Biomere

COMMUNITY BLOG

OCULAR TOXICITIES CAUSED BY ANTI-CANCER THERAPIES

As per a recent report, the number of anticancer therapies approved for use in humans is 321, and over 98% of the drugs are single agents while 4 are approved therapy combinations[1]. This number is likely to continue growing as the preclinical drug development pipeline includes over 1,600 anticancer therapies and the R&D spend on anticancer therapies is estimated to be about $409 billion by 2028[2]. Anticancer therapies include many different types of modalities including small molecules, monoclonal antibodies including immunotherapies antibody-drug conjugates, radionuclide therapies etc. Most cancer therapies have a broad range of reported side effects that can range from mild to severe and can sometimes be fatal. Ocular toxicity has been frequently reported in several clinical studies for different anticancer modalities and range from mild and reversible to chronic and severe complications[3].

Several chemotherapies have been reported to cause adverse ocular effects. For example, the antimetabolite chemotherapy drug capecitabine that is used in combination with docetaxel for various cancers including colorectal and breast cancers has been reported to reduce vision, induce irritation, conjunctivitis, corneal deposits etc[3]. Another example is the widely used breast cancer drug Tamoxifen that has been reported to cause corneal disease (keratopathy) as well as retinopathy, cataracts and optic never damage[3]. Monoclonal antibodies targeting different cancer antigens have also been reported to cause ocular issues. One example is the VEGF inhibitor, bevacizumab, which has been reported to cause ocular hyperemia and issues in the posterior pole of the eye[3]. Bevacizumab is widely used to treat several metastatic cancer types so monitoring ocular issues is essential during and after the treatment regimen.

Interestingly, immune checkpoint inhibitors (ICI) have been reported to have lower levels of ocular toxicity – a 2022 study analyzed about 1,300 patients treated with ICIs and found ocular adverse effects in about 10% of patients[4]. The most common ocular effect was corneal toxicity followed by optic nerve issues and uveitis/scleritis[4]. Interestingly, ocular effects were more commonly seen in patients treated with nivolumab and pembrolizumab compared to patients treated with other ICIs such as ipilimumab[4], which suggests different mechanisms of action on ocular tissues. Additionally, combination regimens such as ipilimumab-nivolumab had higher occurrence of ocular effects. While the numbers and severity of ocular adverse effects is relatively low, it is critical to monitor ocular toxicities as ICIs are tested and prescribed for an increasing number of cancer indications. It is likely that the actual number of patients with ocular effects will increase significantly as the total number of patients being treated with ICIs increases.

Antibody-drug conjugates (ADC) are some of the most promising anticancer therapies. As of 2024, 13 ADCs have been approved by the FDA and over 100 ADCs are reported to be in clinical trials[5]. However, based on clinical trial data, ocular toxicity is being reported as the most common adverse effect. One of the primary adverse effects is the development of corneal epithelial inclusions or microcyst-like bodies. The microcyst-like bodies have been reported to develop as ADC dose and treatment duration increase[6]. These bodies have been reported to induce eye irritation, blurred vision and can also cause corneal epithelial cell death. Interestingly, the pseudomicrocysts disappear after the treatment regimen is complete but it is important to monitor the long-term impact of the microcysts on eye tissues. Another ocular adverse effect is conjunctivitis which also resolves after treatment is complete[6].

Taken together, ocular toxicities have been reported to be induced by multiple anticancer therapies but severe adverse effects are rare. However, as ADCs, ICIs and other modalities are likely be used for more cancer indications, it is essential to monitor ocular toxicities during preclinical development and clinical trials.

References:

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