

Significance of Single vs. Combination Immunotherapies

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DESCRIPTION

While immunotherapies have made great strides in the fight against cancer, this is not a universal situation. Different types of immunotherapy have different side effects, and some are more effective than others for certain cancers. In addition, the patient's overall health, the strength of their immune system, and the type of cancer all play a role in which immunotherapy is available and will have the greatest chance of being effective.

After consideration of all relevant factors, including potential autoimmune toxicity, then it may be determined a single or combination therapy regimen, including all standard and novel cancer therapies (chemotherapy, radiation, molecularly targeted therapies), may be established to increase the likelihood of successful treatment. The potential synergy provided by combination therapies could make the tumor more immunogenic, thereby increasing the efficacy of immunotherapy.

Radiation therapy has been shown to stimulate immune mediators, thereby enhancing the antitumor immune response. Combining radiation with immunotherapy could increase the efficacy seen with single-agent immunotherapy. Combination therapies may enable more personalized cancer treatment to provide the maximum potential benefits of each therapeutic agent.

Advances in immunotherapy are focused on the potential to initiate a self-sustaining immune response against cancer cells, resulting in long-term clinical benefits and a reduced incidence of recurrence. While individual immunotherapy regimens have shown increasing response rates and durability in all cancer types, a high percentage of patients still do not respond, and the potential for tumors to become resistant over time to these agents still exists.

Therefore, research has focused on the possibility of combining immunotherapy with current clinical therapies alongside other immunotherapeutic agents in the hope of improving response rates and long-term outcomes for patients. However,

combination therapies have their own clinical and economic aspects that must not be overlooked.

Boosting the immune response has the potential to put the immune system into overdrive, leading to severe and sometimes critical autoimmune reactions, which may be further exacerbated by combination with other therapy with similar effects on the immune response. In addition, single-agent immunotherapy alone is expensive, so the use of another therapeutic agent adds to the already increased costs.

Future studies must consider these challenges and potential changes in the dose of therapies in combination with other therapeutic agents, the order of therapies, the selection of meaningful endpoints, and the selection of appropriate patient populations.

While immune checkpoints are used to prevent T lymphocytes from turning against normal cells, tumors have found ways to exploit these pathways, complicating potential therapeutic mechanisms. However, currently, combination immunotherapy regimens often focus on immune checkpoint inhibitors, the PD1/PD-L1 axis, and Cytotoxic T-lymphocyte Antigen 4 (CTLA-4). Combinations of PD-1 and CTLA-4 inhibitors are currently being evaluated in clinical trials for multiple malignancies, including gastric, breast, bladder, pancreatic, kidney, lung, and ovarian cancers. In addition, phase 1 and 2 trials combining PD-1 with radiotherapy are on-going with promising preliminary results.

Benefits

Immunotherapy is administered for a maximum of two years. It will then be stopped. This can naturally be a very anxious and scary time; to seemingly be taken away from a treatment that works. Immunotherapy can;

- Educate the immune system to recognize and attack specific cancer cells.
- Provide the body with additional components to strengthen the immune response.
- Boost immune cells to help them eliminate cancer.

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