17TH ANNUAL CONFERENCE OF THE BRITISH HIV ASSOCIATION (BHIVA)

British HIV Association BHIVA

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SSAT ST STEPHEN'S AIDS TRUST

BHIVA 2011

Clinical features and outcome in 61 patients with HIV associated Multicentric Castleman's disease

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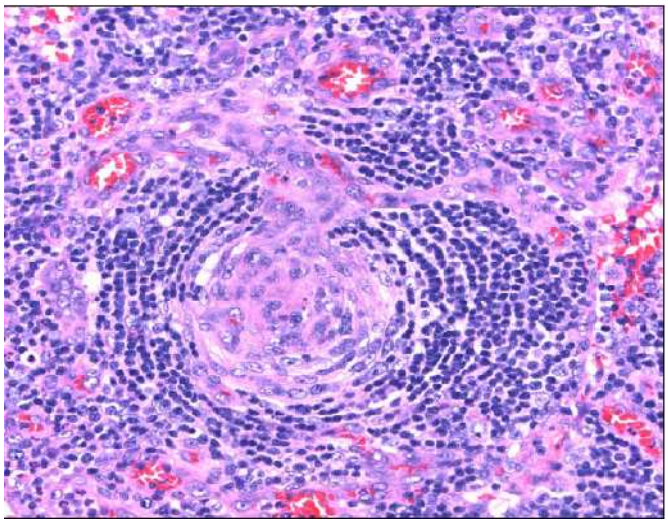
Castleman's disease



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HIV Castleman's disease

	Hyaline vascular	Plasmablastic
Localised		
Multicentric		HIV-MCD

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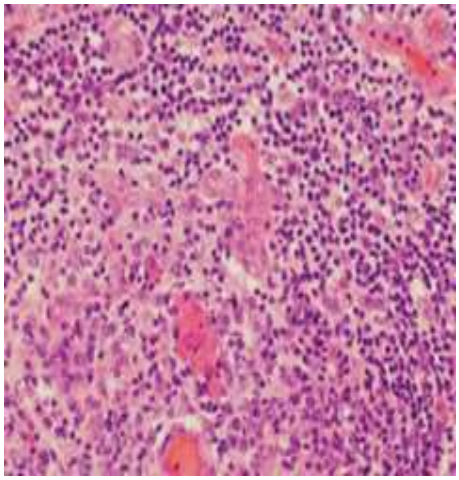
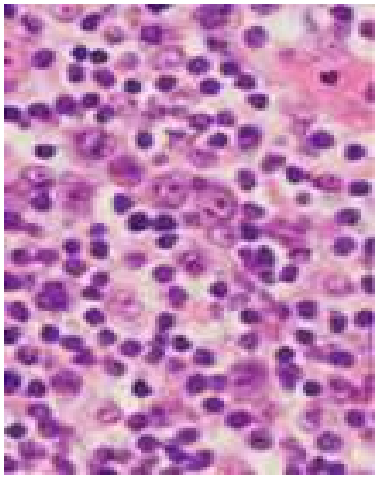
Mantle zone with large lymphoid cells with prominent nucleoli (plasmablasts)





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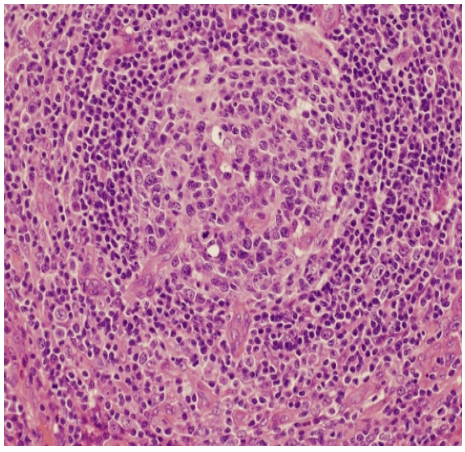
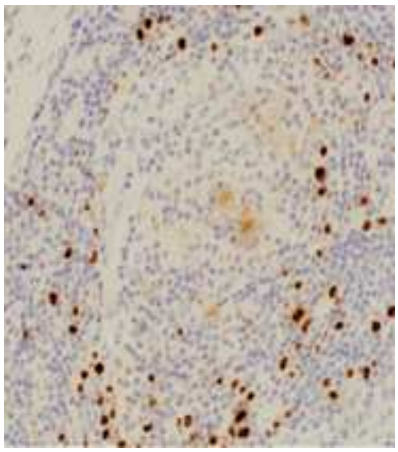
Plasmablasts infected by HHV8





HHV8 LANA staining

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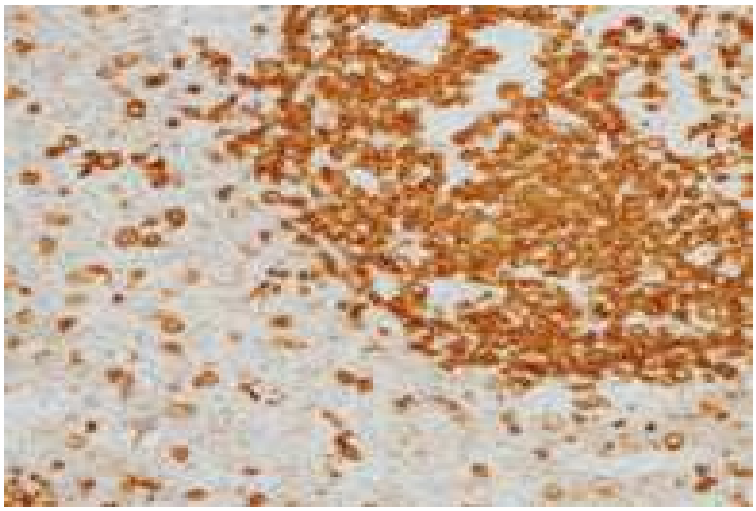
Plamablasts CD20+



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Castleman's Clinical Presentation

Fever, night sweats, weight loss

Localised or diffuse lymphadenopathy

Hepatosplenomegaly

Anaemia, hypoalbuminaemia, polyclonal hypergammaglobulinaemia

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What's an attack of MCD?

1. Fever
2. At least 3 of the following:
   - Lymphadenopathy
   - Splenomegaly
   - Oedema
   - Pleural effusion
   - Ascites
   - Cough
   - Nasal obstruction
   - Xerostomia
   - Rash
   - Central neurologic symptoms
   - Jaundice
   - Autoimmune haemolytic anaemia
3. Serum C-reactive protein level > 20 mg/L (in the absence of any other cause)

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Single institution cohort study

Cohort study to examine:

1. Clinical features of MCD
2. Treatment outcomes

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Features at diagnosis
MCD at CWH (n=61)

Mean Age	42 years
Male	87%
Prior AIDS	38%
Median CD4 count (range)	234/mm^3 (41-1400)
On HAART >3m	25/59 (42%)
On HAART & VL<50 copies	11/25 (44%)
Median duration symptoms (range)	3 months (0.5-24)

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Frequency of clinical criteria
in 61 MCD patients

Fever	98%
C-reactive protein >20mg/L in the absence of any other aetiology	92%
Peripheral lymphadenopathy	100%
Enlarged spleen	95%
Oedema	18%
Pleural effusion	18%
Ascites	8%
Cough	61%
Nasal obstruction	40%
Xerostomia	40%
Rash (including KS=33)	62%
Central neurologic symptoms	66%
Jaundice	14%
Autoimmune haemolytic anaemia	43%
Fewer than 3 criteria met*	10%

*But nasal obstruction and xerostomia only prospectively collected on 20 patients

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Other MCD features

Clinical features not seen in the classification

Hepatomegaly	40/61 (66%)
Kaposi's sarcoma	33/61(54%)
Pulmonary involvement	28/60 (47%)

Plasma KSHV levels measured at MCD diagnosis for 45 patients-

Detectable KSHV DNA:

Median $\log_{10}$ plasma HHV8 DNA load copies/mm^3 was 5.3 (range 2.3-8.7)

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HIV MCD treatment options

Splenectomy

HAART

Vinblastine

Etoposide

Interferon α

Ganciclovir

Anti IL6 receptor blocking antibody

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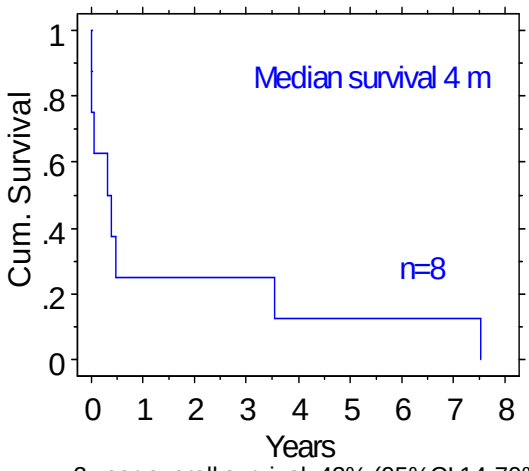
Survival pre 2002



2 year overall survival 42% (95%CI 14-70%)
5 year overall survival 33% (95% CI 6-60%)

cf: (Oksenhendler et al 1996)
Largest published series
n=20
Median survival 14m

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Algorithm of care for MCD (2002-2006)

MCD diagnosed in LN

MCD diagnosed following splenectomy

Rituximab 375mg/m^2 x4

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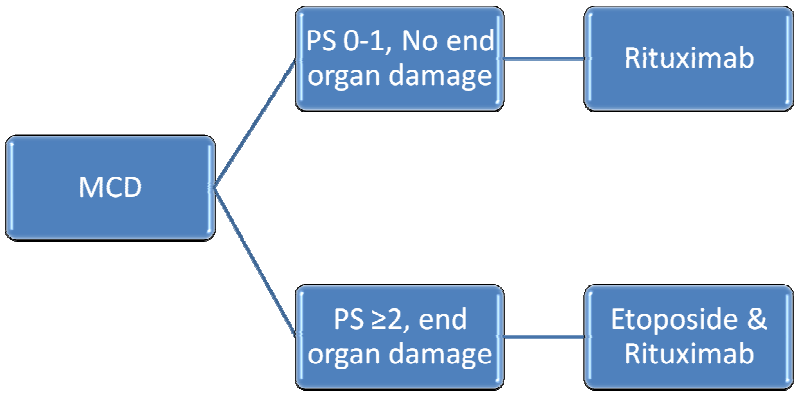
New risk-stratified algorithm 2006-



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Rituximab-based therapy

49 patients since 2003

35 rituximab monotherapy

14 rituximab & etoposide

	2 year OS (95% CI)
All 49:	94% (87-100%)
Rituximab monotherapy:	97% (87-100%)
Rituximab & etoposide:	86% (68-100%)

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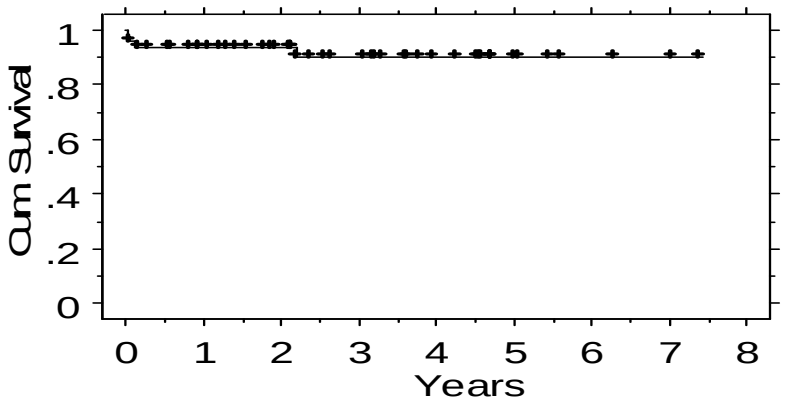
Overall survival of 49 patients treated with rituximab-based therapy



2 year overall survival 94% (CI 87-100%)
5 year overall survival 90% (CI 81-100%)

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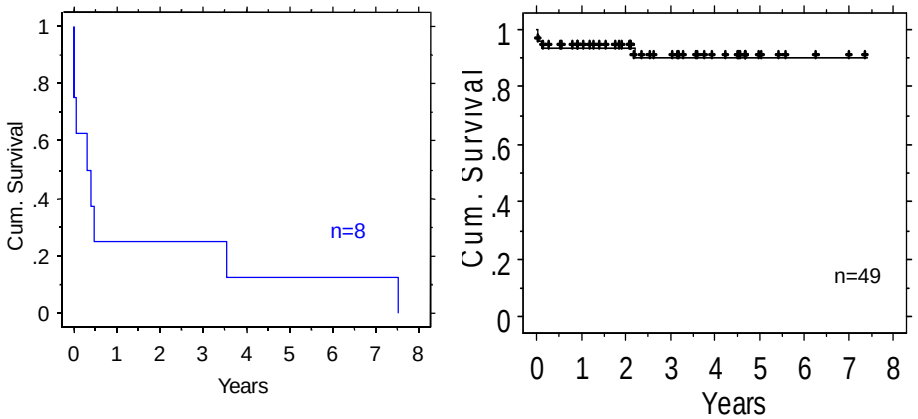
Overall survival pre/post Rituximab



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Response rates

46 patients: achieved resolution of systemic symptoms and fevers

45 patients: radiological response

- 1 Complete Response (2%)
- 34 Partial Response (76%)
- 10 Stable Disease (22%)

Incidence of developing lymphoma: 28/1000 patient years

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Post-treatment analysis

4/49 patients died:

- 3 pts within 10 days of starting treatment (were on ITU)

- 1 patient developed plasmablastic lymphoma 2 years after treatment for MCD – died of progressive lymphoma despite systemic chemotherapy

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Post-treatment analysis

Median KSHV DNA load fell from 126,000 copies/mm^3 at diagnosis to undetectable at 3 months post treatment in 28/37 (76%)

8/46 patients relapsed

- Median time to relapse 2 years
- All successfully retreated and alive in remission
- Re-treatment with Rituximab monotherapy – 6
- Re-treatment with Rituximab & chemotherapy - 2

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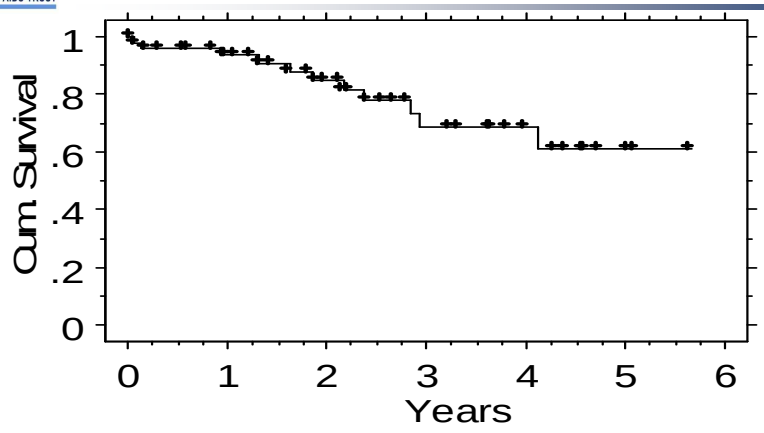
Disease-free survival of 49 patients treated with rituximab-based therapy



2 year relapse-free survival: 85% (CI 74-95%)
5 year relapse-free survival: 61% (CI 40-82%)

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Factors not influencing overall or relapse free survival (p>0.1)

Using Prognostic modelling

Age

Gender

CD4 cell count

ECOG PS>2

Plasma KSHV load

On HAART therapy

Addition of etoposide

Factors influencing OS and RFS

Low plasma viral load – associated with longer OS (p=0.031), but no difference in relapse-free survival

MOF score>3: associated with worse OS (p=0.0007) and worse RFS (0.0066)

MCD and KS

24 patients had KS at time of MCD diagnosis

Received rituximab based treatment

9 (38%) experienced progression of KS within 3 months of rituximab

8 required systemic anthracycline chemotherapy

No difference between rituximab only and rituximab and etoposide treatments

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Conclusion

Largest series of HIV MCD

Dramatic improvement in survival since introduction of Rituximab based therapy, 5 year survival 90% compared to 33% prior to Rituximab use, log rank $p<0.0001$)

Survival has tripled since 2002

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