AIM WITH IMMUNOTHERAPY FOUNDATION

Tremelimumab-actl

An HCP Tool from AIM with Immunotherapy

Tremelimumab-actl (Imjudo®) is an antibody that binds to cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4). Through this directed binding, it blocks the interaction between the immune cell and the cancer cell. Since the interaction is designed to dampen the immune response, tremelimumab-actl reactivates the immune system to target the cancer.

The drug has several indications. Tremelimumab-actl is indicated for the treatment of adult patients with unresectable **hepatocellular carcinoma** in combination with durvalumab. It is also indicated for the treatment of adult patients with metastatic **non-small cell lung cancer** (with no sensitizing epidermal growth factor receptor mutation or anaplastic lymphoma kinase genomic tumor aberrations – *EGFR/ALK* wild type) in combination with durvalumab and platinum-based chemotherapy.

Clinical trial results with tremelimumab-actl

In the HIMALAYA study (NCT03298451), which was a randomized (1:1:1 for tremelimumab-actl with durvalumab:durvalumab:sorafenib), open-label, multicenter study in patients with unresectable hepatocellular carcinoma who had not received prior systemic treatment:

- The median overall survival for tremelimumab-actl combined with durvalumab was 16.4 months versus 13.8 months for sorafenib.
- The median progression-free survival for tremelimumab-actl combined with durvalumab was 3.8 months versus 4.1 months for sorafenib.
- Complete response was achieved in 3.1% of patients treated with the combination versus 0% for sorafenib.
- Partial response was achieved in 17.0% of patients treated with the combination versus 5.1% for sorafenib.

In the POSEIDON study (NCT03164616), a randomized, multicenter, active-controlled, open-label trial for patients with NSCLC and wild-type *ALK/EGFR* and without previous therapy:

- The median overall survival for tremelimumab-actl combined with durvalumab was 14.0 months versus 11.7 months for platinum-based chemotherapy (depending upon the type of NSCLC).
- The median progression-free survival for tremelimumab-actl combined with durvalumab was 6.2 months versus 4.8 months for platinum-based chemotherapy.
- The overall response rate was 39% among patients treated with tremelimumab-actl combined with durvalumab versus 24% of patients treated with platinum-based chemotherapy.
- Follow up studies after 5 years showed that overall survival benefit is greater among those with higher tumor mutation burden in their cancer.

Molecular biology and pharmacology

The therapeutic is referred to as immunotherapy, immune checkpoint inhibitor, and/or an anti-CTLA-4 antibody. It is a negative regulator of CTLA-4, T-cell activity. The antibody binds to CTLA-4 and thereby blocks the interaction between CTLA-4 and its ligand/binding partners, CD80 and CD86. Without this binding, the T-cells are no longer connected to the cancer cell and no longer silenced. Instead, the T-cells are activated. As a result, there will be a decrease in tumor growth and an increase in T-cells within the tumors.

DRUG DOSING AND ADMINISTRATION

The drug is administered as an intravenous infusion over 60 minutes. With combinations, tremelimumab-actl is administered first, before durvalumab. Wait 60 minutes after the infusion of tremelimumab-actl before administering durvalumab (over 60 minutes) and then chemotherapy if it applies.

Tremelimumab-actl comes in two different dosage strengths. All drugs should be administered as separate intravenous infusions. In addition, the drugs should not be co-administered through the same infusion line.

Dose Guidance

Cancer Type	Weight 30 kg and more	Weight less than 30 kg
Hepatocellular carcinoma	300 mg (w/durvalumab 1500 mg) cycle 1/day 1 followed by durvalumab 1500 mg every 4 weeks	4 mg/kg (w/durvalumab 20 mg/kg) cycle 1/day 1 followed by durvalumab 20 mg/kg every 4 weeks
Non-small cell lung cancer	75 mg every 3 weeks (w/durvalumab 1500 mg & chemo) for 4 cycles occurring on weeks 0, 3, 6, and 9; followed by durvalumab 1500 mg alone every 4 weeks with pemetrexed therapy every 4 weeks, and a fifth 75 mg dose with durvalumab dose 6, at week 16	1 mg/kg every 3 weeks (w/durvalumab 20 mg/kg & chemo) for 4 cycles occurring on weeks 0, 3, 6, and 9; followed by durvalumab 20 mg/kg every 4 weeks with pemetrexed therapy every 4 weeks, and a fifth 1 mg/kg dose with durvalumab dose 6 at week 16

Infusion-Related Reaction

Depending on the severity and type of reaction, the infusion of tremelimumab-actl may be slowed, interrupted or even permanently discontinued.

SIDE EFFECTS AND MANAGEMENT

In the clinical trials, patients with unresectable **hepatocellular carcinoma reported common adverse reactions** (≥20%) as abdominal pain (20%), diarrhea (27%), fatigue (26%), musculoskeletal pain (22%), pruritus (23%), and rash (32%). Lab abnormalities (≥40%) include alkaline phosphatase increased, alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, bilirubin increased, hemoglobin decreased, lymphocytes decreased and sodium decreased. Five-year follow up studies reported no late-onset treatment-related serious effects.

Among patients with metastatic **NSCLC, the most common adverse reactions** (≥ 20%) of patients included decreased appetite (28%), diarrhea (22%), fatigue (36%), musculoskeletal pain (29%), nausea (42%), and rash (27%).

Warnings and Precautions

There are several warnings associated with tremelimumab-actl. These include embryo-fetal toxicity, immune-mediated adverse reactions, and infusion-related reactions.

Embryo-Fetal Toxicity

The drug can cause harm to the fetus. Females of reproductive potential are advised to use effective contraception during treatment and for 3 months after the last dose.

Infusion-Related Reactions

For Grade 1 or 2 infusion-related reactions, interrupt or slow the rate of infusion and consider premedication for subsequent infusions. If a reaction manifests as Grade 3 or Grade 4, then permanently discontinue the infusion.

Immune-Mediated Adverse Reactions

For agents that target immune checkpoints, like tremelimumab-actl, immune-mediated adverse reactions are possible. This is especially possible given that tremelimumab-actl targets the inhibition of the CTLA-4 pathway and is used in combination with durvalumab, which removes the inhibition of the PD-L1 pathway. Together, this drug combination has the potential to induce an adverse reaction mediated by the immune system.

By inducing a massive inflammatory reaction of the immune system, damage to organs is possible. Depending on where the damage occurs, it can manifest as immune-mediated colitis, dermatologic reactions, endocrinopathies (adrenal insufficiency, hypophysitis, thyroid disorders, etc.), hepatitis, nephritis, pancreatitis, pneumonitis, rejection of solid organ transplantation, or life threatening myocarditis, pericarditis, myelitis, or myasthenic syndrome.

Depending on the severity and type of reaction, the drug may be withheld or permanently discontinued. Clinicians should monitor for early identification of immune-mediated adverse reactions for management. Patients should have their liver enzymes evaluated at baseline and then again before each does, along with creatine, adrenocorticotropic hormone levels, and thyroid function.

If tremelimumab-actl and durvalumab causes a reaction that requires interruption or discontinuation, administration of systemic corticosteroid therapy (1 to 2 mg/kg per day prednisone or the equivalent, sometimes at least 40 mg per day) is necessary until it improves to Grade 1 or less. Then the taper is initiated for at least 1 month. If this is not sufficient for a patient, consider systemic immunosuppressants. The table below provides more information for the immune-mediated adverse events.

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Management of other notable side effects of tremelimumab-actl

Adverse event	Common management guidance
Colitis	Grade 2 – Withhold Grade 3 or 4 – Permanently discontinue
Dermatologic conditions	**Suspected** Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), or drug rash with eosinophilia and systemic symptoms (DRESS) – Withhold **Confirmed** SJS, TEN, DRESS – Permanently discontinue
Endocrinopathies	Grade 3 or 4 – Withhold until medically stable or if severe, permanently discontinue
Hepatitis with **no** tumor involvement in the liver	Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) increases to more than three and up to eight times the upper limit of normal (ULN) – **Withhold** Or Total bilirubin increases to more than 1.5 to three times the ULN – **Withhold** AST or ALT increases to more than eight times ULN – **Permanently discontinue** Or Total bilirubin increases to more than three times ULN – **Permanently discontinue**
Hepatitis with tumor involvement in the liver	Baseline aspartate aminotransferase (AST) or alanine aminotransferase (ALT) is more than one and up to three times the upper limit of normal (ULN) and increases to more than five and up to 10 times ULN – **Withhold** Or The baseline AST or ALT is more than three and up to five times ULN and increases to more than eight and up to 10 times ULN – **Withhold** AST or ALT increases to more than 10 times ULN – **Permanently discontinue** Or Total bilirubin increases to more than three times ULN – **Permanently discontinue**
Myocarditis	Grade 2, 3, or 4 – Permanently discontinue
Nephritis with renal dysfunction	Grade 2 or 3 increased blood creatine – Withhold Grade 4 increased blood creatine – Permanently discontinue
Neurological toxicities	Grade 2 – Withhold Grade 3 or 4 – Permanently discontinue
Pneumonitis	Grade 2 – Withhold Grade 3 or 4 – Permanently discontinue

QUESTIONS & ANSWERS

Q. **What dose modifications are recommended for adverse reactions?**

A. There are no dose reductions recommended for the treatment of tremelimumab-actl. For any Grade 3 immune-mediated reactions, the drug should be withheld. For Grade 4 reactions, the drug should be permanently discontinued. For recurrent, severe Grade 3 reactions, discontinue the drug as well.

Q. **What should patients tell their providers about before receiving tremelimumab-actl?**

A. If patients are pregnant or planning to become pregnant, they need to tell their providers. The drug carries lethal harm to developing fetuses. An effective method of birth control is required during treatment and then for 3 months following the last dose. Breastfeeding patients need to also tell their provider.

If a patient has an immune problem, they need to tell their providers because tremelimumab-actl may trigger underlying immune conditions. This includes Crohn's disease, ulcerative colitis, and/or lupus. Nervous system conditions like myasthenia gravis or Guillain-Barré syndrome should be disclosed.

Q. **What else should I tell my patients who will receive tremelimumab-actl?**

A. The first day of treatment, Week 0 in the treatment cycle, patients will receive multiple infusions with a break between these – it will be a long day of treatment. First, they will receive an infusion of tremelimumab-actl over 60 minutes, followed by a 60-minute break. Second, they will receive an infusion of durvalumab over 60 minutes. For patients with NSCLC (not hepatocellular carcinoma) this will be followed by an infusion with platinum-containing chemotherapy. During infusions, patients will be monitored for signs of infusion-related reactions.

Q. **What are the most common side effects of tremelimumab-actl when used in combination with durvalumab among adult patients?**

A. For those with unresectable hepatocellular carcinoma, the most common side effects include abdominal pain, diarrhea, feeling tired, itchiness, muscle pain, and rash.

For those with NSCLC, the most common side effects include decreased appetite, diarrhea, feeling tired or weak, muscle or bone pain, nausea, and rash.

PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

American Cancer Society
https://www.cancer.org/

Bristol Myers Squibb Medication Guides
Information about idecabtagene vicleucel.
ABECMA.com
1-888-805-4555

NIH: National Cancer Center
https://www.cancer.gov/

FINANCIAL ASSISTANCE

Pfizer Patient Assistance Program
Provides free Pfizer medicines to eligible patients through their doctor's office or at home.
https://www.pfizerrxpathways.com/resources/patients

Cancer Financial Aid Coalition
Facilitates communication, educates and advocates for patients.
www.cancerfac.org

Centers for Medicare and Medicaid Services (CMS)
Apply to determine if you are eligible for government assistance.
www.cms.gov or www.medicare.gov
1-800-633-4227

Lazarex Foundation
Provides assistance with travel costs for clinical trial participation. Ask your social work counselor for a referral if you have been consented to a clinical trial for melanoma.
www.lazarex.org

Needymeds
Database to search for free or low-cost medications, help with medical transportation and other resources.
www.needymeds.org

Patient Advocate Foundation
Provides assistance with mediation, financial stability, and other assistance. Funds subject to availability. Patient must meet their eligibility for financial assistance.
www.patientadvocate.org
1-800-532-5274

The Sam Fund for Young Adult Survivors of Cancer
Assists cancer survivors ages 21-39 with their transition into post-treatment life. This program distributes grants and scholarships in an effort to enable survivors to pursue goals.
www.thesamfund.org
info@thesamfund.org

PRESCRIPTION ASSISTANCE

CancerCare Co-Payment Assistance Foundation
Helps with the cost of medication. Availability of funds for patients with Stage IV melanoma subject to availability.
www.cancercarecopay.org
1-866-552-6729

Medicine Assistance Tool
Database to search for patient assistance resources offered by pharmaceutical companies.
www.medicineassistancetool.org/

Patient Advocate Foundation Co-Pay Relief
Provides direct financial support to patients who medically qualify. Availability of funds for patients with Stage IV melanoma subject to availability.
www.copays.org
1-866-512-3861

Good Days
Formerly known as the Chronic Disease Fund. Provides assistance with insurance co-pays, and prescription medications. Funds subject to availability. www.mygooddays.org

HealthWell Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Availability of funds for patients with Stage IV melanoma subject to availability. Patient must also meet eligibility for financial assistance.
www.healthwellfoundation.org or grants@healthwellfoundation.org
1-800-675-8416

The Assistance Fund, Inc
Provides prescription copay and financial assistance, including health insurance premiums. Availability of funds for patients with Stage IV melanoma subject to availability.
www.theassistancefund.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Availability of funds for patients with Stage IV melanoma subject to availability.
www.panfoundation.org
1-866-316-PANF (7263)

Patient Assistance Program
Comprehensive database of patient assistance programs offering free medications.
www.rxassist.org
info@rxassist.org

HOUSING

American Cancer Society – Hope Lodge
Provides free housing during treatment appointments. Requires a referral from your social worker.
www.cancer.org/
1-800-227-6333

American Cancer Society – Extended Stay America
Partnership to offer discounted rooms for patients who have to be away from home for cancer treatment.
https://www.cancer.org/about-us/our-partners/extended-stay-america.html
1-800-227-2345

Healthcare Hospitality Network
Connects patients and their caregivers looking for lodging near their healthcare provider
https://members.hhnetwork.org/locate-a-house
1-800-318-8861

Joe's House
Helping patients with cancer find lodging throughout the U.S.
https://www.joeshouse.org/lodging?state=0
1-877-563-7468

National Council of State Housing Agencies
Emergency rental assistance programs available by state. Federal grants still available in some areas.
https://www.ncsha.org/emergency-housing-assistance/

TRANSPORTATION (AIR AND GROUND)

Air Charity Network
Provides access for people in need who are seeking free air transportation to specialized health care facilities
http://aircharitynetwork.org/
1-877-621-7177

Corporate Angel Network
Nonprofit organization that helps cancer patients by arranging free travel on corporate aircraft
https://www.corpangelnetwork.org/
info@corpangelnetwork.org
1-914-328-1313

Medicaid
Ground transportation only. Sets up rides and provides mileage reimbursement for Medicaid patients only.
1-877-633-8747

Mercy Medical Angels
Provides free medical transportation (flights, gas cards, bus and train tickets) for patients with financial needs who need to travel more than 50 miles. Patients must meet their eligibility for financial assistance.
www.mercymedical.org/

Pilots for Patients
Provides free flights to people in need of medical treatment. Patient must be medically stable to fly and be ambulatory. Ask your social worker about a referral.
www.pilotsforpatients.org
1-318-322-5112

ADDITIONAL RESOURCES

IMJUDO® (tremelimumab-actl). Highlights of prescribing information. Revised January 2024. Updated August 2024. Accessed May 2025. AstraZeneca. Available at: https://den8dhaj6zs0e.cloudfront.net/50fd68b9-106b-4550-b5d0-12b045f8b184/0102c6fd-de8a-4b43-afa3-2a2c2115d472/0102c6fd-de8a-4b43-afa3-2a2c2115d472_viewable_rendition__v.pdf

Johnson ML, Cho BC, Luft A et al. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. *J Clin Oncol*. 2023;41(6):1213-1227. doi: 10.1200/JCO.22.00975.

Peters S, Oliner KS, L'Hernault A et al. Durvalumab with or without tremelimumab in combination with chemotherapy in first-line metastatic non-small-cell lung cancer: outcomes by tumor mutational burden in POSEIDON. *ESMO Open.* 2025;10(5):105058. doi: 10.1016/j.esmoop.2025.105058.

Rimassa L, Chan SL, Sangro B et al. Five-year overall survival update from the HIMALAYA study of tremelimumab plus durvalumab in unresectable HCC. *J Hepatol*. 2025:S0168-8278(25)00226-0. doi: 10.1016/j.jhep.2025.03.033.