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Documents

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Chemotherapy, bevacizumab, and cetuximab in metastatic colorectal cancer.

Dialog eLinks

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Accession number & update

2009072510 20090226.

Source

New England Journal of Medicine, {New–Engl–J–Med}, 5 February 2009, vol. 360, no. 6, p. 563–572, 26 refs, CODEN: NEJMA, eISSN: 1533–4406, ISSN: 0028–4793. Publisher: Massachussetts Medical Society, 860 Winter Street, Waltham, MA 02451–1413, USA.

Author(s)

Tol–Jolien, Koopman–Miriam, Cats–Annemieke, Rodenburg–Cees–J, Creemers–Geert–J–M, Schrama–Jolanda–G, Erdkamp–Frans–L–G, Vos–Allert– H, Van–Groeningen–Cees–J, Sinnige–Harm–A–M, Richel–Dirk–J, Voest– Emile–E, Dijkstra–Jeroen–R, Vink–Börger–Marianne–E, Antonini–Ninja–F, Mol–Linda, Van–Krieken–Johan–H–J–M, Dalesio–Otilia, Punt–Cornelis–J–A.

Author affiliation

Dr. C. J. A. Punt: Department of Medical Oncology, Radboud University Nijmegen Medical Center, P.O. Box 9101, 6500 HB Nijmegen, Netherlands. Email: c.punt@onco.umcn.nl.

Abstract

background Fluoropyrimidine–based chemotherapy plus the anti–vascular endothelial growth factor (VEGF) antibody **bevacizumab** is standard first–line treatment for metastatic colorectal cancer. We studied the effect of adding the anti–epidermal growth factor receptor (EGFR) antibody cetuximab to a combination of capecitabine, oxaliplatin, and **bevacizumab** for metastatic colorectal cancer. methods We randomly assigned 755 patients with previously untreated metastatic colorectal cancer to capecitabine, oxaliplatin, and **bevacizumab** (CB regimen, 378 patients) or the same regimen plus weekly cetuximab (CBC regimen, 377 patients). The primary end point was progression–free survival. The mutation status of the KRAS gene was evaluated as a predictor of outcome. results The median progression–free survival was 10.7 months in the CB group and 9.4 in the CBC group (P=0.01). **Quality–**of–life scores were lower in the CBC group. The overall survival and response rates did not differ significantly in the two groups. Treated patients in the CBC group had more grade 3 or 4 adverse events, which were attributed to cetuximab–related adverse cutaneous effects. Patients treated with cetuximab who had tumors bearing a mutated KRAS gene had significantly decreased progression–free survival as compared with cetuximab–treated patients with wild–type–KRAS tumors or patients with mutated–KRAS tumors in the CB group. conclusions The addition of cetuximab to capecitabine, oxaliplatin, and **bevacizumab** resulted in significantly shorter progression–free survival and inferior quality of life. Mutation status of the KRAS gene was a predictor of outcome in the cetuximab group. (ClinicalTrials.gov number, NCT00208546.) Clinical Trail registration number: NCT00208546 (ClinicalTrials.gov).

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2009.

Publication date

20090205.

In vivo activity of novel capecitabine regimens alone and with bevacizumab and oxaliplatin in colorectal cancer xenograft models.

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2009025025 20090204.

Source

Molecular Cancer Therapeutics, {Mol−Cancer−Ther}, 1 January 2009, vol. 8, no. 1, p. 75−82, 40 refs, CODEN: MCTOC, ISSN: 1535−7163. Publisher: American Association for Cancer Research Inc., 150 South Independence Mall West, Philadelphia, PA 19106−3483, USA.

Author(s)

Kolinsky−Kenneth, Shen−Ben−Quan, Zhang−Yu−E, Kohles−Joseph, Dugan−Ute, Zioncheck−Thomas−F, Heimbrook−David, Packman−Kathryn, Higgins−Brian.

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Abstract

Modifying the capecitabine dosing schedule from 14 days on, 7 days off (14/7) to 7 days on, 7 days off (7/7) may enable higher doses and improved antitumor efficacy in colorectal cancer xenografts. Capecitabine 14/7 (267 or 400 mg/kg) and 7/7 (467 or 700 mg/kg) schedules in doublet and triplet combinations with optimally dosed **bevacizumab** (5 mg/kg) and oxaliplatin (6.7 mg/kg) were studied in female athymic nude mice bearing HT29 colorectal xenografts. Additional studies of suboptimally dosed **bevacizumab** (2.5 mg/kg) and capecitabine 7/7 (360 mg/kg) were done in a similar Colo205 tumor xenograft model. Monotherapy and combination regimens were administered to groups of 10 animals and compared with vehicle controls. In the HT29 model, tumor growth inhibition and increase in life span (ILS) were significantly greater with capecitabine 7/7 than with 14/7 ($P < 0.05$). The additional benefit of capecitabine 7/7 versus 14/7 was biologically significant according to National Cancer Institute criteria (>25% ILS). Adding **bevacizumab** to capecitabine 7/7 resulted in significantly greater survival relative to either agent alone ($P < 0.0001$). When oxaliplatin was added, efficacy was significantly better with the triplet combination including capecitabine 7/7 (tumor growth inhibition >100% and ILS 234%) compared with 14/7 (95% and 81%, respectively). In the Colo205 model, combination therapy with capecitabine 7/7 plus **bevacizumab** resulted in significantly greater survival relative to either agent alone ($P < 0.0001$). In conclusion, in athymic nude mice bearing moderately thymidine phosphorylase−expressing HT29 or Colo205 colorectal xenografts, a capecitabine 7/7 schedule permits increased drug delivery compared with traditional 14/7 regimens, greatly improving monotherapy activity without major toxicity.

Publication year

2009.

Publication date

20090101.

Clinical use of anti−vascular endothelial growth factor monoclonal antibodies in metastatic colorectal cancer.

Accession number & update

2008524555 20081201.

Source

Pharmacotherapy, {Pharmacotherapy}, November 2008, vol. 28, no. 11 PART 2, p. 23S−30S, 49 refs, CODEN: PHPYD, ISSN: 0277−0008. Publisher: Pharmacotherapy Publications Inc., 750 Washington Street, Boston, MA 02111, USA.

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Abstract

Vascular endothelial growth factor (VEGF) is the most potent proangiogenic factor and has been identified as an important target of cancer therapy. Blocking endothelial cell VEGF activity inhibits tumor angiogenesis; normalizes tumor vasculature, facilitating improved chemotherapy delivery; and prevents the recruitment of progenitor cells from the bone marrow. **Bevacizumab,** the only United States Food and Drug Administration (FDA)−approved anti−VEGF agent, is a monoclonal antibody that inhibits the binding of VEGF to VEGF receptors. The addition of **bevacizumab** to standard first− and second− line chemotherapy regimens for the treatment of metastatic colorectal cancer improves overall and progression−free survival times and increases the time to disease progression. Studies are evaluating **bevacizumab** as adjuvant therapy. The optimal **bevacizumab** dosage is unknown, but 5 mg/kg every 2 weeks is currently recommended for initial therapy. A surrogate efficacy marker is needed to optimize **bevacizumab** use, both for dose and patient selection; the clinical applicability of several surrogate efficacy markers is being evaluated. Generally, **bevacizumab** is well tolerated; however, several serious adverse effects that may occur (e.g., hypertensive crisis) can usually be appropriately prevented or managed. Although current recommendations suggest the administration of the first **bevacizumab** dose over 90 minutes to prevent infusion−related hypersensitivity reactions, recent study results show that 5 and 10 mg/kg can safely be administered over 10 and 20 minutes, respectively. Whether the addition of **bevacizumab** to metastatic colorectal cancer treatment regimens is a cost−effective treatment option is unknown; health economic studies are needed. When used for FDA−approved indications or for off−label indications being evaluated in select clinical trials, Medicare reimburses for **bevacizumab** therapy.

Publication year

2008.

Publication date

20081100.

Bevacizumab in older patients and patients with poorer performance status.

Dialog eLinks

Full text available at 

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17145521 Medline 20061201.

Source

Seminars in oncology, {Semin−Oncol}, Oct 2006, vol. 33, no. 5 Suppl 10, p. S19−25, 34 refs, ISSN: 0093−7754.

Author(s)

Hoff−Paulo−M.

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Abstract

It is a common belief that older patients and those with less−than− ideal performance status do not tolerate chemotherapy as well as other patients. In fact, many otherwise−healthy older patients with metastatic colorectal cancer are not treated with chemotherapy. There is strong evidence that the addition of **bevacizumab** to the combination of irinotecan, 5−fluorouracil, and leucovorin or to 5−fluorouracil and leucovorin has substantial clinical benefits in patients 65 years of age or older and in those with Eastern Cooperative Oncology Group performance status 1 or 2. The treatment is generally well tolerated, without apparent negative effects on quality of life. However, the toxicity profile differs slightly, and the risk of arterial thrombotic events with **bevacizumab−**containing regimens, while relatively low, is higher in older patients than in younger patients. Clinicians should weigh the potential survival benefits against the risk of adverse events when choosing therapy for older patients with metastatic colorectal cancer and for those with poorer performance status.

Publication year

2006.

Publication date

20061000.

Systemic therapy for advanced or metastatic colorectal cancer: National Comprehensive Cancer Network guidelines for combining anti− vascular endothelial growth factor and anti−epidermal growth factor receptor monoclonal antibodies with chemotherapy.

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Pharmacotherapy, {Pharmacotherapy}, November 2008, vol. 28, no. 11 PART 2, p. 18S−22S, 9 refs, CODEN: PHPYD, ISSN: 0277−0008. Publisher: Pharmacotherapy Publications Inc., 750 Washington Street, Boston, MA 02111, USA.

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Dr. P. F. Engstrom: Fox Chase Cancer Center, 333 Cottman Avenue, Philadelphia, PA 19111−2497, USA. Email: pf_engstrom@fccc.edu.

Abstract

During the past decade, new therapies for colorectal cancer have emerged that significantly prolong survival times. The introduction of these new agents has resulted in changes in colorectal cancer treatment patterns; clinicians are now able to optimize therapy and minimize toxicity by developing individualized patient treatment plans using a variety of agents. Biologic agents, including **bevacizumab,** an anti−vascular endothelial growth factor (VEGF) monoclonal antibody, and cetuximab and panitumumab, anti−epidermal growth factor receptor (EGFR) monoclonal antibodies, are among the new therapies now recommended by the National Comprehensive Cancer Network (NCCN) colon and rectal cancer treatment guidelines for use in first−, second−, and /or third−line colorectal cancer therapy According to the NCCN guidelines, patients with advanced or metastatic colorectal cancer who are without contraindications are candidates to receive the anti−VEGF and anti−EGFR monoclonal antibodies at some point during the treatment course.

Publication year

2008.

Publication date

20081100.

Health−related quality of life impact of bevacizumab when combined with irinotecan, 5−fluorouracil, and leucovorin or 5−fluorouracil and leucovorin for metastatic colorectal cancer.

Dialog eLinks

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2008456892 20081001.

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Oncologist, {Oncologist}, September 2008, vol. 13, no. 9, p. 1021−1029, 17 refs, CODEN: OCOLF, eISSN: 1549−490X, ISSN: 1083−7159. Publisher: AlphaMed Press, 318 Blackwell St. Suite 260,

Durham, NC 27701−2884, USA.

Author(s)

Kabbinavar−Fairooz−F, Wallace−Joel−F, Holmgren−Eric, Yi−Jing, Cella− David, Yost−Kathleen−J, Hurwitz−Herbert−I.

Author affiliation

Dr. F. F. Kabbinavar: Division of Hematology/Oncology, UCLA School of Medicine, 10945 LeConte Avenue, Los Angeles, CA 90095−7059, USA. Email: fkabbina@mednet.ucla.edu.

Abstract

Purpose. To compare the time to deterioration in health−related quality of life (HRQoL) in patients with previously untreated metastatic colorectal cancer receiving a 5−fluorouracil (5−FU)−based chemotherapy regimen with or without the addition of **bevacizumab** (BV) in two randomized, placebo−controlled studies. Patients and Methods. Prespecified HRQoL endpoints in the phase II (Study 2192) and phase III (Study 2107) studies were time to deterioration in HRQoL, measured by the Functional Assessment of Cancer Therapy−Colorectal (FACT−C) Colorectal Cancer Subscale (CCS), Trial Outcome Index (TOI−C), and FACT−C total score. Time to deterioration in HRQoL was evaluated for patients with baseline and postbaseline assessments, using the stratified log−rank test. Results. In the pivotal phase III trial, HRQoL baseline and postbaseline CCS scores were available for 127 patients receiving irinotecan, 5−FU, and leucovorin (LV) (IFL) and 122 patients receiving IFL plus BV. The time to deterioration in HRQoL did not differ significantly between treatment groups as measured by the CCS, TOI−C, or FACT−C total score. In the phase II study, baseline and postbaseline CCS scores were available for 77 and 89 patients receiving 5−FU and LV and 5−FU and LV plus BV, respectively. In that study, the time to deterioration in HRQoL was similar between groups as measured by the CCS and TOI−C scores, but was significantly longer in the 5−FU and LV plus BV arm than in the 5−FU and LV plus placebo arm for the FACT−C total score. Conclusions. When added to 5−FU chemotherapy, BV significantly prolonged overall survival and progression−free survival without compromising HRQoL. ©AlphaMed Press.

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2008.

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20080900.

Targeted therapies in the treatment of colorectal cancer: what managed care needs to know.

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15546221 Medline R 20040101.

Source

Journal of managed care pharmacy : JMCP, {J−Manag−Care−Pharm}, Oct 2004, vol. 10, no. 5 Suppl B, p. S2−13; quiz S14−7, 114 refs, ISSN: 1083−4087.

Author(s)

Schwartz−Rowena−N, Blanke−Charles−D, Pesko−Larry−John.

Author affiliation

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Abstract

OBJECTIVE: This review is designed to explore the disease, its current treatment, the expanding field of antiangiogenic treatments, and the implications of these advances for the managed care patient. DATA SOURCES: This article is based, in part, on presentations given by the authors in a continuing education symposium presented during the Academy of Managed Care Pharmacy.s 16th Annual Meeting and Showcase, April 1, 2004, in San Francisco. CONCLUSIONS: Colorectal cancer (CRC) is the third most common cancer in the United States, and the second− leading non.gender−specific cause of cancer

deaths. If the cancer is caught soon enough (before node involvement and metastasis occur), there is a strong chance of survival; however, only slightly more than one third of cases are detected that soon. Emerging treatments that target only the cancer cells are increasing the length of survival for those who are diagnosed at later stages of the disease.

Publication year

2004.

Publication date

20041000.

Bevacizumab: A review of its use in metastatic colorectal cancer.

Dialog eLinks

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2008116266 20080601.

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Drugs, {Drugs}, 2008, vol. 68, no. 4, p. 487–506, 64 refs, CODEN: DRUGA, ISSN: 0012–6667. Publisher: Adis International Ltd, 41 Centorian Drive, Private Bag 65901, Mairangi Bay, Auckland 10, 1311, New Zealand.

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McCormack–Paul–L, Keam–Susan–J.

Author affiliation

P. L. McCormack: Wolters Kluwer Health / Adis, 41 Centorian Drive, Mairangi Bay, North Shore 0754, Auckland, New Zealand. Email: demail@adis.co.nz.

Abstract

Bevacizumab (Avastin®) is a recombinant, humanized monoclonal antibody against vascular endothelial growth factor (VEGF) that is used to inhibit VEGF function in vascular endothelial cells and thereby inhibit tumour angiogenesis, upon which solid tumours depend for growth and metastasis. The addition of **bevacizumab** to fluoropyrimidine–based chemotherapy, with or without irinotecan or oxaliplatin, in both the first– and second–line treatment of metastatic colorectal cancer, significantly increased median progression–free survival or time to disease progression in most randomized controlled trials. **Bevacizumab** was generally, but not always, associated with a survival advantage; in phase III trials, the increases in median overall survival attributable to **bevacizumab** were 4.7 months with first–line therapy and 2.1 months with second–line therapy. In some studies, patients experienced clinical improvement without an apparent overall survival benefit. **Bevacizumab** had acceptable tolerability, with the majority of adverse events being generally mild and clinically manageable. However, from the UK National Health Service perspective, **bevacizumab** was not considered to be cost effective in combination with bolus fluorouracil/folinic acid or irinotecan/bolus fluorouracil/folinic acid. Additional pharmacoeconomic analyses from different perspectives and using clinical data for combinations with the more efficacious infusional fluorouracil/folinic acid plus oxaliplatin or irinotecan chemotherapy regimens are required. Although cost effectiveness may be a concern, the combination of **bevacizumab** and fluoropyrimidine–based chemotherapy has potential in the treatment of metastatic colorectal cancer.

Publication year

2008.

Publication date

20080000.

Bevacizumab in colorectal cancer.

Dialog eLinks

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15490497 Medline R 20040101.

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The New England journal of medicine, {N–Engl–J–Med}, 14 Oct 2004, vol. 351, no. 16, p. 1690–1; author reply 1690–1, ISSN: 1533–4406.

Author(s)

Sharieff–Waseem.

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2004.

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20041014.

Commentary.

Dialog eLinks

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2008094204 20080301.

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Colorectal Disease, {Colorectal–Dis}, March 2008, vol. 10, no. 3, p. 218–221, 24 refs, CODEN: CODIF, eISSN: 1463–1318, ISSN: 1462–8910. Publisher: Blackwell Publishing Ltd, 9600 Garsington Road, Oxford, OX4 2XG, UK.

Author(s)

Gerard–J–P, Francois–E, Follana–P.

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Publication year

2008.

Publication date

20080300.

The cost–effectiveness of bevacizumab in the first–line treatment of metastatic colorectal cancer in England and Wales.

Dialog eLinks

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Accession number & update

2007549933 20071101.

Source

European Journal of Cancer, {Eur–J–Cancer}, November 2007, vol. 43, no. 17, p. 2487–2494, 21 refs, CODEN: EJCAE, ISSN: 0959–8049. Publisher: Elsevier Ltd, Langford Lane, Kidlington, Oxford, OX5 1GB, UK.

Author(s)

Tappenden–P, Jones–R, Paisley–S, Carroll–C.

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Abstract
Background: **Bevacizumab** is a humanised monoclonal antibody, which has demonstrated significant activity in metastatic colorectal cancer. The aim of this study is to estimate the cost−effectiveness of adding **bevacizumab** to chemotherapy for patients with untreated metastatic colorectal cancer. Methods: A decision−analytic model was developed to estimate the lifetime costs and benefits of adding **bevacizumab** to irinotecan plus FU/LV (IFL) or 5−FU/LV alone. Effectiveness outcomes, health utilities and resource use data were derived from recent **bevacizumab** RCTs and from the literature. Results: Adding **bevacizumab** to IFL costs approximately œ62,857 per QALY gained. Adding **bevacizumab** to 5−FU/LV costs approximately œ88,436 per QALY gained. The acquisition cost of **bevacizumab** is a key determinant of its cost− effectiveness. The probability that **bevacizumab** has a cost− effectiveness ratio that is better than œ30,000 per QALY gained is close to zero. Conclusions: Given high acquisition costs in relation to clinical benefits, **bevacizumab** is unlikely to represent a cost− effective use of NHS resources.

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2007.
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20071100.

Symptom burden for patients with metastatic colorectal cancer treated with first−line FOLFOX or FOLFIRI with and without bevacizumab in the community setting.

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2007510867 20071001.
Source
Supportive Cancer Therapy, {Supportive−Cancer−Ther}, September 2007, vol. 4, no. 4, p. 233−240, 18 refs, ISSN: 1543−2912. Publisher: Cancer Information Group, LP, 3500 Maple Avenue, Suite 750, Dallas, TX 75219, USA.

Author(s)
Fortner−Barry−V, Schwartzberg−Lee−S, Stepanski−Edward−J, Houts−Arthur− C.
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Dr. B.V. Fortner: SOS/ACORN, 1770 Kirby Pkwy, Memphis, TN 38138, USA. Email: bfortner@sosacorn.com.

Abstract
Background: FOLFOX (oxaliplatin/leucovorin/5−fluorouracil) and FOLFIRI (irinotecan/leucovorin/5−fluorouracil) with or without **bevacizumab** have become standard−of−care regimens in first−line treatment of metastatic colorectal cancer. However, there is a paucity of symptom burden information regarding these regimens from the patient perspective in community oncology. Patients and Methods: This retrospective chart review and telephone interview study examined patients with first−line metastatic colorectal cancer from 5 community oncology centers treated with FOLFOX or FOLFIRI with and without **bevacizumab.** Patient−reported outcomes were taken from the Patient Care Monitor 1.0 Revised, a validated tablet computer−based **questionnaire** that measures symptom burden and several scales of functioning and quality of life. A subset of patients completed structured telephone interviews about the impact of treatment on practical activities and income. Results: Eighty−eight patients with an average age of 62 years were included. Patients completed a median of 8 cycles of treatment. The most common moderate to severe symptom complaint was fatigue. Gastrointestinal symptoms were common but did not cluster in one regimen versus another. Neuropathy−related symptoms were also common across all regimens except FOLFIRI without **bevacizumab.** Nausea and neutropenia were

common indications for concomitant medications. One third reported work and other activity interference, and care produced out−of−pocket expenditures in excess of $1000. Conclusion: Although sample size was small in the FOLFIRI− based regimens, patient reports and chart records suggested that there was not a systematic difference between FOLFOX and FOLFIRI regimens in type of symptom. The addition of **bevacizumab** did not appear to increase symptom burden.

Publication year

2007.

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20070900.

Systematic review and economic evaluation of bevacizumab and cetuximab for the treatment of metastatic colorectal cancer.

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Health Technology Assessment, {Health−Technol−Assess}, March 2007, vol. 11, no. 12, p. iii−103, 162 refs, CODEN: HTASF, ISSN: 1366−5278. Publisher: National Co−ordinating Centre for HTA, Bouldrewood, Mail Point 728, Highfield, Southhampton, UK.

Author(s)

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Abstract

Objectives: To assess the clinical effectiveness and cost− effectiveness of **bevacizumab** and cetuximab in the treatment of individuals with metastatic colorectal cancer (CRC). Data sources: Searches of main electronic databases were conducted in April and May 2005. Review methods: For the assessment of **bevacizumab,** trials were included if they recruited participants with untreated metastatic CRC for first−line treatment. Only trials comparing **bevacizumab** in combination with irinotecan and/or established fluorouracil (5−FU)− containing or releasing regimens given as first−line therapy were included. For the assessment of cetuximab, trials were included if they recruited participants with epidermal growth−factor receptor− expressing metastatic CRC who had previously failed irinotecan− including therapy. Independent cost−effectiveness models of **bevacizumab** and cetuximab were developed using survival modelling methods. Results: Adding **bevacizumab** to irinotecan in combination with 5−FU/folic acid (FA) plus irinotecan resulted in a statistically significant increase in median overall survival (OS) of 4.7 months. Adding **bevacizumab** to 5−FU/FA resulted in a non−significant increase in median OS of 3.7 months within one study and 7.7 months in another. Adding **bevacizumab** to irinotecan, fluorouracil and leucovorin (IFL) resulted in a statistically significant increase in median progression−free survival (PFS) of 4.4 months. Adding **bevacizumab** to 5−FU/FA resulted in a statistically significant increase in median PFS of 3.7 months, and a statistically significant increase in time to disease progression of 3.8 months compared to FU/FA alone. An overall tumour response rate of 44.8% was reported for **bevacizumab** plus IFL compared to 34.8% for IFL plus placebo. This addition was statistically significant. The addition of **bevacizumab** to 5−FU/FA resulted in a significant difference in tumour response rate within one study, but not another. **Bevacizumab** in combination with IFL or 5− FU/FA was observed to result in an increase of grade 3/4 adverse events. The independent health economic assessment suggests that the cost−effectiveness of **bevacizumab** plus IFL is unlikely to be better than œ46,853 per life−year gained (LYG); the cost−utility of **bevacizumab** plus IFL is unlikely to be better than œ62,857 per quality−adjusted life−year (QALY) gained. The cost−effectiveness of **bevacizumab** plus 5−FU/FA versus 5−FU/FA is unlikely to be better than œ84,607 per LYG; the cost−utility of **bevacizumab** plus 5−FU/FA versus 5−FU/FA is unlikely to be better than œ88,658 per QALY gained. A Phase II trial reported a

median OS duration of 8.6 months for patients receiving cetuximab plus irinotecan, plus a median time to progression of 4.1 months, a tumour response rate of 22.9% and suggested that treatment with cetuximab in combination with irinotecan is associated with significantly more adverse events (any grade 3 or grade 4 adverse event) than cetuximab monotherapy. The single arm study of cetuximab plus irinotecan reported a median OS duration of 8.4 months, a median time to progression of 2.9 months and a tumour response rate of 15.2%. The cost−effectiveness model suggested that the expected survival duration of patients receiving cetuximab plus irinotecan is 0.79 years (9.5 months) when the proposed continuation rule is applied. In order for cetuximab plus irinotecan to achieve a cost−utility ratio of œ30,000 per QALY gained, treatment with cetuximab plus irinotecan must provide an additional 0.65 life years (7.8 months) over treatment with active/best supportive care, implying that survival in the active/best supportive care group must be 0.14 life years (1.7 months) or less. Conclusions: The trials indicate that **bevacizumab** in combination with 5−FU/FA, and **bevacizumab** in combination with IFL, is clinically effective in comparison to standard chemotherapy options for the first−line treatment of metastatic CRC. The health economic analysis suggests that the marginal cost−utility of **bevacizumab** plus IFL versus IFL is unlikely to be better than œ62,857 per QALY gained, and the marginal cost−utility of **bevacizumab** plus 5−FU/FA versus 5−FU/FA is unlikely to be better than œ88,658 per QALY gained. There is no direct evidence to demonstrate whether cetuximab in combination with irinotecan improves health−related quality of life or OS in comparison to active/best supportive care or oxaliplatin plus 5−FU/FA, although the evidence on tumour response rates suggests that cetuximab plus irinotecan has some clinical activity. While it is difficult to surest whether cetuximab represents value for money, indirect comparisons suggest that the incremental cost−utility of cetuximab plus irinotecan is unlikely, to be better than œ30,000 per QALY gained. This review highlights a number of areas for further research, including clarifying the true impact of, first−line **bevacizumab** in combination with irinotecan and/or infusional 5−FU/FA, without subsequent **bevacizumab** treatment following disease progression, on OS in patients with metastatic CRC who are representative of the typical population of CRC patients in England and Wales. Further research concerning the impact of therapies on health−related quality of life is essential.

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20070300.

Bevacizumab's role in treating advanced colorectal cancer.

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Community Oncology, {Community−Oncol}, May 2007, vol. 4, no. 5, p. 295−296, 14 refs, ISSN: 1548−5315. Publisher: Elsevier Oncology, 46 Green Street, 2nd Floor, Huntington, NY 11743, USA.
Author(s)
Jones−Matthew−P.
Author affiliation
Dr. M.P. Jones: West Virginia University Hospitals−East, Martinsburg, WV, USA. Email: mjones@wvuh−east.org.
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Addition of bevacizumab to bolus fluorouracil and leucovorin in first– line metastatic colorectal cancer: Results of a randomized phase II trial.

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Journal of Clinical Oncology, {J–Clin–Oncol}, 2005, vol. 23, no. 16, p. 3697–3705, 33 refs, CODEN: JCOND, ISSN: 0732–183X. Publisher: American Society of Clinical Oncology, 330 John Carlyle Street, Suite 300, Alexandria, VA 22314, USA.

Author(s)

Kabbinavar–Fairooz–F, Schulz–Joseph, McCleod–Michael, Patel–Taral, Hamm–John–T, Hecht–J–Randolph, Mass–Robert, Perrou–Brent, Nelson– Betty, Novotny–William–F.

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Abstract

Purpose: **Bevacizumab,** a monoclonal antibody against vascular endothelial growth factor, increases survival when combined with irinotecan–based chemotherapy in first–line treatment of metastatic colorectal cancer (CRC). This randomized, phase II trial compared **bevacizumab** plus fluorouracil and leucovorin (FU/LV) versus placebo plus FU/LV as first–line therapy in patients considered nonoptimal candidates for first–line irinotecan. Patients and Methods: Patients had metastatic CRC and one of the following characteristics: age 65 years, Eastern Cooperative Oncology Group performance status 1 or 2, serum albumin 3.5 g/dL, or prior abdominal/pelvic radiotherapy. Patients were randomly assigned to FU/LV/placebo (n = 105) or FU/LV /bevacizumab (n = 104). The primary end point was overall survival. Secondary end points were progression–free survival, response rate, response duration, and quality of life. Safety was also assessed. Results: Median survival was 16.6 months for the **FU**/LV/bevacizumab group and 12.9 months for the FU/LV/placebo group (hazard ratio, 0.79; P = .16). Median progression–free survival was 9.2 months (FU/LV /bevacizumab) and 5.5 months (FU/LV/placebo); hazard ratio was 0.50; P = .0002. Response rates were 26.0% **(FU**/LV/bevacizumab) and 15.2% (FU /LV/placebo) (P = .055); duration of response was 9.2 months (FU/LV /bevacizumab) and 6.8 months (FU/LV/placebo); hazard ratio was 0.42; P = .088. Grade 3 hypertension was more common with **bevacizumab** treatment (16% v 3%) but was controlled with oral medication and did not cause study drug discontinuation. Conclusion: Addition of **bevacizumab** to FU/LV as first–line therapy in CRC patients who were not considered optimal candidates for first–line irinotecan treatment provided clinically significant patient benefit, including statistically significant improvement in progression–free survival. © 2005 by American Society of Clinical Oncology.

Publication year

2005.

Publication date

20050000.

Bevacizumab, a humanized anti–angiogenic monoclonal antibody for the treatment of colorectal cancer.

Dialog eLinks

Full text available at Roche Link >

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2007074855 20070301.

Source

Journal of Clinical Pharmacy and Therapeutics, {J−Clin−Pharm−Ther}, February 2007, vol. 32, no. 1, p. 1−14, 84 refs, CODEN: JCPTE, eISSN: 1365−2710, ISSN: 0269−4727. Publisher: Blackwell Publishing Ltd, 9600 Garsington Road, Oxford, OX4 2XG, UK.

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Abstract

Angiogenesis is the process by which new blood vessels are created from pre−existing vessels. It is essential for the growth and development of normal cells and tissues during embryonic and neonatal development and of tumour cells. Solid tumours rely on having an extensive network of blood vessels for growth and survival. The key mediator of angiogenesis, vascular endothelial growth factor−A (VEGF− A), is critical for the growth of tumours and their subsequent metastasis and is known to initiate angiogenesis. **Bevacizumab** is a humanized immunoglobulin G monoclonal antibody that binds to VEGF with high specificity, thereby blocking VEGF−mediated signalling pathways and thus angiogenesis. Clinical trials have shown that **bevacizumab** is effective in prolonging survival in patients with metastatic colorectal cancer (CRC) when combined with standard chemotherapy. Consequently, **bevacizumab** has been approved in combination with 5− fluorouracil−based chemotherapy for first−line treatment of patients with metastatic CRC. **Bevacizumab** is generally well tolerated in most patients and does not exacerbate the adverse events associated with conventional chemotherapy. **Bevacizumab−**related side effects are generally manageable; however, monitoring for hypertension, gastrointestinal perforation, bleeding, proteinuria and thromboembolism is advised, especially in patients with predisposing factors. In addition to demonstrated survival benefits, the convenient dosing schedule and lack of interactions should ensure the successful integration of this novel agent into clinical practice. © 2007 The authors.

Publication year

2007.

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20070200.

Assessing the combination of FOLFOX or FOLFIRI with bevacizumab, cetuximab, or both in metastatic colorectal cancer.

Accession number & update

2006572768 20060101.

Source

Community Oncology, {Community−Oncol}, September 2006, vol. 3, no. 9, p. 593−598, 31 refs, ISSN: 1548−5315.

Author(s)

Venook−Alan−P, Blanke−Charles−D, Goldberg−Richard−M, Reinke−Denise−K, Sutherland−Susan, Taylor−John−R, McAllister−Pamela, Schilsky−Richard− L.

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Abstract

This article is the first in a new series that details available clinical trials and offers information on how you and your practice can participate. The CALGB/SWOG 80405 trial is designed to assess the optimal combination of biological agents and chemotherapy for the first−line treatment of patients with advanced

or metastatic colorectal cancer.

Publication year
2006.

Publication date
20060900.

Long–term treatment with bevacizumab for patients with metastatic colorectal cancer: Case report.

Dialog eLinks
Full text available at Roche Link >

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2006333649 20060101.

Source
Clinical Colorectal Cancer, **{Clin–**Colorectal–Cancer}, May 2006, vol. 6, no. 1, p. 66–69, 17 refs, CODEN: CCCLC, ISSN: 1533–0028.

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Hurwitz–Herbert–I, Honeycutt–Wanda, Haley–Sherri, Favaro–Justin.

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Abstract
Bevacizumab is a monoclonal antibody to vascular endothelial growth factor that has demonstrated increased overall survival when added to standard chemotherapy regimens for metastatic colorectal cancer. Herein we report the cases of 2 patients who demonstrated prolonged survival times of almost 5 and 6 years, respectively, on various chemotherapy regimens that also included **bevacizumab.** Throughout most of their disease course, these patients maintained a good quality of life, with some adjustments of chemotherapy doses because of side effects. **Bevacizumab** was generally well tolerated in long–term use.

Publication year
2006.

Publication date
20060500.

Bevacizumab and cetuximab for colorectal cancer.

Dialog eLinks
Full text available at Roche Link >

Accession number & update
2006243169 20060101.

Source
Drug and Therapeutics Bulletin, {Drug–Ther–Bull}, May 2006, vol. 44, no. 5, p. 37–40, 29 refs, CODEN: DRTBA, ISSN: 0012–6543.

Abstract
Every year in the UK, around 16,000 people die from colorectal cancer, the second commonest cause of death from cancer in the UK after lung cancer. Over half of all people with colorectal cancer eventually die of metastatic disease. While median survival has increased with optimal use of combination chemotherapy, only a small minority of patients are still alive 5 years after diagnosis of metastases. **Bevacizumab** (pronounced be–va–see–zoo–mab) (Avastin – Roche) and cetuximab (se–tuks–ee–mab)

(Erbitux– Merck) are two new monoclonal antibodies licensed for treating patients with metastatic colorectal cancer. Here we assess their efficacy and safety.

Publication year
2006.

Publication date
20060500.

Can the addition of bevacizumab to IFL chemotheraoy improve outcome in colorectal cancer?

Dialog eLinks
Full text available at Roche Link >

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2005265737 20050101.

Source
Nature Clinical Practice Gastroenterology and Hepatology, {Nat–Clin– Pract–Gastroenterol–Hepatol}, December 2004, vol. 1, no. 2, p. 72–73, 5 refs, ISSN: 1743–4378.

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Publication year
2004.

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20041200.

Bevacizumab can be safely combined with FOLFOX or XELOX.

Dialog eLinks
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2005160908 20050101.

Source
Oncology Report, {Oncol–Rep}, March 2005, no. SPRING, p. 43–44, 1 ref, ISSN: 1548–5323.

Author(s)
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Publication date
20050300.

Bevacizumab adds survival benefit in colorectal cancer.

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2005100344 20050101.

Source

Lancet Oncology, {Lancet–Oncol}, 1 March 2005, vol. 6, no. 3, p. 136, CODEN: LOANB, ISSN: 1470–2045.

Author(s)

Susman–Ed.

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20050301.

Bevacizumab in colorectal cancer (2) (multiple letters).

Dialog eLinks

Full text available at Roche Link >

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2004437609 20040101.

Source

New England Journal of Medicine, {New–Engl–J–Med}, 14 October 2004, vol. 351, no. 16, p. 1690–1691, CODEN: NEJMA, ISSN: 0028–4793.

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2004.

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20041014.

Bevacizumab improves the efficacy of 5–fluorouracil/leucovorin in patients with advanced colorectal cancer.

Dialog eLinks

Full text available at Roche Link >

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2004386338 20040101.

Source

Clinical Colorectal Cancer, **{Clin–**Colorectal–Cancer}, July 2004, vol. 4, no. 2, p. 89–91, 6 refs, CODEN: CCCLC, ISSN: 1533–0028.

Author(s)

Price–Nancy, Chu–Edward, Jain–Vinay–K.

Publication year

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Publication date
20040700.

Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer.

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2004238674 20040101.

Source
New England Journal of Medicine, {New–Engl–J–Med}, 3 June 2004, vol. 350, no. 23, p. 2335–2342, 19 refs, CODEN: NEJMA, ISSN: 0028–4793.

Author(s)
Hurwitz–Herbert, Fehrenbacher–Louis, Novotny–William, Cartwright– Thomas, Hainsworth–John, Heim–William, Berlin–Jordan, Baron–Ari, Griffing–Susan, Holmgren–Eric, Ferrara–Napoleone, Fyfe–Gwen, Rogers– Beth, Ross–Robert, Kabbinavar–Fairooz.

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Abstract
BACKGROUND: **Bevacizumab,** a monoclonal antibody against vascular endothelial growth factor, has shown promising preclinical and clinical activity against metastatic colorectal cancer, particularly in combination with chemotherapy. METHODS: Of 813 patients with previously untreated metastatic colorectal cancer, we randomly assigned 402 to receive irinotecan, bolus fluorouracil and leucovorin (IFL) plus **bevacizumab** (5 mg per kilogram of body weight every two weeks) and 411 to receive IFL plus placebo. The primary end point was overall survival. Secondary end points were progression–free survival, the response rate, the duration of the response, safety, and the quality of life. RESULTS: The median duration of survival was 20.3 months in the group given IFL plus **bevacizumab,** as compared with 15.6 months in the group given IFL plus placebo, corresponding to a hazard ratio for death of 0.66 (P<0.001). The median duration of progression– free survival was 10.6 months in the group given IFL plus **bevacizumab,** as compared with 6.2 months in the group given IFL plus placebo (hazard ratio for disease progression, 0.54; P<0.001); the corresponding rates of response were 44.8 percent and 34.8 percent (P=0.004). The median duration of the response was 10.4 months in the group given IFL plus **bevacizumab,** as compared with 7.1 months in the group given IFL plus placebo (hazard ratio for progression, 0.62; P=0.001). Grade 3 hypertension was more common during treatment with IFL plus **bevacizumab** than with IFL plus placebo (11.0 percent vs. 2.3 percent) but was easily managed. CONCLUSIONS: The addition of **bevacizumab** to fluorouracil–based combination chemotherapy results in statistically significant and clinically meaningful improvement in survival among patients with metastatic colorectal cancer. Copyright © 2004 Massachusetts Medical Society.

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2004.

Publication date
20040603.

Search Strategy

No.	Database	Search term	Info added since	Results
1	MEYY	monoclonal ADJ antibodies	unrestricted	81516
2	MEYY	ANTIBODIES–MONOCLONAL.MJ.	unrestricted	35350
3	MEYY	2 AND bevacizumab	unrestricted	1269
4	MEYY	colorectal ADJ cancer	unrestricted	31236
5	MEYY	COLORECTAL–NEOPLASMS.MJ.	unrestricted	27636
6	MEYY	quality ADJ of ADJ life	unrestricted	66758
7	MEYY	QUALITY–OF–LIFE.DE. OR HEALTH–STATUS.DE.	unrestricted	94082
8	MEYY	qaly	unrestricted	2419
9	MEYY	quality	unrestricted	374455
10	MEYY	lifestyle	unrestricted	26764
11	MEYY	LIFE–STYLE.DE. OR QUESTIONNAIRES.W..DE.	unrestricted	184855
12	MEYY	health ADJ utility	unrestricted	596
13	MEYY	HEALTH–STATUS–INDICATORS.DE. OR HEALTH–SURVEYS.DE. OR OUTCOME–ASSESSMENT–HEALTH–CARE.DE.	unrestricted	64557
14	MEYY	value ADJ of ADJ life	unrestricted	2900
15	MEYY	VALUE–OF–LIFE.DE. OR QUALITY–ADJUSTED–LIFE–YEARS.DE. OR HEALTH–STATUS.DE.	unrestricted	40988
16	MEYY	time ADJ trade ADJ off	unrestricted	441
17	MEYY	OUTCOME–ASSESSMENT–HEALTH–CARE.DE.	unrestricted	31840
18	MEYY	3 AND 5 AND (17 OR 15 OR 13 OR 11 OR 7) AND LG=EN AND HUMAN=YES	unrestricted	9
19	EMYY	Bevacizumab.W..MJ.	unrestricted	1620
20	EMYY	Colorectal–Cancer.MJ.	unrestricted	21596
21	EMYY	quality ADJ of ADJ life	unrestricted	96588
22	EMYY	QUALITY–OF–LIFE.DE. OR QUESTIONNAIRE.W..DE. OR HEALTH–STATUS.DE. OR SCORING–SYSTEM.DE.	unrestricted	315113
23	EMYY	quality	unrestricted	348033

24	**EMYY**	**lifestyle**	**unrestricted**	**40286**
25	**EMYY**	**LIFESTYLE.W..DE.**	**unrestricted**	**29245**
26	**EMYY**	**qaly**	**unrestricted**	**2223**
27	**EMYY**	**QUALITY−ADJUSTED−LIFE−YEAR.DE.**	**unrestricted**	**4250**
28	**EMYY**	**health ADJ utility**	**unrestricted**	**542**
29	**EMYY**	**HEALTH−SURVEY.DE.**	**unrestricted**	**65049**
30	**EMYY**	**health ADJ status**	**unrestricted**	**39377**
31	**EMYY**	**HEALTH−STATUS.DE.**	**unrestricted**	**34798**
32	**EMYY**	**value ADJ of ADJ life**	**unrestricted**	**0**
33	**EMYY**	**time ADJ trade ADJ off**	**unrestricted**	**418**
34	**EMYY**	**TIME−TRADE−OFF.DE.**	**unrestricted**	**12**
35	**EMYY**	**19 AND 20 AND (22 OR 25 OR 27 OR 29 OR 31 OR 34) AND LG=EN AND HUMAN=YES**	**unrestricted**	**22**
36	**EMYY MEYY**	**combined sets 18, 35**	**unrestricted**	**31**
37	**EMYY MEYY**	**dropped duplicates from 36**	**unrestricted**	**6**
38	**EMYY MEYY**	**unique records from 36**	**unrestricted**	**25**

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