CPAG Summary Report for Clinical Panel –URN 1674, Stereotactic ablative radiotherapy for small-cell lung cancer

The Benefits of the Proposition			
No	*Metric*	*Grade of evidence*	*Summary from evidence review*
1.	Survival	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.
2.	Progression free survival	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.
3.	Mobility	Not measured	
4.	Self-care	Not measured	
5.	Usual activities	Not measured	
6.	Pain	Not measured	
7.	Anxiety / Depression	Not measured	
8.	Replacement of more toxic treatment	Not measured	
9.	Dependency on care giver / supporting independence	Not measured	
10.	Safety	Adverse events identified [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.
11.	Delivery of intervention	Not measured	

Other health metrics determined by the evidence review			
No	Metric	Grade of evidence	Summary from evidence review
1.	Local control	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.
2.	Disease- or recurrence-free survival	A	Disease- or recurrence-free survival is 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.
3.	Radiological response	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.
4.	Local failure-free survival	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.
5.	Distant metastasis-free survival	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.
6.	Disease-specific survival	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.

** 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.