NHS England

Evidence review: Stereotactic Ablative Radiotherapy for Small Cell Lung Cancer

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First published: October 2017

Updated: Not applicable

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Contents

1. Introduction

- Stereotactic ablative radiotherapy (SABR) is a radiotherapy technique which involves the use of a high radiation dose delivered in a small number of fractions, and allows sparing of the surrounding healthy normal tissues. It is associated with lower rates of acute and late morbidity. The technique requires specialist positioning equipment and imaging (NHS England 2013).
- Primary lung cancer, which means the cancer first appeared in the lungs, is one of the most common and serious types of cancer. Over 41,000 people are diagnosed with the condition every year in the UK (NHS Choices 2017). Lung cancer mainly affects older people. Although people who have never smoked can develop lung cancer, smoking is the main cause, accounting for about 90% of cases (NHS Choices 2017).
- Primary lung cancers fall into two histological categories, small cell and non small cell. Small cell lung cancer (SCLC), the subject of this evidence review, is less common than non small cell lung cancer, and usually spreads faster.
- The appropriate treatment for SCLC depends on how far it has spread (the stage) and the general health of the patient. Treatment options include surgery, radiotherapy and chemotherapy. Treatment may be curative or palliative (NICE 2011).
- Usually SCLC is treated with chemotherapy, either on its own or in combination with radiotherapy, as the cancer has often spread by the time it is diagnosed. Surgery is an option if the cancer has not spread but this is uncommon; chemotherapy or radiotherapy may be given after surgery to help reduce the risk of the cancer recurring (NICE 2011).
- Some suggest that SABR may be a suitable treatment for early lung cancer. In 2013, NHS England published a commissioning policy (NHSCB/B01/P/a) on the use of SABR as a treatment option in the management of patients with non-small cell lung cancer not suitable for surgery (NHS England 2013). However, NHS England does not commission SABR for SCLC.
- NICE does not include SABR among the treatments which it recommends in its clinical guideline for small cell lung cancer (NICE 2011).

2. Summary of results

- We found one systematic review and two other studies.
- The studies were small, including in total 190 participants, with some duplication between two studies in the systematic review.
- All the studies were uncontrolled, apart from one reported comparison of SABR versus SABR plus chemotherapy.
- The systematic review by Alongi et al 2017 was descriptive and included no comparisons. It summarised four uncontrolled studies, with a total of 108 participants with stage I to III SCLC; a fifth study, a case report, was included without further description. There was some duplication between two of the studies included. The studies reported local control[1] of between 82% (crude rate) and 100% at 36 months, overall survival of between 48% at 24 months and 76% at 24 months, and disease-specific survival of between 75% at 12 months

[1] Local control is the absence of radiological evidence of further growth of the cancer at its site of origin.

and 86% at 36 months.

- Progression-free survival at 24 months was 22% after SABR and 67% after SABR plus chemotherapy, the latter results being described as “significantly higher”.
- Verma et al 2017 reported an uncontrolled study of 74 people with stage 1 SCLC treated with SABR. A complete radiological response was reported in 19/76 lesions (25%), a partial response in 29/76 (38%), stable disease in 13/76 (17%) and progression in 3/76 (4%). Local control at one year was 97%, and at three 3 years was 96%. Local failure-free survival[2] at one year was 97% and at three years was 97%. Distant metastasis-free survival at one year was 73%, and at three years was 63%. Disease-free survival at one year was 59% and at three years was 54%, with a median disease-free survival of 49.7 months. Disease-specific survival[3] at one year was 84% and at three years was 64%, with a median disease-specific survival of 52.3 months. Overall survival at one year was 71% and at three years was 35%, with a median overall survival of 17.8 months.
- Ly et al 2013 reported an uncontrolled study of 8 people with stage 1 SCLC treated with SABR. Overall survival at one year was 88% and at three years was 37%, with a median overall survival of 22 months. Recurrence-free survival[4] at one year was 50% and at three years was 38%, with a median recurrence-free survival of 8.4 months.
- Alongi et al 2017 reported one grade 2 adverse reaction (chest wall toxicity) and five grade 3 adverse reactions (4 oesophagitis, 1 neutropenia) (n=29). Verma et al (2017) reported pneumonitis after treatment of 15 lesions (grade 1 adverse reaction: 9/76 lesions (12%), grade 2: 3/76 lesions (4%), grade 3: 1/76 lesions (1%)), grade 1 dermatitis after treatment of 1/76 lesions (1%), grade 2 fatigue after treatment of 1/76 lesions (1%) and grade 2 chest wall pain after treatment of 3/76 lesions (4%).
- We found no relevant cost utility studies.
- We found no studies which evaluated the clinical and cost-effectiveness of SABR in subgroups of patients.
- Taken together, the evidence that we found does not indicate whether there are any benefits from SABR in the treatment of early stage SCLC compared to standard care (surgery, chemotherapy with or without conventional radiotherapy). All the studies were uncontrolled; none compared SABR to an alternative treatment. This means that we cannot draw any conclusions about whether SABR increases the quality or duration of life compared with alternatives, nor whether any potential benefits are justified by its costs.
- SABR has adverse effects but they do not appear to be common or serious enough to cast doubt on its suitability for use.

[2] Local failure-free survival is survival without relapse or the addition of another systemic therapy.
[3] Disease-specific survival is survival without death from SCLC. All other causes of death are censored (ie disregarded in the analysis).
[4] Recurrence-free survival is survival with no apparent recurrent tumour at specified intervals after completion of SABR. The term is synonymous with disease-free survival.

3. Methodology

- The methodology to undertake this review is specified by NHS England in their 'Guidance on conducting evidence reviews for Specialised Commissioning Products' (2016).
- A description of the relevant Population, Intervention, Comparison and Outcomes (PICO) to be included in this review was prepared by NHS England's Policy Working Group for the topic (see section 9 for the PICO).
- The PICO was used to search for relevant publications in EMBASE, MEDLINE and the Cochrane Library (see section 10 for search strategy).
- The search dates for publications were between 1 January 2007 and 2 August 2017.
- The titles and abstracts of the results from the literature searches were assessed using the criteria from the PICO. Full text versions of papers which appeared potentially useful were obtained and reviewed to determine whether they were appropriate for inclusion. The best quality papers which matched the PICO were selected for inclusion in this review.
- Evidence from all papers included was extracted and recorded in evidence summary tables, critically appraised and their quality assessed using National Service Framework for Long term Conditions (NSF-LTC) evidence assessment framework (see section 7 below).
- The body of evidence for individual outcomes identified in the papers was graded and recorded in grade of evidence tables (see section 8 below).

4. Results

We found one systematic review (Alongi et al 2017), which included four uncontrolled studies; a fifth study, a case report, was included without further description. We found two other uncontrolled studies (Ly et al 2013 and Verma et al 2017).

The studies were small, including in total 190 participants, with some duplication between two studies in Alongi et al 2017.

All the studies were uncontrolled, apart from one reported comparison of progression-free survival after SABR versus after SABR plus chemotherapy.

Participants were mostly adults with stage I SCLC; Alongi et al 2017 included no more than 25 (23%) participants with more advanced tumours. SABR regimes varied, with participants receiving at least 30 Gy[5] and in most cases 50 Gy.

We found no relevant cost utility studies.

What is the evidence on clinical effectiveness of using SABR in different treatment scenarios compared with existing treatments for small cell lung cancer histology, limited stage (T1-T2bN0M0, 8th edition)?

The clinical efficacy outcomes reported in the studies, all of which were uncontrolled, were overall survival, local control, disease-free survival, progression-free survival, radiological response, local

[5] A gray (Gy) is the unit of radiotherapy delivered, and is defined as the absorption of one joule of radiation energy per kilogram of matter.

failure-free survival, distant metastasis-free survival and disease-specific survival.

Overall survival

We found three studies which reported this outcome.

Alongi et al 2016 included four uncontrolled studies reporting this outcome at different timepoints. Overall survival rates were 72% at 32 months (1 study, n=8), 76% at 24 months (1 study, n=64 with some duplication), 63% at 12 months (1 study, n=6) and 48% at 24 months (estimated rate) (1 study, n=29).

Verma et al 2017 (n= 74) reported overall survival rates of 71% at one year and 35% at three years, with median survival of 17.8 months.

Ly et al 2013 (n= 8) reported overall survival rates of 88% at one year and 37% at three years, with median survival of 22 months.

Local control

We found two studies which reported this outcome.

Four of the five studies in the systematic review by Alongi et al 2016 reported local control rates at different timepoints: 100% at 36 months (n=8), 89% at 24 months (n=64 with some duplication), 100% at 12 months (n=6) and 82% (crude rate, duration of observation not reported) (n=29).

Verma et al 2017 reported local control rates of 97% at one year and 96% at three years.

Disease-free survival

We found two studies which reported this outcome.

Verma et al 2017 reported disease-free survival of 59% at one year and 54% at three years, with median disease-free survival of 49.7 months.

Ly et al 2013 reported disease-free survival of 50% at one year and 38% at three years, with median disease-free survival of 8.4 months.

Progression-free survival

We found one study which reported this outcome

Alongi et al 2016 included two studies which reported this outcome at different timepoints. Progression-free survival was estimated at 27% at 24 months (n=29). In another study (n=64), it was reported as 22% after SABR and 67% after SABR plus chemotherapy; this was “significantly higher” with SABR plus chemotherapy but the results of significance tests were not reported.

Radiological response

We found one study which reported this outcome.

Verma et al 2017 reported complete response in 19/76 lesions (25%), partial response in 29/76 lesions (38%), stable disease in 13/76 lesions (17%) and disease progression in 3/76 lesions (4%). The response was unknown in 12 participants.

Local failure-free survival

We found one study which reported this outcome.

Verma et al 2017 reported local failure-free survival of 97% at one year and 97% at three years.

Distant metastasis-free survival

We found one study which reported this outcome.

Verma et al 2017 reported distant metastasis-free survival rates of 73% at one year and 63% at three years.

Disease-specific survival

We found two studies which reported this outcome.

Alongi et al 2016 included three studies reporting this outcome at different timepoints. Disease-specific survival rates were 86% at 36 months (n=8), 79% at 24 months (n=64 with some duplication) and 75% at 12 months (n=6).

Verma et al 2017 reported disease-specific survival of 84% at one year and 64% at three years. The median disease-specific survival was 52.3 months.

What is the evidence relating on the safety of SABR in different treatment scenarios compared with existing treatments for small cell lung cancer histology, limited stage (T1-T2bN0M0, 8th edition)?

We found two studies reported the incidence of adverse effects after SABR.

The systematic review by Alongi et al 2016 included four studies reporting safety outcomes. The adverse events were not meta-analysed.

One of the studies reported no adverse reactions of grade 2 or worse (n=8), one reported no adverse reactions of grade 3 or worse (n=64 with some duplication), one reported one grade 2 adverse reaction (chest wall toxicity) (n=6) and one reported five grade 3 adverse reactions (4 oesophagitis, 1 neutropenia) (n=29).

Verma et al 2017 reported, after treatment of 76 lesions in 74 people, nine "cases" with grade 1 pneumonitis (12%), three with grade 2 pneumonitis (4%) and one with grade 3 pneumonitis (1%). Verma et al 2017 also reported one "case" with grade 1 dermatitis (1%), one with grade 2 fatigue (1%), three with grade 2 chest wall pain (4%) and one with chest wall pain of unknown grade (1%). It is unclear whether the proportions are of participants or lesions.

What is the evidence on the cost effectiveness of SABR in different treatment scenarios compared with existing treatment for small cell lung cancer histology, limited stage (T1-T2bN0M0, 8th edition)?

We do not know. We found no relevant cost utility studies.

Does the evidence of clinical and cost-effectiveness identify any subgroups of patients with small cell lung cancer histology, limited stage (T1-T2bN0M0, 8th edition), who would gain greater benefit from using SABR compared with existing treatments?

No. We found no studies relevant to this question.

5. Discussion

We found a number of small studies which report the outcomes which follow the use of SABR for stage I and stage IIA SCLC; one also included a few participants with stage III disease. However, these do not provide useful evidence on the clinical effectiveness of the treatment: none of the studies reported the results of treatments other than SABR, so we cannot say whether the outcomes would have been different without SABR.

Furthermore, many of the participants in the studies also received chemotherapy, making it more difficult to determine any specific effect of SABR. The only comparative study we found reported a significant impact from the use of chemotherapy, when added to SABR. There were no comparative studies for SABR over alternative treatments.

SABR is associated with adverse effects, including pneumonitis, dermatitis and chest wall pain. However, these were generally not severe.

We found no evidence about the cost effectiveness of SABR for SCLC, nor about whether there are any subgroups in whom SABR is more effective. No studies reported quality of life.

Randomised controlled trials are needed to provide reliable estimates of the incremental benefit of SABR over alternative treatments. These could also explore its effectiveness in different categories of participant, and provide evidence on its cost-effectiveness.

6. Conclusion

Taken together, the evidence that we found does not indicate whether there are any benefits from SABR in the treatment of early stage SCLC. We cannot conclude anything about whether it increases the quality or duration of life, nor whether any potential benefits are justified by its costs.

SABR has adverse effects but they do not appear to be common or serious enough to cast doubt on its suitability for use.

7. Evidence Summary Tables

Use of SABR to treat SCLC									
Study reference	**Study Design**	**Population characteristics**	**Intervention**	**Outcome measure type**	**Outcome measures**	**Results**	**Quality of Evidence Score**	**Applicability**	**Critical Appraisal Summary**
Alongi et al 2017	R1 – systematic review of existing research without meta-analysis	108 people reported in five uncontrolled studies (n=1, 6, 8, 29 and 64 with some duplication), with stage I to III SCLC*: Stage I: 73 (66%) Stage II: 12 (11%), of which 4 (4%) were stage IIA and 8 (7%) were not specified as stage IIA or IIB Stage III: 17 (16%) Stage not reported: 6 (6%). Median follow-up: 12 to 32 months.	SABR, 30 to 60 Gy in 1 to 10 fractions. 78 participants (with some duplication) also received chemotherapy, with agents including carboplatin, cisplatin, etoposide and irinotecan.	Primary Clinical effectiveness	Overall survival (4 studies)	72% at 36 months (n=8), 76% at 24 months (n=64 with some duplication), 63% at 12 months (n=6) and 48% at 24 months (estimated rate) (n=29).	8	Direct	All studies were uncontrolled, so provide no information on the specific effects of SABR. No meta-analysis was carried out, perhaps due to heterogeneity of the different studies. Most participants also received chemotherapy, which may account for some of the reported results. 17 participants (16%) had stage III SCLC, which is outside the scope of this evidence review. Up to a further 8 (7%) with stage II disease may have had stage IIB SCLC, also outside the scope of this evidence review. We nevertheless included this review because most participants were within the scope of the PICO. Better results might be obtained in people with earlier stage cancers. There is some duplication of results, with an "update" of the n=8 study also included in the n=64 study. The numbers of fractions reported in the text and in Table 1A are discrepant; here we report the latter. One study, a care report, was not further reported in the systematic review.
				Primary Clinical effectiveness	Local control (4 studies)	100% at 36 months (n=8), 89% at 24 months (n=64 with some duplication), 100% at 12 months (n=6) and 82% (crude rate) (n=29).			
				Primary Clinical effectiveness	Disease-specific survival (3 studies)	86% at 36 months (n=8), 79% at 24 months (n=64 with some duplication) and 75% at 12 months (n=6).			
				Primary Progression-free survival	Progression-free survival at 24 months (2 studies)	27% at 24 months (estimated rate) (n=29), SABR 22%, SABR plus chemotherapy 67%, "significantly higher" with SABR plus chemotherapy but significance not reported (n=64).			
				Primary Safety	Adverse effects (4 studies)	No adverse reactions of Grade 2 or worse (n=8), no adverse reactions of Grade 3 or worse (n=64 with some duplication), one Grade			

						2 adverse reaction (chest wall toxicity) (n=6), 5 Grade 3 adverse reactions (4 oesophagitis, 1 neutropenia) (n=29).			
Verma et al 2017	P1 – uncontrolled study 24 hospitals in the United States of America	74 people with 76 stage I SCLC, treated between 2005 and 2015. Median age 72 years, 50% male, 67/74 (88%) inoperable because of co-morbidity, "nearly all" because of cardio-pulmonary disease. Median follow-up 18 months.	SABR: 50 Gy in 5 fractions (37%), 50 Gy in 4 fractions (24%), 54 Gy in 3 fractions (11%). 45/74 (59%) of participants also received chemotherapy, most commonly with a platinum agent plus etoposide. 17/74 (23%) also had prophylactic cranial irradiation.	Primary Clinical efficacy	Radiological response**	Complete response 19/76 lesions (25%), partial response 29/76 (38%), stable disease 13/76 (17%) and progression 3/76 (4%).	7	Direct	12 patients without a reported radiological response. Toxicity is reported as "cases" with the number of lesions, not participants, as the denominator. It is unclear whether the proportions are of participants or lesions.
				Primary Clinical efficacy	Local control[6]	1 year 97%, 3 years 96%.			
				Primary Clinical efficacy	Local failure-free survival[7]	1 year 97%, 3 years 97%.			
				Primary Clinical efficacy	Distant metastasis-free survival	1 year 73%, 3 years 63%.			
				Primary Clinical efficacy	Disease-free survival	1 year 59%, 3 years 54%. Median 49.7 months			
				Primary Clinical efficacy	Disease-specific survival	1 year 84%, 3 years 64%. Median 52.3 months			
				Primary Clinical efficacy	Overall survival	1 year 71%, 3 years 35%. Median 17.8 months			
				Primary Safety	Adverse effects	Pneumonitis: grade 1 9/76 lesions (12%), grade 2 3/76 lesions (4%), grade 3 1/76 lesions (1%) Dermatitis: grade 1 1/76 lesions (1%).			

[6] Local control is the absence of radiological evidence of further growth of the cancer at its site of origin.
[7] Local failure-free survival is survival without relapse or the addition of another systemic therapy.

						Fatigue: grade 2 1/76 lesions (1%). Chest wall pain: grade 2 3/76 lesions (4%), unknown grade 1/76 lesions (1%).			
Ly et al 2013	P1 – uncontrolled study 1 hospital in Houston, United States	8 people with stage I SCLCs, treated between 2007 and 2011. Median age 74 years, 50% male, all inoperable. Median follow-up: 16.3 months.	SABR: 50 Gy in 4 fractions. 5/8 (63%) of participants also received chemotherapy, with cisplatin plus etoposide (3) or carboplatin plus etoposide (2).	Primary Clinical efficacy	Overall survival	1 year 88%, 3 years 37%. Median 22 months	7	Direct	The study separately reported 3 participants treated for recurrent SCLC, which we have not included here.
				Primary Clinical efficacy	Recurrence-free survival	1 year 50%, 3 years 38%. Median 8.4 months			

* The scope specified in the PICO for this evidence review is "T1-T2bN0M0, 8th edition", which corresponds to stage I and stage IIA only. Stage IIB lung cancers differ from stage IIA in that there is metastasis in the ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension, but no distant metastasis. Stage III lung cancers have larger and more invasive primary tumours and more widespread lymph node involvement in the chest, but again no distant metastases.

** Defined using the Response Evaluation Criteria in Solid Tumours:

Complete response: Disappearance of all target lesions

Partial response (PR): At least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD

Stable disease: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started

Progressive disease (PD): At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions.

8. Grade of evidence tables

Use of SABR to treat SCLC					
Outcome Measure	**Reference**	**Quality of Evidence Score**	**Applicability**	**Grade of Evidence**	**Interpretation of Evidence**
Overall survival	Alongi et al 2017	8	Direct	A	Overall survival is the proportion of participants alive at specified intervals after completion of SABR. The SR by Alongi et al 2016 included 4 uncontrolled studies reporting this outcome at different timepoints as follows: 72% at 36 months (n=8), 76% at 24 months (n=64 with some duplication), 63% at 12 months (n=6) and 48% at 24 months (estimated rate) (n=29). Improved overall survival would be of great benefit to patients. We found no evidence that SABR improves overall survival in SCLC, as the lack of controlled studies means that we cannot tell whether SABR improved this outcome.
	Verma et al 2017	7			
	Ly et al 2013	7			
Local control	Alongi et al 2017	8	Direct	A	Neither study defined local control, but in general it means the absence of radiological evidence of further growth of the cancer at its site of origin. The SR by Alongi et al 2016 included 4 uncontrolled studies reporting this outcome at different timepoints as follows: 100% at 36 months (n=8), 89% at 24 months (n=64 with some duplication), 100% at 12 months (n=6) and 82% (crude rate) (n=29). Improved local control would benefit patients if it lead to fewer local symptoms or better overall prognosis. We found no evidence that SABR improves local control in SCLC as the lack of controlled studies means that we cannot tell whether SABR improved this outcome.
	Verma et al 2017	7	Direct		
Disease- or	Verma et al 2017	7	Direct	A	Disease- or recurrence-free survival is

recurrence-free survival (the terms are used synonymously in these studies)	Ly et al 2013	7			the proportion of participants alive with no apparent recurrent tumour at specified intervals after completion of SABR. Verma et al 2017 reported disease- or recurrence-free survival at 1 year of 59% and at 3 years of 54% (median 49.7 months). Ly et al 2013 reported disease- or recurrence-free survival at 1 year of 50% and at 3 years of 38% (median 8.4 months). Improved disease- or recurrence-free survival would be of benefit to patients. We found no evidence that SABR improves disease- or recurrence-free survival in SCLC, as the lack of controlled studies means that we cannot tell whether SABR improved this outcome.
Incidence of adverse effects	Alongi et al 2017 Verma et al 2017	8 7	Direct	A	Adverse effects are unintended harmful effects ascribed to treatment. The SR by Alongi et al 2016 included 4 uncontrolled studies reporting this outcome at different timepoints as follows: No adverse reactions of grade 2 or worse (n=8), no adverse reactions of grade 3 or worse (n=64 with some duplication), one grade 2 adverse reaction (chest wall toxicity) (n=6), 5 grade 3 adverse reactions (4 oesophagitis, 1 neutropenia) (n=29). These adverse effects would have caused patients pain and distress. Fewer adverse effects from SABR would be of benefit to patients. These results appear reliable.
Radiological response	Verma et al 2017	7	Direct	B	Radiological response is the proportion of participants alive with tumours whose appearance at imaging falls into different categories**. Verma et al 2017 reported complete response in 19/76 lesions (25%), partial response in0 29/76 (38%), stable disease in 13/76 (17%) and progression in 3/76 (4%).

					Improved radiological response would benefit patients if it lead to fewer local symptoms or better overall prognosis. We found no evidence that SABR improves radiological response in SCLC as the lack of controlled studies means that we cannot tell whether SABR improved this outcome.
Local failure-free survival	Verma et al 2017	7	Direct	B	Local failure-free survival is not defined by Verma et al 2017. In general, it is defined as survival without relapse or the addition of another systemic therapy. Verma et al 2017 reported local failure-free survival rates of 97% at 1 year and 97% at 3 years. Improved failure-free survival would benefit patients if it lead to fewer local symptoms or better overall prognosis. We found no evidence that SABR improves local failure-free survival in SCLC as the lack of controlled studies means that we cannot tell whether SABR improved this outcome.
Distant metastasis-free survival	Verma et al 2017	7	Direct	B	Distant metastasis-free survival is survival without the detection of distant metastases. Verma et al 2017 reported distant metastasis-free survival rates of 73% at 1 year and 63% at 3 years. Improved distant metastasis-free survival would benefit patients if it lead to fewer local symptoms or better overall prognosis. We found no evidence that SABR improves distant metastasis-free survival in SCLC as the lack of controlled studies means that we cannot tell whether SABR improved this outcome.
Progression-free survival	Alongi et al 2017	8	Direct	B	Progression-free survival is survival with no apparent increase in the size of the target tumour at specified intervals after completion of SABR. Alongi et al 2016 included 2 studies

					reporting this outcome as follows: 27% at 24 months (estimated rate) (n=29), SABR 22%, SABR plus chemotherapy 67%, “significantly higher” with SABR plus chemotherapy but significance not reported (n=64). Improved progression-free survival would be of benefit to patients if it lead to fewer local symptoms or better overall prognosis. We found no evidence that SABR improves progression-free survival in SCLC. The lack of studies comparing outcomes with and without SABR means that we cannot tell whether SABR improved this outcome.
Disease-specific survival	Alongi et al 2017	8	Direct	A	Disease-specific survival is survival without death from SCLC. All other causes of death are censored (ie disregarded in the analysis). The SR by Alongi et al 2016 included 3 uncontrolled studies reporting this outcome at different timepoints as follows: 86% at 36 months (n=8), 79% at 24 months (n=64 with some duplication) and 75% at 12 months (n=6). Improved disease-specific survival would benefit patients if it lead to fewer local symptoms or better overall prognosis. We found no evidence that SABR improves disease-specific survival in SCLC. The lack of controlled studies means that we cannot tell whether SABR improved this outcome.
	Verma et al 2017	7	Direct		

** Defined using the Response Evaluation Criteria in Solid Tumours:

Complete response: Disappearance of all target lesions

Partial response (PR): At least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD

Stable disease: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started

Progressive disease (PD): At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions.

9. Literature Search Terms

P – Patients / Population Which patients or populations of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?	Patients diagnosed with small cell lung cancer histology, limited-stage (T1-T2bN0M0, 8th edition)
I – Intervention Which intervention, treatment or approach should be used?	Stereotactic ablative radiotherapy (SABR).
C – Comparison What is/are the main alternative/s to compare with the intervention being considered?	Any treatment for small cell lung cancer histology, limited stage (T1-T2bN0M0, 8th edition)
O – Outcomes What is really important for the patient? Which outcomes should be considered? Examples include intermediate or short-term outcomes; mortality; morbidity and quality of life; treatment complications; adverse effects; rates of relapse; late morbidity and re-admission; return to work, physical and social functioning, resource use.	Clinical effectiveness - Cancer specific survival - Overall survival - Local control - Adverse events/complications - Quality of life (including patient reported outcome measures) Cost effectiveness - Resource utilization - Attendances Any other outcome
Assumptions / limits applied to search	Inclusion Criteria All study designs except case reports published in peer-reviewed journals in the English language Exclusion Criteria Extensive-stage small cell lung cancer. Abstracts. Conference papers. Papers published greater than 10 years ago.

10. Search Strategy

We searched PubMed, Embase and Cochrane Library limiting the search to papers published in English and last 10 years. We excluded conference abstracts, commentaries, letters, editorials and case reports. We also searched TRIP and NICE Evidence Search.

Search date: 2 August 2017

Embase search

1	*lung cancer/
2	*lung carcinoma/ or exp *non small cell lung cancer/ or *small cell lung cancer/
3	(((small cell or non-small cell or nonsmall cell) adj2 (cancer? or carcinoma?)) or sclc or nsclc).ti,ab.
4	(lung adj2 (cancer? or carcinoma?)).ti.
5	1 or 2 or 3 or 4
6	stereotactic body radiation therapy/
7	stereotactic procedure/ and radiotherapy/
8	(stereotactic adj2 (radiotherap* or radiation therap*)).ti,ab.
9	(sbrt or sabr).ti,ab.
10	6 or 7 or 8 or 9
11	5 and 10
12	limit 11 to (english language and yr="2007 -Current")
13	conference*.pt.
14	12 not 13
15	limit 14 to "reviews (maximizes specificity)"
16	limit 14 to "therapy (best balance of sensitivity and specificity)"
17	limit 14 to "economics (maximizes sensitivity)"
18	mortality/ or cancer mortality/
19	survival/ or exp cancer survival/ or overall survival/
20	exp "quality of life"/
21	(mortality or death? or survival).ti,ab.
22	(complication? or adverse event? or adverse effect? or side effect? or harm*).ti.
23	("quality of life" or qol or hrqol or hr-qol or hqol).ti,ab.
24	treatment outcome/ or exp treatment failure/
25	((treatment or cancer) adj5 outcome?).ti,ab.
26	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27	14 and 26
28	15 or 16 or 17 or 27

11. Evidence Selection

- Total number of publications reviewed: 113
- Total number of publications considered potentially relevant: 21
- Total number of publications selected for inclusion in this briefing: 3

12. References

Alongi F, Arcangeli S, De Bari B, Giaj-Levra N, Fiorentino A, Mazzola R, Trovo M 2017. Stage-I small cell lung cancer: A new potential option for stereotactic ablative radiation therapy? A review of literature. *Crit Rev Oncol Hematol* 112: 67-71.

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