Pre-HCT Treatment for Hodgkin's / Non-Hodgkin's Lymphoma

This appendix is intended to provide additional information on:

- Common pre-HCT treatments for lymphoma,
- Lines of therapy,
- Cycles, and
- How to report the best response to lines of therapies.

NOTE: Reporting second or subsequent stem cell transplants
When using the Hodgkin's and Non-Hodgkin's Lymphoma Pre-HCT Data Form (2018) to report a second or subsequent transplant, please check the box at the top of the form and continue with question 129. *Lines of therapy questions do not need to be completed for second or subsequent transplants.*

Common Pre-HCT Treatments

Chemotherapy: The following chemotherapy regimens are common initial and salvage treatments for Hodgkin's / Non-Hodgkin's Lymphoma.

Common Chemotherapy Regimens			
Hodgkin's Lymphoma		**Non-Hodgkin's Lymphoma**	
MOPP	Nitrogen Mustard (mustine, mechlorethamine) Vincristine (VCR, Oncovin) Procarbazine (Mutalane) Prednisone*	**CVP**	Cyclophosphamide (Cytoxan) Vincristine (VCR, Oncovin) Prednisone*
ABVD	Doxorubicin (Adriamycin) Vinblastine (Velban, VLB) Bleomycin (BLM, Blenoxane) Dacarbazine (DTIC)	**CHOP**	Cyclophosphamide (Cytoxan) Doxorubicin (Adriamycin) Vincristine (VCR, Oncovin) Prednisone*
BEACOPP	Bleomycin (BLM, Blenoxane) Etoposide (VP-16, VePesid) Doxorubicin (Adriamycin) Cyclophosphamide (Cytoxan) Vincristine (VCR, Oncovin) Procarbazine (Mutalane) Prednisone*	**FND**	Fludarabine (Fludara) Mitoxantrone (Novantrone) Dexamethasone*
VBM	Vinblastine (Velban, VLB) Bleomycin (BLM, Blenoxane) Methotrexate (MTX)	**ESHAP**	Etoposide (VP-16, VePesid) Methylprednisolone* Cisplatin (Platinol, CDDP) Cytarabine (Ara-C)

Stanford V	Vinblastine (Velban, VLB) Doxorubicin (Adriamycin) Bleomycin (BLM, Blenoxane) Nitrogen Mustard (mustine, mechlorethamine) Etoposide (VP-16, VePesid) Prednisone*	**DHAP**	Dexamethasone Cytarabine (Ara-C) Cisplatin (Platinol, CDDP)
ICE	Ifosfamide (Ifex) Mesna† Etoposide (VP-16, VePesid) Carboplatin (Paraplatin)	**MINT**	Ifosfamide (Ifex) Mesna† Mitoxantrone (Novantrone) Paclitaxel (Taxol)‡
ESHAP	Etoposide (VP-16, VePesid) Methylprednisolone* Cisplatin (Platinol, CDDP) Cytarabine (Ara-C)	**ICE**	Ifosfamide (Ifex) Mesna† Etoposide (VP-16, VePesid) Carboplatin (Paraplatin)
BEAM	Carmustine (BCNU) Etoposide (VP-16, VePesid) Cytarabine (Ara-C) Melphalan‡	**BEAM**	Carmustine (BCNU) Etoposide (VP-16, VePesid) Cytarabine (Ara-C) Melphalan‡

* These drugs are reported on questions 46 and 95, “Corticosteroids.”

† Mesna is not considered part of the chemotherapy regimen and should not be reported as such. It is used to bind acrolein, a metabolite of ifosfamide and cyclophosphamide, which are known to be toxic to the bladder. Mesna is used to reduce the incidence of hemorrhagic cystitis and hematuria in these patients.

If the recipient received any of the above regimens or other chemotherapies, select “yes” (question 31 or 80), and select “yes” or “no” for each of the drugs listed (in questions 35-62 or 84-111).

‡ If the recipient received an additional drug that is not listed as part of a Pre-HCT treatment, select “Yes” for question 62 or 111 and report the drug on question 63 or 112.

Often, the addition of Rituximab (Anti-CD20, Rituxan) to a regimen is indicated by an “R-” before or after the chemotherapy regimen abbreviation. For example, Rituximab with the CHOP regimen is often abbreviated as “R-CHOP” or “CHOP-R.”

Lines of Therapy and Cycles

Line of Therapy: A line of therapy is a specific set of orders used to treat a patient's disease. To determine distinct lines of therapy, it is important to consider the intent of treatment and the protocol of the ordered course of treatment. A line of therapy is used to bring the recipient's disease into complete remission (initially or post-relapse), maintain complete remission, or reduce the tumor burden within a recipient. After the line of therapy has been given, restaging assessments (e.g., PET/CTs or bone marrow biopsies) are often done to determine the disease response. Based on the evaluation, additional lines of therapy may be initiated. For example, a recipient may be treated with a line of therapy to induce a complete response (CR). If, after the first line of therapy is completed, restaging exams show that the disease is resistant (refractory), a second line of therapy will often be used to achieve CR. The first and second lines of therapy should be reported separately because two distinct protocols were used to try to induce CR.

Additional lines of therapy may be used to maintain the recipient's CR status, or to treat relapsed or progressive disease. If a new line of therapy is instituted based on the results of a restaging exam, it is usually considered a distinct line of therapy.

More than two lines of chemotherapy: Recipients with lymphoma may have numerous lines of therapy prior to transplant depending on the aggressiveness of their disease. When submitting the paper version of the form for a recipient with more than two lines of therapy, check the box on the bottom of page three, copy the "Pre-HSCT Treatment for Non-Hodgkin's Lymphoma / Hodgkin's Lymphoma" section and complete a "Line of Therapy" section for each line of therapy administered. The FormsNet™ application allows multiple lines of therapy to be reported. Complete a "Line of Therapy" section for each line of therapy administered prior to the start of the preparative regimen.

Stem cell priming for autologous transplant: stem cell priming using chemotherapeutic drugs for autologous peripheral blood stem cell transplant is usually a distinct line of therapy and should be reported on questions 75 and 124, "Was this line of therapy given for stem cell priming?" This process is commonly called "stem cell mobilization." An example of stem cell priming/mobilization is the use of ifosfamide, carboplatin, and etoposide (ICE) with or without rituximab. This regimen reduces the number of cancer cells and increases the number of peripheral blood stem cells in the blood stream. The peripheral blood stem cells may then be collected, cryopreserved, stored, and later infused for autologous stem cell transplant.

NOTE: Preparative regimen for stem cell transplant
The preparative regimen for transplant should not be reported as a line of therapy, because it is reported on the Pre-TED (Form 2400) and/or Recipient Baseline Data (Form 2000).

Cycle: A cycle consists of one full treatment (per protocol) and the rest period before the next cycle begins. Sometimes a line of therapy may include just one cycle, but more commonly there are several cycles in a single line of therapy. In Example 1 below, a patient received one line of therapy consisting of six cycles.

*Example 1***:** A patient is diagnosed with B-cell NHL and initial treatment with R-CHOP chemotherapy begins on January 4, 2010.

Cycle	Day of Cycle	Treatment
One	Day 1	375 mg/m^2 rituximab on 1/4/10 750 mg/m^2 cyclophosphamide on 1/4/10 50 mg/m^2 doxorubicin on 1/4/10 1.4 mg/m^2 vincristine on 1/4/10
	Days 1-5	100 mg prednisone on 1/4/10-1/8/10
	Days 6-21	Rest 1/9/10-1/24/10
Two	Day 1	375 mg/m^2 rituximab on 1/25/10 750 mg/m^2 cyclophosphamide on 1/25/10 50 mg/m^2 doxorubicin on 1/25/10 1.4 mg/m^2 vincristine on 1/25/10
	Days 1-5	100 mg prednisone on 1/25/10-1/29/10
	Days 6-21	Rest 1/30/10-2/14/10
Three	Day 1	375 mg/m2 rituximab on 2/15/10 750 mg/m^2 cyclophosphamide on 2/15/10 50 mg/m^2 doxorubicin on 2/15/10 1.4 mg/m^2 vincristine on 2/15/10
	Days 1-5	100 mg prednisone on 2/15/10-2/19/10
	Days 6-21	Rest 2/20/10-3/7/10
Four	Day 1	375 mg/m2 rituximab on 3/8/10 750 mg/m^2 cyclophosphamide on 3/8/10 50 mg/m^2 doxorubicin on 3/8/10 1.4 mg/m^2 vincristine on 3/8/10
	Days 1-5	100 mg prednisone on 3/8/10-3/12/10
	Days 6-21	Rest 3/13/10-3/28/10
Five	Day 1	375 mg/m2 rituximab on 3/29/10 750 mg/m^2 cyclophosphamide on 3/29/10 50 mg/m^2 doxorubicin on 3/29/10 1.4 mg/m^2 vincristine on 3/29/10
	Days 1-5	100 mg prednisone on 3/29/10-4/2/10
	Days 6-21	Rest 4/3/10-4/18/10

Six	Day 1	375 mg/m2 rituximab on 4/19/10 750 mg/m^2 cyclophosphamide on 4/19/10 50 mg/m^2 doxorubicin on 4/19/10 1.4 mg/m^2 vincristine on 4/19/10
	Days 1-5	100 mg prednisone on 4/19/10-4/23/10
	Days 6-21	Rest 4/24/10-5/9/10

Example 1: Completing the Form

Question 30: Was therapy given between diagnosis and the start of the Preparative regimen? Yes

Question 31: Chemotherapy .....Yes
Question 32: Date therapy started..... 01 04 2010
Question 33: Date therapy stopped..... 04 19 2010
Question 34: Number of cycles 06
Questions 35-63:..... rituximab, corticosteroids, cyclophosphamide, doxorubicin, vincristine

Question 64: Radiation Therapy..... No

Question 70: Surgery ..... No

Question 75: Was this line of therapy given for stem cell priming? ..... No

Example 2: A patient is diagnosed with advanced stage (Stage III or IV) Hodgkin's Lymphoma and initial treatment with Stanford V begins on November 1, 2010, followed by radiotherapy.

Cycle	Week of Cycle	Treatment
One	Week 1	6 mg/m^2 vinblastine on 11/1/10 25 mg/m^2 doxorubicin on 11/1/10 6 mg/m^2 nitrogen mustard on 11/1/10 40 mg/m^2 prednisone every other day
	Week 2	1.4 mg/m^2 vincristine on 11/8/10 5 U/m^2 bleomycin on 11/8/10 40 mg/m^2 prednisone every other day
	Week 3	6 mg/m^2 vinblastine on 11/15/10 25 mg/m^2 doxorubicin on 11/15/10 60 mg/m^2 etoposide on 11/15/10 and 11/16/10 40 mg/m^2 prednisone every other day
	Week 4	1.4 mg/m^2 vincristine on 11/22/10 5 U/m^2 bleomycin on 11/22/10 40 mg/m^2 prednisone every other day

Two	Week 1	6 mg/m^2 vinblastine on 11/29/10 25 mg/m^2 doxorubicin on 11/29/10 6 mg/m^2 nitrogen mustard on 11/29/10 40 mg/m^2 prednisone every other day
	Week 2	1.4 mg/m^2 vincristine on 12/6/10 5 U/m^2 bleomycin on 12/6/10 40 mg/m^2 prednisone every other day
	Week 3	6 mg/m^2 vinblastine on 12/13/10 25 mg/m^2 doxorubicin on 12/13/10 60 mg/m^2 etoposide on 12/13/10 and 12/14/10 40 mg/m^2 prednisone every other day
	Week 4	1.4 mg/m^2 vincristine on 12/20/10 5 U/m^2 bleomycin on 12/20/10 40 mg/m^2 prednisone every other day
Three	Week 1	6 mg/m^2 vinblastine on 12/27/10 25 mg/m^2 doxorubicin on 12/27/10 6 mg/m^2 nitrogen mustard on 12/27/10 40 mg/m^2 prednisone every other day
	Week 2	1.4 mg/m^2 vincristine on 1/3/10 5 U/m^2 bleomycin on 1/3/10 40 mg/m^2 prednisone every other day
	Week 3	6 mg/m^2 vinblastine on 1/10/11 25 mg/m^2 doxorubicin on 1/10/11 60 mg/m^2 etoposide on 1/10/11 and 1/11/11 prednisone tapering
	Week 4	1.4 mg/m^2 vincristine on 1/17/11 5 U/m^2 bleomycin on 1/17/11 prednisone tapering
	Week 1	36 Gy involved-field radiation therapy to all sites >5 cm
	Week 2	

Example 2: Completing the Form

Question 30: Was therapy given between diagnosis and the start of the Preparative regimen? . Yes

Question 31: Chemotherapy ..... Yes
Question 32: Date therapy started 11 01 2010
Question 33: Date therapy stopped 12 27 2010
Question 34: Number of cycles 03
Questions 35-63: ..... bleomycin, doxorubicin, etoposide, vinblastine, nitrogen mustard, prednisone, vincristine
Question 64: Radiation Therapy ..... Yes
Question 65: Date therapy started 01 24 2011
Question 66: Date therapy stopped 02 04 2011
Question 67: Mediastinum ..... No
Question 68: Other Site(s) ..... Yes

Question 69: Specify other sites ..... *specify involved field sites*

Question 70: Surgery..... No

Question 75: Was this line of therapy given for stem cell priming? ..... No

Best Response to Line of Therapy

To evaluate the best response to a line of therapy, assessments of disease are performed before, during, and/or after a line of therapy. For example, a disease may be assessed at diagnosis and after the first line of therapy. To determine the disease response to a line of therapy, use the following definitions:

Best Response	Definition
Complete remission (CR)	Complete disappearance of all known disease for ≥ 4 weeks
CR undetermined (CRu)	As above, with the exception of persistent scan abnormalities of unknown significance
Partial remission (PR)	≥ 50% reductions in the greatest diameter of all sites of known disease, and no new sites
No response / stable disease (NR / SD)	< 50% reduction in the greatest diameter of all sites of known disease
Progressive disease (PD)	Increase in the size of known disease sites, or new sites of disease
Not tested / Unknown	No evaluation performed or results unknown

NOTE: Bone Marrow Involvement

If the recipient has lymphomatous involvement in the bone marrow, the infiltrate must be cleared upon subsequent biopsy to be considered in CR. If the morphology is unclear, the immunohistochemistry should be negative. New or recurrent involvement within the bone marrow indicates relapsed or progressive disease.

Example 3: A patient presents to her primary physician with cervical adenopathy, weight loss, night sweats, and fever. An “eyes to thighs” staging PET scan shows evidence of disease in a solitary 5 cm x 3 cm mass in the neck. Upon lymph node biopsy, a diagnosis of Hodgkin’s Lymphoma is made. After three cycles of Stanford V plus local radiotherapy (using the same regimen and dates as in example 2), re-staging exams are done.

The restaging scans done on February 14, 2011, show the neck mass has shrunk to 3 cm x 2 cm. Since the diameter of the mass has decreased < 50%, the best response following this treatment is “no response / stable disease.”

Example 3: Filling Out the Form

Question 30: Was therapy given between diagnosis and the start of the Preparative regimen? Yes

Question 31: Chemotherapy ..... Yes
Question 32: Date therapy started..... 11 01 2010
Question 33: Date therapy stopped..... 12 27 2010
Question 34: Number of cycles 03
Questions 35-63:..... bleomycin, doxorubicin, etoposide, vinblastine, nitrogen mustard, prednisone, vincristine

Question 64: Radiation Therapy..... Yes
Question 65: Date therapy started..... 01 24 2011
Question 66: Date therapy stopped..... 02 04 2011
Question 67: Mediastinum..... No
Question 68: Other Site(s)..... Yes
Question 69: Specify other sites..... cervical lymph nodes

Question 70: Surgery ..... No

Question 75: Was this line of therapy given for stem cell priming? ..... No

Question 76: Best Response to Line of Therapy ..... NR/SD
Question 77: Date response established..... 02 14 2011

Example 4: A patient presents with recently diagnosed B-cell Non-Hodgkin's Lymphoma. Staging scans show active disease in cervical, axial, inguinal, and paraaortic lymph nodes. The recipient is started on R-CHOP chemotherapy on January 3, 2011, and receives six cycles.

Cycle	Day of Cycle	Treatment
One	Day 1	375 mg/m^2 rituximab on 1/3/11 750 mg/m^2 cyclophosphamide on 1/3/11 50 mg/m^2 doxorubicin on 1/3/11 1.4 mg/m^2 vincristine on 1/3/11
	Days 1-5	100 mg prednisone on 1/3/11-1/7/11
	Days 6-21	Rest 1/7/10-1/23/10
Two	Day 1	375 mg/m^2 rituximab on 1/24/11 750 mg/m^2 cyclophosphamide on 1/24/11 50 mg/m^2 doxorubicin on 1/24/11 1.4 mg/m^2 vincristine on 1/24/11
	Days 1-5	100 mg prednisone on 1/24/11-1/28/11
	Days 6-21	Rest 1/28/11-2/13/11

Three	Day 1	375 mg/m^2 rituximab on 2/14/11 750 mg/m^2 cyclophosphamide on 2/14/11 50 mg/m^2 doxorubicin on 2/14/11 1.4 mg/m^2 vincristine on 2/14/11
	Days 1-5	100 mg prednisone on 2/14/11-2/18/11
	Days 6-21	Rest 2/18/11-3/6/11
Response to treatment	PET/CT scans to determine response to first three cycles in the first line of therapy (3/5/11)	
Four	Day 1	375 mg/m^2 rituximab on 3/7/11 750 mg/m^2 cyclophosphamide on 3/7/11 50 mg/m^2 doxorubicin on 3/7/11 1.4 mg/m^2 vincristine on 3/7/11
	Days 1-5	100 mg prednisone on 3/7/11-3/11/11
	Days 6-21	Rest 3/11/10-3/27/10
Five	Day 1	375 mg/m^2 rituximab on 3/28/11 750 mg/m^2 cyclophosphamide on 3/28/11 50 mg/m^2 doxorubicin on 3/28/11 1.4 mg/m^2 vincristine on 3/28/11
	Days 1-5	100 mg prednisone on 3/28/11-4/1/11
	Days 6-21	Rest 4/1/11-4/17/11
Six	Day 1	375 mg/m^2 rituximab on 4/18/11 750 mg/m^2 cyclophosphamide on 4/18/11 50 mg/m^2 doxorubicin on 4/18/11 1.4 mg/m^2 vincristine on 4/18/11
	Days 1-5	100 mg prednisone on 4/18/11-4/22/11
	Days 6-21	Rest 4/22/11-5/8/11
Response to treatment	PET/CT scans to determine response to first line of therapy	

Restaging scans on 3/5/11 show a complete response to R-CHOP therapy with no evidence of disease on the PET/CT scan. As per protocol, three additional cycles of R-CHOP are given.

The patient notices swollen groin lymph nodes a month and a half after completing their first line of therapy. A PET/CT scan is done on 6/20/11 and shows that disease in the inguinal nodes has returned. The physician determines the recipient should receive an autologous PBSC transplant and uses ICE for salvage chemotherapy and peripheral blood stem cell mobilization on 7/4/11.

Cycle	Day of Cycle	Treatment
One	Days 1 and 3	100 mg/m^2 etoposide x 2 doses on 7/4/11 and 7/6/11
	Days 2	5000 mg/m^2 ifosfamide on 7/5/11 AUC=5 carboplatin on 7/5/11 100 mg/m^2 etoposide x 2 doses on 7/5/11
	Days 4-14	Rest 7/7/11-7/17/11
Two	Days 1 and 3	100 mg/m^2 etoposide x 2 doses on 7/18/11 and 7/20/11
	Days 2	5000 mg/m^2 ifosfamide on 7/19/11 AUC=5 carboplatin on 7/19/11 100 mg/m^2 etoposide x 2 doses on 7/19/11
	Days 4-14	Rest 7/21/11-7/31/11
Three	Days 1 and 3	100 mg/m^2 etoposide x 2 doses on 8/1/11 and 8/3/11
	Days 2	5000 mg/m^2 ifosfamide on 8/2/11 AUC=5 carboplatin on 8/2/11 100 mg/m^2 etoposide x 2 doses on 8/2/11
	Days 4-14	Rest 8/4/11-8/14/11
Response to treatment	PET/CT scans to determine response to second line of therapy	
Stem Cell Mobilization	Peripheral blood stem cells will be collected over a period of days for cryopreservation in preparation for autologous stem cell transplant.	

The recipient underwent stem cell collection following the third cycle of ICE treatment/stem cell mobilization. The product was cryopreserved. Restaging scans on 9/5/11, one month after completion of the third cycle, confirmed the recipient has sustained a partial remission with a > 50% reduction in the longest diameter of all sites of disease in the inguinal and paraaortic nodal regions. The physician indicates that the recipient should proceed with autologous PBSC transplant.

Example 4: Completing the Form

First Line of therapy

Question 30: Was therapy given between diagnosis and the start of the Preparative regimen? Yes

Question 31: Chemotherapy ..... Yes
Question 32: Date therapy started.....01 03 2011
Question 33: Date therapy stopped.....04 18 2011
Question 34: Number of cycles 06
Questions 35-63:.....corticosteroids, cyclophosphamide, doxorubicin, rituximab, vincristine

Question 64: Radiation Therapy .....No

Question 70: Surgery .....No

Question 75: Was this line of therapy given for stem cell priming? .....No

Question 76: Best Response to Line of Therapy ..... CR

Question 77: Date response established.....03 05 2011
Question 78: Did disease relapse/progress following this line of therapy?..... Yes
Question 79: Date of relapse/progression 06 20 2011

Second Line of therapy

Question 80: Chemotherapy ..... Yes
Question 81: Date therapy started.....07 04 2011
Question 82: Date therapy stopped.....08 01 2011
Question 83: Number of cycles 03
Questions 84-112:.....carboplatin, etoposide, ifosfamide

Question 113: Radiation Therapy.....No

Question 119: Surgery .....No

Question 124: Was this line of therapy given for stem cell priming? ..... Yes

Question 125: Best Response to Line of Therapy ..... PR
Question 126: Date response established.....09 05 2011
Question 127: Did disease relapse/progress following this line of therapy?.....No

References:

Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol. 2007;25:579-586.

Skeel, Roland T. *Handbook of Cancer Chemotherapy*. 7th ed. Vol. 236. Philadelphia: Lippincott Williams & Wilkins, 2007. Print.