Bevacizumab

ACG: A-0491 (AC)
Link to Codes

MCG Health
Ambulatory Care
27th Edition

Clinical Indications

- Bevacizumab may be indicated when **1 or more** of the following are present:
  - Intravitreal administration needed, as indicated by **ALL** of the following:
    - Age 18 years or older
    - Eye condition appropriate for bevacizumab treatment, as indicated by **1 or more** of the following:
      - Diabetic macular edema[A](53)(54)(55)(56)(57)(58)(59)N
      - Macular edema following retinal vein occlusion[B](68)(69)(70)N
      - Myopic choroidal neovascularization[C]N
      - Neovascular age-related macular degeneration[D](56)(84)(85)(86)(87)N
    - No concurrent ocular or periocular infection
  - Systemic administration needed, as indicated by **ALL** of the following(1)(97)(98):
    - Age 18 years or older
    - Malignancy appropriate for bevacizumab treatment, as indicated by **1 or more** of the following:
      - Cervical cancer and **ALL** of the following[E](99)(100)(101)(102):N
        - Administered in combination with other agents (eg, paclitaxel and topotecan, paclitaxel and cisplatin with or without pembrolizumab)
        - Persistent, recurrent, or metastatic disease
      - Colon or rectal cancer (metastatic) and **ALL** of the following[F](106)(107)(108)(109):N
        - Treatment scenario includes **1 or more** of the following:
          - First-line therapy and administered in combination with other agents (eg, intravenous 5-fluorouracil-based, irinotecan-based, or oxaliplatin-based chemotherapy)(114)
          - Second-line therapy and administered in combination with other agents (eg, irinotecan-based or oxaliplatin-based chemotherapy)
        - Metastatic disease(115)
        - No coadministration of cetuximab or panitumumab(116)
      - Hepatocellular carcinoma and **ALL** of the following[G](117)(118)(119)(120)(121):N
        - Administered in combination with atezolizumab(123)
        - Child-Pugh class A liver disease
        - Metastatic or unresectable disease
        - Previously untreated disease
      - Malignant glioma and **ALL** of the following[H](124)(125)(126)(127)(128):N
        - Glioma type is **1 or more** of the following:
          - Anaplastic astrocytoma
          - Anaplastic oligodendroglioma
          - Glioblastoma multiforme
          - Mixed anaplastic oligoastrocytoma
        - Indication for systemic therapy is **1 or more** of the following:
          - Recurrent disease(136)(137)
          - Salvage therapy[I](138)
      - Mesothelioma and **ALL** of the following[J](139)(140)(141):N
        - Administered as combination therapy with pemetrexed and either cisplatin or carboplatin, or as maintenance monotherapy

- Unresectable disease

- Non-small cell lung cancer and **ALL** of the following[K](32)(143)(144)(145):
  - Administration in combination with other agents (eg, erlotinib; carboplatin and paclitaxel, with or without atezolizumab) or as monotherapy for maintenance(32)(152)
  - Indication for systemic therapy is **1 or more** of the following:
    - Locally advanced disease
    - Metastatic disease
    - Recurrent disease
    - Unresectable disease
  - Nonsquamous histology
- Ovarian (epithelial), fallopian tube, or primary peritoneal cancer and **1 or more** of the following(153)(154)(155):
  - Primary adjuvant therapy for stage II to IV disease, and administered with other agents (eg, carboplatin plus paclitaxel, olaparib), or maintenance monotherapy[L]
  - Recurrent platinum-resistant (ie, progression of disease within 6 months of completion of 4 or more cycles of platinum-based therapy) disease, and administered in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan[M]
  - Recurrent platinum-sensitive disease, and administered in combination with carboplatin plus paclitaxel, gemcitabine, or pegylated liposomal doxorubicin, with subsequent monotherapy with bevacizumab[N](167)
- Renal carcinoma and **ALL** of the following[O](168)(169)(170)(171)(172):
  - Administered as monotherapy or combined with other agents (eg, interferon alfa, everolimus, temsirolimus, erlotinib, capecitabine, gemcitabine)
  - Unresectable, recurrent, or metastatic disease

- No central nervous system metastasis
- No current or recent wound dehiscence
- No current therapeutic anticoagulation
- No major surgery planned or completed within 28 days of use
- No recent hemoptysis or other serious hemorrhage(1)
- No surgical incision, or surgical incision healed

Evidence Summary

Background

Bevacizumab is a recombinant human monoclonal IgG1 antibody that reduces angiogenesis in neoplastic and other cells.(1)(2) **(EG 2)**

Criteria

For diabetic macular edema, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** Meta-analyses and systematic reviews demonstrated that all vascular endothelial growth factor inhibitors appear to have some activity against diabetic macular edema,(57) with some clinical trial evidence suggesting that aflibercept may improve best-corrected visual acuity (measured by Early Treatment Diabetic Retinopathy Study (ETDRS) letters) significantly compared with bevacizumab, without a statistically significant difference compared with ranibizumab.(60) **(EG 1)** Systematic reviews found moderate-quality evidence that intravitreal bevacizumab provides a clinical benefit as compared with photocoagulation.(57)(58) **(EG 1)** A randomized trial with 2-year follow-up concluded that intravitreal bevacizumab improved visual acuity in the short term; however, this beneficial effect diminished over time.(61) **(EG 1)** A meta-analysis of studies comparing efficacy and safety of intravitreal triamcinolone vs intravitreal bevacizumab for diabetic macular edema found evidence that triamcinolone may be more effective, but the authors indicated that additional randomized studies are needed to determine and confirm which patients might benefit the most from either drug.(62) **(EG 1)** A randomized study of 660 adults with diabetic macular edema who received either intravitreal aflibercept, ranibizumab, or bevacizumab found that after 1 year, visual acuity improvement was comparable with all 3 drugs in those with mild initial visual acuity loss.(63) **(EG 1)** A follow-up study for up to 2 years found that all 3 groups showed continuing improvement in visual acuity, with similar improvement across all 3 drugs in eyes with better baseline acuity.(64) **(EG 1)** A systematic review and meta-analysis of 8 randomized controlled trials (817 eyes) evaluating the efficacy of intravitreal ranibizumab or bevacizumab combined with intravitreal steroids for the treatment of diabetic macular edema found no difference in both the mean change in visual acuity and central macular thickness at 6-month to 2-year follow-up compared with vascular endothelial growth factor inhibitor therapy alone. Additionally, combination therapy was associated with an increased rate of cataract development and raised intraocular pressure.(65) **(EG 1)**

For macular edema following retinal vein occlusion, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** Meta-analyses and systematic reviews have confirmed the efficacy and safety of vascular endothelial growth factor inhibitors for treatment of central retinal vein occlusion for up to 26 to 52 weeks.(71)(72)(73)(74) **(EG 1)** A meta-analysis found randomized controlled studies that indicate that patients with branch retinal vein occlusion experience a significant benefit with intravitreal bevacizumab, as compared with placebo, in terms of improvement in both central foveal thickness and visual acuity over periods of up to 24 months.(75) **(EG 1)** A randomized study assigned 52 eyes of 52 patients with branch retinal vein occlusion to monotherapy with either intravitreal triamcinolone or bevacizumab, or to both. After 6 months, the group receiving bevacizumab alone had better visual

acuity than the other 2 groups.(69) **(EG 1)** A randomized noninferiority trial of 463 patients with macular edema due to central retinal vein occlusion compared treatment with bevacizumab, aflibercept, or ranibizumab and found, at 100 weeks' follow-up, mean gains in best-corrected visual acuity letter scores of 9.8, 15.1, and 12.5 in patients treated with bevacizumab, aflibercept, and ranibizumab, respectively. The authors found that bevacizumab was not noninferior compared with ranibizumab.(76) **(EG 1)** A randomized controlled trial of 98 patients with either central or branch retinal vein occlusion found that intravitreal bevacizumab and ranibizumab had similar efficacy in improving both macular thickness and visual acuity after 6 months.(77) **(EG 1)** Specialty society guidelines state that bevacizumab is an effective treatment for macular edema due to retinal vein occlusion.(78)(79) **(EG 2)**

For myopic choroidal neovascularization, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. **(RG A2)** A meta-analysis and systematic review of 6 randomized studies of 594 patients with myopic choroidal neovascularization found low to moderate evidence that bevacizumab and ranibizumab are effective in treating this condition for up to a period of 1 to 2 years.(81) **(EG 1)** A specialty society consensus statement recommends that vascular endothelial growth factor inhibitor therapy should be the first-line treatment for patients with myopic choroidal neovascularization.(82) **(EG 2)**

For neovascular age-related macular degeneration, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** A randomized controlled trial of 131 patients receiving either intravitreal bevacizumab, standard care at the time of study (verteporfin or pegaptanib), or sham injection found significant improvement in visual acuity and contrast sensitivity in the bevacizumab group after 1 year.(88)(89) **(EG 1)** In a multicenter randomized single-blind trial, 1208 patients with neovascular age-related macular degeneration were assigned to receive intravitreal injections of either bevacizumab or ranibizumab, either monthly or as needed with monthly evaluation. After 1 year, bevacizumab and ranibizumab had equivalent effects on visual acuity when administered according to the same schedule.(83) **(EG 1)** These results were maintained at 2-year follow-up.(90)(91)(92) **(EG 1)** Randomized trials (of 610, 501, 441, and 327 patients with neovascular age-related macular edema) reported equivalent outcomes with either ranibizumab or bevacizumab at 1-year follow-up.(87)(93)(94)(95) **(EG 1)** A meta-analysis of randomized studies (with a total of 2686 patients receiving either bevacizumab or ranibizumab for neovascular age-related macular edema) confirmed that bevacizumab and ranibizumab had comparable positive effects on visual acuity after 1 year, but bevacizumab was associated with a higher risk of serious systemic adverse events.(96) **(EG 1)** A specialty society guideline recommends bevacizumab as a management option for patients with age-related neovascular macular degeneration.(84) **(EG 2)**

For cervical cancer (recurrent, persistent, or metastatic), evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** A randomized controlled study of 452 patients with recurrent, persistent, or metastatic cervical cancer assigned patients to the standard chemotherapy regimens of cisplatin plus paclitaxel or topotecan plus paclitaxel, with or without bevacizumab. The addition of bevacizumab to any regimen was associated with significant improvement in median overall survival (16.8 months vs 13.3 months), median progression-free survival (8.2 months vs 6.0 months), and response rate (49% vs 36%) without significant deterioration in health-related quality of life.(103)(104)(105) **(EG 1)**

For colon or rectal cancer (metastatic), evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** A systematic review and meta-analysis of 7 randomized controlled trials (3588 patients) evaluating the efficacy of bevacizumab for first-line treatment of metastatic colorectal cancer found that bevacizumab in combination with 5-fluorouracil-based chemotherapy was associated with prolonged progression-free and overall survival.(110) **(EG 1)** A systematic review and meta-analysis identified 8 studies and found that FOLFOXIRI-Bev (eg, fluorouracil, oxaliplatin, and irinotecan plus bevacizumab) therapy resulted in a pooled overall and curative resection rate of liver metastases of 39.1% and 28.1%, respectively, and a median overall survival of 30.2 months in patients previously diagnosed with unresectable metastatic colorectal cancer.(111) **(EG 1)** An open-label phase III trial of 820 patients with unresectable metastatic colorectal cancer that progressed after discontinuing first-line bevacizumab plus chemotherapy randomized patients to second-line chemotherapy (oxaliplatin-based or irinotecan-based) with or without bevacizumab; the addition of bevacizumab in second-line therapy was associated with an improvement in median overall survival (11.2 months vs 9.8 months) and median progression-free survival (5.7 months vs 4.1 months).(112) **(EG 1)** A meta-analysis (including 13 randomized studies) found that administration of the anti-EGFR antibody drugs (cetuximab or panitumumab) plus chemotherapy was associated with a likely survival benefit compared with administration of bevacizumab plus chemotherapy in patients with left-sided origination of colorectal cancer, while patients with right-sided disease had improved progression-free survival and overall survival associated with treatment with bevacizumab plus chemotherapy.(113) **(EG 1)**

For hepatocellular carcinoma, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. **(RG A2)** An open-label phase III trial of 501 patients with metastatic or unresectable hepatocellular carcinoma (all of whom had Child-Pugh class A liver disease, and none of whom had received prior systemic therapy) compared treatment with either combination atezolizumab plus bevacizumab or sorafenib and found, at a median follow-up of 8.6 months, that atezolizumab plus bevacizumab was associated with longer overall and progression-free survival compared with sorafenib.(117) **(EG 1)** A meta-analysis of 8 studies (342 patients) evaluating the efficacy of bevacizumab combined with erlotinib for advanced hepatocellular carcinoma found pooled objective response and disease control rates of 12.6% and 60.3%, respectively, a 16-week progression-free survival rate of 50.2%, and 6-month and 12-month overall survival rates of 74% and 43.7%, respectively. However, the authors noted that 7 of the included studies lacked a comparator arm, and there was high heterogeneity among the studies; further high-quality trials were recommended.(122) **(EG 1)**

For malignant glioma, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. **(RG A2)** A systematic review and meta-analysis of 11 randomized trials

(3743 patients) evaluating the efficacy of anti-angiogenic therapy for high-grade glioma found evidence that bevacizumab prolongs progression-free survival in newly diagnosed and recurrent glioblastoma; however, the impact on quality of life remains uncertain.(129) **(EG 1)** A randomized controlled study of 921 newly diagnosed patients found that the addition of bevacizumab to initial therapy had no effect upon quality of life during the progression-free period.(130) **(EG 1)** In a randomized controlled study of 921 patients with supratentorial glioblastoma, bevacizumab or placebo was added to a universal regimen of radiotherapy plus temozolomide. While bevacizumab significantly improved progression-free survival and maintenance of baseline health-related quality of life and performance status, overall survival did not improve, and significantly more adverse events were noted with bevacizumab.(131) **(EG 1)** Another randomized study of 978 patients with newly diagnosed central glioblastoma found no improvement in overall survival with bevacizumab added to radiotherapy plus temozolomide, although progression-free survival improved from 7.3 months to 10.7 months.(132)(133) **(EG 1)** A phase III randomized trial of 369 patients with recurrent glioblastoma (all of whom had been treated with temozolomide and radiation) compared further treatment with nivolumab or bevacizumab and found, at a median follow-up of 9.5 months, that bevacizumab was associated with longer progression-free survival, with no difference in overall survival seen between the groups; investigator-assessed objective response was higher with bevacizumab as compared with nivolumab (23.1% and 7.8%, respectively).(134) **(EG 1)** A phase III randomized controlled trial of 437 patients with progressive glioblastoma after chemoradiation found that treatment with lomustine plus bevacizumab was associated with improved median progression-free survival compared with lomustine monotherapy (4.2 months vs 1.5 months, respectively); however, there was no difference in overall survival between the treatment groups. Combination therapy was associated with increased grade 3 to 5 adverse effects, including pulmonary embolism and arterial hypertension.(135) **(EG 1)**

For malignant pleural mesothelioma, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. **(RG A2)** An open-label phase III randomized trial of 448 patients with unresectable pleural mesothelioma compared treatment with cisplatin plus pemetrexed with and without bevacizumab and found that treatment with bevacizumab was associated with prolonged overall and progression-free survival.(140) **(EG 1)** Specialty society practice guidelines and an expert consensus guideline recommend bevacizumab combined with pemetrexed and cisplatin(142) or carboplatin for first-line therapy of unresectable malignant pleural mesothelioma.(139)(141) **(EG 2)**

For non-small cell lung cancer, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** Meta-analyses of randomized controlled trials reported that bevacizumab is effective in improving response rate as well as progression-free(146) and overall survival in selected patients with advanced disease.(147)(148)(149) **(EG 1)** However, some authors feel that improvement in overall survival is debatable.(150) **(EG 2)** An open-label phase III randomized trial of 228 patients with advanced (stage IIIB or IV) or recurrent, EGFR-positive, nonsquamous non-small cell lung cancer compared treatment with erlotinib with and without bevacizumab and found, at 12.4-month follow-up, that bevacizumab was associated with prolonged progression-free survival.(151) **(EG 1)** Oncology practice guidelines recommend bevacizumab for advanced or metastatic non-small cell lung cancer as part of a combination chemotherapy regimen or as monotherapy maintenance; bevacizumab is not recommended for patients with squamous cell non-small cell lung cancer.(32)(152) **(EG 2)**

For ovarian (epithelial), fallopian tube, or primary peritoneal cancer, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** An open-label randomized study of 361 patients with histologically confirmed epithelial ovarian, fallopian tube, or primary peritoneal cancer that had progressed within 6 months of completion of platinum-based therapy found that the addition of bevacizumab to chemotherapy was associated with a statistically significant improvement in median progression-free survival (3.4 months vs 6.7 months) and a significantly higher objective response rate (27.3% vs 11.8%).(153) **(EG 1)** For patients with platinum-sensitive recurrent ovarian cancer, a randomized study of 484 patients found, at a median follow-up of 24 months, that patients treated with bevacizumab plus gemcitabine had improved progression-free survival compared with patients treated with gemcitabine plus placebo (12.4 months vs 8.4 months, respectively); however, at a median follow-up of 58.2 months, the 2 groups had comparable overall survival.(156)(157) **(EG 1)** A randomized study of 674 patients with recurrent platinum-sensitive epithelial ovarian, primary peritoneal, or fallopian tube cancer assigned patients to treatment with chemotherapy (consisting of carboplatin and paclitaxel) with or without bevacizumab; a secondary intervention assessing the role of cytoreduction was also studied but has not yet been reported. At a median follow-up of 49.6 months, intention-to-treat analysis showed that the chemotherapy-plus-bevacizumab group was associated with improved median survival as compared with the chemotherapy-alone group (42.2 months vs 37.3 months, respectively), but the difference was not statistically significant. However, the authors identified an error in treatment-free interval stratification data for 7% of patients, and sensitivity analysis did reveal a difference between treatment groups that was statistically significant.(158) **(EG 1)** A double-blind phase III trial randomly assigned 1873 women who had undergone debulking surgery for newly diagnosed stage III or stage IV epithelial ovarian cancer to either chemotherapy alone (ie, carboplatin plus paclitaxel), chemotherapy plus 5 cycles of bevacizumab, or chemotherapy plus 21 cycles of bevacizumab; median progression-free survival in the 3 groups was 10.3 months, 11.2 months, and 14.1 months, respectively.(159) **(EG 1)** Oncology practice guidelines and a systematic review recommend bevacizumab as a part of treatment strategies for recurrent platinum-resistant or platinum-sensitive epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.(160)(161)(162)(163) **(EG 2)** An open-label phase III trial of 406 patients with stage IIIB or IV ovarian cancer (all of whom had recurrent disease after treatment with platinum chemotherapy combined with bevacizumab) compared further treatment with chemotherapy (carboplatin plus paclitaxel, gemcitabine, or liposomal doxorubicin) alone or combined with bevacizumab and found, at a median follow-up of 20.1 months, that bevacizumab was associated with longer median progression-free survival compared with chemotherapy alone.(164) **(EG 1)** An open-label phase III trial of 682 patients with recurrent ovarian, primary peritoneal, or fallopian tube cancer compared further treatment with bevacizumab combined with either carboplatin plus gemcitabine or carboplatin plus liposomal doxorubicin and found that carboplatin plus liposomal doxorubicin was associated with longer progression-free and overall survival compared with carboplatin plus gemcitabine.(165) **(EG 1)**

For renal cell carcinoma, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. **(RG A2)** An open-label phase III randomized trial of 915 patients with previously untreated, unresectable, locally advanced or metastatic renal cell carcinoma (all with clear cell or sarcomatoid histology) compared treatment with either the combination of atezolizumab plus bevacizumab or sunitinib monotherapy and found that combination therapy was associated with prolonged progression-free survival compared with sunitinib. However, no difference in overall survival was seen between the groups, and longer-term follow-up was recommended.(173) **(EG 1)** A multicenter double-blind phase III trial of 649 previously untreated patients found that the combination of bevacizumab plus interferon alfa-2a produced a significantly higher objective tumor response rate and a longer mean duration of progression-free survival, but a statistically nonsignificant increase in overall survival, as compared with interferon given alone. However, more than half of patients in both study arms received at least one postprotocol antineoplastic therapy, which may have confounded the overall survival analysis.(174) **(EG 1)** A randomized double-blind phase II trial of 116 patients with metastatic clear cell renal cell carcinoma compared treatment with bevacizumab or placebo and found, at a median follow-up of 27 months, that bevacizumab was associated with longer progression-free survival and time to disease progression compared with placebo.(175) **(EG 1)** A phase II study of 39 patients with metastatic clear cell renal cell cancer (all of whom had failed first-line anti-vascular endothelial growth factor therapy) evaluating subsequent therapy with the combination of bevacizumab and temsirolimus found, at a median follow-up of 37 months, a 6-month progression-free survival rate of 50.9% and median overall survival of 18.2 months.(176) **(EG 2)** A phase II trial of 34 patients with metastatic or unresectable sarcomatoid renal cell cancer treated with the combination of capecitabine, gemcitabine, and bevacizumab found median progression-free survival of 5.5 months and median overall survival of 12 months.(177) **(EG 2)** Specialty society guidelines and a review article recommend bevacizumab plus interferon as first-line therapy for unresectable, metastatic, or relapsing predominantly clear cell renal carcinoma.(169)(178)(179) **(EG 2)**

Inconclusive or Non-Supportive Evidence

For breast cancer, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** Meta-analyses and systematic reviews of randomized controlled studies reported improvement in progression-free survival and overall response rate but no incremental improvement in overall survival.(3)(4)(5) **(EG 1)** A randomized controlled trial of 4994 patients with HER2-negative breast cancer (all of whom had lymph node-positive or high-risk lymph node-negative disease) compared 4 cycles of adjuvant chemotherapy (doxorubicin and cyclophosphamide) combined with bevacizumab or placebo, followed by 12 cycles of paclitaxel with or without bevacizumab, and found no difference in 5-year overall or invasive disease-free survival among the groups.(6) **(EG 1)** An open-label randomized phase III trial of 800 patients with HER2-negative breast cancer randomized to receive standard chemotherapy (eg, docetaxel, fluorouracil, epirubicin, cyclophosphamide) with or without neoadjuvant bevacizumab found, at 3.5-year follow-up, that among patients with a pathologic complete response, the addition of neoadjuvant bevacizumab was not associated with improvement in disease-free survival and overall survival compared with standard chemotherapy.(7) **(EG 1)** A pooled analysis from 2 randomized trials with a total of 749 patients (all of whom had unresectable, locally advanced or metastatic, hormone receptor-positive, HER2-negative breast cancer) comparing treatment with endocrine therapy with and without bevacizumab found, at a median follow-up of 34 months, that bevacizumab was associated with longer progression-free survival and a higher overall response rate compared with endocrine therapy alone. However, the authors noted there was no difference in overall survival seen between the groups, and that bevacizumab was associated with an increase in grade 3 and higher toxicities (eg, hypertension, proteinuria, cardiovascular events) leading to death.(8) **(EG 1)** A health technology appraisal and expert consensus guidelines note that bevacizumab may be considered in select cases of advanced breast cancer.(9)(10)(11) **(EG 2)**

For central serous chorioretinopathy, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A meta-analysis and systematic review of interventions for central serous chorioretinopathy found 4 low-quality studies that showed no incremental difference in visual acuity after 6 months of treatment with either ranibizumab or bevacizumab. The authors indicated that additional study is needed.(12) **(EG 1)**

For choroidal neovascularization secondary to angioid streaks, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A retrospective case series of 52 eyes (39 patients) with choroidal neovascularization secondary to angioid streaks treated as needed with bevacizumab (13 eyes), ranibizumab (33 eyes), or a combination (6 eyes) found, at a mean follow-up of 33.8 months, that treatment slowed the progression of choroidal neovascularization but did not prevent progressive visual loss. Further prospective randomized studies were recommended.(13) **(EG 2)** A prospective case series of 18 patients with non-subfoveal choroidal neovascularization with angioid streaks treated with intravitreal bevacizumab found no change in best-corrected visual acuity at 12 months, with subsequent worsening at 24 and 36 months.(14) **(EG 2)** A retrospective review of 20 patients (23 eyes) with choroidal neovascularization due to angioid streaks treated with intravitreal bevacizumab found, at a mean follow-up of 23 months, that treatment stabilized vision in affected eyes. Prospective randomized trials were recommended.(15) **(EG 2)**

For corneal neovascularization, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A meta-analysis of the effectiveness of bevacizumab for corneal neovascularization found 7 clinical studies, consisting primarily of small uncontrolled case series, suggesting efficacy, but the authors caution that larger, confirmatory, randomized controlled studies are necessary.(16) **(EG 2)**

For endometrial cancer, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A phase II randomized trial of 108 patients with advanced or recurrent endometrial cancer compared treatment with chemotherapy (carboplatin and paclitaxel) with and without bevacizumab and found that patients treated with bevacizumab had longer progression-free and overall survival compared with patients treated with chemotherapy alone,

though the differences did not reach statistical significance. However, the authors noted that the small number of included patients limited the results, and further studies were recommended.(17) **(EG 1)** An expert consensus guideline states that bevacizumab alone or combined with carboplatin and paclitaxel is a treatment option for recurrent, metastatic, or high-risk disease, based on phase II and retrospective studies.(18) **(EG 2)**

For gastric or gastroesophageal cancer, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A multicenter open-label randomized trial of 1063 patients with resectable esophagogastric adenocarcinoma compared perioperative treatment with the combination of epirubicin, cisplatin, and capecitabine with and without bevacizumab and found, at a median follow-up of 38.4 months, no difference in overall, progression-free, or disease-free survival between the groups; patients treated with bevacizumab had a higher incidence of wound healing complications and postoperative anastomotic leak (especially among those patients who underwent esophagogastrectomy).(19) **(EG 1)** A multinational randomized placebo-controlled trial of 774 patients with advanced gastric cancer reported that bevacizumab in combination with chemotherapy was associated with increased response rate and progression-free survival; however, the trial did not achieve its primary objective of a projected increase in overall survival.(20) **(EG 1)** An expert consensus guideline does not include bevacizumab as a treatment option for gastric or gastroesophageal cancer.(21)(22) **(EG 2)**

For head and neck cancer, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A phase III randomized trial of 403 patients with recurrent or metastatic squamous cell cancer of the head and neck compared platinum-based chemotherapy with and without bevacizumab and found that bevacizumab was associated with longer progression-free survival and a higher overall response rate compared with chemotherapy alone, with no difference in overall survival seen between the groups. However, bevacizumab was associated with more grade 3 or higher toxicities compared with chemotherapy alone, and further trials were recommended.(23) **(EG 1)** An expert consensus guideline does not include bevacizumab as a treatment option for head and neck cancer.(24) **(EG 2)**

For melanoma, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A phase III trial of 1343 patients (all with American Joint Committee on Cancer (AJCC) stage IIB, IIC, or III cutaneous melanoma) compared postoperative adjuvant therapy with bevacizumab or surveillance and found, at a median follow-up of 6.4 years, that although bevacizumab was associated with improvement in 5-year disease-free interval, there was no difference in overall survival or distant metastasis-free interval between the groups; the authors concluded that bevacizumab could not be recommended as standard adjuvant therapy in patients at high risk of disease recurrence.(25) **(EG 1)** A randomized phase II study of 214 previously untreated patients with advanced disease reported that the addition of bevacizumab to carboplatin plus paclitaxel did not meet the primary study objective of a statistically significant improvement in progression-free survival.(26) **(EG 1)**

For neovascular glaucoma, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A meta-analysis and systematic review studying the subconjunctival use of ranibizumab or bevacizumab to inhibit scar formation after trabeculectomy for glaucoma found 5 randomized controlled trials involving 177 eyes; however, the studies were heterogeneous and of low quality, and the authors stated that the evidence was insufficient to refute or support the use of ranibizumab or bevacizumab for this indication.(27) **(EG 1)** A systematic review evaluating intravitreal anti-vascular endothelial growth factors for treatment of neovascular glaucoma (including 2 studies of bevacizumab) found inconsistent effects on post-treatment intraocular pressure and visual acuity; further studies were recommended.(28) **(EG 1)**

For neuroendocrine tumors, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A consensus guideline and a systematic review found evidence that bevacizumab may be associated with improved response and progression-free survival, but the authors indicated that larger studies are necessary and that bevacizumab should not be used for this indication outside of a clinical trial.(29)(30) **(EG 2)**

For non-small cell lung cancer, adjuvant therapy for early-stage disease, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** An open-label, multicenter, randomized, phase III trial of 1501 patients with resected stage IB to IIIA non-small cell lung cancer found, at 50.3-month follow-up, that the addition of bevacizumab to 4 cycles of adjuvant cisplatin-based chemotherapy did not improve overall survival compared with chemotherapy alone and resulted in more reported high-grade toxicities. The authors concluded that bevacizumab should not be used in this setting.(31) **(EG 1)** An expert consensus guideline does not include bevacizumab as a recommended treatment option for adjuvant treatment of early disease.(32) **(EG 2)**

For ocular histoplasmosis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A retrospective chart review of 54 eyes with ocular histoplasmosis treated with either intravitreal bevacizumab or ranibizumab found, at an average of 26.8 months' follow-up, that treatment was associated with improved visual acuity. Due to lack of direct comparison or control, further prospective randomized trials were recommended.(33) **(EG 2)** A retrospective case series of 140 patients (150 eyes) with ocular histoplasmosis treated with intravitreal bevacizumab alone or combined with verteporfin photodynamic therapy found, at a mean follow-up of 21.1 months, no difference between the groups; both treatments resulted in visual stabilization in most patients. The authors recommended further randomized trials.(34) **(EG 2)** A review article notes that bevacizumab has been evaluated for treatment of ocular histoplasmosis only in case series, with good results.(35) **(EG 2)**

For pancreatic cancer, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A meta-analysis of randomized controlled studies found that bevacizumab was associated with moderate improvement in overall response rate in patients with advanced pancreatic cancer but not in progression-free survival or overall survival.(36) **(EG 1)** A systematic review and network meta-analysis of various chemotherapy combinations for pancreatic cancer could not find significant incremental improvement from the addition of bevacizumab to any regimen.(37) **(EG 1)**

For pterygium, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A meta-analysis of 18 randomized controlled trials (1045 eyes) evaluating the efficacy of bevacizumab for the treatment of pterygium found that treatment with bevacizumab was associated with reduced recurrence rates, especially in patients with a primary pterygia or those who received a conjunctival autograft. However, the authors noted that significant heterogeneity among the included studies limited the results, including different administration routes of the medication, different types of pterygium, and variable follow-up; the authors recommended further long-term studies.(38) **(EG 1)**

For radiation retinopathy, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A retrospective cohort study of patients with ciliary body or choroidal melanoma treated with plaque radiotherapy compared outcomes in patients who received postradiation bevacizumab (1131 patients) with those who did not receive bevacizumab (117 patients) and found, at up to 48-month follow-up, that bevacizumab was associated with better median logMAR (Snellen equivalent) visual acuity compared with those who did not receive bevacizumab. However, the authors noted that the lack of a randomized control group limited the results, and further studies were recommended.(39) **(EG 2)** A retrospective case series of 78 patients with radiation maculopathy compared intravitreal bevacizumab, triamcinolone, and dexamethasone implant and found no difference between the groups in central foveal thickness or visual improvement. The authors recommended further prospective randomized studies.(40) **(EG 2)** A retrospective review of 120 patients with radiation retinopathy treated with intravitreal bevacizumab or ranibizumab found, at a mean treatment interval of 38 months, that 80% of patients who received 3 or more injections remained within 2 lines of their initial visual acuity or better, with few acute or long-term side effects noted. However, due to the uncontrolled nature of the review, the authors noted that outcome assessments were limited.(41) **(EG 2)** A retrospective study of 418 patients compared intravitreal bevacizumab with no injection for prevention of macular edema and found, at 2-year follow-up, that bevacizumab was associated with less macular edema, vision loss, and poor visual acuity compared to no intervention; further controlled prospective studies were recommended.(42) **(EG 2)**

For retinal angiomatous proliferation, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A randomized study assigned 50 patients with early or moderate disease to either intravitreal bevacizumab or ranibizumab; each group demonstrated comparable significant improvement after 1 year. However, there was no untreated control group, and the authors indicated that large randomized studies are needed.(43) **(EG 1)**

For retinopathy of prematurity, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** Meta-analyses and systematic reviews have found that the vast majority of published studies on the use of vascular endothelial growth factor inhibitors for retinopathy of prematurity consist of case series, retrospective cohort studies, and nonrandomized studies that show possible benefit; however, the authors stress that high-quality studies are needed to better assess and confirm appropriate dosing, timing, and longer-term adverse effects.(44)(45) **(EG 1)**

For vitreal hemorrhage prophylaxis after vitrectomy, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A systematic review and meta-analysis of 12 randomized controlled trials (654 eyes) found evidence to support the preoperative use of intravitreal bevacizumab to prevent the incidence of early (within 4 weeks), but not late (1 to 6 months), postoperative vitreal cavity hemorrhage.(46) **(EG 1)** For proliferative diabetic retinopathy treated with vitrectomy, a randomized controlled trial of 107 eyes in 91 patients reported that best-corrected visual acuity was no different between the control group and the groups treated with either preoperative or intraoperative intravitreal bevacizumab.(47) **(EG 1)** However, a subsequent randomized study of 156 patients undergoing pars plana vitrectomy for proliferative diabetic retinopathy suggested that those receiving bevacizumab 5 to 10 days preoperatively may fare better than those receiving it 1 to 3 days preoperatively in terms of visual acuity and postoperative complications. The authors recommended further studies to evaluate potential dosing and timing in relation to clinical outcomes in this population.(48) **(EG 1)** Meta-analyses have found that while adjuvant intravitreal bevacizumab appeared to diminish intraoperative complications and early postoperative hemorrhage, additional studies are necessary to determine optimal doses and intervals for injection.(49)(50)(51)(52) **(EG 1)**

References

1. Avastin (bevacizumab) injection, for intravenous use. Physician Prescribing Information [Internet] Genentech, Inc. 2022 Sep Accessed at: https://www.avastin.com/. [created 2004; accessed 2022 Nov 11] [Context Link 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12]
2. Garcia J, et al. Bevacizumab (Avastin®) in cancer treatment: A review of 15 years of clinical experience and future outlook. Cancer Treatment Reviews 2020;86:Online. DOI: 10.1016/j.ctrv.2020.102017. [Context Link 1] View abstract...
3. Wagner AD, Thomssen C, Haerting J, Unverzagt S. Vascular-endothelial-growth-factor (VEGF) targeting therapies for endocrine refractory or resistant metastatic breast cancer. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD008941. DOI: 10.1002/14651858.CD008941.pub2. [Context Link 1] View abstract...
4. Partridge AH, et al. Chemotherapy and targeted therapy for women with human epidermal growth factor receptor 2-negative (or unknown) advanced breast cancer: American Society of Clinical Oncology Clinical Practice Guideline. Journal of Clinical Oncology 2014;32(29):3307-3329. DOI: 10.1200/JCO.2014.56.7479. [Context Link 1] View abstract...

5. Wei J, Luo Y, Fu D. Early and late outcomes of bevacizumab plus chemotherapy versus chemotherapy alone as a neoadjuvant treatment in HER2-negative nonmetastatic breast cancer: a meta-analysis of randomized controlled trials. OncoTargets and Therapy 2018;11:9049-9059. DOI: 10.2147/OTT.S186816. [Context Link 1] View abstract...
6. Miller KD, et al. Double blind phase III trial of adjuvant chemotherapy with and without bevacizumab in patients with lymph node-positive and high-risk lymph node-negative breast cancer (E5103). Journal of Clinical Oncology 2018;36(25):2621-2629. DOI: 10.1200/JCO.2018.79.2028. [Context Link 1] View abstract...
7. Earl HM, et al. Disease-free and overall survival at 3.5 years for neoadjuvant bevacizumab added to docetaxel followed by fluorouracil, epirubicin and cyclophosphamide, for women with HER2 negative early breast cancer: ARTemis Trial. Annals of Oncology 2017;28(8):1817-1824. DOI: 10.1093/annonc/mdx173. [Context Link 1] View abstract...
8. Martin M, et al. Evaluating the addition of bevacizumab to endocrine therapy as first-line treatment for hormone receptor-positive metastatic breast cancer: a pooled analysis from the LEA (GEICAM/2006-11_GBG51) and CALGB 40503 (Alliance) trials. European Journal of Cancer 2019;117:91-98. DOI: 10.1016/j.ejca.2019.06.002. [Context Link 1] View abstract...
9. Bevacizumab in Combination With a Taxane for the First-Line Treatment of Metastatic Breast Cancer. NICE Technology Appraisal Guidance TA214 [Internet] National Institute for Health and Care Excellence. 2011 Feb (NICE reviewed 2013) Accessed at: https://www.nice.org.uk/guidance/. [accessed 2022 Oct 22] [Context Link 1]
10. Gradishar WJ, et al. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 4.2022; 2022 Jun Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1]
11. Gennari A, et al. ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer. Annals of Oncology 2021;32(12):1475-1495. DOI: 10.1016/j.annonc.2021.09.019. (Reaffirmed 2022 Aug) [Context Link 1] View abstract...
12. Salehi M, Wenick AS, Law HA, Evans JR, Gehlbach P. Interventions for central serous chorioretinopathy: a network meta-analysis. Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD011841. DOI: 10.1002/14651858.CD011841.pub2. [Context Link 1] View abstract...
13. Giacomelli G, et al. Long-term follow-up of choroidal neovascularization due to angioid streaks with pro re nata intravitreal anti-VEGF treatment. Ophthalmologica 2017;238(1-2):44-51. DOI: 10.1159/000477498. [Context Link 1] View abstract...
14. Iacono P, Battaglia Parodi M, La Spina C, Bandello F. Intravitreal bevacizumab for nonsubfoveal choroidal neovascularization associated with angioid streaks: 3-year follow-up study. American Journal of Ophthalmology 2016;165:174-178. DOI: 10.1016/j.ajo.2016.03.017. [Context Link 1] View abstract...
15. Alagoz C, et al. Intravitreal bevacizmab in the treatment of choroidal neovascular membrane due to angioid streaks. Retina 2015;35(10):2001-2010. DOI: 10.1097/IAE.0000000000000605. [Context Link 1] View abstract...
16. Papathanassiou M, Theodoropoulou S, Analitis A, Tzonou A, Theodossiadis PG. Vascular endothelial growth factor inhibitors for treatment of corneal neovascularization: a meta-analysis. Cornea 2013;32(4):435-444. DOI: 10.1097/ICO.0b013e3182542613. [Context Link 1] View abstract...
17. Lorusso D, et al. Carboplatin-paclitaxel compared to Carboplatin-Paclitaxel-Bevacizumab in advanced or recurrent endometrial cancer: MITO END-2 - A randomized phase II trial. Gynecologic Oncology 2019;155(3):406-412. DOI: 10.1016/j.ygyno.2019.10.013. [Context Link 1] View abstract...
18. Abu-Rustum NR, et al. Uterine Neoplasms. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 1.2022; 2021 Nov Accessed at: https://www.nccn.org/. [accessed 2022 Aug 11] [Context Link 1]
19. Cunningham D, et al. Peri-operative chemotherapy with or without bevacizumab in operable oesophagogastric adenocarcinoma (UK Medical Research Council ST03): primary analysis results of a multicentre, open-label, randomised phase 2-3 trial. Lancet Oncology 2017;18(3):357-370. DOI: 10.1016/S1470-2045(17)30043-8. [Context Link 1] View abstract...
20. Ohtsu A, et al. Bevacizumab in combination with chemotherapy as first-line therapy in advanced gastric cancer: a randomized, double-blind, placebo-controlled phase III study. Journal of Clinical Oncology 2011;29(30):3968-3976. DOI: 10.1200/JCO.2011.36.2236. [Context Link 1] View abstract...
21. Ajani JA, et al. Gastric Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 2.2022; 2022 Jan Accessed at: https://www.nccn.org/guidelines/. [accessed 2022 Aug 10] [Context Link 1]
22. Ajani JA, et al. Esophageal and Esophagogastric Junction Cancers. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 3.2022; 2022 Jul Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1]
23. Argiris A, et al. Phase III randomized trial of chemotherapy with or without bevacizumab in patients with recurrent or metastatic head and neck cancer. Journal of Clinical Oncology 2019;37(34):3266-3274. DOI: 10.1200/JCO.19.00555. [Context Link 1] View abstract...
24. Pfister DG, et al. Head and Neck Cancers. NCCN Clinical Practice Guideline in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 2.2022; 2022 Apr Accessed at: https://www.nccn.org/. [accessed 2022 Aug 11] [Context Link 1]
25. Corrie PG, et al. Adjuvant bevacizumab for melanoma patients at high risk of recurrence: survival analysis of the AVAST-M trial. Annals of Oncology 2018;29(8):1843-1852. DOI: 10.1093/annonc/mdy229. [Context Link 1] View abstract...
26. Kim KB, et al. BEAM: a randomized phase II study evaluating the activity of bevacizumab in combination with carboplatin plus paclitaxel in patients with previously untreated advanced melanoma. Journal of Clinical Oncology 2012;30(1):34-41. DOI: 10.1200/JCO.2011.34.6270. [Context Link 1] View abstract...
27. Cheng JW, Cheng SW, Wei RL, Lu GC. Anti-vascular endothelial growth factor for control of wound healing in glaucoma surgery. Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD009782. DOI: 10.1002/14651858.CD009782.pub2. [Context Link 1] View abstract...
28. Simha A, Aziz K, Braganza A, Abraham L, Samuel P, Lindsley KB. Anti-vascular endothelial growth factor for neovascular glaucoma. Cochrane Database of Systematic Reviews 2020, Issue 2. Art. No.: CD007920. DOI: 10.1002/14651858.CD007920.pub3. [Context Link 1] View abstract...

29. Boudreaux JP, et al. The NANETS consensus guideline for the diagnosis and management of neuroendocrine tumors: well-differentiated neuroendocrine tumors of the jejunum, ileum, appendix, and cecum. Pancreas 2010;39(6):753-766. DOI: 10.1097/MPA.0b013e3181ebb2a5. [Context Link 1] View abstract...
30. Abdel-Rahman O, Fouad M. Bevacizumab-based combination therapy for advanced gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs): a systematic review of the literature. Journal of Cancer Research and Clinical Oncology 2015;141(2):295-305. DOI: 10.1007/s00432-014-1757-5. [Context Link 1] View abstract...
31. Wakelee HA, et al. Adjuvant chemotherapy with or without bevacizumab in patients with resected non-small-cell lung cancer (E1505): an open-label, multicentre, randomised, phase 3 trial. Lancet Oncology 2017;18(12):1610-1623. DOI: 10.1016/S1470-2045(17)30691-5. [Context Link 1] View abstract...
32. Ettinger DS, et al. Non-Small Cell Lung Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 3.2022; 2022 Mar Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1, 2, 3, 4, 5]
33. Nielsen JS, Fick TA, Saggau DD, Barnes CH. Intravitreal anti-vascular endothelial growth factor therapy for choroidal neovascularization secondary to ocular histoplasmosis syndrome. Retina 2012;32(3):468-472. DOI: 10.1097/IAE.0b013e318229b220. [Context Link 1] View abstract...
34. Cionni DA, et al. Analysis of outcomes for intravitreal bevacizumab in the treatment of choroidal neovascularization secondary to ocular histoplasmosis. Ophthalmology 2012;119(2):327-332. DOI: 10.1016/j.ophtha.2011.08.032. [Context Link 1] View abstract...
35. Diaz RI, Sigler EJ, Rafieetary MR, Calzada JI. Ocular histoplasmosis syndrome. Survey of Ophthalmology 2015;60(4):279-295. DOI: 10.1016/j.survophthal.2015.02.005. [Context Link 1] View abstract...
36. Tian W, Ding W, Kim S, Xu X, Pan M, Chen S. Efficacy and safety profile of combining agents against epidermal growth factor receptor or vascular endothelium growth factor receptor with gemcitabine-based chemotherapy in patients with advanced pancreatic cancer: a meta-analysis. Pancreatology 2013;13(4):415-422. DOI: 10.1016/j.pan.2013.04.195. [Context Link 1] View abstract...
37. Gresham GK, Wells GA, Gill S, Cameron C, Jonker DJ. Chemotherapy regimens for advanced pancreatic cancer: a systematic review and network meta-analysis. BMC Cancer 2014;14:471. DOI: 10.1186/1471-2407-14-471. [Context Link 1] View abstract...
38. Sun Y, Zhang B, Jia X, Ling S, Deng J. Efficacy and safety of bevacizumab in the treatment of pterygium: an updated meta-analysis of randomized controlled trials. Journal of Ophthalmology 2018;2018:4598173. DOI: 10.1155/2018/4598173. [Context Link 1] View abstract...
39. Shields CL, et al. Visual outcome at 4 years following plaque radiotherapy and prophylactic intravitreal bevacizumab (every 4 months for 2 Years) for uveal melanoma: comparison with nonrandomized historical control individuals. JAMA Ophthalmology 2020;138(2):136-146. DOI: 10.1001/jamaophthalmol.2019.5132. [Context Link 1] View abstract...
40. Seibel I, Hager A, Riechardt AI, Davids AM, Boker A, Joussen AM. Antiangiogenic or corticosteroid treatment in patients with radiation maculopathy after proton beam therapy for uveal melanoma. American Journal of Ophthalmology 2016;168:31-39. DOI: 10.1016/j.ajo.2016.04.024. [Context Link 1] View abstract...
41. Finger PT, Chin KJ, Semenova EA. Intravitreal anti-VEGF therapy for macular radiation retinopathy: a 10-year study. European Journal of Ophthalmology 2015;26(1):60-66. DOI: 10.5301/ejo.5000670. [Context Link 1] View abstract...
42. Shah SU, et al. Intravitreal bevacizumab at 4-month intervals for prevention of macular edema after plaque radiotherapy of uveal melanoma. Ophthalmology 2014;121(1):269-275. DOI: 10.1016/j.ophtha.2013.08.039. [Context Link 1] View abstract...
43. Parodi MB, et al. Intravitreal bevacizumab versus ranibizumab for the treatment of retinal angiomatous proliferation. Acta Ophthalmologica 2013;91(3):267-273. DOI: 10.1111/j.1755-3768.2011.02265.x. [Context Link 1] View abstract...
44. VanderVeen DK, Melia M, Yang MB, Hutchinson AK, Wilson LB, Lambert SR. Anti-vascular endothelial growth factor therapy for primary treatment of type 1 retinopathy of prematurity: a report by the American Academy of Ophthalmology. Ophthalmology 2017;124(5):619-633. DOI: 10.1016/j.ophtha.2016.12.025. [Context Link 1] View abstract...
45. Popovic MM, Nichani P, Muni RH, Mireskandari K, Tehrani NN, Kertes PJ. Intravitreal antivascular endothelial growth factor injection versus laser photocoagulation for retinopathy of prematurity: A meta-analysis of 3,701 eyes. Survey of Ophthalmology 2021;66(4):572-584. DOI: 10.1016/j.survophthal.2020.12.002. [Context Link 1] View abstract...
46. Smith JM, Steel DH. Anti-vascular endothelial growth factor for prevention of postoperative vitreous cavity haemorrhage after vitrectomy for proliferative diabetic retinopathy. Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD008214. DOI: 10.1002/14651858.CD008214.pub3. [Context Link 1] View abstract...
47. Ahn J, Woo SJ, Chung H, Park KH. The effect of adjunctive intravitreal bevacizumab for preventing postvitrectomy hemorrhage in proliferative diabetic retinopathy. Ophthalmology 2011;118(11):2218-2226. DOI: 10.1016/j.ophtha.2011.03.036. [Context Link 1] View abstract...
48. Castillo J, Aleman I, Rush SW, Rush RB. Preoperative Bevacizumab Administration in Proliferative Diabetic Retinopathy Patients Undergoing Vitrectomy: A Randomized and controlled trial comparing interval variation. American Journal of Ophthalmology 2017;183:1-10. DOI: 10.1016/j.ajo.2017.08.013. [Context Link 1] View abstract...
49. Zhang ZH, et al. Vitrectomy with or without preoperative intravitreal bevacizumab for proliferative diabetic retinopathy: a meta-analysis of randomized controlled trials. American Journal of Ophthalmology 2013;156(1):106-115.e2. DOI: 10.1016/j.ajo.2013.02.008. [Context Link 1] View abstract...
50. Martinez-Zapata MJ, et al. Anti-vascular endothelial growth factor for proliferative diabetic retinopathy. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD008721. DOI: 10.1002/14651858.CD008721.pub2. [Context Link 1] View abstract...
51. Simunovic MP, Maberley DA. Anti-vascular endothelial growth factor therapy for proliferative diabetic retinopathy: a systematic review and meta-analysis. Retina 2015;35(10):1931-1942. DOI: 10.1097/IAE.0000000000000723. [Context Link 1] View abstract...
52. Zhao XY, Xia S, Wang EQ, Chen YX. Efficacy of intravitreal injection of Bevacizamab in vitrectomy for patients with proliferative vitreoretinanopathy retinal detachment: A Meta-analysis of Prospective Studies. Retina 2018;38(3):462-470. DOI: 10.1097/IAE.0000000000001584. [Context Link 1] View abstract...

53. Michaelides M, et al. A prospective randomized trial of intravitreal bevacizumab or laser therapy in the management of diabetic macular edema (BOLT study) 12-month data: report 2. Ophthalmology 2010;117(6):1078-1086.e2. DOI: 10.1016/j.ophtha.2010.03.045. [Context Link 1, 2] View abstract...
54. Ford JA, Elders A, Shyangdan D, Royle P, Waugh N. The relative clinical effectiveness of ranibizumab and bevacizumab in diabetic macular oedema: an indirect comparison in a systematic review. British Medical Journal 2012;345:e5182. [Context Link 1] View abstract...
55. Stewart MW. Anti-VEGF therapy for diabetic macular edema. Current Diabetes Reports 2014;14(8):510. DOI: 10.1007/s11892-014-0510-4. [Context Link 1] View abstract...
56. VEGF inhibitors for AMD and diabetic macular edema. Medical Letter on Drugs and Therapeutics 2015;57(1464):41-42. [Context Link 1, 2] View abstract...
57. Virgili G, Parravano M, Evans JR, Gordon I, Lucenteforte E. Anti-vascular endothelial growth factor for diabetic macular oedema: a network meta-analysis. Cochrane Database of Systematic Reviews 2018, Issue 10. Art. No.: CD007419. DOI: 10.1002/14651858.CD007419.pub6. [Context Link 1, 2, 3] View abstract...
58. Mitchell P, Wong TY, Diabetic Macular Edema Treatment Guideline Working Group. Management paradigms for diabetic macular edema. American Journal of Ophthalmology 2014;157(3):505-513.e1-e8. DOI: 10.1016/j.ajo.2013.11.012. [Context Link 1, 2] View abstract...
59. Ehlers JP, et al. Intravitreal pharmacotherapies for diabetic macular edema: a report by the American Academy of Ophthalmology. Ophthalmology 2022;129(1):88-99. DOI: 10.1016/j.ophtha.2021.07.009. [Context Link 1] View abstract...
60. Veritti D, Sarao V, Soppelsa V, Lanzetta P. Managing diabetic macular edema in clinical practice: systematic review and meta-analysis of current strategies and treatment options. Clinical Ophthalmology (Auckland, N.Z.) 2021;15:375-385. DOI: 10.2147/OPTH.S236423. [Context Link 1] View abstract...
61. Soheilian M, Garfami KH, Ramezani A, Yaseri M, Peyman GA. Two-year results of a randomized trial of intravitreal bevacizumab alone or combined with triamcinolone versus laser in diabetic macular edema. Retina 2012;32(2):314-321. DOI: 10.1097/IAE.0b013e31822f55de. [Context Link 1] View abstract...
62. Zhang Y, Ma J, Meng N, Li H, Qu Y. Comparison of intravitreal triamcinolone acetonide with intravitreal bevacizumab for treatment of diabetic macular edema: a meta-analysis. Current Eye Research 2013;38(5):578-587. DOI: 10.3109/02713683.2013.767351. [Context Link 1] View abstract...
63. The Diabetic Retinopathy Clinical Research Network. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. New England Journal of Medicine 2015;372(13):1193-1203. DOI: 10.1056/NEJMoa1414264. [Context Link 1] View abstract...
64. Wells JA, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema: two-year results from a comparative effectiveness randomized clinical trial. Ophthalmology 2016;123(6):1351-1359. DOI: 10.1016/j.ophtha.2016.02.022. [Context Link 1] View abstract...
65. Mehta H, Hennings C, Gillies MC, Nguyen V, Campain A, Fraser-Bell S. Anti-vascular endothelial growth factor combined with intravitreal steroids for diabetic macular oedema. Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD011599. DOI: 10.1002/14651858.CD011599.pub2. [Context Link 1] View abstract...
66. Epstein DL, Algvere PV, von Wendt G, Seregard S, Kvanta A. Benefit from Bevacizumab for macular edema in central retinal vein occlusion: twelve-month results of a prospective, randomized study. Ophthalmology 2012;119(12):2587-2591. DOI: 10.1016/j.ophtha.2012.06.037. [Context Link 1] View abstract...
67. Ashraf M, Souka AA, Singh RP. Central retinal vein occlusion: modifying current treatment protocols. Eye (London, England) 2016;30(4):505-514. DOI: 10.1038/eye.2016.10. [Context Link 1] View abstract...
68. Yilmaz T, Cordero-Coma M. Use of bevacizumab for macular edema secondary to branch retinal vein occlusion: a systematic review. Graefe's Archive for Clinical and Experimental Ophthalmology 2012;250(6):787-793. DOI: 10.1007/s00417-012-2016-6. [Context Link 1] View abstract...
69. Cekic O, Cakir M, Yazici AT, Alagoz N, Bozkurt E, Faruk Yilmaz O. A comparison of three different intravitreal treatment modalities of macular edema due to branch retinal vein occlusion. Current Eye Research 2010;35(10):925-929. DOI: 10.3109/02713683.2010.496540. [Context Link 1, 2] View abstract...
70. Scott IU, et al. Effect of bevacizumab vs aflibercept on visual acuity among patients with macular edema due to central retinal vein occlusion: the SCORE2 randomized clinical trial. Journal of the American Medical Association 2017;317(20):2072-2087. DOI: 10.1001/jama.2017.4568. [Context Link 1] View abstract...
71. Yeh S, et al. Therapies for macular edema associated with central retinal vein occlusion: A report by the American Academy of Ophthalmology. Ophthalmology 2015;122(4):769-778. DOI: 10.1016/j.ophtha.2014.10.013. (Reaffirmed 2022 Jul) [Context Link 1] View abstract...
72. Ford JA, et al. Treatments for macular oedema following central retinal vein occlusion: systematic review. BMJ Open 2014;4(2):e004120. DOI: 10.1136/bmjopen-2013-004120. [Context Link 1] View abstract...
73. Ho M, Liu DT, Lam DS, Jonas JB. Retinal vein occulsions, from basics to the latest treatments. Retina 2016;36(3):432-448. DOI: 10.1097/IAE.0000000000000843. [Context Link 1] View abstract...
74. Shalchi Z, Mahroo O, Bunce C, Mitry D. Anti-vascular endothelial growth factor for macular oedema secondary to branch retinal vein occlusion. Cochrane Database of Systematic Reviews 2020, Issue 7. Art. No.: CD009510. DOI: 10.1002/14651858.CD009510.pub3. [Context Link 1] View abstract...
75. Spooner K, Hong T, Fraser-Bell S, Chang AA. Current Outcomes of Anti-VEGF Therapy in the Treatment of Macular Oedema Secondary to Branch Retinal Vein Occlusions: A Meta-Analysis. Ophthalmologica 2019;242(3):163-177. DOI: 10.1159/000497492. [Context Link 1] View abstract...
76. Hykin P, et al. Clinical effectiveness of intravitreal therapy with ranibizumab vs aflibercept vs bevacizumab for macular edema secondary to central retinal vein occlusion: a randomized clinical trial. JAMA Ophthalmology 2019;137(11):1256-1264. DOI: 10.1001/jamaophthalmol.2019.3305. [Context Link 1] View abstract...

77. Rajagopal R, et al. Bevacizumab versus ranibizumab in the treatment of macular edema due to retinal vein occlusion: 6-month results of the CRAVE study. Ophthalmic Surgery, Lasers & Imaging Retina 2015;46(8):844-850. DOI: 10.3928/23258160-20150909-09. [Context Link 1] View abstract...

78. Schmidt-Erfurth U, et al. Guidelines for the management of retinal vein occlusion by the European Society of Retina Specialists (EURETINA). Ophthalmologica 2019;242(3):123-162. DOI: 10.1159/000502041. [Context Link 1] View abstract...

79. Flaxel CJ, et al. Retinal Vein Occlusions. Preferred Practice Pattern [Internet] American Academy of Ophthalmology. 2019 Accessed at: https://www.aao.org/. [accessed 2022 Aug 25] DOI: 10.1016/j.ophtha.2019.09.029. [Context Link 1] View abstract...

80. Parodi MB, Iacono P, Kontadakis DS, Zucchiatti I, Cascavilla ML, Bandello F. Bevacizumab vs photodynamic therapy for choroidal neovascularization in multifocal choroiditis. Archives of Ophthalmology 2010;128(9):1100-1103. DOI: 10.1001/archophthalmol.2010.205. [Context Link 1] View abstract...

81. Zhu Y, Zhang T, Xu G, Peng L. Anti-vascular endothelial growth factor for choroidal neovascularisation in people with pathological myopia. Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No.: CD011160. DOI: 10.1002/14651858.CD011160.pub2. [Context Link 1] View abstract...

82. Cheung CMG, et al. Myopic choroidal neovascularization: review, guidance, and consensus statement on management. Ophthalmology 2017;124(11):1690-1711. DOI: 10.1016/j.ophtha.2017.04.028. [Context Link 1] View abstract...

83. The CATT Research Group. Ranibizumab and Bevacizumab for neovascular age-related macular degeneration. New England Journal of Medicine 2011;364(20):1897-1908. DOI: 10.1056/NEJMoa1102673. [Context Link 1, 2] View abstract...

84. Flaxel CJ, et al. Age-Related Macular Degeneration. Preferred Practice Pattern [Internet] American Academy of Ophthalmology. 2019 Accessed at: https://www.aao.org/. [accessed 2022 Aug 25] [Context Link 1, 2]

85. Solomon SD, Lindsley K, Vedula SS, Krzystolik MG, Hawkins BS. Anti-vascular endothelial growth factor for neovascular age-related macular degeneration. Cochrane Database of Systematic Reviews 2019, Issue 3. Art. No.: CD005139. DOI: 10.1002/14651858.CD005139.pub4. [Context Link 1] View abstract...

86. Santarelli M, Diplotti L, Samassa F, Veritti D, Kuppermann BD, Lanzetta P. Advances in pharmacotherapy for wet age-related macular degeneration. Expert Opinion on Pharmacotherapy 2015;16(12):1769-1781. DOI: 10.1517/14656566.2015.1067679. [Context Link 1] View abstract...

87. Berg K, Pedersen TR, Sandvik L, Bragadottir R. Comparison of ranibizumab and bevacizumab for neovascular age-related macular degeneration according to LUCAS treat-and-extend protocol. Ophthalmology 2015;122(1):146-152. DOI: 10.1016/j.ophtha.2014.07.041. [Context Link 1, 2] View abstract...

88. Tufail A, et al. Bevacizumab for neovascular age related macular degeneration (ABC Trial): multicentre randomised double masked study. British Medical Journal 2010;340:c2459. [Context Link 1] View abstract...

89. Patel PJ, Chen FK, Da Cruz L, Rubin GS, Tufail A, ABC Trial Study Group. Contrast sensitivity outcomes in the ABC Trial: a randomized trial of bevacizumab for neovascular age-related macular degeneration. Investigative Ophthalmology & Visual Science 2011;52(6):3089-3093. DOI: 10.1167/iovs.10-6208. [Context Link 1] View abstract...

90. Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group, et al. Ranibizumab and Bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology 2012;119(7):1388-1398. DOI: 10.1016/j.ophtha.2012.03.053. [Context Link 1] View abstract...

91. Scott AW, Bressler SB. Long-term follow-up of vascular endothelial growth factor inhibitor therapy for neovascular age-related macular degeneration. Current Opinion in Ophthalmology 2013;24(3):190-196. DOI: 10.1097/ICU.0b013e32835fefee. [Context Link 1] View abstract...

92. Johnson D, Sharma S. Ocular and systemic safety of bevacizumab and ranibizumab in patients with neovascular age-related macular degeneration. Current Opinion in Ophthalmology 2013;24(3):205-212. DOI: 10.1097/ICU.0b013e32835f8ec0. [Context Link 1] View abstract...

93. IVAN Study Investigators, et al. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. Ophthalmology 2012;119(7):1399-1411. DOI: 10.1016/j.ophtha.2012.04.015. [Context Link 1] View abstract...

94. Kodjikian L, et al. Ranibizumab versus Bevacizumab for neovascular age-related macular degeneration: Results from the GEFAL noninferiority randomized trial. Ophthalmology 2013;120(11):2300-2309. DOI: 10.1016/j.ophtha.2013.06.020. [Context Link 1] View abstract...

95. Schauwvlieghe AM, et al. Comparing the effectiveness of bevacizumab to ranibizumab in patients with exudative age-related macular degeneration. The BRAMD study. PLoS ONE 2016;11(5):e0153052. DOI: 10.1371/journal.pone.0153052. [Context Link 1] View abstract...

96. Kodjikian L, et al. Bevacizumab and ranibizumab for neovascular age-related macular degeneration: an updated meta-analysis of randomised clinical trials. Graefe's Archive for Clinical and Experimental Ophthalmology 2014;252(10):1529-1537. DOI: 10.1007/s00417-014-2764-6. [Context Link 1] View abstract...

97. Adler MJ, Dimitrov DS. Therapeutic antibodies against cancer. Hematology/Oncology Clinics of North America 2012;26(3):447-481, vii. DOI: 10.1016/j.hoc.2012.02.013. [Context Link 1] View abstract...

98. Roviello G, et al. The role of bevacizumab in solid tumours: A literature based meta-analysis of randomised trials. European Journal of Cancer 2017;75:245-258. DOI: 10.1016/j.ejca.2017.01.026. [Context Link 1] View abstract...

99. Abu-Rustum NR, et al. Cervical Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 1.2022; 2021 Oct Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1, 2]

100. Tewari KS, Monk BJ. New strategies in advanced cervical cancer: from angiogenesis blockade to immunotherapy. Clinical Cancer Research 2014;20(21):5349-5358. DOI: 10.1158/1078-0432.CCR-14-1099. [Context Link 1] View abstract...

101. Eskander RN, Tewari KS. Targeting angiogenesis in advanced cervical cancer. Therapeutic Advances in Medical Oncology 2014;6(6):280-292. DOI: 10.1177/1758834014543794. [Context Link 1] View abstract...

102. Bizzarri N, et al. Bevacizumab for the treatment of cervical cancer. Expert Opinion on Biological Therapy 2016;16(3):407-419. DOI: 10.1517/14712598.2016.1145208. [Context Link 1] View abstract...

103. Tewari KS, et al. Improved survival with bevacizumab in advanced cervical cancer. New England Journal of Medicine 2014;370(8):734-743. DOI: 10.1056/NEJMoa1309748. [Context Link 1] View abstract...

104. Penson RT, et al. Bevacizumab for advanced cervical cancer: patient-reported outcomes of a randomised, phase 3 trial (NRG Oncology-Gynecologic Oncology Group protocol 240). Lancet Oncology 2015;16(3):301-311. DOI: 10.1016/S1470-2045(15)70004-5. [Context Link 1] View abstract...

105. Tewari KS, et al. Bevacizumab for advanced cervical cancer: final overall survival and adverse event analysis of a randomised, controlled, open-label, phase 3 trial (Gynecologic Oncology Group 240). Lancet 2017;390(10103):1654-1663. DOI: 10.1016/S0140-6736(17)31607-0. [Context Link 1] View abstract...

106. Benson AB III, et al. Colon Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 1.2022; 2022 Feb Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1]

107. Benson AB III, et al. Rectal Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 1.2022; 2022 Feb Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1]

108. Loupakis F, et al. Initial therapy with FOLFOXIRI and bevacizumab for metastatic colorectal cancer. New England Journal of Medicine 2014;371(17):1609-1618. DOI: 10.1056/NEJMoa1403108. [Context Link 1] View abstract...

109. Biller LH, Schrag D. Diagnosis and treatment of metastatic colorectal cancer: a review. Journal of the American Medical Association 2021;325(7):669-685. DOI: 10.1001/jama.2021.0106. [Context Link 1] View abstract...

110. Baraniskin A, et al. Efficacy of bevacizumab in first-line treatment of metastatic colorectal cancer: A systematic review and meta-analysis. European Journal of Cancer 2019;106:37-44. DOI: 10.1016/j.ejca.2018.10.009. [Context Link 1] View abstract...

111. Tomasello G, Petrelli F, Ghidini M, Russo A, Passalacqua R, Barni S. FOLFOXIRI plus bevacizumab as conversion therapy for patients with initially unresectable metastatic colorectal cancer: a systematic review and pooled analysis. JAMA Oncology 2017;3(7):e170278. DOI: 10.1001/jamaoncol.2017.0278. [Context Link 1] View abstract...

112. Bennouna J, et al. Continuation of bevacizumab after first progression in metastatic colorectal cancer (ML18147): a randomised phase 3 trial. Lancet Oncology 2013;14(1):29-37. DOI: 10.1016/S1470-2045(12)70477-1. [Context Link 1] View abstract...

113. Holch JW, Ricard I, Stintzing S, Modest DP, Heinemann V. The relevance of primary tumour location in patients with metastatic colorectal cancer: A meta-analysis of first-line clinical trials. European Journal of Cancer 2017;70:87-98. DOI: 10.1016/j.ejca.2016.10.007. [Context Link 1] View abstract...

114. Ren T, et al. Efficacy and safety of bevacizumab plus oxaliplatin- or irinotecan-based doublet backbone chemotherapy as the first-line treatment of metastatic colorectal cancer: a systematic review and meta-analysis. Drug Safety 2021;44(1):29-40. DOI: 10.1007/s40264-020-00997-2. [Context Link 1] View abstract...

115. Skelton WP, Franke AJ, Iqbal A, George TJ. Comprehensive literature review of randomized clinical trials examining novel treatment advances in patients with colon cancer. Journal of Gastrointestinal Oncology 2020;11(4):790-802. DOI: 10.21037/jgo-20-184. [Context Link 1] View abstract...

116. Giusti RM, Cohen MH, Keegan P, Pazdur R. FDA review of a panitumumab (Vectibix) clinical trial for first-line treatment of metastatic colorectal cancer. Oncologist 2009;14(3):284-290. DOI: 10.1634/theoncologist.2008-0254. [Context Link 1] View abstract...

117. Finn RS, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. New England Journal of Medicine 2020;382(20):1894-1905. DOI: 10.1056/NEJMoa1915745. [Context Link 1, 2] View abstract...

118. Benson AB III, et al. Hepatobiliary Cancers. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 2.2022; 2022 Jul Accessed at: https://www.nccn.org/. [accessed 2022 Aug 11] [Context Link 1]

119. Haber PK, et al. Evidence-based management of HCC: Systematic review and meta-analysis of randomized controlled trials (2002-2020). Gastroenterology 2021;161(3):879-898. DOI: 10.1053/j.gastro.2021.06.008. [Context Link 1] View abstract...

120. Greten TF, et al. Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of hepatocellular carcinoma. Journal for Immunotherapy of Cancer 2021;9(9):e002794. DOI: 10.1136/jitc-2021-002794. [Context Link 1] View abstract...

121. Su GL, et al. AGA clinical practice guideline on systemic therapy for hepatocellular carcinoma. Gastroenterology 2022;162(3):920-934. DOI: 10.1053/j.gastro.2021.12.276. (Reaffirmed 2022 Mar) [Context Link 1] View abstract...

122. He L, et al. Efficacy of bevacizumab combined with erlotinib for advanced hepatocellular carcinoma: a single-arm meta-analysis based on prospective studies. BMC Cancer 2019;19(1):276. DOI: 10.1186/s12885-019-5487-6. [Context Link 1] View abstract...

123. Llovet JM, et al. Hepatocellular carcinoma. Nature Reviews. Disease Primers 2021;7(1):6. DOI: 10.1038/s41572-020-00240-3. [Context Link 1] View abstract...

124. Omuro A, DeAngelis LM. Glioblastoma and other malignant gliomas: a clinical review. Journal of the American Medical Association 2013;310(17):1842-1850. DOI: 10.1001/jama.2013.280319. [Context Link 1] View abstract...

125. Koukourakis GV. Bevacizumab for malignant brain gliomas. Which is the current evidence? Recent Patents on Inflammation & Allergy Drug Discovery 2015;9(2):136-143. [Context Link 1] View abstract...

126. Narita Y. Bevacizumab for glioblastoma. Therapeutics and Clinical Risk Management 2015;11:1759-1765. DOI: 10.2147/TCRM.S58289. [Context Link 1] View abstract...

127. Tamura R, Tanaka T, Miyake K, Yoshida K, Sasaki H. Bevacizumab for malignant gliomas: current indications, mechanisms of action and resistance, and markers of response. Brain Tumor Pathology 2017;34(2):62-77. DOI: 10.1007/s10014-017-0284-x. [Context Link 1] View abstract...

128. Nabors LB, et al. Central Nervous System Cancers. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 1.2022; 2022 Jun Accessed at: https://www.nccn.org/guidelines/. [accessed 2022 Aug 10] [Context Link 1, 2]

129. Ameratunga M, Pavlakis N, Wheeler H, Grant R, Simes J, Khasraw M. Anti-angiogenic therapy for high-grade glioma. Cochrane Database of Systematic Reviews 2018, Issue 11. Art. No.: CD008218. DOI: 10.1002/14651858.CD008218.pub4. [Context Link 1] View abstract...

130. Taphoorn MJ, et al. Health-related quality of life in a randomized phase III study of bevacizumab, temozolomide, and radiotherapy in newly diagnosed glioblastoma. Journal of Clinical Oncology 2015;33(19):2166-2175. DOI: 10.1200/JCO.2014.60.3217. [Context Link 1] View abstract...

131. Chinot OL, et al. Bevacizumab plus radiotherapy-temozolomide for newly diagnosed glioblastoma. New England Journal of Medicine 2014;370(8):709-722. DOI: 10.1056/NEJMoa1308345. [Context Link 1] View abstract...

132. Gilbert MR, et al. A randomized trial of bevacizumab for newly diagnosed glioblastoma. New England Journal of Medicine 2014;370(8):699-708. DOI: 10.1056/NEJMoa1308573. [Context Link 1] View abstract...

133. Fine HA. Bevacizumab in glioblastoma--still much to learn. New England Journal of Medicine 2014;370(8):764-765. DOI: 10.1056/NEJMe1313309. [Context Link 1] View abstract...

134. Reardon DA, et al. Effect of nivolumab vs bevacizumab in patients with recurrent glioblastoma: the CheckMate 143 Phase 3 randomized clinical trial. JAMA Oncology 2020;6(7):1-8. DOI: 10.1001/jamaoncol.2020.1024. [Context Link 1] View abstract...

135. Wick W, et al. Lomustine and bevacizumab in progressive glioblastoma. New England Journal of Medicine 2017;377(20):1954-1963. DOI: 10.1056/NEJMoa1707358. [Context Link 1] View abstract...

136. Seystahl K, Wick W, Weller M. Therapeutic options in recurrent glioblastoma-An update. Critical Reviews in Oncology/Hematology 2016;99:389-408. DOI: 10.1016/j.critrevonc.2016.01.018. [Context Link 1] View abstract...

137. Funakoshi Y, et al. Update on chemotherapeutic approaches and management of bevacizumab usage for glioblastoma. Pharmaceuticals (Basel, Switzerland) 2020;13(12):Online. DOI: 10.3390/ph13120470. [Context Link 1] View abstract...

138. Tan AC, Ashley DM, Lopez GY, Malinzak M, Friedman HS, Khasraw M. Management of glioblastoma: State of the art and future directions. CA - A Cancer Journal for Clinicians 2020;70(4):299-312. DOI: 10.3322/caac.21613. [Context Link 1] View abstract...

139. Ettinger DS, et al. Malignant Pleural Mesothelioma. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 1.2022; 2021 Dec Accessed at: https://www.nccn.org/. [accessed 2022 Aug 11] [Context Link 1, 2, 3]

140. Zalcman G, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. Lancet 2016;387(10026):1405-14. DOI: 10.1016/S0140-6736(15)01238-6. [Context Link 1, 2] View abstract...

141. Popat S, et al. Malignant pleural mesothelioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2022;33(2):129-142. DOI: 10.1016/j.annonc.2021.11.005. (Reaffirmed 2022 Mar) [Context Link 1, 2] View abstract...

142. Kindler HL, et al. Treatment of malignant pleural mesothelioma: American Society of Clinical Oncology clinical practice guideline. Journal of Clinical Oncology 2018;36(13):1343-1373. DOI: 10.1200/JCO.2017.76.6394. (Reaffirmed 2022 Jul) [Context Link 1] View abstract...

143. Planchard D. Bevacizumab in non-small-cell lung cancer: a review. Expert Review of Anticancer Therapy 2011;11(8):1163-1179. DOI: 10.1586/era.11.80. [Context Link 1] View abstract...

144. Hong S, Tan M, Wang S, Luo S, Chen Y, Zhang L. Efficacy and safety of angiogenesis inhibitors in advanced non-small cell lung cancer: a systematic review and meta-analysis. Journal of Cancer Research and Clinical Oncology 2015;141(5):909-921. DOI: 10.1007/s00432-014-1862-5. [Context Link 1] View abstract...

145. Singh N, et al. Therapy for stage IV non-small-cell lung cancer with driver alterations: ASCO living guideline. Journal of Clinical Oncology 2022;40(28):3310-3322. DOI: 10.1200/JCO.22.00824. (Reaffirmed 2022 Aug) [Context Link 1] View abstract...

146. Botrel TE, Clark O, Clark L, Paladini L, Faleiros E, Pegoretti B. Efficacy of bevacizumab (Bev) plus chemotherapy (CT) compared to CT alone in previously untreated locally advanced or metastatic non-small cell lung cancer (NSCLC): systematic review and meta-analysis. Lung Cancer 2011;74(1):89-97. DOI: 10.1016/j.lungcan.2011.01.028. [Context Link 1] View abstract...

147. Cui J, Cai X, Zhu M, Liu T, Zhao N. The efficacy of bevacizumab compared with other targeted drugs for patients with advanced NSCLC: a meta-analysis from 30 randomized controlled clinical trials. PLoS ONE 2013;8(4):e62038. DOI: 10.1371/journal.pone.0062038. [Context Link 1] View abstract...

148. Soria JC, et al. Systematic review and meta-analysis of randomised, phase II/III trials adding bevacizumab to platinum-based chemotherapy as first-line treatment in patients with advanced non-small-cell lung cancer. Annals of Oncology 2013;24(1):20-30. DOI: 10.1093/annonc/mds590. [Context Link 1] View abstract...

149. Lima AB, Macedo LT, Sasse AD. Addition of bevacizumab to chemotherapy in advanced non-small cell lung cancer: a systematic review and meta-analysis. PLoS ONE 2011;6(8):e22681. DOI: 10.1371/journal.pone.0022681. [Context Link 1] View abstract...

150. Snee M. Bevacizumab in non-small cell lung cancer: an overview of practice in the era of molecular testing. Clinical Oncology 2014;26(8):468-472. DOI: 10.1016/j.clon.2014.05.004. [Context Link 1] View abstract...

151. Saito H, et al. Erlotinib plus bevacizumab versus erlotinib alone in patients with EGFR-positive advanced non-squamous non-small-cell lung cancer (NEJ026): interim analysis of an open-label, randomised, multicentre, phase 3 trial. Lancet Oncology 2019;20(5):625-635. DOI: 10.1016/S1470-2045(19)30035-X. [Context Link 1] View abstract...

152. Singh N, et al. Therapy for stage IV non-small-cell lung cancer without driver alterations: ASCO living guideline. Journal of Clinical Oncology 2022;40(28):3323-3343. DOI: 10.1200/JCO.22.00825. (Reaffirmed 2022 Jul) [Context Link 1, 2] View abstract...

153. Pujade-Lauraine E, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial. Journal of Clinical Oncology 2014;32(13):1302-1308. DOI: 10.1200/JCO.2013.51.4489. [Context Link 1, 2, 3, 4] View abstract...

154. Colombo N, Conte PF, Pignata S, Raspagliesi F, Scambia G. Bevacizumab in ovarian cancer: Focus on clinical data and future perspectives. Critical Reviews in Oncology/Hematology 2016;97:335-348. DOI: 10.1016/j.critrevonc.2015.08.017. [Context Link 1] View abstract...

155. Wu YS, Shui L, Shen D, Chen X. Bevacizumab combined with chemotherapy for ovarian cancer: an updated systematic review and meta-analysis of randomized controlled trials. Oncotarget 2017;8(6):10703-10713. DOI: 10.18632/oncotarget.12926. [Context Link 1] View abstract...

156. Aghajanian C, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. Journal of Clinical Oncology 2012;30(17):2039-2045. DOI: 10.1200/JCO.2012.42.0505. [Context Link 1] View abstract...

157. Aghajanian C, Goff B, Nycum LR, Wang YV, Husain A, Blank SV. Final overall survival and safety analysis of OCEANS, a phase 3 trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent ovarian cancer. Gynecologic Oncology 2015;139(1):10-16. DOI: 10.1016/j.ygyno.2015.08.004. [Context Link 1] View abstract...

158. Coleman RL, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncology 2017;18(6):779-791. DOI: 10.1016/S1470-2045(17)30279-6. [Context Link 1] View abstract...

159. Burger RA, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. New England Journal of Medicine 2011;365(26):2473-83. DOI: 10.1056/NEJMoa1104390. [Context Link 1] View abstract...

160. Aravantinos G, Pectasides D. Bevacizumab in combination with chemotherapy for the treatment of advanced ovarian cancer: a systematic review. Journal of Ovarian Research 2014;7:57. DOI: 10.1186/1757-2215-7-57. [Context Link 1] View abstract...

161. Matsumoto K, Onda T, Yaegashi N. Pharmacotherapy for recurrent ovarian cancer: current status and future perspectives. Japanese Journal of Clinical Oncology 2015;45(5):408-410. DOI: 10.1093/jjco/hyv014. [Context Link 1] View abstract...

162. Rossi L, et al. Bevacizumab in ovarian cancer: A critical review of phase III studies. Oncotarget 207;8(7):12389-12405. DOI: 10.18632/oncotarget.13310. [Context Link 1] View abstract...

163. Armstrong DK, et al. Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 3.2022; 2022 Jul Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1]

164. Pignata S, et al. Carboplatin-based doublet plus bevacizumab beyond progression versus carboplatin-based doublet alone in patients with platinum-sensitive ovarian cancer: a randomised, phase 3 trial. Lancet Oncology 2021;22(2):267-276. DOI: 10.1016/S1470-2045(20)30637-9. [Context Link 1] View abstract...

165. Pfisterer J, et al. Bevacizumab and platinum-based combinations for recurrent ovarian cancer: a randomised, open-label, phase 3 trial. Lancet Oncology 2020;21(5):699-709. DOI: 10.1016/S1470-2045(20)30142-X. [Context Link 1] View abstract...

166. Ray-Coquard I, et al. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. New England Journal of Medicine 2019;381(25):2416-2428. DOI: 10.1056/NEJMoa1911361. [Context Link 1] View abstract...

167. Kuroki L, Guntupalli SR. Treatment of epithelial ovarian cancer. British Medical Journal 2020;371:m3773. DOI: 10.1136/bmj.m3773. [Context Link 1] View abstract...

168. Motzer RJ, et al. Kidney Cancer. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 2.2023; 2022 Aug Accessed at: https://www.nccn.org/. [accessed 2022 Aug 10] [Context Link 1]

169. Patard JJ, et al. ICUD-EAU International Consultation on Kidney Cancer 2010: treatment of metastatic disease. European Urology 2011;60(4):684-90. DOI: 10.1016/j.eururo.2011.06.017. (Reaffirmed 2022 Jun) [Context Link 1, 2] View abstract...

170. Unverzagt S, et al. Immunotherapy for metastatic renal cell carcinoma. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD011673. DOI: 10.1002/14651858.CD011673.pub2. [Context Link 1] View abstract...

171. Chowdhury N, Drake CG. Kidney cancer: an overview of current therapeutic approaches. Urologic Clinics of North America 2020;47(4):419-431. DOI: 10.1016/j.ucl.2020.07.009. [Context Link 1] View abstract...

172. Rathmell WK, et al. Management of metastatic clear cell renal cell carcinoma: ASCO guideline. Journal of Clinical Oncology 2022;40(25):2957-2995. DOI: 10.1200/JCO.22.00868. [Context Link 1] View abstract...

173. Rini BI, et al. Atezolizumab plus bevacizumab versus sunitinib in patients with previously untreated metastatic renal cell carcinoma (IMmotion151): a multicentre, open-label, phase 3, randomised controlled trial. Lancet 2019;393(10189):2404-2415. DOI: 10.1016/S0140-6736(19)30723-8. [Context Link 1] View abstract...

174. Escudier B, et al. Phase III trial of bevacizumab plus interferon alfa-2a in patients with metastatic renal cell carcinoma (AVOREN): final analysis of overall survival. Journal of Clinical Oncology 2010;28(13):2144-2150. DOI: 10.1200/JCO.2009.26.7849. [Context Link 1] View abstract...

175. Yang JC, et al. A randomized trial of bevacizumab, an anti-vascular endothelial growth factor antibody, for metastatic renal cancer. New England Journal of Medicine 2003;349(5):427-34. DOI: 10.1056/NEJMoa021491. [Context Link 1] View abstract...

176. Bamias A, et al. The combination of bevacizumab/temsirolimus after first-line anti-VEGF therapy in advanced renal-cell carcinoma: a clinical and biomarker study. International Journal of Clinical Oncology 2019;24(4):411-419. DOI: 10.1007/s10147-018-1361-9. [Context Link 1] View abstract...

177. Maiti A, et al. Phase 2 trial of capecitabine, gemcitabine, and bevacizumab in sarcomatoid renal-cell carcinoma. Clinical Genitourinary Cancer 2017;S1558-7673(17):30238-0. DOI: 10.1016/j.clgc.2017.07.028. [Context Link 1] View abstract...

178. Escudier B, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2019;30(5):706-720. DOI: 10.1093/annonc/mdz056. (Reaffirmed 2022 Jul) [Context Link 1] View abstract...

179. Jonasch E, Gao J, Rathmell WK. Renal cell carcinoma. British Medical Journal 2014;349:g4797. [Context Link 1] View abstract...

Footnotes

[A] For diabetic macular edema, in a randomized trial, bevacizumab was administered by intravitreal injection every 6 weeks for 12 weeks and then as needed with evaluation every 6 weeks.(53) [A in Context Link 1]

[B] For macular edema following retinal vein occlusion, in a randomized trial, bevacizumab was administered by intravitreal injection every 6 weeks for 12 months.(66)(67) [B in Context Link 1]

[C] For myopic choroidal neovascularization, in a randomized trial, bevacizumab was administered by intravitreal injection once monthly for 3 months and then as needed with monthly evaluation.(80) [C in Context Link 1]

[D] For neovascular age-related macular degeneration, in a randomized trial, bevacizumab was administered by intravitreal injection either monthly or as needed with monthly evaluation.(83) [D in Context Link 1]

[E] For cervical cancer (persistent, recurrent, or metastatic), bevacizumab is administered as an intravenous infusion every 3 weeks in combination with one of the following intravenous chemotherapy regimens: cisplatin and paclitaxel, carboplatin and paclitaxel, or topotecan and paclitaxel.(1)(99) [E in Context Link 1]

[F] For colon or rectal cancer (metastatic), bevacizumab is administered as an intravenous infusion every 2 or 3 weeks in combination with chemotherapy (eg, 5-fluorouracil, fluoropyrimidine-oxaliplatin, fluoropyrimidine-irinotecan, or fluoropyrimidine-oxaliplatin). Administration should continue until disease progression or occurrence of unacceptable side effects.(1) [F in Context Link 1]

[G] For hepatocellular carcinoma, bevacizumab is administered intravenously every 3 weeks in combination with atezolizumab.(1) [G in Context Link 1]

[H] For malignant glioma, bevacizumab is administered as an intravenous infusion every 2 weeks. Administration should continue until disease progression or occurrence of unacceptable side effects.(1) [H in Context Link 1]

[I] Salvage therapy may include treatment of symptoms due to radiation therapy necrosis, vasogenic edema, or mass effect.(128) [I in Context Link 1]

[J] For mesothelioma, bevacizumab is administered as an intravenous infusion every 3 weeks in combination with pemetrexed and either cisplatin or carboplatin. Administration should continue until disease progression or occurrence of unacceptable side effects.(139) [J in Context Link 1]

[K] For non-small cell lung cancer, bevacizumab is administered as an intravenous infusion every 3 weeks.(1) Administration should continue until disease progression or occurrence of unacceptable side effects.(32) [K in Context Link 1]

[L] For adjuvant therapy of stage II to IV epithelial ovarian, fallopian tube, or primary peritoneal cancer, bevacizumab is administered as an intravenous infusion every 3 weeks in combination with standard chemotherapy for up to 18 weeks, followed by maintenance monotherapy every 3 weeks. Administration should continue for a total of 66 weeks or until disease progression.(1) For use in conjunction with olaparib, bevacizumab has been evaluated at a dosing interval of every 3 weeks for a total of 15 months.(166) [L in Context Link 1]

[M] For platinum-resistant recurrent ovarian (epithelial), fallopian tube, or primary peritoneal cancer, bevacizumab is administered as an intravenous infusion every 2 weeks in combination with intravenous paclitaxel, pegylated liposomal doxorubicin, or weekly topotecan, or every 3 weeks in combination with intravenous topotecan.(1) Administration should continue until disease progression or occurrence of unacceptable side effects.(153) [M in Context Link 1]

[N] For platinum-sensitive recurrent ovarian (epithelial), fallopian tube, or primary peritoneal cancer, bevacizumab is administered as an intravenous infusion every 3 weeks in combination with either carboplatin-paclitaxel for 6 to 8 cycles, or carboplatin-gemcitabine for 6 to 10 cycles, followed by single-agent monotherapy every 3 weeks.(1) Administration should continue until disease progression or occurrence of unacceptable side effects.(153) [N in Context Link 1]

[O] For metastatic renal cell carcinoma, bevacizumab should be administered every 2 weeks.(1) [O in Context Link 1]

Codes

HCPCS: C9257, J9035, Q5126

Last Update: 9/21/2023 5:41:48 AM
Build Number: 27.2.2023092114759.013030