Letter to the editor

Toxicity of oxaliplatin rechallenge in metastatic colorectal cancer

G. Mauri[1,2], K. Bencardino[2], A. Sartore-Bianchi[1,2] and S. Siena[1,2]

[1]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan, Italy;

[2]Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milan, Italy.

Corresponding Author:

Prof. Salvatore Siena

(*E-mail: salvatore.siena@ospedaleniguarda.it)

© The Author(s) 2018. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com.

Downloaded from https://academic.oup.com/annonc/advance-article-abstract/doi/10.1093/annonc/mdy306/5061139
by University of Western Sydney user
on 31 July 2018

We have read with great interest the article published by Arnold et al. [1] in which the Authors systematically reviewed the options of treatment in patients with metastatic colorectal cancer (mCRC) beyond second line of therapy. Reviewed data supported the use of approved agents such as regorafenib or trifluridine/tipiracil rather than any chemotherapy rechallenge based on evidences of efficacy and safety derived from clinical trials [1].

In their study, according to the criteria of systematic review of the paper, Authors mentioned rechallenge with oxaliplatin by reporting survival data and ≥G3 toxicities from available phase II/III clinical trials but they have omitted to consider the occurrence of oxaliplatin immune-induced syndrome (OIIS).

As described by our group and others, OIIS is a rare but potentially life-threatening side effect characterized by acute onset of thrombocytopenia, fever, renal failure, hemolytic anemia, chills, back pain, and bleeding arising within 24 hours from oxaliplatin administration [2–4]. In 4 cases described in the literature, OIIS was lethal [2]. OIIS has been associated with long term administration of oxaliplatin, occurring most frequently after an average of 16^{th} cycles of oxaliplatin-based regimens [2]. Interestingly, OIIS has been demonstrated to occur earlier if discontinuation and subsequent reintroduction of oxaliplatin takes place. OIIS occurs indeed after average 4 cycles of rechallenge with oxaliplatin, therefore earlier than with continuous administration within the same therapeutic line [2].

The mechanisms underlying OIIS have not been clarified yet, but drug specific antibody production is currently under investigation as the most plausible. Recently, OIIS has been associated with multiple drug-dependent antibodies sensitizing to several compounds and thus potentially jeopardizing continuation of other oncological treatments beyond oxaliplatin [5]. All in all, these evidences the need to consider the risk of OIIS, rare and therefore insidious side effect that may complicate treatment of patients with mCRC beyond second line.

Downloaded from https://academic.oup.com/annonc/advance-article-abstract/doi/10.1093/annonc/mdy306/5061139
by University of Western Sydney user
on 31 July 2018

Funding

Authors are supported by grants from Associazione Italiana Ricerca Cancro grant AIRC 5 x mille [Project ID 51000] Special Program Molecular Clinical Oncology, AIRC Investigator Grant [Project ID 20685], and AIRC 5 x mille [Project ID 21091] Special Program Metastases; CORDIS Community Research and Development Information Service, Horizon 2020 [Project ID 635342] grant Molecularly Guided Trials with Specific Treatment Strategies in Patients with Advanced Newly Molecular Defined Subtypes of Colorectal Cancer (MoTriColor); Fondazione Oncologia Niguarda Onlus, grant Terapia Molecolare dei Tumori and grant Studies to Develop Therapies Against Colorectal Cancer in Young Adults.

Disclosures

SS has acted in a consulting or advisory role to Amgen, Bayer, BMS, Daiichi-Sankyo, Ignyta, Lilly, Merck, Merus, Novartis, Roche, and Sanofi. AS-B has acted in a consulting or advisory role to Amgen, Bayer, Lilly, and Sanofi.

References

1. Arnold D, Prager GW, Quintela A et al. Beyond second-line therapy in patients with metastatic colorectal cancer: a systematic review. Ann. Oncol. Off. J. Eur. Soc. Med. Oncol. 2018; 29(4):835–856.

2. Bencardino K, Mauri G, Amatu A et al. Oxaliplatin Immune-Induced Syndrome Occurs With Cumulative Administration and Rechallenge: Single Institution Series and Systematic Review Study. Clin. Colorectal Cancer 2016; 15(3):213–221.

3. Cobo F, De Celis G, Pereira A et al. Oxaliplatin-induced immune hemolytic anemia: a case report and review of the literature. Anticancer. Drugs 2007; 18(8):973–976.

4. Phull P, Quillen K, Hartshorn KL. Acute Oxaliplatin-induced Hemolytic Anemia, Thrombocytopenia, and Renal Failure: Case Report and a Literature Review. Clin. Colorectal Cancer 2016. doi:10.1016/j.clcc.2016.11.005.

5. Curtis BR, Hsu Y-MS, Podoltsev N et al. Patients treated with oxaliplatin are at risk for thrombocytopenia caused by multiple drug-dependent antibodies. Blood 2018; 131(13):1486–1489.

Downloaded from https://academic.oup.com/annonc/advance-article-abstract/doi/10.1093/annonc/mdy306/5061139
by University of Western Sydney user
on 31 July 2018