



Comment from <i>Insert your name and organisation</i>	Page number <i>Insert 'general' if your comment relates to the whole document</i>	Line/section number	Comment and suggestion for rewording <i>Please insert each new comment in a new row.</i>	Character of comment • 'major' ^a =1 • 'minor' ^b = 2 • 'linguistic' ^c =3 <i>Please indicate your choice by writing the according number in this field, e.g. for major choose "1".</i>	Author's reply
Dr A Sundaramurthy Scotland	11	2.2.2	Age: delete older than 18 on average. Ideally reword that line as : Adult >=18 years of age	3	Accepted.
Dr A Sundaramurthy Scotland	12	2.2.2	Comparison: The standard of care for localized prostate cancer is either surgery or radiotherapy (even if operable). So, PROV.P – comparator should be radiotherapy, surgery or surgery + radiotherapy	1	Included although the corresponding citation is missing
Dr A Sundaramurthy Scotland	13	2.2.2	Definition of conventional radiotherapy >8. My worry is if it's a 10 fraction palliative radiotherapy, how are you going to filter this out. One way of saying this is conventional radical radiotherapy	2	Palliative therapies will be analyzed independently if sufficient information is found (6 th level of priority) according to segmentation of synthesis priorities in Table 2-2. Otherwise, palliative and curative treatments will be jointly synthesized in a single summary of findings table.
Dr A Sundaramurthy Scotland	13	2.2.2	Biochemical control is not relevant in liver or lung cases	2	Ratings adjusted to "7" for liver and lung for this rater.

^a "major": the comment points to a highly relevant aspect and a thorough answer is expected from the author(s)

^b "minor": the comment does not necessarily have to be answered in a detailed manner

^c"linguistic": grammar, wording, spelling or comprehensibility of the document



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Dr A Sundaramurthy Scotland	13	2.2.2	Acute urinary or digestive toxicity or late urinary or digestive toxicity – some are relevant dependent on what is being irradiated. These are irrelevant in lung irradiation. I wonder if it need to be a simple Acute toxicity (RTOG or CTCAE) and Late toxicity (RTOG or CTCAE)	2	General toxicity would be categorized as a safety outcome. This outcomes, considered in the clinical effectiveness domain, have been adjusted to "7" for lung for this rater.
Dr A Sundaramurthy Scotland	13	2.2.2	"Percentage of patients with privative androgenic treatment due to recurrence" I think you are looking at androgen deprivation therapy? It is relevant both in PROV M and PROV P. But not other tumour sites.	2	Ratings adjusted to "7" for liver and lung for this rater.

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Dr A Sundaramurthy Scotland	13	2.2.2	Safety Outcomes. Why are prostate/lung not being looked at for "Number and percentage of patients presenting grade 4 toxicities" Number and percentage of patients with acute toxicities	2	<p>Number and percentage of patients presenting toxicities (prostate) were rated <8 on average, and in preliminary outcome search the authoring team did not find reporting of toxicities by grade nor acuteness.</p> <p>Major radiation complications (presence or absence of grade 2 CTCAE v4 complication) (lung) were rated <8 on average, and in preliminary outcome search "Major systemic therapy complications: presence or absence of grade >2 CTCAE v4 complication (lung)" was found and has been prioritized. On the other hand, "Major surgical complications (presence or absence of grade >2 event) (lung)" was also found in preliminary outcome search and have only been prioritized for metastatic lung cancer.</p> <p>In summary, safety outcomes aggregation by toxicity, acuteness and etiology has been based on preliminary search on how toxicities are reported in published research.</p>

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Dr A Sundaramurthy Scotland	13	2.2.2	This is relevant in PROV P as well if patient undergoes surgery. Major surgical complications (presence or absence of grade >2 event)	2	Included.
Dr A Maciejczyk (Lower Silesian Cancer Centre)	13	2.2.2	In everyday practice, I do not assess late urinary and digestive toxicity in patients with lung cancer - the values 9 and 8 concerned only the evaluation of patients with prostate cancer	2	Late urinary and digestive toxicity rating adjusted to "7" for lung and liver populations for this rater.
Dr A Maciejczyk (Lower Silesian Cancer Centre)	13	2.2.2	In everyday practice, I do not assess biochemical control in patients with lung cancer - the values 8 and 7 concerned mainly prostate cancer	2	Biochemical control rating adjusted to "7" for lung cancer for this rater.

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