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Metronomic oral vinorelbine and lung cancer therapy during the COVID 19 pandemic: A single-center experience

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ABSTRACT

COVID 19 pandemic is a worldwide health emergency. Every single Hospital and Department was forced to radically modify clinical practice decreasing or stopping daily activities. Oncological patients had to carry on treatments in order to prevent disease progression and improve their quality of life. However, many health workers may be a potential source of infection if not tested with swabs but this diagnostic procedure was not suitable universally in Italy. Aiming to reduce hospitalization of our patients with advanced lung cancer, vinorelbine in its metronomic formulation is one of the best strategy. Here, we report the experience with oral vinorelbine in a few patients of our Oncology Department.

Coronavirus pandemic disease forced clinicians and health systems to radically change treatments of oncological patients, especially patients with advanced lung cancer without oncogene-drivers.

During Covid19 pandemic, oncologists worldwide must choose the best strategy for these “frail” patients in order to reduce side effects and maximize the outcomes.

ESMO-Guidelines during Covid19 era [1] shows HIGH PRIORITY for “1st-line treatment including chemotherapy, chemotherapy plus Immunotherapy, Immunotherapy alone or TKIs to improve prognosis, cancer-related symptoms and QoL”. In patients without oncogene-drivers (PDL-1 \geq 50 %, EGFR-mutations, B-RAF mutations, ALK and ROS-1 rearrangements), immunotherapy alone or TKIs are not suitable therapies and chemotherapy - alone or plus immunotherapy – is the treatment of choice.

Conventional chemotherapy with intravenous formulation may induce severe neutropenia causing fever and infectious episodes: pneumonitis can occur in up to 16 % of treated patents [2]. Moreover, it is well known that chemotherapy has immunosuppressive activity [3]. On the other hand, Immune check-point inhibitors are related with risk of interstitial pneumonitis that can occur in about 2% of cancer patients with higher incidence in lung cancer [4].

Therefore, it seems well known that the treatment of patients with not-oncogene addicted lung cancer is a real challenge during COVID-19 era. The choice of best therapy becomes harder in elderly and unfit patients. The first strategy for these patients is simply delaying treatment in order to overcome emergency period, hoping to reduce the impact of side effects. However, this option is not suitable for symptomatic patients that require an immediate treatment to improve

quality of life.

It's reasonable that these patients undergo systematic testing for SARS-CoV-2 at the beginning of treatment [5] but, nevertheless, serum testing is not available worldwide and swabs could not be performed universally in the absence of any symptoms at the moment. Moreover, classical chemotherapy needs to hospitalize patients, first to insert intravenous catheter and second to administer drugs, increasing the risk of COVID 19 infection with pulmonary complications (in Italy many health workers were infected and became contagious). In this scenario, an oral formulation may overcome the need to put a central line and to spend a lot of time in Hospital.

In 2019, a Meta-analysis of metronomic oral vinorelbine has been published [6]: 9 studies, in first and second line, was selected to be included. Results were as follows: median progression-free-survival 4,2 months, median overall survival 8,7 months, grade 3–4 toxicity 15.8 % (main toxicity: anaemia). The authors concluded that “metronomic oral vinorelbine is an active and well-tolerated single-drug chemotherapy regimen in metastatic NSCLC and is a manageable therapy in frail patients”. In 2017, we started to use this oral metronomic formulation with vinorelbine at the dose of 40 mg three times a week (Monday, Wednesday, Friday), continuously. Here, we report our experience in 10 out of 36 treated patients during COVID19 pandemic. Before Coronavirus emergency, our protocol required that patients perform blood test and hospital visit every 4 weeks; after March 8th 2020 (Prime Minister Decree-law, in Italy), we still had 10 patients in treatment with metronomic vinorelbine. So, we decided to avoid hospital visits to these patients following them by phone interviews according their needs. The patients performed blood tests at home by Oncological home-care

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institutions and the oncologist received laboratory reports by fax in order to confirm therapy without risk of haematological renal or liver toxicity. The drugs were delivered at home by volunteers or by patients' relatives. We did not record any grade 3 or 4 side effects in these 10 patients that carried on treatment regularly in this emergency period without need to postpone chemotherapy and avoiding frequent hospital visits. In conclusion, we think that this vinorelbine formulation may be a valuable option allowing to treat frail lung cancer patients during Covid19 era.

CRediT authorship contribution statement

David Rossi: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

None.

References

- [1] ESMO Management and Treatment Adapted Recommendations in the COVID-19 Era: Lung Cancer. *Esmo Open*, (2020) April <https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/lung-cancer-in-the-covid-19-era>.
- [2] D.E. Magee, A.E. Hird, Z. Klassen, et al., Adverse event profile for immunotherapy agents compared with chemotherapy in solid organ tumors: a systematic review and meta-analysis of randomized clinical trials, *Ann. Oncol.* 31 (2020) 50–60.
- [3] G. Lehne, K. Lote, Pulmonary toxicity of cytotoxic and immunosuppressive agents. A review, *Acta Oncol.* 29 (1990) 113–124.
- [4] M. Nishino, N.H. Ramaiya, M.M. Awad, et al., PD-1 inhibitor-related pneumonitis in advanced cancer patients: radiographic patterns and clinical course, *Clin. Cancer Res.* (2016) 6051–6060.
- [5] L. Calabro', Solange Peters, J.C. Soria, et al., Challenges in lung cancer therapy during the Covid-19 pandemic, *Lancet Respir. Med.* (2020), [https://doi.org/10.1016/S2213-2600\(20\)30170-3](https://doi.org/10.1016/S2213-2600(20)30170-3) April 9.
- [6] J.L. Pujol, A. Coffy, A. Camerini, et al., An individual patient-data metaanalysis of metronomic oral vinorelbine in metastatic non-small cell lung cancer, *PLoS One* 14 (8) (2019) e0220988, <https://doi.org/10.1371/journal.pone.0220988> eCollection 2019.