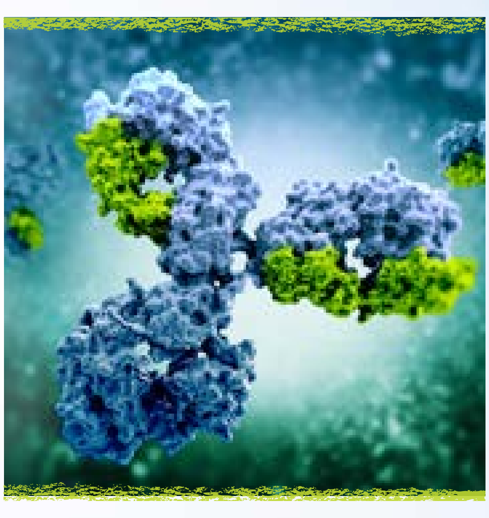
DANYELZA™
(naxitamab-gqgk)
40mg/10mL Injection

Information About DANYELZA® (Naxitamab-gqgk) 40mg/10mL Injection

What is DANYELZA?

DANYELZA is a prescription medicine used with another medicine called GM-CSF (Granulocyte-Macrophage Colony-Stimulating Factor) to treat children 1 year of age and older and adult patients with high-risk neuroblastoma in the bone or bone marrow that has come back (relapsed) or that did not respond to previous treatment (refractory), and has shown a partial response, minor response, or stable disease to prior therapy. DANYELZA is a GD2-binding monoclonal antibody that is given by intravenous (IV) infusion by a healthcare professional (HCP). DANYELZA is approved based on two clinical studies that looked at reducing tumor size. DANYELZA is still being studied to confirm the study results and the clinical benefit of treatment.[1]

How DANYELZA Works



- DANYELZA is a humanized monoclonal antibody that targets GD2, which is found mostly on the surface of neuroblastoma cells. DANYELZA binds to GD2 molecules on neuroblastoma tumor cells to help destroy them.[1]
  - DANYELZA binds to the GD2 target because of the amino acid sequence of its binding site.
  - GD2 is also expressed on skin cells. Because of this, patients may experience severe pain from nerves (neuropathic pain) when receiving DANYELZA. Please see below for serious infusion-related reactions and nervous system problems.
- In studies not conducted in humans, DANYELZA caused tumor cell death by engaging the body's own immune system to target tumor cells via innate or acquired toxicity, antibody dependent cellular cytotoxicity (ADCC), and complement dependent cytotoxicity (CDC).[1]
- DANYELZA is given with another drug called GM-CSF.

Dosing and Administration of DANYELZA

- DANYELZA is a liquid solution that is given through an IV (intravenously) by a healthcare professional. GM-CSF is administered subcutaneously prior to infusion and during infusion. GM-CSF may be administered either by the healthcare provider or the caregiver.[1]
- DANYELZA is given 3 days in one week and this is referred to as Day 1, Day 3, and Day 5. This 1 week of DANYELZA treatment is considered 1 cycle of treatment. Treatment cycles are repeated every 4-8 weeks until disease progression or unacceptable toxicity. Subsequent cycles may be repeated every 8 weeks until disease progression or unacceptable toxicity from first infusion of DANYELZA. The doctor will assess the patient's response to each treatment to determine if treatment should continue.[1]

DANYELZA Clinical Trial Data

DANYELZA was approved under FDA's Accelerated Approval program based on overall response rate (ORR) and duration of response (DOR) seen in two clinical trials that assessed the safety and efficacy of DANYELZA in patients with high-risk neuroblastoma in the bone or bone marrow demonstrated a partial response, minor response, or stable disease to prior therapy. Continued approval may be contingent upon the outcome of ongoing confirmatory clinical trials.[1]

- Study 201 is an ongoing study where patients know they are receiving DANYELZA, and DANYELZA is not being compared with another treatment. It is being conducted at several different locations in the United States as well as other countries. This is done to evaluate the efficacy and safety of DANYELZA in patients with refractory or relapsed high-risk neuroblastoma in the bone or bone marrow and demonstrated a partial response, minor response, or stable disease to prior therapy. Patients with progressive disease were excluded. All patients received at least one systemic therapy to treat disease outside of the bone or bone marrow prior to patient enrollment. 22 patients were evaluated for efficacy during the ongoing study.
- Study 12-230 was a study where patients knew they were receiving DANYELZA, and DANYELZA was not being compared with another treatment. It was conducted at a nationally recognized neuroblastoma center in the United States in patients who had relapsed or refractory high-risk neuroblastoma in the bone or bone marrow and demonstrated a partial response, minor response, or stable disease to prior therapy. Patients with progressive disease were excluded.[1] The study was conducted in two phases. The first phase studied dosing. The second phase evaluated the efficacy and safety of DANYELZA. Patients were required to have received at least one dose of DANYELZA at a dose of 3 mg/kg or greater per infusion and have evaluable disease at baseline according to independent review per the revised International Neuroblastoma Response Criteria (INRC). A total of 117 patients participated in the study and 38 patients were evaluated for efficacy.
- In both studies patients were previously treated with other therapies, which included surgery, chemotherapy, radiation, stem cell transplant, and anti-GD2 therapy.[1]

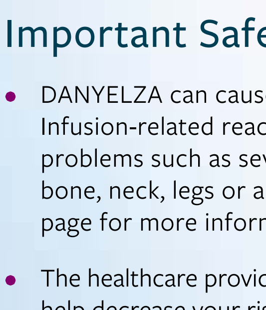
The efficacy of DANYELZA in combination with GM-CSF was measured by overall response rate (ORR) and duration of response (DOR). ORR is defined as the percentage of patients who responded to treatment. ORR includes looking at what is called a complete response (CR) and a partial response (PR). A CR is when patients showed no physical evidence of disease on examination or imaging tests after treatment and a PR is when patients had their cancer reduced by at least half. DOR is defined as the length of time that the tumor continues to respond to treatment without the cancer growing or spreading.

STUDY 201 (22 patients)

Of the patients who received DANYELZA, 45% (10 out of 22 patients) responded to treatment, with either a complete or partial response (overall response rate)

- **36%** (8 out of 22 patients) showed no physical evidence of disease on examination or imaging tests after treatment (complete response)
- **9%** (2 out of 22 patients) had their cancer reduced by at least half (partial response)

STUDY 12-230 (38 patients)



Of the patients who received DANYELZA, 34% (13 out of 38 patients) responded to treatment, with either a complete or partial response (overall response rate)

- **26%** (10 out of 38 patients) showed no physical evidence of disease on examination or imaging tests after treatment (complete response)
- **8%** (3 out of 38 patients) had their cancer reduced by at least half (partial response)

Duration of response

30% (7 patients) — **30% of patients (7 out of 22 patients) had a duration of response ≥6 months** — **6 months**

23% (9 patients) — **23% of patients (9 out of 38 patients) had a duration of response ≥6 months** — **6 months**

Serious Infusion-Related Reactions and Nervous System Problems: Important Safety Information

- DANYELZA can cause serious infusion-related reactions that require immediate medical attention. Infusion-related reactions are common with DANYELZA. DANYELZA can also cause nervous system problems such as severe pain from nerves (neuropathic pain), including pain in the belly (abdomen), bone, neck, legs or arms. Pain is common with DANYELZA and can be severe. Please see the back of this page for more information on these side effects and other side effects of DANYELZA.
- The healthcare provider will give patients certain medicines before and during their DANYELZA infusion to help decrease your risk of getting pain, infusion-related reactions, and nausea or vomiting.
- The healthcare provider may slow down the infusion rate, temporarily stop DANYELZA infusion, or permanently stop treatment with DANYELZA if certain side effects are experienced. Patients will be monitored for side effects for at least 2 hours after each DANYELZA infusion.

Medicines Given to Help with Side Effects:

- Prophylactic medication for pain (e.g., gabapentin)
- Allergy reducers (e.g., antihistamines)
- Nausea reducers (e.g., antiemetics)
- Prescription pain medicine (e.g., opioids)
- General anesthetic (e.g., ketamine)
- Fever reducers (e.g., acetaminophen)
- Drugs that lower inflammation (e.g., corticosteroids)[1]

Please click for full PRESCRIBING INFORMATION AND PATIENT INFORMATION for DANYELZA including Boxed Warning on serious infusion reactions and pain, and talk to your doctor.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about DANYELZA?
DANYELZA may cause serious side effects, including:

- **Serious infusion reactions**. DANYELZA can cause serious infusion-related reactions that require immediate medical attention. Infusion-related reactions are common with DANYELZA. Tell your healthcare provider right away if you get any signs or symptoms during or after your DANYELZA infusion, including:
  - swelling of your face, eyes, lips, mouth, or tongue
  - itching
  - redness on your face (flushing)
  - skin rash or hives
  - trouble breathing
  - cough or wheezing
  - noisy high-pitched breathing
  - feeling faint or dizziness (low blood pressure)
- **Nervous system problems. Talk to your healthcare provider right away if you have new symptoms or worsening of nervous system problems, including:**
  - **Severe pain from nerves (neuropathic pain),** including pain in the belly (abdomen), bone, neck, legs, or arms. Pain is common with DANYELZA and can be severe.
  - **Inflammation of the spinal cord.** Signs or symptoms may include:
    - weakness in your legs or arms
    - bladder and bowel problems
    - pain in back, legs, or stomach (abdomen)
    - numbness
    - tingling
    - burning sensation
  - **Reversible Posterior Leukoencephalopathy Syndrome (RPLS – also known as Posterior Reversible Encephalopathy Syndrome - PRES).** PRES is a condition that affects the brain. Your healthcare provider will monitor your blood pressure and check for any neurologic symptoms after your DANYELZA infusion. Signs or symptoms of PRES may include:
    - severe headache
    - vision changes
    - changes in mental status, such as confusion, disorientation or decreased alertness
    - difficulty speaking
    - weakness in your arms or legs
    - seizures
  - **Numbness, tingling, or burning sensation in the arms or legs.**
  - **Nervous system problems of the eye.** Signs or symptoms may include:
    - unequal pupil size
    - blurred vision
    - trouble focusing your eyes
    - larger pupil size (dilated)
    - decreased ability to see
    - sensitivity to light
  - **Problems urinating or emptying your bladder (prolonged urinary retention).**

Do not receive DANYELZA if you have had a severe allergic reaction to naxitamab-gqgk (the active ingredient in DANYELZA). Ask your healthcare provider if you are not sure.

Before receiving DANYELZA, tell your healthcare provider about all your medical conditions, including if you:

- Have high blood pressure
- Are pregnant or plan to become pregnant. DANYELZA may harm your unborn baby.
  - Your healthcare provider will do a pregnancy test before you start treatment with DANYELZA.
  - Females who are able to become pregnant should use effective birth control (contraception) during treatment and for **2 months** after your last dose of DANYELZA. Talk to your healthcare provider about birth control choices that may be right for you during this time.
  - Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with DANYELZA.
- Are breastfeeding or plan to breastfeed. It is not known if DANYELZA passes into your breast milk. Do not breastfeed during treatment and for **2 months** after your last dose of DANYELZA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of DANYELZA?

DANYELZA may cause serious side effects, including:

- **See "What is the most important information I should know about DANYELZA?"**
- **High blood pressure (hypertension).** High blood pressure is common in people who receive DANYELZA. Your blood pressure will be monitored during your DANYELZA infusion, and at least each day on Days 1 to 8 of each DANYELZA treatment cycle. Tell your healthcare provider right away if you get any signs or symptoms of high blood pressure, including:
  - headaches
  - seizures
  - nausea or vomiting
  - chest pain
  - dizziness
  - visual changes
  - shortness of breath
  - feeling that your heart is pounding or racing (palpitations)
  - nose bleeds

The most common side effects of DANYELZA include:

- fast heart rate
- vomiting
- cough
- nausea
- decreased white blood cell, red blood cell, and platelet counts
- diarrhea
- decreased appetite
- tiredness
- skin rashes
- decreased level of potassium, sodium, and phosphate in the blood
- hives
- fever
- headache
- injection site reaction
- swelling of the body or only in one part of the body
- anxiety
- irritability
- increased liver function blood tests
- decreased blood sugar level
- decreased calcium levels in the blood
- decreased protein levels (albumin) in the blood

These are not all of the possible side effects of DANYELZA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please click for full PRESCRIBING INFORMATION AND PATIENT INFORMATION for DANYELZA including Boxed Warning on serious infusion-related reactions and nervous system problems, and talk to your doctor.

References

1. Y-mAbs Therapeutics (2020). Label on File.

Y-mAbs Therapeutics, Inc.™