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Original Research Article

Real-world utilization and acceptance of biosimilar bevacizumab in metastatic colorectal cancer in India

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ABSTRACT

Background: To describe the patient characteristics and usage pattern of biosimilar bevacizumab for the treatment of metastatic colorectal cancer (mCRC) in India.
Methods: This real-world, retrospective analysis included adult patients receiving biosimilar bevacizumab between April 2021 and March 2022.
Results: A total of 1125 patients with mCRC who received biosimilar bevacizumab-based chemotherapy were included. The mean age at diagnosis was 57.8 years. Majority of the patients were males (71%) and belonged to the age groups of 41-76 years. The primary tumor site was right colon (52.6%) followed by left colon (29.2%) and rectum (17.3%), and tumor grade was reported as high in most (88.7%) of the patients. Majority of the patients received biosimilar bevacizumab-based chemotherapy as first-line therapy (61.3%), followed by second-line (31.9%) and third-line therapy (6.8%). In combination with biosimilar bevacizumab, FOLFOX (folinic acid, 5-fluorouracil, and oxaliplatin) was the most commonly administered chemotherapy regimen (42.9%), followed by CAPOX (capecitabine and oxaliplatin, 26.5%) and FOLFIRI (folinic acid, 5-fluorouracil, and irinotecan, 22.8%).
Conclusions: Biosimilar bevacizumab-based chemotherapy is being widely used in real-world clinical setting in India for the management of patients with mCRC.

Keywords: Bevacizumab, Biosimilar, Metastatic, Colorectal, Cancer

INTRODUCTION

Colorectal cancer (CRC) is the fourth most common cancer in the world. Nearly 1.1 million new cases and 550,000 deaths were reported globally in 2018. CRC accounts for 5.8% of all tumor-related mortality, and it is the fifth most common cause of cancer death.[1] An increased incidence is correlated with advancing age and the median age at diagnosis is approximately 70 years.[2] If diagnosed at an early stage, colorectal cancer is associated with a good prognosis.[3] However, 20-25% of patients present with metastases, and approximately half of the patients with CRC eventually develop metastatic disease.[3,4] Unfortunately, the prognosis is poor for patients presenting with mCRC, and the current five-year survival rate in US is ~13.5%.[3] Also, metastatic disease accounts for the high mortality rates associated with CRC.[3]

The management of mCRC has evolved significantly in the past twenty years, and survival rates have improved during this time. Indeed, the median overall survival (OS) of patients with mCRC in clinical trials is now approximately 30 months, double that of two decades ago.[5] Although several factors have contributed to improved clinical outcomes, a key development has been the introduction of novel biologic therapies targeting either epidermal growth factor signalling or angiogenesis.[6]

Bevacizumab, a monoclonal antibody directed against vascular endothelial growth factor (VEGF), is among these therapies. By inhibiting the action of VEGF, bevacizumab is thought to cause regression of existing tumor vasculature and prevent the development of new blood vessels, thereby inhibiting tumor growth.[7] Bevacizumab is approved by the US Food and Drug Administration (FDA), European Medicine Agency (EMA) and Drugs Controller General of India (DCGI) for the treatment of an array of tumors, including mCRC, Non-Squamous Non-Small-Cell Lung Cancer (NSCLC), metastatic renal cell carcinoma (mRCC), glioblastoma, cervical cancer, and recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.[7, 8]

Bevacizumab is produced through recombinant biotechnology from a Chinese hamster ovary cell line and has a molecular weight of ~149 kD. Intas Pharmaceuticals Limited, India, has developed biosimilar bevacizumab (BEVATAS), which was approved by DCGI on 23rd June 2016. The current study was conducted to evaluate the real-world usage pattern of biosimilar bevacizumab for the treatment of mCRC.

METHODS

Study design

This retrospective analysis involved mCRC patients who received biosimilar bevacizumab based-chemotherapy in India. The data was collected between April 2021 and March 2022 at various centers across India. All treatment decisions were at the investigator's discretion, including individual dose, duration of therapy, and method and frequency of clinical assessments, in accordance with local labelling information and standard clinical practice.

The current study collected data on patient characteristics and treatment utilization patterns. The data collected included age, sex, disease characteristics including tumor site and grade, medical history as well as details of the treatment.

Sample size and statistical analysis

In this real-world study, the patients' data was collected retrospectively without any predetermined sample size. The study did not test any hypothesis and only the observations from patient's records were analyzed. Demographic and baseline characteristics were summarized using descriptive statistics. Categorical variables were summarized with frequency and percentage. Continuous variables were summarized with count, mean, standard deviation, etc. Graphical presentation of data was done using bar chart as appropriate. Statistical analyses were performed using Microsoft excel (Microsoft Corp., USA).

Ethics statement

The study protocol approved by the ACEAS independent ethics committee, Ahmedabad, India. This study was performed in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) guideline and the ethical principles of the Declaration of Helsinki. Since this study involved data retrieval from patient records only, an informed consent of patients was not obtained.

RESULTS

A total of 1125 patients with mCRC and who received biosimilar bevacizumab-based chemotherapy were eligible and included in the analysis. The demographic characteristics of the patients are presented in Table 1. The mean age at diagnosis was 57.8 years, the majority of patients were males (71%) and belonged to the age groups of 41-76 years (90.9%). The most common comorbidities reported were hypertension (49%, 550 patients) and diabetes (42%, 468 patients). The primary tumor site was right colon (52.6%) followed by left colon (29.2%) and rectum (17.3%), and the tumor grade was reported as high in most (88.7%) of the patients.

Table 1: Baseline demographics (N=1125).

Parameters	
Age at diagnosis (years), mean±SD	57.8±10.9
Range	18-100
Age group (years), n (%)	
18-28	21 (1.9)
29-40	56 (5)
41-52	230 (20.4)
53-64	481 (42.8)
65-76	312 (27.7)
77-88	23 (2)
89-100	2 (0.2)
Gender, n (%)	
Men	799 (71)
Women	326 (29)
Body weight, kg, mean±SD	61.6±11.0
Primary tumor site, n (%)	
Left colon	328 (29.2)
Right colon	592 (52.6)
Rectum	195 (17.3)
Not available	10 (0.9)
Grade of tumor at diagnosis, n (%)	
High	998 (88.7)
Low	127 (11.3)

Drug utilization characteristics

Majority of the patients received biosimilar bevacizumab-based chemotherapy as first-line therapy (61.3%), followed by second-line (31.9%) and third-line therapy (6.8%). In combination with biosimilar bevacizumab, FOLFOX (folinic acid, 5-fluorouracil, and oxaliplatin)

was the most commonly administered chemotherapy regimen (42.9%), followed by CAPOX (capecitabine and oxaliplatin, 26.5%) and FOLFIRI (folinic acid, 5-fluorouracil, and irinotecan, 22.8%). The mean number of cycles of bevacizumab administered was 8.

Table 2: Drug utilization characteristics, (N=1125).

Parameters	n (%)
Current line of therapy	
First-line	690 (61.3)
Second-line	359 (31.9)
Third-line	76 (6.8)
Chemotherapy regimen	
FOLFOX	483 (42.9)
FOLFIRI	257 (22.8)
FOLFOXIRI	44 (3.9)
CAPOX	298 (26.5)
Others	43 (3.8)

DISCUSSION

This retrospective study reports a preliminary assessment of the real-world usage patterns of BEVATAS, a biosimilar bevacizumab, for the management of mCRC in Indian oncology setting. The patient characteristics in our study were generally consistent with those of the Indian mCRC patients reported in earlier studies. The average age of CRC in literature is 63 years, similar to that reported in our study (~58 years). CRC is a disease of the elderly, and our study reported that most of the patients belonged to age between 41-76 years. Our study reported a male preponderance. The annual incidence rates for colon cancer are 4.4 (males) and 3.9 (females) per 100,000 people in India.[9,10]

Bevacizumab has been an important biologic agent as the standard of care in the management of several cancers including CRC since its first approval in 2004.[11] Bevacizumab has reported improved outcomes in mCRC as both first- and second-line therapies in combination with chemotherapy in several clinical studies.[12-14] In our study, biosimilar bevacizumab based chemotherapy was used as first-line therapy (61%) or second-line (32%) therapy in majority of the patients.

Bevacizumab has been used in combination with several chemotherapy regimens in the treatment of mCRC. In our study, biosimilar bevacizumab was commonly administered with FOLFOX (folinic acid, 5-fluorouracil, and oxaliplatin; 42.9%), CAPOX (capecitabine and oxaliplatin, 26.5%) and FOLFIRI (folinic acid, 5-fluorouracil, and irinotecan, 22.8%) regimens. Studies have reported an improved disease outcomes with addition of bevacizumab to oxaliplatin-based first-line chemotherapy in patients with mCRC.[15] The addition of bevacizumab to FOLFOX regimen resulted in significantly improved disease outcomes in terms of response rates, progression free survival (PFS) and overall survival (OS) in the randomized phase III Eastern co-operative oncology group study E3200.[14] CCOG-0902 trial has described efficacy and safety of bevacizumab plus CAPOX regimen as first-line therapy in patients with mCRC.[16] FOLFIRI-bevacizumab regimen has been widely used as first-line treatment of mCRC. In a pooled analysis of 29 published trials Petrelli et al concluded that FOLFIRI-bevacizumab improved the disease outcomes as first-line chemotherapy in mCRC patients.[17]

The cost of cancer treatment is a guiding factor for high healthcare expenditures.[18] The oncology treatment cost is estimated to increase In India, with the advent of new and expensive treatment modalities.[19] In such a scenario, the availability of lower cost biosimilar agents will markedly reduce the financial toxicity of cancer treatment.[20] Further, biosimilar use should be encouraged via educating the oncologists on the efficacy and safety, and implementation of government policies in order to comprehend the fiscal advantages.[21,22] Economical alternatives to bevacizumab, biosimilar versions, have entered the Indian market, with several biosimilars of bevacizumab available currently. Despite having the advantage of substantial savings in treatment cost globally, physicians are sceptical in adopting a biosimilar product in view of the scarcity of the utilization data in the extrapolated indications.[23] This retrospective study was conducted to generate data on the utilization patterns of Intas' biosimilar bevacizumab, BEVATAS, in Indian patients with mCRC, and provides valuable insights on its usage in this vital indication.

The current study findings should be interpreted cautiously in view of study limitations in terms of missing data, and potential inconsistency arising from data entry at multiple sites. Overall, the study aimed to evaluate the initial real-world usage patterns of biosimilar bevacizumab in the treatment of mCRC in India. This analysis was not focused to determine the clinical efficacy and safety of biosimilar bevacizumab, and further research is needed to emphasize on these parameters.

CONCLUSIONS

This retrospective, observational study reports the real-world usage of biosimilar bevacizumab, BEVATAS, in Indian patients with mCRC. This study highlights the utilization pattern of Intas' biosimilar bevacizumab. There is a need for additional data with longer follow-up periods to explore clinical outcomes and cost–effectiveness in various patient populations who may be prescribed biosimilars of bevacizumab.

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Conflict of interest: Dr. Deepak Bunger, Dr. Lav Patel, and Mr. Shreekant Sharma are employees of Intas Pharmaceuticals Limited, Ahmedabad, Gujarat, India
Ethical approval: The study was approved by the ACEAS Independent Ethics Committee, Ahmedabad, India

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