Original Research

European practice patterns and barriers to smoking cessation after a cancer diagnosis in the setting of curative versus palliative cancer treatment

Jeroen W.G. Derksen a,b, Graham W. Warren c, Karin Jordan d, Stefan Rauh e, Ruth Vera García f, Deirdre O’Mahony g, Samreen Ahmed h, Peter Vuylsteke i,j, Sinisa Radulovic k, Nikolaos Tsoukalas l, Piotr J. Wysocki m, Markus Borner n, Alvydas Cesas o, Anneli Elmep, Heikki Minn q, Gustav J. Ullenhag r,s, Jeanine M.L. Roodhart a, Miriam Koopman a, Anne M. May b,*

Received 21 May 2020; received in revised form 2 July 2020; accepted 19 July 2020
Available online 29 August 2020

* Corresponding author: Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands.

E-mail address: a.m.may@umcutrecht.nl (A.M. May).

https://doi.org/10.1016/j.ejca.2020.07.020
0959-8049/© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
1. Introduction

Despite the great progress made in supportive care for people with cancer, smoking cessation treatments remain an often-neglected element of cancer care. Smoking by cancer patients and survivors causes adverse cancer treatment outcomes and poor quality of life with a median 50% increased risk of overall mortality and 60% increased risk of cancer-related mortality across cancer diagnoses and treatments [1]. In addition, the effects of continued smoking can result in significant additional cancer-related treatment costs [2]. Smoking cessation after a cancer diagnosis can improve survival [3], and improve outcomes for non—cancer-related health effects that may have a more significant effect on mortality than cancer [4]. Major organisations including the European Society for Medical Oncology (ESMO), American Society of Clinical Oncology (ASCO), American Association for Cancer Research, National Comprehensive Cancer Network, International Association for the Study of Lung Cancer (IASLC), World Health Organisation and others advocate for smoking cessation as a standard part of cancer care [5—12]. However, approximately two-thirds of cancer patients who smoke at diagnosis continue to smoke during follow-up [13].

Evidence-based approaches to increase smoking cessation consist of providing counselling and medications [14]. Before the landmark 2014 Surgeon General’s Report concluding that smoking was a causal factor for poor cancer treatment outcomes [1], large surveys of oncologists demonstrated that while most oncologists asked about tobacco use and advised patients to quit, few offered assistance with quitting [15,16]. There have been considerable efforts to raise awareness of the need to provide smoking cessation as a standard part of cancer care, but there have only been few contemporary surveys of practice patterns to evaluate if improvement has occurred. In addition, no previous surveys have evaluated differences in patterns between the curative and palliative settings. The purpose of this study is to evaluate current practice patterns of oncologists by reporting (1) their perceptions on tobacco use after diagnosis, (2) current practices of tobacco use assessment including provision of cessation support and (3) potential barriers to facilitating cessation support—while distinguishing between the curative and palliative settings.

2. Methods

2.1. Study population

Target respondents included clinical oncologists (i.e. medical oncologists and radiation oncologists) practicing in Europe. In total, 24 national societies for medical or clinical oncology—all partners of ESMO—were invited to participate in this international survey study (Supplement S1). On individual board approval, the societies distributed the survey among
their members and most local coordinators sent two reminders after the initial invitation to complete the survey. The Medical Research Ethics Committee (MREC) of the University Medical Center Utrecht confirmed that the Medical Research Involving Human Subjects Act (WMO) does not apply, and MREC approval is not required under the WMO (reference WAG/mb/19/013713).

2.2. Survey

An online 34-item survey was developed based on the 2013 ASCO survey [15] to assess European practice patterns in clinical oncology and perceptions regarding smoking cessation after a cancer diagnosis. The survey contained questions asking about respondent characteristics, the oncologist’s perceptions of tobacco use in patients with cancer, the oncologist’s interactions with cancer patients, and potential barriers to smoking cessation support (Supplement S2). Respondents were asked about practice patterns and perceptions in both the curative and palliative settings. Except for the respondent’s demographics, most questions could be answered on a five-level Likert scale ranging from always to never, or from strongly agree to strongly disagree. The survey was distributed between 19th September 2019 and 20th December 2019.

2.3. Data analysis

Responses to the survey are presented using descriptive statistics, and compared by treatment setting using the non-parametric Mann–Whitney U test. Statistical analyses were performed using SPSS (version 25.0, IBM Corp, Armonk, NY). To determine the respondent’s smoking status, currently smoking every day or some days per week was classified as being a current smoker, currently no smoking but having smoked more than 100 in a lifetime was classified as being an ever smoker, and never smoking in a lifetime or no current smoking but having smoked less than 100 in a lifetime was classified as being a never smoker.

3. Results

A total of 6235 members of participating medical or clinical oncology societies from Belgium, Denmark,
Estonia, Finland, Germany, Greece, Ireland, Lithuania, Luxembourg, The Netherlands, Poland, Serbia, Spain, Sweden, Switzerland and the United Kingdom (UK) were invited to participate. Of all invited members, 568 (~9.1%) completed the survey for this study, with varying response rates by country ranging from 2% to 44%. After excluding respondents with another profession (18 surgeons and 6 miscellaneous), a total of 544 respondents (~8.7%) were included in this analysis.

3.1. Respondent characteristics

Table 1 shows characteristics of the 544 survey respondents. Most respondents were older than 40 years (73%), and practicing as medical oncologist (90%). Furthermore, 41% of respondents were men, 37% had an MD with a doctorate degree and 50% reported to be working in a university or academic setting. Breast, gastrointestinal and lung tumours were the three most frequently seen primary tumour types of respondents with respectively 49%, 46% and 39%. The majority of respondents reported to spend more than half of their time on patient care (90%). Regarding smoking behaviour, 5% of the clinical oncologists reported to currently smoke, and 17% were classified as ever smoker.

3.2. Perceptions on tobacco and cancer

Responses on questions regarding perceptions towards tobacco use in patients with cancer are shown in Table 2. Oncologists strongly believe that tobacco use negatively impacts treatment outcomes, in both the curative (94%) and palliative settings (74%). Subsequently, 95% of the respondents agreed that smoking cessation should be a standard part of curative cancer treatment, and 63% agreed that it should be standard in the palliative setting as well. Interestingly, 52% reported to not have adequate training in smoking cessation interventions, and 73% indicated that more training in tobacco assessment and cessation interventions is needed. This is especially relevant as 42% found that the treating oncologist would be an appropriate provider of cessation support. The two other most frequently suggested providers were primary care physicians (58%) and clinical support staff such as nurses (56%). A stratification by country showed that primary care physicians were less often (<50%) suggested in Germany, Greece, Luxembourg, Serbia and Sweden, and more often (>75%) in Spain, Switzerland and the UK. The most commonly reported methods in the respondents’ hospital to support patients in tobacco cessation are face-to-face counselling (37%), and the provision of information materials such as pamphlets (29%), but 23% of the respondents reported no knowledge of a dedicated smoking cessation program available in their centre.

3.3. Interactions with the patient

Table 3 shows the oncologists’ practices and communication with the patient. The vast majority of respondents reported to always or most of the time ask patients if they smoke tobacco products, in both the curative (93%) and palliative (78%) settings. Asking about using specific tobacco products was less frequently reported as 57% of oncologists indicated to ask for cigar, pipe, snuff use in the curative setting and 48% in the palliative setting, while the use of electronic cigarettes or devices was reported to be asked always or most of the time by 39% of the oncologists in the curative setting and by 33% in the palliative setting. When asking patients about tobacco use, most oncologists do not use a structured method for the assessment (rarely or never by 69% in the curative setting and 71% in the palliative setting). Although oncologists indicated that they do ask smokers if they want to quit smoking (always or most of the time by 75% in the curative setting and 50% in the palliative setting) and also advise smokers to quit (88% in the curative setting and 54% in the palliative setting), only 39% reported to discuss medication options always or most of the time with curative patients, and 24% with palliative patients. Overall, 69% of the respondents reported to discuss tobacco use and cessation options equally in patients with tobacco-related and non—tobacco-related cancers in the curative setting, and 58% in the palliative setting.

3.4. Barriers for interventions

Oncologists agreed or strongly agreed that the perceived inability to get patients to quit (69% in the curative setting and 61% in the palliative setting), the patient’s resistance (69% in the curative setting and 70% in the palliative setting), the lack of time for counselling (59% in the curative setting and 54% in the palliative setting) and a lack of training in cessation interventions (65% in the curative setting and 61% in the palliative setting) are barriers to facilitate smoking cessation interventions (Table 4). In contrast, very few respondents agreed or strongly agreed that smoking cessation after diagnosis is a waste of time (3% in the curative setting and 14% in the palliative setting, p < 0.001). The oncologist’s own hesitation and ‘not feeling comfortable taking something away patients might enjoy doing’ are more present in the palliative setting since 43% agreed or strongly agreed to this statement, as compared with 13% in the curative setting (p < 0.001). When stratified for tobacco use history, oncologists that are current or former smokers do not differ from never smokers in terms of their own hesitation as a barrier to provide cessation support, neither in the curative setting (p = 0.53) nor in the palliative setting (p = 0.63).
4. Discussion

Among European oncologists who responded to the online survey on smoking cessation in patients with cancer, most reported to believe that tobacco use negatively impacts treatment outcomes, and that smoking cessation interventions should be a part of the multidisciplinary treatment. Most oncologists ask patients for tobacco use and advise those who use tobacco to quit, in both the curative and palliative settings, and with similar frequency for both patients with tobacco-related and non—tobacco-related cancers. Use of specific tobacco products or electronic cigarettes is less frequently interrogated. Barriers to provide cessation support were conceived rather equally between the curative and palliative settings, with a lack in training, the perception of inability to get patients to quit, patient resistance, and a lack of time being the most frequently reported. Oncologists appeared to report higher rates of addressing tobacco in the curative setting as compared with the palliative setting, but except for the oncologist’s own hesitations to take away a pleasurable habit (equally present in currently/former smoking oncologists versus non-smoking oncologists) and disbelief in an effect on outcomes, barriers were remarkably similar between the curative and palliative settings. To the best of our knowledge, this is the first large survey to report the effects of cancer treatment setting on tobacco use assessment and barriers to provide support.

In curative setting patients, results are consistent with the 2013 ASCO [15] and IASLC [16] surveys demonstrating that about 90% of oncologists regularly ask about tobacco use, 80—90% regularly advise patients to quit smoking and 30—40% regularly provide assistance to quit through medications or counselling. In contrast, patients in the palliative setting received consistently lower support with 54% advised to quit and 18—24% provided medications or counselling. This unique finding suggests that oncologists perceive tobacco cessation as less important in the palliative setting, particularly due to the reported hesitations from not feeling comfortable taking something away patients might enjoy doing, and less belief in an effect on outcomes. To date, the evidence on survival benefits in patients with stage IV disease is indeed sparse [17—21];
Table 3
Oncologist’s interactions with cancer patients.

| Question (n = 496) | Setting | Always | Most of the time | Some of the time | Rarely | Never | N/A | p-Value |
|--------------------|---------|--------|------------------|------------------|--------|-------|-----|---------|
| I ask patients if they smoke or use tobacco products | C       | 361 (73%) | 100 (20%) | 22 (4%) | 8 (2%) | 2 (<1%) | 3 (1%) | <0.001 |
| | P       | 260 (51%) | 136 (27%) | 48 (10%) | 41 (9%) | 11 (2%) | 0 (0%) | 0.001 |
| I advise patients who smoke or use tobacco products to stop smoking | C       | 183 (37%) | 97 (20%) | 84 (17%) | 93 (19%) | 35 (7%) | 4 (1%) | <0.001 |
| | P       | 136 (27%) | 102 (21%) | 83 (17%) | 117 (24%) | 55 (11%) | 3 (1%) | 0.02 |
| I discuss medication options such as nicotine replacement, bupropion, varenicline, etc. | C       | 132 (27%) | 63 (13%) | 65 (13%) | 121 (24%) | 108 (22%) | 7 (1%) | 0.28 |
| | P       | 100 (20%) | 64 (13%) | 70 (14%) | 127 (26%) | 130 (26%) | 5 (1%) | 0.001 |
| When asking about tobacco use, I use a structured questionnaire or other structured method for asking questions | C       | 69 (14%) | 43 (9%) | 27 (5%) | 61 (12%) | 279 (56%) | 17 (3%) | 0.28 |
| | P       | 59 (12%) | 38 (8%) | 30 (6%) | 61 (12%) | 293 (59%) | 15 (3%) | 0.001 |

| Question (n = 496) | No. (%) | Yes, I discuss this equally in patients with tobacco-related and non–tobacco-related cancers | Yes, I mostly discuss this with patients with tobacco-related cancers | Yes, I mostly discuss this with patients with non–tobacco-related cancers | N/A | p-Value |
|--------------------|---------|---------------------------------|-------------------------------------------------|-------------------------------------------------|-----|---------|
| My interactions with patients regarding smoking/tobacco use (above questions) | C       | 343 (69%) | 113 (23%) | 8 (2%) | 32 (7%) | 1.00 |
| | P       | 288 (58%) | 126 (25%) | 18 (4%) | 64 (13%) | 0.001 |

C = curative, P = palliative.
* 9% missing, and descriptive statistics of complete cases are presented.

however, the body of evidence is expected to grow in the near future given the current focus on this topic. Nevertheless, still 64% of oncologists disagreed that cessation is a waste of time because of no impact on outcomes.

In contrast to assessing and addressing tobacco use, barriers to support appeared more consistent between the curative and palliative settings. Analysis of the IASLC survey demonstrated that significant predictive barriers to providing medications or counselling were a lack of time for counselling or referral, lack of available resources and lack of training or experience [22]. Our results show that these predictive barriers were remarkably consistent according to cancer treatment intent with 60% versus 55% for lack of time, 56% versus 53% for lack of resources and 65% versus 61% for lack of training or experience for curative versus palliative setting, respectively.

Further comparisons between the current survey and the 2013 surveys [15,16] show that a lack of time and adequate training were more frequently reported compared with 2013, whereas no reimbursement and other financial reasons were less frequently reported. The latter finding might be caused by the nationality of the respondents, because financial health care policies differ between the US and European countries. Our results show a high percentage of oncologists reporting inadequate training and that more training is needed to better support patients, which suggests that oncologists are receptive to additional training regarding smoking cessation support.

Clinicians might feel that smoking cessation should mainly be emphasised in patients with either early stage or curable disease. However, a large review of the literature showed that smoking increases mortality in patients with both early and advanced or metastatic cancer [1]. Moreover, the 2020 Surgeon General’s Report demonstrated that smoking cessation after a cancer diagnosis was associated with improved overall survival [3]. Smoking cessation after a cancer diagnosis has further shown to improve cancer-related survival, risk of second primary cancer and quality of life.
It has recently been shown that providing comprehensive tobacco treatments including intensive counselling and proactive pharmacologic management in the oncologic setting can lead to sustained cessation in almost half of patients with cancer who smoke [38]. In response to these study results, Fiore et al. [39] stated that an effective cessation treatment for patients with cancer who smoke should become the fourth pillar—and an integral and essential component—of comprehensive cancer care, and describe in detail which steps are needed to promote implementation of smoking cessation treatment in cancer care. Moreover, assessment of smoking status and initiation of cessation support should no longer depend on preferences of individual oncologists, but should be automated in electronic health record systems and regulated at the hospital level. Smoking cessation support might, for example, be used as a hospital performance indicator. This approach fits well in the current era in which there is an increased focus on delivering the best oncologic care at the lowest cost to assure an appropriate allocation of resources in health care systems [40]. When new antineoplastic agents are introduced, the efficacy, safety and costs of treatment are currently the main considerations [41]. Continued smoking is a factor that contributes to potential failure of first-line treatment and leads to significant incremental costs to the health care system [2]. Hence, smoking behaviour should be given more consideration, especially when considering its highly modifiable nature.

The inevitable limitation of the current survey study is the presence of selective response. As respondents...
are likely to be oncologists with a higher interest in the role of lifestyle factors, such as smoking, the results may be an optimistic representation of ‘true’ daily practices and perceptions towards tobacco use and cessation support. Although generalisability might be affected by the low response rate (~9.1%), the obtained response rate is in line with other international lifestyle-related surveys in the oncology setting [15,42] and results are highly congruent with prior published surveys using similar or identical questions [15,16]. In general, true practice patterns of oncologists are likely to be worse than our results show, which only strengthens our recommendations of implementing routine smoking behaviour assessments in every patient with cancer and including evidence-based smoking cessation support in the oncologic care path. Another limitation is that, although quitting smoking is relevant at any point in time, surgeons were not included in our target population. Smoking cessation is already receiving increasing attention as a part of surgical prehabilitation programs to improve post-surgical outcomes [43,44], whereas cessation support was expected to be less implemented by oncologists. In addition, this target population was also chosen based on our focus on the palliative setting in which patients are most often seen by oncologists. Nevertheless, supporting patient in quitting smoking remains a multidisciplinary responsibility. Strengths of this study include the large sample of oncologists and participation of 16 European countries, which underpins the broad support for the obtained results. Lastly, the specific distinction between the curative and palliative settings allowed to study the current views towards cessation support in both these settings and to make comparisons between them.

To conclude, this study demonstrates that oncologists appear to address tobacco use more frequently in the curative setting than in the palliative setting. Unfortunately, this study further suggests that practice patterns remain relatively unchanged despite significant advances in the evidence base that smoking negatively affects cancer treatment outcomes. The dominant barriers of lack of time, resources and education suggest that addressing these issues may improve treatment that supports tobacco cessation in both the curative and palliative settings. Given the increasing survival of cancer patients treated with palliative intent, smoking cessation support will be of increasing relevance to improve survivorship and quality of life. We recommend that all cancer patients should be screened for smoking status at diagnosis, and active smokers should have access to evidence-based smoking cessation support to improve cancer treatment outcomes as well as improve outcomes for non–cancer-related health conditions known to be improved with smoking cessation.

**Funding**

The present study is supported by an unrestricted grant from the Province of Utrecht, The Netherlands.

**Role of the funding source**

The funder had no role in the execution of this study, as it includes an unrestricted grant.

**Conflict of interest statement**

The authors have declared no conflicts of interest.

**Acknowledgements**

The authors would like to thank all organisations that distributed this survey among its members. This includes organisations from: Belgium (Belgian Society of Medical Oncology [BSMO], in Belgian: Belgische Vereniging voor Medische Oncologie—Société belge d’Oncologie médicale); Denmark (Danish Society for Medical Oncology, In Danish: Dansk Selskab Klinisk Onkologi [DSKO]); Estonia (Estonian Society of Medical Oncology, in Estonian: Eesti Onkoteraapia Ühing [EOU]); Finland (Finnish Society for Oncology, in Finnish: Suomen Onkologiayhdistys); Germany (Medical Oncology Association as part of the German Cancer Society, in German: Arbeitsgemeinschaft Internistische Onkologie (AIO); Greece (Hellenic Society of Medical Oncology [HeSMO]); Ireland (Irish Society of Medical Oncology [ISMO]); Lithuania (Lithuanian Society for Medical Oncology [LSMO], in Lithuanian: Lietuvos onkologų chemoterapeutų draugija); Luxembourg, (Luxembourg Society of Oncology [SLO], in Luxembourg: Société Luxembourgeoise d’Oncologie); The Netherlands (Dutch Colorectal Cancer Group [DCCG], Dutch Upper GI Cancer Group [DUCG], and the Dutch Neuro-Oncology Society [DNOS]); Poland (Polish Society of Clinical Oncology, in Polish: Polskie Towarzystwo Onkologii Klinicznej [PTOK]); Serbia (Serbian Society of Medical Oncology, in Serbian: Udruženje Medikalnih Onkologa Srbije [UMOS]); Spain (Spanish Society of Medical Oncology, in Spanish: Sociedad Española de Oncología Médica [SEOM]); Sweden (Swedish Society of Oncology, in Swedish: Svensk Onkolologisk Förening [SOF]); Switzerland (Swiss Society of Medical Oncology, in Swiss: Schweizerische Gesellschaft für Medizinische Onkologie [SGMO]); and the United Kingdom (Association of Cancer Physicians [ACP]).

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejca.2020.07.020.
References

[1] US Department of Health and Human Services. The health consequences of smoking-50 years of progress: a report of the surgeon general. Atlanta (GA), 2014.

[2] Warren GW, Cartmell KB, Garrett-Mayer E, Salloum RG, Cummings KM. Attributable failure of first-line cancer treatment and incremental costs associated with smoking by patients with cancer. JAMA Netw Open 2019:2.

[3] US Department of Health and Human Services. Smoking cessation: a report of the surgeon general. Atlanta (GA): Centers for Disease Control and prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.

[4] Warren GW, Alberg AJ, Cummings KM, Dresler C. Smoking cessation after a cancer diagnosis is associated with improved survival. J Thorac Oncol 2020;15(5):705–8.

[5] Postmus PE, Kerr KM, Oudkerk M, et al. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28:1–21.

[6] Planchard D, Popat S, Kerr K, et al. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2019;30:863–70.

[7] Warren GW, Simmons VN. Tobacco use and the cancer patient. In: Cancer: principles & practice of oncology. 11th ed. 2018.

[8] National Comprehensive Cancer Network (NCCN). Smoking cessation guidelines. [cited 4-14-2020]. Available from: www.nccn.org/professionals/physician_gls.

[9] Hanna N, Mulshine J, Wollins DS, Tyne C, Dresler C. Tobacco cessation and control a decade later: American society of clinical oncology policy statement update. J Clin Oncol 2013;31:3147–57.

[10] Toll BA, Brandon TH, Gritz ER, et al. Assessing tobacco use by cancer patients and facilitating cessation: an American Association for Cancer Research policy statement. Clin Canc Res 2013;19:1941–8.

[11] Cummings KM, Dresler CM, Field JK, et al. E-cigarettes and cancer patients. J Thorac Oncol 2014;9:438–41.

[12] Toogawa K, Bhatti L, Tursan d’Espaignet E, et al. Association between smoking during radiotherapy and prognosis in head and neck cancer: a follow-up study. Head Neck 2002;24:1031–7.

[13] Sardari Nia P, Weyler J, Colpaert C, Vermeulen P, Van Marck E, Van Schil P. Prognostic value of smoking status in operated non-small cell lung cancer. Lung Canc 2005;47:351–9.

[14] Basr S, Shannon VR, Eapen GA, et al. Smoking cessation after diagnosis of lung cancer is associated with a beneficial effect on performance status. Chest 2006;130:1764–90.

[15] Chen J, Jiang R, Garces YI, et al. Prognostic factors for limited-stage small cell lung cancer: a study of 284 patients. Lung Canc 2010;67:221–6.

[16] Sloan JA, Zhao X, Novotny PJ, et al. Relationship between deficits in overall quality of life and non-small cell lung cancer survival. J Clin Oncol 2012;30:1498–504.

[17] Al-Mamgani A, van Rooij PH, Woutersen DP, et al. Radiotherapy for T1-2N0 glottic cancer: a multivariate analysis of predictive factors for the long-term outcome in 1050 patients and a prospective assessment of quality of life and voice handicap index in a subset of 233 patients. Clin Otolarngol 2013;38:306–12.

[18] Al-Mamgani A, van Rooij PH, Mehilal R, Verduijn GM, Tans L, Kwa SL. Radiotherapy for T1a glottic cancer: the influence of smoking cessation and fractionation schedule of radiotherapy. Eur Arch Oto-Rhino-Laryngol 2014;271:125–32.

[19] Bloom EL, Oliver JA, Sutton SK, Brandon TH, Jacobsen PB, Simmons VN. Post-operative smoking status in lung and head and neck cancer patients: association with depressive symptomatology, pain, and fatigue. Psycho Oncol 2015;24:1012–9.

[20] Passarelli MN, Newcomb PA, Hampton JM, et al. Cigarette smoking before and after breast cancer diagnosis: mortality from breast cancer and smoking-related diseases. J Clin Oncol 2016;34:1315–22.

[21] Safavy S, Kilday PS, Slezak JM, et al. Effect of a smoking cessation program on sexual function recovery following robotic prostatectomy at Kaiser permanente Southern California. Perm J 2017;21:16–138.

[22] Norn J, Nieder C. Tobacco smoking and cessation and PD-L1 inhibitors in non-small cell lung cancer (NSCLC): a review of the literature. ESMO Open 2019;3:e000406.

[23] Li B, Huang X, Fu L. Impact of smoking on efficacy of PD-1/PD-L1 inhibitors in non-small cell lung cancer patients: a meta-analysis. OncoTargets Ther 2018;11:3691–6.

[24] Beck M, Rodriguez-Abreu D, Robinson AG, et al. Updated analysis of KEYNOTE-024: pembrolizumab versus platinum-based chemotherapy for advanced non-small-cell lung cancer with PD-L1 tumor proportion score of 50% or greater. J Clin Oncol 2019;37:537.

[25] Robinson CD, Gonzalez-Feliciano A, Mucci LA, Markt SC. Smoking cessation among men following cancer diagnosis: a matched cohort study. J Cancer Surviv 2018;12:786–93.

[26] Gritz ER, Fingeret MC, Viderne DJ, Lavey AB, Mehta NV, Reece GP. Successes and failures of the teachable moment - smoking cessation in cancer patients. Cancer 2008;106:17–27.

[27] Cinciripini PM, Karam-Hage M, Kypriotakis G, et al. Association of a comprehensive smoking cessation program with smoking abstinence among patients with cancer. JAMA Netw Open 2019;2.
[39] Fiore MC, D’Angelo H, Baker T. Effective cessation treatment for patients with cancer who smoke—the fourth pillar of cancer care. JAMA Netw Open 2019;2.

[40] Petrucci CM, Hyland A. Understanding the financial consequences of smoking during cancer treatment in the era of value-based medicine. JAMA Netw Open 2019;2:e191713.

[41] European Medicines Agency. How EMA evaluates medicines for human use. 2020 [cited; Available from: www.ema.europa.eu/en/about-us/what-we-do/authorisation-medicines/how-ema-evaluates-medicines.

[42] Hardcastle SJ, Kane R, Chivers P, et al. Knowledge, attitudes, and practice of oncologists and oncology health care providers in promoting physical activity to cancer survivors: an international survey. Support Care Canc 2018;26:e9711–9.

[43] Carli F, Silver JK, Feldman LS, et al. Surgical prehabilitation in patients with cancer: state-of-the-science and recommendations for future research from a panel of subject matter experts. Phys Med Rehabil Clin 2017;28:49–64.

[44] van Rooijen S, Carli F, Dalton S, et al. Multimodal prehabilitation in colorectal cancer patients to improve functional capacity and reduce postoperative complications: the first international randomized controlled trial for multimodal prehabilitation. BMC Canc 2019;19:98.