CORSO EDUCAZIONALE

GRUPPO LINFOMI IN PAZIENTI CON IMMUNODEFICIT

**Milano, Best Western Hotel Madison**

29 maggio 2026

# Il linfoma di Burkitt: presente e futuro

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# Disclosures of Name Surname

| Company name | Research support | Employee | Consultant | Stockholder | Speakers bureau | Advisory board | Other |
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| Gilead/Kite | x | | | | | | x |
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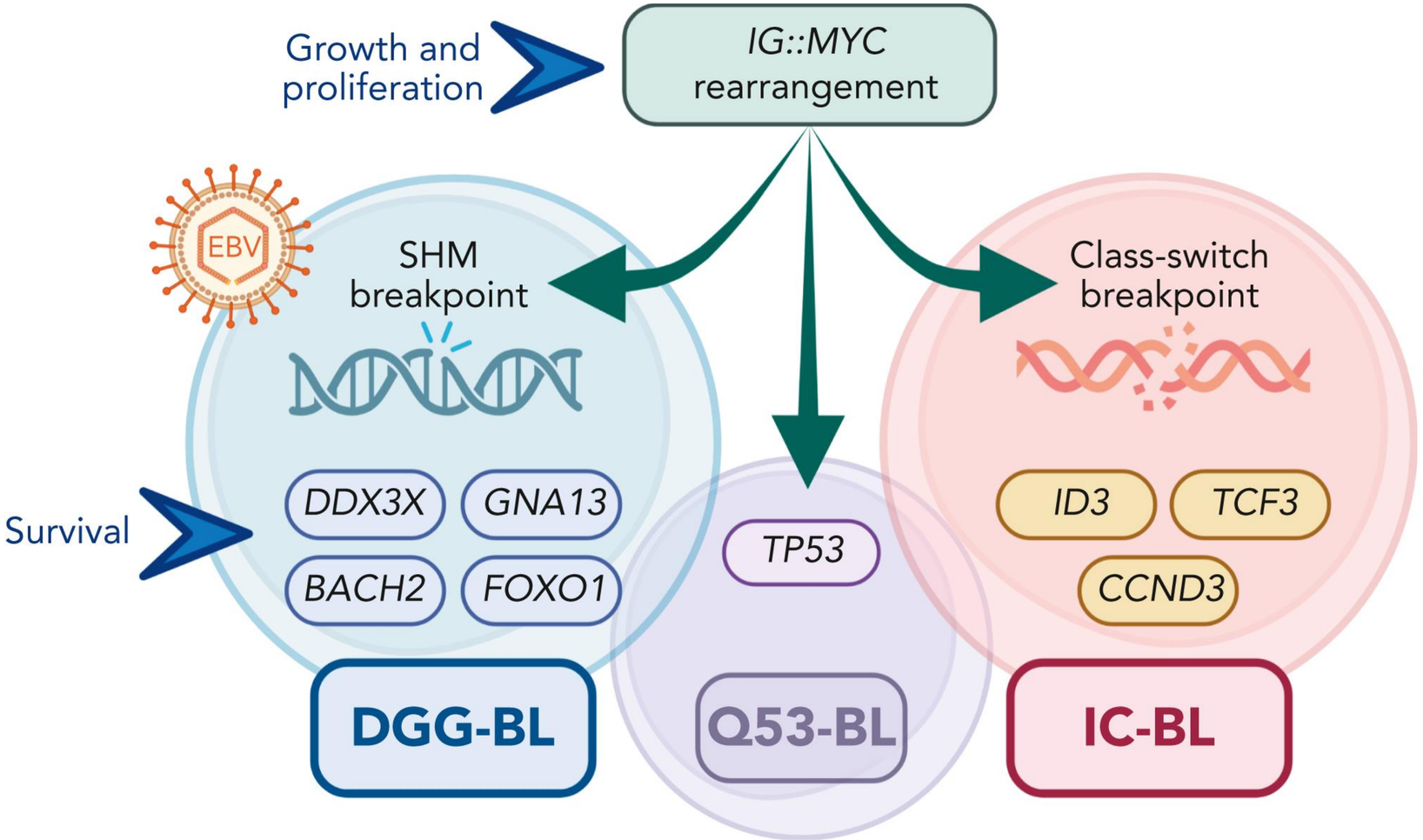
- Classification and risk factors
- **New biological insights**
- Treatment strategies in the present and future

**Table 1.** Epidemiologic and Clinical Features of Burkitt's Lymphoma Variants.*

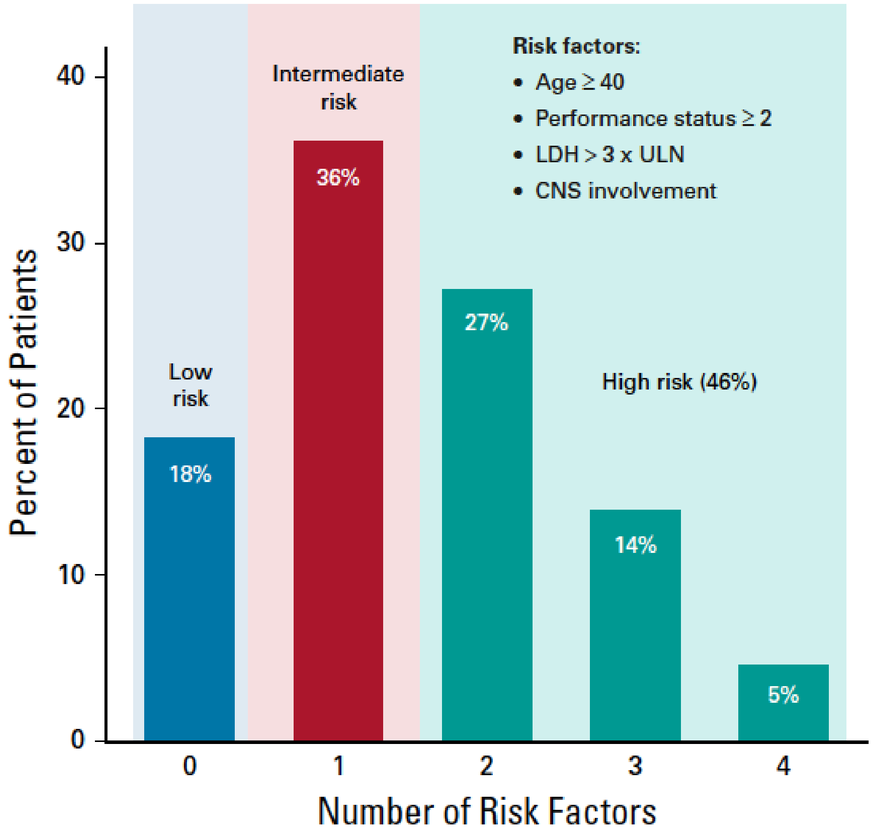
| Feature | Endemic Variant | Sporadic Variant | Immunodeficiency-Associated Variant |
|---|---|---|---|
| Incidence | 3–6 cases per 1000 children; 30–50% of all childhood cancers and approximately 90% of lymphomas in high-risk areas | 30–50% of childhood lymphomas; 1–2% of adult lymphomas | 40% of lymphomas that are associated with HIV; antiretroviral therapy has not decreased this risk |
| Geographic distribution | Equatorial Africa and Papua New Guinea; incidence correlated with regions where *Plasmodium falciparum* malaria is holoendemic | Worldwide | Worldwide |
| Age | Median: 6–9 yr | Predominantly affects children and adolescents; incidence peaks occur at ages 10, 40, and 75 yr | Median: 40–45 yr |
| Male:female ratio | 2:1 | 3:1 | 1:1 |
| Anatomical sites | Previously, jaw and orbit; now, abdomen, thyroid, ovaries, kidneys, adrenal glands, breasts; often spares lungs and spleen | Large abdominal masses common; ileocecal region most common site; may also be present in the head and neck, involving sinus or oropharynx; ovaries, kidneys, breasts | More nodal involvement than other variants; most common sites of extranodal involvement are gastrointestinal tract and bone marrow |
| CNS involvement | <10% of cases; cranial-nerve palsies or paralysis of the legs | 10–20% of cases, mostly leptomeningeal | 20–30% of cases |
| Bone marrow involvement | Occasional; leukemia not common | 30–35% of cases | Frequent |
| Associated with EBV | 95–100% of cases | 20–30% of cases; higher incidence among older adults | 25–40% of cases |

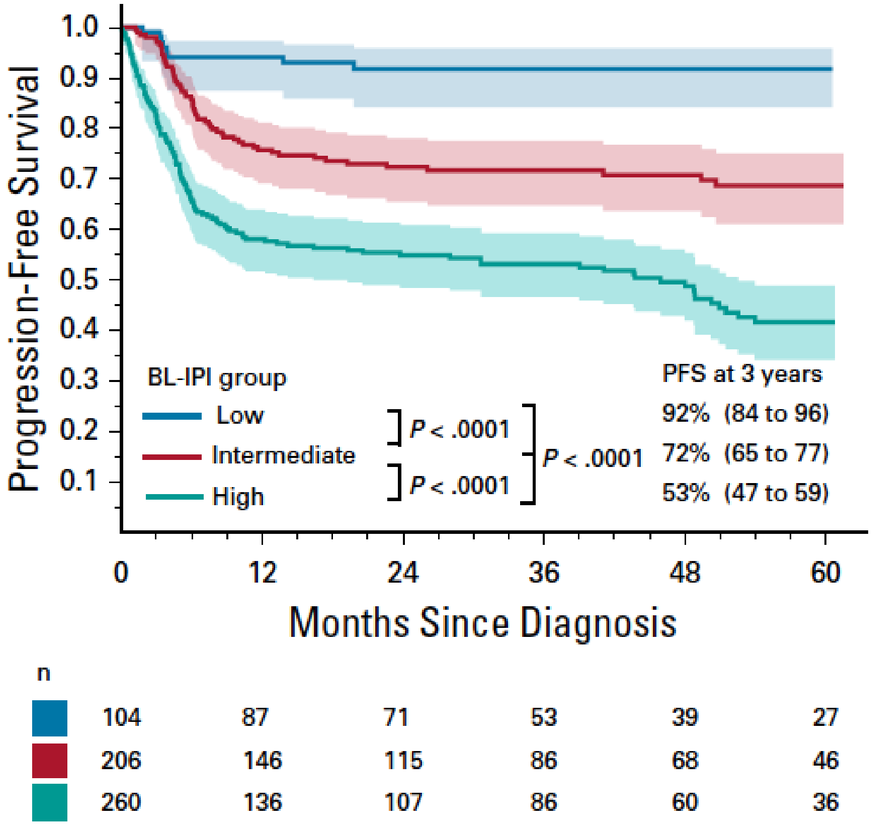
Roschewski, Staudt, Wilson. N Engl J Med 2022




Olszewski, Blood 2023
Thomas et al, Blood 2023

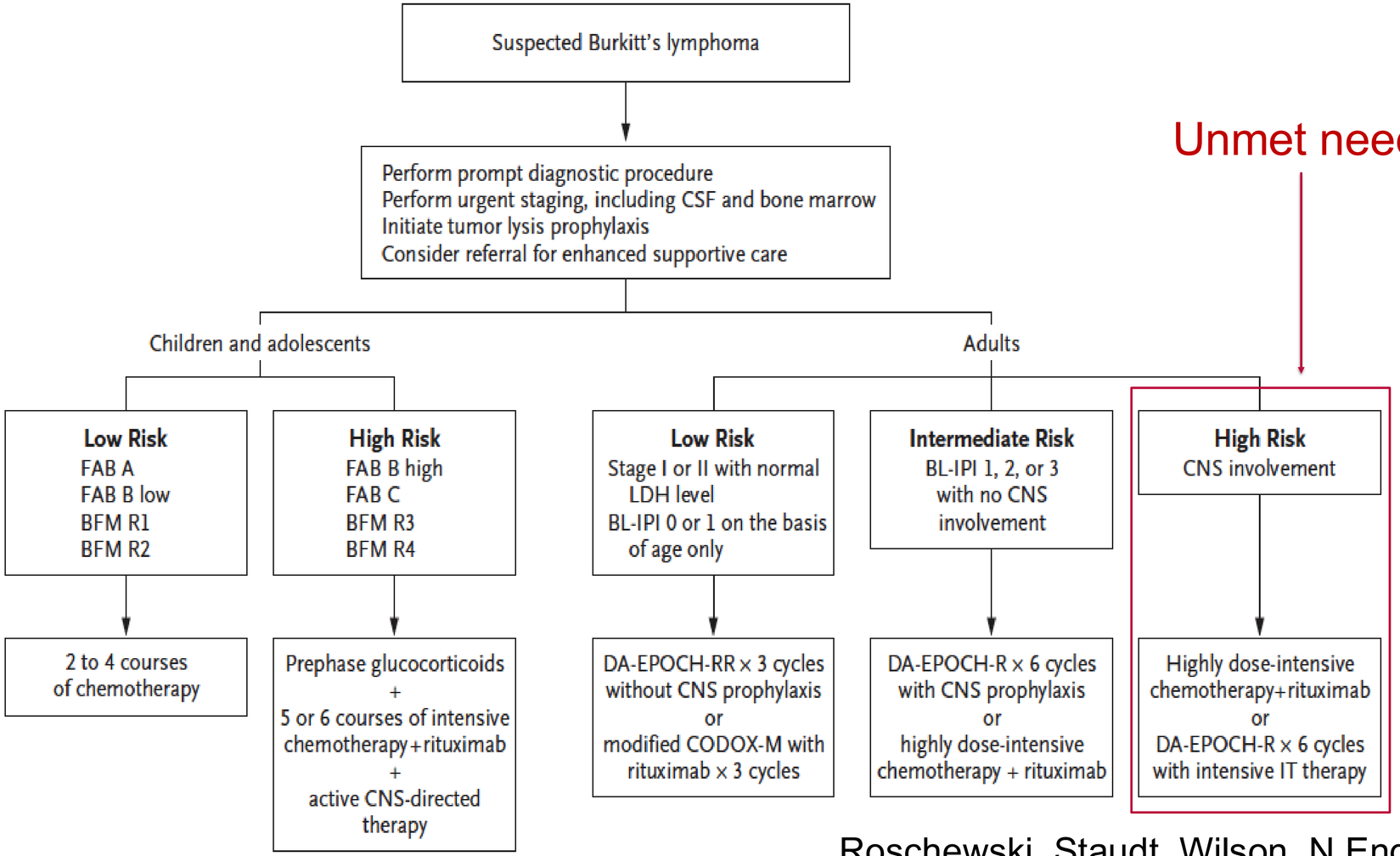
# Burkitt Lymphoma International Prognostic Index (BL-IPI)



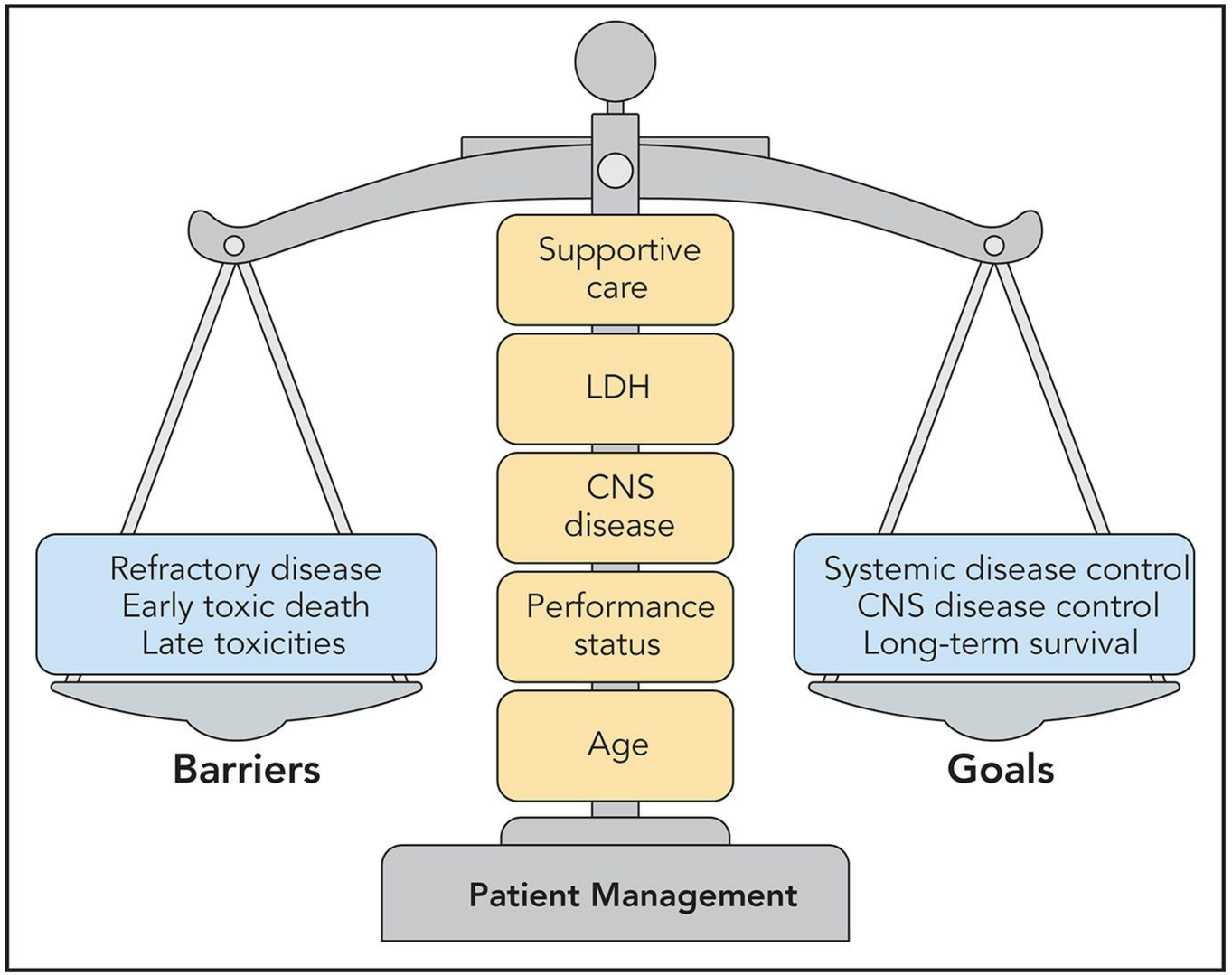

Olszewski et al. J Clin Oncol 2021

# Risk-Adapted Approach to Burkitt Lymphoma



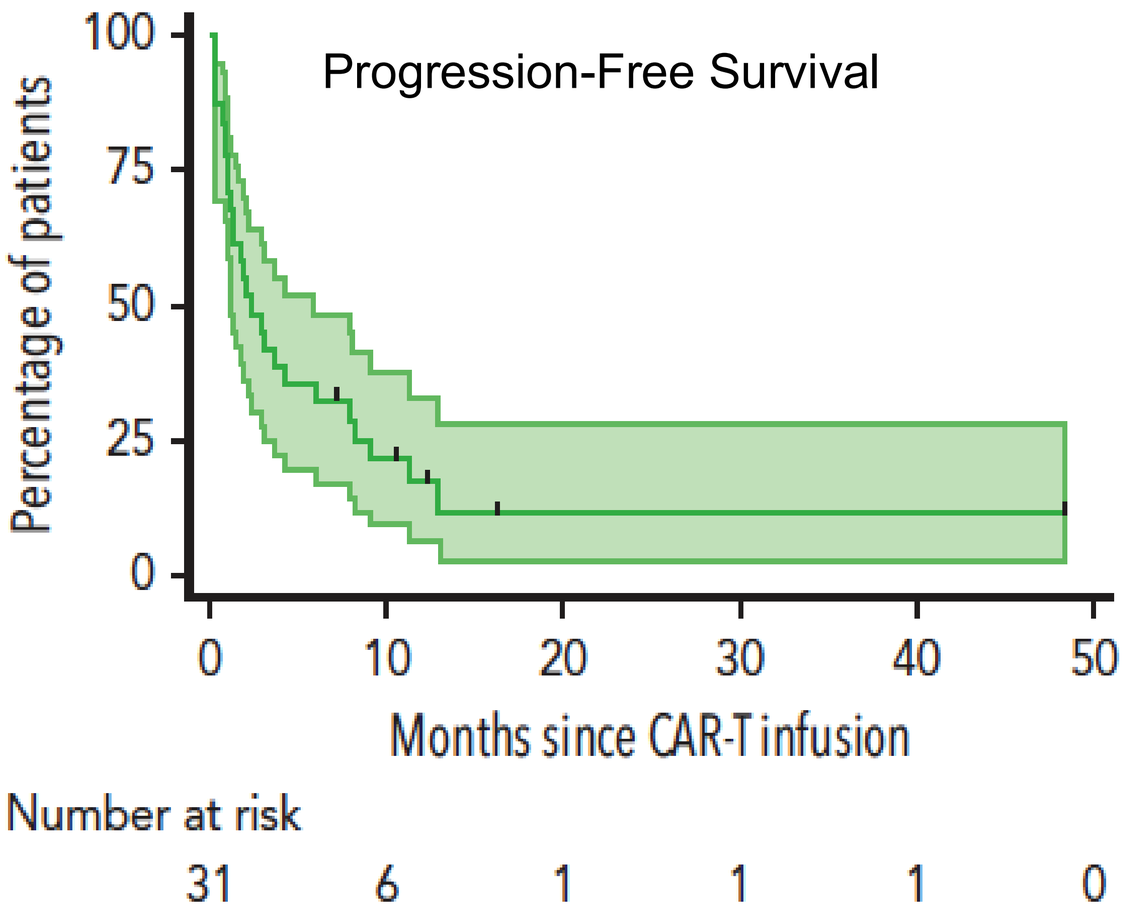

Roschewski, Staudt, Wilson. N Engl J Med 2022

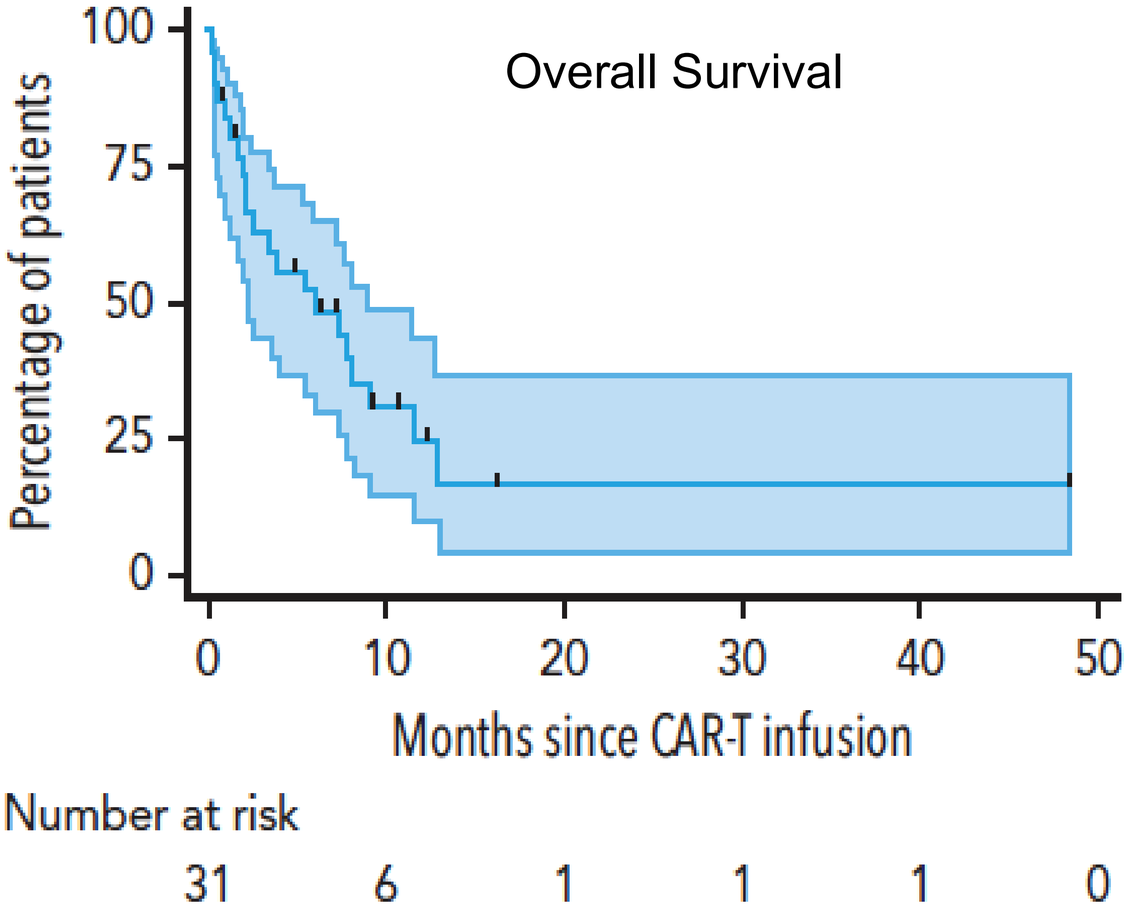
# Balancing Act in Adults with Intermediate-Risk Burkitt lymphoma




Roschewski, M. Blood 2021

# Anti-CD19 CAR T-cell Therapy in Relapsed Burkitt Lymphoma




Courtesy of Mark Roschewski, MD

Samples et al. *Blood* 2025 Jun 5;145(23):2762-22767

# Suboptimal results with (R)-CHOP in BL

| | |
|---|---|
| High Intensity | GMALL<br>R-HyperCVAD<br>CODOXM-IVAC<br>R-daEPOCH<br>LMB |
| Higher toxicity | high disease burden<br>HIV +<br>elderly<br>comorbidities<br>**limited resources settings** |

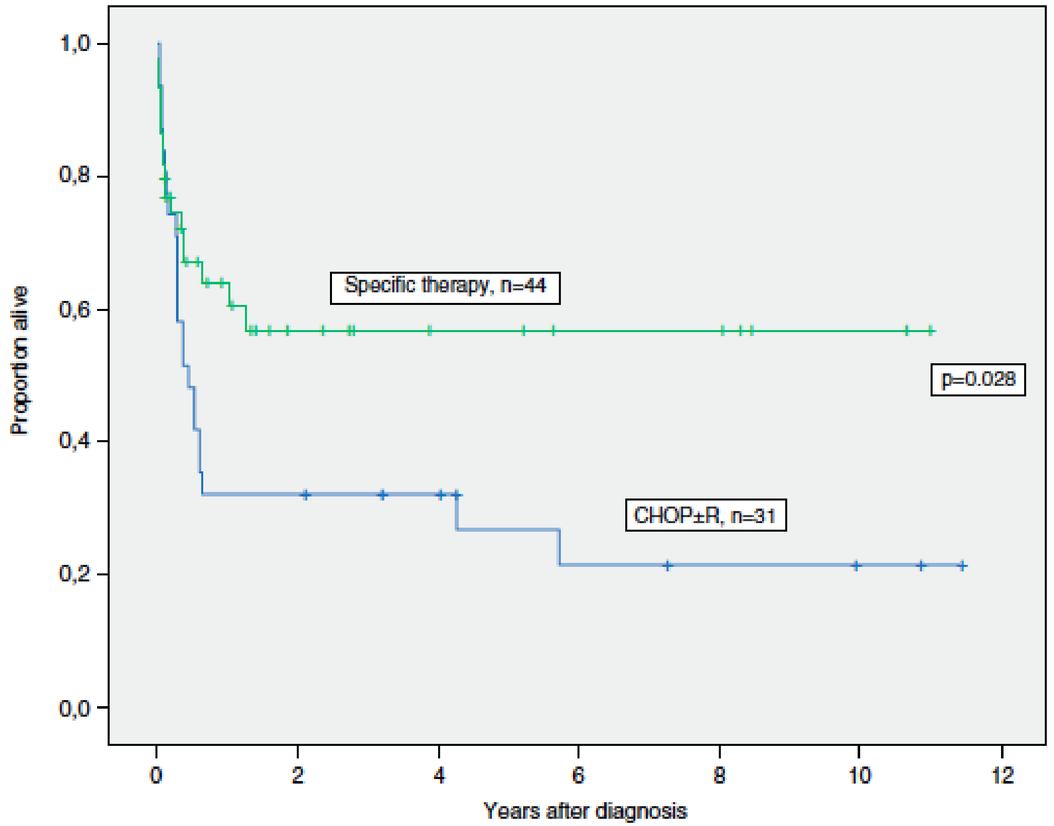
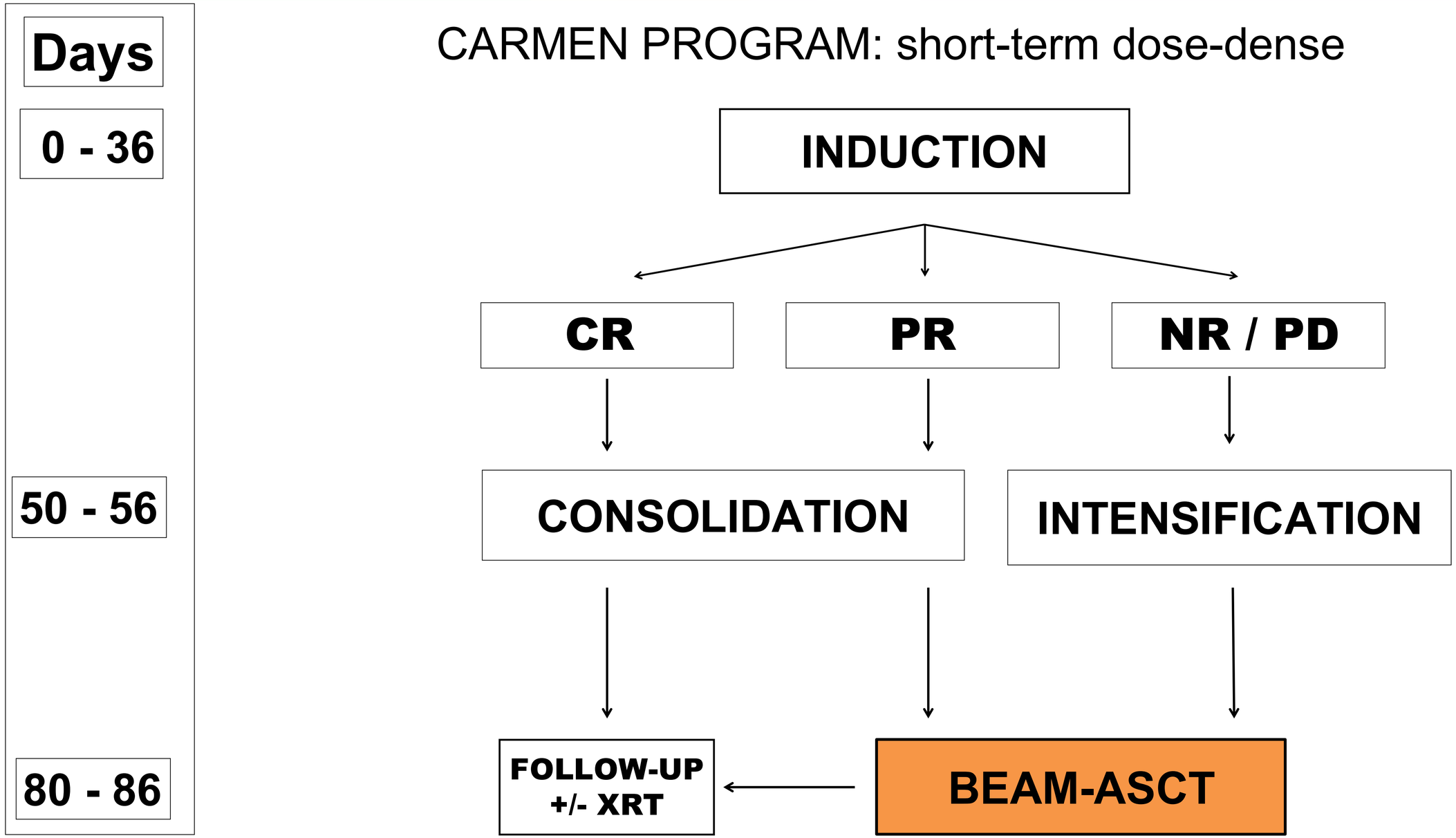



**Figure 2.** Overall survival probability in groups A (CHOP) and B (PETHEMALAL3/97 and BURKIMAB protocols).

Xicoy et al, Med Clin 2010

# CARMEN PROGRAM: short-term dose-dense



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Luca Fumagalli[3]
Marco Foppoli[1]
Silvia Mappa[1]
Silvia Govi[1]
Massimo Di Nicola[4]
Giuseppe Rossi[2]
Umberto Tirelli[5]
Federico Caligaris-Cappio[1]
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## Safety and activity of a new intensive short-term chemoimmunotherapy in HIV-positive patients with Burkitt lymphoma


*British Journal of Haematology*, 2012, **159**, 237–255

bjh research paper

## A dose-dense short-term therapy for human immunodeficiency virus/acquired immunodeficiency syndrome patients with high-risk Burkitt lymphoma or high-grade B-cell lymphoma: safety and efficacy results of the "CARMEN" phase II trial

Andrés J. M. Ferreri,[1] Chiara Cattaneo,[2] Arben Lleshi,[3] Luisa Verga,[4] Bernardino Allione,[5] Fabio Facchetti,[6] Maurilio Ponzoni,[7,8] Marco Foppoli,[1] Daris Ferrari,[9] Luigi Rigacci,[10] Lorenza Pecciarini,[7] Giovanni Donadoni,[1] Luca Fumagalli,[11] Marianna Sassone,[1] Teresa Calimeri,[1] Giuseppe Rossi,[2] Michele Spina[3,*] and Alessandro Re[2,*]

**Summary**

A few prospective trials in HIV-positive patients with Burkitt lymphoma (BL) or high-grade B-cell lymphoma (HGBL) have been reported. Investigated therapies have shown good efficacy but relevant safety problems, with high rates of interruptions, severe mucositis, septic complications, and fungal infections. Here, we report the results of a multicentre phase II trial addressing a new dose-dense, short-term therapy aimed at maintaining efficacy and improving tolerability. The experimental programme included a 36-day polychemotherapy induction followed by high-dose cytarabine-based

REGULAR ARTICLE

blood advances

## Safety and efficacy of a dose-dense short-term therapy in patients with MYC-translocated aggressive lymphoma

Andrés J. M. Ferreri,[1] Piera Angelillo,[1] Federico Erbella,[1] Chiara Cattaneo,[2] Luisa Verga,[3] Arben Lleshi,[4] Bernardino Allione,[5] Maurilio Ponzoni,[6,7] Fabio Facchetti,[8] Chiara Pagani,[2] Marco Foppoli,[1] Lorenza Pecciarini,[6] Marianna Sassone,[1] Sara Steffanoni,[1] Elena Flospergher,[1] Giuseppe Rossi,[2] Michele Spina,[4] and Alessandro Re[2]

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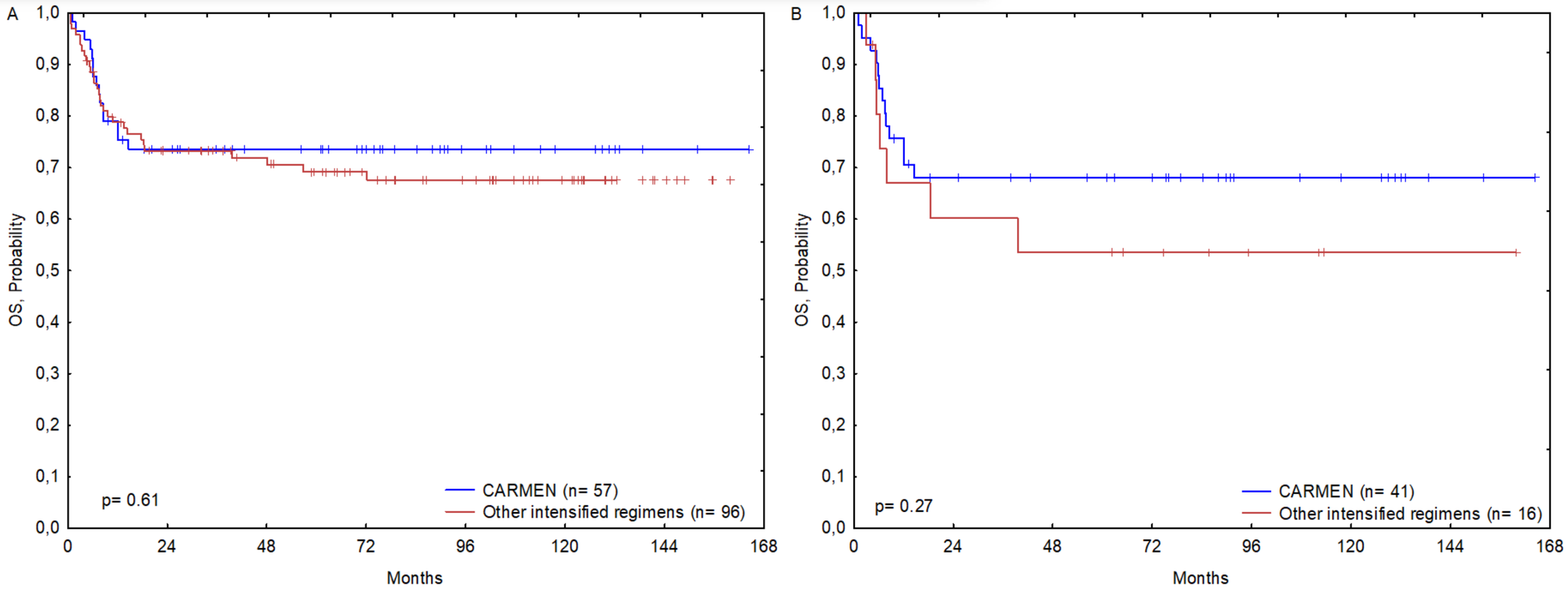
# THE SHORT-TERM DOSE-DENSE "CARMEN" THERAPY IS BETTER TOLERATED AND EVENLY EFFECTIVE THAN OTHER INTENSIFIED REGIMENS IN BOTH HIV-NEGATIVE AND HIV-POSITIVE PATIENTS (PTS) WITH BURKITT LYMHOMA

P. Angelillo, F. Erbella, C. Pagani, E. Ravano, L. Verga, F. Cavallo, M.C. Quattrocchi, P. Fiore, C. Cattaneo, G. Rindone, E. Amaducci, F. Pagni, L. Bandiera, L. Pecciarini, A. Passi, S. Maifredi, L. Lorenzi, L. Molinaro, L. Bongiovanni, T. Calimeri, E. Flospergher, F. Marino, G. Cassanello, S. Marktel, S. Mastaglio, F. Palumbo, L. Saliani, M. Quattrone, A. Carmagnola, M. Ponzoni, M. Spina, A. Re, A.J.M. Ferreri

10 centers Italy
Study population: 153 patients
Median follow-up: 84 months (range 10 – 189)




Angelillo et al, ICML 2025

**Table: Main toxic events (expressed as patients affected by at least one event)**

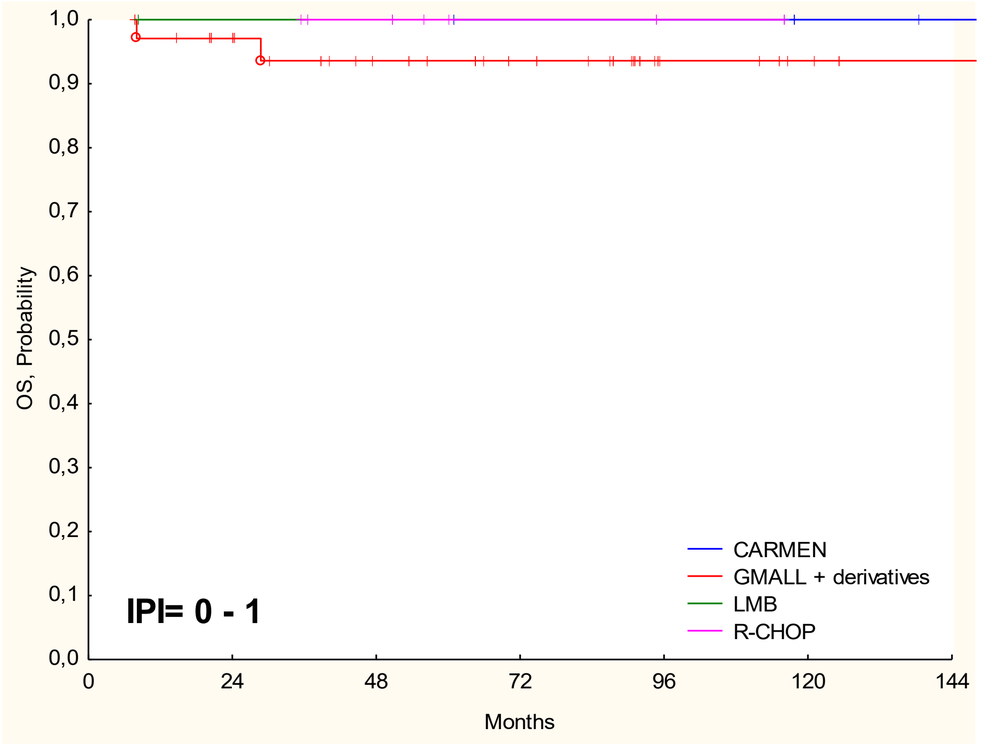
| | N° | Toxic deaths | Interruptions or dose reductions | Grade ≥3 Non-hematologic toxicity | Grade ≥3 infections | Grade ≥3 opportunistic infections |
|---|---|---|---|---|---|---|
| HIV-positive pts CARMEN | 41 | 2 ( 5%) | 5 (12%) | 15 (37%) | 6 (15%) | 3 ( 7%) |
| HIV-positive pts Controls | 16 | 1 ( 6%) | 9 (56%) | 12 (75%) | 14 (88%) | 6 (38%) |
| p value | | 0.83 | 0.0005 | 0.009 | 0.00001 | 0.005 |
| HIV-negative pts CARMEN | 16 | 0 ( 0%) | 1 ( 6%) | 4 (25%) | 5 (31%) | 1 ( 6%) |
| HIV-negative pts Controls | 80 | 9 (11%) | 26 (33%) | 46 (58%) | 51 (64%) | 5 ( 6%) |
| p value | | 0.17 | 0.03 | 0.01 | 0.01 | 0.67 |
| Whole series CARMEN | 57 | 2 ( 4%) | 6 (11%) | 19 (33%) | 11 (19%) | 4 ( 7%) |
| Whole series Controls | 96 | 10 (10%) | 35 (36%) | 58 (60%) | 65 (68%) | 11 (11%) |
| p value | | 0.12 | 0.0005 | 0.001 | 0.00001 | 0.37 |

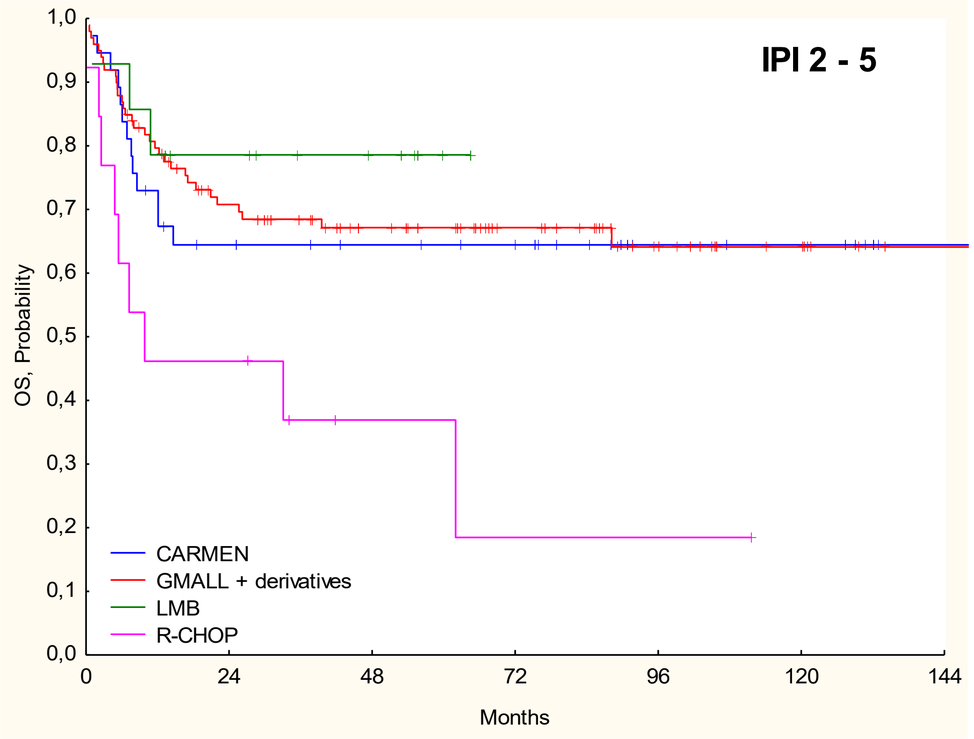
# CARMEN: present and near future


EHA HIV Lymphoma Network


International
Burkitt Lymphoma
Network

# SAFETY AND EFFICACY OF CARMEN vs OTHER STANDARDIZED CHEMOTHERAPY COMBINATIONS: INTERNATIONAL RETROSPECTIVE SERIES OF HIV-POSITIVE PATIENTS AFFECTED BY BURKITT LYMPHOMA




19 centers (?) from Germany, Italy, Spain, France, and Croatia.
Total series: 267 patients
Study population: 222 patients
Median follow-up: 65 months (range 7 – 164)

Study of the EHA HIV Lymphoma Network


ST. MARY'S HOSPITAL LACOR
1959
EMERGENCY


AI-REAL
Aggressive Infection Related East Africa Lymphoma
Precise and Timely Diagnosis
Patients and Parents Empowerment
Capacity Building
HAVE YOU SEEN THIS?
WHAT IS IT?
Swollen Face
Loose Teeth
Swollen Eyes
Swollen Abdomen
Swollen Testicles
This may be Burkitt's Lymphoma Cancer
If a child has the above, take the child to the nearest Health Centre.
If you are at a Health Centre & see a child with symptoms described above, refer the child to St. Mary's Hospital Lacor for diagnosis & management of Burkitt's Lympoma.
This is a child who got treatment for Burkitt,s Lymphoma from St. Mary's Hospital Lacor
BEFORE TREATMENT
AFTER TREATMENT
ST MARY'S HOSPITAL LACOR
FOR ASSISTANCE CALL THESE PHONE NUMBER
AI-REAL PROJECT OFFICE:
+256-772 593 901
+256-774 243 773
+256-779 757 910
+256-782 701 866
+256-393 252 856
HEALTH CENTRE
AFENET
NIHR National Institute for Health Research
UKaid
OXFORD
ONCOLOGY

# INCTR 03-06: epidemiology 2010- 2012

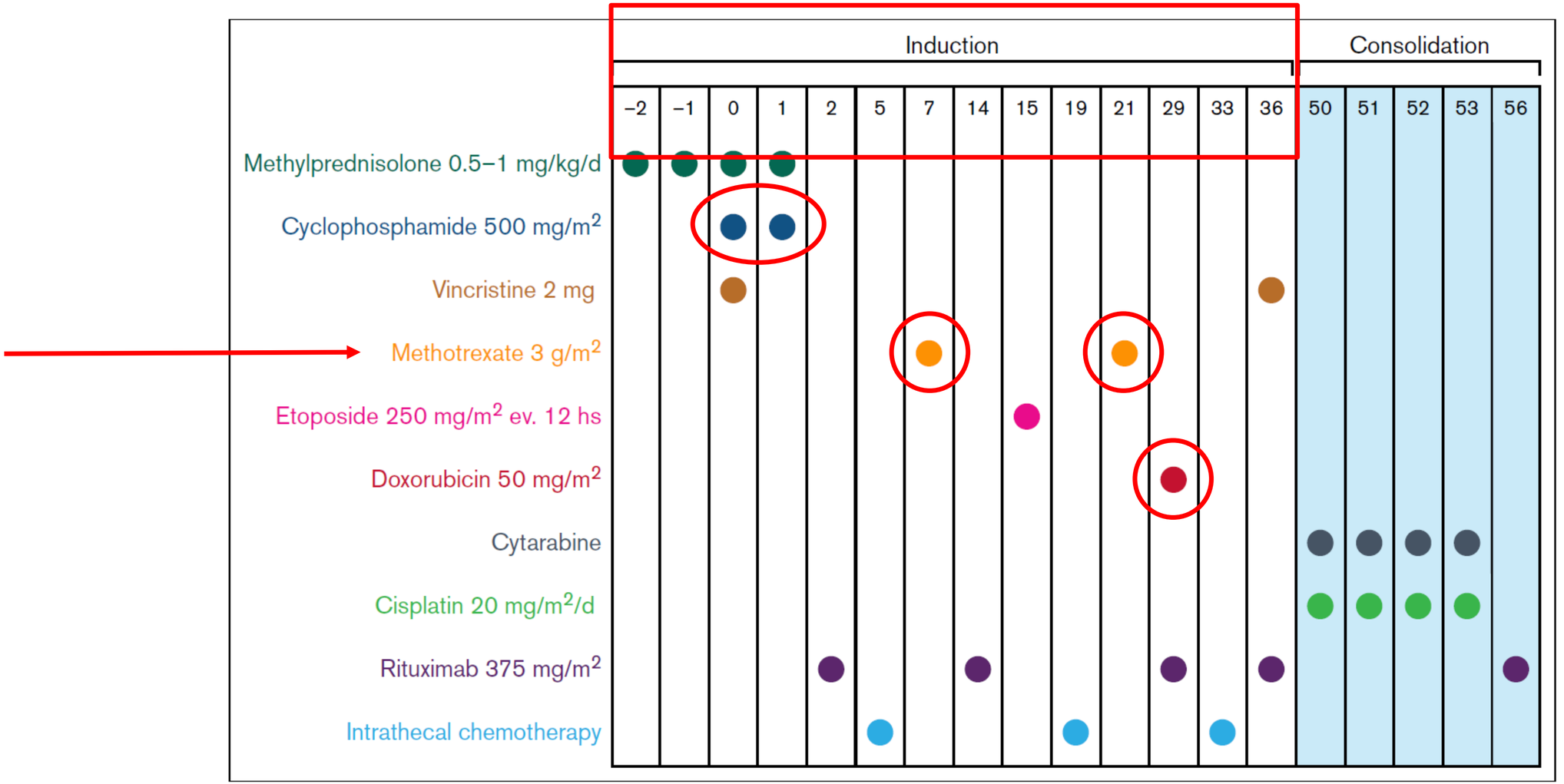
| | |
|---|---|
| ***Number of Patients*** | **118** |
| *Median Age* | 8 years |
| M:F | 77:41 |
| HIV | 1 |
| ***Sites of Disease at Presentation*** | |
| Abdominal/Pelvic | 93 (79%) |
| Jaw | 50 (42%) |
| CNS (CSF and/or CN Palsies) | 29 (25%) |
| Chest | 15 (13%) |
| Lymphadenopathy | 14 (12%) |
| Paralysis | 13 (11%) |
| Orbit | 11 (9%) |
| Bone Marrow | 7 (of 67 evaluated) |
| ***Multiple Sites of Disease*** | 104 of 112 (6 had no BM exam) |

Courtesy of Calbi V. and INCTR

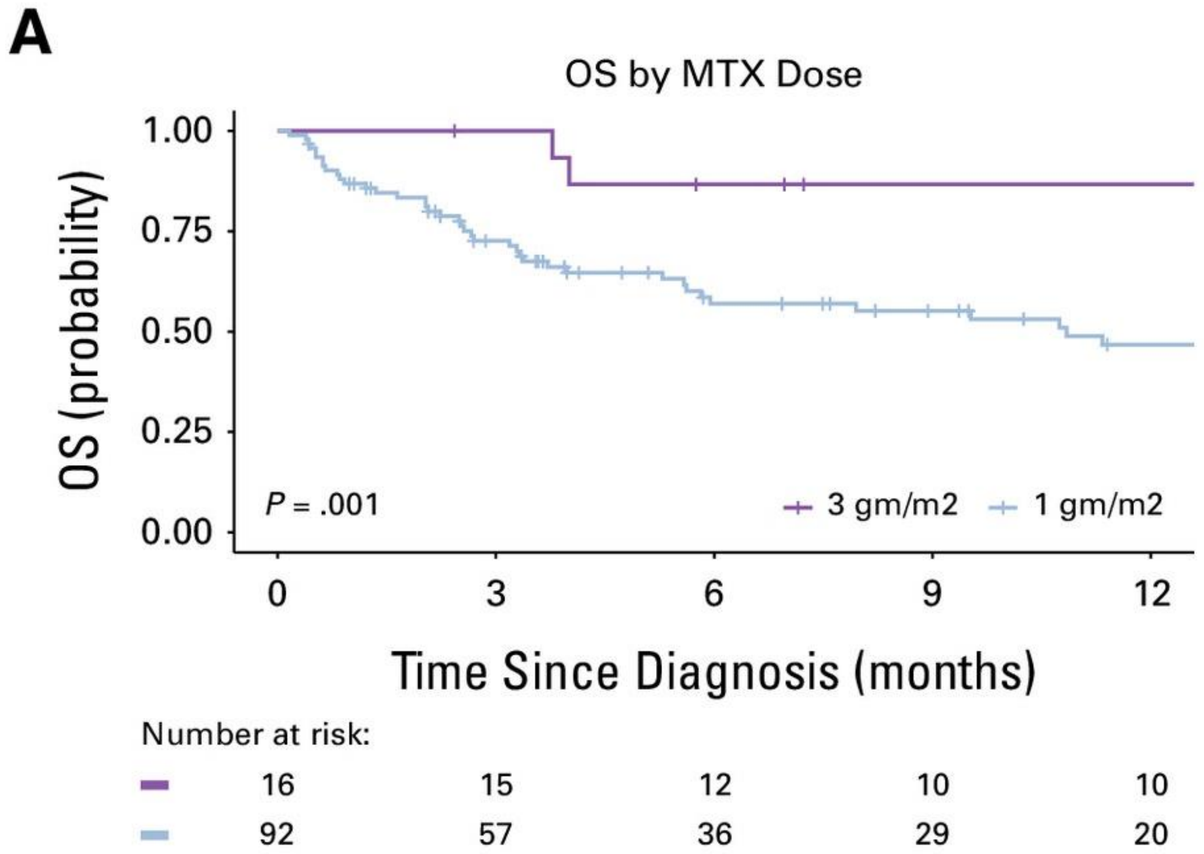

- First Line Treatment:
  - Low risk: COM + IT therapy
  - High risk: (R)- CHOP +/- IT

- (Second-Line Treatmen: (R)-DHAP +/- IT)

**EFS 20-30% (CNS progression in systemic remission)**


Induction
Consolidation
−2
−1
0
1
2
5
7
14
15
19
21
29
33
36
50
51
52
53
56
Methylprednisolone 0.5–1 mg/kg/d
Cyclophosphamide 500 mg/m2
Vincristine 2 mg
Methotrexate 3 g/m2
Etoposide 250 mg/m2 ev. 12 hs
Doxorubicin 50 mg/m2
Cytarabine
Cisplatin 20 mg/m2/d
Rituximab 375 mg/m2
Intrathecal chemotherapy

# High-Dose Methotrexate Usage Without Drug-Level Monitoring in Advanced Pediatric Mature B-Cell Non-Hodgkin Lymphoma in a Resource-Limited Setting in Malawi




Mzikamanda et al, Ped Oncol 2025

# Plasma EBV DNA: A Promising Diagnostic Marker for Endemic Burkitt Lymphoma

*Rena R. Xian[1,2], Tobias Kinyera[3,4], Isaac Otim[3,4], Joshua N. Sampson[5], Hadijah Nabalende[3,4], Ismail D. Legason[3,4], Jennifer Stone[2], Martin D. Ogwang[3,4], Steven J. Reynolds[6], Patrick Kerchan[3,7], Kishor Bhatia[5], James J. Goedert[5], Sam M. Mbulaiteye[5†] and Richard F. Ambinder[1,2*†]*

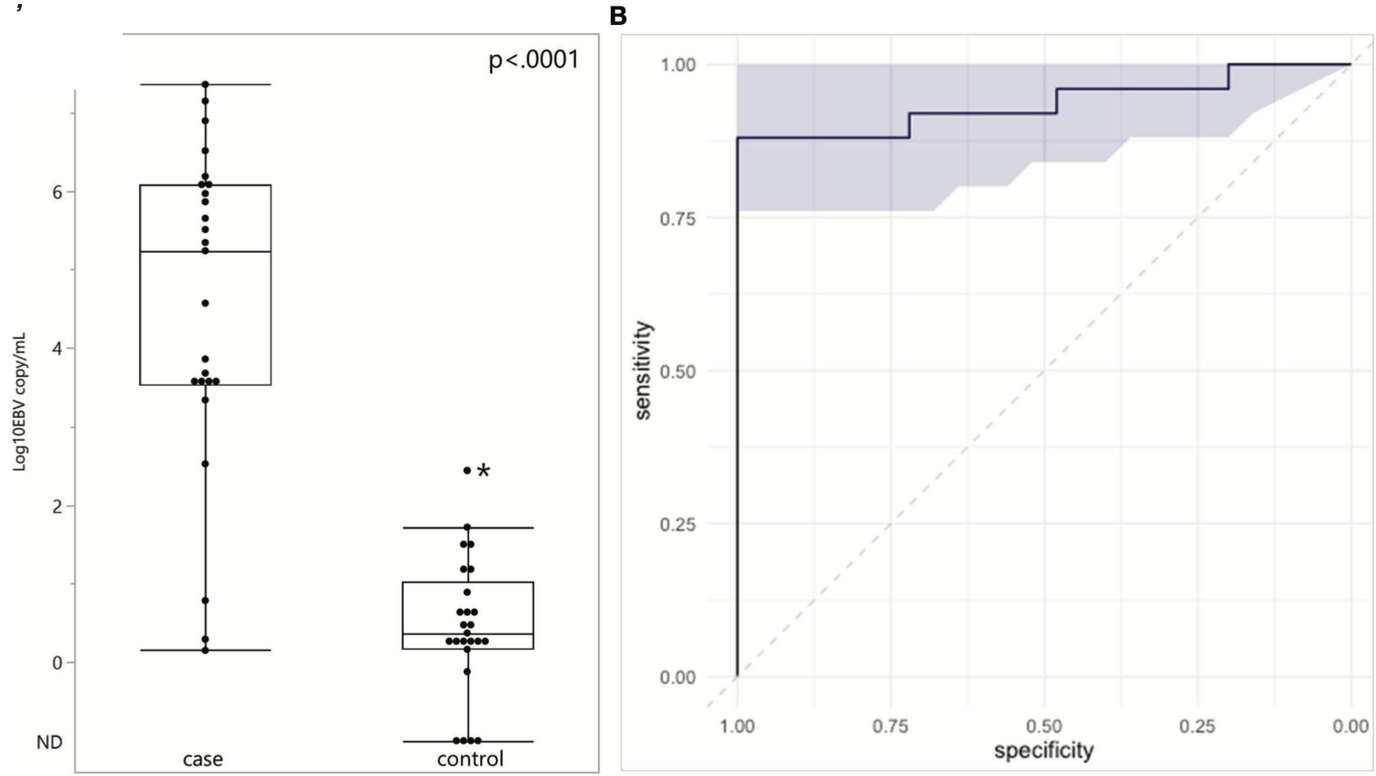



**FIGURE 1** | Plasma EBV quantification in endemic Burkitt Lymphoma. **(A)** Plasma EBV levels in 25 children with eBL and 25 controls. ND, Not Detected. **(B)** ROC analysis curve based on EBV quantification and shaded area represents 95% confidence intervals. *Indicates outlier.

Xian et al, Front Oncol. 2021

# TAKE HOME MESSAGES

- Sustainability: Optimize existing resources

- Biological insight > tailored therapy

*«Arrivando a ogni nuova città il viaggiatore ritrova un suo passato che non sapeva più d'avere…»*

Italo Calvino, Le città invisibili

thank you

- CARMEN co-chairs: A. Re (Brescia) and M. Spina (Aviano)
- M. Foppoli, P. Angelillo, F. Erbella, P. Fiore (HSR)
- Other CARMEN centers:
  - H. San Gerardo, Monza (L. Verga et al.)
  - H. Niguarda, Milano (E. Ravano et al.)
  - Città della Salute, Turin (F. Cavallo et al.)

I.R.C.C.S. Ospedale San Raffaele
Gruppo San Donato


M. Federico & S. Luminari (Italy),
Maria Gomes da Silva (Portugal),
Astrid Pavlovski (Argentina),
Carlos Chiattone (Brazil),
Alejandro Martin Garcia & Maria Rodriguez Socorro Pinilla (Spain)

María A. Torres (Venezuela),
Brady Beltrán (Perú),
Alana von Glassenap (Paraguay)

Mr. Martin Ogwang
Dr. Venice Omona
Dr. Sam Mbulaiteye
Dr. Fiddy Obalim, MBCHB
Dr. Isaac Otim
And all the Pediatric and Pathology team

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International Burkitt Lymphoma Network