



Single-institution analysis of the prevalence, indications and outcomes of end-of-life radiotherapy

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ABSTRACT

Background: Radiotherapy plays an important role for symptom control in advanced stage cancer patients. Yet patients need to be carefully selected, and its use and benefits must be weighed against time spent under treatment and patient priorities in the last phase of life. In this study, we assess prevalence, indications and outcomes of radiotherapy close to death.

Methods: We screened all radiotherapy treatments performed at the Department of Radiation Oncology of the University Hospital Zurich between January 2010 and December 2019 to identify those which occurred near patients' end-of-life. Analyzed data was extracted from the database of the Comprehensive Cancer Center Zurich, the treatment planning system Aria® and the electronic medical records system KISIM®.

Results: Within 60 days of death, 377 radiotherapy courses were prescribed to 280 patients, which constitutes 3.4% of all radiotherapy courses administered over the last decade at our department. Within 60–31, 30–8, and 7–0 days to death 164, 159, and 54 radiotherapy courses were prescribed, respectively. The most frequent treatment sites were brain (N = 122, 32%) and bone (N = 119, 32%), and there was no statistically significant difference in treatment site between the three sub-groups. The most common regimen was 10x3Gy (N = 130, 35%) in all three sub-groups (p = 0.23). Radiotherapy finished more than one week before death was associated with high completion rates (>80%) and treatment benefit (>55%).

Conclusion: Patient selection and survival prognostication remains challenging for radiation oncologists. While radiotherapy achieved high completion and success rates until one week before death, treatment within one week of death should be restricted to carefully selected patients or avoided altogether.

Introduction and background

Radiotherapy (RT) constitutes a treatment modality with a very favorable risk profile for symptom control in advanced stage cancer patients [1,2]. Palliative RT has proven to be effective for the treatment of painful bone metastasis and for stabilizing symptomatic as well as emergency situations like hemoptysis or spinal cord compression [3–6].

Several studies have shown that experienced physicians tend to systematically overestimate patients' survival, even when prognostic factors and scoring systems are employed [7,8]. This may contribute to both the prescription of longer RT courses despite the recommendation for hypofractionated schedules as well as potentially overly aggressive treatment regimens. As a result, RT may be administered near the end-

of-life (EoL) without having a positive effect on quality-of-life (QoL) [2,9,10]. Instead, such treatments carry the risk of depriving patients of valuable EoL time spent outside hospitals close to their loved ones, realizing key priorities in the last phase of life. Hence even though the World Health Organization recommends RT in the management of cancer patients in adults as well as adolescents, and the guidelines of the European Society of Medical Oncology and the American Society of Clinical Oncology intend to help navigate treatment decisions in advanced stage cancer patients, selecting the right palliative treatment strategy for any individual patient remains challenging for treating physicians. Appropriately managed, palliative RT regimens, even when prescribed close to death, have the potential to improve QoL, as, for example, emergent or analgesic effects of RT may start to take effect

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hours or days after treatment has begun or been completed [11–14].

As the prognostication of patient survival remains an inexact science and as the commonly used EoL cut-off of 30 days seems to have been chosen arbitrarily, this single-institution analysis at a tertiary comprehensive cancer center in Switzerland aims at comparing EoL RT in patients according to the historical definition with groups of patients who had a longer and a shorter prognosis. For all three groups, we assess the prevalence, review the indications and treatment rationales, and quantify the outcomes of EoL RT.

Materials and methods

We screened all RTs conducted at the Department of Radiation Oncology of the University Hospital Zurich between January 2010 and December 2019 to identify those which were occurred near EoL. The list of analyzed patients was extracted and compiled using the Record and Verify System Aria® (Version 15, Varian®), the central database and tumor registry of the Comprehensive Cancer Center Zurich.

Demographic patient data were retrieved from the hospital's electronic medical records system KISIM®. Extracted variables included gender, tumor histology, date of birth, date of death, treatment modality, dates of treatment, metastatic status at primary diagnosis, place of death, treatment intent, treatment completion, reason for treatment discontinuation, treatment indication, treatment site, treatment outcome, clinical performance status, and the existence of an advance healthcare directive at the time of treatment start. If missing, the performance status was derived from available data. Treatment outcome per RT course was assessed *qualitatively* via a thorough review of electronic medical records and all available follow-up information: Treatment benefit was defined as pre-therapeutic symptom load not having worsened ("symptom control") or having been improved ("symptom improvement"). Data on treatment dates, fractionation and dosage schedules were obtained from Aria®. All data was encoded. This review, as part of a project series, was approved by the Swiss Cantonal Ethics Committee (BASEC ID #2019-02488).

Descriptive statistics were computed for all demographic and treatment variables. EoL RT patients were subsequently stratified in order to compare and contextualize outcomes in three different patient sub-groups who received RT 60–31 days, 30–8 days and 7–0 days before death. For multiple sub-group comparison, the non-parametric Kruskal-Wallis-test was used. Statistical significance was set at $p < 0.05$. To facilitate comparability with other studies, the nomenclature RT_{DD} , increasingly commonly applied in the literature, was consistently used to label treatments taking place within a certain time interval in days before death [15]. EoL RT was defined as taking place within 60 days of death for the purposes of this analysis. For all statistical analysis, the statistical software package *Stata*® (Version v16.1.) was utilized.

Results

Contextualization of patient population

Between 2010 and 2019, 10,980 patients received 22,164 RT courses at our department, 64.8% ($N = 14,370$) and 35.2% ($N = 7794$) of which had a curative and a palliative intent, respectively. The 280 patients having received EoL RT courses within the last decade, thus constitute 2.6% of all patients treated at our department. The 370 EoL RT courses with a palliative intent represent 4.8% of all prescribed palliative RT courses. The 7 EoL RT courses with a curative intent make up a negligible proportion of 0.05% of all prescribed curative RT courses over the past decade at our department.

Patient characteristics

For the 280 patients having received EoL RT, the median age at primary diagnosis was 65 (interquartile range (IQR), 55–72) years, with

the majority of patients being male ($N = 168$, 66%). All patients had a histologically verified cancer diagnosis. The two most common primary cancer entities were lung ($N = 123$, 44%; non-small cell lung cancer (NSLC), small-cell lung cancer (SCLC), and mesothelioma) and melanoma ($N = 76$, 27%), accounting together for about 70% of all cases. More than two thirds of patients were metastatic at primary diagnosis, with the most common metastatic sites being lung ($N = 82$, 44%) and bone ($N = 74$, 40%). The performance status was higher or equal to 70% of the Karnofsky Performance Score (KPS) in 57% ($N = 160$) of patients at the time of consult when treatment was prescribed. The median interval from the time of primary diagnosis to RT start was 7.7 (IQR, 1.4–20.8) months. Forty-five (16%) patients had completed an advance healthcare directive prior to RT start. For the majority of patients ($N = 184$, 66%), the place of death was the inpatient setting. Thirty-five (13%), 23 (8%), and 8 (3%) patients died at home, in a nursing home and at a hospice, respectively. Thirty (11%) patients were lost to follow-up; the date of death was assessed through death registries. Patient characteristics are shown in Table 1.

Treatment characteristics

A total of 377 EoL RT courses was prescribed to 280 patients (mean: 1.35 courses per patient, median: 1 course per patient, range: 1–6 courses). An interdisciplinary tumor board was involved in the treatment decision in 38% ($N = 142$) of all prescribed RT courses. The treatment intent was palliative in $N = 370$ (98%) RT courses. A curative treatment regimen was prescribed in seven courses (2%) for lung, head & neck, brain and esophageal cancer patients. In more than 70% of treatment courses, the RT indication was pain or symptomatic brain/spinal metastasis ($N = 273$, 73%). Less frequently, indication was dyspnea/hemoptysis, asymptomatic brain/spinal metastasis or bleeding.

Table 1
Patient characteristics.

Data variables	Patients (n = 280)
Age at primary diagnosis in years, median (IQR)	65 (55–72)
Male gender, n (%)	186 (66)
Primary tumor site, n (%)	
Lung	123 (44)
Melanoma	76 (27)
CNS	32 (11)
Head & Neck	13 (5)
Colorectal	8 (3)
Other ¹	28 (10)
Presence of metastasis at primary diagnosis, n (%)	187 (67)
Metastatic sites at primary diagnosis, n (%)	
Lung	82 (44)
Bone	74 (40)
Brain	51 (27)
Liver	46 (25)
Other ²	145 (78)
Karnofsky performance status (KPS), n (%)	
≥ 70	160 (57)
< 70	120 (43)
Overall survival from date of primary diagnosis in months, median (IQR)	7.7 (1.4–20.8)
Advance healthcare directive prior to RT start, n (%)	45 (16)
Place of death, n (%)	
Inpatient	184 (66)
Home	35 (13)
Unknown	30 (11)
Nursing home	23 (8)
Hospice	8 (3)

Abbreviations: CNS = Central nervous system; IQR = interquartile range; RT = Radiation therapy.

¹ Includes breast, bone/soft tissue, esophageal, gynecological, hematologic, liver, thyroid, and pancreatic cancer.

² Includes adrenal glands, leptomeningeal disease, lymph nodes, mediastinum, orbita, skull base, spinal cord, and visceral organs.

Brain and bone were the most common treatment sites comprising more than 60% (N = 241) of all courses. In 23% (N = 85) of courses the primary tumor was irradiated. The median number of fractions was 10 (IQR, 5–10), the median dose per fraction was 3 (3–4) Gy, and 85% (N = 321) of RT courses consisted of more than 5 fractions. Median duration of RT was 11 (IQR, 6–16) days. With 83% (N = 311) the large majority of EoL RT courses was completed. When a RT course had to be discontinued, a general deterioration of the patient's performance status due to disease progression was identified as the cause in 77% (N = 51) of cases. The treatment aim was reached in N = 197 of RT courses, having led to a patient benefit in 52% of treatments. Treatment characteristics are summarized in Table 2.

Sub-group analysis

For sub-group analysis, the data on RT courses was stratified using time of RT application to create three distinct groups: treatments within 60 to 31 days before death (RT_{D60-31}), 30 to 8 days before death (RT_{D30-8}), and 7 to 0 days before death (RT_{D7-0}). This resulted in N = 164 (43.5%) courses in the RT_{D60-31} group, N = 159 (42.2%) in the RT_{D30-8} group, and 54 (14.3%) in the RT_{D7-0} group. Median patient age at time of radiotherapy treatment was 66 (IQR, 56–73), 65 (IQR, 53–73), and 54 (IQR, 56–72) for patients receiving RT_{D60-31}, RT_{D30-8}, and RT_{D7-0}, respectively. No statistically significant difference was observed with

Table 2
Treatment characteristics.

Data variables	RT courses (n = 377)
RT courses per patient, mean; median (range)	1.35; 1 (1–6)
Tumor board involvement in RT decision, n (%)	142 (38)
Palliative RT treatment intent, n (%)	370 (98)
Treatment indication, n (%)	
Pain	168 (45)
Symptomatic brain/spinal metastasis	105 (28)
Dyspnea/hemoptysis	33 (9)
Asymptomatic brain/spinal metastasis	32 (8)
Bleeding	20 (5)
Definitive ¹	7 (2)
Other ²	12 (3)
Treatment site, n (%)	
Brain	122 (32)
Bone	119 (32)
Primary	85 (23)
Soft tissue	29 (8)
Lymph node	12 (3)
Other ³	10 (3)
Fractionation schedule and dose	
Planned fractions, median (IQR)	10 (5–10)
1, n (%)	37 (10)
2–4, n (%)	19 (5)
5, n (%)	78 (21)
6–9, n (%)	23 (6)
10, n (%)	130 (35)
greater than 10, n (%)	90 (24)
Dose per fraction, median (IQR)	3 (3–4) Gy
RT treatment duration in days, median (IQR)	11 (6–16)
RT course completion, n (%)	311 (83)
Reasons for RT course discontinuation, n (%)	
General deterioration of performance status	51 (77)
Patient compliance	10 (15)
Pain exacerbation	2 (3)
Other ⁴	3 (5)
RT course treatment benefit, n (%)	197 (52)

Abbreviations: Gy = Gray; IQR = interquartile range; RT = Radiation therapy.

¹ Includes one case of chemo-sensitization and one case of radiochemotherapy for glioblastoma.

² Includes cholestasis, inferior vena cava syndrome, among others.

³ Includes adrenal glands, lung, mediastinum, orbita, skull base, spinal cord, and visceral organs.

⁴ Includes side effects, suicide and wound healing disorder.

respect to patient age (p = 0.47). Two thirds of courses were administered to male patients: 67.1% in RT_{D60-31}, 67.3% in RT_{D30-8}, and 66.7% in RT_{D7-0} (p = 1.00). Between the three sub-groups no statistically significant difference in KPS was observed (p = 0.59). A tumor board was involved in the treatment decision of 36.0% (N = 59), 41.5% (N = 66), and 31.5% (N = 17) of RT_{D60-31}, RT_{D30-8}, and RT_{D7-0} treatments, respectively (p = 0.35). Between the three sub-groups, there was also no significant difference in treatment indications (p = 0.52): pain was the most common indication in RT_{D60-31}, RT_{D30-8}, and RT_{D7-0}, with N = 72 (43.9%), N = 71 (44.7%) and N = 25 (46.3%), respectively. Symptomatic brain/spinal metastasis was the second most common indication and represented 25.6% (N = 42), 30.2% (N = 48), and 27.8% (N = 15) in RT_{D60-31}, RT_{D30-8}, and RT_{D7-0}, respectively. Dyspnea/hemoptysis, asymptomatic brain/spinal metastasis, bleeding and other indications were less common in all three sub-groups. There was no statistically significant difference between fractionation schedules either, with a median of 10 fractions prescribed to patients in all three sub-groups (p = 0.23). Statistically significant differences between the three sub-groups were observed with respect to RT course discontinuation rate, which was 6.1% (N = 10) and 17.0% (N = 27) in the RT_{D60-31} and RT_{D30-8} sub-groups, respectively, compared to 53.7% (N = 29) in the RT_{D7-0} sub-group (p < 0.001). Treatment benefit was also significantly different between sub-groups (p < 0.001): While RT courses were deemed beneficial in 81.7% (N = 134) and 58.5% (N = 93) of RT_{D60-31} and RT_{D30-8} sub-groups, respectively, treatment failure in RT_{D7-0}, was 94.4% (N = 51). For a tabulation of the variables for the three sub-groups, see Table 3.

Discussion

Summary of key results

Within 60 days of death, 377 RT courses were prescribed to 280 patients, which represents 3.4% of all RT courses prescribed over the last decade at our department. The most frequent EoL RT sites were brain (32%) and bone (32%). Of all prescribed EoL courses, 83% were completed as planned. Treatment was deemed beneficial for patients in 52% EoL courses. Treatment discontinuation rates and patient benefit after RT were favorable for all patients except when RT was performed in their last week. The most commonly prescribed RT regimen was 10x3Gy, independently of the three sub-groups.

Treatment intent

No significant differences with respect to basic patient and treatment characteristics were identified in the three sub-groups RT_{D60-31}, RT_{D30-8} and RT_{D7-0}. No statistically significant difference in treatment indications was observed between sub-groups, providing no evidence for the hypothesis that patients who were treated closer to EoL had a higher proportion of highly palliative or emergent RT indications. The patients who were prescribed a curative EoL RT died of causes not related to RT. It remains challenging for physicians to predict and differentiate patient-individual life expectancy between 1 and 2 months, few weeks and only one week and to identify patients who may or may not qualify for and benefit from EoL RT.

Fractionation schedules

This is also supported by the fact that prescribed RT courses consisted of 10 or more fractions in almost 60% of cases and were associated with a median of 10 days spent under therapy. Prescribed regimens did not differ among sub-groups (p = 0.23). Such RT schedules have widely been considered too long for an EoL situation [10], yet remain common and were similarly reported in other studies: Guadagnolo et al. (2012) found that 20% of patients in a large population-based cohort of elderly patients who received RT within 30 days of death spent 10 days under

Table 3
Comparison of three different treatment sub-groups.

Data variables	RT _{D60-31}	RT _{D30-8}	RT _{D7-0}	χ^2 -prob.
# of RT courses (n, %)	164 (43.5)	159 (42.2)	54 (14.3)	
Age at RT (median, IQR)	66 (56–73)	65 (53–73)	66 (56–72)	0.4658
Male gender (n, %)	110 (67.1)	107 (67.3)	36 (66.7)	0.9963
KPS at RT start (n, %)				0.5932
≥ 70	107 (65.2)	89 (56.0)	32 (59.3)	
< 70	57 (34.8)	70 (44.0)	22 (40.7)	
Tumor board decision (n, %)				0.3545
Yes	59 (36.0)	66 (41.5)	17 (31.5)	
No	105 (64.0)	93 (58.5)	37 (68.5)	
Treatment intent (n, %)				0.5156
Curative	4 (2.4)	3 (1.9)	0 (0.0)	
Palliative	160 (97.6)	156 (98.1)	54 (100.0)	
Treatment indication, n (%)				0.5235
Pain	72 (43.9)	71 (44.7)	25 (46.3)	
Symptomatic brain/spinal metastasis	42 (25.6)	48 (30.2)	15 (27.8)	
Dyspnea/hemoptysis	11 (6.7)	14 (8.8)	8 (14.8)	
Asymptomatic brain/spinal metastasis	20 (12.2)	10 (6.3)	2 (3.7)	
Bleeding	10 (6.1)	8 (5.0)	2 (3.7)	
Definitive	4 (2.4)	3 (1.9)	0 (0.0)	
Other ¹	5 (3.0)	5 (3.1)	2 (3.7)	
Fractions (median, IQR)	10 (5–10)	10 (5–12)	10 (5–12)	0.2280
RT course completion (n, %)				<0.001
Yes	154 (93.9)	132 (83.0)	25 (46.3)	
No	10 (6.1)	27 (17.0)	29 (53.7)	
RT course benefit (n, %)				<0.001
Yes	134 (81.7)	93 (58.5)	3 (5.6)	
No	30 (18.3)	66 (41.5)	51 (94.4)	
Median time of last RT to death in days (n, IQR)	44 (39–53)	19 (13–24)	4 (2–6)	<0.001
Proportion of EoL period spent under therapy (median %, IQR)	21 (13–28)	41 (24–55)	70 (54–82)	<0.001

Abbreviations: EoL = End of life; IQR = Interquartile range; KPS = Karnofsky Performance Score; RT = Radiotherapy; RT_{Dxx} = Radiotherapy having taken place xx days before a patient's death.

¹ Includes cholestasis, inferior vena cava syndrome, among others.

treatment [10]. While longer treatment periods may be justified when patients have an outlook onto several months of life, shorter RT regimens should become commonplace in patients with a very short lifespan [16]. With the most common RT indication being pain (45%) and the most common fractionation scheme being 10x3Gy (35%), the causes for the negligence of shorter schedules such as 5x4Gy or 1x8Gy may be due to challenging survival prognostication and existing remuneration incentives.

Discontinuation rate

The majority of the EoL RT courses (83%) were completed as planned. Of the 377 prescribed EoL RT courses, 66 stopped early, resulting in an effective discontinuation rate of 17%. Though comparability is challenging due to varying definitions of EoL and patient selection, when putting this figure into perspective to other studies having focused exclusively on patients with palliative RT near EoL, e.g., by using a

certain cut-off date, this rate is low. Berger et al. (2014) reported a discontinuation rate of 78% in 52 cancer patients who died within 30 days of end of RT. Similarly, Toole et al. (2012) found a RT discontinuation rate of 52% in a cohort of 63 patients who died shortly after RT [9,17]. When compared to studies assessing the rate of EoL RT in a broader cohort of patients treated with palliative RT, the discontinuation rate in our study was comparable. While Wu et al. (2019) and Grade et al. (2019) reported discontinuation rates of 12% and 12.6% in 518 and 214 cancer patients, respectively, Anshushaug et al. (2015) reported 18% of all RTs cancelled in 616 cancer patients [6,15,18]. For a comparative overview of selected studies, see Table 4. When looking at different sub-groups, course completion was only 46.3% in the RT_{D7-0} sub-group, which was significantly lower than in the RT_{D30-8} (83.0%) and RT_{D60-31} (93.9%) sub-groups ($p < 0.001$).

Treatment benefit

Upon reviewing the patients' medical records, more than one third of the EoL RT courses achieved the intended palliative treatment benefit (52%). When looking at the three different sub-groups, a beneficial outcome was observed in only 6% of RT courses in the RT_{D7-0} sub-group, which is in strong contrast to the benefit rates of 82% in the RT_{D60-31} and 59% in the RT_{D30-8} sub-group ($p < 0.001$). This low benefit rate is not surprising and indicates that many patients treated within one week of death had little benefit in the form of symptom control or QoL improvements. However, the results here underline the suggestion that RT may be a valuable treatment option even in patients with a life expectancy of 30 days only, where a palliative treatment benefit was achieved in more than one third of the patients in this cohort.

Survival prognostication

These findings reinforce the need to develop a comprehensive prognostic assessment to improve accuracy of physicians' prediction of survival and weigh options of symptom control through EoL RT versus best supportive or hospice care. It is indicated that institutions systematically scrutinize their clinical practice and pattern of care by reviewing the use of palliative RT in patients at the EoL, as some centers have already done [15]. One additional metric seen in the literature to compare across studies is RT_{D30}, the proportion of patients having received RT within one month of death. There is even recommendation that RT_{D30} should lie below 10%, which may be challenged on the basis of the EoL RT completion and success rates reported in this study, however [15]. In comparable studies, the rate of RT_{D30} ranges between 8% and 100%, depending on the patient cohort analyzed, the cut-off time point chosen for EoL analysis as well as the denominator for the comparative analysis (see Table 4). RT_{D30} in this patient group was 57% when compared to patients treated within 2 months of death. When put into perspective with all palliative RT courses prescribed at our tertiary center over the last decade, RT_{D30} was 2.7%.

Advance care planning and place of death

Today, advance care planning and patient-centered care are considered an important pillar of cancer care [19]. Only 16% of patients had completed their advance healthcare directive before consultation for RT. Despite this, treating physicians should acknowledge that cancer care at the EoL includes highly individual decisions, with QoL improvement often being a top priority. When looking at place of death, the larger proportion of 66% of patients died in an inpatient setting, either on the palliative care wards or in another acute care hospital bed. Given that the analyzed patients represent a selected and vulnerable group suffering from incurable, metastatic cancer close to the EoL, it is yet not surprising that the proportion of patients dying in an acute care facility is higher than the Swiss population average which is close to 40% [20].

Table 4
Overview of selected studies examining the use of palliative RT near death.

First author (year)	Patient cohort	Time period	Primary cancer type	RT _{D30} , n (%)	Discontinued RT treatments, n (%)
Wu et al. (2019) [15]	518 cancer patients treated with palliative RT	2012–2016	All histologies	125 (24%)	63 (12%)
Grade et al. (2019) [6]	214 cancer patients treated in 238 palliative RT courses	2014	All histologies	N/A	27 (12.6%)
Anshushaug et al. (2015) [18]	616 cancer patients treated with RT, CT or RCT	2005, 2009	All histologies	61 (8%)	11 (18%)
Ellsworth et al. (2014) [21]	339 patients receiving RT for bone metastasis	2007–2012	All histologies	89 (26%)	N/A
Berger et al. (2014) [9]	52 cancer patients who died within 30 days of RT	2009–2011	All histologies	N/A	41 (78%)
Toole et al. (2012) [17]	63 cancer patients who died shortly after RT	2008–2011	All histologies	63 (100%)	33 (52%)

Abbreviations: CT = Chemotherapy; EoL = End of life; N/A = Not available; RCT = Radio-Chemo-Therapy; RT = Radiotherapy; and RT_{D30} = Radiotherapy within 30 days of death.

Tumor board involvement

Of note, only 38% of RT decisions were discussed in an organ-specific tumor board. This rather low rate may be due to the fact that palliative RT indications, especially for pain control or airway management, are typically summoned under symptom management, which does not necessarily require interdisciplinary involvement, potentially allowing for a quicker RT initiation.

Shortcomings

Limitations of this study arise from its retrospective nature. The results do not lend themselves to causal inferences. Also, other university centers may see different practices and a different patient mix, though they all tend to care for patients with advanced, incurable cancer. The lack of systematic assessment of patient reported outcomes, which represents a general challenge in studies with a palliative patient cohort, is a further shortcoming. Overall, despite its limitations, this study sheds light on the highly personalized and patient-centered decision-making at the EoL in our department, where treating radiation oncologists are often confronted with severely ill patients demanding treatment while having to weigh various aspects for and against RT in the absence of reliable prognostic scoring systems.

Conclusion

Survival prognostication and patient selection for EoL RT remains challenging for radiation oncologists. While EoL RT until one week before death was characterized by high completion and treatment benefit rates, which were almost comparable to RT administered within 60–30 days of death, treatment prescribed within one week of death, often had to be discontinued. The utilization of EoL RT therefore needs to be carefully weighed, also taking into account patient preferences for the last phase of life.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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