HLHRUXO STUDY INFORMATION SHEET

OVERVIEW

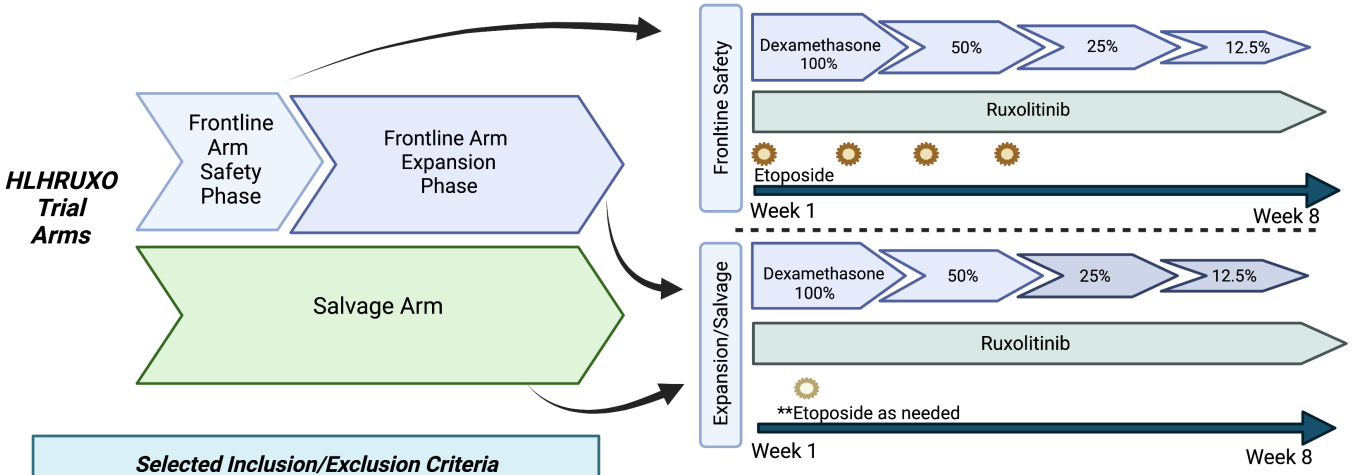
The North American Consortium for Histiocytosis (NACHO) is conducting a clinical study to examine the efficacy and tolerability of the Janus Kinase (JAK) inhibitor ruxolitinib (Jakafi®) given in combination with dexamethasone and etoposide (if needed) for the treatment of children with newly diagnosed or relapsed/refractory hemophagocytic lymphohistiocytosis (HLH).

Ruxolitinib is being examined because it inhibits signaling downstream of multiple cytokines that are elevated in HLH, including interferon (IFN)-gamma, interleukin (IL)-2, IL-6, IL-10, IL-12, among others.

Because of its broad anti-cytokine activity, ruxolitinib holds potential to synergize with other HLH-directed agents such as steroids and/or etoposide to more effectively reduce the inflammation that occurs in HLH.

STUDY APPROACH

HLHRUXO is a multi-site Phase Ib/II, two-arm (Frontline and Salvage), non-randomized, study of ruxolitinib given in combination with dexamethasone and etoposide if needed.



Selected Inclusion/Exclusion Criteria
Inclusion: *1. Active Disease* *2. >/=6 weeks of age to </=22 years of age* *3. Salvage: previous treatment of HLH with standard of care therapy with reactivation or failure to respond to therapy*
Exclusion: *1. Malignancy or rheumatologic disorder* ***Prior Therapy Exclusions:*** *1. Frontline: any HLH-directed therapy except steroids or anakinra* *2. Salvage: any JAK inhibitor, emapalumab, tocilizumab, alemtuzumab in last 3 months*

HLHRUXO Therapy Overview		
Dexamethasone	Start Week 1 and wean every 2 weeks	
Ruxolitinib	Start Week 1, continue to end of Week 8	
Etoposide	Frontline Safety	Frontline Expansion *AND* Salvage Arm
	Weekly x 4 doses, continued based on response	Added as needed based on response

The study has an overall duration of approximately 52 weeks. In the Frontline Arm Safety Phase patients will receive ruxolitinib in addition to dexamethasone and etoposide for 8 weeks. Once 6 patients have successfully completed the Frontline Arm Safety Phase, the Frontline Arm Expansion Phase will open.

On the Frontline Arm Expansion Phase and the Salvage Arm, patients will receive ruxolitinib and dexamethasone. If HLH responds favorably, these patients will continue ruxolitinib and dexamethasone for 8 weeks. Patients whose HLH does not respond favorably, will have etoposide added. Etoposide will be administered weekly up to week 8. After week 8, patients with primary (genetic, familial) HLH should proceed to allogeneic hematopoietic stem cell transplntation, while those with secondary (non-genetic, non-familial) HLH should wean off therapy, disease status permitting. If needed, ruxolitinib will be provided as a part of this study for up to one year for patients who require continuation therapy.

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PATIENTS ELIGIBLE FOR TREATMENT

All patients must have active disease based on presence of >5 of 8 HLH-2004 diagnostic criteria for those with secondary HLH or HLH of unknown etiology at diagnosis, or >4 of 8 HLH-2004 diagnostic criteria for those with primary HLH. Patients must be and be ≥6 weeks to ≤ 22 years of age.

To be eligible for for the ***Frontline Arm***, patients must not have received any other HLH-directed therapy except for up to 2 weeks of steroids or anakinra at any dose.

To be eligible for the ***Salvage Arm***, HLH must have failed to adequately respond or reactivated after previous standard of care therapy (etoposide, ATG, dexamethasone). Patients must not have received JAK inhibitors or other anti-cyokine therapies (such as tocilizumab, emaplaumab) in the 3 months prior to enrolling.

For more information about inclusion/ exclusion criteria, please go to ClinicalTrials.gov (NCT04551131).

HOW TO ENROLL PATIENTS

Please contact the HLHRUXO team at: HLHRUXO@stjude.org
Study website: nacho-consortium.org

PRINCIPAL INVESTIGATORS

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COLLABORATING SITES

Atrium Health Levine Children's Hospital, Charlotte, NC, **Dr. David Gass**

Children's Hospital of Orange County, Orange, CA, **Dr. Lilibeth Torno**

Children's Hospital of Philadelphia, Philadelphia, PA, **Dr. David Teachey**

Children's National, Washington DC, **Dr. Birte Wistinghausen**

Children's Wisconsin, Milwaukee, WI, **Dr. Julie-An Talano**

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