology, NVRO section neuro-oncology (Dutch Society for Radiotherapy and Oncology). Romania: CFMR (Romanian College of Medical Physicists). UK: Society and College of Radiographers, MRC UK (Medical Research Council), RCR (Royal College of Radiologists), BTOG (British Thoracic Oncology Group). Belgium: BVRO/ABRO (Belgian Association of Oncological Radiotherapy). Switzerland: SAKK (Clinical cancer research group). Germany: DEGRO (German Society for Radiotherapy and Oncology). Italy: Postgraduate School of Medical Oncology and Radiotherapy, AIRO (Italian Association of Radiotherapy and Oncology). Ireland: Cancer Trials Ireland. EORTC LCG (European Organisation for Research and Treatment of Cancer Lung Cancer Group), ROG (Radiation Oncology Group), ERS (European Respiratory Society) and ESMO YOC (European Society for Medical Oncology Young Oncologist Committee).

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejca.2018.01.067.

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