Expanding the Utility of Leukine®, an FDA-Approved Treatment for Hematopoietic Acute Radiation Syndrome (H-ARS), as a Medical Countermeasure (MCM) to Counter Higher Priority and Emerging Chemical, Biological and Radio-Nuclear Threats

Leukine is a yeast-derived recombinant human granulocyte-macrophage colony-stimulating factor (rhu GM-CSF) that plays a critical role in host defense and stimulating immunity. Leukine was first approved in 1991 to reduce the incidence of severe and life-threatening infection following induction chemotherapy in patients with myeloid leukemia and was subsequently approved for four other oncology indications. In 2018, FDA approved Leukine to treat patients exposed to myelosuppressive doses of radiation (H-ARS) based upon its effectiveness in increasing survival after exposure in the setting of minimal supportive care that mimics the limited resource environment in a radio-nuclear mass casualty event.

Partner Therapeutics is developing Leukine to treat sulfur mustard (HD) induced myelosuppression. By leveraging data supporting Leukine's approval for H-ARS and safety and efficacy data from patients receiving Leukine after mustard-derived chemotherapeutic agents, PTx aims to rapidly generate required data to bridge a treatment gap for warfighters exposed to HD. The initial objective will be to deliver updated clinical practice guidelines (CPGs) on treatment for HD exposure with an ultimate objective of FDA approval under the "Animal Rule."

When used as an agent of chemical warfare, HD would likely spread by aerosol transmission resulting in inhalational, dermal, and ocular exposure. Dermal and respiratory HD exposures typically result in permeating systemic exposure triggering bone marrow (BM) suppression, which leads to myelosuppression and pancytopenia. HD symptoms include headache, nausea, vomiting, epigastric pain, leukopenia, thrombocytopenia and anemia. Leukopenia was reported in patients requiring hospitalization after exposure during World War I, World War II and the Iran-Iraq War. Mortality was reported in all cases where leukocyte counts dropped below 200/µl. Hematological damage is the primary driver of long-term hospitalization and severe hematological damage is the primary cause of mortality.

There are no products approved to treat myelosuppressive effects of HD exposure. Clinical chemotherapeutic and therapeutic radiation data, as well as data from Non-Human Primate (NHP) ARS studies, support Leukine's potential use in HD exposure. Leukine accelerates recovery from BM suppression and pancytopenia which reduces the rate of infection and septicemia. These data suggest that Leukine is likely to provide the same benefits after HD exposure.

Lovelace Biomedical Research Institute's NHP HD model produces BM suppression and pancytopenia and the inhalation route used for exposure is consistent with exposure in most human casualties. A pilot study, currently underway, will confirm HD exposure levels in the animal model generate clinical and hematological outcomes consistent with those reported in literature on human exposures.

Leukine treatment following HD exposure is hypothesized to enhance recovery and decrease duration and severity of pancytopenia. A placebo-controlled study of Leukine in LBRI's model will be completed during October 2022. Animals will be exposed to an HD dose expected to produce leukopenia, thrombocytopenia and reticulocytopenia. During the 28-day study period, animals will be evaluated for changes in hematological parameters, immune response, clinical signs, pathology, and weight. A full description of the model and key results evaluating Leukine's effects in treating HD-induced myelosuppression generated from the pilot and the placebo-controlled studies will be presented at the conference.

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