Pediatric Lymphoma – Update from the Children’s Oncology Group

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CR, PR, SD or PD?

Baseline

Post 2 cycles of Rx
CR, PR, SD or PD?

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Objectives

• To review staging and response criteria used in current COG Hodgkin Lymphoma Studies: Focus on AHOD 1331

• To review of anatomic imaging (CT, MRI) and functional imaging (PET/CT and PET/MRI) in response assessment

• Introduce dose reduction strategies in PET/CT

• To introduce the audience to efforts aimed at reducing surveillance imaging in pediatric Hodgkin Lymphoma
• **Staging**

- Ann Arbor Criteria (anatomic stage, ± “B” Sx)
- **Bulk Disease:** *Independent Predictor of Outcome*
  - May increase risk stratification: Bulky IIB = High Risk
  - Transthoracic diameter based on upright CXR
  - Maximum diameter of non-mediastinal nodal mass ≥ 6 cm either axial or craniocaudal dimension. *This is new from prior protocols*

- Bone marrow Involvement on FDG-PET
  - Diffuse vs focal bone and bone marrow disease
  - Still obtaining BM biopsy at Dx
Mediastinal Bulk: Mass > 1/3 diameter of transthoracic diameter at level of diaphragm

13.8 cm
31.5 cm
~ 44%
Non-Mediastinal Bulky Disease

> 6 cm

4.8 cm

7.0 cm

Courtesy of Kathleen McCarten, MD
Cluster of Many Small Nodes: NOT Bulky Disease

Courtesy of Kathleen McCarten, MD
HD: PET and Bone/BM Involvement

Focal vs Diffuse Bone Marrow Uptake
Interim Response Assessment:

FDG-PET after two cycles of chemoRx predicts treatment failure and progression free survival

Hutchings et al. (2006) Blood 107: 52

Friedman D L et al. JCO 2014;32:3651
Deauville Workshop on Interim PET

- Baseline PET/CT: prior to initiation of Rx.
- Interim-PET: must be performed early during induction chemotherapy (after 2 cycles).
- Patients achieving complete metabolic response (FDG -) are considered CR: *independent of residual disease on CT*
- Visual analysis using a 5-point scale
  - SUV is still investigational
- Preferable reference scale should be the mediastinum and the liver.

Deauville Criteria for Interim FDG-PET

1. No FDG uptake above surrounding background
2. FDG uptake ≤ mediastinal blood pool
3. FDG uptake > mediastinal blood pool but ≤ liver
4. Moderate increase in FDG uptake compared to liver
5. Marked increase FDG uptake compared to liver

COG: Anatomic imaging still required at Interim PET
- MRI or Contrast-enhanced CT
- May be I+ low dose attenuation correction CT (CT/Ac)
- PET/MRI: still investigational

Meignan et al. Leukemia & Lymphoma (2009) 50: 1257
Anatomic Imaging Requirements for COG

- **I+ CT: Dx, f/u**
- **I+ CT/Ac: f/u**
- **MRI: Dx, f/u**
Interim post Cycle 2 PET Response

- FDG-PET positive is defined as Deauville scores 4 or 5 (SRL)
- FDG-PET negative is defined as Deauville scores 1, 2, or 3 (RRL)

End chemotherapy PET (PET 5) Response

- FDG-PET positive is defined as Deauville scores 3, 4, or 5 (IMR)
- FDG-PET negative is defined as Deauville scores 1 or 2 (CMR)
All FDG+ sites are now ≤ MBP and liver: “Deauville 2”
Post-2 Cycle Interim Assessment: FDG+ sites are > MBP but ≤ liver = “Deauville 3”
Residual Metabolically Active Disease:

Deauville 4

Deauville 4 or 5
Spleen: Complete Metabolic Response

Residual contrast CT abnormality decreased by >50% or is <1cm. in diameter

No residual PET avidity

No focal splenic PET avidity

Baseline

Post therapy Negative

Courtesy of Kathleen McCarten, MD

CHILDREN'S ONCOLOGY GROUP
Hodgkin Lymphoma Surveillance

- 216 patients (< 21 yo) Rx’d on POG 9425
  - Correlated stage, time to recurrence, relapse site, & survival (OS).
  - Median follow-up of 7.4 years
  - Impact of Surveillance Imaging in Detecting Relapse

- 25/216 relapses (11.6%).
  - Median time to relapse was 7.6 months (0.2-48.9 months).
  - 19 (76%) relapses were detected based on symptoms, lab or PE
  - 4/216 patients relapse > 1 year post-Rx and were asymptomatic

- Main determinant of survival: Time to relapse
  - Whether detected by Sx or Imaging

Surveillance Imaging in HD - What is the Impact on Survival?

POG 9425
- > 8 years of follow-up
- 25/216 relapses
- Median time to relapse = 7 months

Pediatric HD Surveillance Recommendations

History/PE/routine labs: q3 mo x 1 yr, q 6 mo x 2 years, yearly thereafter

Off-therapy Hodgkin Lymphoma Imaging Surveillance

- CT
- FDG/PET*
- CXR

0 12 24 36 48 60 months

End of Rx

Impact of Reduced Surveillance

- **AHOD 0031**
  - ~1700 patients w/ 11 off-therapy scans
    - Baseline and q3 mo for first 12 mo off therapy
    - 6 between years 1-5
    - ~10,000 off Rx scans in pts with > 90% survival
  - Modeling CT exposure -> 8 new cancers from surveillance imaging alone

- **Cost**
  - CMS rate of $376.16 per chest CT
  - Additional ~$2300 per patient
  - Cost to the health care system of ~ $3.84 million for the 1700 patients enrolled

Bulky Stage III Disease, resolution of splenic disease, and CR (Deauville 2) by FDG-PET

Baseline

Post 2 cycles of Rx
Summary

• **Staging**
  – Bulk Disease: CXR for LMA; 6 cm by CT or MRI for other sites, in any dimension

• **Response**
  – International criteria: PET based response
  – I+ CT for measurement and XRT planning
    • Low dose CT/Ac with contrast and MRI also allowed

• **Deauville Criteria** for PET response

• Changes to **surveillance imaging**