Editorial

The multidisciplinary lung cancer team meeting: increasing evidence that it should be considered a medical intervention in its own right

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In men and women combined, lung cancer is currently the most often diagnosed cancer and the leading cause of cancer-related death. Progress in improving overall survival (OS) has generally been slow and incremental, with expensive therapies approved on the back of modest gains. For example, Nivolumab was approved for 2nd line therapy in patients with advanced (stage IIIB/IV) squamous and non-squamous non-small cell lung cancer (NSCLC) on the basis of a 3.2- and 2.8-month gain in median OS respectively (1,2). To put this into context, the American Society of Clinical Oncology (ASCO) recommendations for "meaningful outcomes in clinical trials" set the bar at an extension in OS of 2.5–3 and 3.25–4 months compared with standard therapy (assuming little or no increase in toxicity) for patients with advanced squamous and non-squamous cancer respectively (3). Keeping these figures in mind, it is therefore noteworthy that as far back as 2005, single-center data from Scotland was published showing a gain in median OS of 3.4 months in patients with inoperable NSCLC (predominantly stage IIIB/IV) following the introduction of a multidisciplinary lung cancer team (MDT) in 1998 (4). More patients in the 2001 cohort (data prospectively collected) underwent staging and the survival of patients with stage III disease doubled compared with 1997 (retrospective data), despite a stage drift towards more advanced disease. Chemotherapy use rose from 7% to 23% and the use of palliative care alone dropped from 58% to 44%.

More contemporary data from Stone *et al.* in Australia, backs this up and refocuses attention on the prognostic importance of the lung cancer MDT (5). Their team was established in 2006 and they recently published a single-center post-hoc analysis of institutional registry data prospectively collected between January 2006 and December 2012. The registry included all patients with a tissue diagnosis of lung cancer. Patients who were presented in the MDT (n=295) and those who were not (n=902), were compared. The maximum rate of referral to the MDT was 40.8%, in 2011. Patients discussed in the MDT tended to be younger and were more likely to have early-stage disease. The authors found that the unadjusted 1-, 2- and 5-year survival probability was higher in the MDT group for all stages of NSCLC. After a multivariate analysis (that considered factors like age, sex, performance status, pathology, stage, and year of diagnosis), 5-year OS was significantly better in the MDT group: the hazard ratio (HR) was 0.7 [95% confidence interval (CI): 0.58–0.85] and there was an early and sustained separation of the Kaplan-Meier curves (Figure 1 in their paper). Unfortunately, absolute OS data (e.g., in months/years) was not provided, but the 5-year NSCLC survival probability in the MDT group was a very respectable 0.61 for stage IIIA, 0.38 for stage IIIB and 0.28 for stage IV. It is notable that in the 7-year study period only 295/1,197 patients (24.6%) with a tissue diagnosis were presented at the MDT, or between 28–62 patients/year. The lung cancer MDT apparently

met weekly for one hour. Assuming for example, 48 meetings/year, this means that the number of patients included in their study who were discussed was between 0.6 and 1.3/week. Even allowing for the fact that patients without a tissue diagnosis would also have been discussed, such patients as the authors indicate, are typically in the minority. What the rest of the MDT time was spent on, and why three-quarters of patients with a tissue diagnosis were not discussed is uncertain. Treatment characteristics were not available and so could not be analyzed.

Interestingly, Boxer *et al.*, also from Australia, published data from the period 2005–2008, partially overlapping with Stone *et al.* and although they found a significantly higher use of radiotherapy in stage I–IV NSCLC (66% *vs.* 33%) and chemotherapy in stage IV NSCLC (46% *vs.* 29%), surprisingly, this did not translate into an impact on survival (6). In contrast with Stone *et al.*, 76% of all newly diagnosed lung cancer patients were discussed at their MDT meeting. However, there are other studies that also support a link between the MDT and better survival in lung cancer (7,8). Bydder and colleagues from Australia (9), motivated by the fact that in Forrest *et al.* the cohorts were separated by 4 years which they speculated might have influenced the results, performed a single institution analysis of patients with inoperable NSCLC (predominantly stage IIIB/IV) treated in a single year (2006). They too found that median OS was significantly longer in patients whose case was presented at the MDT, although the margin was smaller (31 days *vs.* 3.4 months), and the OS in the non-MDT group was considerably longer, than in Forrest *et al.* (208 days *vs.* 3.2 months). One-year survival was 15% higher in the MDT group (33% *vs.* 18%). Rogers *et al.* from Australia analyzed all newly diagnosed cancer patients between 2009–2012, including 593 with lung cancer of whom 60% were presented at an MDT meeting within 60 days of diagnosis (10). They found that the MDT group had a significantly lower mortality after adjusting for age, stage, comorbidity and treatment: HR 0.62; 95% CI: 0.50–0.76. Bilfinger *et al.* from the United States analyzed 4,271 patients from a 14-year period (2002–2016), 1956 (46%) of whom were treated in the institution's MDT program (7). Consistent with Stone *et al.*, the 1-, 3-, 5- and 10-year survival rates were significantly better in the MDT group, across stages. Using Cox proportional hazard models and propensity matching to try and address potential biases, they showed that 5-year OS was significantly better in the MDT group of patients: HR 0.65; 95% CI: 0.54–0.77. Absolute OS data (months/years) was not presented. It is notable that the HRs in Stone *et al.* (0.7), Rogers *et al.* (0.62), and Bilfinger *et al.* (0.65), are similar. Tamburini *et al.* from Italy have also recently published a propensity matched analysis and found that patients undergoing surgical resection for NSCLC before (2008–2012) the introduction of an MDT meeting had a worse 1-year survival compared with those having their resection afterwards (2012–2015) (8).

Taken together, these data suggest that the lung cancer MDT meeting may be an important therapeutic intervention. While the data do not represent the highest level of evidence, the survival gain in some of the analyses is comparable to what is being seen with new medical therapies and consistent with the ASCO definition of a meaningful outcome (1-3). In a disease as serious as lung cancer, this kind of return on a case discussion by a multidisciplinary medical team that typically lasts a few minutes (11,12), and is associated with no toxicity to the patient, is just too interesting to ignore. While it would be easy to dismiss the results of the studies as being due to bias and confounders, statistical attempts to account for these have not altered the conclusion. While the MDT sounds like a novel concept, there is nothing new about discussing patient care with colleagues. There is a long history of doing this in medicine to try and achieve the best outcome for patients, and reports of tumor boards date back more than 50 years (13,14). Where the modern concept of an MDT differs for example, is that in many instances the size of the team has increased, it has been given a central role in the organization of oncology services and national cancer policy, and has become compulsory (11,15). 'Service-friendly' metrics like an increase in the completeness of staging, better adherence to guidelines, changes to the initial management plan in a substantial proportion of cases, opportunities for clinical trial recruitment, or a speeding up of the diagnostic and treatment pathway, while not survival end points, are nonetheless important patient-centered outcomes (16-18). That said however, there is no doubt that seeing the MDT as a potential therapeutic intervention that may influence survival, changes the perception of it.

Despite this, there have been persistent concerns about the effectiveness, efficiency, cost-effectiveness and time demands of MDT meetings (19,20). While caution is necessary in talking about MDTs in terms that are too general, or that suggest all teams are equal (11), these concerns need to be heeded. Escalating healthcare costs are problematic and the time burden associated with MDT meetings has often fallen disproportionately on certain specialties like radiology and pathology, two essential

members of the team (11). The recent introduction of specialized molecular tumor boards and the rise in MDT meetings facilitated by videoconferencing between cancer centers and their partner institutes will lead to yet more demands on time (21,22). Against this background, there are several challenges facing researchers, individual clinical teams, hospital administrators and policy makers. These include: (I) deciding whether there is a more robust way to accumulate convincing evidence of a survival benefit from the MDT meeting, accepting that a randomized study is unlikely to be ethical in many countries since such meetings are already written into policy and considered the standard of care that a patient can expect to have access to (11); (II) accepting that for various reasons, it may not be possible for all patients in all centers to be discussed, and identifying which patients stand to gain the most from being presented at an MDT (23); (III) identifying the features of an MDT meeting that allow it to influence survival (these might include for example, MDT composition, communication within the team, influence of hierarchy), accepting that they might vary depending on the operating environment, for example, socio-geographic and cultural factors, and the level of resources that are available in the particular center or country; (IV) determining the leanest possible configuration of an effective MDT meeting to maximize the cost-effectiveness and reach as many patients as possible; (V) providing teams with the tools and resources to implement, run and improve their MDT meeting (24); (VI) providing clinicians with the tools and time needed to prepare for the meeting; (VII) ensuring efficient administration of 'live' and remote (e.g., videoconferencing) MDT meetings, including completeness of information (including for example, scans and pathology specimens from external centers) and effective discussion, free of distractions (e.g., smart phones); (VIII) keeping the team discussion patient centered, including where necessary adequate representation of patient preferences and ensuring adequate communication with their general practitioner (25); and (IX) ensuring that the costs associated with the meeting are represented in the treatment cost, and that staff schedules take the preparation time and the meeting itself into consideration.

Cancer policy and national plans, mean that lung cancer MDT meetings are here for the foreseeable future. However, the weight of the available data (in particular for NSCLC), imperfect as it is, suggests there may actually be a clinically relevant prognostic and therapeutic role for the MDT meeting. Accumulating 'better' evidence is likely to take time, and local efforts should be focused on refining the intervention (the meeting), and leveraging it to give as many lung-cancer patients access, with the goal of improving their survival.

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Footnote

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