EARLY CONSOLIDATION WITH HIGH DOSE THERAPY AND AUTOLOGOUS STEM CELL TRANSPLANTATION IN HIV-ASSOCIATED NON HODGKIN LYMPHOMA AT HIGH RISK (aa-IPI 2-3) RESULTS OF A MULTICENTER PHASE II STUDY

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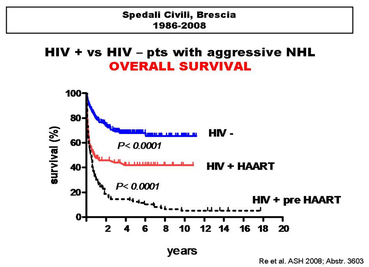
BACKGROUND

- **NHL in HIV+ pts is more aggressive compared to the general population**
- Outcome of HIV-NHL with adverse prognostic features is not satisfactory with standard therapy (R-CHOP) and IPI is the main prognostic factor (IPI int-high risk: 2y OS < 50%)
- **Stem cell mobilization has been shown to be feasible in HIV+ pts with lymphoma (Re et al, Haematologica 2012)**
- There are no prospective studies addressing the role of high dose therapy (HDT) and autologous stem cell transplantation (ASCT) as up-front consolidation in HIV-NHL
- **HDT with ASCT has been shown to be feasible, safe and active in HIV-NHL in the salvage setting (Re et al, Blood 2009)**



Stem cell mobilization in HIV seropositive patients with lymphoma

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Table 5. Stem cell mobilization and remobilization attempts in 155 HIV positive patients.

Attempt	N pts	N success	N optimal
1	155	113	74
2	25*	9#	2*
3	3	0	
4	2	0	

*Including 2 patients in whom > 2 x 10^6 $CD34^+$ cells/kg had been obtained at the 1st attempt and had a second one to achieve >5.# including 2 patients in whom > 2 x 10^6 $CD34^+$ cells/kg was obtained after pooling 1st + 2nd attempts.

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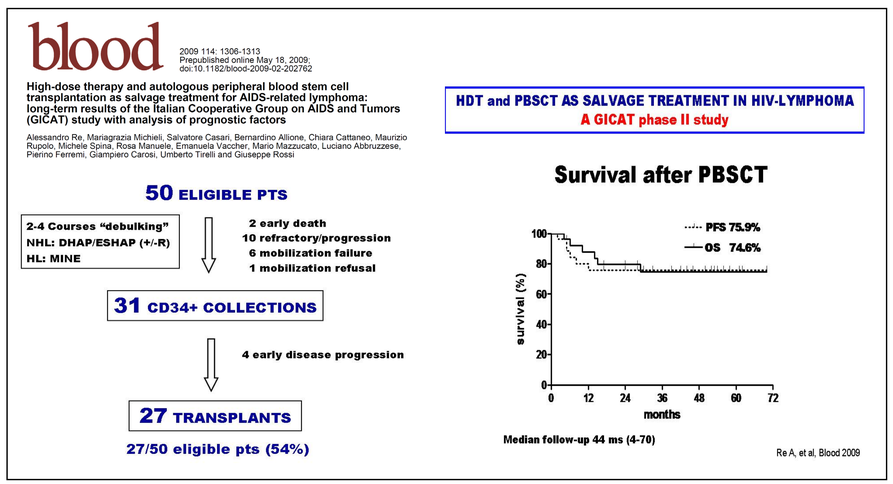


AIM OF THIS STUDY

- To define the role of HDT and ASCT in the upfront treatment of HIV-associated NHL at high risk, in terms of efficacy and toxicity.
- We report the results of a multicenter prospective study including HDT and ASCT as consolidation after first-line treatment of HIV-associated NHL at high risk

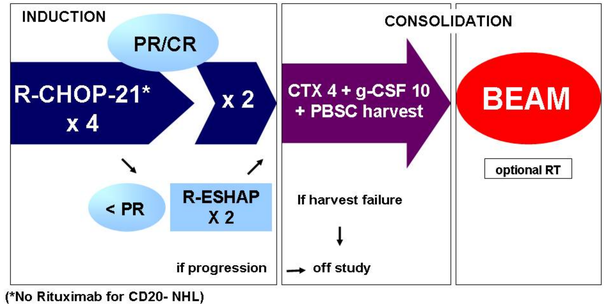
INCLUSION CRITERIA

- HIV + pts with untreated aggressive NHL (DLBCL, Plasmablastic, Anaplastic)
- Age 18-60 ys
- aaIPI 2-3
- Stage IB-IV

EXCLUSION CRITERIA

- Burkitt, lymphoblastic lymphoma, PEL
- P.S. > 2
- E.F. <50%, DLCO < 50%, Creatinine >2 mg/dl, ALT >3X nv, P.T. <70%, N<1500/cmm, plt<100000/cmm
- CD4+ < 50/cmm and/or virologic failure to HAART
- CNS or meningeal lymphoma
- Active major opportunistic infection
- HBV-DNA pos

STUDY DESIGN



(*No Rituximab for CD20- NHL)

HAART

- HAART is mantained during the entire treatment program
- Pts with plasmablastic lymphoma are allowed to receive CHOP-14

PRIMARY ENDPOINT

- Overall survival at 2 years

STATISTICAL PLAN

- To test a 20% increase of 2-ys OS with experimental treatment (R-CHOP + ASCT) compared to standard (R-CHOP)
- Expected accrual: 43 pts
- First step: > 8/15 pts alive at 2 years to continue the trial

RESULTS

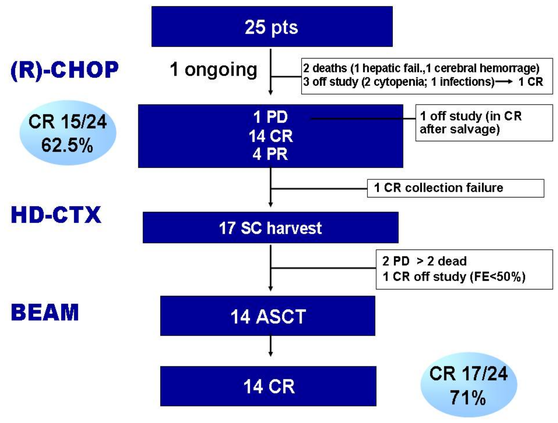
PATIENTS' CHARACTERISTICS

Patients registered	**29***
Patients enrolled	**25**

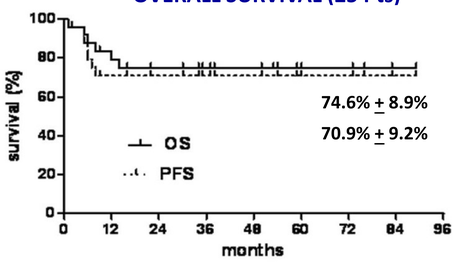
* 3 screening failure; 1 lost before starting therapy

Age (median)	48 ys (27-62)
M/F	15 / 10
Histology: DLBCL	19 (76%)
Plasmablastic	5 (20%)
Anaplastic ALK -	1 (4%)
aaIPI: 2	13 (52%)
3	12 (48%)
WHO PS >1	14 (56%)
LDH > NV	22 (88%)
Stage: III	7 (28%)
IV	18 (72%)
B symptoms	16 (64%)
> 1 extranodal site	12 (48%)
Bulky disease (> 7 cm)	8 (32%)
Risk groups (IPI)	
Eterosexual	12 (48%)
Omosexual	2 (8%)
unknown	3 (12%)
HIV previously unknown	7 (28%)
Prior AIDS	2 (8%)
Prior HAART	17 (68%)
HAART duration before NHL dx	2 ys (0-15)
HIV duration before NHL dx	6 ys (0-26)
CD4+ count (median)	255/mL (51-571)
Detectable HIV-viremia	14 (56%)
Median HIV-viremia	51 cp/mL (0- >500.000)
HCV +	10 (40%)
Anti HBc +	13 (52%)

PATIENTS' FLOW-CHART

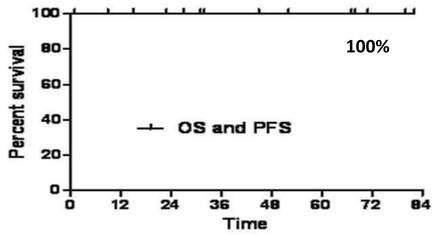


OVERALL SURVIVAL (25 Pts)



Median follow-up 50 ms (2-89 ms)

SURVIVAL AFTER TRANSPLANT (14 Pts)



Median follow-up 38.5 ms (1-82 ms)

TOXICITY/INFECTION after ASCT

TOXICITY (WHO 2-4)
- grade 2: GI (5) Hepatic (2)
- grade 3: GI (5) Hepatic (1)
- grade 4: GI (1)

FEVER/INFECTION BEFORE ENGRAFTMENT
(FUO) (9); VZV infection (1); Sigmoiditis (1); CMV infection (1); Cl.Difficile colitis (1)

WITHIN 100 DAYS AFTER ENGRAFTMENT
CMV infection (1); FUO (2)

AFTER 100 DAYS Acute cholecystitis (1); Bacterial pneumonia(1)

CONCLUSIONS

- This is the first prospective trial addressing the role of HDT/ASCT in first-line treatment of HIV-NHL
- 58% of pts were able to complete the entire treatment program and ASCT was well tolerated
- The OS in this series of "high risk" pts is satisfactory. No relapses occurred in pts who received ASCT, after a prolonged follow-up
- HDT/ASCT seems an effective way to consolidate first response and improve outcome in HIV-NHL at high risk
- Further improvement could result from an increase of the rate of pts who receive ASCT