Durvalumab

An HCP Tool From AIM with Immunotherapy

Durvalumab (Imfinzi) is a Programmed Cell Death-Ligand 1 (PD-L1) blocking antibody and therefore an immune checkpoint inhibitor drug. This toolkit is based on the indication of durvalumab for the treatment of adult patients with unresectable, Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Multiple indications

Durvalumab has multiple indications. Current approvals for durvalumab include:

- Adult patients with metastatic NSCLC with no sensitizing epidermal growth factor receptor mutations or anaplastic lymphoma kinase genomic tumor aberrations: Durvalumab In combination with tremelimumab-actl and platinum-based chemotherapy as first line treatment
- Extensive-stage small cell lung cancer: Durvalumab in combination with etoposide and either carboplatin or cisplatin as first line therapy
- Adult patients with locally advanced or metastatic biliary tract cancer: Durvalumab in combination with gemcitabine and cisplatin
- Adult patients with unresectable hepatocellular carcinoma: Durvalumab in combination with tremelimumab-actl
- Adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient: Durvalumab approved in combination with carboplatin and paclitaxel followed by durvalumab as a single agent as maintenance treatment

Clinical trial results

The PACIFIC phase 3 global clinical trial (NCT02125461) established the effectiveness and safety of durvalumab for the care of patients with unresectable, Stage III NSCLC.

- Median progression-free survival was 16.9 months with durvalumab versus 5.6 months with placebo
- The 12-month progression-free survival rate was 55.9% with durvalumab and 35.3% with placebo
- The 18-month progression-free survival rate was 44.2% with durvalumab and 27.0% with placebo
- Median time to death or distant metastasis was 23.2 months with durvalumab versus 14.6 months with placebo

Five-year survival data from this trial showed robust and durable benefit of durvalumab. An estimated 42.9% of patients receiving durvalumab remained alive at 5 years, compared to 33.4% in placebo arm. In addition, 33.1% of patients who received durvalumab were alive without evidence of disease progression at 5 years.

The observational, retrospective PACIFIC-R study (NCT03798535) assessed whether the benefit of durvalumab from the clinical trial is achieved in real world clinical practice. The median overall survival was not reached after ~3 years of follow-up. Over 60% of all patients were alive. Progression-free survival outcome with durvalumab was favorable and comparable to outcomes in the PACIFIC study.

DRUG DOSAGE AND ADMINISTRATION

Durvalumab is administered as an intravenous infusion over 60 minutes. It is given for either every two or four weeks until disease progression, unacceptable toxicity, or a maximum of 12 months, depending on indication and intent of treatment.

For patients with Stage III NSCLC of weight ≥30 kg, 10 mg/kg is given every two weeks or 1,500 mg every four weeks. For patients of weight <30 kg, 10 mg/kg is given every two weeks.

The measurement and evaluation of liver enzymes, creatinine, and thyroid function tests are performed at baseline and periodically during treatment.

No dose reductions or modifications for durvalumab are recommended. The drug is withheld for severe, Grade 3, immune-mediated adverse reactions. For Grade 4 immune-mediated adverse reactions or recurrent severe Grade 3 reactions not responsive to corticosteroid dosing within 12 weeks, durvalumab is permanently discontinued.

SIDE EFFECTS AND MANAGEMENT

The most common adverse reactions (≥20%) of durvalumab in patients with unresectable, Stage III NSCLC are cough (40%), fatigue (34%), pneumonitis/radiation pneumonitis (34%), upper respiratory tract infections (26%), dyspnea (25%), and rash (23%). The percentage of patients will adverse reactions occurred at all grades. Approximately 18% of patients reported diarrhea on durvalumab. Other adverse reactions occurring in <10% of patients were dysphonia, dysuria, night sweats, peripheral edema, and increased susceptibility to infections.

Infusion-related reactions are possible and occurred in 2.2% of patients receiving durvalumab as a single agent. Complications of allogenic HSCT can occur. This drug may cause fetal toxicity. Females with the potential of reproduction should be advise of the risk and use contraception.

Immune-related adverse events

Severe or fatal immune-mediated toxicities may occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PD-L1 blocking antibody. Usually these occur during treatment with the drug, but they can also manifest after drug discontinuation.

The possibilities of immune-mediated adverse reactions can manifest as colitis, dermatologic adverse reactions, endocrinopathies, hepatitis, nephritis and renal dysfunction, pancreatitis, pneumonitis, and solid organ transplant rejection. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.

Management

For durvalumab no dose reductions or modifications are recommended. Withhold for severe (Grade 3) immune-mediated adverse reactions and permanently discontinue durvalumab for life-threatening (Grade 4) and severe, recurrent Grade 3 reactions. In the clinical trial, PACIFIC, that examined the safety of durvalumab, the drug was discontinued due to adverse reactions in 15% of patients. The most common adverse reactions leading to durvalumab discontinuation were pneumonitis or radiation pneumonitis whereby fatal pneumonia occurred in <2% of patients.

When durvalumab reactions require interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or the equivalent) until improvement to ≤Grade 1. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Administration of systemic immune-suppressants should be considered in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Management of administration with notable side effects of durvalumab

Adverse event	Common management guidance
Pneumonitis	Grade 2: Withhold Grade 3 or 4: Permanently discontinue
Colitis	Grade 2: Withhold Grade 3: Withhold or permanently discontinue Grade 4: Permanently discontinue
Endocrinopathies	Grade 3 or 4: Withhold until stable or permanently discontinue depending on severity
Hepatitis with no tumors in the liver	Withhold: ALT or AST increases to more than 3 and up to 8 times the upper limit normal (ULN) or total bilirubin increases to more than 1.5 and up to 3 times ULN Permanently discontinue: ALT or AST increases to more than 8 times ULN or total bilirubin increases to more than 3 times the ULN
Hepatitis with liver tumors	Withhold: AST or ALT is more than 1 and up to 3 times ULN at baseline and increases to more than 5 and up to 10 times ULN or AST or ALT is more than 3 and up to 5 times ULN at baseline and increases to more than 8 and up to 10 times ULN Permanently discontinue: ALT or AST increases to more than 10 times ULN or total bilirubin increases to more than 3 times ULN
Intestinal Perforation	Any Grade: Permanently discontinue
Myocarditis	Grade 2, 3 or 4: Permanently discontinue
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine: Withhold Grade 4 increased blood creatinine: Permanently discontinue

AIM WITH IMMUNOTHERAPY FOUNDATION

QUESTIONS & ANSWERS

Q. How long will patients stay on durvalumab?

A. Patients with Stage III NSCLC are administered an intravenous infusion of durvalumab on a cycle every 2, 3, or 4 weeks for up to 12 months. Clinicians will determine how long a patient will receive the drug. Infusions usually last 60 minutes.

Q. What is the most important information to know about durvalumab?

A. Durvalumab can cause the immune system to attack normal organs and tissues in the body because it works by generating a response from the immune system. Sometimes, this response can elicit life-threatening problems. These can be severe and happen during or after treatment with the drug.

Q. How can a health care provider identify a severe infusion reaction?

A. Patients who experience severe infusion reactions usually develop the following symptoms: chills or shaking, dizziness, facial swelling, feeling of impending passing out, fever, flushing, itching, pain in the back or neck, rash, and shortness of breath or wheezing.

Q. What symptoms may indicate that a patient who is receiving durvalumab is also experiencing hormone gland problems from treatment?

A. Hormone gland problems may manifest as headaches that will not subside or are otherwise unusual. Other indicates can be: changes in mood or behavior, constipation, dizziness, eye problems, extreme fatigue, fainting, feeling cold, feeling more hungry than usual, forgetfulness, hair loss, increased sweating, irritability, rapid heartbeat, sensitivity to light, urinating more than usual, and weight loss or gain.

Q. What are possible side effects of durvalumab therapy in adults with NSCLC?

A. Patients who were given durvalumab most commonly cough, feeling tired, inflammation of the lungs, rash, shortness of breath and upper respiratory tract infections.

PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

American Cancer Society
Patient programs, services, 24/7 hotline, etc
https://www.cancer.org/

National Cancer Institute
Information about cancer types, treatment, side effects, find a clinical trial, etc
https://www.cancer.gov/

FINANCIAL ASSISTANCE

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
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
800-532-5274

The Sam Fund for Young Adult Survivors of Cancer
The Sam Fund for Young Adult Survivors of Cancer assists 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 specific cancers is 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. Funds subject to availability.
https://copays.org
1-866-512-3861

Good Days
Provides assistance with insurance co-pays, and prescription medications. Funds subject to availability.
www.mygooddays.org

Health Well Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Funds for patients 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. Funds subject to availability.
www.theassistancefund.org
https://tafcares.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Funds 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
318-322-5112

ADDITIONAL RESOURCES

Antonia SJ, Villegas A, Daniel D et al. Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. *N Engl J Med*. 2017;377(20):1919-1929. doi: 10.1056/NEJMoa1709937.

Filippi AR, Bar J, Chouaid C et al. Real-world outcomes with durvalumab after chemoradiotherapy in patients with unresectable stage III NSCLC: interim analysis of overall survival from PACIFIC-R. *ESMO Open*. 2024;9(6):103464. doi: 10.1016/j.esmoop.2024.103464.

Spigel DR, Faivre-Finn C, Gray JE et al. Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. *J Clin Oncol*. 2022;40(12):1301-1311. doi: 10.1200/JCO.21.01308.

IMFINZI (durvalumab) [prescribing information]. Wilmington, DE, USA and Cambridge, England: AstraZeneca Pharmaceuticals LP. 2024. Available at: https://den8dhaj6zs0e.cloudfront.net/50fd68b9-106b-4550-b5d0-12b045f8b184/9496217c-08b3-432b-ab4f-538d795820bd/9496217c-08b3-432b-ab4f-538d795820bd_viewable_rendition__v.pdf