Regorafenib for metastatic colorectal cancer in community setting: A multicentre retrospective analysis in Hong Kong

Lam KO[1], Lee KC[2], Lee VHF[1], Sze HCK[1], Chiu JWY[3], Leung Roland[3], Yau T[3]

[1] Department of Clinical Oncology, LKS Faculty of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong
[2] Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital, Hong Kong
[3] Department of Medicine, LKS Faculty of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Background

The efficacy of regorafenib in refractory metastatic colorectal cancer has been demonstrated in two international phase III randomized controlled trials, the CORRECT and the CONCUR study, but the data in community setting is scarce. To evaluate the use of regorafenib in community setting, we perform a multicenter retrospective analysis in Hong Kong

Method

Patients were eligible for treatment with regorafenib if they have failed all available systemic agents including fluoropyrimidine, oxaliplatin, irinotecan, bevacizumab, and cetuximab or panitumumab if RAS wild-type tumor. Individual patient data was retrieved from the Department of Clinical Oncology and the Department of Medicine, Queen Mary Hospital and the Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital, Hong Kong. Beside demographic, efficacy and toxicity data, pattern of prescription and treatment suspension were collected.

Results

From July 2013 to January 2015, 28 patients were treated with regorafenib for metastatic colorectal cancer in a non-clinical trial setting. The median age of patients was 62 (Range 45-77) and most of them had good performance status (ECOG 0-1: 89.3%). Majority of patients presented with synchronous metastasis (64.3%) and had metastases involving multiple organs at the time of regorafenib treatment (92.9%). Sixty-four percent of tumors was RAS wild-type. Patients have received a median of three prior lines of treatment and the median time interval from date of first line therapy to the start of regorafenib was 24.3 months.

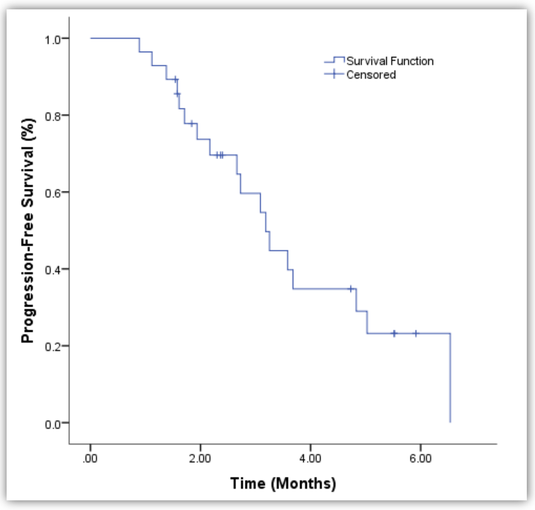
Fifteen patients were started at 160mg daily and 9 of them required further dose reduction or suspension during subsequent cycles. Irrespective of the starting dose, 77% of additional dose reduction occurred at the first and second cycles. The main reason for dose reduction or treatment suspension was due to hand-foot syndrome followed by deranged liver function. For those who started at lower dose or required dose reduction during treatment, 14 of 22 patients were able to re-escalate the dose.

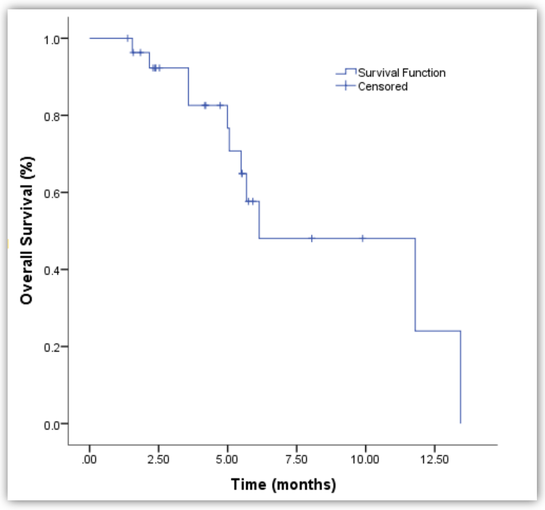
Adverse events of any grade occurred in all patients. There was one case of grade 4 anaemia due to per rectal bleeding but no treatment related death was observed. The commonest grade 3 non-haematolgic adverse event were hand-foot syndrome (25%), elevated AST (14.3%)/ ALT (10.7%), elevated bilirubin (3.6%), hypoalbuminaemia (3.6%), fatigue (3.6%), diarrhea (3.6%) and bleeding (3.6%). The most common grade 3 haematologic adverse events were anaemia (7.1%) and thrombocytopenia (3.6%).

After a median follow-up time of 4.9 months: 18 of the 28 patients have progressed and the median progression-free survival was 3.2 months (95% CI 2.5-3.9 months) while 11 of the 28 patients have died and the median survival was 6.1 months (95% CI: 1.4-10.9 months). Treatment response was uncommon and only 1 patient achieved a partial response. Nine of nineteen patients were able to receive further systemic treatment after stopping regorafenib.

Table 1. Pattern of Regorafenib dose modification

Initial dose	
160mg	53.6 %
Further dose reduction	
No	53.6%
Once	25.0%
Twice	21.4%
Timing of dose reduction	
1st cycle	23.1%
2nd cycle	53.8%
Later	23.1%
Reasons of dose reduction	
Hand-Foot Syndrome	69.2%
Deranged liver function	23.1%
Others	7.7
Dose re-escalataion	
No	36.4
Once	50.0
Twice	13.6





Conclusions

The efficacy and toxicity profile of regorafenib in the community setting were comparable to those reported in phase III clinical trials. Dose reduction and treatment interruption was common but dose re-escalation is feasible.

Reference: 1. Grothey A, et al. Lancet 2013; 2. Li J, et al. Lancet Oncol 2015.

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