



Major review

Ophthalmic complications of targeted cancer therapy and recently recognized ophthalmic complications of traditional chemotherapy



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ABSTRACT

As our understanding of cancer pathophysiology has increased, so have the number of targeted therapeutic agents available. By targeting specific molecules involved in tumorigenesis, targeted therapeutic agents offer the potential for significant efficacy against tumor cells while minimizing the adverse effects. We highlight the recently recognized ophthalmic complications of targeted cancer therapy, as well as recently recognized complications of traditional chemotherapeutic agents.

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1. Introduction

The National Cancer Institute defines targeted cancer therapy as “drugs or other substances that block the growth and spread of cancer by interfering with specific molecules involved in tumor growth and progression.”^A Currently over 40 targeted therapies are in clinical trials. By targeting specific molecules involved in cancer tumorigenesis, rather than all rapidly dividing cells, targeted therapy offers the theoretical advantage of tumoricidal efficacy with minimal adverse effects.

The specific ophthalmic complications of targeted cancer therapy vary by drug and range in severity from mild ocular

irritation to significant visual loss. We highlight the known ophthalmic complications of the various targeted therapies that are being utilized with increasing frequency in cancer treatment. We will also discuss recently recognized ophthalmic complications of nontargeted traditional chemotherapeutic agents.

2. EGFR inhibitors

Epidermal growth factor receptor (EGFR) and its downstream signaling pathways play an important role in cancer

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proliferation and survival. Targeted EGFR inhibitors include EGFR tyrosine kinase inhibitors erlotinib (Tarceva) and gefitinib (Iressa®) and monoclonal antibodies directed against EGFR, cetuximab (Erbix) and panitumumab (Vectibix). EGFR

tyrosine kinase inhibitors are for non-small cell lung cancer and pancreatic cancer,^{62,92} and EGFR monoclonal antibodies are used for advanced colorectal cancer and head and neck cancers.^{6,106}

Table 1 – Summary of drugs, their indications, and their common and rare ophthalmic adverse effects

Drugs and Indications	Adverse Effects	
	Common	Rare
EGFR Inhibitors Squamous cell carcinoma Non-small cell lung cancer Pancreatic cancer Colon cancer	Trichalomegaly Trichiasis Abberant last growth Conjunctivitis Blepharitis Dry eye syndrome	Corneal thinning Persistent Corneal erosions Periorbital dermatitis Diffuse Punctate Keratitis
Imatinib (Gleevec) Chronic myeloid leukemia Gastrointestinal stromal tumor	Periorbital edema Epiphora Subconjunctival hemorrhage	Optic disc edema Optic neuritis Cystoid macular edema Macular ischemia
Perifosine Colorectal cancers Waldenström macroglobulinemia Gastrointestinal stromal tumor	Ulcerative keratitis	Progressive corneal ring infiltrate
Denileukin difitox Cutaneous T-cell lymphoma	None	Pigmentary retinopathy
Trastuzumab (Herceptin) Breast cancer Gastric cancer	Dry eye Blurred vision Epiphora Conjunctivitis	Vision loss Macular edema
Rituximab Non-Hodgkin lymphoma Chronic lymphocytic leukemia		Eyelid edema Scleral edema Macular edema
MEK inhibitors Metastatic melanoma Colorectal cancer Non-small cell lung cancer	Acneiform rash Blurred vision	Central serous chorioretinopathy Retinal vein occlusion Uveitis
Ipilimumab Metastatic melanoma	Uveitis Conjunctivitis	Orbital inflammation Orbital apex/cavernous sinus inflammation Retinal edema
BRAF inhibitors Metastatic melanoma Thyroid cancer	Squamous cell carcinoma	
Docetaxel (Taxotere) Breast cancer Metastatic non-small cell lung cancer Prostate cancer Stomach cancer Head and neck cancer	Epiphora Canilicular stenosis	Cystoid macular edema
S-1 Gastric cancer Colorectal cancer Pancreatic Cancer	Epiphora Canilicular stenosis	
Bisphosphonates Osteoporosis Paget disease of bone Bone metastases Multiple myeloma		Uveitis Conjunctivitis Keratitis Scleritis Orbital inflammation

Name of drugs are given in bold and indications are listed below each drug name/class.

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