Protocol Plain Language Summary

A clinical study of pembrolizumab in children with advanced melanoma, solid tumors, or lymphomas (MK-3475-051)

Protocol title: A Phase I/II Study of Pembrolizumab (MK-3475) in children with advanced melanoma or a PD-L1 positive advanced, relapsed, or refractory solid tumor or lymphoma (KEYNOTE-051)

Why is this study needed?

Researchers are looking for new ways to treat children with different types of melanoma (skin cancer), solid tumors, and lymphomas (blood cancers) that are any of these:

- **Advanced**, which means cancer spread in the body or cannot be removed with surgery
- **Relapsed,** which means cancer has come back after it had responded to previous treatment (**responded** means it stopped growing, gets smaller, or disappeared)
- **Refractory**, which means cancer did not respond to previous treatment

Pembrolizumab is an immunotherapy, which is a treatment that helps the immune system fight cancer. Researchers want to learn if different doses of pembrolizumab:

- Can cause at least 1 of the types of cancer to get smaller or go away
- Are safe and how well children tolerate (manage) the treatment

Who will take part in this study?

About 320 children with cancer will be in this study. They will be 6 months to 18 years old and:

- Have certain types of cancer
- Not have tumors on their brain stem
- Have certain gene mutations (a change in a person's DNA) or **biomarkers**, which are substances made by cancer that can be detected in blood, tissues, or other body fluids. Biomarkers may show how well cancer responds to a treatment.

What treatments are being given during the study?

All children in this study will receive **pembrolizumab (the study medicine)** given through a needle into a vein as an intravenous (IV) infusion. Children will receive pembrolizumab once every 3 weeks for up to about 2 years. Some children may receive 1 more year of pembrolizumab (3 years total).

How is this study designed?

This study has 2 parts:

- **Part 1** will learn about the safety of different doses of pembrolizumab in up to 36 children and choose a dose to use in Part 2. Researchers will start by giving the low dose of pembrolizumab to the first children. Researchers will check to see if there are any safety concerns or medical problems before giving higher doses. Researchers will choose a dose to use in Part 2 based on safety data and how well it may work.
- **Part 2** will learn more about the safety and effects of the chosen dose in a larger number of children.

The children, the children's caregivers, and researchers will know which treatment the child takes because everyone receives pembrolizumab (also called an open-label study).

During the study, children may have tumor, blood, urine, and imaging tests, and have physical examinations. Children or their caregivers will answer questions about their health. After treatment, researchers will check on the children over the phone. Children may be in this study for up to 5 years total.

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

Main goals	How they will be measured
To learn about the **dose limiting toxicities (DLTs)** of pembrolizumab during Part 1 – **DLTs** are medical problems related to study medicine that prevent giving a higher dose	The number of children who have a DLT at the highest dose of pembrolizumab during the first 3 weeks of treatment
To learn about **safety** and how well children **tolerate** pembrolizumab	The number of children who: • Have an **adverse event (AE)** – An AE is a health problem that happens or worsens during a study • Stopped treatment due to an AE
To learn about the **objective response rate (ORR)** of children with different types of cancer who receive pembrolizumab	**ORR** is the number of children who have the cancer get smaller or go away during the study

Other goals	How they will be measured
To learn what happens to different doses of pembrolizumab in the body over time	Researchers will measure the amount of pembrolizumab in blood samples at different time points during the study
To learn about the **immune system response** of children who receive pembrolizumab	Researchers will measure the amount of a protein called interleukin 2 (IL-2) in blood samples during the first 22 days of treatment. IL-2 is a protein in the immune system that can help fight cancer.
To learn how different types of cancer **respond** after receiving pembrolizumab	During the study, researchers will measure: • **Duration of response**: the average length of time from when cancer first responds to treatment until cancer gets worse • **Disease control rate**: the number of children who have the cancer stop growing, get smaller, or go away • **Progression-free survival**: the average length of time a child is alive from the start of treatment until the cancer gets worse or death due to any cause • **Overall survival**: the average length of time that children live from the start of treatment until death due to any cause • **ORR** measured using a different tool than the tool used for the main goal
To learn about changes in levels of certain **biomarkers** and compare biomarker levels to other goals	Researchers will measure changes in the level of certain biomarkers and compare biomarker levels to other goals such as ORR during the study

What are the possible benefits and risks?

Children in this study may not benefit from treatment, such as having cancer stop growing or go away. More information about benefits and risks may be found in the Investigator's Brochure, Protocol, and Informed Consent documents.