Optic and Otic Side Effects of Molecular Targeted Therapies

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Objectives: *To discuss the optic and otic toxicities associated with molecular targeted therapies including description, presentation, grading, and management of these toxicities.*

Data Sources: *PubMed, CINAHL, the Cochrane Library and nursing text books.*

Conclusion: *Although targeted therapies often do not have the same systemic toxicities as chemotherapy, they have their own unique side effects. Optic and otic toxicities are seen with a variety of targeted therapies and, although these are not life-threatening toxicities, they do have the potential to severely impair a patient's quality of life.*

Implications for Nursing Practice: *Baseline optic and otic assessments along with periodic assessments throughout treatment can lead to early recognition of problems with the eyes or ears. Recognition and treatment of these problems will help maintain the patient's quality of life.*

Key Words: *Optic, eye, ear, targeted therapy, molecular targeted therapy, ototoxicity*

Molecular targeted therapies generally inhibit several pathways needed for the survival of cancer cells. These agents are more tumor specific than chemotherapeutic agents with fewer toxicities; however, they do have their own unique set of both on-target and off-target effects. Although relatively uncommon, toxicities can occur in the eye and its adnexa, the anterior segment, and/or the posterior segment. The adnexa includes the eyelid, eyebrows, and lacrimal system. The anterior segment includes the crystalline lens, iris, and cornea; while the posterior segment includes the retina, choroid, optic disc, and vitreous humor

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0749-2081/3003-$36.00/0.
http://dx.doi.org/10.1016/j.soncn.2014.05.004

(see Fig. 1). The eyes are particularly sensitive to targeted therapies because several of the signaling molecules targeted in anti-cancer therapy are also present in ocular tissue.[1,2] Ototoxicities can occur because of effects of the agent on either the cochlear and vestibular cells of the inner ear or on the acoustic nerve.[3]

A variety of targeted agents have the potential to cause ocular and otic complications. Agents associated with ocular toxicities include cetuximab, bevacizumab, panitumumab, imitanib, erlotinib, afatinib, and gefitinib (see Table 1).[1,2,4] The mitogen-activated protein kinase (MEK) pathway has more recently been identified as a potential target for several cancer types. MEK inhibitors are a novel class of drugs under investigation in a variety of tumor types. However, several of these agents have been shown to exhibit ocular toxicities.[4] Agents that have been associated with otic complications include dasatinib, imatinib, sorafinib, trastuzumab, and cetuximab (see Table 2).[5]

Presentation

Ocular Complications

Ocular toxicities caused by targeted therapies manifest as blepharitis, epiphora, conjunctivitis, or trichomegaly. Blepharitis is characterized by inflammation of the eyelids. Cetuximab is associated with ocular toxicities, such as blepharitis, in 80% of patients with 15% of cases being severe.[6,7] Gefitinib has also been associated with blepharitis in early studies of the drug.[1] Patients with blepharitis complain of eye irritation and redness. When the blepharitis occurs around the eyelashes and follicles it is considered anterior blepharitis and is less common than posterior blepharitis. Posterior blepharitis is characterized as inflammation of the inner eye around the meibomian glands. These glands secrete an oily substance that creates a thin coating, helping tears to spread over the eye and keep them from evaporating. Because this allows the eyes to remain lubricated, posterior blepharitis is often accompanied by dry eye syndrome, conjunctivitis, and keratitis.[8]

Epiphora, commonly known as watery eyes, occurs when there is an increased production of tears or when the tears cannot drain properly from the eye. While other conditions such as blepharitis, foreign bodies, droopy lower eyelids, and allergies can cause epiphora, it can also be caused by cancer treatments. Agents known to contribute to epiphora include bevacizumab and imitanab. Epiphora is categorized according to one of four

TABLE 1.
Ocular Toxicities

Agent	Toxicity
Cetuximab	Blepharitis
	Trichomegaly
Bevacizumab	Epiphora
Panitumumab	Epiphora
Imitanib	Epiphora
Erlotonib	Conjuncivitis
	Trichomegaly
Aftatinib	Conjuncivitis
	Epiphora
Gefitinib	Trichomegaly
	Conjuncivitis

Data from references 1,2, and 4.

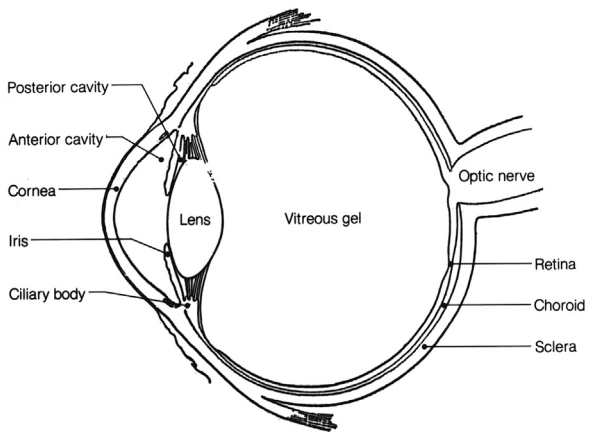

FIGURE 1. **Lateral view of the eye. National Cancer Institute, 2001. Available from https://visualsonline.cancer.gov/details.cfm?imageid=1767.**

TABLE 2.
Otic Toxicities

Agent	Toxicity
Dasatinib	Tinnitus
	Vertigo
Imatinib	Tinnitus
	Vertigo
Sorafannib	Tinnitus
Dasatinib	Vertigo
Sumitinib	Vertigo
Tastuzumab	Vertigo
Cetuximab	Vertigo

Data from Cianfrone et al.[5]