



OLIGO-AIRO: a national survey on the role of radiation oncologist in the management of OLIGO-metastatic patients on the behalf of AIRO

Rosario Mazzola¹ · Barbara Alicja Jereczek-Fossa^{2,3} · Paolo Antognoni⁴ · Nadia Di Muzio^{5,6} · Luca Nicosia¹ · Andrea Lancia⁷ · Ivan Fazio⁸ · Silvia Chiesa⁹ · Mattia F. Osti¹⁰ · Stefano Pergolizzi¹¹ · Davide Franceschini¹² · Piercarlo Gentile¹³ · Luca Triggiani¹⁴ · Filippo Alongi^{1,15}

Received: 11 February 2021 / Accepted: 9 March 2021
© Springer Science+Business Media, LLC, part of Springer Nature 2021

Abstract

In the last years, several evidences demonstrated the role of stereotactic body radiotherapy (SBRT) in the oligometastatic disease and the possibility to increase survival in selected patients. In 2020 the study group “biology and treatment of the oligometastatic disease” of the Italian Association of Radiotherapy and Clinical Oncology (AIRO) conducted a survey evaluating the attitude of physicians in treating the oligometastatic disease and the definition of it. An electronic questionnaire was administered online to the society members. 105 questionnaires were returned. 78% responders considered as oligometastatic a disease with ≤ 5 metastases. The majority of the responders (77%) treated > 50 patients in the last year, and 89% responders agreed in considering every oligometastatic tumor susceptible to local treatments. Regarding the clinical management of the oligometastatic disease, the majority of the responders (66%) suggested an interdisciplinary discussion. When choosing a treatment option for fit patients with a single oligometastatic focus, 52% of the responders agreed in proposing only SBRT. In the case of unfit patients with a single oligometastatic lesion the agreement was in favor of the SBRT alone (89%). In the oligoprogressive setting, 41% responders opted to continue the current systemic treatment and to add SBRT, while in the case of oligoresidual disease, 70% responders was in favor of adding SBRT and continuing the current systemic treatment. In conclusions, the survey illustrated the current agreement and prescribing attitude for oligometastatic patients in Italy. The non-homogenous agreement in some clinical scenarios suggest the need of more robust evidence.

Keywords Stereotactic body radiotherapy · SBRT · SABR · Oligometastatic disease · Survey

Introduction

During the last years, the role of the Radiation Oncologist has dramatically evolved in the multidisciplinary arena of the oligometastatic disease. In this setting, the old belief of relegating the Radiation Oncologists with a palliative role has been supplanted by the concrete opportunity of playing a leading position among other oncological professionals. Such advances are related to a multifactorial process: (1) the increasing amount of literature evidence from the theory of Hellman and Weichselbaum until to randomized trials attesting the crucial role of metastases directed therapy

in the oligometastatic disease, (2) the progressive enlargement of biological knowledge behind the delivery of high doses irradiation that allow clinicians to graduate the intent of the treatment (ablative or immunostimulatory), (3) the recent greater effectiveness of even more types of systemic therapies that favorably modified the natural history of the polymetastatic disease creating scenarios of oligo-clonal resistance, (4) the improvement or early detection of oligometastatic foci by means of more sensitive and accurate imaging modalities [1–8].

To date, it remains mandatory to homogenize the clinical applications of metastasis directed therapy (MDT) in the field of Radiation Oncology. In this sense, the scientific societies have educational duties including the monitoring of the perception of their members on this topic issue through a monothematic survey. The main aim of the current survey was to explore and define the role of Italian Radiation

✉ Luca Nicosia
lucanicosia.rg@gmail.com

Extended author information available on the last page of the article

Oncologists in the management of oligometastatic patients endorsed by the Italian Association of Radiotherapy and Clinical Oncology (AIRO).

Material and methods

The questionnaire consisted of 16 single-choice questions and two multiple-choice questions, and was prepared by the AIRO “biology and treatment of the oligometastatic disease” Study Group. The questionnaire was sent via e-mail on May 2020 to all the AIRO members registered in 2019 (775). All subjects were invited to anonymously fill in the electronic form within 30 days. Topics included personal working and educational information, criteria for the definition of the oligometastatic disease, responders’ clinical attitude to the treatment of the oligometastatic disease in different clinical scenario, combination of Stereotactic body Radiotherapy (SBRT) with other treatment modalities. For each question, the agreement was considered reached when more than 80% responders chose the same response.

Results

General considerations and definition of the oligometastatic disease

In total, 105 AIRO members answered the questionnaire (15%). More than 60% of the responders were 35–55 years old (Question 1), 73% worked in a non-academic hospital (Question 3), and only 25% of the responders worked in a research Center (Question 2).

The survey depicted a general agreement in considering as oligometastatic a disease with ≤ 5 metastases (78%) (Question 4; Fig. 1a). Similarly, 70% of responders did not consider the involvement of a single organ as a limitation

for the definition of the oligometastatic disease (Question 5). Regarding the continuing scientific education on the oligometastatic disease (Question 9), including the reading of scientific articles or the consultation of other information sources during the last year, 19% of the responders examined < 5 sources, 39% between 5 and 10 sources, 31% between 10 and 50, and 11% > 50 sources. The responders expressed a general agreement (92%) on the need to draft a position paper on the behalf of Italian Association of Medical Oncology (AIOM)-AIRO working group on the definition of the oligometastatic disease (Question 10).

The majority of the responders (77%) treated > 50 patients in the last year (Question 11; Fig. 1b), but only 39% of them treated a large volume of oligometastatic patients in the last year (Question 12). Interestingly 13% of the responders treated < 10 oligometastatic patients in the last year (Question 12).

Management of the oligometastatic disease

In question 13 (multiple answers allowed) the responders were asked to choose which oligometastatic tumor was considered amenable to a MDT in their own Centers. There was a general agreement (89%) in considering every oligometastatic tumor susceptible to local treatments. When analyzing the specific histology, 29% of the responders chose prostate cancer, 23% lung histology, 19% breast cancer, 18% colorectal disease, and 16% renal tumor.

The most frequent oligometastatic site susceptible to local treatment in each Center was lymph node (46%), followed by bone (45%), lung (40%), brain (36%), and liver (7%) (Question 14, multiple answers allowed). Nevertheless, there was a consensus (80%) in considering every oligometastatic site susceptible to local treatment. The median number of oligometastatic lesions per patient treated in each Center was 2 for 55% of the responders, 3 metastases in 22% of the cases, > 3 lesions in 12%, and 1 in 11% (Question 15).

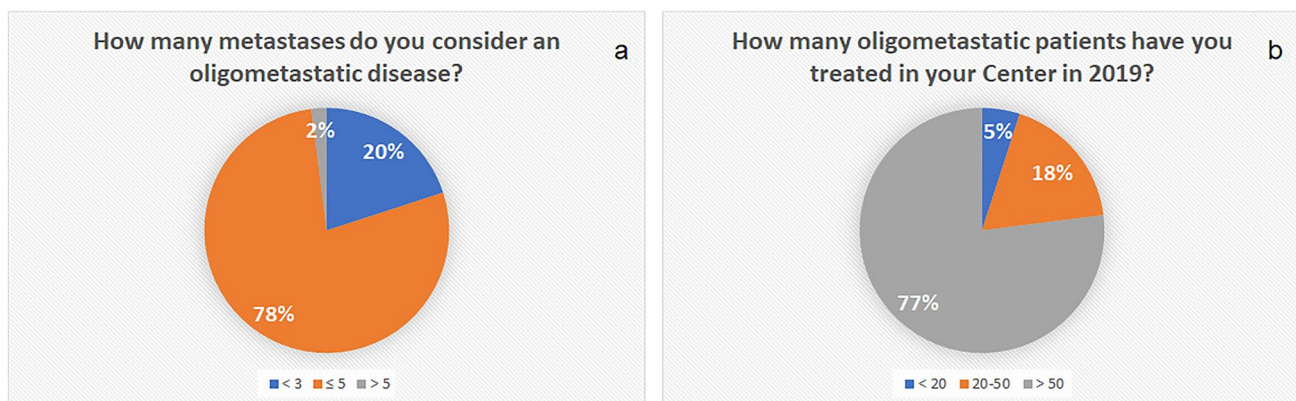


Fig. 1 a: Survey question number 4; b: survey question number 11

Regarding the clinical management of the oligometastatic disease (Question 16), the majority of the responders (66%) suggested an interdisciplinary discussion, 20% were in favor of exclusive management by the Radiation Oncologist, 14% opted for an evaluation case by case, and no responders chose an exclusive surgical or pharmacological management.

Decision strategy of the oligometastatic disease

When choosing a treatment option for fit patients with a single oligometastatic focus (Question 6), 52% of the responders agreed in proposing only SBRT, the combination of SBRT and systemic therapy was the second option (30%), and 18% of the responders considered exclusive surgery. Interestingly, no responders considered systemic therapy alone as a viable treatment option. On the contrary, in the case of unfit patients with a single oligometastatic lesion (Question 7), the consensus has shifted in favor of the SBRT alone (89%), while the combination of SBRT and systemic therapy was 9%, and surgery alone 2%. In the case of patients with > 1 oligometastatic lesion, the responders did not reach a consensus about the treatment strategy to propose (Question 8): 42% chose the combination of SBRT and a new systemic treatment line, 39% opted to continue the same systemic treatment line and to add SBRT, 17% proposed SBRT alone, and 2% a new systemic treatment line.

In the oligoprogressive setting (progression to 1–3 new lesions) (Question 17; Fig. 2), 41% of the responders opted to continue the current systemic treatment and to add SBRT, 38% chose a systemic treatment switch plus SBRT, 1% a new systemic treatment line, and no responders opted for surgery. In the case of oligoresidual disease (persistence of 1–3 lesions during systemic therapy) (Question 18; Fig. 3), 70% of the responders was in favor of adding SBRT and continuing the current systemic treatment, 18% opted for a

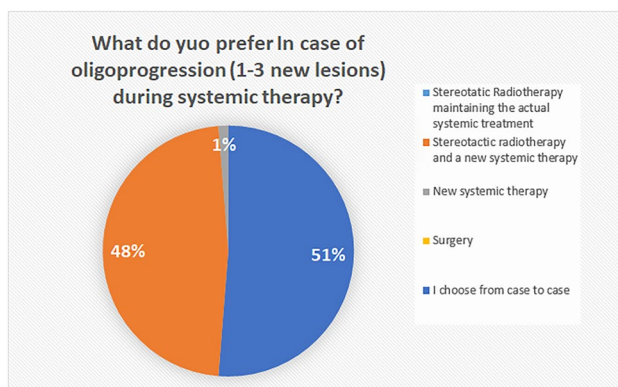


Fig. 2 Survey question number 17

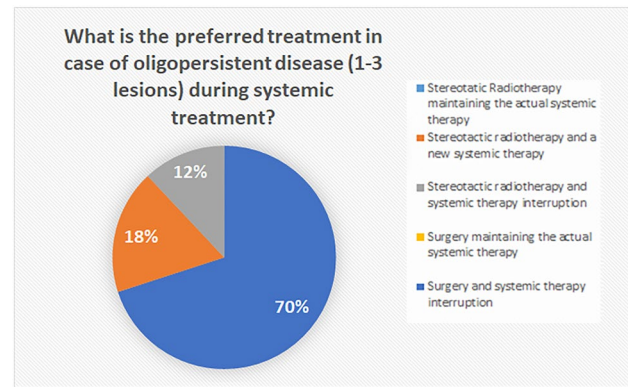


Fig. 3 Survey question number 18

systemic treatment switch plus SBRT, 12% chose SBRT and the interruption of the systemic treatment.

Discussion

The Radiation Oncologist is actually facing a change of his own professional role in the management of metastatic patients. This transformation is mainly related to the increasing recognition of the oligometastatic disease, amenable of local approaches. Moreover, the development of ablative irradiation techniques, also known as SBRT or MDT allowed clinicians to offer this therapeutic opportunity more frequently [9]. Apart from the rationale for treating the oligorecurrent disease with controlled primary cancer, the integration with systemic therapies in the oligopersistent or oligoprogressive scenarios represents an interesting trend in the daily clinical practice. On the other hand, the possibility to delay the systemic therapy administration when MDT is adopted as upfront therapy could help to enlarge the therapeutic armamentarium/sequences [10–12]. The feeling of AIRO members herein involved is in line with this last clinical evidence. In fact, there was a general agreement (89%) in considering any kind of oligometastatic tumor susceptible to local treatments. Moreover, 59% responders considered every oligometastatic site susceptible to local therapy. Globally, the median number of oligometastatic lesions/patient treated in each Center was less than 3 in more than 85% of the responders.

The present survey was focused specifically on the clinical management of the oligometastatic disease. Therefore, a limitation could be not having planned questions regarding technical aspects like treatment dose and fractionation. Moreover, the technology availability needed to administer SBRT was not explored.

Interesting points have emerged regarding the decision-making strategy in the case of oligometastases diagnosis.

SBRT remains the first treatment option in the case of single lesion either in the case of fit or unfit patients. Of contrast, a consensus was not reached in the case of more than one lesion. Recently, the numeric criteria for considering a disease as oligometastatic was largely revised by several editorials, provocatively postulating the overcoming of the sole numeric limit in favor of a more global vision of the patients' disease, and a deeper interfacing with systemic therapy [13]. In the next future, new treatment approaches could be hypothesized. For example, selected low-volume metastatic disease may benefit from the sole ablative irradiation to all the active sites, meanwhile in the high-volume disease a combination of high-dose irradiation to limited sites low-dose radiotherapy to remaining lesions could enhance systemic responses especially in the context of Immune-Oncology [14]. With this in mind, the scientific societies will have to work to produce evidence and acquire subsequently awareness in their own means [15]. Much effort was made by the European Society for Radiotherapy and Oncology and the European Organisation for Research and Treatment of Cancer by promoting the OligoCare registry which aims to identify patient, tumor, stage, and treatment characteristics that affect overall survival of patients treated with SBRT for oligometastatic disease [12]. The results of the OligoCare prospective cohort trial might improve the daily clinical practice.

Conclusion

The present survey, with its results, is a clear and detailed picture of Italian Scientific Radiation Oncology Community in 2020, concerning the new awareness to be crucial among the other oncological professional figures in the decision-making process and in the therapeutic management of oligometastatic patients.

Acknowledgements The Authors thank the Scientific Committee and Board of the AIRO for the critical revision and final approval of the manuscript (Nr. 1/2021).

Declarations

Conflict of interest The authors declare that they have no conflict of interest to disclose.

References

- Mazzola R, Jereczek-Fossa BA, Franceschini D, Tubin S, Filippi AR, Tolia M, Lancia A, Minniti G, Corradini S, Arcangeli S, Scorsetti M, Alongi F. Oligometastasis and local ablation in the era of systemic targeted and immunotherapy. *Radiat Oncol*. 2020;15(1):92.
- Iyengar P, Wardak Z, Gerber DE, Tumati V, Ahn C, Hughes RS, Dowell JE, Cheedella N, Nedzi L, Westover KD, Pulipparacharuvil S, Choy H, Timmerman RD. Consolidative radiotherapy for limited metastatic non-small-cell lung cancer: a phase 2 randomized clinical trial. *JAMA Oncol*. 2018;4(1):e173501.
- Gomez DR, Blumenschein GR Jr., Lee JJ, Hernandez M, Ye R, Camidge DR, Doebele RC, Skoulidis F, Gaspar LE, Gibbons DL, Karam JA, Kavanagh BD, Tang C, Komaki R, Louie AV, Palma DA, Tsao AS, Sepesi B, William WN, Zhang J, Shi Q, Wang XS, Swisher SG, Heymach JV. Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study. *Lancet Oncol*. 2016;17(12):1672–82.
- Ost P, Reynders D, Decaestecker K, Fonteyne V, Lumen N, De Bruycker A, Lambert B, Delrue L, Bultjijnck R, Claeys T, Goetghebeur E, Villeirs G, De Man K, Ameye F, Billiet I, Joniau S, Vanhaverbeke F, De Meerleer G. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. *J Clin Oncol*. 2018;36(5):446–53.
- Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, Mulroy L, Lock M, Rodrigues GB, Yaremko BP, Schellenberg D, Ahmad B, Senthil S, Swaminath A, Kopek N, Liu M, Moore K, Currie S, Schlijper R, Bauman GS, Laba J, Qu XM, Warner A, Senan S. Stereotactic ablative radiotherapy for the comprehensive treatment of oligometastatic cancers: long-term results of the SABR-COMET phase II randomized trial. *J Clin Oncol*. 2020;38(25):2830–8.
- Triggiani L, Mazzola R, Magrini SM, Ingrosso G, Borghetti P, Trippa F, Lancia A, Detti B, Francolini G, Matrone F, Bortolus R, Fanetti G, Maranzano E, Pasqualetti F, Paiar F, Bonù ML, Magli A, Bruni A, Mazzeo E, Franzese C, Scorsetti M, Alongi F, Jereczek-Fossa BA, Ost P, Buglione M. Metastasis-directed stereotactic radiotherapy for oligoprogressive castration-resistant prostate cancer: a multicenter study. *World J Urol*. 2019;37(12):2631–7.
- Mazzola R, Francolini G, Triggiani L, Napoli G, Cuccia F, Nicotia L, Livi L, Magrini SM, Salgarello M, Alongi F. Metastasis-directed Therapy (SBRT) Guided by PET-CT (18)F-CHOLINE Versus PET-CT (68)Ga-PSMA in Castration-sensitive oligorecurrent prostate cancer: a comparative analysis of effectiveness. *Clin Genitourin Cancer*. 2020;S1558–7673(20):30191–9.
- De Bleser E, Jereczek-Fossa BA, Pasquier D, Zilli T, Van As N, Siva S, Fodor A, Dirix P, Gomez-Iturriaga A, Trippa F, Detti B, Ingrosso G, Triggiani L, Bruni A, Alongi F, Reynders D, De Meerleer G, Surgo A, Loukili K, Miralbell R, Silva P, Chander S, Di Muzio NG, Maranzano E, Francolini G, Lancia A, Tree A, Deantoni CL, Ponti E, Marvaso G, Goetghebeur E, Ost P. Metastasis-directed therapy in treating nodal oligorecurrent prostate cancer: a multi-institutional analysis comparing the outcome and toxicity of stereotactic body radiotherapy and elective nodal radiotherapy. *Eur Urol*. 2019;76(6):732–9. <https://doi.org/10.1016/j.eururo.2019.07.009>.
- Jereczek-Fossa BA, Bortolato B, Gerardi MA, Dicuonzo S, Arienti VM, Berlinghieri S, Bracelli S, Buglione M, Caputo M, Catalano G, Cazzaniga LF, De Cicco L, Di Muzio N, Filippone FR, Fodor A, Franceschini D, Frata P, Gottardo S, Ivaldi GB, Laudati A, Magrini SM, Mantero E, Meaglia I, Morlino S, Palazzi M, Piccoli F, Romanelli P, Scorsetti M, Serafini F, Scandolaro L, Valdagni R, Orecchia R, Antognoni P, Lombardy Section of the Italian Society of Oncological Radiotherapy (Associazione Italiana di Radioterapia Oncologica-Lombardia, AIRO-L). Radiotherapy for oligometastatic cancer: a survey among radiation oncologists of Lombardy (AIRO-Lombardy), Italy. *Radiol Med*. 2019;124(4):315–22. <https://doi.org/10.1007/s11547-018-0972-6>.

10. Kobiela J, Spsychalski P, Marvaso G, Ciardo D, Dell'Acqua V, Kraja F, Błażyńska-Spsychalska A, Łachiński AJ, Surgo A, Glynne-Jones R, Jereczek-Fossa BA. Ablative stereotactic radiotherapy for oligometastatic colorectal cancer: systematic review. *Crit Rev Oncol Hematol*. 2018;129:91–101.
11. Kucharczyk MJ, So J, Gravis G, Sweeney C, Saad F, Niazi T. A combined biological and clinical rationale for evaluating metastasis directed therapy in the management of oligometastatic prostate cancer. *Radiother Oncol*. 2020;152:80–8.
12. Guckenberger M, Lievens Y, Bouma AB, Collette L, Dekker A, Nandita MD, Dingemans AMC, Fournier B, Hurkmans C, Lecouvet FE, Meattini I. 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(1):e18–28.
13. Palma DA, Bauman GS, Rodrigues GB. Beyond oligometastases. *Int J Radiat Oncol Biol Phys*. 2020;107(2):253–6.
14. Patel RR, Verma V, Barsoumian H, Ning MS, Chun SG, Tang C, Chang JY, Lee PP, Gandhi S, Balter P, Dunn JD, Chen D, Puebla-Osorio N, Cortez AM, Welsh JW. Use of multi-site radiation therapy as systemic therapy: a new treatment approach personalized by patient immune status. *Int J Radiat Oncol Biol Phys*. 2020;S0360–3016(20):34114–6.
15. D'Angelillo RM, Francolini G, Ingrosso G, Ravo V, Triggiani L, Magli A, Mazzeo E, Arcangeli S, Alongi F, Jereczek-Fossa BA, Pergolizzi S, Pappagallo GL, Magrini SM. Consensus statements on ablative radiotherapy for oligometastatic prostate cancer: a position paper of Italian Association of Radiotherapy and Clinical Oncology (AIRO). *Crit Rev Oncol Hematol*. 2019;138:24–8. <https://doi.org/10.1016/j.critrevonc.2019.03.014>.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Authors and Affiliations

Rosario Mazzola¹ · Barbara Alicja Jereczek-Fossa^{2,3} · Paolo Antognoni⁴ · Nadia Di Muzio^{5,6} · Luca Nicosia¹  · Andrea Lancia⁷ · Ivan Fazio⁸ · Silvia Chiesa⁹ · Mattia F. Osti¹⁰ · Stefano Pergolizzi¹¹ · Davide Franceschini¹² · Piercarlo Gentile¹³ · Luca Triggiani¹⁴ · Filippo Alongi^{1,15}

¹ Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, via Don Sempreboni 5, 37034 Negrar, Verona, Italy

² Department of Radiotherapy, IEO European Institute of Oncology IRCCS, Milan, Italy

³ Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy

⁴ Radiation Oncology Centre, Ospedale di Circolo e Fondazione Macchi, ASST Dei Sette Laghi, Varese, Italy

⁵ Department of Radiotherapy, IRCCS San Raffaele Scientific Institute, Milan, Italy

⁶ University Vita-Salute San Raffaele, Milan, Italy

⁷ Radiation Oncology Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

⁸ Radiation Therapy Unit, Casa di Cura Macchiarella, Palermo, Italy

⁹ UOC di Radioterapia Oncologica, Dipartimento Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia,

Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo A. Gemelli 1, 00168 Rome, Italy

¹⁰ Radiotherapy Oncology, Department of Medicine and Surgery and Translational Medicine, Sapienza University of Rome, S. Andrea Hospital, Rome, Italy

¹¹ Department of Radiation Oncology, University of Messina, Messina, Italy

¹² Department of Radiotherapy, Humanitas Clinical and Research Center—IRCCS, Via Manzoni 56, 20089 Rozzano, Milan, Italy

¹³ Radiation Oncology Unit, UPMC Hillman Cancer Center, San Pietro Hospital FBF, Rome, Italy

¹⁴ Department of Radiation Oncology, Brescia University, Piazza Spedali Civili, 1, 25100 Brescia, Italy

¹⁵ University of Brescia, Brescia, Italy