STUDENTS' CORNER
LETTER TO THE EDITOR

Arfolitixorin: An unmet need in the management of metastatic colorectal cancer

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Madam, Arfolitixorin [6R]-5,10-methylenetetrahydrofolate (6R-MTHF) is a folate-based contemporary prodrug that FDA has approved for Phase III study.[1] It is a refined form of folate, which boosts cytotoxic 5-fluorouracil (5-FU) competence, thereby enhancing tumour mortality in carcinoma cells. This drug is currently used in patients who underwent therapeutic regimens with advanced colorectal cancer (CRC) as reported by Isofol Medical AB.[2]

Conventional treatment for advanced colorectal cancer relies on cytotoxic drugs initially, but drug resistance poses challenges. Chemotherapy, has systemic toxicity and lacks tumour specificity, driving the exploration of targetted therapies like monoclonal antibodies and immunotherapeutic approaches (ACT, vaccines, cytokines) to address limitations and enhance outcomes, thus this is where Arfolitixorin emerge as a potential treatment option.[3] Unlike traditional folate-based prodrugs like leucovorin and levoleucovorin, Arfolitixorin doesn't need multi-step metabolic activation, making it highly beneficial for advanced colorectal cancer patients. A genomic analysis at Östra Hospital in Gothenburg found that ~75% of metastatic colorectal cancer patients lack the potential to effectively metabolize folate-based drugs, rendering them ineffective, but Arfolitixorin provides a new ray of hope for these patients.[2]

In a developing country like Pakistan, the prevalence of colorectal cancer is 5.6%.[4] Moreover, advanced mCRC with liver and lung involvement has a five-year survival of only 10-15%. Thus most patients with mCRC are treated with 5-FU. Following therapy, they become susceptible to the side-effects including anaemia, diarrhoea, bruising, bleeding, and mucositis etc. To counter such effects folinic acid is co-administered. Despite this regimen, the conversion of folinic acid to MTHF is inefficient, leading to suboptimal levels of MTHF. In such cases, a drug such as Arfolitixorin can be beneficial as it does not require conversion leading to a concurrent rise in MTHF levels in tumour cells thus causing efficient regression of tumour cells. Some potential adverse effects of Arfolitixorin include diarrhoea, nausea, vomiting, stomatitis, leucopenia, neutropenia, thrombocytopenia, ocular toxicity, paresthesia, fatigue, and neuropathy, which seemed to be the equivalent of conventional folate based prodrugs and not more pronounced, eliciting it as a better treatment candidate due to its effectiveness.[5] Arfolitixorin can be considered a broad-spectrum medication for the standard-care treatment for metastasized & non-metastasized CRC as well as other cancers including breast cancer, pancreatic cancer, head and neck cancers, and stomach cancers because in such cancers conventional folate-based drugs are also administered. Further clinical trials must be conducted to predict the safety and efficiency of Arfolitixorin.

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