

HODGKIN LYMPHOMA

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Disclosure Information

I have no financial relationships to disclose relevant to the content of this presentation

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Topics

- Improving outcomes
 - Better efficacy
 - Lower toxicity
- Special situations
 - Pregnancy
 - HIV
 - Elderly

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Hodgkin Lymphoma Successes

- High overall cure rate.
- Treatment is generally well-tolerated.
- Modern treatment = fewer long term side effects

BUT. . .

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Challenges

- Some patients are not cured with current standard treatment.
- Significant rate of long-term complications
 - 2nd malignancies
 - cardiac, pulmonary toxicity
 - neuropathy

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Questions


- Is ABVD still standard for all patients?
- Can treatment be tailored to risk?
- Can treatment be tailored to early PET response?
- In which patients is RT necessary?
- Transplant at Relapse
- Special situations:
 - Elderly, pregnancy, HIV

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Choice of Regimen

Efficacy

High cure rate with initial regimen
(or good ability to salvage those who fail)



Late Side Effects

- Cardiac toxicity
- Pulmonary toxicity
- Second malignancy
- MDS/AML
- Infertility
- Neuropathy

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Localized HL, Stage I-II
Evolution of Treatment

- 1960s: Large RT fields
- 1970s: Staging lap and more limited RT
- 1980s: Chemotherapy and EFRT
- 1990s: Chemotherapy and limited IFRT
- **Current US standard:**
ABVD x 4(-6) + IFRT 30Gy

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Advanced HL, Stage III-IV
Evolution of Treatment

- 1960s: MOPP
- 1980s: ABVD
- 1990s: RT not necessary in CR
- 2000s: Newer regimens:
 - Stanford V
 - Lower doses, weekly
 - BEACOPP (esc and standard)
 - Higher doses, q 2weeks
- **Current US standard:**
ABVD x 6-8, no RT

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“Modern” ABVD

- UK LY09 (n=406, Ph 3) 3yFFS 75%
Johnson, JCO, 2005
- Ital Intgrp (n=112, Ph 3) 8yFFS 88%
ASH 2008
- Nwstrn/S’hampton (n=40) 5yEFS 87%
Evens, Br J Haem, 2007

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Newer Regimens for HL

- Stanford V
 - bleomycin
 - etoposide
 - doxorubicin
 - mustard
 - vincristine
 - vinblastine
 - prednisone
 - RT to >5cm
- low cumul doses of dox and bleo
- no reported AML
- BEACOPP^{esc}
 - bleomycin
 - etoposide
 - doxorubicin
 - cyclophosphamide
 - vincristine
 - procarbazine
 - prednisone
 - +/- RT
- escalated doses of cyclophos, etoposide
- more toxic than ABVD

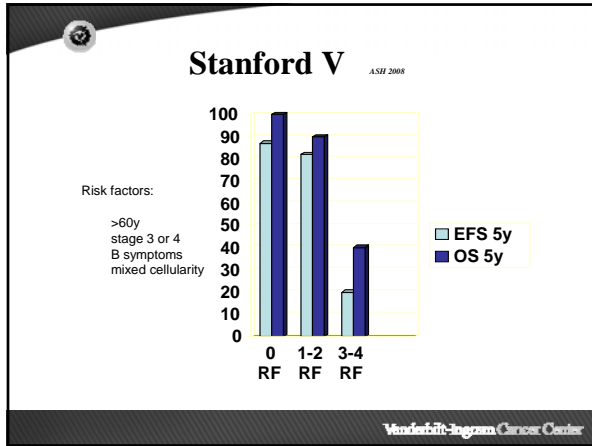
GHSg HD9, ASH 2007

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**Choice of Regimen
Advanced Stage**

- Background
 - ABVD: 75-87% PFS
 - Stanford V: Ph2 87% PFS,
 - UK study: High risk group much worse
 - BEACOPP^{esc}: Ph 3 FFS 87%
 - Toxicity concerns

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BEACOPP^{esc} GHSB HD9, ASH 2007

	COPP/ ABVD	BEACOPP ^{esc}
all	64%	82%
IPS 0-1	78	91
2-3	59	83
4-7	54	71

10yEFS

- grade 3-4 toxicity
 - neutropenia >95%
 - thrombocytopenia >70%
 - infection 22%
- sAML in 3.2% at 10y

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- ### StV vs ABVD ASH 2008, abst 370
- 520 pts: X (52%), B (74%), or St III-IV (51%)
 - IPS: 37% LR, 54% IR, 9% HR
 - 5y PFS: 76% ABVD, 74% St V (NS)
 - No diff by IPS
 - Pulm tox sl more in ABVD, nonpulm sl more in St V
 - ECOG 2496 results soon
- Van de Ven Cancer Center

GHSB HD 12
ASH 2008, Abstr 1588

- HD9 "established" BEACOPP_{esc} x8 as the standard in advanced HD
- Toxicity recognized
- BEACOPP_{esc} x8 (BE) vs BEACOPP_{esc} x4 then BEACOPP_{baseline} x4 (4+4)

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GHSB HD 12
ASH 2008, ABSTR 1588

- N=1571
- Grade 3-4 tox in 97%
- No sig diff in 5yPFS, 86%
- 77 second malignancies, 1.5% MDS
- New standard for GHSB

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GSHG HD 14

- Stage I-IIA with large med mass, high ESR, extranodal, some B pts
- N=1010
- ABVD x 4 vs BEACOPP_{esc} X2 +ABVD x2
- All received IFRT 30Gy
- 3yFFTF 90% ABVD vs 96% 2+2

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Conclusions

Choice of Regimen for Advanced/Unfavorable HL

- BEACOPP looks very good, concern about toxicity. Needs comparison to "modern" ABVD in advanced pts
- Stanford V: variable results. Poor for high risk?
 - Await ECOG 2496
- For now- ABVD

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Early PET is Prognostic in HL

- Published studies
 - Gallamini, 2006, Hutchings, 2006
- Abst 1460, CALGB, adv pts
 - PET2 neg vs pos: 2yPFS 87% vs 47%
- Abst 1450: early stage pts
 - PET2 neg vs pos: 2yFFS 95% vs 46%

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Response-Adapted Therapy Based on Early PET Abstr 2592

- N=102. Stage 1-4 (80% I/II).
- ABVD x3.
- PET neg(87 pts)--> observed. 82(94%) in CR at 18 mos
- "PET/CT PR" (14 pts)--> ABVD x 3 + IFRT. 12 CRs (85%). 11 (78%) in CR at 18 mos.
- EFS 18mos 92%

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Response-Adapted Therapy Based on Early PET Abstr 369

- N=331, stage I/IIA
- PET after ABVD x 3
- If neg --> obs
- If pos --> ABVD #4 + IFRT
- PET pos in 21% (high)
- 96% PFS at 13mos

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Response-Adapted Therapy Based on Early PET abstr 2594

- 21 pts with pos PET after ABVD x 2
- Historically 12% 2y FFS
- 19 treated with BEACOPPesc x 4 then BEACOPPstd x 4.
- 15/19 alive without relapse at 14 mos

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Conclusions
Response Adapted Therapy after Early PET

- Pos PET2 = poor outcome
 - Unclear that changing therapy changes outcome, but suggested by this small study
- Neg PET2 = good outcome
 - some suggestion that treatment can be de-escalated.
- Need more studies and follow up

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Transplant for HL

- ASCT vs chemotherapy
 - Relapse at < 1 yr: 41 vs 12% FTF
 - Relapse at > 1 yr: 75 vs 44%
- Risk factors for poor outcome include
 - Less than CR to salvage
 - High IPS
 - Relapse in prior RT field

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Importance of neg PET and neg CT before ASCT for HL abst 776

- 198 pts rel/ref HL at MSKCC
- Treated with ICE to best response then treated with HDCT / ASCT
- 3 groups by response to ICE
 - Gallium or PET pos (FI+)
 - FI neg, residual mass by CT
 - No residual mass

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Importance of neg PET and neg CT before ASCT for HL abst 776

	5y EFS	5y OS
NRM	86%	93
FI-, RM	71	79
FI +	41	51

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HL and Pregnancy

- 0.5 - 1% of HL patients are pregnant
- Small series and case reports
- Staging- avoid radiation to the extent possible:
 - CXR, shielded
 - Abd U/S or MR rather than CT

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HL and Pregnancy


- Treatment
 - Majority require no immediate treatment
 - 50% can go to term without intervention
 - Therapeutic RT not recommended
 - Alkylating agents, especially in the first or second trimester are associated with spontaneous abortion and fetal malformations
 - ABVD has been used in all trimesters without obvious detriment to fetus/child

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HL and Pregnancy

- Alternative is vinblastine
 - Min toxicity, not known to be teratogenic in humans
- After delivery, patients can be treated in a standard fashion, but staging may be inaccurate and they should receive a full 6-8 courses of chemotherapy.
 - 17 pts at BCCA, 13 alive, 2 dead of HL. 17 normal children


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HL in the HIV Patient

- HIV infected pts are at 5- 10 fold risk of HL
- More aggressive and unusual presentation and course
- Challenge of drug interactions and infections
- With HAART and standard chemotherapy, 60-70% 5y survivals are reported
- Relapsed patients are eligible for curative ASCT

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HL in the Elderly

- Worse outcomes
 - Worse histologic subtypes?
 - Reduced organ function
 - Reluctance to give full dose treatment
- Recommendations
 - Full standard treatment when possible
 - If necessary, bleo may be omitted
 - If doxorubicin is contraindicated, etoposide can be substituted

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