

# Immunotherapy for Liver Cancer

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## Introduction

The immune system of the body helps to fight the infections and diseases. It is made up of white blood cells (WBC), organs and tissues of lymph system. Immunotherapy is one type of biological therapy, a type of treatment that restores the ability of the immune system of the body. The immunotherapy helps body to fight the infections and diseases. It is used in the treatment of cancer. Immunotherapy can stimulate immune system responses to fight liver cancer better. Liver is a vital organ that carry out essential function that involves detoxification, metabolism of fat and sugars and drug processing. Liver cancer is frequently spread to other organs like breasts or lungs. Often, liver cancer begins in liver cells called hepatocytes, which are the chief functional cells of liver performing multiple metabolic, endocrine and secretory functions.

## Types of Liver Cancer

**Hepatocellular carcinoma (HCC):** is the common type of liver cancer. Chronic liver disease like cirrhosis caused by hepatitis virus often is the cause of hepatocellular carcinoma.

**Cholangiocarcinoma:** is the cancer formed in the bile duct (slender tubes), that carry digestive bile fluids.

**Hepatoblastoma:** is a rare cancer commonly found in children of 3-4 years of age. This cancer doesn't spread to other parts of body.

**Risk factors:** HCC is commonly seen in people who heavily use alcohol and have fat accumulated in the liver and diabetes. Hepatitis infection and long-term liver diseases, chance of error in DNA replication while repairing a damaged tissue is high that may lead to cancer.

**Preventive vaccine:** Hepatitis B vaccine was named as the first anti-cancer vaccine as it prevents chronic infections caused by hepatitis B virus, thereby preventing liver cancer. Hepatitis B vaccine (HEPLISAV-B) is a preventive cancer vaccine that helps in preventing the development of liver cancer caused by hepatitis B virus.

**Diagnosis of HCC:** HCC can be diagnosed by Blood tests, computer tomography (CT) and magnetic Resonance, imaging (MRI), biopsy.

**Treatment:** Depends on the size and location of cancer, liver function and general health of the patient. Surgery, liver transplant surgery, killing cancer cells with heat or cold, chemotherapy, radiation therapy, targeted drug therapy, immunotherapy.

**Immune checkpoint inhibitors:** are also called as immunomodulators. Immune system uses checkpoints to prevent from targeting healthy cells of body. To initiate immune response, the proteins on the immune cells need to be activated. Cancer cells use these checkpoints and become invisible to immune system.

**Pd-1 and Pd-L1 inhibitors:** are checkpoint inhibitor anti-cancer drugs. The cancer cells use the immune proteins surrounding them to hide from immune targeting. These inhibitors block the binding of PD-1 and PD-L1, which helps in boosting the immune response to cancer cells.

Atezelizumab (Tecentriq) is a checkpoint inhibitor, targets the PD-L1 protein present at the surface of the cells. blocking this protein enhances the immune response to cancer cells. This drug can be used in combination with Bevacizumab (Avastin).

Pembrolizumab (Ketruda) and NIVOLUMAB (OPDIVO) are checkpoint inhibitor drugs that target PD-1 which boosts the cancer fighting immune response.

**CTLA-4 Inhibitors:** these drugs block another protein of the T-cells (immune cells) named as CTLA-4 and enhances the immune response. Ipilimumab (Yervoy) is a CTLA-4 inhibitor that can be used in combination with Nivolumab (Opdivo) in treatment of liver cancer.

**Side effects:** The checkpoint inhibitor drugs or immunomodulators may cause side effects including fever, cough, nausea, tiredness, skin rash, loss of appetite, pain in muscle or joints and diarrhea. Some rare side effects are infusion reactions and autoimmune reactions. CTLA-

4 inhibitor drugs seem to cause more serious side effects compared to PD-1 and PD\_L1 inhibitors.

The advanced therapy and promising drugs with encouraging results with PD-1 inhibitors are emerging and tremendous interest in immunotherapy raises hope that better combinations of drugs will be available in treatment of liver cancer.

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