Burkitt lymphoma treatment in UCI

**Patient Numbers**

- **173** patients enrolled with suspected BL (Jul 2012 – Jul 2014)
- **121 (70%)** were confirmed to be BL
  - **103 (85.1%)** received 1st line COM
  - **15 (12.4%)** Died before treatment
  - **3 (2.4%)** Refused treatment
- **52 (30%)** were non-BL
  - 13 (25%) LL
  - 3 (6%) RMS
  - 4 (8%) Retinoblastoma
  - 4 (8%) Other NHL
  - 3 (6%) PNET
  - 21 (40%) Other
  - 2 (4%) No Cancer

**Responses to 1st line COM+IT MTX**
- 70 (68%) had complete response
- 18 (17%) had partial or progressive disease
- 13 (Died during treatment)
- 2 Loss to Follow Up

**Current Status overall**
- 56 (46%) Disease free
- 52 (43%) Died
- 8 (7%) Lost to follow-up
- 5 (4%) Refused treatment
Objective To describe 12-month overall survival (OS) for endemic Burkitt lymphoma (eBL) treated with CHOP in Lilongwe; and examine risk factors associated with 12-month OS.
Method Children ≤18 years with newly diagnosed, pathologically confirmed eBL were enrolled in June 2013–March 2015 in the prospective Kamuzu Central Hospital (KCH) Lymphoma Study. During this period, staging and supportive care were standardized, as was treatment with COP prephase followed by CHOP for 6 cycles as tolerated. Children were actively traced when lost. We assessed 12-month Kaplan-Meier OS, and risk factors for mortality using adjusted Cox proportional hazards. Follow-up was calculated from enrollment until death or loss to follow-up.
Results Sixty-two children with eBL were treated with CHOP between June 1, 2013 and March 31, 2015. Median age was 8.7 years (IQR 6.8–11.3), 40 (65%) were male, and 1 was HIV-infected. Forty-nine (79%) presented with stage III/IV disease, 27 (44%) with abdominal disease, 51 (81%) had Lansky performance score ≤70, and 19 (31%) weight-for-age z-score ≤−2. Baseline median white blood cells were 8.6 x 10^3/μL (IQR 6.6–12.5), absolute neutrophils 4.2 x 10^3/μL (IQR 2.7–6.8), hemoglobin 9.9 g/dL (IQR 8.6–11.3), platelets 448 x 10^3/μL (IQR 310–599), albumin 3.4 g/dL (IQR 2.9–3.9) and lactate dehydrogenase (LDH) 696 IU/L (IQR 381–1415). As of March 31, 2015, 6 (9.7%) patients were lost to follow-up and estimated 12-month OS was 35% (95% CI 22–51%). Mortality was associated with age > median (HR 2.1, p = 0.04), weight-for-age z-score ≤−2 (HR 2.0, p = 0.06), LDH > median (HR 2.3, p = 0.03), and performance status ≤70 (HR 3.2, p = 0.05). Of 32 deaths, 17 were attributed to disease progression, 11 treatment, and 4 uncertain causes.
Conclusion Compared to published experience using less intense regimens, CHOP did not clearly improve outcomes for mostly advanced eBL in Lilongwe. However, CHOP may be appropriate for some children, and adjudicated deaths were more often due to disease than treatment. Older age, low weight, and higher LDH were associated with worse 12-month OS. Better risk stratification to more appropriately match higher treatment intensity to higher-risk children would likely improve outcomes.
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P: prednisolone, D: Doxorubicin, C: Cyclophosphamide, V: Vincristine, 
MTX: Methotrexate, Ara-C: Cytarabine, HC: Hydrocortisone
**Consolidation**

(starts 2 weeks after completion of induction)

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**Induction:**
C 300mg/m² + V 1mg/m² dl
P 40mg/m² for 4 weeks, followed by tapering dose
IT MTX 12mg + IT AraC 30mg + IT HC 30mg d3, 10, 17, 24
C 1200mg/m² + V 2mg/m² d8, 15, 22, 29, 36
Ara-C 60mg/m² d8, 29

**Consolidation:**
C: 1200mg/m² d2, 23
Ara-C: 75mg/m² SC d1–4, 22-25, 29-32
IT MTX 12mg + IT AraC 30mg, + IT HC 30mg d4, 25, 32
Treatment schema and events according to the treatment arm.

Flow chart of the trial.

Registration
762 eligible

105 not eligible for randomization
34 response to COP < 20%
11 protocol modification
4 early death
38 refusal
13 physician decision
5 mistake

Randomization
657 patients

164 assigned to COPADM2, M1 (standard)
4 excluded
2 other pathology
1 no data
1 LFU 43 days
160 analyzed

163 assigned to COPADM2, no M1
2 excluded
1 other pathology
1 no data
161 analyzed

167 assigned to COPADMI, M1
6 excluded
1 CNS +
5 other pathology
161 analyzed

163 assigned to COPADMI, no M1
8 excluded
1 CNS +
6 other pathology
1 no data
155 analyzed

Kaplan-Meier curves for survival, EFS, and FFS. Vertical bars denote 95% CI of the actuarial rates.