Provider decision regret – a useful method for analysis of palliative thoracic re-irradiation for lung cancer?

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Abstract

Background: The overall usefulness of palliative thoracic re-irradiation depends on the balance between efficacy, survival and toxicity, and is difficult to judge from previous studies. In the absence of patient-reported data, we developed a method for provider decision regret that addresses the question “would we re-irradiate this patient again in light of the known outcome?” Furthermore, we analyzed different reasons for decision regret and defined a subgroup at increased risk.

Patients and Methods: A retrospective analysis of 33 patients with lung cancer re-irradiated with 17-45 Gy was performed. Reasons for decision regret included re-irradiation within the last 30 days of life, immediate radiological progression after re-irradiation (as opposed to stable disease or objective response), radiation myelopathy, any grade 4-5 toxicity, grade 3 pneumonitis, other grade 3 toxicity in the absence of a symptomatic benefit or a time period of at least 3 months without worsening of the treated tumor.

Results: Median survival time was 5.2 months (95% confidence interval 3.4-7.0 months). Symptomatic and radiological responses were observed. Provider decision regret was declared in 12 patients (36%, two patients with grade 3 pneumonitis, three patients with a short survival (radiotherapy during the last 30 days of life), seven patients with progression). Decision regret was declared only in patients with ECOG performance status (PS) 2 or 3 and was associated with time interval to re-irradiation <6 months.

Conclusion: Our data support the usefulness and acceptable side effect profile of palliative re-irradiation for lung cancer. Patients with reduced PS are at increased

risk of futile treatment. Future research should aim at prediction of immediate disease progression (the prevailing cause of decision regret). Evaluation of provider decision regret has the potential to improve the way we learn from retrospective databases and should also be considered for other scenarios where high-quality prospective outcome data are lacking.

Keywords: lung cancer, radiotherapy, re-irradiation, symptom palliation, decision regret

Re-irradiation for symptom palliation has long been used in a large number of different clinical scenarios [1], including advanced lung cancer [2]. It has also been shown that selected patients with non-small cell lung cancer (NSCLC) are able to tolerate high-dose re-irradiation, which aims beyond relief of symptoms [3-5]. In contrast to other indications, no randomized trials of lung cancer re-irradiation have been published [6]. Evidence is derived mainly from few small single-arm prospective studies and a considerable number of retrospective analyses. Most of these reported limited data about the overall usefulness of palliative re-irradiation and did not fully answer the following questions. Did re-irradiation result in symptom relief or prolong the time without worsening of the thoracic tumor? Was survival long enough to justify re-irradiation as compared to simpler palliative and supportive interventions? Did re-irradiation cause high-grade toxicity? We were interested in analyzing the usefulness of re-irradiation based on a composite endpoint integrating all the aspects mentioned above, resembling the concept of uncomplicated cure in first-line settings. Furthermore, we asked the question “do we regret our decision to offer re-irradiation in light of the observed outcome or would we do it again?” In the absence of patient-reported data, this kind of provider-based retrospective decision regret analysis may shed additional light on the current controversies around palliative thoracic re-irradiation.

## Patients and Methods

This is a retrospective single-institution study based on a previously described database that is maintained in order to analyze the quality of care for patients with

lung cancer at our institution [7]. Staging information in the database relates to the TNM 7th edition and response data to RECIST 1.1. All patients re-irradiated for in-field or marginal recurrence to overlapping thoracic target volumes between 2011 and 2018 were identified from the database and included in the study. The following criteria for decision regret were applied: re-irradiation within the last 30 days of life, immediate radiological progression after re-irradiation (as opposed to stable disease or objective response), radiation myelopathy, any grade 4-5 toxicity (CTC AE version 4.0), grade 3 pneumonitis, other grade 3 toxicity in the absence of a symptomatic benefit or a time period of at least 3 months without worsening of the treated tumor. We arbitrarily decided that grade 3 toxicities other than pneumonitis might be acceptable if “compensated” by a benefit from re-irradiation, but we acknowledge that patient-reported data and judgements would be preferable to confirm this perspective. Grade 2 pneumonitis was registered as well. Re-irradiation was offered on a case-by-case basis, irrespective of target volume size, time interval and previous dose, and without applying any standardized dose constraints, except for spinal cord where we used our previously published risk model to ensure the patients had a low or intermediate risk of myelopathy [8]. Patients with interstitial lung disease or grade ≥2 pneumonitis after initial radiotherapy were not re-irradiated. No lower limit was applied for any lung function parameter. A 3-D conformal technique was used and, when available, the initial treatment plan was co-registered to the re-irradiation plan. Motion management (4-D computed tomography (CT), deep inspiration breath hold) and positron emission tomography were not mandatory. Dose-fractionation regimens were

individualized. Dose was prescribed to the reference point, and the clinical target volume received at least 95% of the prescribed dose, unless coverage was reduced to protect normal tissues. Variable minimum planning target volume coverage was accepted, however the 90% isodose was to enclose 98% of the volume whenever feasible. Follow-up took place every three months and included clinical examination and chest and abdomen CT. Symptoms were not quantified on any particular assessment scale. The electronic patient records (including physician and oncology nurse notes) and radiology reports were assessed to collect follow-up data. Date of death was also registered in these records. Survival was calculated from the first day of re-irradiation.

## Results

Thirty-tree patients were analyzed (22 males; two largest histology groups: 19 with squamous cell, 6 with small cell (SCLC) tumors). Only 8 patients (24%) had received a curative regimen as their first treatment. Fifteen patients had received systemic treatment before re-irradiation (chemotherapy, targeted agents, immune checkpoint inhibitors). More than 10 different fractionation regimens were used in first line (median dose 39 Gy), e.g., 2 fractions of 8.5 Gy (day 1 and 8; 21%), 10 fractions of 3 Gy (15%), and 15 fractions of 2.8 Gy (12%). Comparable heterogeneity was observed for re-irradiation (Table 1, median dose 30 Gy). In 6 cases (18%), re-irradiation dose was higher than the previous dose. Common regimens included 2 fractions of 8.5 Gy (n=10, 30%) and 10 fractions of 3 Gy (n=7, 21%). Eight patients (24%) received two courses with identical fractionation, e.g.,

10 fractions of 3 Gy or 2 fractions of 8.5 Gy. The median time interval from first to second radiotherapy was 10 months (minimum 3 months, maximum 61 months). Eight patients (24%) were re-irradiated after less than 6 months and 6 (18%) after more than 2 years. All patients completed their prescribed course of re-irradiation. The median age at re-irradiation was 70 years (range 47-86) and 12 patients (40%) were 75 or older. Eastern Cooperative Oncology Group (ECOG) performance status (PS) was 0-1 in 7 patients (21%), 2 in 15 patients (45%), and 3 in the remaining 11 patients (33%). The reason for re-irradiation was superior vena cava compression (n=2), nodal relapse at the margin of the previous target volume (n=1), consolidation of chemotherapy response (n=1), thoracic pain (n=7), lung symptoms (dyspnea, cough, hemoptysis; n=9), and in-field imaging progression (n=13). Pain improved in 3 of 7 cases. Lung symptoms improved in 3 of 9 cases. Regarding the 14 patients with imaging progression/nodal relapse, 5 obtained partial remissions and 8 stable disease. Fifteen patients (45%) had documented imaging progression in the re-irradiated region before death, and this was often the cause of death. Eleven patients (33%) were not in contact with the hospital in the final phase before death, and therefore the cause of death was defined as unknown after review of the patient records.

The median overall survival time was 5.2 months (95% confidence interval 3.4-7.0 months) and 4 patients (12%) were alive 1 year after the start of re-irradiation. Responders (imaging or symptoms) had better survival than patients with stable or progressive disease as their best response (Figure 1). One patient developed grade 2 and two grade 3 pneumonitis (overall 9% ≥ grade 2). Radiation myelopathy

or grade 4-5 toxicity was not observed. Grade 1-2 esophagitis, fatigue and asthenia were recorded in up to 30%.

The retrospective chart review resulted in provider decision regret in 12 patients (36%). Two of these decisions were triggered by grade 3 pneumonitis, three from short survival (radiotherapy during the last 30 days of life; in one case combined with lack of efficacy), and seven from lack of efficacy. Decision regret was declared only in patients with ECOG PS 2 or 3. All 12 patients were scheduled to spend no more than 10 working days on re-irradiation. Shorter time interval showed a statistical trend towards decision regret ($p=0.09$ for <6 months vs. at least 6 months). The rates were 63% (<6 months), 32% (6-24 months), and 17% (>24 months). Gender, age, presence of SCLC and a diagnosis of stage IIIB or IV disease were not associated with decision regret (chi-square test $p>0.1$). Median overall survival in the decision regret subgroup was 2.0 months. Regarding all PS 3 patients, median overall survival was 3.5 months (maximum 11.5 months).

## Discussion

Despite increasing numbers of systemic treatment options and continuous improvement of local therapies, many patients with lung cancer relapse [9-11]. Palliative thoracic re-irradiation may contribute to symptom improvement and, in some cases, improved survival due to its ability to delay the process of tumor growth. These aims (symptom control, growth control) were also the most common reasons for referral in the present study. However, less than 50% of the patients had documented improvement of lung symptoms, pain and tumor size on CT

imaging. Retrospective chart review is not the best method to evaluate symptom improvement and quality of life. Patient-reported outcome data and decision regret analyses provide a better picture of the usefulness of treatment. However, such information is not available in the literature of palliative thoracic re-irradiation. The fact that responders had better survival than non-responders (Figure 1) supports the potential role of re-irradiation. Ideally, patients unlikely to respond would be spared the burden of treatment. Yet, internationally accepted models of response prediction are not available in this setting. Decision-making also has to acknowledge the potential of serious toxicity from thoracic radiotherapy.

In the absence of patient-reported data we were interested in exploring alternative ways to judge the usefulness of palliative thoracic re-irradiation. Since it is unknown if some of our patients did regret their decision to undergo treatment, we decided to create criteria for provider decision regret. Those included short survival (radiotherapy during the last 30 days of life, an endpoint also evaluated in different other recent studies [12, 13]), lack of efficacy (defined as immediate thoracic disease progression without a period of stable or shrinking disease), and serious toxicity (myelopathy, any grade 4-5, selected grade 3). Of course, other criteria could have been selected. However, the present ones may serve as a starting point from which future recommendations can be derived, if the radiation oncology community agrees that this type of chart review adds value to the way we learn from real-world databases. Based on the present decision regret criteria, we found that we would not offer re-irradiation again to 36% of the patients who actually

received it. The main cause was lack of efficacy. Only 3 (9%) and 2 patients (6%) had received radiotherapy during the last 30 days of life, and developed serious toxicity (grade 3 pneumonitis), respectively. In general, overall survival and toxicity profile do not discourage palliative thoracic re-irradiation.

We did not perform detailed analyses of cumulative doses and correlations of outcome and dosimetric data in this relatively small cohort with heterogeneous treatment approaches, due to limited statistical power and lack of ability to validate our findings. However, it appears that regimens such as 17 Gy in 2 fractions and 30-39 Gy in 10-13 fractions are feasible, even in our population of mostly elderly patients with compromised ECOG PS. Both, patients with SCLC and NSCLC were among those who derived benefit from re-irradiation. If needed to reduce the biologically effective dose to organs at risk, two daily fractions of 1.5-2 Gy can be prescribed. Eventually, fractionation should be chosen taking into account aim (symptom relief or tumor cell kill), survival prognosis, and tolerance of critical structures.

As shown in Tables 2-4 the previous studies reported quite heterogeneous outcomes after re-irradiation to median doses that often were in the range of 30-40 Gy. However, toxicity rates were acceptable and responses were observed in all studies, though survival beyond 12 months was relatively unlikely. Kramer et al. [17] confirmed this observation, using 2 fractions of 8 Gy given with one week split. The median overall survival was 5.6 months and 71% of patients had partial or

complete relief of one or more of their symptoms. Relief of dyspnea, hemoptysis, and cough was observed in 35%, 100%, and 67%, respectively. Karnofsky performance status (KPS) improved in 45% patients. The overall median duration of symptom relief was 4 months. Poltinnikov et al. [23] were the first to report on the use of hypofractionated stereotactic re-irradiation (SBRT) in patients previously treated with concurrent chemoradiotherapy. The median dose of the hypofractionated schedule was 32 Gy (range, 4-42 Gy), with a median fraction size of 4 Gy (range, 2.5-4.2 Gy) delivered 3-5 times per week. Five patients also received concurrent chemotherapy. Radiologic response was observed in 5 (29%), and stable disease in another 5 (29%) patients. The median survival from the start of re-irradiation was 5.5 months. Symptom resolution was observed in 85% of symptomatic patients. No grade 3 or higher side effects were observed. Survival outcomes were better in the study by Patel et al. [24]. Previous median radiation dose was 61.2 Gy with a median 8-month interval from previous radiation. The median re-irradiation dose was 30 Gy (SBRT, n=26). Two-year actuarial local control was 65% (survival 37%). Fifty-five percent of patients reported acute/chronic grade 1 and 2 toxicities. No grade 3 or higher toxicities were reported. High-dose SBRT will not be discussed in detail because our study has focused on palliative regimens. Since brachytherapy is limited to patients with accessible, endoluminal disease this approach will not be discussed either.

Few studies have provided data on predictive factors for radiation pneumonitis after palliative re-irradiation. Due to the low number of events, we refrained from

further evaluation. Recently, Ren et al. analyzed 67 patients, 18 of whom with grade 3-4 pneumonitis [25]. Multivariate analysis revealed that mean lung dose (MLD) of the initial plan, V5 of the composite plans, and overlap-V5/re-V5 were independent predictors for grade ≥ 3 pneumonitis. However, independently validated models are lacking. Most previous studies date back to the pre-immunotherapy era. Even if our experience is limited to two patients (nr. 13 and 14, Table 1) who received PD1 inhibitors between first and second radiotherapy, toxicity problems such as pneumonitis were not encountered.

Despite inherent limitations of small retrospective studies our data showed that even patients with ECOG PS3 did not have a uniformly poor prognosis. Nevertheless, decision regret was only declared in patients with PS2-3, meaning that PS is an important factor to consider during decision-making. Time interval <6 months also played a role. In contrast, age and stage were not of high relevance. The fact that patients with retrospective provider decision regret were scheduled to spend no more than 10 working days on re-irradiation suggests that the prescribing physician was aware of the serious prognosis and potential for futile treatment. However, the underlying clinical information was probably too complex to be reflected in the limited data extracted for this study. A previous study performed in the first-line palliative irradiation setting revealed that PS, serum lactate dehydrogenase, C-reactive protein, liver/adrenal gland metastases, and extrathoracic disease status significantly predicted survival [7]. The poor prognosis patients survived for a median of 0.8 months. It would be interesting to analyze

whether or not blood biomarkers or other parameters, e.g., imaging features, also could be helpful in predicting futile re-irradiation. In conclusion, this study supports the usefulness and acceptable side effect profile of palliative re-irradiation for lung cancer and encourages research towards prediction of immediate disease progression (the prevailing cause of decision regret).

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Table 1. Patient data

| Number | Baseline information (1. radiotherapy) | First regimen, response | Second regimen, previous treatment | Clinical information (2. radiotherapy), indication | Results | Decision regret (reason) |
|---|---|---|---|---|---|---|
| 1 | Male, ASCC T4 left lung, relapse after surgery and CTx, stage IIIB | July 2013, 13 fr of 3 Gy, partial response | December 2013, 10 fr of 3 Gy, none | 68 yr, PS 2<br>pain | OS 7.7 mo<br>pain improved<br>death from met | No |
| 2 | Male, SCC T2 left lung, stage IIIA and brain met | January 2012, 10 fr of 3 Gy, partial response | October 2013, 17 fr of 2.5 Gy, CTx | 73 yr, PS 1<br>radiological progress | OS 16.6 mo<br>stable disease<br>unknown cod | No |
| 3 | Male, LC mediastinal nodes, relapse after surgery and CTx, stage IIIA | July 2011, 15 fr of 2.8 Gy, partial response | April 2012, 15 fr of 2 Gy and 3 fr of 2.5 Gy, none | 58 yr, PS 1<br>pain | OS 7.6 mo<br>pain improved<br>partial response<br>unknown cod | No |
| 4 | Female, no histology, left lung, new lesion after SBRT | May 2012, 10 fr of 3 Gy, stable disease | October 2012, 10 fr of 3 Gy, none | 70 yr, PS 3<br>pain | OS 9.5 mo<br>pain improved<br>death from prog | No |
| 5 | Male, SCC T4 right lung, stage IIIB | December 2012, 10 fr of 3 Gy, stable disease | July 2013, 10 fr of 3 Gy, none | 73 yr, PS 2, liver met<br>v. cava compression | OS 3 mo<br>stable disease<br>death from met | No |
| 6 | Female, SCC T4 left lung, stage IIIB | December 2013, 2 fr of 8.5 Gy, stable disease | September 2014, 10 fr of 3 Gy, none | 77 yr, PS 2<br>lung symptoms | OS 6.4 mo<br>symptoms | No |

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|---|---|---|---|---|---|---|
| | | | | | improved<br>unknown cod | |
| 7 | Male, SCC T3 right lung, stage IIIB, primary CTx | May 2014, 15 fr of 2.8 Gy and 5 fr of 2.6 Gy, partial response | December 2016, 20 fr of 1.75 Gy BID, CTx* | 79 yr, PS 1<br>radiological progress | OS 7.4 mo<br>partial response<br>death from prog | No |
| 8 | Female, SCC T2 left lung, stage I | December 2012, 35 fr of 2 Gy, partial response | January 2015, 13 fr of 3 Gy, none | 68 yr, PS 3<br>radiological progress | OS 11.5 mo<br>stable disease<br>unknown cod | No |
| 9 | Female, SCC T3 left lung, stage IIIA | March 2015, 15 fr of 3 Gy, partial response | April 2016, 2 fr of 8.5 Gy, none | 85 yr, PS 3<br>lung symptoms | OS 10.7 mo<br>symptoms improved<br>death from prog | No |
| 10 | Male, SCC T2 left lung, stage I, local and nodal progress after SBRT | March 2013, 3 fr of 20 Gy, partial response | April 2015, 15 fr of 2.8 Gy, CTx* | 70 yr, PS 1<br>radiological progress | OS 36 mo<br>(ongoing)<br>relapse free | No |
| 11 | Male, SCC T3 right lung, stage IV, primary CTx | June 2015, 2 fr of 8.5 Gy, stable disease | February 2016, 8 fr of 4 Gy, CTx* | 64 yr, PS 2<br>radiological progress | OS 17.5 mo<br>stable disease<br>death from prog | No |
| 12 | Male, no histology, T4 left lung, pleural met | April 2016, 2 fr of 8.5 Gy, stable disease | July 2016, 2 fr of 8.5 Gy, none | 86 yr, PS 2<br>pain | OS 4.4 mo<br>not improved<br>unknown cod | No |

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|---|---|---|---|---|---|---|
| 13 | Male, no histology, T4 right lung, stage IIIB | February 2016, 13 fr of 3 Gy*, stable disease | January 2017, 5 fr of 5.5 Gy, PD1 inhibitor | 47 yr, PS 3<br>lung symptoms | OS 6.7 mo<br>not improved<br>unknown cod | No |
| 14 | Male, SCC T2 right lung, stage IIIA | August 2016, 15 fr of 2.8 Gy*, stable disease | August 2017, 26 fr of 1.5 Gy BID, PD1 inhibitor | 67 yr, PS 3<br>lung symptoms | OS 3.5 mo<br>improved<br>partial response<br>death from cachexia and infection | No |
| 15 | Male, SCC T3 left lung, stage IV, primary CTx | September 2017, 2 fr of 8.5 Gy, partial response | April 2018, 2 fr of 8.5 Gy, CTx* | 68 yr, PS 2<br>radiological progress | OS 4.0 mo<br>partial response<br>death from prog | No |
| 16 | Male, SCC T4 right lung, stage IIIB | July 2016, 10 fr of 3.75 Gy, partial response | December 2016, 2 fr of 8.5 Gy, none | 81 yr, PS 3<br>pain | OS 2.0 mo<br>not improved<br>death from prog | Yes (Prog) |
| 17 | Female, SCC T4 left lung, stage IIIB, induction CTx and converted from radical to palliative RT | December 2014, 1 fr of 2 Gy and 2 fr of 8.5 Gy, stable disease | April 2015, 2 fractions of 8.5 Gy, none | 74 yr, PS 3<br>radiological progress | OS 5.6 mo<br>local progress<br>unknown cod | Yes (Prog) |
| 18 | Male, adeno T4 right lung, stage IV, primary CTx | June 2015, 2 fr of 8.5 Gy, stable disease | October 2015, 2 fr of 8.5 Gy, CTx* | 57 yr, PS 2<br>pain | OS 1.9 mo<br>not improved<br>death from prog | Yes (Prog) |

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|---|---|---|---|---|---|---|
| 19 | Male, no histology, left lung, local progress after SBRT | July 2012, 3 fr of 20 Gy, partial response | September 2013, 10 fr of 3 Gy, none | 66 yr, PS 2, adrenal met radiological progress | OS 5.3 mo local progress unknown cod | Yes (Prog) |
| 20 | Female, SCC T3 left lung, stage IIIA | April 2014, 35 fr of 2 Gy* partial response | September 2015, 7 fr of 4 Gy, CTx* | 56 yr, PS 2 lung symptoms | OS 3.0 mo not improved death from prog | Yes (Prog) |
| 21 | Male, adeno T2 right lung, stage IV, primary CTx | September 2015, 2 fr of 8.5 Gy, stable disease | May 2016, 2 fr of 8.5 Gy, none | 70 yr, PS 3 lung symptoms | OS 1.7 mo not improved death from pneumonia | Yes (Prog) |
| 22 | Male, SCC left lung, stage IV, primary CTx | November 2013, 10 fr of 3 Gy, stable disease | September 2014, 10 fr of 3 Gy, none | 75 yr, PS 3 pain | OS 1.6 mo not improved death from prog | Yes (Prog) |
| 23 | Female, SCC T3 right lung, stage IIIA, primary CTx | July 2015, 2 fr of 8.5 Gy partial response | October 2015, 2 fr of 8.5 Gy, CTx* | 75 yr, PS 2 radiological progress | OS 5.2 mo stable disease gr 3 pneumonitis death from met | Yes (Tox) |
| 24 | Male, SCC T1 right lung, stage IV, CTx contraindication | October 2015, 10 fr of 4.25 Gy, partial response | September 2016, 16 fr of 2 Gy BID, none | 76 yr, PS 2 lung symptoms | OS 4.0 mo not improved gr 3 pneumonitis unknown cod | Yes (Tox) |

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|---|---|---|---|---|---|---|
| 25 | Male, SCC T4 left lung, stage IIIB | April 2016, 5 fr of 4 Gy, stable disease | August 2016, 10 fr of 3 Gy, none | 63 yr, PS 2<br>lung symptoms | OS 1.3 mo<br>not improved<br>death from prog | Yes (OS and Prog) |
| 26 | Male, adeno T2 right lung, stage IIIA | November 2014, 33 fr of 2 Gy*, partial response | January 2017, 2 fr of 8.5 Gy, targeted therapy | 83 yr, PS 3<br>lung symptoms | OS 0.3 mo<br>not improved<br>death from prog | Yes (OS) |
| 27 | Male, SCC T4 right lung, stage IIIB | April 2010, 15 fr of 2.8 Gy partial response | January 2011, 2 fr of 8.5 Gy, v. cava stent and CTx* | 63 yr, PS 3<br>v. cava compression | OS 0.5 mo<br>death from fall | Yes (OS) |
| 28 | Female, SCLC extensive disease, left lung | June 2013, 10 fr of 3 Gy consolidation after CTx, stable disease | November 2014, 15 fr of 3 Gy, none | 59 yr, PS 0<br>radiological progress | OS 12.5 mo<br>partial response<br>adrenal met<br>unknown cod | No |
| 29 | Male, SCLC limited disease, left lung | September 2006, 15 fr of 2.8 Gy*, partial response | October 2011, 14 fr of 2.5 Gy, CTx* | 52 yr, PS 1<br>nodal relapse | OS 7 mo<br>stable disease<br>death from met | No |
| 30 | Male, SCLC limited disease (yet malignant pleural effusion), right lung, CTx and sequential RT | January 2015, 30 fr of 1.5 Gy BID and 4 fr of 2 Gy, partial response | March 2017, 9 fr of 3 Gy, CTx* | 73 yr, PS 2<br>consolidation of CTx response | OS 7 mo<br>stable disease<br>gr 2 pneumonitis after 2.5 mo CTx for local progress<br>death from prog | No |

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|---|---|---|---|---|---|---|
| 31 | Female, SCLC limited disease, right lung, CTx and sequential RT | January 2016, 34 fr of 1.5 Gy BID, complete response | June 2017, 6 fr of 4 Gy, none | 79 yr, PS 2 radiological progress | OS 4.5 mo partial response unknown cod | No |
| 32 | Female, SCLC limited disease, right lung | April 2016, 30 fr of 1.5 Gy BID*, partial response | August 2017, 7 fr of 3.5 Gy, CTx* | 77 yr, PS 1, lung met radiological progress | OS 3.9 mo stable disease death from prog | No |
| 33 | Female, SCLC limited disease, right lung, CTX alone, later RT for mediastinal relapse | October 2017, 5 fr of 4 Gy, partial response | June 2018, 5 fr of 5 Gy, none | 79 yr, PS 2 radiological progress | OS 1.7 mo stable disease liver met death from met | No |

SCC: squamous cell cancer, ASCC: adenosquamous cell cancer, LC: large cell cancer, SCLC: small cell cancer

CTx: systemic chemotherapy

PS: Eastern Cooperative Oncology Group performance status

OS: overall survival from first date of re-irradiation

Met: distant metastases

Cod: cause of death

SBRT: stereotactic body radiotherapy

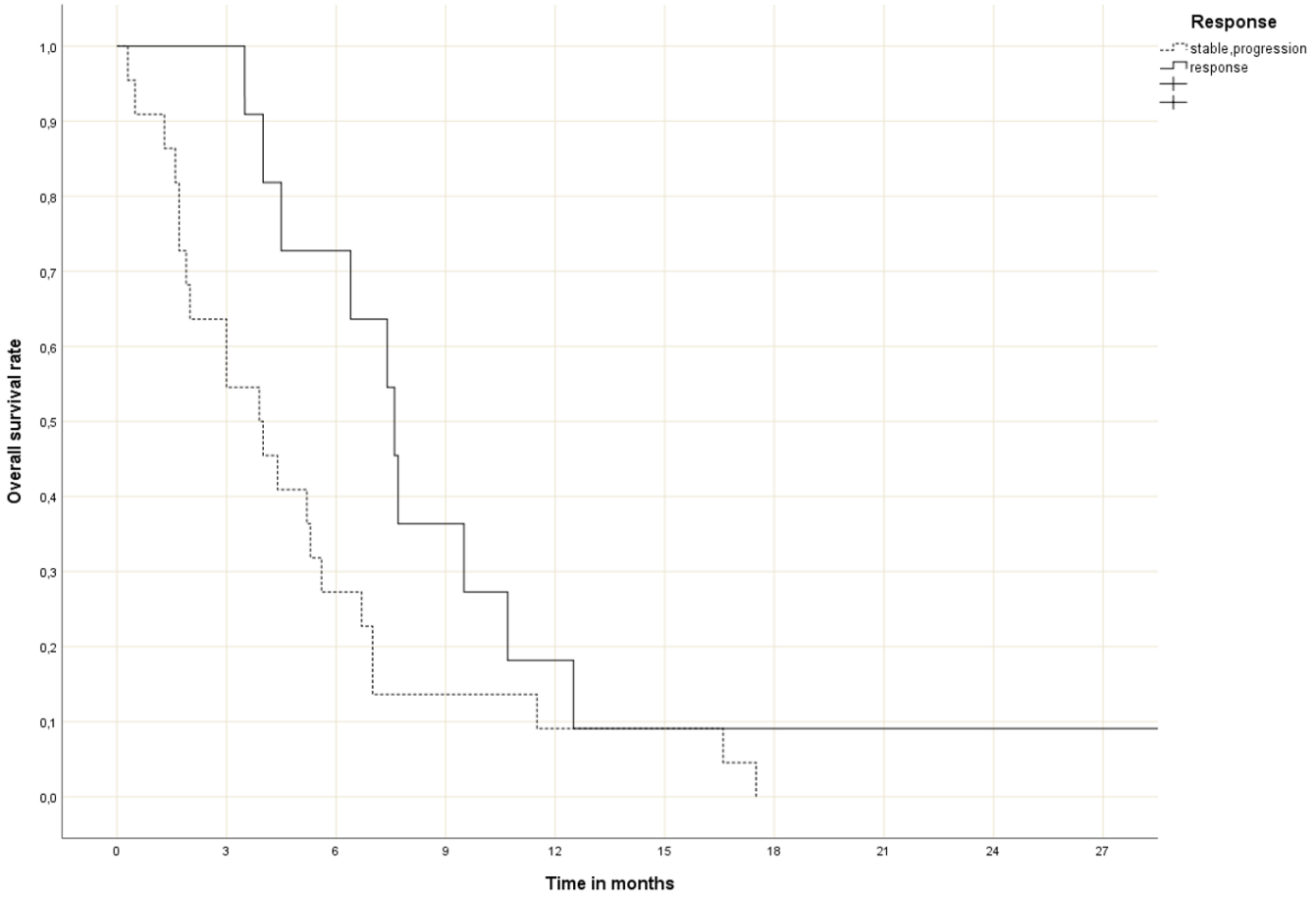
Prog: thoracic disease progression

Tox: radiation-induced toxicity

BID: two fractions per day, minimum interval 6 hours

*including concomitant platinum-based chemotherapy

Figure 1. Actuarial overall survival (Kaplan-Meier curves) for 11 responders (imaging or symptoms) and 22 patients with stable or progressive disease (median 7.6 vs. 3.9 months, p=0.05, log-rank test).




| | | | | |
|---|---|---|---|---|
| **Numbers at risk** | **11** | **8** | **2** | **(responders)** |
| | **22** | **6** | **2** | |