Phase II trial evaluating an ex-US on-demand chemotherapy delivery strategy at room temperature for patients with stage III or IV Hodgkin's Lymphoma

Background: In the US and other high resource countries, stage III and IV Hodgkin's lymphoma is potentially curable with 6 year overall survival above 90%.[1] In low resource countries, overburdened public health departments struggle with the high cost of diagnosis and treatment especially as it regards procurement of chemotherapy drugs. While some patients in those countries do have access to private clinics that provide state of the art care, the majority of patients receive care through publicly funded hospitals and clinics. These public hospitals and clinics may not be able to reliably procure and dispense curative intent chemotherapy, turning potentially curable illnesses into chronic and sometimes fatal illnesses.

Internationally, drug prices are opaque, due in part to rebates and relationships between manufacturers, distribution companies, hospitals, pharmacies and pharmacy benefit managers. Smaller hospitals and low resource countries may struggle to navigate this complex system.

During a short stay in a country in Eastern Africa as part of an ASH approved collaboration between US and local Hematology/Oncology physicians, I witnessed first hand the brilliance and hard work of local physicians, but also the limits of their care when consistent, reliable chemotherapy was not available.

In high resource countries, the longstanding generic chemotherapy cocktail for Hodgkin's lymphoma, ABVD (adriamycin, bleomcyin, vinblastine and dacarabazine), is usually stored between 2 and 8 degrees celsius. This type of storage may not be possible in lower resources countries where reliable electricity is not universal. There is data to show that these drugs retain their potency without constant refrigeration if kept away from direct sunlight and used within 24 hours.[2]

In an effort to reduce barriers to curative intent chemotherapy of Hodgkin's lymphoma, I have founded a company that aims to purchase the generic drugs necessary for treatment from pharmaceutical manufacturing companies and act as the direct distributor to public cancer hospitals in low resource countries with minimal profit margin, not to exceed 15%. This pilot study will act as an attempt to treat 10 Hodgkin's lymphoma patients in this manner and report on the challenges and successes.

Given the limited availability of Radiation Oncology and imaging for response assessment, patients will be treated without Radiation Therapy and response will be tailored to the local hospital's standard of care, with at least CBC, BMP and a physical exam done before each treatment and at the end of treatment. For those patients with stage I or II disease, treatment will be considered complete after 4 cycles.

Phase of Study: II
Estimated Monthly Accrual: 1
Proposed Minimum Sample Size: 10
Estimated Date the Study can Begin: 6/1/2025
Projected Accrual Dates: 6/1/25-5/31/26
Funding Sources: None
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Hypotheses:

Primary Outcome Null Hypothesis: Treating patients in the developing world for Hodgkin's lymphoma using ABVD delivered by room temperature using an effective altruistic delivery model is not realistic and is not feasible.

Primary Outcome Alternate Hypothesis: Treating patients in the developing world for Hodgkin's lymphoma using ABVD delivered by room temperature using an effective altruistic delivery model is realistic and is feasible.

Eligibility Criteria:

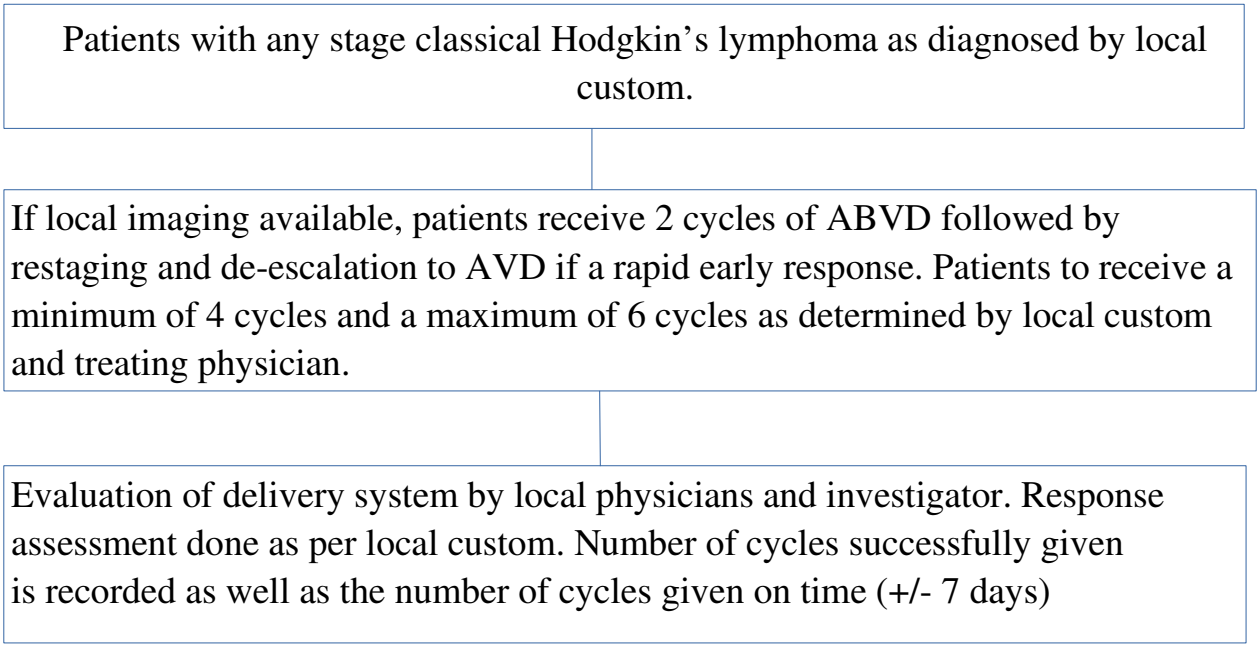
1. Patients must be >= 16 years of age
2. Patients must have the ability to understand and the willingness to sign an informed consent document in the language of their choosing.
3. Patients must have an ECOG performance status of 0-2.ECOG PS can be higher if due solely to their disease.
4. Patients must have a documented pathologic diagnosis of classical Hodgkin's lymphoma. Lymphocyte predominant HL patients are ineligible.
5. Patients must not have any known allergies, hypersensitivity or intolerance to corticosteroids, adriamycin, bleomycin, vinblastine, or dacarbazine.
6. Patients with all stages of HL are eligible. The number of cycles and the use of consolidative curative intent radiation therapy is left up to the discretion of the treating physician with no fewer than 4 cycles of ABVD and no more than 6 cycles with each including lasting 28 days and including a day #1 and day #15 treatment day.
7. Patients must have measurable disease as determined by local custom. If local custom allows CT or PET imaging, those will be included at diagnosis, as an interim scan between cycles 2 and 4 and as an end of treatment scan.
8. Patients must have adequate organ function as defined below:
    a. Creatinine clearance > 30 ml/min
    b. Absolute neutrophil count >= 1000/mm3, unless BM involvement, then > 500/mm3
    c. Untransfused platelet count >=75,000/mm3, unless BM involvement, then > 50,000/mm3
    d. Hemoglobin >= 8 g/dL, unless BM involvement, then > 6 g/dL
    e. Total bilirubin <= 1.5 X ULN (institution upper limit of normal)
    f. AST and ALT <= 3 X ULN
9. Patient must have received no more than one cycle of ABVD prior to enrollment.

10. Patients must not be pregnant or breast feeding and must agree to ongoing pregnancy testing during treatment.
11. Patients infected with Human immunodeficiency virus (HIV) must be on effective anti-viral therapy.
12. Patients with concurrent active malignancy outside of cutaneous non-melanoma skin cancers are excluded.
13. Patients with known history of cardiomyopathy with LVEF <= 40% are excluded. If local custom does not include echocardiography, patients must not have evidence of heart failure before their first treatment or prior to any treatment.
14. Patients with peripheral neuropathy >= CTC grade 2 are excluded
15. Patient must not have any serious medical or psychiatric illness that could, in the investigator's opinion, potentially interfere with the completion of treatment according to the protocol.

Statistical considerations:

Given the unusual nature of this intervention, it is difficult to define a baseline. One baseline of low resource countries is non-treatment and therefore any intervention is statistically important. It is beyond the scope of this study to retrospectively investigate prior outcomes of HL in each hospital that accrues patients. Therefore, this will be an "observational" study using a common sense approach to treating this disease and describing any successes and failures prospectively:

Schema:



Treatment Plan:

Administration Schedule for ABVD

a. All doses are based on actual body weight

b. Each cycle is 28 days and is composed of a d1 and d15 dose

c. Both arms will receive standard ABVD as described below

d. All patients will receive prophylactic and as needed anti-emetics as described below

e. Number of cycles to be determined by treating physician according to the clinical stage but will be no less than four cycles and no more than six cycles. Bleomycin dosing after 2 cycles determined by the treating physician.

f. If local custom and available, pulmonary function done prior to treatment and every two cycles

g. If local custom and available, anthrayclines delivered through central catheter.

Treatment Calendar:

	d1c1	d15c1	d1c2	d15c2	d1c3*	d15c3	d1c4	d15c4	d1c5	d15c5	d1c6	d15c6
Zofran 16 mg po d1												
Decadron 8 mg pod2, 3, 4, 16, 17, 18												
Adriamycin 25 m2/m2												
Bleomycin 10 Units/m2												
Vinblastine 6 mg/m2												
Dacarbazine 375 m2/m2												

* as per RATHL, if imaging available, Bleomycin will be dropped after 2 cycles for rapid early response

Bibliography:

1. Ansell, S. Echelon-1. NEJM 2022;387:310-20
2. ASHP Injectable drug information ISBN: 978-1-58528-743-7