NCCN 11th Annual Congress:
Hematologic Malignancies™

# Early-stage Classical Hodgkin Lymphoma (CHL): Can We Eliminate Radiation Therapy for Most Patients?

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# Learning Objectives

- Describe the challenges associated with the management of early stage CHL and the need to develop individualized treatment options
- Review the evidence from recent clinical trials evaluating the use of chemotherapy alone for early stage CHL
- To understand the evolving criteria used in interpretation of PET scans (Deauville Criteria)
- To understand the potential use and limitations of PET scans in guiding treatment decisions in early stage CHL

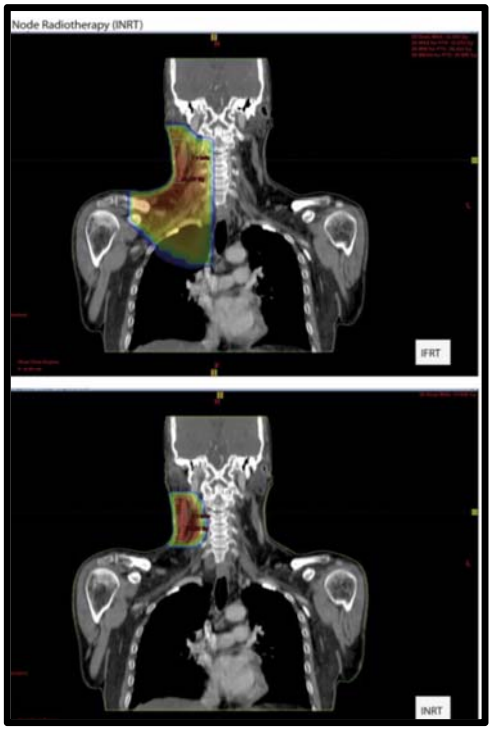
# Stage I-II Classical Hodgkin Lymphoma (CHL)
# Evolution of "The Gold Standards"

- Late 1960's-1970's: Extensive Radiation Therapy (RT)
- Late 1970's-1990's: Aggressive combined modality therapy (CMT) with extended field RT
- Mid 1990's: Reduced intensity CMT with involved field RT
- Current CMT: Further reduction in chemotherapy with involved nodal/involved site RT
- Current focus: PET-adapted strategies to assess if RT can be eliminated

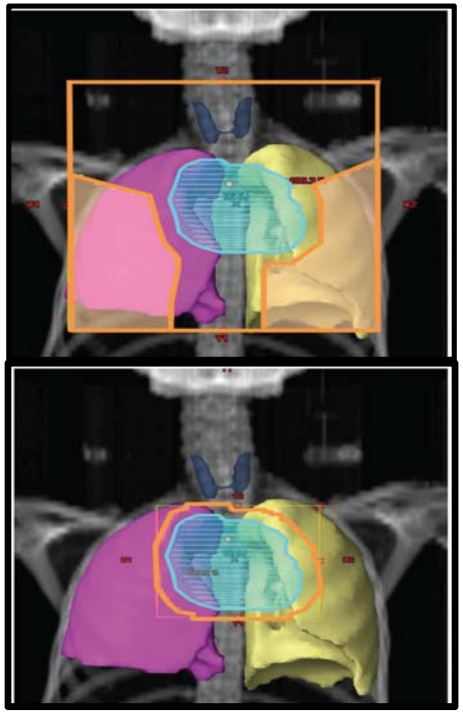
## Evolution of Radiation Therapy

- Involved Field Radiation Therapy (IFRT)
  - Treats entire lymphoid regions defined by arbitrary anatomic landmarks
- Involved Site Radiation Therapy (ISRT)
  - Targets only the specific volume initially involved with minimal margins
- Involved Nodal Radiation Therapy (INRT)
  - Special case of ISRT where pre-chemo PET-CT in treatment position required
  - More accurate volume definition of treatment field

# Evolution of RT: IFRT vs INRT

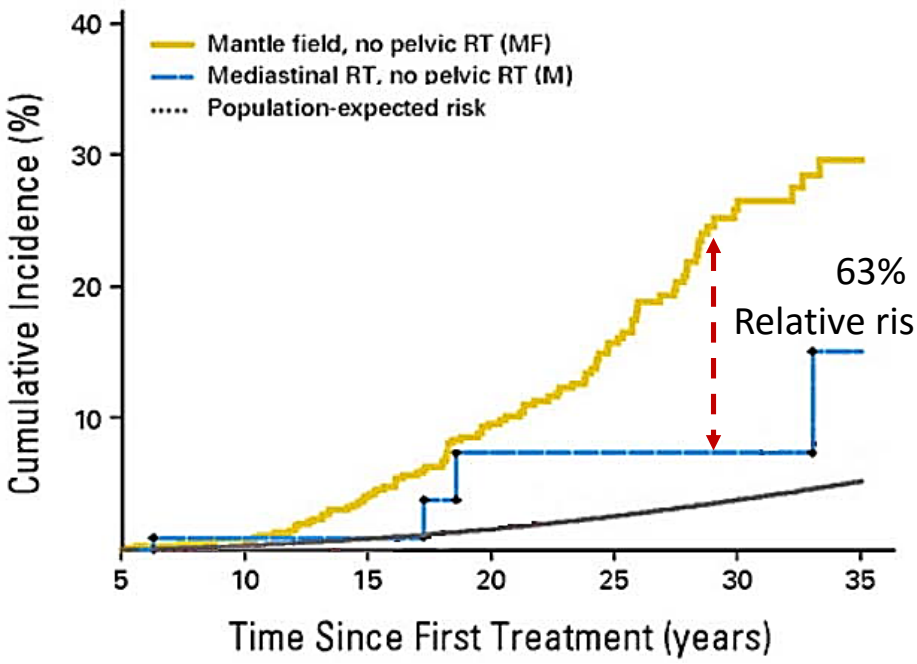



Maraldo MV, et al. *Int J Radiat Oncol Biol Phys*. 2013;85(4):1057-1065.



Campbell BA, et al. *Ann Oncol*. 2012;23(5):1259-1266.

# Implications for Transition to IFRT
# Clinical Evidence of Reduction in Breast Cancer Risk




63% reduction in
Relative risk of breast cancer

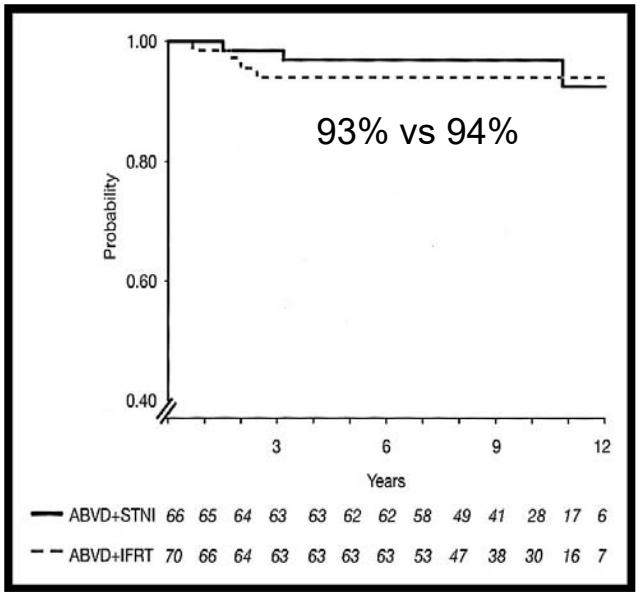
De Bruin M L et al. *J Clin Oncol.* 2009;27(26): 4239-4226.

# Stage I-II CHL

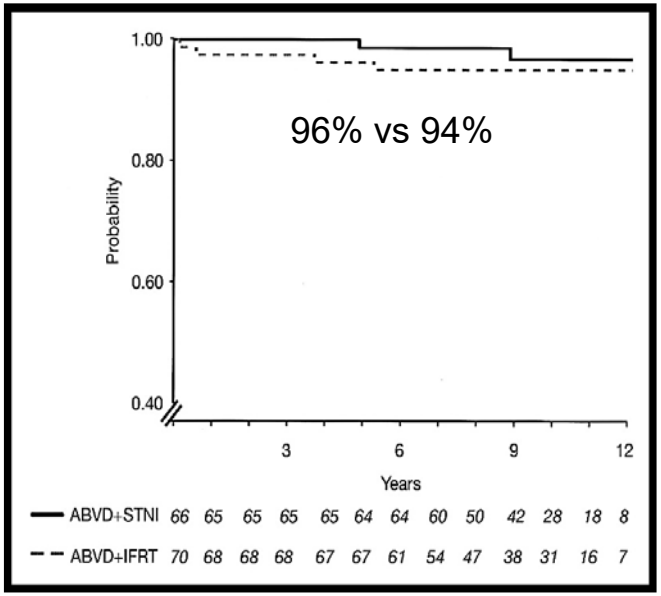
## ABVD X 4 + IFRT: Established Standard of Care

### Long-Term Results (12 years)

Freedom From Progression (FFP)




Overall Survival (OS)




Bonadonna G, et al. *J Clin Oncol.* 2004;22(14):2835-2841.

# Stage I-II CHL: Key Issues

- Definition of “favorable” vs “unfavorable” early stage disease
- Can risk-adapted strategies be employed to omit radiation therapy?
- Considerations for the treatment of patients with bulky mediastinal disease
- Future considerations
  - Incorporation of novel agents
  - Identification of biological subsets to guide therapy

# Stage I-II CHL: Key Issues

- Definition of “favorable” vs “unfavorable” early stage disease

# Risk Factors in Early Stage CHL

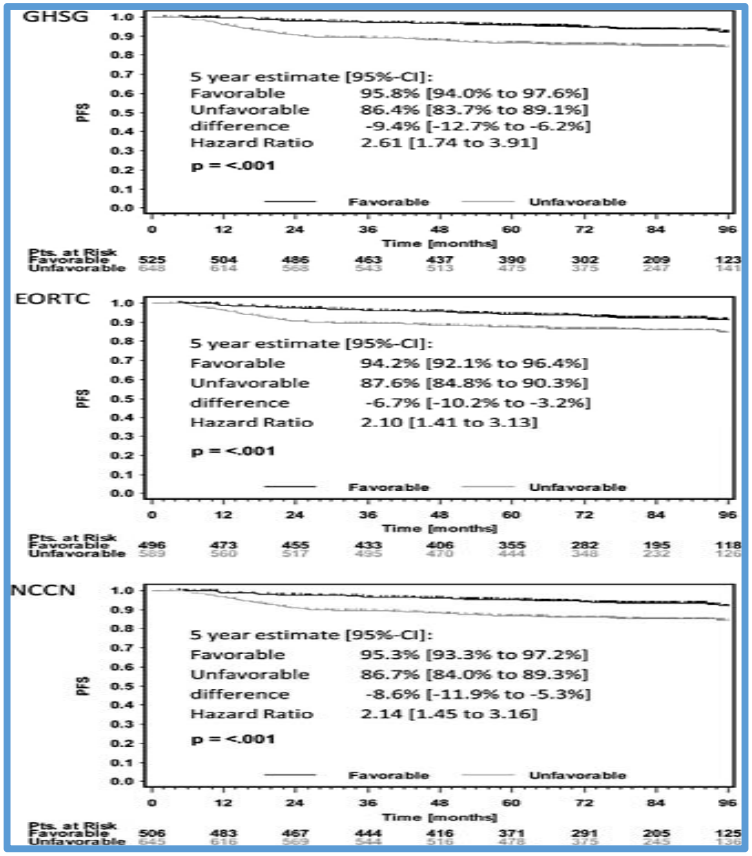
## Risk Factors: Variably defined

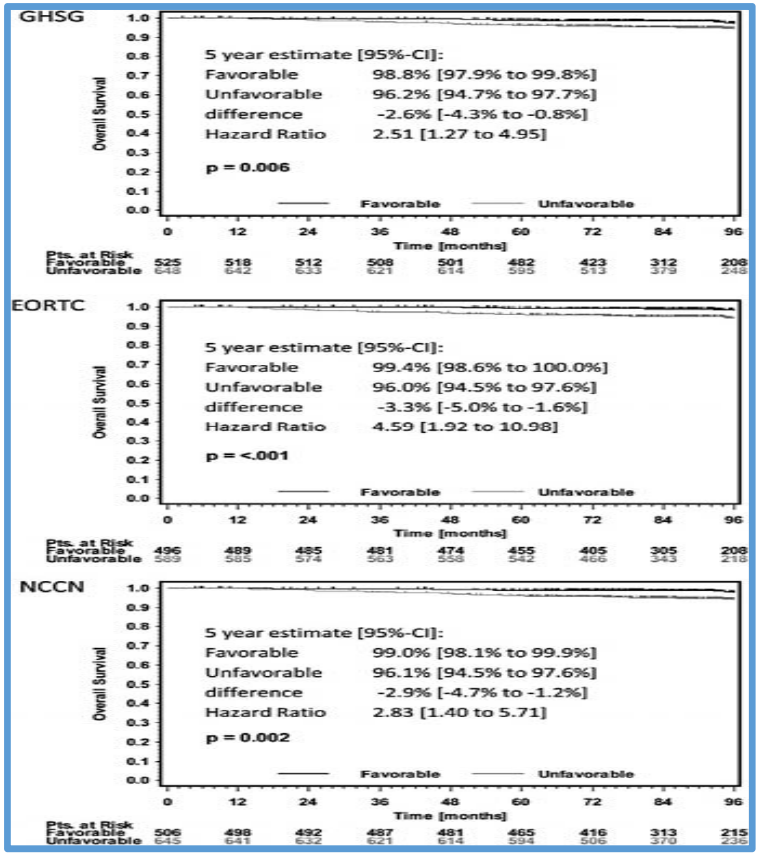
| GHSG | EORTC | NCCN |
|---|---|---|
| Large mediastinal mass (ratio ≥ 1/3)* | Large mediastinal mass (ratio ≥ 0.35) | Large mediastinal mass (ratio > 1/3) |
| | | Bulk > 10 cm |
| | Age ≥ 50 years | |
| ≥1 extranodal lesion* | | |
| ESR ≥ 50 (A) or ≥ 30 (B) | ESR ≥ 50 (A) or ≥ 30 (B) | ESR ≥ 50 (A) |
| | | B-symptoms |
| ≥3 nodal areas (out of 11 GHSG areas) | ≥4 nodal areas (out of 5 supra-diaphragmatic. EORTC areas) | ≥4 nodal regions (out of 17 Ann Arbor regions) |

Klimm B, et al. *Ann Oncol.* 2013;24(12):3070-3076.

# Outcomes in Early stage CHL Using Risk Definitions: GHSG, EORTC, or NCCN

## All definitions work largely because of significant overlap in risk factors

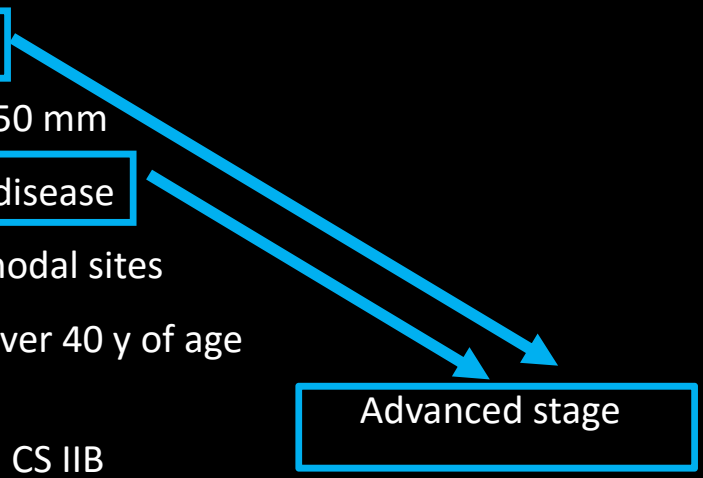



Klimm B, et al. *Ann Oncol*. 2013;24(12):3070-3076.

# HL Clinical Trial Treatment Groups
# Europe vs North America

| Europe (GSHG, GELA, EORTC) | | USA/Canada |
|---|---|---|
| | Stage | |
| Early favorable | CS I, IIA, B<br>No risk factors | Limited stage |
| Early unfavorable | CS I, IIA, B | |
| (Intermediate) | B Sx<br>ESR > 50 mm<br>Bulky disease<br>> 2-3 nodal sites<br>Men over 40 y of age | |
| Advanced stage | CS III-IV,<br>Selected CS IIB | Advanced stage |



Courtesy Connors JM, et al. *53rd ASH Annual Meeting*. 2010 education session.

# Early Stage Classical Hodgkin Lymphoma (CHL)

## Expected outcomes and goals of therapy in 2016

| | % Cure Rate | Therapeutic Priority |
|---|---|---|
| **Early Favorable (Stage I-II)** | **90** | **Reduce Toxicity** |
| **Early Unfavorable (stage I, II with risk factors)** | **80-85** | **Increase Efficacy *without* any increase in toxicity** |

Risk Factors: Variably defined

- Large mediastinal mass
- Extranodal lesions
- ≥ 3 nodal sites
- ↑ ESR
- age > 40
- MC histology

# Case 1: Early Stage CHL

- 36-year-old woman presents with a 2-month h/o pruritus. She denies fevers, night sweats, or weight loss
- Exam: well appearing and has a 2 cm L neck mass
- PET/CT scan: bilateral supraclavicular nodes measuring ~ 2 cm (SUV 6-8) and an upper mediastinal node measuring 5 x 2 cm (SUV 11.1)
- Excisional biopsy: classical HL, nodular sclerosing type
- Labs: WBC 5.6 K/µL with a normal differential, Hgb 12.7 g/dL, plt 154 K/µL, ESR 45, normal renal and hepatic function
- Final Diagnosis: Stage II A CHL

# Case 1: Therapy Choices for Stage IIA disease

1: ABVD x 2 + 20 Gy ISRT

2: ABVD x 4 + 30 Gy ISRT

3: Stanford V 8 weeks + 30 Gy ISRT

4: ABVD x 2 + Esc BEACOPP x 2 + ISRT

5: ABVD x 3-4

6: ABVD x 6

Bonadonna G, et al. *J Clin Oncol.* 2004;22(14):2835-2841, Engert A, et al. *N Engl J Med.* 2010;363(7):640-652
Eich HT, et al. *J Clin Oncol.* 2010;28(27):4199-4206, von Tresckow B, et al. *J Clin Oncol.* 2012;30(9):907-913
Advani RH, et al. *Ann Oncol.* 2013;24(4):1044-1048, Radford J, et al. *N Engl J Med.* 2015;372(17):1598-1607
Meyer RM, et al. *N Engl J Med.* 2012; 366(5):399-408, Raemaekers JM, et al. *J Clin Oncol.* 2014;32(12):1188-1194

# Combined Modality Therapy in CT Era
# Overall Survival > 94% in Early stage CHL

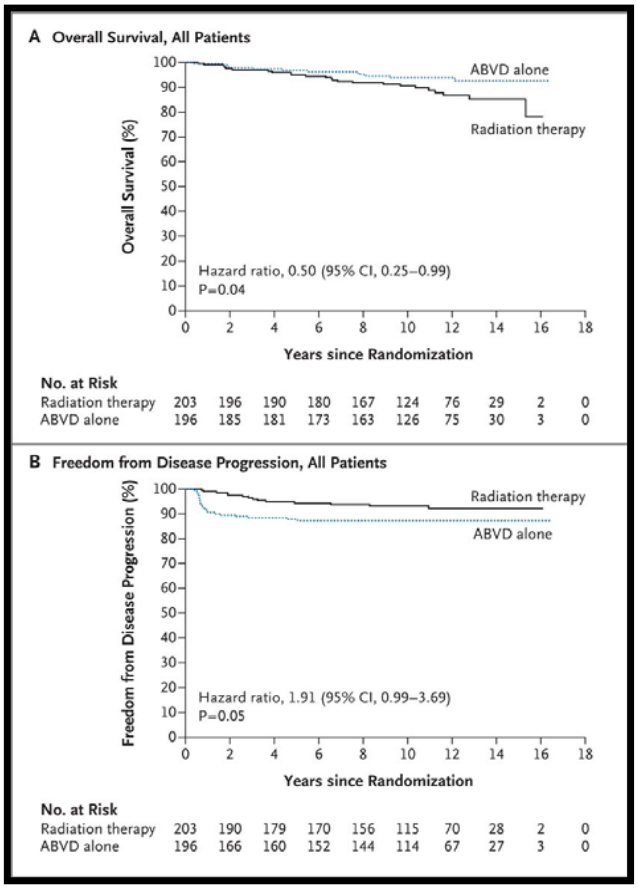
| Study | N | Chemo | RT | OS (%) | Years |
|---|---|---|---|---|---|
| Milan INT | 70 | ABVD | IF 30 Gy | 94 | 12 |
| GHSG HD10 | 1190 | ABVD | IF 20-30 Gy | 94.5 | 10 |
| GHSG HD11 | 1395 | ABVD Esc BEACOPP | IF 30 Gy | 94.5 | 10 |
| GHSG HD14 | 1431 | ABVD 2+2 | IF 30 Gy | 95 | 5 |
| EORTC H9U | 277 | ABVD | IF 30 Gy | 95 | 4 |
| Stanford/Kaiser G4 | 87 | Stanford V | IF 30 Gy | 94 | 12 |

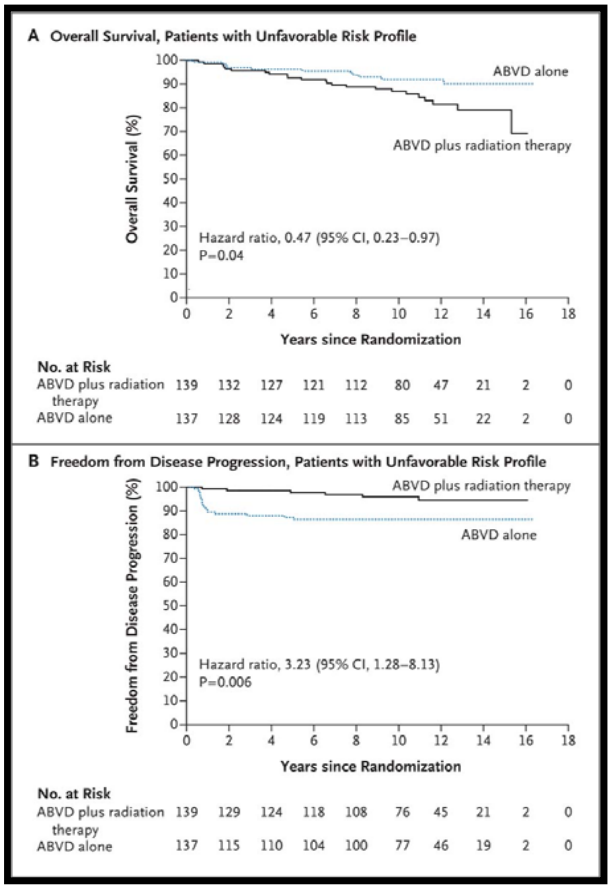
Bonadonna G, et al. *J Clin Oncol.* 2004;22(14):2835-2841, Engert A, et al. *N Engl J Med.* 2010;363(7):640-652. Eich HT, et al. *J Clin Oncol.* 2010;28(27):4199-4206., von Tresckow B, et al. *J Clin Oncol.* 2012;30(9):907-913. Advani RH, et al. *Ann Oncol.* 2013;24(4):1044-1048.

# Questions

- Can favorable patients receive less treatment?
- Should early stage unfavorable patients receive more treatment?
- Can we better select patients for chemotherapy alone?

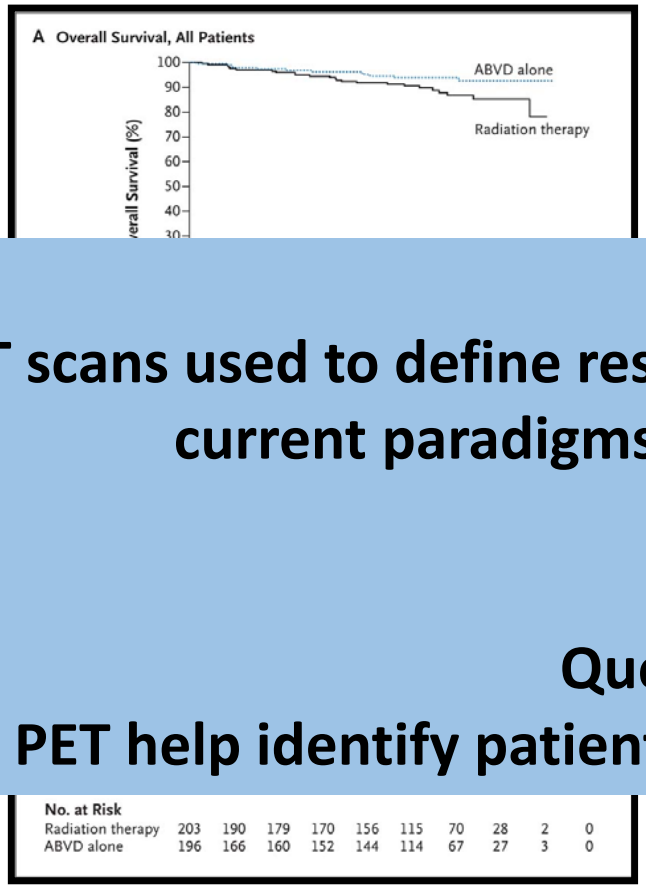
# NCIC H6 Trial: CT Adapted Therapy
# Overall Survival and Freedom From Disease Progression

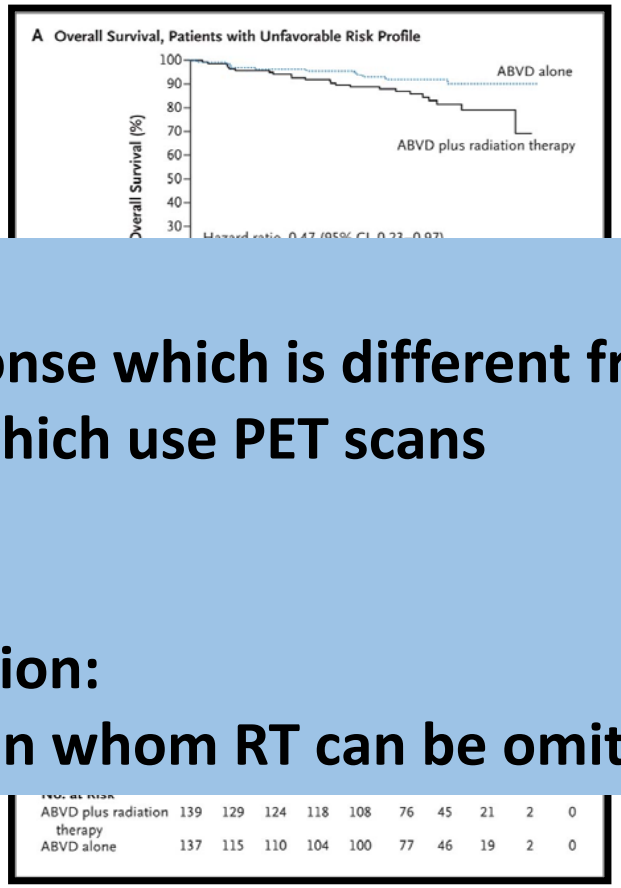



Meyer RM, et al. *N Engl J Med.* 2012;366(5):399-408.

# NCIC H6 Trial: CT Adapted Therapy
# Overall Survival and Freedom From Disease Progression




**CT scans used to define response which is different from current paradigms which use PET scans**

**Question:**
**Can PET help identify patients in whom RT can be omitted?**

Meyer RM, et al. *N Engl J Med.* 2012;366(5):399-408.

# PET/CT Imaging
# Potential Uses In CHL

- Staging: YES
- Response assessment: YES
  - End of therapy (EOT)

- ***Treatment modification based on PET/CT***
  - ***EOT***
  - ***Interim***

- Can modification of Rx based on EOT or interim PET/CT have the potential to select patients for treatment escalation or de-escalation?

- Do these modifications have the potential to improve outcomes?

# Report 'Wording' Nightmares for Clinicians

Common report

- Excellent response, there is minimal residual uptake in a para aortic node which could represent treated disease. Residual lymphoma cannot be excluded.

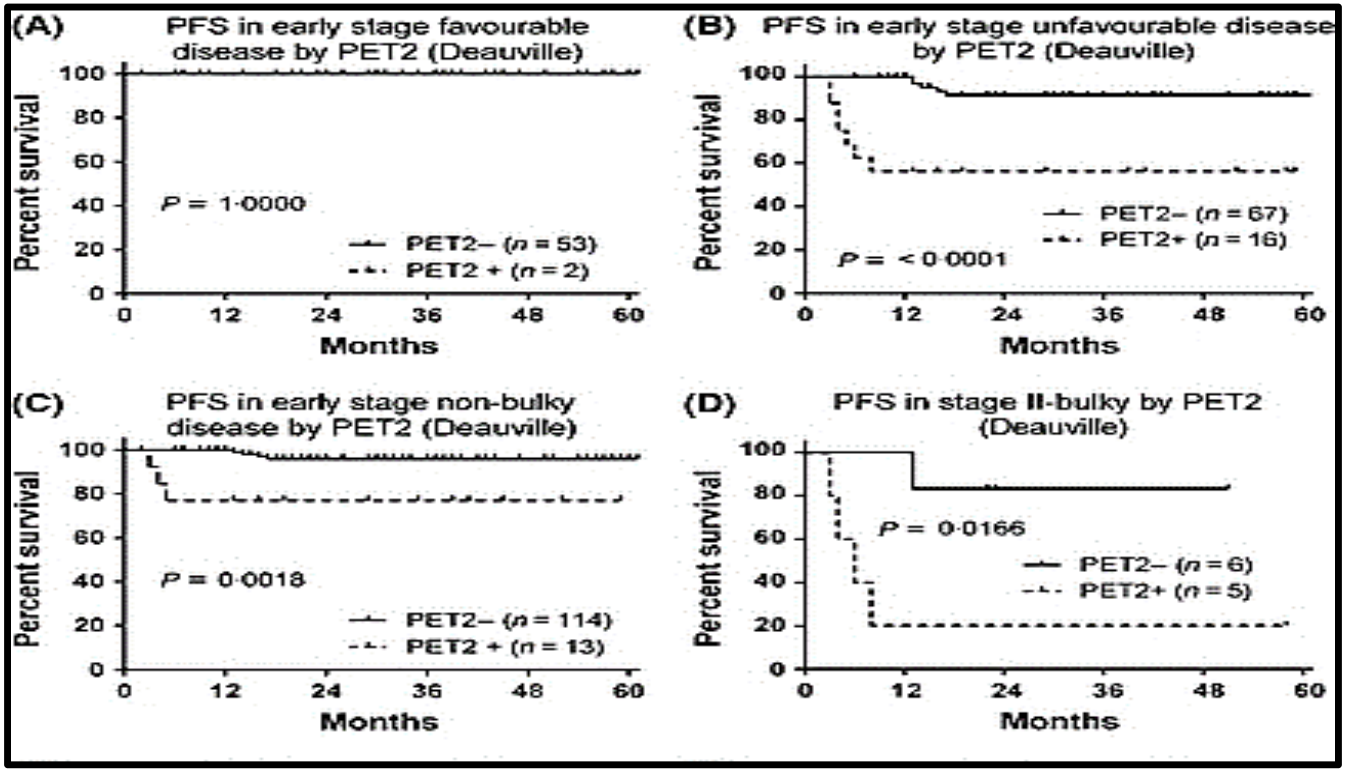
# Deauville 5-Point Scoring System

Score
1 No uptake
2 Uptake ≤ mediastinum
3 Uptake > mediastinum but ≤ liver
4 Uptake moderately higher than liver
5 Uptake markedly higher than liver and/or new lesions
X New areas of uptake unlikely to be related to lymphoma

Barrington SF, et al. *J Clin Oncol.* 2014;32(27):3048-3058.

# The Prognostic Value of Interim PET Scan in Patients With Early Stage CHL

## MD Anderson retrospective study using Deauville Criteria



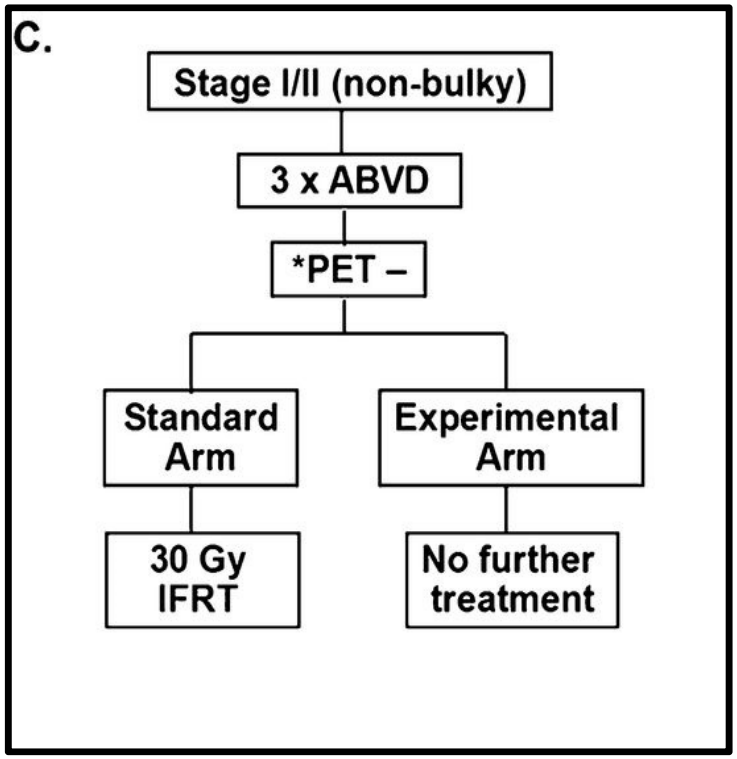

Oki Y, et al. *Br J Haematol.* 2014;165(1):112-116.

## Early Stage CHL

# Does a reduction in therapy based upon a negative interim PET impact PFS?

## Prospective Studies

# UK NCRI RAPID Trial: Stage I-IIA Non-Bulky




## PET scores after 3 cycles ABVD and treatment allocation

- Following 3 cycles ABVD 571 pts had a PET scan:
  - Score 1, 301 (52.7%)
  - Score 2, 125 (22.0%) –
  - Score 3, 90 (15.7%) –
  - Score 4, 32 (5.6%)
  - Score 5, 23 (4.0%) +
- 420 of 426 PET –ve pts randomised to IFRT (209) or NFT (211)
  - 6 not randomised; pt choice 3, clinician choice 2, error 1
- 25 of 209 pts randomised to IFRT did not receive this treatment:
  - patients declined 19
  - died 5
  - pneumonia 1

≥7% difference in PFS

~ 36% would have been considered unfavorable by GHSG or EORTC criteria

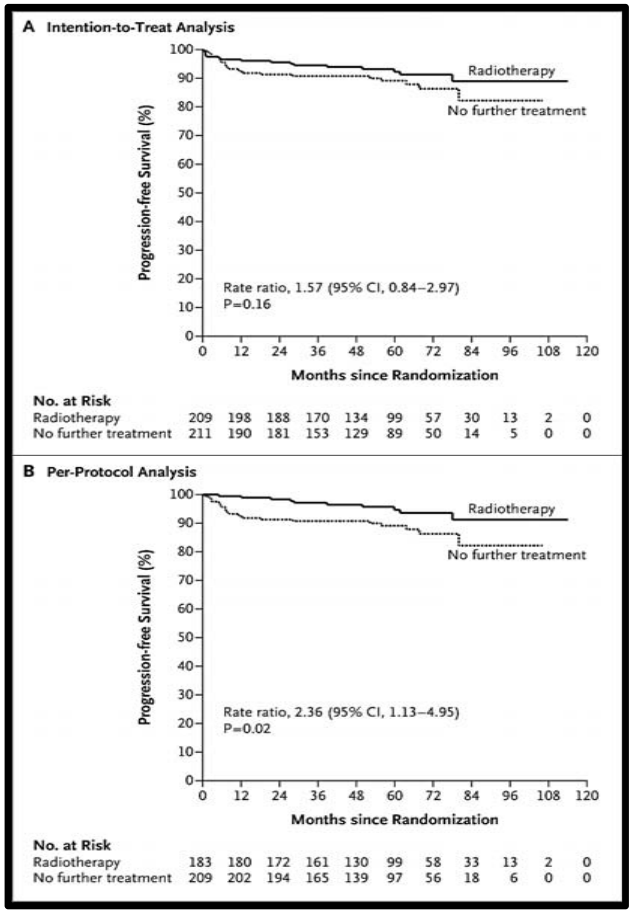
Radford J, et al. *N Engl J Med.* 2015;372(17):1598-1607.

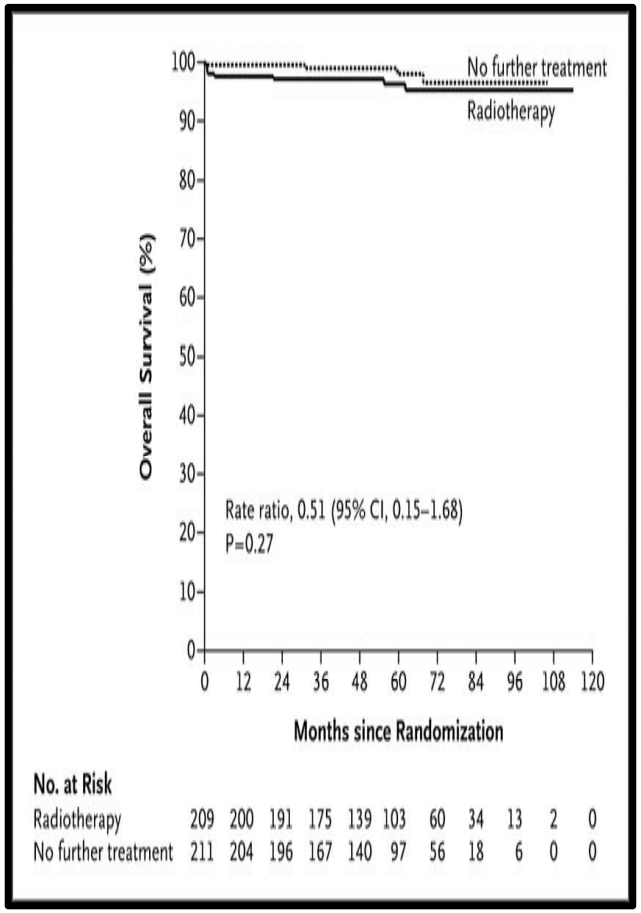
# UK NCRI RAPID Trial: Patient Characteristics

| Characteristic | Negative PET Findings | | Positive PET Findings (N=145) |
|---|---|---|---|
| | Radiotherapy (N=209) | No Further Treatment (N=211) | |
| Age — yr | | | |
| Median | 34 | 34 | 36 |
| Range | 16–74 | 16–75 | 18–75 |
| Sex — no. (%) | | | |
| Male | 103 (49.3) | 107 (50.7) | 96 (66.2) |
| Female | 106 (50.7) | 104 (49.3) | 49 (33.8) |
| Ann Arbor stage — no. (%)* | | | |
| IA | 69 (33.0) | 70 (33.2) | 48 (33.1) |
| IIA | 140 (67.0) | 141 (66.8) | 97 (66.9) |
| Favorable pretreatment features — no./total no. (%)† | | | |
| EORTC criteria[14] | 118/184 (64.1) | 122/185 (65.9) | 85/158 (53.8) |
| GHSG criteria[15,24] | 114/175 (65.1) | 136/184 (73.9) | 97/153 (63.4) |

Radford J, et al. *N Engl J Med.* 2015;372(17):1598-1607.

# UK NCRI RAPID Trial: Stage I-IIA Non-Bulky



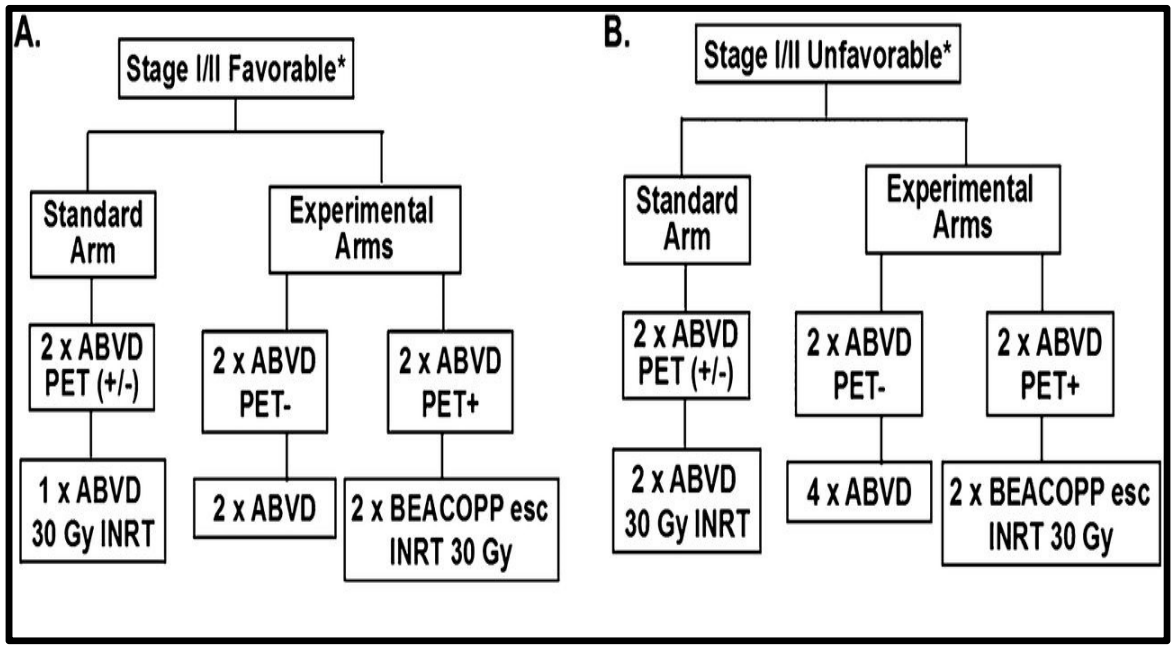




Radford J, et al. *N Engl J Med*. 2015;372(17):1598-1607.

# UK NCRI RAPID Trial: Conclusions

- Overall excellent outcomes
- PET score after 3 cycles ABVD had prognostic value in terms of EFS but EORTC/GHSG pre-treatment stratification did not
- PET score 5 is a particularly adverse feature
  - 5 episodes of progression and 3 HL deaths in 23 patients
- Findings need to be validated in other series of patients with early stage CHL
- If confirmed the role of PET in individualized treatment planning is strengthened

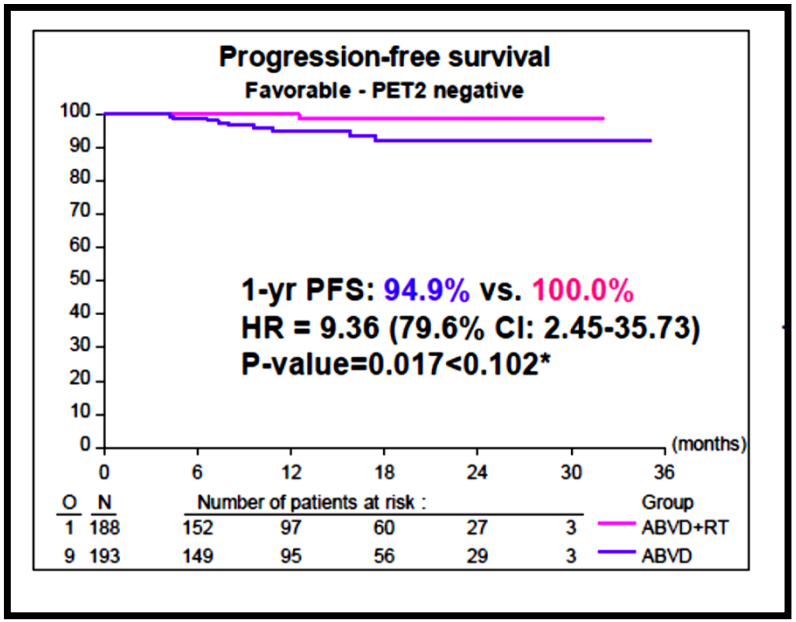
# EORTC H10 Trial: Randomized Trial
# Early FDG-PET Scan Guided Treatment Adaptation



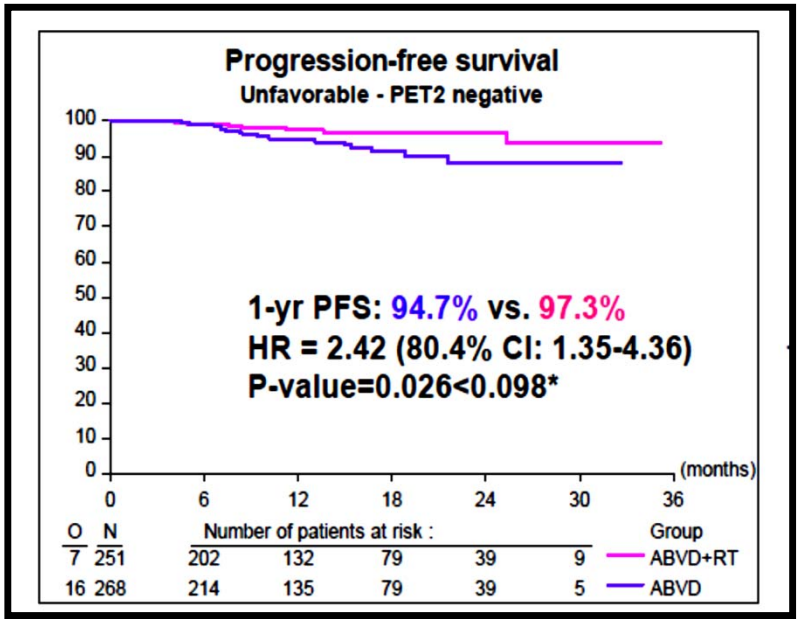

- PET scans scored according to the International Harmonization Project criteria
  - PET negative: Deauville score 1 or 2

Raemaekers JM, et al. *J Clin Oncol.* 2014;32(12):1188-1194.

# EORTC H10 Trial: PET– Group
## Futility Confirmed in Both Arms




| Events | 1 | 9 |
|---|---|---|
| Relapse | 1 | 9 |
| Death w/o relapse | 0 | 0 |




| Events | 7 | 16 |
|---|---|---|
| Relapse | 7 | 15 |
| Death w/o relapse | 0 | 1 |

Raemaekers JM, et al. *J Clin Oncol.* 2014;32(12):1188-1194.

# 5-Point Scale (Deauville Criteria) for Interpretation of Interim-PET scans

1. No uptake
2. Uptake ≤ mediastinum
3. Uptake > mediastinum but ≤ liver

Negative scan

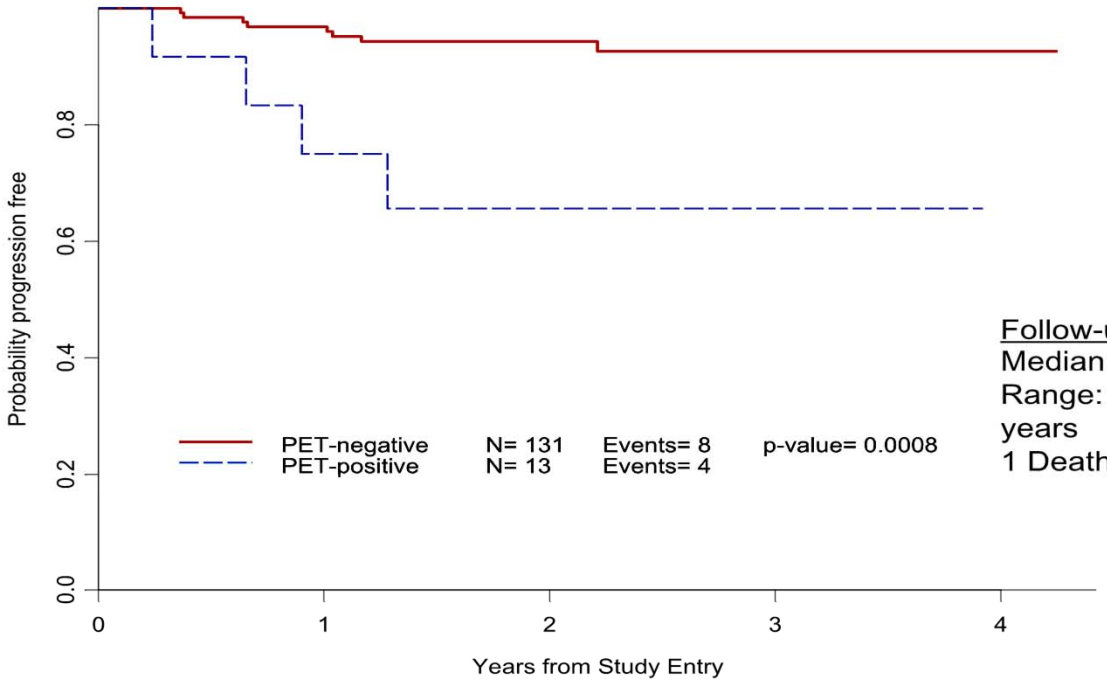
4. Moderately increased uptake compared to liver
5. Markedly increased uptake compared to liver or new areas of FDG uptake

Positive scan

Barrington SF et al. *J Clin Oncol* 2014;32(27):3048-3058.

# CALGB 50604 Progression Free Survival

## Post cycle 2 ABVD PET- and PET+ Patients




Follow-up time
Median: 2.1 years
Range: < 1month – 4.3 years
1 Death (Suicide – PET +)

| | Est. 3-yr PFS | Hazard Ratio |
|---|---|---|
| PET - | 92% (84%-96%) | 6.04 (1.82-20.08) |
| PET + | 66% (32%-86%) | |

Courtesy Dr Strauss ASH 2015

# Stage I-II CHL: Key Issues

## Considerations in patients with bulky mediastinal disease

- Responses not reported separately for bulk vs other factors in most studies
- Therapy varies across different study groups
  - GHSG: bulk alone: treated on early stage unfavorable studies
    - ie, HD11 and HD14
  - GHSG: bulk + EN/B symptoms: treated on advanced stage studies
    - HD15 (esc BEACOPP x 6)
  - North America: By and large treated as advanced disease

# Randomized Phase III Studies Which Included Stage I-II X CHL

**Table** Results of Randomized Phase III Trials That Include Patients With Stage I–IIX Hodgkin Lymphoma

| Study (% bulky mediastinal mass) | Treatment Arm | N | Median Follow-up (yrs) | Overall Response Rate (%) | Outcome (% of pts) | Overall Survival (%) |
|---|---|---|---|---|---|---|
| **North American Trials** | | | | | | |
| ECOG 2496 (subset with stage I–IIX mediastinal HL)[33] (100%) | ABVD × 6–8 + 36 Gy IFRT | 136 | 5.47 | 82 | 5-yr FFS: 85 | 5-yr: 95 |
| | Stanford V | 131 | 5.47 | 86 | 5-yr FFS: 77 | 5-yr: 92 |
| **European Trials (Bulky subsets were not separately reported.)** | | | | | | |
| EORTC H9-U[35,36] (NR) | ABVD × 6 + 30 Gy IFRT | 276 | NR | 87 | 4-yr EFS: 94 | 4-yr: 96 |
| | ABVD × 4 + 30 Gy IFRT | 277 | NR | 86 | 4-yr EFS: 89 | 4-yr: 95 |
| | BEACOPP × 4 + 30 Gy IFRT | 255 | NR | 84 | 4-yr EFS: 91 | 4-yr: 93 |
| EORTC H10-U[37] (NR) | ABVD × 4 + 30 Gy INRT | 251 | 1.1 | NR | 1-yr PFS: 97.3 | NR |
| | ABVD × 2; if PET negative, ABVD × 4 (total 6); if PET positive, escalated BEACOPP × 2 + 30 Gy INRT | 268 | 1.1 | NR | 1-yr PFS: 94.7 | NR |
| GHSG HD11[25] (17% to 22%) | ABVD × 4 + 30 Gy IFRT | 356 | 7.6 | 94.7 | 5-yr PFS: 87.2 | 5-yr: 94.3 |
| | ABVD × 4 + 20 Gy IFRT | 347 | 7.6 | 92.8 | 5-yr PFS: 82.1 | 5-yr: 93.8 |
| | BEACOPP × 4 + 30 Gy IFRT | 341 | 7.6 | 94.4 | 5-yr PFS: 87.9 | 5-yr OS: 94.6 |
| | BEACOPP × 4 + 20 Gy IFRT | 351 | 7.6 | 94.6 | 5-yr PFS: 87.0 | 5-yr OS: 95.1 |
| GHSG HD14[19] (18.7%) | ABVD × 4 + 30 Gy IFRT | 765 | 3.6 | 95.0 | 5-yr PFS estimate: 89.1 | 5-yr estimate: 96.8 |
| | Escalated BEACOPP × 2 + ABVD × 2 + 30 Gy IFRT | 763 | 3.6 | 95.7 | 5-yr PFS estimate: 95.4 | 5-yr estimate: 97.2 |
| **GHSG Advanced-Disease Protocols (Includes patients with stage I–IIX plus extranodal sites or B symptoms. Bulky subsets were not separately reported.)** | | | | | | |
| GHSG HD9[39] (bulky disease in 58% to 68% of pts; stage IIB in 9% to 16%) | COPP/ABVD × 8 | 261 | 10.2 | 85 | 10-yr FFTF: 64 | 10-yr: 75 |
| | Baseline BEACOPP × 8 | 469 | 9.3 | 88 | 10-yr FFTF: 70 | 10-yr: 80 |
| | Escalated BEACOPP × 8 | 466 | 8.9 | 96 | 10-yr FFTF: 82 | 10-yr: 86 |
| GHSG HD12[40] (large mediastinal mass in 27.6% to 29.2%; stage IIB in 12.7% to 17.1%) | Escalated BEACOPP × 8 | 787 | 6.5 | 93.0 | 5-yr FFTF: 86.4 | 5-yr: 92 |
| | Escalated BEACOPP × 4 followed by baseline BEACOPP × 4 | 787 | 6.5 | 91.1 | 5-yr FFTF: 84.8 | 5-yr: 90.3 |
| GHSG HD15[41] (large mediastinal mass in 29% to 30%; stage IIB in 15% to 17%) | Escalated BEACOPP × 8 | 705 | 4.0 | 90.1 | 5-yr FFTF: 84.4 | 5-yr: 91.9 |
| | Escalated BEACOPP × 6 | 711 | 4.0 | 94.2 | 5-yr FFTF 89.3 | 5-yr: 95.3 |
| | Baseline BEACOPP × 8 | 710 | 48 mo | 92.4 | 5-yr FFTF 85.4 | 5-yr: 94.5 |

Percival ME, et al. *Oncology.*2014;28(3):253-256, 258-260, C3.

# Randomized Phase III Studies Which Included Stage I-II X CHL

**Table** Results of Randomized Phase III Trials That Include Patients With Stage I–IIX Hodgkin Lymphoma

| Study (% bulky mediastinal mass) | Treatment Arm | N | Median Follow-up (yrs) | Overall Response Rate (%) | Outcome (% of pts) | Overall Survival (%) |
|---|---|---|---|---|---|---|
| **North American Trials** | | | | | | |
| ECOG 2496 (subset with stage I–IIX mediastinal HL)[33] (100%) | ABVD × 6–8 + 36 Gy IFRT | 136 | 5.47 | 82 | 5-yr FFS: 85 | 5-yr: 95 |
| | Stanford V | 131 | 5.47 | 86 | 5-yr FFS: 77 | 5-yr: 92 |
| **European Trials (Bulky subsets were not separately reported.)** | | | | | | |
| EORTC H9-U[35,36] (NR) | ABVD × 6 + 30 Gy IFRT | 276 | NR | 87 | 4-yr EFS: 94 | 4-yr: 96 |
| | ABVD × 4 + 30 Gy IFRT | 277 | NR | 86 | 4-yr EFS: 89 | 4-yr: 95 |
| | BEACOPP × 4 + 30 Gy IFRT | 255 | NR | 84 | 4-yr EFS: 91 | 4-yr: 93 |
| | BEACOPP × 4 + 20 Gy IFRT | 351 | 7.6 | 94.6 | 5-yr PFS: 87.0 | 5-yr OS: 95.1 |
| GHSG HD14[19] (18.7%) | ABVD × 4 + 30 Gy IFRT | 765 | 3.6 | 95.0 | 5-yr PFS estimate: 89.1 | 5-yr estimate: 96.8 |
| | Escalated BEACOPP × 2 + ABVD × 2 + 30 Gy IFRT | 763 | 3.6 | 95.7 | 5-yr PFS estimate: 95.4 | 5-yr estimate: 97.2 |
| **GHSG Advanced-Disease Protocols (Includes patients with stage I–IIX plus extranodal sites or B symptoms. Bulky subsets were not separately reported.)** | | | | | | |
| GHSG HD9[39] (bulky disease in 58% to 68% of pts; stage IIB in 9% to 16%) | COPP/ABVD × 8 | 261 | 10.2 | 85 | 10-yr FFTF: 64 | 10-yr: 75 |
| | Baseline BEACOPP × 8 | 469 | 9.3 | 88 | 10-yr FFTF: 70 | 10-yr: 80 |
| | Escalated BEACOPP × 8 | 466 | 8.9 | 96 | 10-yr FFTF: 82 | 10-yr: 86 |
| GHSG HD12[40] (large mediastinal mass in 27.6% to 29.2%; stage IIB in 12.7% to 17.1%) | Escalated BEACOPP × 8 | 787 | 6.5 | 93.0 | 5-yr FFTF: 86.4 | 5-yr: 92 |
| | Escalated BEACOPP × 4 followed by baseline BEACOPP × 4 | 787 | 6.5 | 91.1 | 5-yr FFTF: 84.8 | 5-yr: 90.3 |
| GHSG HD15[41] (large mediastinal mass in 29% to 30%; stage IIB in 15% to 17%) | Escalated BEACOPP × 8 | 705 | 4.0 | 90.1 | 5-yr FFTF: 84.4 | 5-yr: 91.9 |
| | Escalated BEACOPP × 6 | 711 | 4.0 | 94.2 | 5-yr FFTF 89.3 | 5-yr: 95.3 |
| | Baseline BEACOPP × 8 | 710 | 48 mo | 92.4 | 5-yr FFTF 85.4 | 5-yr: 94.5 |

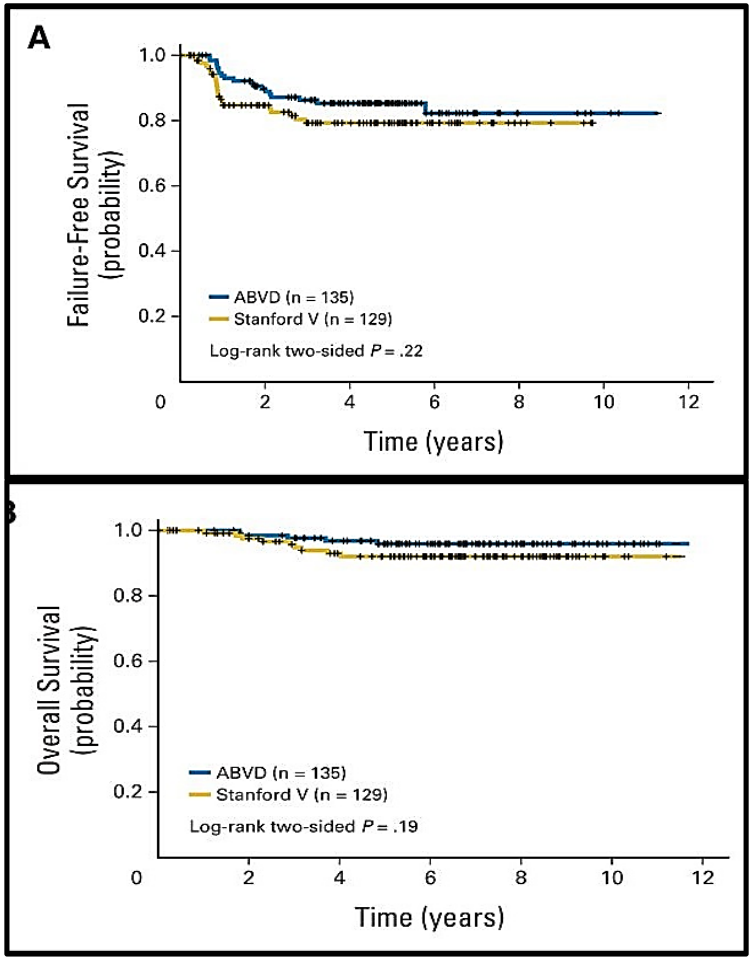
E2496: reported outcomes specifically in patients with bulky disease

Other studies have included 9-25% of patients with bulky disease

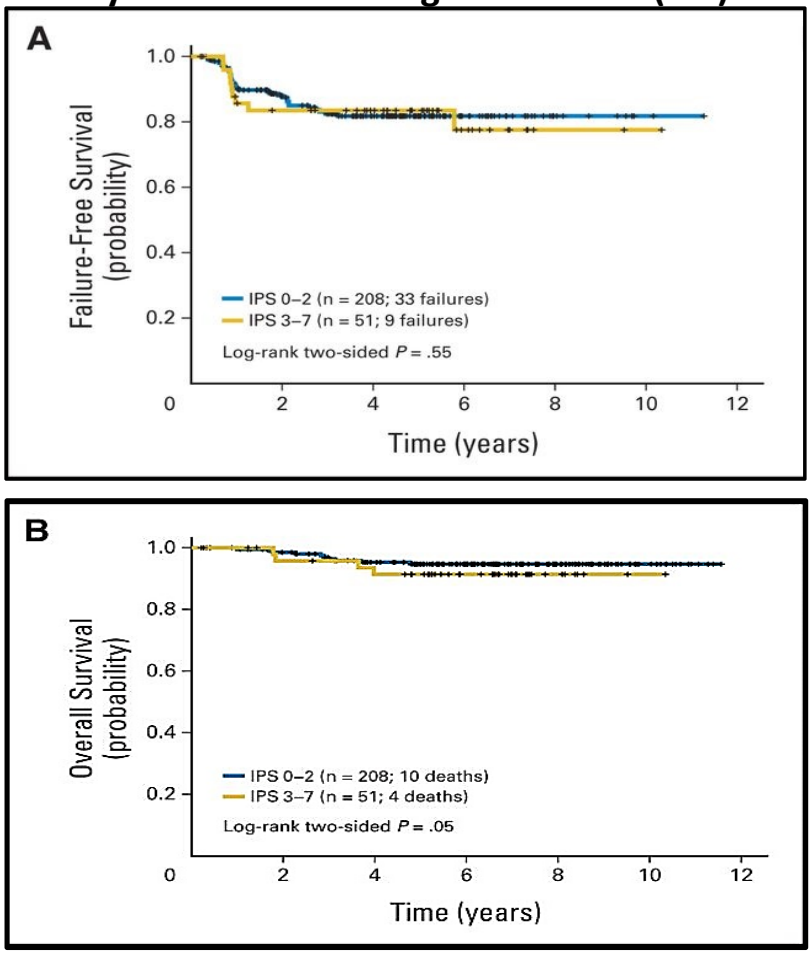
Percival ME, et al. *Oncology.*2014;28(3):253-256, 258-260, C3.

# E2496: Results in Stage I-II Bulky Mediastinal CHL

## By Treatment Arm

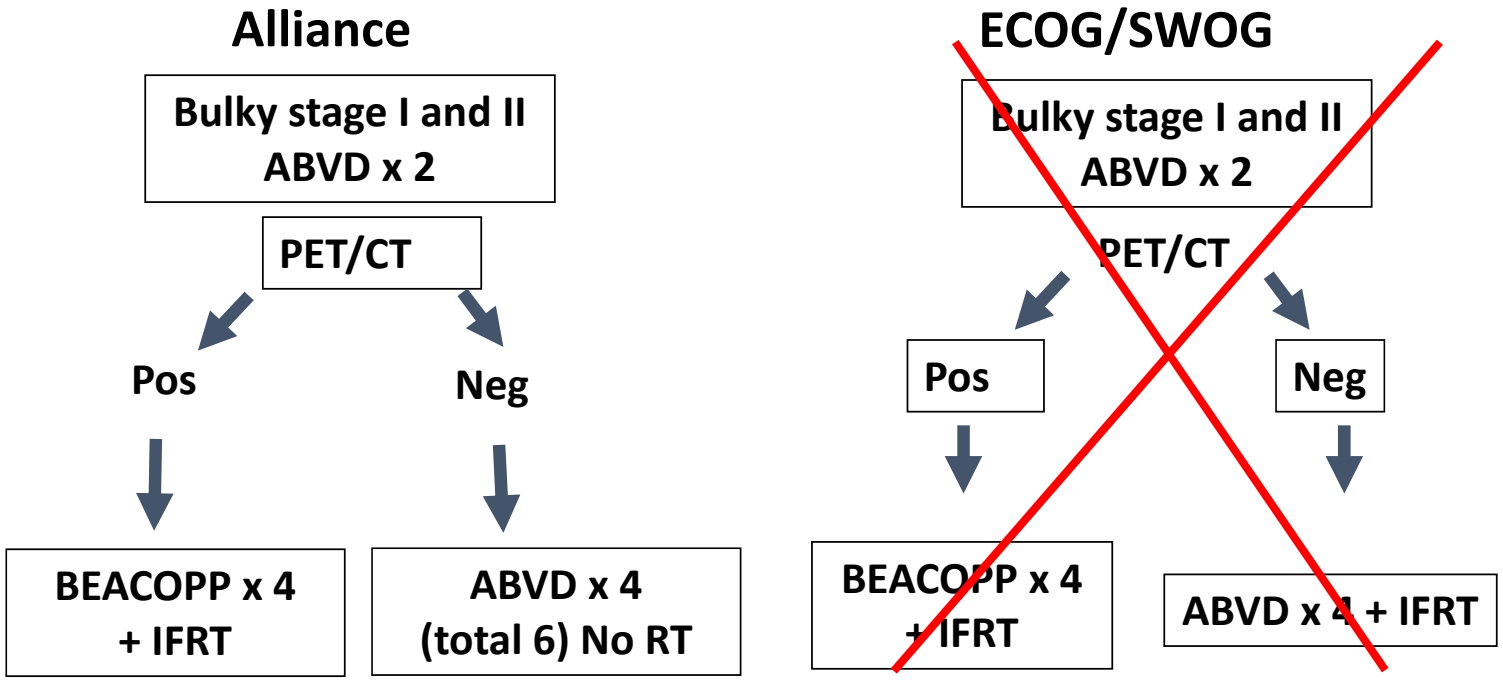



## By International Prognostic Score (IPS)



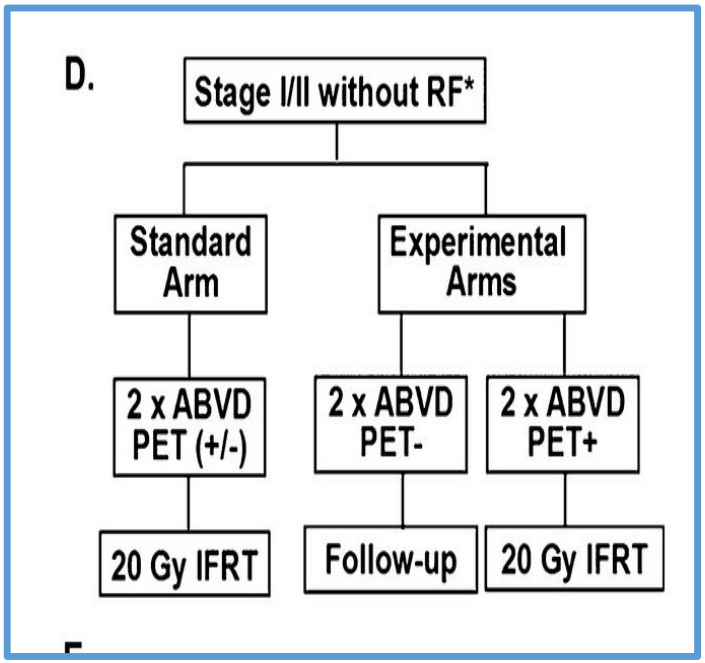

Advani RH, et al. *J Clin Oncol.* 2015;33(17):1936-1942.

# North American Studies in Bulky CHL: Risk- and PET-Adapted

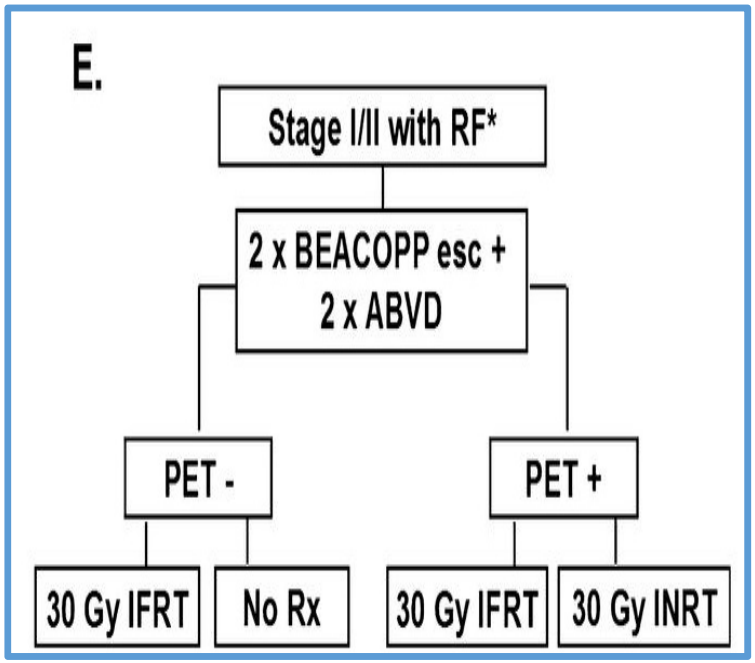


# GHSG: Ongoing Trials in Early Stage CHL

**HD 16**




**HD 17**




Risk Factors: > 2 nodal areas, ESR ≥ 50 (no B sympt)
ESR ≥ 30 (B sympt), MMR > 0.33 (no B sympt/or EN sites)

Evens AM and Kostakoglu L. *Blood*. 2014;124(23):3356-3364.

# Early Stage CHL: Summary of Prospective Trials

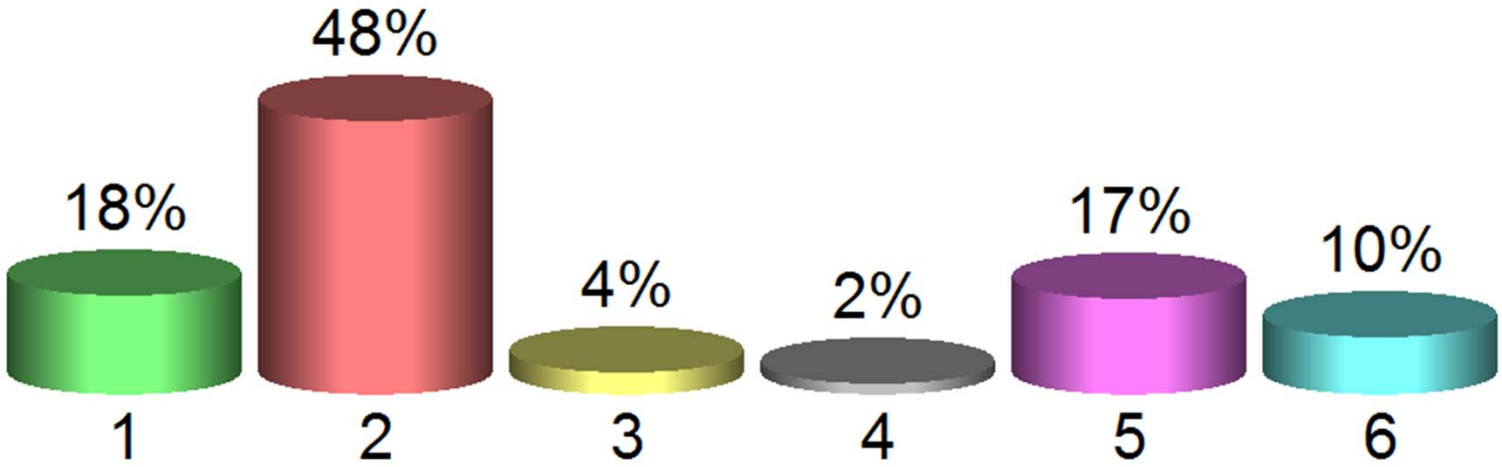
- Prognosis of patients with early favorable and unfavorable CHL is excellent
- PET negative patients (Deauville 2) after 2-3 cycles of ABVD
  - Excellent outcome, but experience slightly more treatment failure than those receiving RT
  - INRT/ISRT appears adequate to prevent relapse and may have fewer long-term/late effects than previously seen with IFRT
  - No difference in OS, but follow-up of PET-adapted therapy is very short
- CALGB: Deauville 3
  - Avoids RT in more patients.
  - Esc BEACOPP does not improve outcomes in PET positive patients
  - Need better front line therapy

***CRITICAL TO HAVE PET-CT REPORTS BASED ON DEAUVILLE CRITERIA IF RESPONSE ADAPTED THERAPY IS BASIS FOR TREATMENT DECISIONS***

## Audience Polling Results

### Case 1: Therapy Choices for Stage IIA disease

1: ABVD x 2 + 20 Gy ISRT
2: ABVD x 4 + 30 Gy ISRT
3: Stanford V 8 weeks + 30 Gy ISRT
4: ABVD x 2 + Esc BEACOPP x 2 + ISRT
5: ABVD x 3-4
6: ABVD x 6




Bonadonna G, et al. *J Clin Oncol.* 2004;22(14):2835-2841, Engert A, et al. *N Engl J Med.* 2010;363(7):640-652
Eich HT, et al. *J Clin Oncol.* 2010;28(27):4199-4206, von Tresckow B, et al. *J Clin Oncol.* 2012;30(9):907-913
Advani RH, et al. *Ann Oncol.* 2013;24(4):1044-1048, Radford J, et al. *N Engl J Med.* 2015;372(17):1598-1607
Meyer RM, et al. *N Engl J Med.* 2012; 366(5):399-408, Raemaekers JM, et al. *J Clin Oncol.* 2014;32(12):1188-1194

## Case 1: Therapy Choices for 36 y female with Stage IIA disease

3 nodal sites (bil neck and upper mediastinum)
GHSG: unfavorable
NCCN and EORTC: favorable

1: ABVD x 2 + 20 Gy ISRT

2: ABVD x 4 + 30 Gy ISRT

3: Stanford V 8 weeks + 30 Gy ISRT

4: ABVD x 2 + Esc BEACOPP x 2 + ISRT

5: ABVD x 3-4 (If interim PET negative)

6: ABVD x 6

# Early-stage CHL:
# Can We Eliminate Radiation Therapy for Most Patients?

## Optimizing Therapy

### Considerations

### Chemotherapy Alone

- Females < age 35 yr
- Axillary and mediastinal involvement

### Considerations

### Combined Modality Therapy

- Patients with favorable disease, especially when it is possible to limit the duration of chemotherapy
- Patients with a positive interim PET scan (~ 25%)
- Patients with bulky mediastinal adenopathy

# Early-stage CHL
# Can We Eliminate Radiation Therapy for Most Patients?

## Balancing Risk With Benefit for the Individual

**Disease Control**

**Optimal Survivorship**

## Stage I-II CHL: Future Considerations

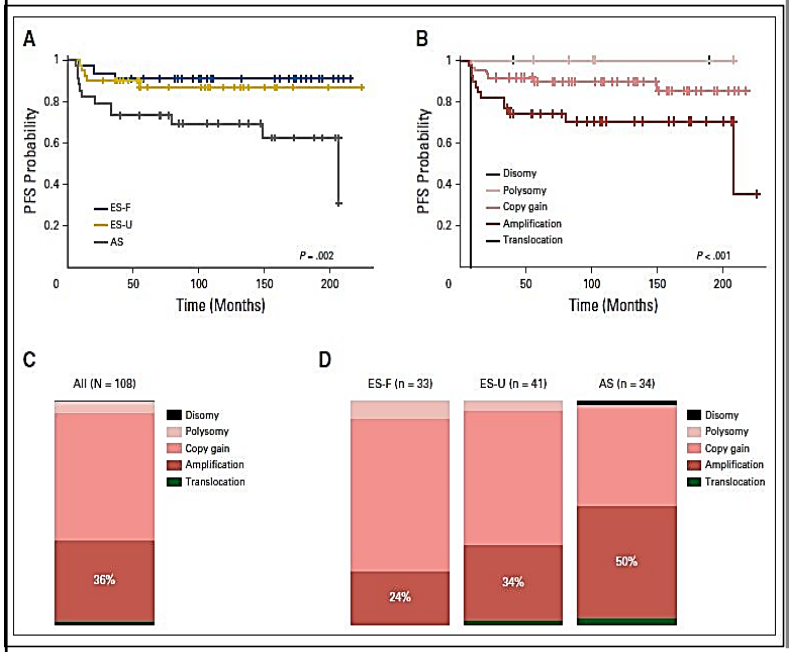
- Incorporation of novel agents
- Identification of biological subsets to guide therapy

## Incorporation of Novel Agents

- Brentuximab Vedotin
- Check Point Inhibitors (Nivolumab, Pembrolizumab)
- Studies combining these agents with AVD (doxorubicin, vinblastine, and dacarbazine) are ongoing in the front line setting

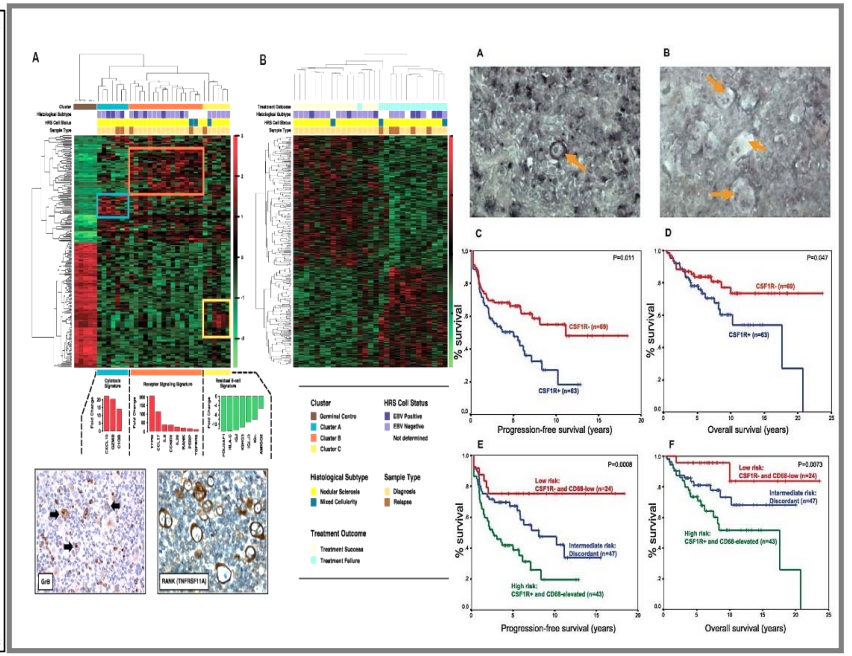
# Identification of biological subsets to guide therapy
# Molecular markers to define risk

## Frequency of 9p24.1 Genetic Alterations and Outcomes




Roemer et al *J Clin Oncol.* 2016;34(23):2690-2697.

## GEP of mico dissected Hodgkin RS cells correlates with treatment outcome in CHL




Steidl et al *Blood.* 2012; 120: 3530-3540.

# NCCN Member Institutions