Protocol Plain Language Summary

A clinical study of pembrolizumab in children and young people with classical Hodgkin lymphoma (MK-3475-667)

Protocol Title: An Open-label, Uncontrolled, Multicenter Phase II Trial of MK-3475 (Pembrolizumab) in Children and Young Adults with Newly Diagnosed Classical Hodgkin Lymphoma with Inadequate (Slow Early) Response to Frontline Chemotherapy (KEYNOTE 667)

Why is this study needed?

Researchers are looking for new ways to treat children and young people with **classical Hodgkin Lymphoma (cHL)**. **cHL** is cancer in the lymphatic system that causes swollen lymph nodes and tumors in the body. The lymphatic system is a network of tissues and organs that are part of the body's immune system. **Chemotherapy** and **radiation therapy** are often used to treat children with a new diagnosis of cHL. Chemotherapy is medicine that destroys cancer cells or stops them from growing, and radiation therapy is treatment that uses beams of intense energy (like X-rays) to shrink or get rid of tumors. Many children with cHL that get these treatments are cured, but some children are not cured.

Pembrolizumab (study medicine) is an immunotherapy, which is a treatment that helps the immune system fight cancer. The goal of this study is to learn if treating children and young people with pembrolizumab and chemotherapy helps the cancer shrink or go away.

Who will take part in this study?

About 340 children and young people with a new diagnosis of cHL will be in the study. They will be between the ages of 3 to 25 years and**:**

- Did not have another type of cancer in the past 3 years
- Have not received treatment for cHL

What treatments are being given during the study?

All children and young people in the study will receive:

- Chemotherapy, given through a needle in a vein as an intravenous (IV) infusion, with or without a steroid medicine taken by mouth. Some of the children and young people in the study will then go on to receive:
- Pembrolizumab- given by IV infusion, with or without radiation therapy.

How is this study designed?

Children and young people in this study will be divided into two groups, depending on the stage of cHL (how far along cancer is in the body) when the person is diagnosed.

- Group 1- low risk
- Group 2- high risk

Each group will receive 2 cycles of treatment including several different chemotherapy medicines for about one month. Then, an imaging test will be done to see if the cHL responded to the chemotherapy. If the person's cancer responds to the first treatment, this is called a **rapid early responder (RER).** Their study doctor will follow up with RERs and will give them further treatment if they need it.

If the person's cancer does not respond to the treatment, this is called a **slow early responder (SER).** SERs will receive 2 or 4 more cycles of chemotherapy treatment and will also receive pembrolizumab.

After another imaging test, people will receive more pembrolizumab treatment. Pembrolizumab will be given every 3 weeks for up to about a year, with or without radiation therapy.

Both the people in the study and the researcher will know which study treatment a person is getting (open-label study). During the study, people may give urine and blood samples, have tumor and imaging tests, and have physical examinations. A person may be in the study for up to about 9 years.

What are the goals of this study and how will they be measured?

Main goal	How it will be measured
To learn the **objective response rate (ORR)** of people who receive pembrolizumab with chemotherapy	**ORR** is the number of people whose cancer responds to treatment (gets smaller or goes away). Doctors who are not part of the study will measure this in group 1 and 2 SERs.

Other goals	How they will be measured
To learn about the **Positron Emission Tomography (PET)** negativity rate in children and young people who receive pembrolizumab and chemotherapy	PET is an imaging test for cHL. A negative test means that cHL cannot be seen or can only be seen in certain areas of the body. Researchers will measure the number of people with a negative test in: • Group 1 and 2 SERs • Group 1 after first chemotherapy treatment
To learn about the **event free survival (EFS)** in children and young people who receive pembrolizumab and chemotherapy	EFS is the length of time people live without the cancer growing, spreading, or coming back. Researchers will measure this in: • Group 1 and 2 SERs (up to 2 years after the study start) • Group 1 and 2 RERs (up to 3 years after study start)
To learn about the **overall survival (OS)** in children and young people who receive pembrolizumab and chemotherapy	OS is the length of time that people live from the start of the study until death from any cause. Researchers will measure OS in: • Group 1 and 2 SERs • Group 1 and 2 RERs
To learn about the radiation therapy that children and young people receive	Researchers will describe the number of times and doses that children and young people received radiation therapy.
To learn about a biomarker (a substance made by a tumor that can be detected in blood) in cHL	Researchers will measure the amount of a biomarker called **TARC** in people's blood samples at several time points
To learn about safety and how well people tolerate pembrolizumab in combination with chemotherapy	The number of people who: - Had an adverse event (AE) – An AE is a health problem that happens or worsens during a study - Stopped treatment due to an AE

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.