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# Therapeutic potential and critical analysis of trastuzumab and bevacizumab in combination with different chemotherapeutic agents against metastatic breast/colorectal cancer affecting various endpoints

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ABSTRACT

Researchers are working day and night across the globe to eradicate or at least lessen the menace of cancer faced by the mankind. The two very frequently occurring cancers faced by the human beings are metastatic breast cancer and metastatic colorectal cancer. The various chemotherapeutic

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agents like anthracycline, cyclophosphamide, paclitaxel, irinotecan, fluorouracil and leucovorin etc., have been used impressively for long. But the obstinate character of metastatic breast cancer and metastatic colorectal cancer needs more to tackle the threat. So, the scientists found the use of monoclonal antibodies trastuzumab (Herceptin®) and bevacizumab (Avastin®) for the same. The current study critically investigates the therapeutic potential of trastuzumab and bevacizumab in combination with various chemotherapeutic agents against metastatic breast cancer and metastatic colorectal cancer. To the best of our knowledge, this is the very first critical analysis showing percent wise increase in various positive endpoints like median time to disease progression, median survival, and progression free survival etc. for the treatment of metastatic breast/colorectal cancer using trastuzumab and bevacizumab in combination with different chemotherapeutic agents and provides the rational for the success and failure of the selected monoclonal antibodies.



## 1. Introduction

Earlier the primary treatment for cancer was surgery and radiation. But it was a common notion of the physicians that the cancer cannot be cured for long or it comes back shortly after being operated upon and radiation therapy being done to the patient. The emergence of chemotherapy in 1960s has made the cancer treatment a bit more sophisticated and helped to reduce the recurrence rate. It has the capacity to induce objective remission in large percentage of patients (Brambilla et al., 1976; Carter, 1972; Russell et al., 1978).

The process of recurrence of cancer is known as relapse and is considered as one of the most daunting task among the challenges in cancer care. At the time of relapse, the patient or their family members feel more pity and complicated than even during at first diagnosis. The main reason thought to be considered behind the relapse is that few of the cancer cells survived the basic treatments like surgery, radiation and chemotherapy given to the patients.

Almost all cytotoxic chemotherapeutic agents share a similar mechanism of action. They work by stopping or slowing the growth of rapidly dividing cancer cells and interfere with their DNA metabolism or mitosis. But the very complex and frequent complications linked with these agents are central and peripheral nervous system toxicity which often leads to reduction in the prescribed amount of the drugs and sometimes their cessation (Chrissa and Athanassios, 2009). The common drawback associated with chemotherapeutic drugs is their inability to differentiate between the normal and cancerous cells. So the chemotherapeutic drugs are chosen very judiciously by the physicians.

## 2. Chemotherapeutic drugs against cancer

The common chemotherapeutic drugs used for different types of cancers are as follows:

### 2.1. Carboplatin (Paraplatin)

Carboplatin is a known anti-cancerous, cytotoxic chemotherapeutic drug classified as an alkylating agent. It is usually administered intravenously (IV) and is commonly used for the treatment of ovary, head and neck, and lung cancers (Wheate et al., 2010; Apps et al., 2015).

The common side effects experienced by almost 30% of the patients are low blood counts (red blood cells, white blood cells and platelets). The other frequent adverse reactions are nausea, vomiting, diarrhea etc.

### 2.2. Cisplatin (Platinol, Platinol-AQ)

Cisplatin works as alkylating, cytotoxic drug used in cancer chemotherapy. It is one of the most potent antitumor agents known, displaying clinical activity against a large range of tumors (Zahid, 2003). It is administered intravenously (IV) as an infusion. It is useful in the treatment of bladder, ovary and testicle cancers.

The possible side effects associated with the use of cisplatin are decrease in blood cell counts, allergic reactions like rashes and/or labored breathing, nausea, vomiting, hearing loss, fluctuations in blood electrolytes, kidney damage etc.

### 2.3. Cyclophosphamide (Cytoxan, Neosar)

It is one of the most lucrative and extensively used antineoplastic drugs used for the treatment of lymphoma, breast cancer, and ovarian carcinoma. It is also a very potent immunosuppressive agent used in blood and marrow transplantation (BMT) (Ashkan et al., 2009). It is administered either intravenously (IV) or given orally to the patient.

The likely side effects associated with the use of cyclophosphamide are decrease in blood cell counts, nausea, vomiting, abdominal pain, decreased appetite, hair loss (reversible), bladder damage, fertility impairment, lung or heart damage (with high doses), secondary malignancies (very rare).

### 2.4. Doxorubicin (Adriamycin)

This chemotherapeutic drug has a vast utility in cancer oncology but its use is associated with very fatal side effects known as cardiomyopathy (Emmanuel and William, 1983). It has been widely used for the treatment of solid and hematologic malignant conditions like breast cancer, lymphoma, and multiple myeloma. It is administered intravenously to the patient.

The commonly linked side effects with this drug are decrease in blood cell counts, mouth ulcers, hair loss (reversible), nausea, vomiting etc.

### 2.5. Fluorouracil (5-FU)

It is widely used in the treatment of colon, breast, stomach, and head and neck, but drug resistance remains a significant limitation to the clinical use of 5-FU (Daniel et al., 2003). It is also administered intravenously to the cancer patient.

The common side effects of the use of this drug are decrease in blood cell counts, diarrhea, mouth ulcers, photosensitivity, dry skin etc.