



Diagnosis and Therapy in Chronic Lymphocytic Leukemia

Supported by an educational grant from Cephalon Oncology

Disclosures

- Amy H. Seung, PharmD, BCOP has no significant financial relationships to disclose.
- Neisha L. Griffith, MS, RPh is a speaker and consultant for Amgen
- Several of the agents as well as regimens discussed are in investigational use at this time and are not currently approved by the FDA.

Learning Objectives

- Know how previous treatment regimens have made refractory disease more difficult to re-treat
- Identify the therapies appropriate for treating CLL and the side effects attendant on these treatments
- Be familiar with the novel biologic agents that are used for treating CLL
- Be aware of the reimbursement issues associated with the different therapies



Treatment Strategies in B-Chronic Lymphocytic Leukemia

Amy Hatfield Seung, PharmD, BCOP
Clinical Specialist, Hematologic Malignancies
The Johns Hopkins Hospital,
Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

Objectives

- After attending the presentation, the participant will be able to:
 - Differentiate prognostic features in CLL
 - Assess different first line treatment strategies
 - Compare therapies for refractory disease
 - Identify treatment-specific toxicities

Natural History of CLL

- Indolent disease
 - Median age at diagnosis 65-70 years
 - Incurable
 - Some patients 10-year survival
 - Watchful waiting until progression
- Progressive disease
 - Over 50% are at risk for progression
 - Subgroup at risk for accelerated disease progression

Clinical Presentation

- Asymptomatic 25%
- Symptoms
 - Lymphadenopathy 50-90%
 - Splenomegaly 25-55%
 - Hepatomegaly 15-25%
 - B symptoms 5-10%
 - Infections, Autoimmune disorders infrequent
- Laboratory Abnormalities
 - WBC $>100,000/\text{mm}^3$ 30%
 - Lymphocytosis
 - Hgb <11 g/dL 31%
 - Platelet $<100,000/\text{mm}^3$ 16%

Rai and Binet Staging Systems

- Differentiates into 3 stages based on
 - Lymphocytosis
 - Lymphadenopathy
 - Organomegaly
 - Bone marrow failure
- Staging not enough information to predict prognosis
- Some early stage patients will have rapidly progressing disease

Prognostic Factors

Historical Parameters	Good	Poor
Morphology	Typical	Atypical
Bone marrow histology	Nondiffuse pattern	Diffuse pattern
Lymphocyte doubling	>12 months	<12 months
Serum markers (LDH, thymidine kinase, sCD23, B-2 microglobulin)	Normal	Elevated
Biological Parameters	Good	Poor
Cytogenetic abnormalities	Normal, del13q	del11q, del17p
CD38 expression	<30%	>30%
IgVH gene mutation status	Mutated	Germline
ZAP-70 expression	Low	High

Cytogenetic Abnormalities

Abnormality	Frequency (%)	Median Survival (months)
del 13q (sole abnormality)	36%	133
Normal	18%	111
Trisomy 12	14%	114
del11q	17%	79
del17p	7%	32
Others (del3q, del6q, trisomy 8q, t(14q32))	8%	Not evaluated

Prognostic Groups

- Patients differentiated into groups based on risk of progression
 - Factors
 - Stage of disease
 - Cytogenetic abnormalities
 - Biologic markers
- Prognostic Groups
 - Low
 - Intermediate
 - High

Prognostic Risk Groups for Early Stage

Risk Group	Median Survival (years)	Median Treatment Free Interval (years)	Immediate Treatment
Low	>15	>5	No
Intermediate	10	3-4	No
High	3-8	1-4	Clinical Trial
Symptomatic	2-6	None	Yes

Challenge

Will early aggressive treatment of high risk CLL patients result in higher rates of long term survival or longer time to progression?

Indications for Initiation of Therapy

- Bone marrow failure
- Thrombocytopenia
- Severe lymphadenopathy
- Lymphocyte doubling time < 6 months
- Constitutional symptoms

Specific Patient Factors for Guiding Therapy

- Age
- Performance Status
- Comorbidities
 - Including current infection status
- Organ dysfunction
- Goals of Therapy
 - Palliation
 - Maximal response with prolonged progression free survival

Assessment of Response

- Overall Response Rate
 - Complete Response
- Progression Free Survival
- Time to Treatment
 - Time from diagnosis until treatment is initiated
- Duration of Response
- Minimal Residual Disease (MRD)
- Toxicities

First line Treatment Strategies

- Conventional therapies
 - Noncurative
 - Treat only when symptomatic or progressive
- Single agents
- Combination chemotherapy
- Chemoimmunotherapy
- None of randomized trials for first line therapy have shown a difference in overall survival

Single Agents

- Chlorambucil
- Purine analogues
 - Fludarabine
 - Cladribine
 - Pentostatin
- Comparison of chlorambucil vs. fludarabine (N=544)
 - ORR 37% vs. 63%
 - CR 4% vs. 20%
 - TTP 14 vs. 20 months
 - OS No difference
- Addition of steroids to an alkylator or purine analogue
 - No evidence of increased efficacy and greater toxicity

Rai KR et al. N Engl J Med. 2000; 343:1750.

Wierda WG. Hematology Am Soc Hematol Educ Program 2006; 285-294.

Steurer M et al. Cancer Treat Rev. 2006; 32: 377-89.

Fludarabine vs. Fludarabine/ Cyclophosphamide

Phase III Trials	ORR	CR	PFS (months)
Eichhorst ¹ , N=375 Flu 25mg/m ² IV x 5 days vs. Flu 30mg/m ² IV x 3 days/Cyclo 250mg/m ² IV x 3 days Cycled every 28 days (max 6 cycles)	83% 94%	7% 24%	37 48
Flinn ² , N=278 Flu 25mg/m ² IV x 5 days vs. Flu 20mg/m ² IV x 5 days/Cyclo 600mg/m ² IV x 1 day Cycled every 28 days (max 6 cycles)	60% 74%	5% 23%	19 32
Catovsky ³ , N=777 Flu 25mg/m ² IV x 5 days vs. Flu 25mg/m ² IV/Cyclo 250mg/m ² IV x 3 days vs. Chlorambucil 10mg/m ² PO x 7 days cycles Cycled every 28 days(max 6 cycles–12 chlorambucil)	80% 94% 72%	15% 38% 7%	5 y rate 10% 36% 10%

¹ Eichhorst BF et al. Blood. 2006; 107:885 .

³ Catovsky D et al. Lancet. 2007; 370:230

² Flinn IW et al. J Clin Oncol. 2007; 25:793.

Rituximab

- Single agent
 - N=44
 - 375mg/m² IV weekly x 4 weeks
 - Repeated every 6 months for 4 courses
 - ORR 58%, CR 9%
 - Median follow up 20 months
 - 2 year estimated PFS 49 months

Chemoimmunotherapy

Select Prospective Trials	ORR	CR	PFS (months)
Keating ¹ , Tam ² Prospective Phase II, N= 224 Flu 25 mg/m ² IV x 3 days Cyclophosphamide 250 mg/m ² IV x 3 days Rituximab 375-500 mg/m ² IV x 1 day Cycled every 28 days (Max 6 cycles)	95%	70%	Failure free survival at 4 y 69%
Byrd ³ Prospective Randomized Phase II, N=104 Concurrent: Flu 25mg /m ² IV x 5 days Rituximab 375 mg/m ² IV x 1 day Cycled every 28 days (Max 6 cycles), 2 mo observation, then weekly rituximab x 4 weeks Sequential: Flu 25 mg/m ² IV x 5 days Cycled every 28 days (Max 6 cycles) 2 mo observation, then weekly rituximab x 4 weeks	90%	47%	-----
	77%	28%	-----

¹ Keating MJ et al. J Clin Oncol. 2005; 23:4079-88.

³ Byrd JC et al. Blood 2003; 101: 6-14.

² Tam CS et al. Blood. 2008 Apr 14. Epub ahead of print.

Alemtuzumab versus Chlorambucil

Randomized, Multicenter, Open Label Phase II Trial

Alemtuzumab
30 mg IV 3x/week
Maximum of 12 weeks
N=149

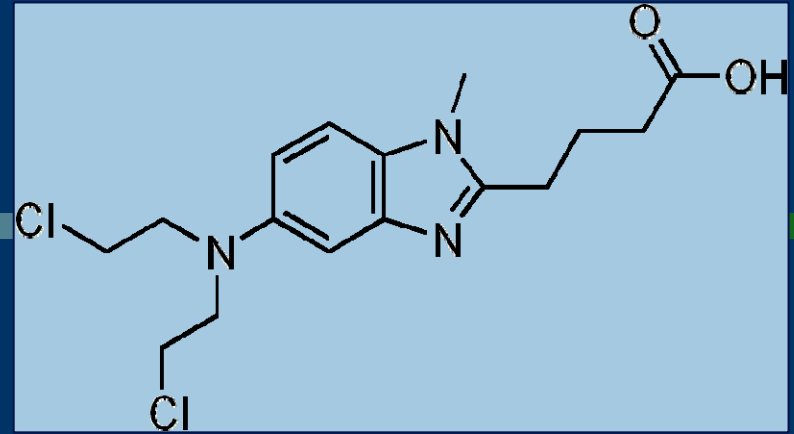
vs.

Chlorambucil
40 mg/m² PO
every 28 days
Maximum of 12 cycles
N=148

Results	A	C	P value
ORR	83%	55%	p<0.0001
CR	24%	2%	p<0.0001
PFS (months)	14.6	11.7	P=0.0001
OS (median 24.6 months follow up)	84%	84%	NS

Bendamustine

- FDA approved March 2008
 - Available in Europe in 1971
- Bifunctional alkylating agent
 - Additive purine analogue activity
 - Low cross resistance
- Dosing
 - 100 mg/m² IV over 30 minutes on Days 1, 2 every 28 days for 6 cycles
 - For relapsed or refractory patients, 70mg/m² IV over 30 minutes on Days 1, 2 every 28 days
 - Dose reductions and delays for Grade 4 hematologic toxicity
 - Caution in patients with renal and/or hepatic dysfunction
 - No formal studies



Bendamustine Toxicities

- Most common
 - Fever, nausea, vomiting
- Myelosuppression (pancytopenia)
 - Neutropenia 28% (Grade 3/4 24%), thrombocytopenia 23%, anemia 19%
 - Nadir in 3rd week
- Infections
- Infusion-related reactions
 - Fever, chills, pruritus and rash
 - Rare anaphylaxis reported
- Tumor lysis syndrome
- Rash
- Premedications
 - Antiemetics

Bendamustine versus Chlorambucil

Randomized, Multicenter, Open Label Phase II Trial

Bendamustine
100mg/m² IV on Days 1,2
Every 28 days
Maximum of 6 cycles
N=139

vs.

Chlorambucil
0.8 mg/kg PO on Days 1,15
every 28 days
Maximum of 6 cycles
N=125

Results	Bend	C	P value
ORR	68%	39%	p<0.0001
CR	30%	2%	p<0.0001
PFS (months)	21.7	9.3	P=0.0001
OS (median 18.5 months follow up)	--	--	NS

Duration of Therapy

- Complete remission
- Unacceptable toxicity
- No evidence of continued improvement
 - Plateau

Minimal Residual Disease

- Many patients who achieve a CR will have MRD
 - MRD found by flow cytometry or polymerase chain reaction (PCR)
- Eradication of MRD
 - Should it be a goal?
 - Only in clinical trials thus far
 - Absence of disease associated with greater PFS
- Consolidation with alemtuzumab or rituximab
 - Optimal dosing and schedule to be determined

Selection of a Second or Third or Fourth Regimen

- Outcomes for refractory regimens highly influenced by prior therapies
- Previous alkylator therapy then retreatment with combination alkylator therapy
 - ORR 22-62%, Few CRs
 - ↑ Response rates to purine analogues
- Duration of response
 - Initial response >6-12 months, rechallenge with initial regimen
- Once refractory to both alkylator and purine analogues, outcome is poor
 - Median survival < 1 year

Select Regimens for Previously Treated Patients

Therapy

Fludarabine

Fludarabine/ Cyclophosphamide (FC)¹

Fludarabine/Cyclophosphamide/Mitoxantrone (FCM)²

Bendamustine/Mitoxantrone³

¹ O'Brien SM et al. J Clin Oncol. 2001; 19:1414-20.

² Bosch F et al. Br J Haematol. 2002; 119:976-84.

³ Koppler H et al. Leuk Lymphoma. 2004; 45:911-3.

Rituximab Containing Regimens

Therapy

Fludarabine/Cyclophosphamide/Rituximab (FCR)¹

Pentostatin/Cyclophosphamide/Rituximab (PCR)²

Rituximab (Escalated doses³ or Thrice Weekly⁴)

Bendamustine/Rituximab⁵

¹ Wierda W et al. J Clin Oncol. 2005;23: 4070-8.

² Lamanna N et al. J Clin Oncol. 2006;24:1575-81.

³ O'Brien SM et al. J Clin Oncol. 2001; 19:2165-70.

⁴ Byrd JC et al. J Clin Oncol. 2001; 19:2153-64.

⁵ Fischer K et al. Blood. 2007 110: Abstract 3106.

Alemtuzumab Containing Regimens

Therapy

Alemtuzumab¹

Fludarabine/Alemtuzumab²

Alemtuzumab/Rituximab³

Fludarabine/Cyclophosphamide/Rituximab/Alemtuzumab (CFAR)⁴

¹ Keating MJ et al. Blood. 2002; 99:3554-61

² Elter T et al. J Clin Oncol. 2005; 23:7024-31.

³ Faderl S et al. Blood. 2003; 101:3413015.

⁴ Wierda WG et al. Blood. 2005;106: (Abstract 719)

Stem Cell Transplantation

- Autologous vs. Allogeneic vs. Nonmyeloablative
- Consider for younger patients
 - Failure of first line therapy with fludarabine
 - Relapse <12 months
 - del 17p by FISH
- No studies comparing standard chemotherapy to transplant
 - Retrospective analysis – potential survival advantage to autologous transplant versus chemotherapy
- No studies directly comparing different transplant options

Flavopiridol

- Synthetic flavone
 - Inhibits cyclin-dependent kinases
 - Antiproliferative, apoptosis-inducing properties
 - ORR 50%
- Phase II Trial N=42
 - 3 dosing cohorts, 30-minute loading dose followed by 4 hour infusion weekly for 4 of 6 weeks
 - PR: 19 (45%)
 - 5/12 (42%) PR in poor risk cytogenetic disease
 - Median response duration > 12 months
 - Toxicities
 - Tumor lysis syndrome

Oblimersen

- Bcl-2 directed antisense oligonucleotide
 - Downmodulates mRNA levels
 - Decreased bcl-2 protein levels
 - Induces apoptosis
- Randomized Phase III Trial, N=241
 - Inclusion: relapsed or refractory, prior fludarabine therapy
 - Fludarabine 25 mg/m² IV x 3 days + cyclophosphamide 250 mg/m² IV x 3 days
 - +/- oblimersen 3 mg/kg/day IV continuous infusion x 7 days beginning 4 days prior to chemo
 - Maximum 6 cycles
- Primary endpoint
 - ORR: Chemotherapy only (N=121) 7% vs. Chemo + oblimersen (N=120) 17% (P=.025)
 - CR/PR associated with extended TTP and PFS (P<0.0001)
 - Toxicities
 - Oblimersen (thrombocytopenia, cytokine release reactions, tumor lysis)
 - No difference in infections between groups

Lumiliximab

- Anti-CD23 primatized anti-CD23 macaque/human chimeric monoclonal antibody
- Inhibits IgE secretion
- Phase I dose escalation trial
 - N=46 patients
 - No CR or PR
 - ↓ in absolute lymphocyte counts 42/46 (91%) of patients
 - ↓ Reduction in lymphadenopathy 52% (17/33)
- Toxicities
 - Most common: headache, constipation, nausea, and cough
 - Grade 3 or 4: neutropenia and dyspnea (15%)

Infection-Related Risks

- Pathogenesis
 - Primary disease
 - Therapies
- Lymphopenia
- Neutropenia
- Recurrent infections
- Pulmonary infections most common site

Specific Infections

Therapy	Infections
Alkylator	Bacterial
Purine analogues	<i>Candida</i> , <i>Aspergillus</i> , HSV, <i>Pneumocystis</i>
Rituximab	No significant infections
Alemtuzumab	HSV, CMV, <i>Candida</i> , <i>Aspergillus</i>

Prophylaxis and Management Strategies

- Immunoglobulin
- Prophylactic oral antibiotics
 - Pneumocystis
 - Viral
- Duration of prophylaxis extended
- Weekly CMV PCR
- Myeloid growth factor support

Autoimmune Hemolytic Anemia

- Initiation of therapy
 - Fludarabine-containing regimens
- Management
 - Corticosteroids
 - Immunoglobulin
 - Rituximab
 - Immunosuppression

Conclusions

- Increasing information on aggressive disease related to specific prognostic features
 - Benefit of early initiation of treatment for high risk early stage patients to be determined
- Purine analogue with alkylator therapy +/- rituximab
 - ↑ ORR, PFS, duration of response
 - No difference in OS
 - Therapies should be selected based on patient-specific goals and factors
- Incorporation of monoclonal antibodies and evolving agents into treatment strategies may offer increased responses for specific patients



Understanding Reimbursement

Niesha Griffith, M.S., R.Ph.

Director of Pharmacy

The Arthur G. James Cancer Hospital at

The Ohio State University

Columbus, Ohio

Objectives

- After attending the presentation, the participant will be able to:
 - Explain reimbursement issues as they apply to both the inpatient and outpatient setting
 - Discuss reimbursement issues associated with the different therapies
 - Describe the methods for minimizing write-offs and maximizing revenue

Inpatient Reimbursement

- Medicare Inpatient Prospective Payment System (IPPS) – Part A
 - Paid according to Diagnosis Related Group (DRG)
 - In 2008, 538 DRGs were expanded to 745 Medicare Severity (MS-DRGs)
 - Reimbursement should now more accurately reflect the severity of the illness and the level of services provided

Inpatient Reimbursement

- Medicare IPPS
 - Optional reporting of 27 quality measures as a pay-for-performance initiative
 - Failure to report results in 3.4% penalty
 - Includes measures for acute myocardial infarction, heart failure, pneumonia, surgical care, mortality, and patients' experience of care

Inpatient Reimbursement

- Medicaid
 - State mandated so different rules apply
 - Often a per diem rate (usually a lower percentage of a Medicare DRG)
- Other third party payers
 - DRG - similar
 - Per diem
 - Percent of charges
 - Case rate

Inpatient Reimbursement

- No separate reimbursement for medications except carve-outs
 - Medicare – factor products
 - Other payers – negotiated

Outpatient Reimbursement

- Medicare Physician Fee Schedule (MPFS) – Part B
 - Paid for each individual component of a service
 - Medications are individually reimbursed and paid at average sales price (ASP) + 6%
 - ASP is calculated on the basis of manufacturer-reported sales data for hospitals, pharmacies, physician offices, and others
 - Reflects promotions, discounts, and rebates, but it does not reflect 340B program discounts or data from competitive acquisition program providers
 - Updated quarterly

Outpatient Reimbursement Medicare OPPS

- Medicare Outpatient Prospective Payment System (OPPS) – Part B
 - Paid according to Ambulatory Payment Classification (APC) – a service procedure or item (including medications) with an established payment rate
 - Medications (when reimbursed) are paid at ASP + 5%
 - Some medications are packaged into the APC payment (when cost is less than \$60)

Outpatient Reimbursement Medicare OPPS

- Some medications reimbursed separately
 - New medications (C9399)
 - Reimbursed at 95% of Average Wholesale Price (AWP)
 - Must put National Drug Code (NDC) # of the medication in the remarks field
 - Pass-through drugs and biologicals (J codes)
 - Reimbursed at a rate that is equivalent to the payment they would receive in a physician's office setting
 - Higher reimbursement related to “newness and relative cost”

Outpatient Reimbursement Medicare OPPS

Pass-through Drugs and Biologicals

- Temsirolimus injection
- Abatacept injection
- Anadulafungin injection
- Decitabine injection
- Eculizumab injection
- Ibandronate sodium injection
- Idursulfase injection
- Micafungin sodium injection
- Natalizumab injection
- Ranibizumab injection
- Tigecycline injection
- Hyaluronidase recombinant
- Reclast[®] (zoledronic acid) injection
- Nelarabine injection
- Panitumumab injection

Outpatient Reimbursement Medicare OPPS

- Some medications reimbursed separately
 - Non-Pass through drugs and biologicals (J codes)
 - Reimbursed at ASP + 5%
 - “Preadministration related services” for Intravenous Immunoglobulin (IVIG) (also applies to physician offices)
 - Anti-emetics (J codes - IV, Q codes - PO)
 - Dolasetron
 - Granisetron
 - Ondansetron
 - Palonosetron

Outpatient Reimbursement Medicare OPPS

- Medications are reimbursable if indication for use is:
 - A Food and Drug Administration (FDA) labeled indication
 - Approved via a National or Local Coverage Determination (NCD,LCD)
 - Listed in one of the Centers for Medicare & Medicaid Services (CMS) -approved compendia
 - American Hospital Formulary Service (AHFS) *Drug Information*
 - Thompson Healthcare's *Drugpoints*
 - NCCN *Drugs and Biologicals Compendium*
- There is no preauthorization process for off-label uses of medications

Outpatient Reimbursement Medicare OPPS

- NCD – policies that establish the extent to which Medicare will cover specific services, procedures or technologies on a nation-wide basis
 - Examples: aprepitant, erythropoiesis stimulating agents (ESAs), factor products, iron therapy (IV)

Outpatient Reimbursement Medicare OPPS

- LCD – rules or decision by a Medicare fiscal intermediary (FI) about coverage for a particular service based on whether it is reasonable and necessary
 - May expand on an NCD, but can not be in direct contradiction to the NCD
 - Examples: bevacizumab, colony stimulating factors, ESAs, IVIG, rituximab

Outpatient Reimbursement Medicare OPPS

- If using a medication for an off-label indication, the patient must be requested to sign an advance beneficiary notice (ABN)
 - Explains reason for ABN, alternative treatment options, and potential obligation for payment if CMS does not approve use
 - May be completed by physician designee, but must be signed by patient and physician
 - Must have ABN on file to appeal denial

Outpatient Reimbursement Medicare OPPS

- Two approaches for appealing a denied claim:
 - Appeal for an individual patient
 - Submit the claim and wait for the denial
 - Provide Phase III clinical trial data from a peer-reviewed journal

Outpatient Reimbursement Medicare OPPS

- Two approaches for appealing a denied claim:
 - Request modification of the LCD via a “reconsideration packet”
 - Submit request in writing from a physician
 - Provide Phase III clinical trial data from a peer-reviewed journal and published evidence-based guidelines (if available)
 - Identify other FIs who reimburse for the indication in question

Outpatient Reimbursement Medicare OPPS

Peer-reviewed Medical Journal Listing

- American Journal of Medicine
- Annals of Internal Medicine
- The Journal of the AMA
- Journal of Clinical Oncology
- Blood
- Journal of the National Cancer Institute
- The New England Journal of Medicine
- British Journal of Cancer
- British Journal of Hematology
- British Medical Journal
- Cancer
- Drugs
- European Journal of Cancer
- Lancet
- Leukemia
- Annals of Oncology
- Biology of Blood and Marrow Transplantation
- Bone Marrow Transplantation
- Gynecologic Oncology
- Clinical Cancer Research
- International Journal of Radiation, Oncology, Biology, and Physics
- Journal of the National Comprehensive Cancer Network (NCCN)
- Radiation Oncology
- Annals of Surgical Oncology
- Journal of Urology
- Lancet Oncology

Outpatient Reimbursement

- Medicaid
 - State mandated so different rules apply
 - Often a percent of charges or APC - similar reimbursement
- Other third party payers
 - APC - similar
 - Percent of charges
 - Case rates

Outpatient Reimbursement

- Other third party payers
 - Use “predetermination” process for off-label indications
 - Provide literature and seek approval *PRIOR* to medication administration
 - Request patients sign a notice of non-coverage (NONC)

Case

- BD a 57yr (70kg) male newly diagnosed Chronic Lymphocytic Leukemia (CLL)
 - Complete Blood Count (CBC):
 - White Blood Count (WBC) 110,000/mcL (70% Lymphs)
 - Hemoglobin 9.8 g/dl
 - Platelet 92,000/mcL
 - Cytogenetics:
 - Deletion 11q
 - Trisomy 12
 - Rai Stage III, Binet Stage C

CLL Therapy

- Day 1:
 - NaCl 0.9% 1 liter over 2 hours
 - Dexamethasone 12mg PO x1
 - Granisetron 1mg PO x1
 - Fludarabine 25mg/m² IV over 30 minutes
 - Cyclophosphamide 250mg/m² IV over one hour
 - Rituximab 375mg/m² IV

CLL Therapy

- Day 2, 3:
 - NaCl 0.9% 1 liter over 2 hours
 - Dexamethasone 12mg PO x1
 - Granisetron 1mg PO x1
 - Fludarabine 25mg/m² IV over 30 minutes
 - Cyclophosphamide 250mg/m² IV over one hour

Medication Cost vs. Reimbursement

Drug Therapy Day 1, 2, 3	AWP	Contract Price without Discounts	ASP +5%
Fludarabine 25mg/m ²	\$629.68	\$393.45	\$367.38
Cyclophosphamide 250mg/m ²	\$28.38	\$14.64	\$17.11
Rituximab 375mg/m ²	\$2,932.72	\$2,346.18	\$2,381.61
Granisetron 1mg	\$177.06	\$157.35	\$140.85
Total Price	\$3,767.84	\$2,911.62	\$2,906.95

Prices based on a 70 kg patient

Six Months Later

- At follow-up, WBC reveals recurrent disease
 - Days 1,2:
 - Bendamustine 70mg/m² IV over 30-60 minutes

Medication Cost vs. Reimbursement

Drug Therapy Day 1, 2	AWP	Contract Price without Discounts	95% of AWP
Bendamustine 70mg/m ²	\$3,588.44	\$3,074.40	\$3,409.02

Prices based on a 70 kg patient

Tips for Minimizing Write-Offs and Maximizing Revenue

- Educate pharmacists, nurses and physicians regarding reimbursement rules
 - Compendia, NCDs, LCDs
- Be proactive with formulary process
 - Add restrictions for use
 - Standardize ordering to guide appropriate use
- Review of billing systems
 - Ensure billing units and multipliers are correct
- Require pre-authorization for all high cost medications

Tips for Minimizing Write-Offs and Maximizing Revenue

- Review reimbursement of high cost medications
- Utilize pharmaceutical manufacturer medication assistance programs
- Get to know your Medicare reimbursement specialist
- Review claim denials
- Use the appeal process
- Establish a multi-disciplinary reimbursement committee
- Hire a pharmacy reimbursement specialist

Resources

- Am J Health-Syst Pharm Nov, 1 2006 Suppl
- Am J Health-Syst Pharm Jan, 15 2008 Suppl
- ASHP Pharmaceutical Reimbursement Resource Center
 - http://www.ashp.org/s_ashp/docs/files/SPPM_Pharmacy_Reimbursement.pdf
- Pharmacy Practice News
 - “Reimbursement Matters” Column