Liver toxicity in colorectal cancer patients treated with first line FOLFIRI-containing regimen: a single institution experience

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Background

Hepatotoxicity represent a relevant issue regarding clinical management of metastatic colorectal cancer patients. This retrospective study evaluated patterns of liver toxicity in patients treated with FOLFIRI-based regimens, and the possible protective effect of S-Adenosylmethionine supplementation.

Patients and methods

156 mCRC patients receiving a FOLFIRI backbone-based regimen were included in this analysis. Liver enzymes levels (AST, ALT, total bilirubin, gamma-glutamyltransferase, alkaline phosphatise) were assessed before starting the treatment (basal value) and then before every therapy course. R ratio and the AST/ALT ratio was calculated in patients developing liver toxicity. 46 out of 156 patients received an oral supplementation of SAMe (400 mg twice a day).

Results

AST, ALT and alkaline phosphatase (AP) showed a significant modification after the beginning of first line treatment. Specifically, both AST level (123.87 vs 41.05U/l; P <0.001), ALT level (94.48 vs 39.80 U/l; P=0.004) and AP (289.0 vs 172.44 U/l; P=0.02) were found to be significantly increased during the first three months of treatment. In the entire CRC population the calculated R ratio was 3.96 (3.25-4.51). In all the three regimens the calculated R ratio was between 2 and 5 (FOLFIRI=4.10; BEVA-FOLFIRI=3.76; CETUXIMAB-FOLFIRI=4.35), without any statistical differences between regimens, supporting a mixed pattern of hepatic injury. Globally, 25 (16.02%) patients out of 156 needed course delays and 12 (7.69%) patients received a dose reduction, and only three patients (1.92%) stopped the first line therapy due to liver toxicity. In details, Grade 3-4 hypertransaminasemia, was less frequently observed in the small group of patients treated with SAMe (2.17% vs 16.37%; P=0.029). In addition, patients treated with SAMe supplementation required in a lower number chemotherapy course delays (4.35% vs 20.90%, P=0.020).

	FOLFIRI-based without SAMe (110 pts)	FOLFIRI-based with SAMe (46 pts)	P value
Courses delays	23 (20.90%)	2 (4.35%)	0.020
Dose reduction	10 (9.09%)	2 (4.35%)	0.494
Chemotherapy discontinuation	2 (18.18%)	1 (2.17%)	0.623
Hypertransaminase (G3-4)	18 (16.37%)	1 (2.17%)	0.029
Hyperbilirubinemia (G3-4)	9 (8.18%)	3 (6.52%)	0.898

	FOLFIRI	BEVA-FOLFIRI	CETUXIMAB-FOLFIRI
Median R Ratio (95% CI)	4.10 (3.65-5.31)	3.76 (2.99-4.78)	4.35 (3.42-5.34)
Median AST/ALT Ratio (95% CI)	0.89 (0.71-1.08)	1.12 (0.74-1.39)	0.88 (0.69-1.27)

Global median R Ratio: 3.96 (3.25-4.51)
Global median AST/ALT Ratio: 0.95 (0.8-1.26)

Conclusions

For the first time in literature, patterns of FOLFIRI-based chemotherapy-induced liver injury have been indirectly defined upon the evaluation of the R-Ratio. SAMe supplementation prevented hepatotoxicity in a specific group of mCRC patients treated with FOLFIRI-containing regimens reducing Grade 3-4 hypertransaminasemia and treatment delays.

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