Use of Genetics and Diet in Inflammatory Bowel Disease for Treatment with Checkpoint Inhibitor Blockade and resulting Gastrointestinal Toxicity

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Supplemental Video

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Background/Knowledge Gap:
Colitis associated with checkpoint blockade therapy has pathophysiology similarities to Inflammatory Bowel Disease (IBD), such as Crohn's Disease and Ulcerative Colitis. The inflammatory colitis toxicity from checkpoint blockade is also similar to clinical symptoms experienced in patients with IBD.

Methods/Design:
We will briefly review the pathophysiology, dietary, and genetic factors associated with IBD. Dietary modifications with the SCD, FODMAP, BRAT, lactose elimination, low-residue and more target specific portions of the upper, middle, and lower affected gastrointestinal tract. We further relate how these principles can be applied to patients experiencing inflammatory bowel toxicity secondary to checkpoint blockade.

Results/Findings:
Checkpoint molecules are cell surface receptors on immune cells that mediate suppression and augmentation of the immune response. Mechanistically, checkpoint molecules and other immunomodulatory molecules, such as TNF-alpha upregulated in IBD, are the same molecules up-regulated in inflammatory and cancerous processes, such as colon and small intestinal cancer. Blocking these checkpoints can not only inhibit the cascade of inflammation, but also result in toxic side effects from that same cascade. Current guidelines towards treatment go beyond corticosteroids, such as prednisone, to achieve remission. Specific genetic markers give rise to downstream immune checkpoints also associated with the pathophysiology of Crohn's and ulcerative colitis.

Conclusions/Implications:
The balance of the toxicity in the application of these inhibitors relies heavily on the symptoms of IBD patients and established diagnostic criteria. Some of these toxicities include, but are not limited to, mucositis, hypothyroidism, hypophysis, rash, hepatotoxicity, pancreatitis, pneumonitis, colitis and more. Criteria can help achieve a mediated point of toxicity and treatment for IBD patients.

Learning Objectives
1. Identify how genetics can impact checkpoint inhibitors behind the inflammation and blockade of colitis
2. Apply the pathophysiology of lifestyle and diet changes made in Crohn's disease and ulcerative colitis to treatment of inflammatory bowel toxicity
3. Compare the checkpoint inhibitor toxicity levels, symptoms, and factors in both Crohn's disease and ulcerative colitis

References and Resources
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1,44-62

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