HODGKIN LYMPHOMA
Updated February 2016 by Dr. Manna (PGY-5 Hematology Resident, University of Calgary)

Reviewed by Dr. Michelle Geddes (Staff Hematologist, University of Calgary) and Dr. Matt Cheung (Staff Hematologist, University of Toronto)

DISCLAIMER: The following are study notes compiled by the above PGY-5 medical oncology residents and reviewed by a staff medical oncologist. They reflect what we feel is relevant knowledge for graduating medical oncology residents preparing for their final examination. The information has not been surveyed or ratified by the Royal College.

A) PUBLIC HEALTH

EPIDEMIOLOGY
- Incidence: Accounts for 10% of all lymphomas, approximately 0.6% of all cancers diagnosed annually. Bimodal age distribution – one peak in young adults age ~20yo, and one in older adults ~65yo. Slight male predominance

RISK FACTORS
- Environmental/Chemical/Infections: History of EBV infection, Immunosuppression (ie) HIV, Autoimmune disorders (ie) RA, SLE, sarcoidosis
- Genetic: possible genetic susceptibility

B) PRESENTATION & DIAGNOSIS

SYMPTOMS & SIGNS
- Common Symptoms: Asymptomatic lymphadenopathy, alcohol induced pain of lymph nodes, B symptoms (fever, weight loss, night sweats), pruritus, skin lesions, respiratory symptoms due to mediastinal masses (ie) cough, chest pain, SOB
- Common Signs: Cervical lymphadenopathy, SVC syndrome (rare)
- Common Presentations: Painless asymptomatic cervical/supraclavicular lymphadenopathy

INVESTIGATIONS
- Laboratory: CBC, differential, ESR, liver function tests, ALP, electrolytes, Creatinine, Calcium, Albumin, LDH, HIV serology, pregnancy test (in women of childbearing age)
- Diagnostic Imaging: CT scan (neck, chest, abdomen, pelvis), PET
- Diagnostic Procedures: Bone marrow biopsy and aspiration can be omitted from staging
- Other Pretreatment Evaluation Considerations:
  - Cardiac Function: assessment of ejection fraction through Echo or MUGA if patient to receive anthracycline
  - Pulmonary Function: consider baseline pulmonary function studies (for DLCO) if patient to receive bleomycin. Although baseline results do not predict subsequent development of pulmonary bleomycin toxicity
  - Fertility Counseling: patients of childbearing age should receive counseling on effect of treatment and options for fertility preserving measure

PATHOLOGY & MOLECULAR BIOLOGY
- Essential to obtain excisional lymph node biopsy to confirm diagnosis of HL
- WHO Classification of Histologic Subtypes of HL
  - Classical (~95%)
    - Nodular Sclerosis (70%)
    - Mixed Cellularity (20%)
    - Lymphocyte Rich (5%)
    - Lymphocyte Depleted (1%)
Nodular Lymphocyte Predominant
- **Common Histology:** Reed Sternberg Cells
- **Relevant Immunohistochemistry:** CD30+, CD15+, CD20+ (20%), PAX-5+

**STAGING**
- **Ann Arbor Staging:**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Involvement of a single lymph node region or a single extranodal site</td>
</tr>
<tr>
<td>II</td>
<td>Involvement of two or more lymph node regions on the same side of the diaphragm</td>
</tr>
<tr>
<td>III</td>
<td>Involvement of lymph node regions on both sides of the diaphragm</td>
</tr>
<tr>
<td>IV</td>
<td>Diffused/disseminated involvement of one or more extra lymphatic organs or tissues with or without associated lymph node involvement</td>
</tr>
</tbody>
</table>

**Other**
- **B Symptoms:** absence (A) or presence (B) or fever >38.5°C, drenching night sweats, and/or unexplained weight loss of >10% body weight in past 6 months
- **E:** Extranodal disease
- **X:** Bulky disease. Defined as mediastinal mass >1/3 thoracic diameter or any nodal mass >10cm in maximal diameter

**Limited Stage (Stage I-II) Definition of Unfavorable Disease**
- **EORTC** (European Organization for the Research and Treatment of Cancer) Definition:
  - Age >50
  - Bulky mediastinal disease
  - ESR >50 without B symptoms
  - ESR >30 with B symptoms
  - >3 lymph node regions

- **GHSG** (German Hodgkin Study Group) Definition:
  - Bulky mediastinal disease
  - ESR >50 without B symptoms
  - ESR >30 with B symptoms
  - Extranodal disease
  - ≥3 Lymph node groups

**Advanced Stage (Stage III-IV) International Prognostic Score (Hasencleaver Index):**
- Hb <105. Age >45, Male, Stage IV, Lymphopenia <600 (and/or 8% total WBC), Albumin <40, WBC >15

<table>
<thead>
<tr>
<th>Score</th>
<th>5 Yr FFP (%)</th>
<th>5 Yr OS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>88</td>
<td>98</td>
</tr>
<tr>
<td>1</td>
<td>84</td>
<td>97</td>
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<tr>
<td>2</td>
<td>80</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>74</td>
<td>88</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
<td>85</td>
</tr>
<tr>
<td>5 or more</td>
<td>62</td>
<td>67</td>
</tr>
</tbody>
</table>

**PROGNOSIS**
- Majority of patients with HL will be alive in 10 years post treatment (>80%)
- Younger patients with limited disease have very good prognosis (ie) 5 year OS <45yo >90%
- Although most have excellent long term prognosis, approximately 20-25% will relapse with majority in first 3 years following treatment.
GENERAL FOLLOWUP CONSIDERATIONS

- Secondary Cancers post radiotherapy
  - Risk continues beyond 30 years
  - Chest/Axillary RXT: annual mammogram 8-10 years post treatment or at 40 yo (whichever comes first)
  - Age appropriate preventative health care and cancer screening
- Cardiovascular disease
  - At risk if received mediastinal radiation or anthracycline
  - Assess and reduce cardiovascular risk factors (HTN, smoking, Diabetes, lipids)
- Hypothyroidism
  - At risk if received neck/upper mediastinal RXT: annual thyroid function tests
- MDS/Leukemia
  - Low risk with ABVD (increased if RT), at higher risk if received BEACOPP or BEACOPP escalated
  - Annual CBC, evaluate if symptoms
- Fertility
  - At risk especially if received BEACOPP or older age. Lower risk with ABVD
  - Consider referral for reproductive endocrinology, fertility counseling, and options for fertility preserving measure (ie) sperm banking
- Radiation pneumonitis/Lung Fibrosis
  - Rare, evaluate if symptoms

C) TREATMENT

EARLY STAGE (STAGE I-II) CLASSICAL HL
- Bottom Line General Approach:
  - Combined modality therapy for localized disease to improve disease free survival and limit late toxicities.
  - ABVD chemotherapy = Doxorubicin, Bleomycin, Vinblastine, Dacarbazine
  - IFRT = involved field radiation therapy

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>Treatment Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I-II Favorable, Nonbulky</td>
<td>o Favorable disease defined by either EORTC or GHSG criteria</td>
</tr>
<tr>
<td></td>
<td>o Classical HL Stage I-II (all histologies): ABVD X2 cycles, plus IFRT 20Gy</td>
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<td></td>
<td>o For pts who prefer to avoid IFRT: ABVDX2 then PET-CT. If Pet negative then further ABVDX2, if PET positive then IFRT</td>
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<tr>
<td></td>
<td>o Stage IA Nodular Lymphocyte predominant in peripheral nodal sites: IFRT alone</td>
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<tr>
<td></td>
<td>o Stage IA Nodular Sclerosis with high neck or epitrochlear nodes &lt;3cm: IFRT alone</td>
</tr>
<tr>
<td></td>
<td>o Assessment of response to therapy evaluated with PET-CT (or CT)</td>
</tr>
<tr>
<td>Stage I-II Unfavorable, Nonbulky</td>
<td>o Unfavorable disease defined by either EORTC or GHSG criteria</td>
</tr>
<tr>
<td></td>
<td>o Classical HL Stage I-II (all histologies): ABVD X4 cycles, plus IFRT 30Gy</td>
</tr>
<tr>
<td></td>
<td>o Assessment of response to therapy evaluated with PET-CT (or CT)</td>
</tr>
<tr>
<td>Stage I-II Bulky</td>
<td>o Bulky: mediastinal mass &gt;1/3 thoracic diameter or any nodal mass &gt;10cm</td>
</tr>
<tr>
<td></td>
<td>o ABVD X6 cycles plus IFRT 30Gy to prior bulk site</td>
</tr>
</tbody>
</table>
- **Important Clinical Trials:**

**Early, Favorable**

| GHSG HD7 Trial: Two Cycles of Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine plus Extended-Field Radiotherapy is Superior to Radiotherapy Alone in Early Favorable Hodgkin’s Lymphoma: Final Results of the GHSG HD7 Trial  
Engert et al. JCO 2007. 25(3): 3495-3502 |

| Regimen | ● 30Gy Extended Field Radiotherapy (EFRT) + 10Gy to involved field  
● vs ABVD X2 + 30Gy EFRT + 10Gy IFRT |
| Primary Endpoint | ● Freedom from treatment failure |
| Inclusion/Exclusion Criteria | ● Early stage (Stage I or II), newly diagnosed  
● Hodgkin’s lymphoma with favorable prognosis  
● Without clinical risk factors (large mediastinal mass, extranodal disease) |
| Size (N) | ● 650 patients |
| Results | Comparison are Radiation alone vs Combined modality  
○ **FFRF:** 7 yr rates 67% vs 88%, p<0.0001. Due to more relapses after radiation only (22% vs 3%)  
○ **CR:** 95% vs 94%  
○ **OS:** at 7 years 92% vs 94%, p=0.43 |
| Conclusion | Combined modality consisting of 2 cycles of ABVD plus EFRT is more effective than EFRT alone. |
Early, Favorable

GHSG HD10 Trial: Reduced treatment intensity in patients with early-stage Hodgkin's lymphoma
Engert et al. NEJM 2010;363(7):640

| Regimen | ● ABVD X4 → 30Gy Radiation  
| ABVD X4 → 20Gy Radiation  
| ABVD X2 → 30Gy Radiation  
| ABVD X2 → 20Gy Radiation |

| Primary Endpoint | ● Freedom from treatment failure |

| Inclusion/Exclusion Criteria | ● Early stage (Stage I or II) HL with favorable prognosis |

| Size (N) | ● 1370 patients |

| Results | ● No significant difference between 4 and 2 cycles ABVD.  
| o 5yr FFTF (93% vs 91.1%),  
| o 5yr OS (97.1% vs 96.6%),  
| o 5yr PFS (93.5% vs 91.2%)  
| ● No significant difference between 30 and 20 Gy IFRT  
| o 5yr FFTF (93.4% vs 92.9%)  
| o 5yr OS (97.7% vs 97.5%)  
| o 5yr PFS (93.7% vs 93.2%) |

| Toxicity | ● Significant difference in major toxicity between 4 and 2 cycles ABVD (all events 52% vs 33%) including leukopenia, infections, hair loss  
| ● Significant differences in major toxicity between 30 and 20 Gy IFRT (all events 8.7% vs 2.9%) including dysphagia, mucositis |

| Conclusion | In patients with early-stage Hodgkin's lymphoma and a favorable prognosis, treatment with ABVD×2 + 20 Gy IFRT is as effective as, and less toxic than, ABVD ×4 + 30 Gy IFRT |
Early, Unfavorable


Eich et al. JCO 2010; 28(27): 4199-206

<table>
<thead>
<tr>
<th>Regimen</th>
<th>2×2 factorial design (to demonstrate superiority of BEACOPP over ABVD and noninferiority of 20Gy compared with 30Gy IFRT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>o A:</td>
<td>ABVD ×4 +30Gy IFRT</td>
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<tr>
<td>o B:</td>
<td>ABVD ×4 +20Gy IFRT</td>
</tr>
<tr>
<td>o C:</td>
<td>BEACOPP (baseline) ×4 +30Gy IFRT</td>
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<tr>
<td>o D:</td>
<td>BEACOPP (baseline) ×4 +20Gy IFRT</td>
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**Primary Endpoint**
- Freedom from treatment failure

**Inclusion/Exclusion Criteria**
- Early stage, newly diagnosed, unfavorable
- Age 16-75

**Size (N)**
- 1395 patients

**Results**
- At 5 years: FFTF 85%, OS 94.5%, PFRS 86%
- BEACOPP more effective than ABVD +20Gy IFRT (5yr FFTF difference 5.7%)
- No difference between BEACOPP and ABVD +30Gy IFRT (5yr FFTF difference 1.6%)
- BEACOPP +20Gy was not inferior to BEACOPP 30Gy

**Toxicity**
- Treatment related toxicity occurred more often in arms with intensive therapy

**Conclusion**
- Dose escalation using BEACOPP didn’t significantly improve outcome in early unfavourable HL. ABVD ×4 should be followed by 30Gy IFRT
Early Favorable & Unfavorable

<table>
<thead>
<tr>
<th>NCIC/ECOG HD6 Study <strong>Canadian</strong></th>
<th>ABVD alone versus radiation-based therapy in limited-stage Hodgkin's lymphoma</th>
<th>Meyer et al. NEJM 2012;366(5);399</th>
</tr>
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<tbody>
<tr>
<td>Chemotherapy plus radiation treatment is effective in controlling stage IA or IIA nonbulky Hodgkin's lymphoma in 90% of patients but is associated with late treatment-related deaths. Chemotherapy alone may improve survival because it is associated with fewer late deaths</td>
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**Regimen**
- ABVD X 4-6 cycles for both favorable and unfavorable
- Vs Radiation
  - SNRT alone (if favorable)
  - or ABVDX2 + SNRT (if unfavorable)
- SNRT = subtotal nodal radiation

**Primary Endpoint**
- 12yr OS

**Inclusion/Exclusion Criteria**
- Previously untreated stage IA or IIA nonbulky Hodgkin Lymphoma
- Favorable or unfavorable risk profiles
- Unfavorable: age >39, ESR >50, mixed cellularity or lymphocyte deplete histology, ≥4 sites of disease

**Size (N)**
- 405 patients

**Results**
Comparisons are ABVD alone vs SNRT groups
- **12yr OS, higher in ABVD-only:** 94% vs 87%, p=0.04
- **Rate of Freedom from disease progression, lower in ABVD-only:** 87% vs 92%, p=0.05
- **Event free survival, no difference:** 85% vs 80%, p=0.60

Subset analysis according to risk profile
- Favorable risk: No sig. difference in any outcome
- Unfavorable risk: results similar to primary analysis
  - OS higher in ABVD only group (92% vs 81%, p=0.04)
  - Rate of Freedom from disease progression lower in ABVD only (86% vs 94%, p=0.006)
  - Rate of EFS no difference (83% vs 78%, p=0.74)

**Toxicity**
- ABVD alone: 6 died from HL or early treatment complication, 6 died from other cause
- Radiation therapy: 4 deaths from HL or early toxic effects, 20 from other cause
- More pts in radiation-therapy group than ABVD-only group who had second cancers (23 vs. 10) and who had cardiac events (26 vs. 16)

**Conclusion**
ABVD therapy alone, as compared with treatment that includes SNRT, improves the rate of long-term OS in pts with stage IA or IIA nonbulky HL. Furthermore, the rates of 87% for 12-year freedom from disease progression and 94% for OS with ABVD alone suggest that this treatment can now more confidently be considered to be a therapeutic option for this population

**Comments**
Premature closure of the trial: based on the availability of new data from a trial by EORTC, which showed excellent outcomes with combination therapy that included involved-field radiation therapy

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**ADVANCED STAGE (III + IV) CLASSICAL HL**

- **Bottom Line General Approach:**
  - Stage III or IV HL (Some trials also include Stage IIB)
  - IPS score for prognostication
  - 6 cycles ABVD or escalated BEACOPP (especially if 4-7 risk factors by IPS) +/- IFRT if PET positive residual mass or bulky disease
- Escalated BEACOPP Risks:
  - Infection, Infertility, Increased risk MDS/AML (0.9%)

### Important Clinical Trials:

**GHSG HD9 Trial: Standard and Increased-Dose BEACOPP Chemotherapy Compared with COPP-ABVD for Advanced Hodgkin's Disease**  
Diehl et al. NEJM 2003; 348: 2386-05

<table>
<thead>
<tr>
<th>Regimen</th>
<th>COPP-ABVD ×8</th>
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<tbody>
<tr>
<td></td>
<td>Vs BEACOPP ×8</td>
</tr>
<tr>
<td></td>
<td>Vs escalated BEACOPP ×8</td>
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<td>Each followed by local radiotherapy when indicated</td>
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**Mechanism of Action of Experimental Drug**

- **COPP-ABVD**: cyclophosphamide, vincristine, procarbazine, prednisone alternating with doxorubicin, bleomycin, vinblastine, dacarbazine
- **BEACOPP**: bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone

**Primary Endpoint**
- Freedom from treatment failure

**Inclusion/Exclusion Criteria**
- Newly diagnosed HL unfavorable stage IIB, IIIA/B, or IV
- Age 15-65yo

**Size (N)**
- 1201 patients

**Results**
- Comparisons are COPP-ABVD vs BEACOPP vs escBEACOPP
  - **FFTF at 5yrs**: 69%, 76%, 87%
  - **OS at 5yrs**: 83%, 88%, 91%
  - **Early Progression**: 10%, 8%, 2%
  - **CR**: 85%, 88% 96%

**Toxicity**
- Increased toxicity with esc BEACOPP (cytopenias, infection)

**Conclusion**
- EscBEACOPP is superior to COPP-ABVD with respect to FFTF + OS

**Other Comments**
- Enrollment in COPP-ABVD group stopped in 1996 owing to inferior results (trial enrolled from 1993-1998)
- BEACOPP protocol included regular GSF and built in adjustment
| Regimen                                                                 | • BEACOPP$_{\text{escalated}}$ ×8  
• vs BEACOPP$_{\text{escalated}}$ ×4 + BEACOPP$_{\text{baseline}}$ ×4 (4+4 arm)  
• Each followed by local radiotherapy when indicated |
<table>
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<tbody>
<tr>
<td>Primary Endpoint</td>
<td>• Freedom from treatment failure</td>
</tr>
<tr>
<td>Inclusion/Exclusion Criteria</td>
<td>• Newly diagnosed HL stage IIB with large mediastinal mass or extranodal lesions and stages III or IV</td>
</tr>
<tr>
<td>Size (N)</td>
<td>• 1670 patients</td>
</tr>
<tr>
<td>Results</td>
<td>Comparisons are BEACOPP$_{\text{escalated}}$ vs 4+4 arm</td>
</tr>
<tr>
<td>• FFTF at 5yrs: 86.4% vs 84.8%</td>
<td></td>
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<tr>
<td>• 5yr OS: 92% vs 90.3%</td>
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</tr>
<tr>
<td>• FFTF was inferior without RT (90.4% vs 87%) particularly in those with residual disease after chemo but not in those with bulk in CR after chemo</td>
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</tr>
<tr>
<td>Toxicity</td>
<td>• Similar toxicity in both arms (cytopenias, infection)</td>
</tr>
<tr>
<td>Conclusion</td>
<td>The reduction of BEACOPP to the 4 + 4 regimen did not substantially reduce severe toxicity but might decrease efficacy. Our results do not support the omission of consolidation RT for patients with residual disease</td>
</tr>
</tbody>
</table>
**GHSG HD15 Trial: Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin’s lymphoma: a randomised, open-label, phase 3 non-inferiority trial**

Engert et al. The Lancet 2012; 379(9829): 1791-1799

| Regimen | ● BEACOPP<sub>escalated</sub> ×8  
|         | ● Vs BEACOPP<sub>escalated</sub> ×6  
|         | ● Vs BEACOPP<sub>14</sub> ×8  
|         | ● Persistent mass post chemo ≥2.5cm and PET positive received 30Gy IFRT (PET 2 wks after last BEACOPP course) |
| Primary Endpoint | ● Freedom from treatment failure |
| Inclusion/Exclusion Criteria | ● Newly diagnosed advanced stage HL aged 18-60yo |
| Size (N) | ● 2182 patients |
| Results | Comparisons are B<sub>escalated</sub> ×8 vs B<sub>escalated</sub> ×6 vs B<sub>14</sub> ×8  
|         | ● FFTF @ 5yrs: 84.4%, 89.3%, 85.4%  
|         | ● OS: 91.9%, 95.3%, 94.5%  
|         | ● NPV for PET @ 12mo: 94.1% (225/2126 received IFRT) |
| Toxicity | ● B<sub>esc</sub> ×8 showed higher mortality (7.5%) than B<sub>esc</sub> ×6 (4.6%) and B<sub>14</sub> ×8 (5.2%) mainly due to treatment related events (2.1%, 0.8%, 0.8%) and secondary malignancies (1.8%, 0.7%, 1.1%) |
| Conclusion | Treatment with 6 cycles of BEACOPP<sub>escalated</sub> followed by PET-guided radiotherapy was more effective in terms of FFTF and less toxic than 8 cycles of BEACOPP<sub>escalated</sub> or BEACOPP<sub>14</sub>. Thus, 6 cycles of BEACOPP<sub>escalated</sub> should be the treatment of choice for advanced stage Hodgkin’s lymphoma. PET done after chemotherapy can guide the need for additional radiotherapy in this setting |

**RELAPSED /REFRACTORY CLASSICAL HL**

- **Bottom Line General Approach:**
  - **Refractory Disease:** Failure to achieve remission or relapse at <3months after completing therapy
  - **Relapsed Disease:** Early 3-12 months versus Late >12months (better prognosis)
  - Confirm relapse with tissue biopsy and complete restaging. False positive PET-CT causes include local inflammation post therapy, sarcoidosis, deposition of brown fat, infection.
  - Identify sites of relapse, initial presenting stage and stage at relapse, previous therapy received (radiation alone, or combined modality), time to relapse, comorbidities
  - If initial therapy radiation alone: ABVD ×6 +/- IFRT if localized relapse outside original radiotherapy field
  - If initial therapy included chemotherapy: Re-induction with salvage chemotherapy followed by autologous stem cell transplant +/- IFRT to prior bulk site at relapse. Salvage chemotherapy options include:
    - GDP (Gemcitabine, Dexamethasone, Cisplatin)
    - DICEP (Dose Intensive Cyclophosphamide, Etoposide, Cisplatin)
    - DHAP (Dexamethasone, Cytarabine, Cisplatin)
  - For Second/Subsequent relapse
    - Palliative chemotherapy for those with symptoms (GDP, vinblastine, CHVVP, MOPP, gemcitabine single agent)
    - Allogeneic stem cell transplant (if eligible, with chemosensitive disease, time to relapse >1year following auto-HSCT)
    - Brentuximab vedotin if failed initial chemotherapy and failed auto-HSCT
- **Prognosis**: Relapse rates 20-25% depending on stage. Salvage therapy can achieve responses in approximately 50%, however long term disease free survival following relapse therapy less common.

- **Important Clinical Trials**:

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Authors</th>
<th>Journal</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aggressive conventional chemotherapy compared with high-dose chemotherapy with autologous haemopoietic stem-cell transplantation for relapsed chemosensitive Hodgkin’s disease: a randomised trial</td>
<td>Schmitz et al.</td>
<td>Lancet</td>
<td>2002</td>
</tr>
</tbody>
</table>

| Regimen | ● Four cycles Dexa- BEAM (dexamethasone, carmustine, etoposide, cytarabine, melphalan)  
|         | ● Vs 2 cycles Dexa- BEAM → high-dose BEAM → auto-HSCT |
| Primary Endpoint | ● Freedom from treatment failure |
| Inclusion/Exclusion Criteria | ● Age 16-60 with relapsed HL |
| Size (N) | ● 161 patients |
| Results | ● FFTS @ 3 yrs: BEAM-HSCT (55%) vs Dexa-BEAM (34%) p=0.019  
|         | ● OS: did not differ significantly |
| Conclusion | High-dose BEAM and auto-HSCT improves FFTF in patients with chemosensitive first relapse of HL irrespective of length of initial remission |

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin’s lymphoma</td>
<td>Younes et al.</td>
<td>JCO</td>
<td>2012</td>
</tr>
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</table>

| Regimen | ● Open-label, phase II study evaluating efficacy and safety of brentuximab vedotin  
|         | ● Brentuximab vedotin 1.8mg/kg IV q3wks (max 16 cycles) |
| Mechanism of Action of Experimental Drug | ● Brentuximab vedotin: antibody drug conjugate directed to protein CD30 which is expressed in classical HL and systemic anaplastic large cell lymphoma |
| Primary Endpoint | ● ORR |
| Inclusion/Exclusion Criteria | ● Relapsed or refractory HL after auto-SCT  
|         | ● Histologically documented CD-30 positive HL |
| Size (N) | ● 102 patients |
| Results | ● ORR: 75%  
|         | ● CR: 34% pts  
|         | ● Median PFS: 5.6months  
|         | ● Median duration of response: 20.5 months  
|         | ● Median observation time >1.5years: 31 pts alive and free of progressive disease |
| Toxicity | ● Peripheral sensory neuropathy, nausea, fatigue, neutropenia, diarrhea |
| Conclusion | Brentuximab was associated with manageable toxicity and induced objective responses in 75% of patients with R/R HL after auto-SCT. Durable CRs approaching 2 years were observed |

**Nodular Lymphocyte Predominant HL**

- **Background**:
  - Uncommon subtype (5% of all cases), indolent course, good survival
Slight male predominance, median age 37yo. Typically present with peripheral adenopathy, not contiguous.

Immunohistochemistry: negativity for CD30, CD15

Associated with progressive transformation of germinal centers, T-cell rich B cell lymphoma, diffuse large B cell lymphoma

**Bottom Line General Approach:**

- No standard therapy
- Early Stage: IFRT, combined modality ie ABVD, or observation
- Advanced stage: Combined modality ie ABVD +/- rituximab if CD20+

**REFERENCES**

- Alberta Health Services Guidelines
- UptoDate
- Canadian Cancer Society
- Odette Cancer Centre Guidelines