Immuno-Oncology at a Glance

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What’s immuno-oncology (I-O)

Improved survival remains a challenge in some advanced cancers. 5-year survival remains poor for many patients with metastatic solid tumors.¹ There is an ongoing need for new treatments and therapeutic modalities for patients with advanced cancers.²

Pillars of Cancer Therapies

I-O therapies are being investigated in an attempt to utilize the body’s own immune system to fight diseases.³⁻⁵

The immune system and cancer: immunoediting

The process by which the immune system recognizes, destroys, and sculpts tumors is known as **immunoediting**. There are 3 phases in immunoediting:

1. **ELIMINATION** (cancer immunosurveillance) – Cancer cells are detected by the immune system and/or eliminated. Tumor cells not destroyed may enter the equilibrium phase.
2. **EQUILIBRIUM** (cancer dormancy) – Some cancer cells persist but the immune system prevents tumor outgrowth.
3. **ESCAPE** (cancer progression) – Resistant variant cells acquire the ability to evade immune detection or elimination. This results in clinically apparent disease.

The goal of I-O therapy is to restore the ability of the immune system to eliminate cancer cells by either **activating the immune system** directly, or by **inhibiting mechanisms of suppression** by tumors.

Some tumors may **escape** the immune system by interfering with various mechanisms of immune system activation and suppression.

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Players in the immune response against cancer

**Tumor-associated antigens**
- Are abnormal cell substances/proteins (tumor antigens) which can be recognized and responded to by the immune system

**Antigen-presenting cells (APC)**
- Take up antigens from infected or malignant cells and process them into shorter peptide segments
- Present antigens to T cells to mobilize an immune response

**T cells**
- Have T-cell receptors, which can recognize tumor-associated antigens
- Play a major role in killing infected or malignant cells when activated
- Help perpetuate ongoing immune responses

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### Players in the immune response against cancer

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<th>B cells</th>
<th>Antibodies</th>
<th>NK cells</th>
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| • Display B-cell receptors, which can bind free floating antigens in the blood or lymph.  
• Once activated, B cells differentiate to become plasma cells which can secrete large quantities of antibodies against a specific antigen. | • Are secreted by activated B cells, called plasma cells.  
• Tag antigen-containing cells for attack by other parts of the immune system, or neutralize their targets directly by blocking important mechanisms. | • Can recognize infected or malignant cells innately without contact with an antigen-presenting cell or antibody (this allows NK cells to launch rapid responses against stressed cells).  
• Can also attack based on recognition of antibodies on a cell surface. |

Tumor-associated antigens can cause an immune response

PRACTICAL AND SAFETY CONSIDERATIONS

Potential patterns of response to I-O therapy

Therapies that affect the immune system may not induce a measurable impact on tumor growth immediately after administration. Potential effects may be seen weeks to months after initial administration.

Immediate response

Lack of tumor shrinkage but a slowing of tumor progression

Tumor regression after early radiographical progression

Early but clinically insignificant progression

There is also the potential that patients may not respond to therapy.

Pseudo-progression and I-O therapy

Apparent progression upon radiographic imaging after initial I-O therapy can actually be a sign of pseudo-progression. Pseudo-progression may occur when T cells infiltrate the tumor site and cause tumors to flare or new lesions to appear upon imaging. 

Adverse effects (AEs)

Tumor cells arise from normal cells in our body so some tumor-associated antigens may also be associated with normal, healthy cells. By ‘activating’ the immune system with I-O therapy, a major concern is that the immune system will attack normal, healthy cells along with tumor cells.¹

Clinical implications of immune-associated AEs

• AEs can be serious and potentially fatal
• Remain vigilant throughout and after treatment
• Educate and encourage patients to monitor for and report symptoms of immune-associated AEs
• Not all AEs can be managed and some patients may have to discontinue treatment
  – To give patients the best chance of therapeutic success, follow management guidelines for immune-associated AEs