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Editorial

Role of targeted therapy in ophthalmic tumors

Rajendra P Maurya[1]*, **Kokil Tiwari**[1]

[1] *Regional Institute of Ophthalmology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India*

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With ongoing advancements in oncology, targeted therapy have revolutionized treatment of malignancies and brought a paradigm shift.[1] Targeted therapy is a rapidly evolving field in oncology with new informations and several advantages.

Targeted therapies in cancer treatment focus on specific proteins involved in cancer growth, minimizing side effects compared to traditional chemotherapy. In this therapy newer molecular treatment options can target and block the level of signaling pathway. It inhibits blood vessel formation, induces cancer cell death, and delivers toxins directly to cancer cells. They offer advantages like fewer side effects, effectiveness in certain genetic mutations, and the ability to combine with immunotherapy, chemotherapy, and radiotherapy for enhanced results. Overall, targeted therapies provide a precise and effective approach to cancer treatment, promising improved patient outcomes with personalized care.[1,2]

Targeted therapy for ocular malignancies is still in the early trial stage. Data regarding long-term safety, efficacy and outcome are still not available. Below are some targeted therapies recommended in ophthalmic malignancies.

1. Eyelid Tumors

Novel targeted therapies in case of eyelid tumors like basal cell carcinoma (BCC) which comprise of 80-90% of malignant eyelid tumors, squamous cell carcinoma (SCC) 5-10% cases, have been reported.

With a better understanding of the pathogenesis of BCC, novel therapies which target Sonic Hedgehog (SHH) signaling pathway are being developed.

Vismodegib- it selectively targets the extracellular domain of the SMO protein and inhibits its function which inactivates SHH signaling pathway.[3,4] The SSH is a secreted protein that binds to tumor suppress gene (transmembrane receptor complex) PTCH1 (patched) which intern inactivate the SMO (smoothened). Vismodegib is a small molecule approved for use in case of locally advanced and non-resectable metastatic BCC. Vismodegib inhibits SMO and allowing normal functioning of PTCH1. In a study by TANG et al., it was found that vismodegib had statistically fewer surgeries. 54% of patients had to stop the drug due to adverse events like myocardial infarction, ischemic stroke etc.[5] It is also beneficial as neoadjuvant therapy before resection of the tumor. According to Ally et al. it reduced the actual surgical defect area by 27% compared with pretreatment estimates.[6] Trials like ERIVANCE were pivotal for FDA approval for its use in metastatic BCC.[7]

Sonidegib is a SMO inhibitor used as an additional oral therapy for metastatic BCC. BOLT trial propulsed its use in metastatic BCC and established its safety and efficacy.

Cetuximab is a chimeric monoclonal antibody that inhibits EGFR and inhibits downstream activation of its numerous pathways. It is under phase 2 trial for patients with metastatic and unresectable SCC.[8]

* *Corresponding author.*
E-mail address: mauryarp_bhu@yahoo.com (R. P. Maurya).

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Gefitinib is the first oral EGFR inhibitor which selectively inhibits tyrosine kinase activity by bloackage of autophosphorylation. It has been extensively researched as neoadjuvant agent for locally aggressive or recurrent cutaneous SCC. It reported an overall response rate of 45%.[9]

Vemurafenib is a novel therapy which inhibits BRAF, it was approved for treatment of BRAF-mutated unresectable or metastatic malignant melanoma(MM).[10–12]

Dabrafenib a selective BRAF inhibitor and Trametinib a selective MEK inhibitor have also been reported for treatment of cutaneous malignant melanoma.

Various novel proteins have been utilized in therapies of sebaceous cell carcinoma by inhibiting EGFR. Reported side effects are skin toxicity, rash, pustular follicular eruption, trichomegaly which can further lead to corneal ulceration and conjunctivitis.[9]

2. Orbital Neoplasms

Targeted therapies have been approved for various orbital neoplasms as well. Optic nerve sheath meningiomas have shown some benefit with these therapy. Immunotherapy with Rituximab and targeted therapy with Ibrutinib have been employed in treatment of ocular adnexal lymphomas. Selumetinib a MEK inhibitor has been approved by FDA for treatment of pediatric Neurofibromatosis Type 1 for children older than 2 with inoperative plexiform neurofibromatosis.[13]

3. Intraocular Tumors

Uveal melanoma is the commonest intraocular malignancies of adulthood. Genetic alteration has been found in uveal melanoma (maturations of genes coding for GNAQ/GNA11) which lead to activation of G-protein in coupled pathways like PKC, MAPK and P13K. Immune checkpoint inhibitors like Nivolumab, Pembrolizumab and atezolizumab have been approved for treatment of metastatic melanoma. Belzupacap Sarotalocan or AU-O11 are recommended for uveal melanoma which selectively binding to malignant melanoma cells and causing acute tumor necrosis.

Advances in understanding the pathogenesis of eyelid tumors have led to the development of effective targeted therapies advances in understanding the pathogenesis of eyelid tumors have led to the development of effective targeted therapies. Targeted therapies have emerged as a promising approach in the treatment of ocular malignancies. They have lead to improved patient outcomes and better personalized treatment.Although it is still in its early stages of development it offers a hopeful and exciting future for ocular oncology.

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Author biography

Rajendra P Maurya, Rajendra P Maurya, Editor in Chief IJCEO, Associate Professor & I/c Orbit, Ocular Oncology and Oculoplasty Unit Regional Institute of Ophthalmology,
Institute of Medical Sciences,
Banaras Hindu University, Varanasi, (UP), India
https://orcid.org/0000-0001-9343-6003

Kokil Tiwari, Junior Resident

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