Clinical impact of Neutropenia and Febrile Neutropenia in metastatic colorectal cancer patients treated with FOLFOXIRI/bevacizumab: pooled analysis of TRIBE and TRIBE2 studies

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A. Sbrana, D. Rossini, S. Lonardi, D. Santini, G. Tomasello, C. Antoniotti, R. Moretto, F. Marmorino, E. Cortesi, M. Ronzoni, S. Noventa, G. Peverelli, C. Carlomagno, T.P. Latiano, S. Cordio, E. Fea, F. Paolieri, C. Cremolini, A. Falcone, A. Antonuzzo on behalf of the GONO (Gruppo Oncologico del Nord Ovest) investigators

INTRODUCTION

FOLFOXIRI/bevacizumab (bev) is a valid option as first-line therapy for unresectable metastatic colorectal cancer (mCRC), as reported in TRIBE and TRIBE-2 trials [1,2].

TRIBE trial^[1] was a phase-III, randomized clinical trial that randomized patients (pts) to receive either FOLFIRI plus bev or FOLFOXIRI plus bev as a first line of treatment for mCRC.

TRIBE-2 trial^[2] was a phase-III trial in which previously untreated pts with unresectable mCRC were randomized to FOLFOX/bev followed by FOLFIRI/bev after disease progression (PD) (arm A) or FOLFOXIRI/bev followed by the reintroduction of the same regimen after PD (arm B).

Neutropenia (N) and febrile neutropenia (FN) are possible side effects of FOLFOXIRI/bev, but their clinical impact is often debated. Here we aim at thoroughly describing N and FN associated with FOLFOXIRI/bev in order to estimate their clinical relevance.

METHODS

Safety data of 1,175 patients enrolled in the TRIBE and TRIBE2 studies were reviewed.

The incidence and severity of N and FN, and the use of G-CSF in the triplet/bev and in the doublets/bev arms were compared using the Chi-square or the Fisher exact test as appropriate.

Characteristics	% patients
Sex (M / F)	42 / 58
Median Age (range)	61 (29 – 75)
ECOG PS (0 /1-2)	88 / 12
Synchronous Metastases (Y / N)	85 / 15
Prior Adjuvant CT (Y / N)	7 / 93
Primary Tumor Site (right / left / rectum / NA)	35 / 43/ 20 / 2
Liver Only (1 / >1)	26 / 74
Resected Primary (Y / N)	58 / 42

RESULTS

Characteristics	Overall Population N=1175	FOLFOXIRI + Bevacizumab N = 586	FOLFOX/FOLFIRI + Bevacizumab N = 589	p
Prophylactic G-CSF	34	29 (4.9%)	5 (0.8%)	-
Neutropenia ≥ G3	394	276 (49.9%)	118 (20.2%)	< 0.001
Febrile Neutropenia	66	41 (7.4%)	25 (4.3%)	0.041
MASCC Score <21 (Single episodes)	78	13/48 (27.1%)	4/30 (13.3%)	0.17
G-CSF Use (Single cycles)	1069/ 9908	799/4804 (16.6%)	270/5104 (5.3%)	< 0.001

CONCLUSIONS

FOLFOXIRI plus bev was associated with a higher risk of N and FN than doublets + bevacizumab. However, the risk of FN was lower than 10%, thus not requiring a systematic use of primary G-CSF prophylaxis.

The majority of FN episodes was associated with a good MASCC score, thus having a limited clinical impact.

The vast majority of FN episodes occurred in the first two months of treatment, suggesting a closer monitoring of this adverse event during the first courses of therapy.

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References

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