Abstract selection for HL

I’m not Bruce Cheson.....

...however I will do my best.
The following abstracts were selected for oral presentation (three slides) by the chairmen of the session

• A 102 Pavlovsky A: Treatment of all stages of Hodgkin Lymphoma adapted to the results of PET-CT after 3 cycles of ABVD.

• A 112 Gallamini A: Multicenter clinical study with early treatment intensification in High-risk Hodgkin Lymphoma (HL) patients, with a positive FDG-PET scan after two ABVD courses.

• A 115 Borra A. Cost-effectiveness of interim PET response adapted therapy in ABVD-treated, advanced-stage Hodgkin Lymphoma.
A 104 Dann AJ
Tailored HL therapy based on predefined risk factors and interim PET/CT preliminary report on 191 patients on Israel National Hodgkin Study

Early favorable pts: ABVD x 2 →PET→(-): INRT
→PET→(+): ABVD x 2 + INRT

Early unfavorable pts: ABVD x 2 →PET→(-): ABVD x 2 + INRT
→PET→(+): ABVD x 4 – INRT

Advanced, IPS 0-2: ABVD x 2 →PET→(-): ABVD x 4 No Rt
ABVD x 2 →PET→(+): EB x2 + BB x 4 + Rt

Advanced, IPS 3-7: EB x 2 →PET→(-): ABVD x 4 No Rt
EB x 2 →PET→(+): EB x2 + BB x 4 + Rt

Advanced-stage Pts: 2-y PFS 88%; NPV of PET-2: 92%
-Interpretation key for interim-PET not validated on an observational cohort of pts.
-Specificity and PPV not very good.
A 105 Kobe C
Assessment of residual bulky tumor using FDG-PET in patients with advanced-stages after completion of chemotherapy. Final report of the GHSG HD 15 trial

2182 patients with advanced-stage HL treated with various BEACOPP containing regimens
740 showed a residual mass with a diameter ≥ 2.5 cm.
In 712/740 the follow-up was >than 12 months
All 740 patient underwent PET/CT scan . The scans were reviewed by an expert panel
548 (74%) were PET-negative, 192 (26%) PET-positive.
Only 31/548 PET-negative patients relapsed. The NPV of PET was 94%
- Low PPV for PET-positive patients.
- No mention on confirmatory biopsy for PET-positive pts.
- No mention on the number and location of the residual FDG-avid foci
A 107 Radford J.
UK NCRI RAPID trial in patients with clinical stage IA/IIA Hodgkin Lymphoma: an update following attainment of the recruitment target.

Patients with non-bulky stage IA/IIA HL a PET scan is performed after 3 ABVD cycles Patients with a negative interim scan (Deauville score 1 and 2) are randomized between IFRT or no further treatment. Patients with a positive interim scan (Deauville score 3-5) are treated with a 4° ABVD cycle and IFRT

In 05/11 601 pts were registered
Patients with score 1 & 2 (Interim-PET negative) were 426 (74.6%);
Patients with score 3-% (Interim-PET negative) were 145 (25.4%)
420/426 PET-negative patients were randomized to IFRT or no further treatment
After a median of 34.1 months 389/420 (92.6%) are alive and progression-free
- No baseline PET scan
- Relative high number of interim PET positive patients (25.4%)
A 108 Markova J: The role of FDG-PET in early and late therapy assessment of patients with advanced Hodgkin Lymphoma treated with BEACOPP

69 patients with advanced-stage HL treated with 6/8 cycles of BEACOPP
PET/CT performed after 4 cycles (PET-4), at the end of the therapy (PET 6/8) and 3 months later, during follow-up ((PET-3m)
Median f-up 55 months
NPV for PET-4, PET 6/8, PET-3m were 98%, 95%, 97%.
4-y PFS for PET-4 neg and PET-4 pos were 96% and 78%
4-y PFS for PET6/8 neg. and PET6/8 pos were 95% and 78%
Patients with large mediastinal mass contributed to nearly all PET-4 and PET-8 positive patients
- Very low PPV (14% in the previous report)
- Criteria for PET positivity: residual FDG uptake higher than background.
A 109 Simoni Z.:
Interim PER-CT in Hodgkin’s lymphoma. The Hungarian experience

89 patients enrolled in a prospective study between 2007 and 2011 in Debrecen University
47% in early stage, 41% asymptomatic
Therapy ABVD or EBVD x 6 ± consolidation or IF radiotherapy
PET negative in 55%, MRU in 28%, positive in 17%.
EFS: 84% in the negative and 20% in the positive interim-PET patients
- No data on concordance rate among reviewers
- Overall predictive value very good; however subset analysis is needed
A 110 Mounier N.: 
Early determination of treatment sensitivity in HIV-related HL by FDG-PET after two cycles of ABVD chemotherapy.

44 HIV-related HL patients enrolled in 9 European centers
Median CD4 values 394/mm$^3$
Viral load present in 7/44 patients
42 received concomitant HAART
20 early stage, 24 stage III and IV
Interim-PET scan interpretation Key: Deauville score (1-3 neg; 4-5 pos.)
Treatment ABVD x 6 ± consolidation Rt.
77% in CCR at a median FU of 18 months
39 (88%) patients with PET-2 negative, 5 (12%) with PET-2 positive
2-y EFS for PET-2 negative and positive 88% and 12%, respectively.
- Very good. but confirmatory results
Clinical abstracts selected for oral presentation

- Pavlovsky A
  Treatment for all stages of Hodgkin Lymphoma adapted to the result of PET-CT after 3 cycles of ABVD
Treatment for all Stages of Hodgkin’s adapted to the Result of PET-CT after 3 Cycles of ABVD. Preliminary Results in 193 Patients.


Dr. A. Pavlovsky and co-authors have no conflicts of interest to declare.

**OBJECTIVES:**

- Reduce therapy in patients who achieve early CR with negative PET-CT in all stages of HL.

- Intensify treatment, only in patients with positive PET-CT after 3 cycles of ABVD, improving their otherwise bad prognosis.

- Achieve CR, EFS and OS, as good as in our historical control, when we used 3 or 6 cycles of ABVD plus IFRT in all patients.

**Patient’s characteristics at diagnosis**

<table>
<thead>
<tr>
<th># = 193 evaluable</th>
<th>Male / Female</th>
<th>Age yrs. median (range)</th>
<th>Stage I-II no B</th>
<th>III-IV B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>84 / 109</td>
<td>30 (16-80)</td>
<td>125 (65%)</td>
<td>68 (35%)</td>
</tr>
<tr>
<td>Bulky (%)</td>
<td>33 (17%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPS*</td>
<td>0 - 1</td>
<td>85 (47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=172</td>
<td>2 - 3</td>
<td>75 (39%)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>&gt;= 4</td>
<td>12 (14%)</td>
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</table>
Treatment for all Stages of Hodgkin’s adapted to the Result of PET-CT after 3 Cycles of ABVD. Preliminary Results in 193 Patients.


RESULTS:

ABVD x 3 (n=193) (100%)

- Negative PET (CR) (n=148) (77%)
  - PR (n=40)
  - PD (n=5)
- Positive PET (n=45) (23%)
  - ABVD x 3/ IFRT
  - ESHAP x 3

END OF TREATMENT

EFS and OS in HL with PET-TC adapted therapy

Total relapse = 21/178 (11%)
Median follow up 39 months (3 – 71)

Dr. A. Pavlovsky and co-authors have no conflicts of interest to declare.
(A102) Treatment for all for all Stages of Hodgkin’s adapted to the Result of PET-CT after 3 Cycles of ABVD. Preliminary Results in 193 Patients.


Multivariate analysis for EFS

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<th>P</th>
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<tbody>
<tr>
<td>Age</td>
<td>0.046</td>
</tr>
<tr>
<td>Stage</td>
<td>0.17</td>
</tr>
<tr>
<td>Extra nodal areas</td>
<td>0.96</td>
</tr>
<tr>
<td>Bulky Disease</td>
<td>0.76</td>
</tr>
<tr>
<td>PET +3</td>
<td>0.001</td>
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CONCLUSIONS:

- With PET-CT adapted therapy after 3 cycles of ABVD, 148 pts (77%) received only 3 cycles of ABVD as initial therapy with an EFS and OS 83% and 97% at 36 months.
- The overall EFS and OS are comparable to our historical control with a significant reduction of chemo and radiotherapy.
- PET-CT +3 and age > 60 yrs. are the only significant factors for EFS.
- Three cycles of ABVD is an adequate treatment for patients who achieve early CR with a negative PET-TC+3.

Historic comparison

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th># pts</th>
<th>CR (%)</th>
<th>EFS (%) at 36 months</th>
<th>OS (%) at 36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL - 96 1</td>
<td>584</td>
<td>91</td>
<td>75</td>
<td>93</td>
</tr>
<tr>
<td>HL - 05 2</td>
<td>193</td>
<td>92</td>
<td>80</td>
<td>97</td>
</tr>
</tbody>
</table>

1 61 % ABVD x 6, 100% IFRT.
2 23 % ABVD x 6, 23% IFRT.

5 pts received ESHAP/ASCT in 1st line.

Dr. A. Pavlovsky and co-authors have no conflicts of interest to declare.
Clinical abstracts selected for oral presentation

A 112 Gallamini A:

Multicenter clinical study with early treatment intensification in High-risk Hodgkin Lymphoma (HL) patients, with a positive FDG-PET scan after two ABVD courses.
Multicentre clinical study with early treatment intensification in high-risk Hodgkin Lymphoma (HL) patients, with a positive FDG-PET scan after two ABVD courses.

Gallamini A, Tarella C., Patti C., Gianni AM, Bolis S., Trentin L., Biggi A., Chauvie S., Mennitto MR, Rambaldi A.
HL IIB-IV B. IPS 0-7

ABVD x 2

CT-PET

+ -

R

BEACOPP-esc. x 4
R-BEACOPP-esc. x 4

CT-PET

- -

BEACOPP-bas. x 4
R-BEACOPP-bas. x 4

CT-PET

GITIL HD0607 Protocol

CT-PET

ABVD x 4

Follow up

Rescue

Consolidation Rx therapy
No Consolidation Rx therapy

Assess response on completion of treatment
PET-2 review results (130 / 337 pts.)

Overall, 130/337 non-negative PET-2 were uploaded & reviewed: 51/130 turned out positive (score 4-5) and 79/130 negative (score 1-3).

Percentage of PET-2 +: 51/337 (15.1%)

The median time from PET uploading in the website to review was 1.22 days.

The binary concordance rate (score 1-3 vs. 4-5) among reviewers was very good, and ranged from 0.75 to 0.92 (Cohen's k coefficient); overall concordance rate (1-3 vs. 4-5) was 0.83 (Krippendorf's alpha).
HD 0607 INTERIM ANALYSIS (13.05.2011) on a cohort of patients who completed the therapy with a mean f-up of 403 (± 163) days

122

ABVD x 2

PET-2

17

BEACOPP / R-BEACOPP

13 0 4

CR PR RE

105

ABVD x 4 +/- Rx therapy

CR PR RE

101 0 4

Relative Dose Intensity for R-BEACOPP: 96.7%
Relative dose intensity for BEACOPP: 92.7%
Relative dose intensity for ABVD: 97.8%
Clinical abstracts selected for oral presentation

A 115 Borra A.

Cost-effectiveness of interim PET response adapted therapy in ABVD-treated, advanced-stage Hodgkin Lymphoma.
COST-EFFECTIVENESS OF INTERIM PET RESPONSE ADAPTED THERAPY IN ABVD-TREATED, ADVANCED-STAGE HODGKIN’S LYMPHOMA

1Borra A, 2Marchetti M, 3Biggi A, 4,5Chauvie S, 4Stancu A, 4Cerello P, 1Gallamini A

1Hematology Department, S. Croce e Carle Hospital, Cuneo, Italy
2Hematology Unit, Internal Medicine Department C. Massaia Hospital, Asti, Italy
3 Nuclear Medicine Department, S. Croce e Carle Hospital, Cuneo, Italy
4National Institute of Nuclear Physics (INFN), Turin, Italy
5Medical Physics Unit, S. Croce e Carle Hospital, Cuneo, Italy
PET-2 response adapted treatment strategy for advanced-stage HL patients (Retrospective study N= 160)

- PET-2 negative
  ABVD → ABVD (N= 137)
  - 95%
  - 91%

- PET-2 positive
  ABVD → eBEACOPP (N=23)
  - 62%

Markov model
Cost of the “classic” ABVD therapy (A-T)

- 6 ABVD
  - No RxT (60%)
  - RxT (40%)
    - RC
      - No RC
        - IGEV
          - ASCT
            - 15% DHAP + AlloSCT
              - No AlloSCT

Cost Calculations:
- 3000€ x 40% = 1200 €
- 43519.3 x 30% = 13055.61 €
- 79639.9 x 15% = 11945.9 €
- 245.5 + 41.4 € = 286.9 €
Cost of the PET-driven strategy (A/B-T)

- **2ABVD**
  - 20% PET-2+
    - 4BEe +4BEb
      - RC
      - No RC
      - 3097.96€ x 20% = 619.53€
      - IGEV
      - ASCT
      - DHAP +AlloSCT
      - No AlloSCT
      - 2266.50€

- **PET-2- 80%**
  - 4ABVD
    - 1058,50€
    - 1082.37€
    - 32% RxT
    - No RxT 48%
    - RC
    - No RC
    - 152.96€ x 80% = 122.37€
    - IGEV
    - ASCT
    - DHAP +AlloSCT
    - No AlloSCT
    - 115.09€ +2108.7€ = 2223.79€

- **Cost**
  - 81.85€ + 13.8€ = 95.30€
Results

<table>
<thead>
<tr>
<th>ABVD “classical”</th>
<th>ABVD. PET-adapted</th>
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<tr>
<td>€ 29,050</td>
<td>€ 27,861</td>
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Cost saving € 1189 per patient!