Immunotherapies and Their Toxicities in Oncology: What is here and what is coming

VCH Family Medicine Rounds Jan 8 2025 — **Zoom AI summary**

Dr Maryam Soleimani

Immune Checkpoint Inhibitors in Oncology

Dr Soleimani discussed the objectives of the meeting, which included reviewing common toxicities of immune checkpoint inhibitors and introducing novel immunotherapies in oncology. She explained the role of immune checkpoints in the immune system and how cancer cells exploit this system to evade destruction. She then discussed the development of immune checkpoint inhibitors, such as anti-CTLA-4 and anti-PD-1/PD-L1 antibodies, to prevent the interaction between tumor cells and T cells. Dr Soleimani also mentioned the potential of combining immune checkpoint inhibitors with other treatments like targeted therapies, oral medications, or chemotherapy. Lastly, she highlighted the risk of immune-related adverse events due to the massive T cell response.

Managing Immune-Related Adverse Events

Dr Soleimani discussed the management of immune-related adverse events (irAEs) in patients who have received immunotherapy. She emphasized the importance of early recognition and management of these side effects, as they can become severe and life-threatening if not addressed promptly. Dr Soleimani highlighted that any organ system can be involved in irAEs, and patients who develop severe toxicities often have the best response in terms of disease control. She also noted that the risk of developing an irAE is never completely zero, even after a long time since the last treatment.

Dr Soleimani then focused on three common groups of irAEs: dermatologic, gastrointestinal, and endocrinopathies. She explained that the management of these side effects typically involves the use of steroids, with the goal of tapering down the dose as quickly as possible. She also mentioned the importance of involving dermatology in the management of severe skin rashes and the need for close monitoring in severe cases. Dr Soleimani concluded by stating that while these side effects can be challenging to manage, they are now a routine part of cancer treatment.

Gastrointestinal Toxicity and Hepatotoxicity Risks

Dr Soleimani discussed gastrointestinal toxicity, focusing on hepatotoxicity. She highlighted that while rare, it can be severe and potentially fatal if not promptly recognized and managed. She emphasized that the risk is highest with the use of a Ctla 4 inhibitor, such as ipilimumab, which is often used in conjunction with another immune checkpoint inhibitor. Dr Soleimani noted that immunemediated hepatitis can be asymptomatic and may require a high dose of steroids, with a slow taper, and possibly additional immunosuppressive agents. She stressed the importance of involving hepatology early on and monitoring liver enzymes closely. High-grade toxicity requires hospital management due to the risk of fulminant liver failure.

Colitis: She emphasized the importance of establishing a baseline for bowel movements to identify any changes. Dr Soleimani also highlighted that a pre-existing diagnosis of Crohn's or ulcerative colitis is not an absolute contraindication for using these inhibitors, but it does require careful management. She mentioned that the use of proton pump inhibitors, family history of inflammatory bowel disease, and the use of the Ctla 4 inhibitor are risk factors for colitis. Dr Soleimani also discussed the management of colitis, including the use of steroids and the potential need for additional immune suppression. She shared a case of a patient who developed severe colitis and required a total colectomy, but also experienced exceptional response to treatment.

Endocrinopathies

Lastly, Dr Soleimani discussed endocrinopathies, including hyperthyroidism, type 2 diabetes, and hypophysitis, which can be asymptomatic or present with mild symptoms. She stressed the importance of monitoring these conditions and initiating appropriate treatment when necessary.

Immune Checkpoint Inhibitors and CAR T

Dr Soleimani discussed the use of immune checkpoint inhibitors and CAR T-cell therapy in cancer treatment. She explained that immune checkpoint inhibitors are a standard of care, while CAR T-cell therapy is mainly used in hematologic cancers and is still under active investigation for solid tumors. Dr Soleimani highlighted the high cost and resource-intensive nature of CAR T-cell therapy, as well as its associated toxicities, including cytokine release syndrome, immune effector cell-associated hematotoxicity, and the potential for secondary malignancies. She also mentioned the importance of close monitoring and the involvement of the leukemia and bone marrow transplant team in managing these patients.

Bispecific T-Cell Engagers, cancer vaccines and TILS

Dr Soleimani discussed the potential of bispecific T-cell engagers (BiTEs) in oncology, highlighting their advantages over CAR T-cell therapy. She explained that BiTEs can be mass-produced, have fewer off-target side effects, and are quickly administered. Dr Soleimani also introduced two newer classes of drugs: cancer vaccines and TILs therapy. Cancer vaccines, which target tumor-associated antigens or tumor-specific antigens, are still in research stages, with questions remaining about their side effects, optimal use, and safety profile. TILs therapy, similar to CAR T-cell therapy, involves isolating tumor-infiltrating lymphocytes from a tumor sample, expanding them, and then reinfusing them into the patient after depleting their current circulating T cells. Dr Soleimani concluded by stating that these therapies are rapidly evolving and will likely become more widely used in the next few years.

T-Cell Immunotherapy for Metastatic Melanoma

Dr Soleimani discussed the current state of T-cell immunotherapy (TILs) and its potential in treating metastatic melanoma. She highlighted that there is no Health Canada approved indication for TILs, but there is one in the US for a drug called amtag v, used for heavily pretreated metastatic melanoma. Dr Soleimani also mentioned that TILs are a resource-intensive

treatment requiring inpatient monitoring and administration. She noted that the treatment has shown promising results, with a 31.4% response rate in a phase 2 clinical trial involving 153 patients. However, she also pointed out that the treatment's side effects are significant, including cytopenias, increased risk of infection, and renal impairment. Dr Soleimani concluded by noting that TILs are rapidly evolving, with new drugs and mechanisms of action being developed, but challenges remain in predicting response, improving toxicity profiles, and optimizing delivery methods.

Immunotherapy Advancements and Treatment Duration

Dr Soleimani discussed the advancements in immunotherapy treatments in BC, highlighting the development of an advanced immunotherapies committee to address the challenges of these treatments. She addressed a participant’s question about the duration of immunotherapy treatments, explaining that some have a finite time period while others are indefinite, and that re-challenging patients with immunotherapy after a relapse is a topic of ongoing research. Dr Soleimani also responded to another question about the magnitude of effect and life prolongation from these therapies, stating that they are highly effective for many patients but the response varies depending on the tumor type and treatment agent. She emphasized the need for better biomarkers to predict patient response to these treatments.