Review Article on Medical Oncology: Challenges in 2022

Prostate cancer—what about oligometastatic disease and stereotactic ablative radiotherapy?—a narrative review

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Background and Objective: Oligometastatic prostate cancer (OMPC) encompasses a heterogenous group of clinical entities defined by the timing of the development of metastases. These include *de novo* oligometastatic, oligorecurrent and oligoprogressive prostate cancer (PrCa). We describe the evidence supporting the use of stereotactic ablative radiotherapy (SABR) to the oligometastases to improve patient outcomes in each of these settings.

Methods: Published clinical trials relevant to 'OMPC' and 'SABR' where used for this narrative review.

Key Content and Findings: The driving force behind this narrative review is the constantly evolving field of OMPC with an increasing number of salvage radiotherapy options changing the current treatment paradigm. We now have evidence to support that disease control can be optimised with SABR as shown in several practice changing trials including 'ORIOLE', 'STOMP' for PrCa and 'SABR-COMET' showing a survival advantage with a tumour agnostic salvage approach. We also describe the challenges with data interpretation and cost implications. Challenges include the small sample size for most reported trials, in combination with a lack of cost-efficiency analysis.

Conclusions: SABR is a promising treatment approach for OMPC with a proven clinical benefit in some clinical settings and its use will expand in the future.

Keywords: Stereotactic radiotherapy; oligometastatic prostate cancer; salvage radiotherapy; oligorecurrent prostate cancer

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Introduction

Background

Prostate cancer (PrCa) is currently the most common solid tumour in developed countries and a major cause of mortality (1). The incidence of metastatic PrCa has increased as has the incidence of localised PrCa and this is correlated with a variety of genetic, hereditary and environmental factors, including older age, family history of PrCa and African ethnicity. Nowadays, it has been established that germline or somatic aberrations in the DNA damage repair (DDR) genes are present in 19% of primary

Figure 1 OMPC in different clinical settings, according to the timeline of disease progression. OMPC, oligometastatic prostate cancer.

PrCa and in approximately 23% of metastatic castration-resistant PrCa (2). Incidence of germline *BRCA* genes mutations in newly diagnosed PrCa is 1.2–2%. *BRCA1* and *BRCA2* genes carriers can have around 4- and 8-fold risk of developing PrCa, respectively (3). The treatment of PrCa has been rapidly changed. Namely, androgen receptor (AR) signalling inhibitors downregulate expression of DDR gene expression and increase DNA damage, maximizing the efficacy of PrCa to poly (ADP-ribose) polymerase (PARP) inhibitors. Androgen deprivation therapy (ADT) formulates a status of 'BRCAness' when PARP and AR signalling are concurrently inhibited. As such, PARP inhibitors may be effective even beyond DDR mutated PrCa (4). Given that micro-vessel density represents a predictor of metastasis, targeting angiogenesis is an area of ongoing research (5).

The majority of PrCa cases are diagnosed and treated with localized disease; nevertheless, some patients have metastatic PrCa, either at presentation or following localized disease (6). From the therapeutic point of view, those with high-risk non-metastatic PrCa receive ADT for 3 years that may be combined with radiotherapy. Recently has been reported that combination of abiraterone alone or with enzalutamide with ADT led to significantly higher rates of metastasis-free survival versus ADT alone (7).

Biomarkers have an important role in the selection of patients that may benefit from a particular type of treatment. Within this context, microRNAs, AR variants, bone metabolism, neuroendocrine and metabolite biomarkers are promising candidates, which is crucial in the era of the precision medicine. A luteinising hormone-releasing hormone (LHRH) antagonist for 6 months following stereotactic ablative radiotherapy (SABR) may be considered when treating oligometastatic PrCa (OMPC). The rationale behind that strategy is to enable the safe localisation of the target for SABR planning and delivery and finally to maximize the response to radiotherapy (8). There have been major advances in the management of metastatic PrCa from the use of androgen deprivation therapy alone to the addition of primary chemotherapy (STAMPEDE, CHAARTED), and novel antiandrogens (ENZAMET, STAMPEDE, TITAN) (9-11).

Rationale and knowledge gap

The oligometastatic state was first described by Weichselbaum and Hellman in 1995 and outlines an intermediate stage of cancer between localised disease and widespread metastases. The current definition of OMPC is based on the paradigm that up to 3 or 5 metastatic lesions could be effectively treated with a form of metastasis directed therapy. There are several published trials demonstrating a survival advantage with an aggressive approach of local treatments such as salvage prostatectomy, or salvage ultrahypofractionated radiotherapy. There is robust evidence indicating that AR activates DNA repair pathways, which provides a rationale behind the use of ADT with SABR for hormone-sensitive OMPC (12).

The current nomenclature of OMPC has 3 clearly defined clinical entities, based on the timing of the presentation of metastases. The clinical strategy can vary between presentations, but there is evidence of disease control benefit in all of the following (*Figure 1*):

(I) *De novo* or synchronous: oligometastatic disease at the time of presentation of the primary,
(II) Oligorecurrent or metachronous: limited metastatic recurrence after treatment of primary, and
(III) Oligoprogressive: well controlled metastatic disease with disease progression seen in a limited number of metastases.

Multiple phase II randomised trials have supported the safety and efficacy of using SABR to treat oligometastases. SABR-COMET an international randomised phase II trial in which 99 patients with 1–5 metachronous oligometastases from different primary cancer sites were randomised to receive SABR to all oligometastases or palliative standard of care. A median overall survival (OS) benefit of 22 months

which translated to an absolute survival benefit of 24.6% at 5 years was observed in the patients who received SABR (13).

Objective

Our objective is to offer a clear and objective review of the most important trials in OMPC. This narrative review is aimed at the oncologists who are treating patients with oligometastatic disease. This serves as a platform for reflection of current evidence and aims to stimulate discussion on the optimal stratification of patients and the personalised treatment approach of SABR. We present this article in accordance with the Narrative Review reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-828/rc).

Methods

We used PubMed to identify relevant articles, searching for relevant terms, including 'PrCa', 'Oligometastatic disease', 'SABR'. Relevant papers were reviewed by the authors and the original papers were selected for presentation. A structured review and prioritisation of seminal papers allowed for a flexible way to extract the most relevant references and lay them out in a clinical subgroup format. This narrative review serves as a basis for discussion, but has several limitations. It is not an extensive literature review; several case series and retrospective data reviews were not included.

De novo oligometastatic PrCa

The CHAARTED study demonstrated the benefit of upfront treatment in the metastatic Hormone Sensitive cohort (mHSPC) and identified those patients with high burden disease as those deriving most benefit from the addition of docetaxel chemotherapy (9). Subsequent trials, such as STAMPEDE, confirmed an OS benefit even in the oligometastatic cases (14). In fact, the trialists involved in the STAMPEDE trial agree that upfront chemotherapy should be offered to all patients presenting with mHSPC, regardless of metastatic tumour load. Similarly, the randomised controlled trials using upfront novel antiandrogens found an OS benefit regardless of tumour burden.

Based on the above evidence it would be difficult to resist the urge to offer an upfront chemotherapy or novel antiandrogen treatment in *de novo* oligometastatic cases. The evidence to support the use of a more aggressive radiotherapy approach in mHSPC is not robust and consists of several retrospective studies and a few prospective single arm small trials. In a recently published systematic review of published trials by Rogowski *et al.* the published data do not support the use of SABR in synchronous metastases, other than within a clinical trial (15). Available trials used different definitions for OMPC with some using 2, others 3 or 5 sites as the inclusion criteria. Furthermore, the majority were retrospective and used different fractionations and prescriptions. On the face of robust level 1 evidence the use of upfront chemotherapy or novel antiandrogens, the choice is clear.

Nevertheless, the argument to target the primary PrCa site, in the face of metastatic disease, has shown some promising results in 2 major trials. The HORRAD trial randomised patients with metastatic PrCa to receive ADT or ADT plus prostate external beam radiation therapy (EBRT) (16). Initially, this trial failed to show an OS benefit, but a post-hoc subgroup analysis of men with low burden disease (as per the CHAARTED definition) confirmed a significant OS benefit with the use of EBRT. Similarly, the STAMPEDE Arm H investigated the same question of radiotherapy to the primary in patients with mHSPC, only to confirm the OS benefit for the low burden disease cohort (17). The survival benefit was measured as 7% at 3 years in the STOPCAP meta-analysis (18).

In summary, the use of upfront SABR in *de novo* oligometastatic disease lacks significant support with trial evidence. In this setting the use of systemic anti-cancer treatment (SACT) is the priority. Level 1 evidence based on the STAMPEDE trial support the use of SACT upfront with a significant overall survival advantage (17). Consolidation with prostate radiotherapy, regardless of fractionation, in the low burden mHSPC setting, has shown a clinical advantage.

Oligorecurrent PrCa

In oligorecurrent PrCa metastases develop typically at least 3–6 months after treatment of the primary. These cancers tend to run a more indolent course and have a better prognosis than *de novo* oligometastatic PrCa. It is likely that oligorecurrent PrCa will be diagnosed more frequently with increased use of prostate-specific membrane antigen (PSMA) positron emission tomography (PET) scan, which can detect recurrent disease at earlier time points.

In the ORIOLE trial men with recurrent mHSPC (no

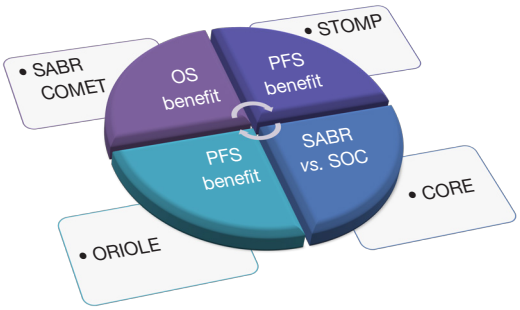

Figure 2 Seminal Trials providing the evidence for salvage SABR. SABR, stereotactic ablative radiotherapy. OS, overall survival; PFS, progression-free survival.

ADT for at least 6 months) and oligometastatic disease (defined as less than 3 metastases) were randomised to salvage SABR or observation. At 6 months 19% of men treated with SABR progressed compared to 61% of those on observation. This trial would have been more applicable to current practice if they used ADT as the comparator (19). Nevertheless, the radiotherapy community was infused with increased optimism and the use of salvage SABR has become mainstream in this setting.

The promise of salvage prostatectomy has not been confirmed in any randomised controlled trials. Such an approach is currently considered experimental and patients should be carefully selected, in view of the associated significant toxicity. The evidence is based on retrospective trials, with 27 single or multicentre trials, showing a risk of urinary incontinence from 30% to 70%, anastomotic urethral stenosis from 10% to 20% and rectal injury from 5% to 10%. The biochemical control rate was noted as between 30% to 100%. The variability of outcomes and risk of severe toxicity makes this option not attractive (20).

The biggest SABR observational study of its kind started in 2015 when the England National Health Service (NHS) decided to assess the novel technology of SABR via commissioning through evaluation (CtE). This single arm, observational, patient registry looked as the evaluation of SABR in oligometastatic (up to 3 lesions) carcinomas. These were metachronous oligometastases with at least a 6 months disease free interval from previous treatment, with a primary endpoint being OS at 1 and 2 years. With 1,422 patients on this registry from 17 NHS trusts the results were impressive with a 1 year OS of 92% and 2 years OS of 79%. There was no comparator arm with excellent toxicity profile and grade III toxicity of 2% (21). NHS England has reviewed the 'Commissioning Through Evaluation' (CTE) data in the UK, as shared with the UK SABR consortium and subsequently approved the expansion of commissioning of salvage SABR for oligometastatic disease.

The CORE trial (A randomised trial of Conventional Care versus Radioablation for Extracranial Oligometastases) randomised patients into the Standard of Care (ADT for PrCa) versus SABR and Standard of Care. The trial has successfully completed recruitment and will publish the results in 2 years (22).

A further multicentre randomised phase II trial of oligorecurrent PrCa, with 3 or fewer lesions, enrolled 62 men and offered salvage SABR to the lesions versus surveillance. The trial was described as 'Surveillance or Metastasis-Directed Therapy for Oligometastatic PrCa recurrence', STOMP trial. As expected those men offered surveillance required ADT within 13 months versus 21 months in the intervention group. The comparator Arm of the trial was surveillance, which at the time reflected the European guidelines for asymptomatic patients. For most clinicians the use of ADT would have been a better reflection of real world practice. The STOMP trial was a hypothesis generating trial, opening the way for future RCTs (*Figure 2*) (23). In summary, the oligorecurrent PrCa patients have more options than before and could be offered salvage radiotherapy treatment, as part of a multidisciplinary approach.

Oligoprogressive PrCa

The role of SABR in oligoprogressive PrCa is being investigated in several clinical trials. This is a growing field and an indication not currently supported by the United Kingdom (UK) CtE SABR commissioning criteria. A Canadian Trial by Dr David Palma set up as a multicentre phase II trial randomising patients with oligoprogressive cancers to standard of care or SABR to all progressing metastatic sites. This is the STOP trial (Stereotactic Radiotherapy for Oligo-Progressive metastatic cancer), not limited to PrCa, but aiming to recruit 90 patients (24).

A PrCa specific trial is also recruiting in the UK for men who progress on a novel antiandrogen (abiraterone or enzalutamide) and develop 1 or 2 targetable lesions. The TRAP trial (Targeted Radiotherapy in Androgen-Suppressed PrCa patients), with a target of 80 patients, who will receive 30 Gy in 5 fractions to the metastatic sites (25). In summary, oligoprogressive PrCa patients offer a separate challenge and have yet to shown to gain a measurable benefit from salvage radiotherapy.

Non-metastatic castrate resistant PrCa (nmCRPC)

The biggest challenge to the approach of targeting OMPC, especially in castrate resistant setting has come from 2 trials. The SPARTAN trial, with its laconic name claimed that if the traditional imaging modalities were used (computerized tomography and bone scans), then a new clinical entity can present a target population opportunity for novel anti-androgens. In the majority of these men, if we were to perform a F-PSMA-PET or Ga-PSMA-PET we would identify metastatic sites, most of them likely candidates for SABR. The benefit in disease-free survival with the introduction of Apalutamide was staggering with a hazard ratio (HR) of 0.06 for prostate-specific antigen (PSA) failure. The median metastasis free survival was 40.5 months with apalutamide compared to 16 months with placebo (26). Such impressive results have not been noted with any SABR trial, which are never powered to demonstrate that, as they are designed as phase II trials. In summary, in the nmCRPC patient cohort we have seen a growth of available systemic treatment options, which have achieved an improvement of outcomes.

Discussion

The key question for researchers is whether the current development of more targeted radiotherapy treatments for PrCa really matters. We have numerous phase II clinical trials currently recruiting, or about to publish the results. Any future SABR trial needs to be an adequately powered multi-institutional phase III trial, with the appropriate standard of care arm. We have done the hypothesis generating work and this is the time to collaborate and aim for better trials with longer follow up periods. PrCa is a chronic disease and needs adequate follow up to prove the value of SABR.

There is no lack of single arm phase II trials to support the use of SABR in OMPC, but no mention of tailoring this treatment based on biomarkers and molecular testing. We know that OMPC is an inherently heterogenous entity with significant biological heterogeneity (27). The European Organisation for Research and Treatment of Cancer (EORTC) has suggested a new classification of 'genuine oligometastatic disease' those with *de novo* or recurrent OMPC, versus the 'induced oligometastatic disease' as those on treatment for metastatic PrCa, who develop oligopersistent or oligoprogressive disease (28).

Several publications have commented on the importance of hormone sensitivity as a biomarker of response to salvage SABR. Franzese *et al*. performed a univariate analysis and identified castrate resistance as a negative predictive biomarker (29). However, Triggiani *et al*. showed excellent 2-year control rates at 92% for hormone sensitive and 90% for castrate resistant disease (30). There is an obvious clinical benefit for local control with SABR, but the castrate resistant cases behave more aggressively and more likely to develop more metastatic sites. The delay to the need for systemic treatment is appealing to many patients, who would like to maintain quality of life.

Health economics-cost efficiency

A salvage strategy to address that risk of nodal relapse outside the treated nodes is needed. The concept of upfront extended nodal radiotherapy (ENRT) in N1 PrCa was proposed as a way to treat non-visible metastatic disease with extended fields. Nevertheless, the radiation toxicity form this approach is significant and some to the toxicity gain from SABR is lost (31).

In order to perform a cost-benefit analysis, current models require an OS benefit that can measurable and compared to the standard of care. Despite the multitude of trials showing a progression-free survival benefit, there is only one trial that has shown the OS advantage; that is the SABR-COMET trial. According to a Markov model assessment of the cost of SABR, based on the results of the COMET-SABR trial the salvage SABR approach in OMPC is cost-effective. The analysis looked at the different treatment options and for 1 lesion the cost was $28k per Quality Adjusted Life Year (QALY) (32). This is well within the current National Institute for Health and Care Excellence (NICE) cut off and patients would be eligible to receive this salvage treatment.

Strengths and limitations

This narrative review serves as a basis for discussion, but has several limitations. Several case series and retrospective data reviews were not incorporated. As a narrative review, the emphasis was placed on identifying the most relevant research to support any claims on the role of SABR in OMPC. The field developing rapidly and several trials are currently recruiting and will be able to answer the questions of best timing and place of SABR.

Conclusion

More evidence is needed to prove the value of SABR in OMPC, not only as a clinically effective treatment modality, but also as cost-effective use of resources for an ever increasing patient population. The experience so far is suggestive of excellent local control and a delay to disease progression. Considering that this is an important surrogate marker for survival, then the promise of better disease control and better outcomes is plausible. Furthermore, palliative care input is patients with metastatic disease is important in addressing patient expectations and manage future disease related issues and symptoms.

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References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin 2018;68:7-30.
2. Boussios S, Rassy E, Shah S, et al. Aberrations of DNA repair pathways in prostate cancer: a cornerstone of precision oncology. Expert Opin Ther Targets 2021;25:329-33.
3. Ghose A, Moschetta M, Pappas-Gogos G, et al. Genetic Aberrations of DNA Repair Pathways in Prostate Cancer: Translation to the Clinic. Int J Mol Sci 2021;22:9783.
4. Shah S, Rachmat R, Enyioma S, et al. BRCA Mutations in Prostate Cancer: Assessment, Implications and Treatment Considerations. Int J Mol Sci 2021;22:12628.
5. Ioannidou E, Moschetta M, Shah S, et al. Angiogenesis and Anti-Angiogenic Treatment in Prostate Cancer: Mechanisms of Action and Molecular Targets. Int J Mol Sci 2021;22:9926.
6. Gillessen S, Armstrong A, Attard G, et al. Management of Patients with Advanced Prostate Cancer: Report from the Advanced Prostate Cancer Consensus Conference 2021. Eur Urol 2022;82:115-41.
7. Attard G, Murphy L, Clarke NW, et al. Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol. Lancet 2022;399:447-60.
8. Saxby H, Mikropoulos C, Boussios S. An Update on the Prognostic and Predictive Serum Biomarkers in Metastatic Prostate Cancer. Diagnostics (Basel) 2020;10:549.
9. Sweeney CJ, Chen YH, Carducci M, et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer. N Engl J Med 2015;373:737-46.
10. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. N Engl J Med 2019;381:13-24.
11. James ND, de Bono JS, Spears MR, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. N Engl J Med 2017;377:338-51.
12. Saxby H, Boussios S, Mikropoulos C. Androgen Receptor

Gene Pathway Upregulation and Radiation Resistance in Oligometastatic Prostate Cancer. Int J Mol Sci 2022;23:4786.
13. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet 2019;393:2051-8.
14. Clarke NW, Ali A, Ingleby FC, et al. Addition of docetaxel to hormonal therapy in low- and high-burden metastatic hormone sensitive prostate cancer: long-term survival results from the STAMPEDE trial. Ann Oncol 2019;30:1992-2003.
15. Rogowski P, Roach M 3rd, Schmidt-Hegemann NS, et al. Radiotherapy of oligometastatic prostate cancer: a systematic review. Radiat Oncol 2021;16:50.
16. Boevé LMS, Hulshof MCCM, Vis AN, et al. Effect on Survival of Androgen Deprivation Therapy Alone Compared to Androgen Deprivation Therapy Combined with Concurrent Radiation Therapy to the Prostate in Patients with Primary Bone Metastatic Prostate Cancer in a Prospective Randomised Clinical Trial: Data from the HORRAD Trial. Eur Urol 2019;75:410-8.
17. Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. Lancet 2018;392:2353-66.
18. Burdett S, Boevé LM, Ingleby FC, et al. Prostate Radiotherapy for Metastatic Hormone-sensitive Prostate Cancer: A STOPCAP Systematic Review and Meta-analysis. Eur Urol 2019;76:115-24.
19. Phillips R, Shi WY, Deek M, et al. Outcomes of Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer: The ORIOLE Phase 2 Randomized Clinical Trial. JAMA Oncol 2020;6:650-9.
20. Matei DV, Ferro M, Jereczek-Fossa BA, et al. Salvage radical prostatectomy after external beam radiation therapy: a systematic review of current approaches. Urol Int 2015;94:373-82.
21. Chalkidou A, Macmillan T, Grzeda MT, et al. Stereotactic ablative body radiotherapy in patients with oligometastatic cancers: a prospective, registry-based, single-arm, observational, evaluation study. Lancet Oncol 2021;22:98-106.
22. Conventional Care Versus Radioablation (Stereotactic Body Radiotherapy) for Extracranial Oligometastases (CORE) (accessed on 23 June 2022); Available online: https://clinicaltrials.gov/ct2/show/record/NCT02759783
23. Ost P, Reynders D, Decaestecker K, et al. Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial. J Clin Oncol 2018;36:446-53.
24. Stereotactic Radiotherapy for Oligo-Progressive Metastatic Cancer (The STOP Trial) (accessed on 23 June 2022); Available online: https://clinicaltrials.gov/ct2/show/NCT02756793
25. Targeted Radiotherapy in Androgen-suppressed Prostate Cancer Patients. (TRAP) (accessed on 23 June 2022); Available online: https://clinicaltrials.gov/ct2/show/NCT03644303
26. Smith MR, Saad F, Chowdhury S, et al. Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. N Engl J Med 2018;378:1408-18.
27. Stewart R, White M, Tan J, et al. SABR in oligometastatic breast cancer: Current status and future directions. Breast 2021;60:223-9.
28. Guckenberger M, Lievens Y, Bouma AB, et al. Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation. Lancet Oncol 2020;21:e18-28.
29. Franzese C, Zucali PA, Di Brina L, et al. The efficacy of Stereotactic body radiation therapy and the impact of systemic treatments in oligometastatic patients from prostate cancer. Cancer Med 2018;7:4379-86.
30. Triggiani L, Alongi F, Buglione M, et al. Efficacy of stereotactic body radiotherapy in oligorecurrent and in oligoprogressive prostate cancer: new evidence from a multicentric study. Br J Cancer 2017;116:1520-5.
31. Soldatov A, von Klot CAJ, Walacides D, et al. Patterns of Progression After (68)Ga-PSMA-Ligand PET/CT-Guided Radiation Therapy for Recurrent Prostate Cancer. Int J Radiat Oncol Biol Phys 2019;103:95-104.
32. Qu XM, Chen Y, Zaric GS, et al. Is SABR Cost-Effective in Oligometastatic Cancer? An Economic Analysis of the SABR-COMET Randomized Trial. Int J Radiat Oncol Biol Phys 2021;109:1176-84.

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