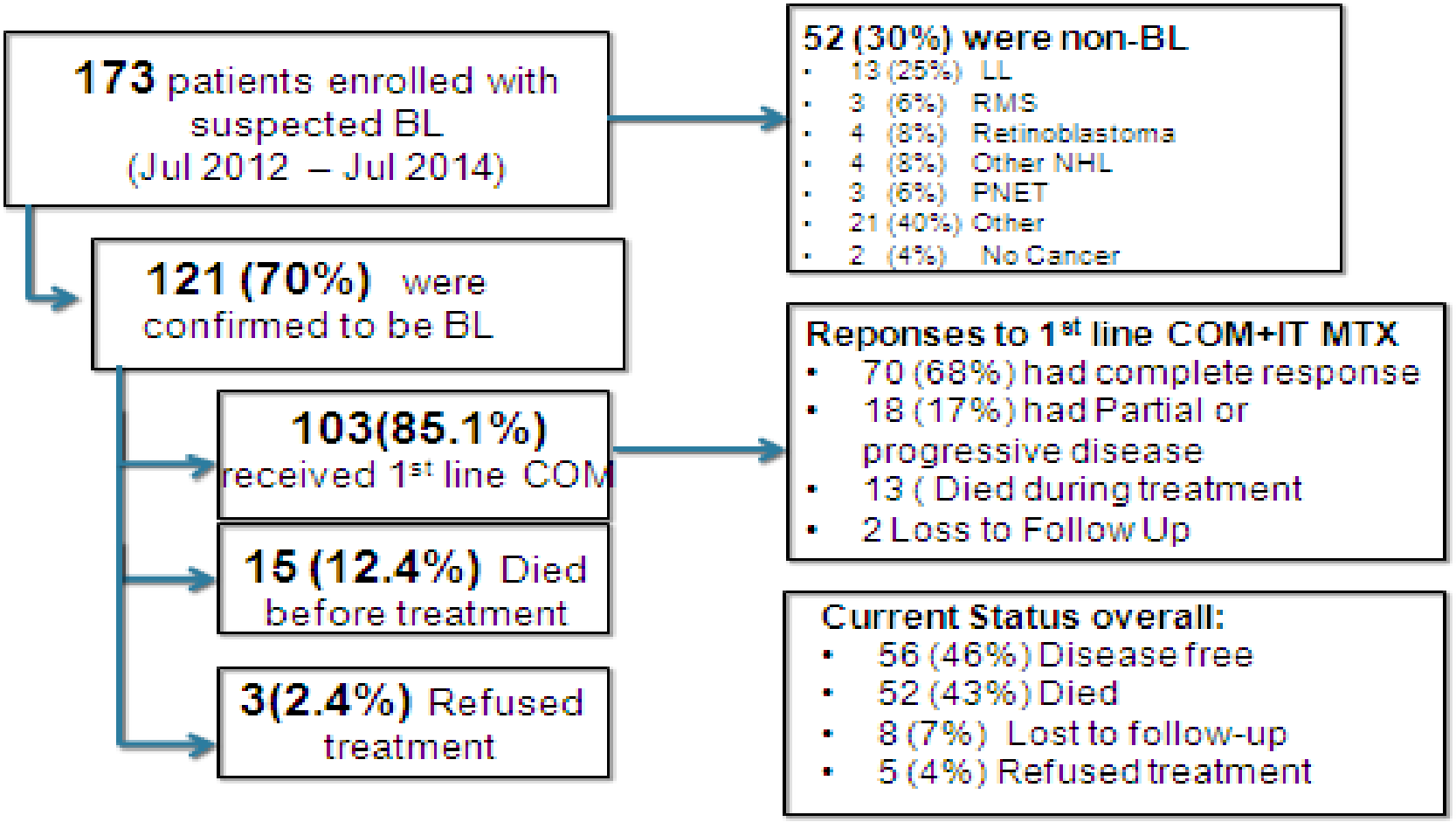
Burkitt lymphoma treatment in UCI

Patient Numbers



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2015

Stanley, Christopher

PREDICTORS OF ONE YEAR SURVIVAL AMONG CHOP-TREATED CHILDREN WITH ENDEMIC BURKITT LYMPHOMA IN LILONGWE, MALAWI

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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 103/μL (IQR 6.6–12.5), absolute neutrophils 4.2 x 103/μL (IQR 2.7–6.8), hemoglobin 9.9 g/dL (IQR 8.6–11.3), platelets 448 x 103/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.

Treatment(Regimen(

Induction(

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
1			**Day 1** P 40mg/m^2 C 300mg/m^2 V 1mg/m^2	**Day 2** P 40mg/m^2	**Day 3** P 40mg/m^2 IT MTX / Ara-C /HC	**Day 4** P 40mg/m^2	**Day 5** P 40mg/m^2
2	**Day 6** P 40mg/m^2	**Day 7** P 40mg/m^2	**Day 8** P 40mg/m^2 D 60mg/m^2 C 1200mg/m^2 V 2mg/m^2	**Day 9** P 40mg/m^2	**Day 10** P 40mg/m^2 IT MTX / Ara-C /HC	**Day 11** P 40mg/m^2	**Day 12** P 40mg/m^2
3	**Day 13** P 40mg/m^2	**Day 14** P 40mg/m^2	**Day 15** P 40mg/m^2 C 1200mg/m^2 V 2mg/m^2	**Day 16** P 40mg/m^2	**Day 17** P 40mg/m^2 IT MTX / Ara-C /HC	**Day 18** P 40mg/m^2	**Day 19** P 40mg/m^2
4	**Day 20** P 40mg/m^2	**Day 21** P 40mg/m^2	**Day 22** P 40mg/m^2 C 1200mg/m^2 V 2mg/m^2	**Day 23** P 40mg/m^2	**Day 24** P 40mg/m^2 IT MTX / Ara-C /HC	**Day 25** P 40mg/m^2	**Day 26** P 40mg/m^2
5	**Day 27** P 40mg/m2	**Day 28** P 40mg/m^2	**Day 29** P 20mg/m^2 D 60mg/m^2 C 1200mg/m^2 V 2mg/m^2	**Day 30** P 20mg/m^2	**Day 31** P 20mg/m^2	**Day 32** P 10mg/m^2	**Day 33** P 10mg/m^2
6	**Day 34** P 10mg/m^2	**Day 35** P 5mg/m^2	**Day 36** P 5mg/m^2 C 1200mg/m^2 V 2mg/m^2	**Day 37** P 5mg/m^2	**Day 38**	**Day 39**	**Day 40**

P: prednisolone, D: Doxorubicine, C: Cyclophosphamide, V: Vincristine,
MTX: Methotrexate, Ara-C: Cytarabine, HC: Hydrocortisone

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Consolidation

(starts 2 weeks after completion of induction):

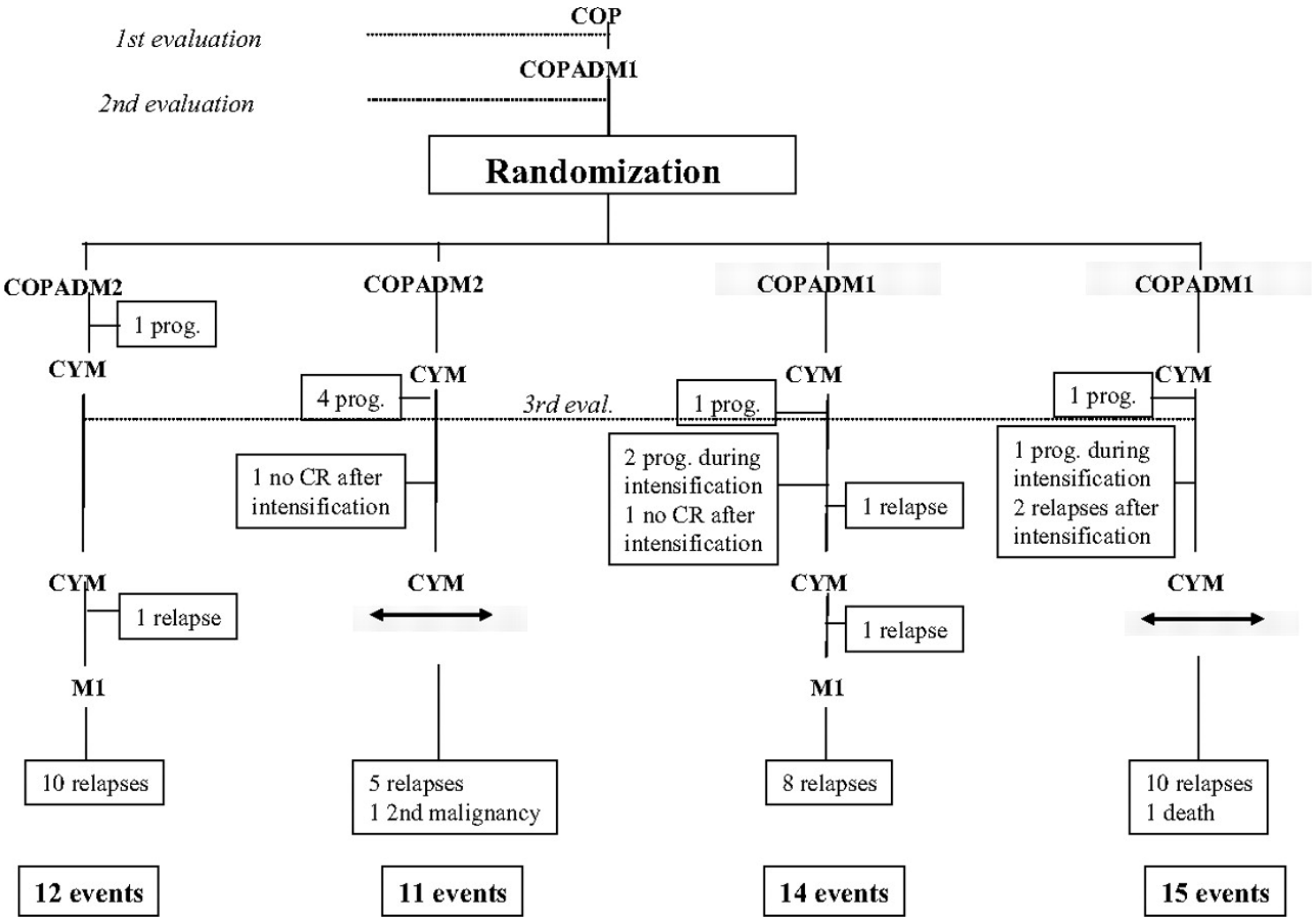
	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
1		Day 1 AraC SC 75mg/m2	Day 2 D 60mg/m^2 C 1200mg/m^2 Ara-C SC 75mg/m2	Day 3 Ara-C SC 75mg/m2	Day 4 IT MTX / Ara-C /HC AraC SC 75mg/m2	Day 5	Day 6
	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13
	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19	Day 20
2	Day 21	Day 22 AraC SC 75mg/m2	Day 23 C 1200mg/m^2 Ara-C SC 75mg/m2	Day 24 Ara-C SC 75mg/m2	Day 25 IT MTX / Ara-C /HC AraC SC 75mg/m2	Day 26	Day 27
3	Day 28	Day 29 AraC SC 75mg/m2	Day 30 Ara-C SC 75mg/m2	Day 31 Ara-C SC 75mg/m2	Day 32 IT MTX / Ara-C /HC AraC SC 75mg/m2	Day 33	

P: prednisolone, D: Doxorubicine, C: Cyclophosphamide, V: Vincristine,
MTX: Methotrexate, Ara-C: Cytarabine, HC: Hydrocortisone

Induction:
C 300mg/m^2 + V 1mg/m^2 d1
P 40mg/m^2 for 4 weeks, followed by tapering dose
IT MTX 12mg + IT AraC 30mg + IT HC 30mg d3,10,17, 24
C 1200mg/m^2 + V 2mg/m^2 d 8, 15, 22, 29, 36
A: 60^{mg}/m^2 d 8, 29

Consolidation:
C: 1200mg/m^2 d 2, 23
A: 60mg/m^2 d 2
Ara-C: 75mg/m^2 SC d 1-4, 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.



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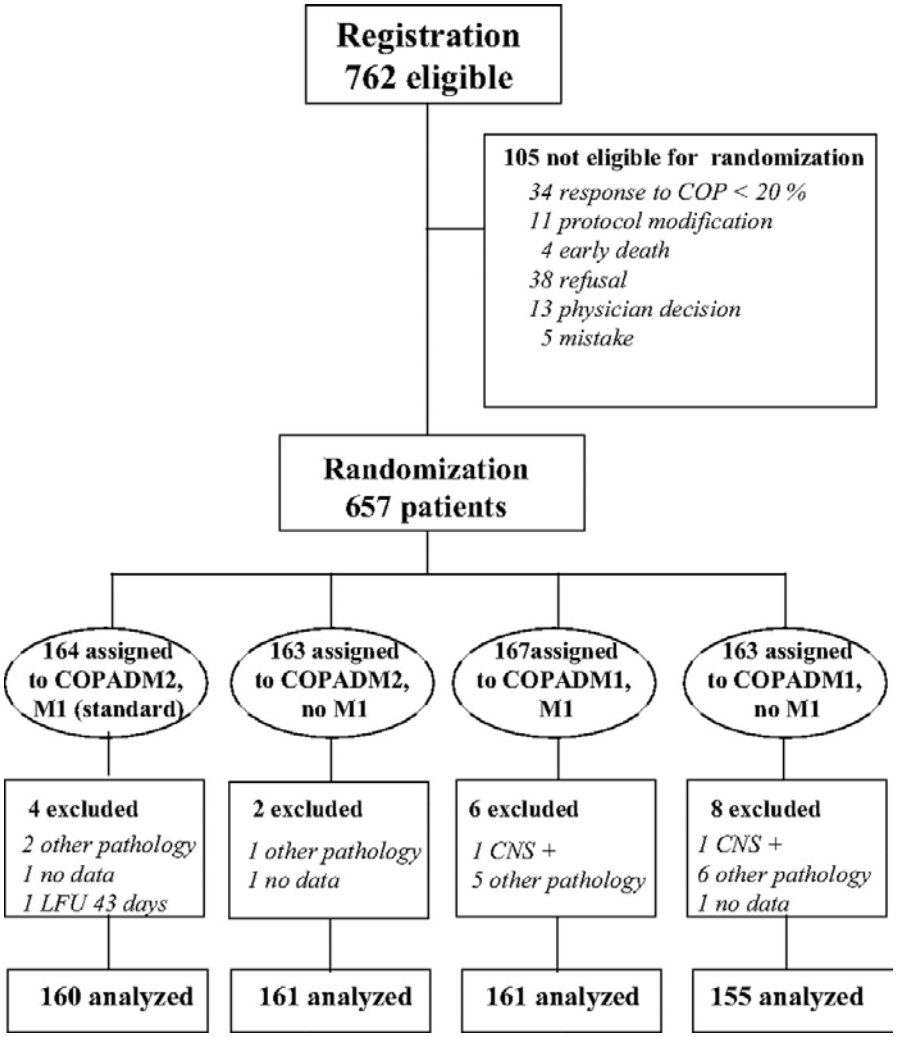
Flow chart of the trial.



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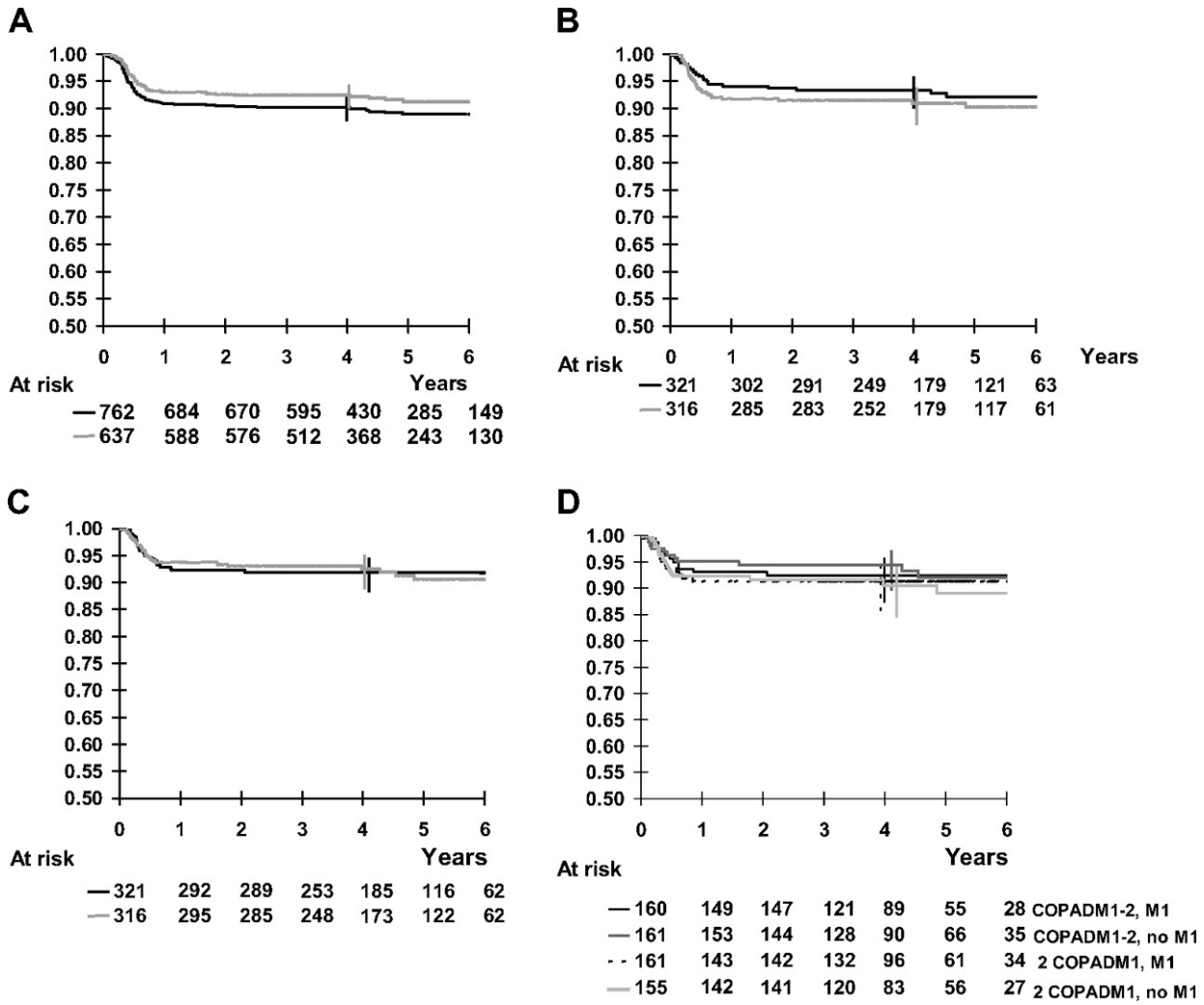
Kaplan-Meier curves for survival, EFS, and FFS. Vertical bars denote 95% CI of the actuarial rates.



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