Circannual variation of efficacy outcomes in patients with newly diagnosed metastatic colorectal cancer and treated with first-line chemotherapy


1 AOU San Luigi Gonzaga, Orbassano
2 Ospedale San Luigi Gonzaga, Orbassano
3 IRCCS, Candiolo
4 Università del Piemonte Orientale, Novara
5 AOU Città della Salute, Torino
6 Università di Brescia, AO Spedali Civili, Brescia

Seasonal variation of initial diagnosis of localized colorectal cancer (stage I-III) has been reported in literature as an independent variable that influences overall survival. On the contrary, no data about such a rhythm in advanced stage patients are actually available. In this study we collected data about 1610 newly diagnosed advanced colorectal cancer patients treated at four independent centers; responses to first line chemotherapy were available for 1495 patients. A strong circadian rhythm in response rate was evident (MESOR 37.7%, double amplitude 11.1%, acrophase in January; p < 0.001). At the time of data cutoff, 1322 patients progressed, with a median progression free survival of 11 months. A circannual rhythmicity of the proportion of patients progressing at 6 months was demonstrated, with MESOR 79%, double amplitude 5.2%, and acrophase in February (p < 0.001). Survival rate at one year showed a synchronized rhythm with MESOR 80.0%, a double amplitude of 4.2% and acrophase in January (p = 0.05). Several interpretation about the genesis of this cyclic variation could be claimed: the rhythm in sunlight exposure and consequently of vitamin D serum levels and folate degradation, the variability in toxic effect intensity of chemotherapy, and the rhythm in the biological behavior of tumor cells. Further investigation on our observation both in preclinical and clinical settings are needed, in order to better clarify the underlying mechanisms.