# Radiation Dose and Fractionation for Limited-stage Small-cell Lung Cancer: Survey of US Radiation Oncologists on Practice Patterns

Matthew J. Farrell,[1] Jehan B. Yahya,[1] Catherine Degnin,[1] Yiyi Chen,[1] John M. Holland,[1] Mark A. Henderson,[1] Jerry J. Jaboin,[1] Matthew M. Harkenrider,[2] Charles R. Thomas, Jr,[1] Timur Mitin[1]

## Abstract

**In the present survey of 309 US radiation oncologists on how they treat limited-stage small-cell lung cancer, substantial variation was found in the dosing and fractionation for thoracic radiotherapy (TRT). Three quarters of the respondents administered once-daily TRT more commonly than twice daily. For twice-daily TRT, most preferred a dose of 45 Gy. For once-daily TRT, the disagreement was greater, with a 60-Gy dose the most common.**

**Background:** Thoracic radiotherapy (TRT) with concurrent chemotherapy is standard for limited-stage small-cell lung cancer (LS-SCLC). However, the optimal dosing and fractionation remain unclear. The National Comprehensive Cancer Network guidelines have recommended either 45 Gy delivered twice daily (BID) or 60 to 70 Gy delivered once daily (QD). However, the current practice patterns among US radiation oncologists are unknown. **Materials and Methods:** We surveyed US radiation oncologists using an institutional review board-approved questionnaire. The questions covered demographic data, self-rated knowledge of key trials, and treatment recommendations. **Results:** We received 309 responses from radiation oncologists. Of the 309 radiation oncologists, 60% preferred TRT QD and 76% acknowledged QD to be more common in their practice. The respondents in academic settings were more likely to endorse BID treatment by both preference ($P = .001$) and actual practice ($P = .009$). The concordance between preferring QD and administering QD in practice was 100%. In contrast, 40% of respondents who preferred BID actually administered QD more often. Also, 15% of physicians would be unwilling to switch from QD to BID and 3% would be unwilling to switch from BID to QD, even on patient request. Most respondents (88%) recommended a dose of 45 Gy for BID treatment. For QD treatment, the division was greater, with 54% recommending 60 Gy, 30% recommending 63 to 66 Gy, and 10% recommending 70 Gy. **Conclusion:** Substantial variation exists in how US radiation oncologists approach TRT dosing and fractionation for LS-SCLC. Three quarters of our respondents reported administering TRT QD most often. The most common doses were 60 Gy QD and 45 Gy BID. The results of the present survey have provided the most up-to-date information on US practice patterns for LS-SCLC.

*Clinical Lung Cancer,* Vol. 20, No. 1, 13-9 
**Keywords:** Dose escalation, Dosing, Hyperfractionated, LS-SCLC, Thoracic radiotherapy

## Introduction

Small-cell lung cancer (SCLC) represents 10% to 15% of lung cancer cases and carries a poor prognosis.[1] At diagnosis, 24% of SCLC patients have limited-stage SCLC (LS-SCLC),[1] defined by the National Comprehensive Cancer Network (NCCN) as stage I-III (T any, N any, M0) disease that can be treated safely with

Abstract presented in part as an oral presentation at the International Association for the Study of Lung Cancer 2017 Chicago Multidisciplinary Symposium in Thoracic Oncology, Chicago, IL, September 14-16, 2017.

[1]Department of Radiation Medicine, Oregon Health & Science University, Portland, OR
[2]Department of Radiation Oncology, Stritch School of Medicine, Loyola University Chicago, Chicago, IL

Submitted: May 6, 2018; Revised: Jul 24, 2018; Accepted: Aug 11, 2018; Epub: Aug 22, 2018

Address for correspondence: Timur Mitin, MD, PhD, Department of Radiation Medicine, Oregon Health & Science University, 3181 Southwest Sam Jackson Park Road, L337, Portland, OR 97239-3098
E-mail contact: mitin@ohsu.edu

1525-7304/$ - see frontmatter 
https://doi.org/10.1016/j.cllc.2018.08.015

definitive radiotherapy.[2] The standard treatment for LS-SCLC involves concurrent chemoradiotherapy and, for patients with a good objective response, prophylactic cranial irradiation.[3-6] Meta-analyses[7,8] and a retrospective analysis[9] showed significant improvement in overall survival when thoracic radiotherapy (TRT) was added to chemotherapy. However, the optimal dose and fractionation schedule remain unclear.[10]

NCCN guidelines—both the version available when the survey was completed[11] and the most recent version at the writing of this report[2]—have recommended 1 of 2 treatment strategies: twice-daily (BID) TRT in 1.5-Gy fractions over 3 weeks to a total dose of 45 Gy or once-daily (QD) TRT in 2.0-Gy fractions over 6 to7 weeks to a total dose of 60 to 70 Gy. The recommendation for BID TRT stemmed from the 1999 Intergroup 0096 study reported by Turrisi et al[3]—a randomized controlled trial of 417 LS-SCLC patients. They demonstrated that the regimen of 45 Gy BID in 3 weeks improved survival compared with 45 Gy QD in 5 weeks, although with a greater rate of grade 3/4 esophagitis using the predominately 2-dimensional treatment planning of that era.[3]

Although the Intergroup 0096 trial established 45 Gy BID as standard treatment, adoption of this regimen has been minimal. Only 11.3% of patients undergoing TRT for LS-SCLC from 1999 to 2012 were treated with this regimen, determined from an analysis of 25,045 patients in the National Cancer Database.[12] Various concerns regarding this schedule have been raised, including the increased toxicity, logistical challenges, and that the dose in the QD arm of the Intergroup 0096 study was not biologically equivalent to the dose in the BID arm. Doses as great as 70 Gy have been shown to be safe for QD administration in LS-SCLC patients.[13,14]

Two trials were designed to compare the 45-Gy BID regimen and dose-escalated QD TRT. The European Organization for Research and Treatment of Cancer 08072/CONVERT (concurrent once-daily vs. twice-daily radiotherapy) trial, which enrolled 547 patients with LS-SCLC, found no significant differences in survival and no major differences in toxicity between 45 Gy BID over 3 weeks and 66 Gy QD over 6.6 weeks.[4] The ongoing Alliance/CALGB (Cancer and Leukemia Group B) 30610/RTOG (Radiation Therapy Oncology Group) 0538 trial is comparing 45 Gy BID over 3 weeks and 70 Gy QD over 7 weeks (a third arm was closed to accrual).[15] The primary endpoint is overall survival. The power analysis is based on the assumption that the 2-year survival will be 8.8% greater in the QD arm than in the BID arm.

Given the ongoing debate and that the NCCN guidelines have endorsed 2 different strategies, it is unknown how patients with LS-SCLC are actually being treated in the United States. We designed an online survey to learn how US radiation oncologists treat LS-SCLC patients. We hypothesized that substantial variation in the practice patterns would be found regarding dosing and fractionation.

## Materials and Methods

### *Survey Instrument Development*

The Oregon Health & Science University institutional review board approved the present study (institutional review board approval no. 000149). The online survey was designed using REDCap, which is managed by the Oregon Clinical & Translational Research Institute.

The survey contained 39 questions. The questions covered demographic information and treatment recommendations for patients with LS-SCLC, including dose, fractionation schedule, timing of TRT with chemotherapy, target volume, elective nodal irradiation, prophylactic cranial irradiation, and memantine use.

Respondents were asked to provide the reasons they preferred QD versus BID TRT. They were given prepared answers and instructed to select all that applied. An "other" option was also provided, allowing respondents to type in their own reasons. Finally, the respondents were asked to rate their knowledge of 3 studies relevant to our analysis—the Intergroup 0096 trial,[3] CONVERT trial,[4] and CALGB 30610 trial. The following options were provided in each case: "I am not familiar with this trial," "I am familiar with this trial but could not provide specific details," and "I am very familiar with this trial and could provide specific details." For the recent CONVERT trial and ongoing CALGB 30610 trial, a fourth option was provided: "I participated in this trial and enrolled patients."

### *Data Collection*

The data sample was collected through an anonymous online questionnaire of US radiation oncologists. Using REDCap, electronic mail invitations were sent to 6954 potential participants from a public database of US radiation oncologists. The invitations contained information about the study, a link to the survey, instructions for completion, and contact information. Invitations were sent in October 2016, and the survey was closed to further responses in December 2016.

### *Statistical Analysis*

The respondents were characterized by self-reported practice setting, practice region, years since completing residency training, number of lung cancer patients treated with definitive intent in the previous year, number of LS-SCLC patients treated in the previous year, and self-rated knowledge of the relevant trials. These characteristics were analyzed for correlations with the responses regarding treatment practice. The $\chi^2$ test or Fisher's exact test in the case of small sample sizes was used to determine differences between groups for categorical variables. The Cochran-Armitage test was used to analyze trends in ordinal variables between groups. Kendall's rank correlation tau was used to evaluate the concordance between physician preference and actual treatment practice for the fractionation schedule. A $P$ value $< .05$ was deemed statistically significant. R, version 3.3.3, software (2017-03-96; R Foundation for Statistical Computing, Vienna, Austria; available at: http://www.r-project.org/) was used for statistical analysis.

## Results

### *Survey Respondents*

Survey invitations were sent to 6954 electronic mail addresses, including many that were inactive or duplicates, because the database contained both personal and institutional electronic mail addresses. Thus, the true number of potential participants was unknown. For context, recent estimates have suggested 4500 to 5000 radiation oncologists are practicing in the United States.[16] We received 732 undeliverable or failed automatic replies, 11 ineligible responses, and 315 completed responses, 309 of which were from

**Table 1** Demographic Information for Radiation Oncologists Who Completed the Survey (n = 309)

| Variable | Respondents, n (%) |
|---|---|
| Practice setting | |
| Private | 182 (58.9) |
| Academic | 127 (41.1) |
| Practice region | |
| Central | 79 (25.6) |
| Northern | 72 (23.3) |
| Pacific | 58 (18.8) |
| Southern | 66 (21.4) |
| Western | 31 (10.0) |
| Other | 3 (1.0) |
| Duration since residency training, y | |
| Currently in residency training | 11 (3.6) |
| 0-2 | 20 (6.5) |
| 3-5 | 49 (15.9) |
| 6-10 | 61 (19.7) |
| >10 | 168 (54.4) |
| Lung cancer patients treated with definitive intent in previous year, n | |
| None | 6 (1.9) |
| 1-2 | 7 (2.3) |
| 3-4 | 13 (4.2) |
| 5-10 | 41 (13.3) |
| >10 | 242 (78.3) |
| LS-SCLC patients treated in previous year, n | |
| <5 | 137 (44.3) |
| ≥5 | 172 (55.7) |

Abbreviation: LS-SCLC = limited-stage small-cell lung cancer.

radiation oncologists. Only the responses from the 309 radiation oncologists were analyzed, and their characteristics are summarized in Table 1.

### *QD Versus BID TRT*

Of the respondents, 60% preferred to administer TRT QD compared with 40% who preferred BID fractionation (Figure 1A). When asked which TRT schedule was more common for their patients, 76% selected QD and 24% selected BID TRT (Figure 1B). Physicians in academic settings, compared with those in private practice, were more likely to prefer BID TRT (51% vs. 33%; $P = .001$) and to use this regimen more commonly in practice (32% vs. 19%; $P = .009$).

Physician preference and actual treatment practice were highly correlated ($P < .0001$), indicating that the actual practice frequently aligned with physician preference. Every respondent who preferred QD TRT did use a QD schedule most often with their patients. In contrast, 40% of respondents who preferred BID TRT actually used a QD schedule more commonly. In addition, even if requested by patients, 15% of the respondents would be unwilling to switch from QD to BID therapy, and 3% would be unwilling to switch from BID to QD therapy. The respondents unwilling to switch schedules were more likely to have > 10 years of experience after residency training ($P = .048$).

### *Physician Reasoning for Fractionation Choice*

The respondents were asked why they preferred QD to BID fractionation, and the results are summarized in Figure 2. For those preferring QD TRT, 19 (10%) chose "other." Ten reported they were not convinced by the data supporting BID over QD therapy, with most citing flaws with the Intergroup 0096 study, in particular, the lack of a biologically equivalent dose in the QD arm. Four cited patient preference or that many patients could not arrange travel for 2 daily visits for treatment. Two reported they were more comfortable with the QD schedule owing to their training and experience. Two referenced the greater rates of esophagitis with BID therapy, which could lead to patients not being able to complete treatment uninterrupted. Finally, 1 noted that QD and BID therapy appeared equivalent based on the data from their home institution.

For those who preferred BID TRT, 15 (12%) chose "other." Nine reported that BID therapy appears superior to QD based on the best available data, including the Intergroup 0096 and CONVERT trials. Three expanded on the shorter treatment duration with BID therapy, which they argued was important for a fast-growing cancer such as SCLC. Two referenced the lower total lung dose with BID therapy and the uncertainty of how high to increase the dose for QD treatment. One noted better local control with BID treatment based on personal experience.

### *Dose for TRT*

When administering QD TRT, more than one half (54.4%) of the respondents preferred a total dose of 60 Gy, followed by 20.4% opting for 66 Gy, 10.0% for 70 Gy, 9.4% for 63 Gy, 5.2% for < 60 Gy, and 0.6% for > 70 Gy (Figure 3A). When administering BID TRT, the vast majority (87.9%) preferred a total dose of 45 Gy, with 5.9% choosing 54 Gy, 2.9% choosing 50 Gy, 2.9% choosing > 54 Gy, and 0.3% choosing 30 Gy (Figure 3B). For QD TRT, the physicians who had treated more lung cancer patients in the previous year were increasingly likely to recommend doses > 60 Gy ($P = .01$). For BID TRT, physicians with > 10 years of experience after residency training were more likely to recommend doses > 45 Gy (18% vs. 4%; $P = .0004$).

### *Self-rated Knowledge of Relevant Trials*

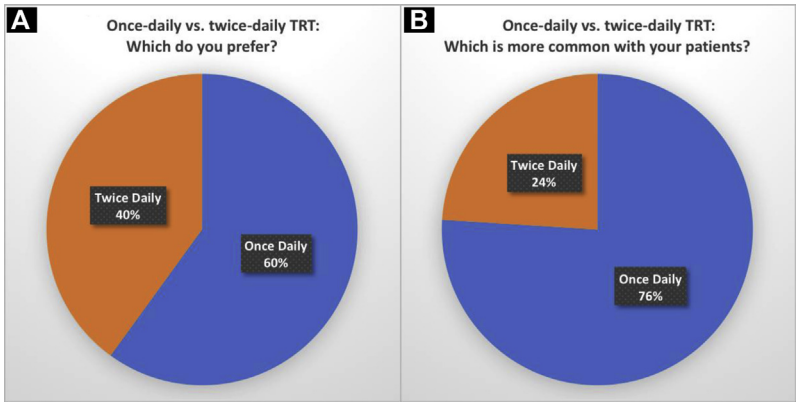
The respondents' self-rated knowledge of the relevant trials is summarized in Table 2. The respondents familiar with the CALGB 30610 trial[3] were more likely to prefer BID TRT ($P = .003$). Knowledge of the CONVERT trial[4] was not significantly associated with a preference for QD versus BID therapy ($P = .10$). Regarding the dose for QD TRT, the respondents who preferred doses > 60 Gy were more likely to be familiar with the CALGB 30610 trial independently ($P = .004$), the CONVERT trial independently ($P = .02$), or with both trials ($P = .01$).

## Discussion

### *Fractionation: A Tale of 2 Schedules*

The current NCCN guidelines present a fork in the road for treatment of LS-SCLC, endorsing TRT in the form of either 45-Gy

**Figure 1** Once-daily (QD) Versus Twice-daily (BID) Thoracic Radiotherapy (TRT). (A) As a General Rule, 184 of 308 Respondents (59.7%) Preferred to Administer QD TRT Compared With 124 (40.3%) Who Preferred BID. (B) When Asked Which Schedule Was More Common With Their Actual Patients, 235 of 309 Respondents (76.1%) Selected QD TRT and 74 (23.9%) Chose BID TRT




BID or 60- to 70-Gy QD.[2] Our survey results have shown that most respondents preferred QD over BID fractionation and more than three quarters administered QD TRT more often to their patients. The present survey was conducted after results of the landmark CONVERT trial had been presented at the 2016 American Society of Clinical Oncology Annual Meeting[17] but before publication of the report in June 2017.[4] The investigators of the CONVERT trial argued that BID TRT should remain the standard of care, because the trial had been designed to show the superiority of QD treatment and failed to do so. Furthermore, in the BID arm, a nonsignificant trend was found toward improved survival, along with lower than expected toxicity, better compliance, and a shorter treatment time. However, because no significant survival differences were found, it remains to be seen to be seen whether radiation oncologists will interpret these results as justification for prescribing QD TRT with an escalated dose. Almost two thirds of our respondents (63%) were familiar with the CONVERT trial, and 99% were familiar with the Intergroup 0096 trial,[3] which

**Figure 2** Physician Reasoning Behind the Choice Between Once-daily (QD) and Twice-daily (BID) Thoracic Radiotherapy (RT). Respondents Were Provided With a Set of Prepared Answers and Asked to Select All Answers That Applied. (A) Of the 184 Respondents Who Preferred QD RT, 130 (70.7%) Selected the First Option, 79 (42.9%) the Second, and 109 (59.2%) the Third. (B) Of the 124 Respondents Who Preferred BID RT, 63 (50.8%) Chose the First Option, 72 (58.1%) the Second, and 52 (41.9%) the Third

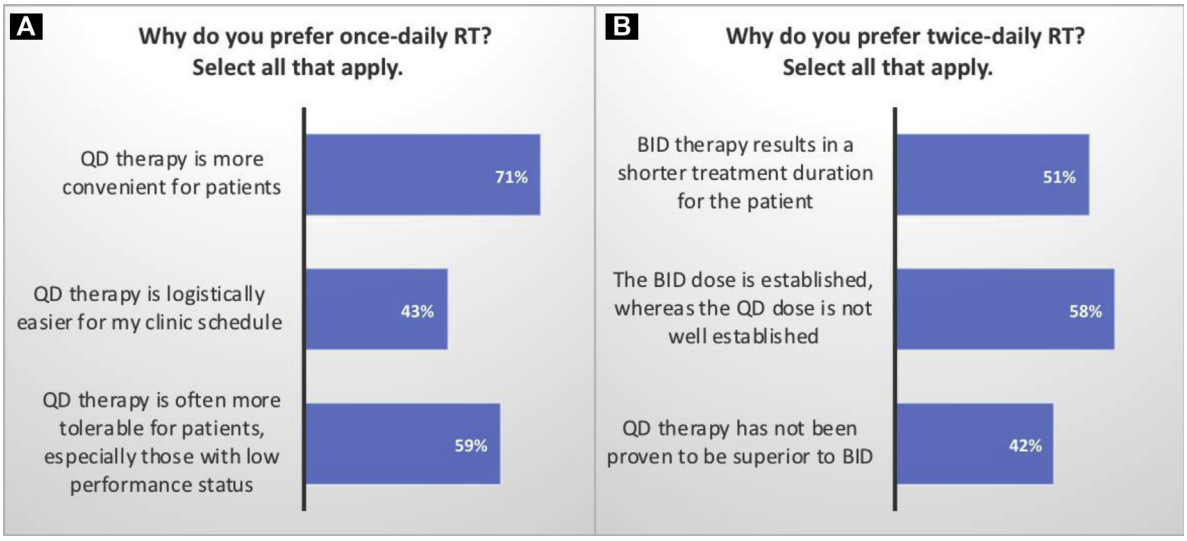
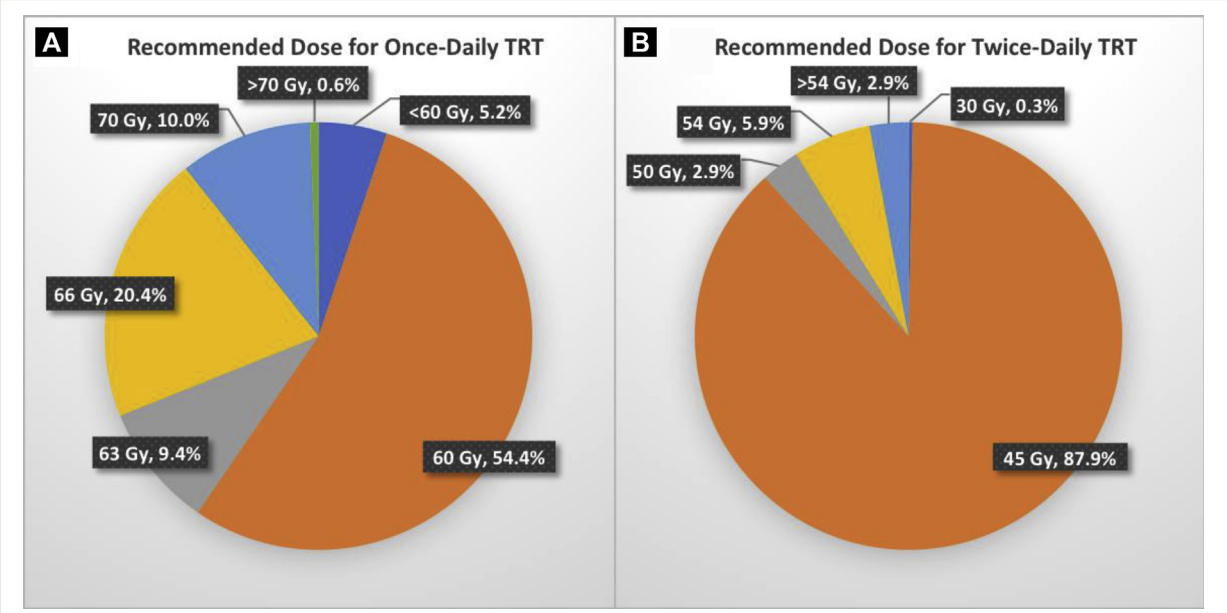


**Figure 3** Preferred Doses for Once-daily (QD) and Twice-daily (BID) Thoracic Radiotherapy (TRT). (A) For QD TRT, 16 of 309 Respondents (5.2%) Recommended < 60 Gy as the Total Dose, 168 (54.4%) Chose 60 Gy, 29 (9.4%) Chose 63 Gy, 63 (20.4%) Chose 66 Gy, 31 (10.0%) Chose 70 Gy, and 2 (0.6%) Chose > 70 Gy. (B) For BID TRT, 1 (0.3%) of 307 Respondents Recommended 30 Gy, 270 (87.9%) Chose 45 Gy, 9 (2.9%) Chose 50 Gy, 18 (5.9%) Chose 54 Gy, and 9 (2.9%) Chose > 54 Gy




showed the superiority of 45-Gy BID compared with 45-Gy QD. Nonetheless, BID treatment was recommended by only a minority of the respondents.

A common concern with BID therapy has been its associated toxicity. In the Intergroup 0096 trial, the rate of grade 3/4 esophagitis was significantly greater in the BID arm (32% vs. 16%).[3] More than one half of our respondents who preferred QD therapy based their decision on the assumption that it will be better tolerated, especially by patients with a low performance status. The CONVERT trial included only patients with a moderate-to-good performance status (Eastern Cooperative Oncology Group performance status of 0-2) and found no significant differences in toxicity rates between the groups, with the exception of the incidence of grade 4 neutropenia being higher in the BID group ($P = .05$). The rate of grade 3/4 esophagitis was 19% in both groups ($P = .85$), lower than expected from the Intergroup 0096 results, perhaps owing to the omission of elective nodal irradiation and advances in the precision of radiation delivery during the past several decades. The ongoing CALGB 30610 trial has mandated elective irradiation of the ipsilateral hilar lymph nodes. Thus, it will be interesting to see how the rates of esophagitis compare with those in the CONVERT trial, which omitted elective nodal irradiation completely. In both trials, 3-dimensional conformal radiotherapy was mandatory, and intensity-modulated radiotherapy was allowed.

A full 40% of those preferring BID TRT did not treat according to this preference, instead using QD TRT with most of their patients. Perhaps this resulted from the logistical difficulty—for both provider and patient—of arranging 2 treatments daily. The most frequently chosen reason for preferring QD therapy was patient convenience, with another common choice being the logistical ease of clinic scheduling—both reasons not tied to the inherent efficacy or toxicity of the treatment. Some facilities might simply not be set up for BID therapy, especially smaller private practices. This could explain why respondents in academic settings were more likely to prefer and use BID therapy, consistent with previous studies showing BID therapy to be more common in academic

**Table 2** Self-rated Knowledge of Relevant Clinical Trials

| Knowledge | Intergroup 0096 (1999)[3] | EORTC 08072/CONVERT (2017)[4] | CALGB 30610/RTOG 0538 (Ongoing) |
|---|---|---|---|
| Not familiar | 3 (1.0) | 115 (37.2) | 32 (10.4) |
| Familiar | 85 (27.5) | 139 (45.0) | 136 (44.2) |
| Very familiar | 221 (71.5) | 51 (16.5) | 99 (32.1) |
| Participated or enrolled patients | NA | 4 (1.3) | 41 (13.3) |

Abbreviations: CONVERT = concurrent once-daily versus twice-daily radiotherapy; EORTC = European Organization for Research and Treatment of Cancer; NA = not applicable; RTOG = Radiation Therapy Oncology Group.

institutions.[12,18] The difficulty in arranging BID therapy might also be why 15% of the physicians who preferred QD TRT would not switch to BID TRT, even if requested by their patients.

### *Dose: Agreement for BID; Disagreement for QD*

For BID TRT, the overwhelming majority of our respondents recommended a total dose of 45 Gy, in line with the NCCN guidelines.[2] Doses > 45 Gy represent overtreatment, because no clinical trial results have supported higher doses. Also, evidence has indicated 45 Gy to be the maximum tolerable dose for BID treatment delivered over 3 weeks.[13] However, 12% of our respondents recommended doses > 45 Gy for BID TRT. The respondents with > 10 years of experience after residency were > 4 times more likely to exceed the recommended dose of 45 Gy than those with less experience. This suggests the need for ongoing education of physicians throughout their careers.

Less unity was found in the recommendations for QD dosing, not surprising given that the NCCN guidelines have endorsed any dose from 60 to 70 Gy. The most commonly chosen reason for preferring BID TRT was that the optimal BID dose was established but the optimal QD dose was not.

The respondents familiar with the CONVERT and CALGB 30610 trials—which used doses of 66 Gy and 70 Gy, respectively—were more likely to recommend doses > 60 Gy for QD TRT. Perhaps knowledge of, or participation in, these trials allowed physicians to be more comfortable with dose escalation.

### *Study Limitations*

The greatest limitation of our study was the low response rate, with a sample size of 309 eligible responses. This low response rate could have resulted from the relative infrequency of treating LS-SCLC patients, the subspecialization of radiation oncology practices, and survey fatigue. Response or participant bias could have affected the results, because differences could have been present between those who completed the survey and those who did not. Our findings should be interpreted with caution, because they might not be representative of US radiation oncologists as a whole. In comparing our sample of radiation oncologists to samples from other recent surveys and an online directory of radiation oncologists, we did not find substantial differences in the demographic data, in terms of practice setting,[19,20] practice region,[21] or number of years in practice.[20]

Also, any unintended bias from us in how the questions were worded or ordered in the survey could have affected the answers given. Recall bias could also have influenced the accuracy of the responses, given that some responses relied on the physicians' memory of recent practice patterns. Finally, it is unknown whether the respondents self-primed their knowledge of the clinical trials asked about in our survey by researching the trials as they completed the survey.

## Conclusion

The goal of the present survey was to broadly sample radiation oncologists in the United States on their management of LS-SCLC. Our survey revealed disunity in how US radiation oncologists approach dosing and fractionation. It was conducted before publication of the landmark CONVERT trial report, which failed to show superiority of 66 Gy QD over the standard schedule of 45 Gy BID. Our data can be used to track changes in practice patterns in the wake of the CONVERT trial to determine whether more physicians do as the investigators of the CONVERT trial suggest and embrace 45 Gy BID as the standard of care. The ongoing CALGB 30610 trial is still many years from completion. If the results are positive, it might bring US providers to a consensus on management; however, if negative, our survey results might hold for years to come.

### *Clinical Practice Points*

- For patients with LS-SCLC, current NCCN guidelines have recommended 2 different treatment strategies: BID TRT delivered in 1.5-Gy fractions to a total dose of 45 Gy or QD TRT delivered in 2.0-Gy fractions to a total dose of 60 to 70 Gy.
- The 1999 Intergroup 0096 trial reported by Turrisi et al[3] established 45-Gy BID as the standard regimen by demonstrating its superiority over 45-Gy QD.
- The 2017 CONVERT trial was designed to show the superiority of 66-Gy QD over 45-Gy BID but failed to do so, finding no significant differences in survival and no major differences in toxicity.
- Our survey of 309 radiation oncologists revealed wide variability in dose and fractionation usage among clinicians.
- Of the respondents, 60% preferred QD over BID fractionation as a general rule, and more than three quarters reported they used QD treatment more commonly with their patients.
- All respondents who preferred QD TRT used QD treatment in actual practice.
- In contrast, 40% of those preferring BID TRT still used QD TRT more commonly.
- Regarding radiation dose, nearly 9 of 10 respondents recommended a total dose of 45 Gy for BID TRT.
- However, for QD TRT, more variation was found, with the most common recommendation being 60 Gy.
- The present survey was conducted before final report of the CONVERT trial; however, our data can be used to track the practice patterns in the aftermath of this landmark trial.
- The ongoing Alliance/CALGB 30610/RTOG 0538 trial—comparing 45 Gy BID and 70 Gy QD—is still years from completion.

## Acknowledgments

The online questionnaire described in this manuscript was created using the REDCap web application, managed by the Oregon Clinical and Translational Research Institute and supported by grant 1 UL1 RR024140 01 from the National Institutes of Health, United States.

## Disclosure

The authors declare that they have no competing interests.

## References

1. Howlader N, Noone AM, Krapcho M, et al, eds. SEER cancer statistics review, 1975-2014. April 2017, based on November 2016 SEER data submission. Available at: https://seer.cancer.gov/csr/1975_2014/. Accessed: March 13, 2018.
2. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Small Cell Lung Cancer (Version 2.2018), Available at: www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed: March 13, 2018.

3. Turrisi AT III, Kim K, Blum R, et al. Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. *N Engl J Med* 1999; 340:265-71.
4. Faivre-Finn C, Snee M, Ashcroft L, et al. Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial. *Lancet Oncol* 2017; 18:1116-25.
5. Aupérin A, Arriagada R, Pignon JP, et al. Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. Prophylactic Cranial Irradiation Overview Collaborative Group. *N Engl J Med* 1999; 341:476-84.
6. Arriagada R, Le Chevalier T, Rivière A, et al. Patterns of failure after prophylactic cranial irradiation in small-cell lung cancer: analysis of 505 randomized patients. *Ann Oncol* 2002; 13:748-54.
7. Pignon JP, Arriagada R, Ihde DC, et al. A meta-analysis of thoracic radiotherapy for small-cell lung cancer. *N Engl J Med* 1992; 327:1618-24.
8. Warde P, Payne D. Does thoracic irradiation improve survival and local control in limited-stage small-cell carcinoma of the lung? A meta-analysis. *J Clin Oncol* 1992; 10:890-5.
9. Lally BE, Geiger AM, Urbanic JJ, et al. Trends in the outcomes for patients with limited stage small cell lung cancer: an analysis of the Surveillance, Epidemiology, and End Results database. *Lung Cancer* 2009; 64:226-31.
10. Slotman B. What is the optimal radiotherapy schedule for limited stage small cell lung cancer? *Lung Cancer* 2017; 105:52-3.
11. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Small Cell Lung Cancer (Version 2.2017), Available at: www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed: November 2, 2016.
12. Schreiber D, Wong AT, Schwartz D, Rineer J. Utilization of hyperfractionated radiation in small-cell lung cancer and its impact on survival. *J Thorac Oncol* 2015; 10:1770-5.
13. Choi NC, Herndon JE, Rosenman J, et al. Phase I study to determine the maximum-tolerated dose of radiation in standard daily and hyperfractionated-accelerated twice-daily radiation schedules with concurrent chemotherapy for limited-stage small-cell lung cancer. *J Clin Oncol* 1998; 16:3528-36.
14. Bogart JA, Herndon JE, Lyss AP, et al. 70 Gy thoracic radiotherapy is feasible concurrent with chemotherapy for limited-stage small-cell lung cancer: analysis of Cancer and Leukemia Group B study 39808. *Int J Radiat Oncol Biol Phys* 2004; 59:460-8.
15. Komaki R, Paulus R, Ettinger DS, et al. Phase II study of accelerated high-dose radiotherapy with concurrent chemotherapy for patients with limited small-cell lung cancer: Radiation Therapy Oncology Group protocol 0239. *Int J Radiat Oncol Biol Phys* 2012; 83:e531-6.
16. The State of Cancer Care in America, 2017: A Report by the American Society of Clinical Oncology. *J Oncol Pract* 2017; 13:e353-94.
17. Faivre-Finn C, Snee M, Ashcroft L, et al. Concurrent once-daily versus twice-daily radiotherapy: an international 2-arm randomized controlled trial of concurrent chemoradiotherapy comparing twice-daily and once-daily radiotherapy schedules in patients with limited stage small cell lung cancer (LS-SCLC) and good performance status. Presented at the 2016 American Society of Clinical Oncology Annual Meeting, Chicago, IL, June 3-7. Abstract 8504.
18. Komaki R, Khalid N, Langer CJ, et al. Penetration of recommended procedures for lung cancer staging and management in the United States over 10 years: a quality research in radiation oncology survey. *Int J Radiat Oncol Biol Phys* 2013; 85:1082-9.
19. Vichare A, Washington R, Patton C, et al. An assessment of the current US radiation oncology workforce: methodology and global results of the American Society for Radiation Oncology 2012 Workforce Study. *Int J Radiat Oncol Biol Phys* 2013; 87:1129-34.
20. Lucey P, Zouzias C, Franco L, Chennupati SK, Kalnicki S, McLellan BN. Practice patterns for the prophylaxis and treatment of acute radiation dermatitis in the United States. *Support Care Cancer* 2017; 25:2857-62.
21. US News & World Report. Find radiation oncologists, Available at: health.usnews.com/doctors/location-index/radiation-oncologists. Accessed: February 9, 2018.