



Key ASH Presentations
Issue 4, 2011

PET Scans in Hodgkin Lymphoma

CME INFORMATION

OVERVIEW OF ACTIVITY

The annual American Society of Hematology (ASH) meeting is unmatched in its importance with regard to advancements in hematologic cancer and related disorders. It is targeted by many members of the clinical research community as the optimal forum in which to unveil new clinical data. This creates an environment each year in which published results from a plethora of ongoing clinical trials lead to the emergence of many new therapeutic agents and changes in the indications for existing treatments across virtually all malignant and benign hematologic disorders. As online access to posters and plenary presentations is not currently available, a need exists for additional resources to distill the information presented at the ASH annual meeting for those clinicians unable to attend but desiring to remain up to date on the new data released there. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the most important emerging data sets from the latest ASH meeting, including expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for hematologic cancer.

LEARNING OBJECTIVES

- Apply the results of new research to the evidence-based use of interim PET scans for patients with advanced-stage Hodgkin lymphoma.
- Recognize the limited role of consolidative radiation therapy for patients with Hodgkin lymphoma who have a negative post-treatment PET scan.

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Advisory Committee: Cephalon Inc, Genentech BioOncology, Seattle Genetics; Paid Research: Cephalon Inc, Genentech BioOncology, Lilly USA LLC, Plexxikon Inc, Seattle Genetics.

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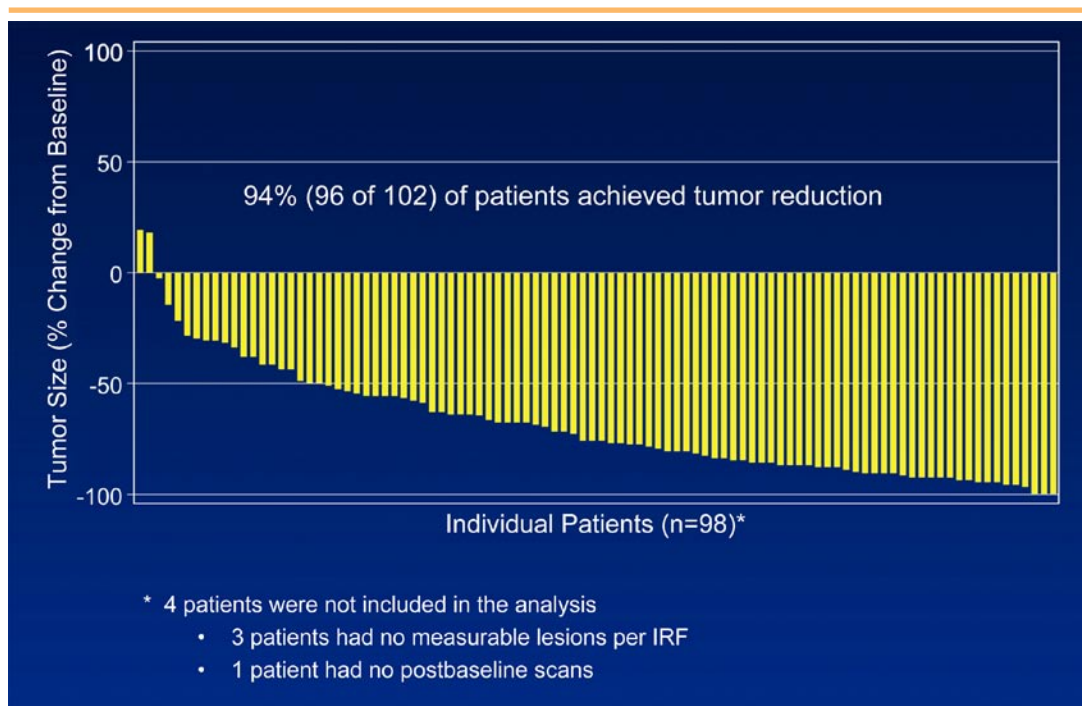
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[Click here for papers on](#) Hodgkin lymphoma.

When one queries lymphoma investigators about the key data sets from the December ASH meeting, at the top of almost every list is a stunning **report** in which 102 patients with Hodgkin lymphoma (HL) and disease progression after a median of 3.5 prior chemotherapy treatments and an autologous stem cell transplant were treated with brentuximab vedotin. "B vedotin" is an immune conjugate, with an antibody against CD30 hooked to an antitubulin agent (monomethyl auristatin E) that is similar to vinblastine.

Like the trastuzumab/maytansine conjugate T-DM1 in breast cancer, B vedotin is thought to deliver the cytotoxic to or into the tumor cell, but the exact mechanism of antitumor effect has yet to be defined. Of great interest, unlike its breast cancer cousin, the naked antibody in B vedotin is not active in heavily pretreated HL.

In this pivotal Phase II, single-arm trial, more than 90 percent of patients had tumor responses (check out the waterfall plot), with 34 percent complete and 40 percent partial remissions. The agent was well tolerated with apparently reversible peripheral neuropathy identified as the only important toxicity. It should come as no surprise that this fascinating agent is quickly tracking through the FDA and being incorporated into ongoing and emerging clinical trials, including as consolidation after transplant and up front with ABVD.



Three other ASH presentations on HL are also profiled in our slide sets:

1. The long-awaited **[Phase III ECOG/Intergroup trial](#)** in locally extensive or bulky advanced HL randomizing between ABVD and Stanford V.

Many were disappointed to see that there was no major efficacy difference between the two arms, and in the US, ABVD remains the standard. In this trial, only patients with bulky mediastinal disease received radiation therapy with ABVD as opposed to essentially a multimodality approach with Stanford V.

2. **[A German study](#)** evaluating PET scanning in patients with advanced-stage HL and a residual mass on CAT scan greater than 2.5 cm after BEACOPP.

Ninety-two percent of patients with negative PETs were disease-free at three years without radiation therapy. Whether this can be extrapolated to ABVD is being debated.

3. **[An Italian study](#)** of interim PET scanning after two cycles of ABVD in patients with both early and advanced disease.

Patients with PET positivity did poorly and should be considered for immediate referral to a tertiary center for clinical trial consideration.

It is worth remembering that while most of the 8,000 patients diagnosed with HL annually in the US are cured, approximately 1,500 (mostly those presenting with advanced disease) are not. Fortunately, for the first time maybe ever there are a number of promising agents in development, including B vedotin, lenalidomide, panobinostat and everolimus, offering new hope that some of these mostly younger patients can be salvaged.

Next up on ASH *5-Minute Journal Club*: Another major paper on B vedotin — this time in anaplastic large cell lymphoma — and other new data in T-cell lymphomas.

Neil Love, MD

[Research To Practice](#)

Miami, Florida

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PET Scans in Hodgkin Lymphoma

Presentations discussed in this issue

Zinzani PL et al. **Early interim ^{18}F -FDG PET in Hodgkin's lymphoma: Evaluation on 304 patients.** *Proc ASH 2010*; [Abstract 3879](#).

Engert A et al. **Assessment of residual bulky tumor using FDG-PET in patients with advanced-stage Hodgkin lymphoma after completion of chemotherapy: Final report of the GHSG HD15 trial.** *Proc ASH 2010*; [Abstract 764](#).

Slides from presentations at ASH 2010 and transcribed comments from a recent interview with Craig Moskowitz, MD (1/3/11)

Early Interim ^{18}F -FDG PET in Hodgkin's Lymphoma: Evaluation on 304 Patients (Italian study)¹

Assessment of Residual Bulky Tumor Using FDG-PET in Patients with Advanced-Stage Hodgkin Lymphoma After Completion of Chemotherapy: Final Report of the GHSG HD15 Trial (German study: slide 6)²

¹Zinzani PL et al.

Proc ASH 2010; Abstract 3879.

²Engert A et al.

Proc ASH 2010; Abstract 764.

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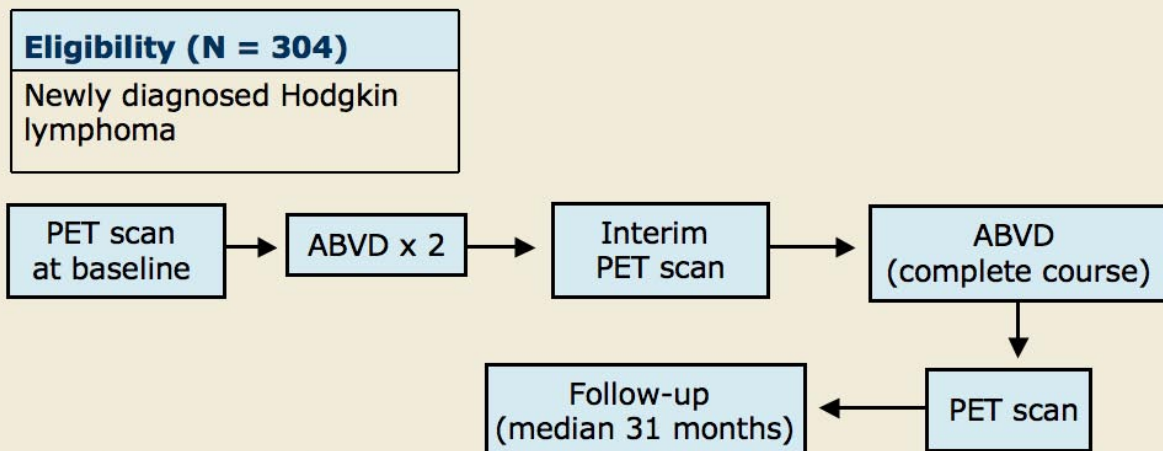
Early Interim ¹⁸F-FDG PET in Hodgkin's Lymphoma: Evaluation on 304 Patients

Zinzani PL et al.

Proc ASH 2010;Abstract 3879.

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Study Schema



Distribution of Patients

147 early stage
157 advanced stage

Zinzani P et al. *Proc ASH 2010;Abstract 3879.*

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Results (from Abstract)

Efficacy Outcome	Positive Interim PET (n = 53)	Negative Interim PET (n = 251)
Complete Remission	24.5%	92.0%
Early Stage (n = 19, 128)	21.0%	97.6%
Advanced Stage (n = 34, 123)	26.4%	88.6%

Comparison between interim PET-positive and interim PET-negative patients indicated a significant association between PET findings and 9-year PFS ($p = 0.0000$) and 9-year overall survival ($p = 0.0000$).

Zinzani P et al. *Proc ASH 2010*;Abstract 3879.

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Author Conclusions

- These results confirm the role of early PET as a significant step forward for the management of both early and advanced-stage Hodgkin lymphoma.
- Interim PET scans may offer the potential for an immediate switch to high-dose treatments, if required.

Zinzani P et al. *Proc ASH 2010*;Abstract 3879.

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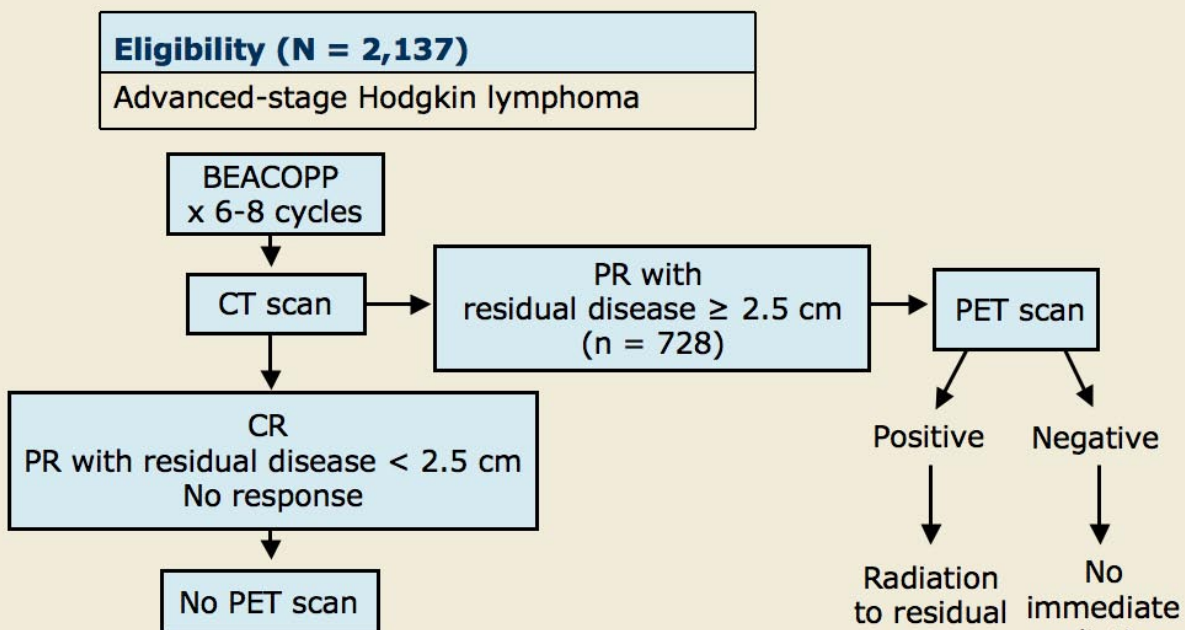
Assessment of Residual Bulky Tumor Using FDG-PET in Patients with Advanced-Stage Hodgkin Lymphoma After Completion of Chemotherapy: Final Report of the GHSG HD15 Trial

Engert A et al.

Proc ASH 2010;Abstract 764.

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Study Schema



Engert A et al. *Proc ASH 2010;Abstract 764.*

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Results (from Abstract)

Patients with PR and Residual Disease \geq 2.5 cm (n = 728)	
PET Negative	74.2%
PET Positive	25.8%

	PET Negative	PET Positive ¹
Negative Prognostic Value	94.6%	—
Lack of Progression Events ² at 3 Years	92.1%	86.1%

¹ Patients with PET-positive disease received immediate radiation.

² Radiation counted as a progression event in PET-negative patients.

Engert A et al. *Proc ASH 2010*;Abstract 764.

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Results (from Abstract)

	Current Trial	Earlier Trials
Radiation after BEACOPP	11%	71%

In addition, there was no difference in PFS or overall survival as compared to earlier trials in advanced-stage HL.

Engert A et al. *Proc ASH 2010*;Abstract 764.

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Author Conclusion

- Patients with a negative PET scan after BEACOPP do not need additional radiation therapy.
 - 94.6% negative prognostic value of negative PET

Engert A et al. *Proc ASH* 2010;Abstract 764.

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Investigator comment on role of PET scan in Hodgkin lymphoma

The study by Zinzani is important. The question in my mind is whether all patients with Hodgkin lymphoma (HL) need the interim PET scan. Approximately 90 percent of patients with early-stage HL are cured in the pre-PET era, and the corresponding proportion in advanced-stage HL is 75 percent. I believe that patients with advanced-stage HL and a positive PET after two cycles fare extremely poorly and should be referred to major academic centers for second-line therapy. For patients who have early-stage HL with positive interim PET, to me that is still a debatable issue.

The presentation by Engert is mainly applicable to patients receiving BEACOPP and to practices that have traditionally administered involved field radiation therapy to patients with residual disease of 2.5 cm or more. This might also be applicable to patients receiving ABVD, but I don't know that. For patients with advanced HL and a negative PET after BEACOPP, there is definitely no role for consolidative radiation therapy anymore.

Interview with Craig Moskowitz, MD, January 3, 2011

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