

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. Pancreatology 20 (2020) 1004-1005

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Letter to Editor

Keywords:

Pancreatic cancer

Carbon ion radiotherapy

Covid-19

Pancreatic cancer: Does a short course of carbon ion radiotherapy worth during COVID-19 outbreak?

> approach is now a challenge for oncologists for several reasons: (i) the increased susceptibility for SARS-CoV-2 infection in relation to the immunosuppressive action of CT; (ii) the need to minimize both the hospital accesses of patients and the exposure of hospital staff to fight viral spread. Under these circumstances, CIRT might be well considered for local control in patients with stable or partial response after systemic CT [8].

> Current practice include Stereotactic Body Radiation Therapy (SBRT) that provides cost-effective, with low acute toxicity rate and shows an improvement of 2-years-overall survival [9]. However SBRT is devoid of CIRT physical and radiobiological advantages. CIRT Japanese experience appears to be effective with results superior in long-terms outcomes compared to conventional RT or concomitant CT/RT and well tolerated with a lower rate of gastrointestinal toxicities requiring hospitalization [10]. In our Italian hadrontherapy facility the schedule of CIRT (4 days weekly for 3 weeks) halve the total accesses in the RT Department compared to conventional RT (5 days for week for 5–6 weeks), as it happens for modern hypofractionated schedules.

> We are aware that results from CIRT are still mono-institutional and there are no phase III trial showing unequivocally the advantages of ions versus photon RT. In addition, European facilities are few and only a very small number of patients might possibly be considered for CIRT. However, we felt useful to remind the oncological community about this option that meets the temporary needs and took the opportunity to revamp interest in this new technology that is short, effective and safe, at least not inferior to SBRT.

Funding

None.

Declaration of competing interest

None.

References

- [1] Data available in: https://www.esmo.org/guidelines/gastrointestinal-cancers/ gastrointestinal-cancers-pancreatic-cancer-in-the-covid-19-era
- Jereczek-Fossa BA, Palazzi MF, Soatti CP, Cazzaniga LF, Ivaldi GB, Pepa M et al on behalf of the CODRAL (Board of Directors of Radiation Oncology Departments in Lombardy) network, COVID-19 Outbreak and Cancer Radiotherapy Disruption in Lombardy, Northern Italy, Clinical Oncology DOI:https://doi. org/10.1016/j.clon.2020.04.007.
- [3] Bogani G, Raspagliesi F. Minimally invasive surgery at the time of Covid-19: the OR staff needs protection. | Minim Invasive Gynecol Epub ahead of print 2020. https://doi.org/10.1016/j.jmig.2020.04.010. pii: \$1553-4650(20)30185-0.
- Tchelebi LT, Haustermans K, Scorsetti M, Hosni A, Huguet F, Hawkins MA, et al. [4] Recommendations on the use of radiation therapy in managing patients with

Coronavirus disease 2019 (COVID-19) is a respiratory highly virulent disorder caused by SARS-COV-2 virus declared pandemic by WHO on March 11, 2020. Italy is one of the most involved Country and the outbreak changed dramatically medicine leading in a mandatory reorganization of health care facilities.

Systemic immunosuppression resulting from tumour and anticancer treatments makes oncological patients more vulnerable to infections, therefore, it's imperative to reduce time spent in hospitals and/or in public environment in order to minimize the epidemic impact.

Regarding pancreatic cancer (PC), the ESMO recommendations in the COVID-19 era [1] consider as "high priority to treat" newly diagnosed resectable PC and locally advanced PC (LAPC). Since, radiotherapy (RT) is an essential component of oncological curative therapy, in this era a shorter RT should be preferred to conventional schedule and, when possible, surgery delayed [2]. The surgical related length of hospitalization, the high risk of pulmonary and postoperative morbidity [3] are unfavourable circumstances to be weighted. As response to pandemic, in several hospitals, surgery has been suspended and possibly relocated to surgical COVID free hubs, impacting on maintaining appropriate waiting times. Therefore, for resectable and borderline PC a neoadjuvant short RT course may reduce the hospitalization period [4]. To overcome the intrinsic radioresistance of PCs, it is essential to safely reach the tumour target with high doses by avoiding surrounding high radiosensitive structures. Carbon ion radiotherapy (CIRT), compared to traditional photon-beam RT, has a peculiar physical selectivity in releasing the dose to the tumour with minimal damage in surrounding tissue [5], decreasing post-radiation morbidity. Further CIRT, compared to photons has a higher relative biological effectiveness. and revealed the ability to suppress metastatic cancer cells capability [6]. CIRT is also effective in eliminating retroperitoneal microinvasion, reducing tumour size, perivascular/lymphatic involvement and improving the resectability rate. Japanese [7] and Italian [6] neoadjuvant short course CIRT trials (8 fractions of CIRT and surgery after 4 weeks) showed no detrimental effect in delaying and safely performing surgery.

Patients with LAPC need to receive chemotherapy (CT) [4]; this





gastrointestinal malignancies in the era of COVID-19. Radiother Oncol Epub ahead of print 2020. https://doi.org/10.1016/j.radonc.2020.04.010.

- [5] Facoetti A, Barcellini A, Valvo F, Pullia M. The role of particle therapy in the risk of radio-induced second tumors: a review of the literature. Anticancer Res 2019;39(9):4613–7.
- [6] Vitolo V, Cobianchi L, Brugnatelli S, Barcellini A, Peloso A. Facoetti A Preoperative chemotherapy and carbon ions therapy for treatment of resectable and borderline resectable pancreatic adenocarcinoma: a prospective, phase II, multicentre, single-arm study. BMC Canc 2019;14(1):922. 19.
- [7] Ebner DK, Shinoto M, Kawashiro S, Isozaki Y, Kamada T, Yamada S. Phase 1/2 trial of preoperative short-course carbon-ion radiation therapy for patients with resectable pancreatic cancer. Int J Radiat Oncol Biol Phys 2017;99:S144.
- [8] Wu L, Zhou Y, Fan Y, Rao S, Ji Y, Sun J, et al. Consolidative chemoradiotherapy after induced chemotherapy is an optimal regimen for locally advanced pancreatic cancer. Front Oncol 2020;9:1543.
- [9] Tchelebi LT, Lehrer EJ, Trifiletti DM, Sharma NK, Gusani NJ, Crane CH, et al. Conventionally fractionated radiation therapy versus stereotactic body radiation therapy for locally advanced pancreatic cancer (CRiSP): an international systematic review and meta-analysis. Cancer 2020. https://doi.org/10.1002/ cncr.32756.
- [10] Kawashiro S, Yamada S, Okamoto M, Ohno T, Nakano T, Shinoto M, et al. Multi-institutional study of carbon-ion radiotherapy for locally advanced pancreatic cancer: Japan carbon-ion radiation oncology study group (J-CROS) study 1403 pancreas. Int J Radiat Oncol Biol Phys 2018;1(5): 1212–21. 101.

Amelia Barcellini, Viviana Vitolo^{*}

National Center of Oncological Hadrontherapy (Fondazione CNAO), Pavia, Italy Lorenzo Cobianchi General Surgery Department, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia, Italy

Francesca Valvo, Barbara Vischioni, Maria Bonora, Maria Rosaria Fiore, Alberto Iannalfi, Giulia Riva, Sara Ronchi, Elena Tornari, Ester Orlandi National Center of Oncological Hadrontherapy (Fondazione CNAO),

Pavia, Italy

* Corresponding author. National Center of Oncological Hadrontherapy (Fondazione CNAO), Strada Campeggi 53, Pavia, Italy. *E-mail address:* vitolo@cnao.it (V. Vitolo).

> 27 April 2020 Available online 12 May 2020