Off-label use of bevacizumab: advanced adenocarcinoma of the pancreas

BlueCross BlueShield Association

Record Status
This is a bibliographic record of a published health technology assessment. No evaluation of the quality of this assessment has been made for the HTA database.

Citation

Authors' objectives
To determine the incremental net benefit of using bevacizumab (Avastin®, Genentech Bio-Oncology) among patients with pancreatic adenocarcinoma. This Assessment updates part of an earlier Assessment on "Off-Label Uses of Bevacizumab: Renal Cell Carcinoma and Other Miscellaneous Non-Colorectal Cancer Indications" (Vol. 21, No. 9).

Authors' conclusions
Adenocarcinoma of the pancreas is a grim disease with limited life expectancy after diagnosis, even after the best treatment current practice can offer. Multiple drugs have been tested as combination therapy with gemcitabine for advanced disease, including both more traditional chemotherapies such as cisplatin and newer, targeted therapies such as erlotinib. Unfortunately, the impact of these additional therapies has been limited or nonexistent. In this type of clinical situation, even small net benefits are often accepted. Bevacizumab was considered promising because it targets vascular endothelial growth factors (VEGFs), which stimulate angiogenesis and are thought to play an important role in pancreatic cancer, and because of an apparently positive effect in a Phase II trial. Unfortunately, the results of two Phase III trials, one of which was stopped early because of the lack of an effect on overall survival and the second of which was recently released, show no incremental benefit in overall survival.

The findings on progression-free survival were inconsistent, although the earlier Phase III trial was cut short. The more recently published trial did report a statistically significant difference in progression-free survival: median of 4.6 months in patients receiving bevacizumab plus gemcitabine and erlotinib versus 3.6 months in the group receiving only gemcitabine and erlotinib. However, few details were given on the methods used to assess progression-free survival, which may be subject to greater measurement error than overall survival. Data on quality of life would also be helpful to assess the value of this difference, but none were reported. In a disease such as advanced pancreatic cancer, where unfortunately life expectancy is short and secondary treatments used after failure of the first course have shown limited efficacy and often are not used, overall survival is the most meaningful primary outcome.

Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel made the following judgments about whether the use of bevacizumab in patients with advanced adenocarcinoma of the pancreas meets the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) criteria.

1. The technology must have final approval from the appropriate governmental regulatory bodies.

The U.S. Food and Drug Administration (FDA) has approved bevacizumab for first- or second-line treatment of metastatic colorectal cancer; for first-line treatment of unresectable, non-squamous, non-small cell lung cancer; for patients who have not received chemotherapy for metastatic, HER2-negative breast cancer; and, as of May 5, 2009, for patients with glioblastoma, with progressive disease after prior therapy. Bevacizumab has not been approved for use in pancreatic cancer.

2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

Sufficient scientific evidence is available on the use of bevacizumab for patients with advanced adenocarcinoma of the pancreas in the form of two Phase III trials.
3. The technology must improve the net health outcome.

The addition of bevacizumab to a treatment regimen does not increase overall survival among patients with locally advanced or metastatic disease.

4. The technology must be as beneficial as any established alternatives.

The established alternatives provided a benefit compared to the previously used regimens (gemcitabine vs. fluorouracil and erlotinib plus gemcitabine vs. gemcitabine alone). The addition of bevacizumab does not provide additional benefit in terms of the primary outcome of interest, overall survival.

5. The improvement must be attainable outside the investigational settings.

Whether the addition of bevacizumab to chemotherapy regimens for advanced pancreatic adenocarcinoma improves health outcomes has not been established in the investigational settings.

Based on the above, use of bevacizumab for patients with advanced adenocarcinoma of the pancreas does not meet the TEC criteria.

*Another trial showed that the addition of erlotinib to gemcitabine resulted in a small but statistically significant difference in overall survival among patients receiving erlotinib (HR=0.82, p=0.038, adjusted for stratification factors).

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