

Handbook for Housestaff/Fellows on J/SO Services

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J/Solid Oncology Handbook: Table of Contents

Section	Page
Key phone numbers	2
“J Medicine: The Big Picture”	4
Autologous transplant patients	6
A. Conditioning Regimens	
B. Infection Prophylaxis	
C. Growth Factors	
Allogeneic transplant patients	7
A. Conditioning Regimens	
B. Infection Prophylaxis	
C. GVHD Prophylaxis	
Prophylaxis in all J patients	9
A. Gut sterilizers/Neutropenic Precautions	
B. Blood Products	
C. TPN	
D. Bleeding prophylaxis	
E. Tumor lysis prophylaxis	
F. Growth Factors	
G. Mucositis	
Complications of Therapy	11
Veno-occlusive Disease	
Graft-versus-Host Disease	
Emergency: Neutropenic Fever	
Emergency: Tumor Lysis Syndrome	
Solid Oncology “The Big Picture”	14
Solid Oncology: Interleukin-2 Guidelines	15
Solid Oncology: Liver Procedures	18
A. RFA	
B. Chemoembolization	
Solid Oncology: Neuro-oncology	19
Communication—Palliative Care	23
Managing Pain—Palliative Care	24
Handy Info for Interns	26
Electrolyte replacement	
Discharge Checklist	
Differential Dx & Workup of Common Problems on J/SO	
Common Chemotherapy Agents	31
Preventing/Managing Chemotherapy Related Emesis	33
Common Chemotherapy Regimens on J/SO	35

Key Phone numbers

Apheresis (Pam Bumerts)	47177
Bed Control	58804
Blood Bank	54968
Bone Marrow Scheduling/Flow	58806
Bone Marrow Bx results/Flow	51039
Donor Services	50888
ER	52112
Hematology Lab	58933
Interventional Radiology	59281

To schedule IT chemo, fax requisition & chemo order to x52776 and give chemo order to pharmacy too

Lab	58080
Panorex films	55634
Palliative Care: Tiffinny Drake	Pager 95983
Pharmacy – 8 th Floor	52652
PICC Service	51424 or page 92788
Radiation Oncology (8-5)	56600
Radiology: CT Abd Reading Room	57107
Radiology Film Library (Chest films)	56471 Will tell you who is reading that day
Radiology: Neuro-radiol Reading Rm	41399
Stem Cell Lab	61013

Sheila Stinnett RN/Clin Dir	66995 or page 95609
Bindu Danee RN/Unit Dir	50848 or page 97634
Frini Chiu MSW-J service	63686 or page 90156
Charlene Vener MSW-Solid Onc	58596 or page 91945
Neela Patel/J-Case Mgr	73150 or page 92367
JoJo Densing/SO-Case Mgr	73348 or page 94352

10East	59761
10West	57215
8East	55033
Charge Nurse (8&10 th floors)	73155 or page 90309

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Tidi Lambert (allo M-Z)	65783 or page 99379
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Kathy Hill (auto M-Z)	65778 or page 90171
Carol Wolf (post-d/c)	63626 or page 93956

Outpatient Follow Up

Appointments Bowyer	66931
Infusion Room Bowyer	56765
Clinic Nurses Station Bowyer	66735
Pharmacy Bowyer	41177
Pharmacy A-level CHS	63784
Dr. Britten	66931 (Bowyer appt)
Dr. DeVos	44221 (100 MP #510)
Dr. Finn	Liver: Deborah Wafer x51645 or Jemel Saffel x51412 Bowyer: Rosa Bishop x57341
Dr. Glaspy (Denise Oseguera NP)	44955 (100 MP #550)

Dr. Hecht	44221 at 100 MP, #510 UCLA or 310/829-5471 or 828-0475 at SM
Dr. Paquette	66931 (200 MP Bowyer Clinic)
Dr. Pinter-Brown	44221 (100 MP #510)
Dr. Ribas	44955 (100 MP, #550)
Dr. Rosove	44955 (100 MP, #550)
Dr. Sadeghi	310/829-5471 or 828-0475 SM or x44955 100 MP #550 UCLA
Dr. Schiller	66931 (200 MP Bowyer Clinic)
Dr. Tap	44955 (100 MP, #550)
Dr. Territo (Carolina Faysman NP)	66931 (Bowyer); Carolina x72868 or pgr 22143
Dr. Timmerman	44221 (100 MP #510)

J-Medicine – Transplant Medicine Service “The Big Picture”

The purpose of this introduction is to provide a general overview of the major classes of patients you will see on the J Med/Transplant service. There are three main classes of patients on J Med: 1) allogeneic transplants (2) autologous transplants and (3) acute leukemias.

Allogeneic Transplants

The goal of an allo-transplant is to establish a new immune/hematopoietic system in the recipient. This procedure is used in situations when the recipient has a primary hematologic malignancy that would preclude the collection of autologous stem cells (such as AML that is refractory to chemotherapy). Increasingly, researchers are aware of the phenomenon that the transplanted immune system may establish an immunologic control against cancers, known as the **GVL** effect (graft vs. leukemia or graft vs. lymphoma). Therefore, allo transplants are also used for malignancies that are incurable with conventional chemotherapy in the hopes of inducing a GVL response. Common situations for this indication include CML, Hodgkins or Non-Hodgkins lymphoma (intermediate or high-grade) that is refractory to conventional and salvage chemotherapy, and low-grade NHL/CLL (which are treatable but not curable with conventional chemotherapy).

One of the dangers of an allo-transplant is the development of acute **graft vs. host disease**. This is an immunologic attack mediated by the new immune system (specifically T-cells) against the host tissues. The main targets of GVH include: liver, (hyperbilirubinemia), skin (rash/exfoliation), and GI (diarrhea/ileus). Allo-transplants are immunologically matched as much as possible pre-transplant in an attempt to minimize GVH and graft rejection. The major histocompatibility antigens (HLA) are used for this purpose. Donor/recipients are tested at the HLA -A,B, and DR loci for compatibility. Unrelated and related donors are available sources for allo donors. Sibling haplo-identical donors (i.e. **a genotype match**) are preferred because of the decreased incidence of severe GVH thought due to minor histocompatibility antigens aside from the HLA loci). Alternatively, a matched unrelated donor (i.e. **MUD**) may be used. Traditionally, allo transplant donors were harvested in the operating room (i.e. a true bone marrow transplant [**BMT**]) with repeated needle aspirations which was a very painful and time-consuming procedure. The current practice is to collect allo donors using growth factors and leukopheresis (i.e. **allo stem cells [PSCT]**).

The allo patients require a specialized level of care and attention. They are typically neutropenic for a prolonged period before engraftment (usually about 3 weeks). They receive multiple medications to prevent GVH (cyclosporine, methylprednisolone, and/or methotrexate). They also receive prophylactic antibiotics against CMV (gancyclovir, IVIG), Pneumocystis (Bactrim), and endogenous flora (“gut sterilizers”). As the counts recover, we watch for the development of GVH rash (esp. hands and behind ears), diarrhea, and hyperbilirubinemia. While GVL is hoped for, GVH is dreaded.

Autologous transplants (AKA: high dose chemotherapy with stem cell rescue)

Autologous transplants are a technique allowing for the delivery of high-doses of chemotherapy (i.e. myeloablative) followed by the infusion of the patient’s own “stem cells” that is reserved for diseases that are chemotherapy-sensitive. Stem cells are collected while the patient is in remission and before admission often by a combination of chemotherapy followed by high dose neupogen (G-CSF) that promotes circulation of stem cells in the peripheral blood. Leukocytes are collected during this period of recovery through leukopheresis and analyzed for the amount of **CD34+** cells (the stem cell marker). This product is frozen. The patient is then admitted to the hospital to receive high doses of chemotherapy +/- radiation (i.e. **conditioning**) followed by stem cell infusion of the previously cryo-preserved product. The patients remain in the hospital until their neutrophil counts recover (usually 8 – 14 days post transplant). There is essentially no risk of GVH in these patients. As the duration of neutropenia and extent of immunosuppression is much less, auto transplants are considerably safer than allo’s. However, because of the absence of the GVL effect, auto transplants are restricted to situations where the underlying disease is considered chemo/radiation responsive and there is no involvement in the patient’s bone marrow. Auto transplants are also used in patients where previous treatment has completely eliminated all evidence of the underlying cancer (often termed a **remission** for leukemia or a **complete response** for lymphoma), but the patient remains at statistically high-risk of relapse. Common indications for auto-transplants include AML in remission, NHL/HD in remission, and multiple myeloma.

Terminology for Transplants

Day of transplant = day 0

Days before transplant = day minus (-) X

Days after transplant = day plus (+) X

Allo-transplants are 5/6 or 6/6 match and either related or unrelated

For presenting patients “Mr X is day minus 2 for a 5/6 unrelated allo -transplant.”

Acute Leukemia

The most common adult acute leukemia is myelogenous (AML). The initial phase in the treatment of these patients is critical. Many patients present with profound cytopenias and/or life-threatening infections. Once the patient is medically optimized, the initial treatment for AML usually consists of a 7 day infusional cytarabine plus 3 days of idarubicin (7+3). The goal of this initial chemotherapy “**induction**” is to get the patient into a “**remission**,” meaning no tumor cells are visible on microscopy of bone marrow biopsy/aspirate and no tumor cells can be detected by flow cytometry. However, remission does not mean cure, because even after remission is achieved by induction chemotherapy, the majority of patients will go onto relapse if no further chemo is given. This is because a small number of leukemic cells remain in the marrow after induction chemotherapy. Thus, after a remission is achieved, patients receive an additional cycle of chemotherapy called “**consolidation**” (usually high-dose cytarabine with mitoxantrone, but occasionally another round of 7+3) and then often receive a third cycle in the form of high-dose chemotherapy followed by an auto-PSCT. If they are not candidates for autologous transplant (because of age or other complicating medical conditions), they will be given a total of 3-4 rounds of consolidation.

Terminology for Chemotherapy

First day of chemotherapy = day 1 (no + or – used)

Mitchell Gross, MD , 6/24/00; Revised Leslie Meserve, MD 6/3/03

Autologous transplant patients

Autologous transplants are used commonly for patients with acute leukemia, multiple myeloma and lymphoma. It is also called “high dose chemotherapy with stem cell rescue” because it allows patients to receive very high doses (myeloablative) of chemo and/or radiation by subsequently replenishing the bone marrow progenitor cells with the patient’s own stem cells collected during remission. So, patients will first be treated with standard chemotherapy and/or radiation for their tumor. When their tumor is in remission (leukemia) or has responded sufficiently (multiple myeloma, non-hodgkins/hodgkins disease), they get neupogen (GCSF) and sometimes cytoxan to stimulate growth/release of stem cells into the peripheral blood and then these are collected from the peripheral blood (by pheresis, prior to their admission to the hospital) or, rarely, by bone marrow collection (almost never done). Then, they get admitted to the hospital and get a “conditioning” regimen that completely ablates their marrow (too toxic / myelosuppressive to give to a patient unless they were going to get stem cells back, or “rescue”). Then, on Day 0, they get their stem cells infused intravenously and these stem cells will find their way back to the bone marrow where they will set up the bone marrow “factory” once again.

Patients need to have an echocardiogram showing an EF>40% prior to getting transplanted. They have to have had BM aspirate/bx or CT scans within 8 wks of admission to show they still have control of their disease.

A. Conditioning Chemotherapy

NHL/HD:

- 1) Cytoxan/BCNU/Etoposide (if patients have received previous anthracycline containing regimen and/or significant radiation)
- 2) TBI/Cytosin/Etoposide (if pt can take more radiation)
- 3) Thiotepa/Mitoxantrone/Cytosin

Acute leukemia: TBI/Cytosin

Myeloma: High-Dose Melphalan

B. Infection Prophylaxis

Antifungal: Nystatin (see neutropenic antibiotic preprinted forms). Some patients may be on a protocol with voriconazole (Drew Winston) and in that case should not be on any other prophylactic antifungal medications.

PCP: Patients with multiple myeloma or any patient with prior history of PCP PNA or any patient receiving steroids get PCP prophylaxis

Bactrim DS TID without leucovorin day of admit thru D-2 then once ANC recovered and plt>20K, restart Bactrim DS TID Sat/Sun with leucovorin x 1mo (duration per pt’s protocol)

If Bactrim-allergic, give Dapsone (100 mg po qd), atovaquone (1500 mg or 10 ml susp qd) or pentamidine (300 mg aerosol. Q mo—arrange with RT)

C. Growth Factors

Auto tx (OTHER THAN AML/CML) get GCSF or GMCSF starting D+3 after transplant. See patient’s protocol.

Allogeneic transplant patients

A. Chemo conditioning:

Patients will get one of the following conditioning regimens prior to their transplant:

- A. TBI/Cytarabine/Cytoxan for patients <40 (total body irradiation, cytarabine 0.5gm/m² iv q12h x 4 Day -5 and -4, and cytoxan 60 mg/kg/d with mesna D-3 and D-2).
- B. TBI/Cytoxan for patients >40 (TBI D-7 to -4, cytoxan 60 mg/kg/d with mesna D-3 and D-2)
- C. High-dose busulfan/Cytoxan for patients of any age (busulfan 0.8 mg/kg iv q6h x 16 doses with dilantin, cytoxan 60 mg/kg/d with mesna d-3 and d-2 (dose 50 mg/kg/dx4d if mismatch))
- D. Busulfan/fludarabine +/-ATG given to patients who were heavily pretreated/older.
- E. High-dose cytoxan/ATG given to patients with aplastic anemia undergoing related 6/6 tx.

*Patients who get **busulfan** conditioning chemo need to be on **dilantin 300 mg ivpb** q day starting with admission until 2 days after busulfan because busulfan infusion is associated with seizures. (Fellow should write for this, just double check)

*Patients who get cytoxan conditioning chemo might get hemorrhagic cystitis (even though mesna given with it). Watch for gross hematuria, change in urine output, etc.

*Patients with Ara-C might get rash, neurotoxicity, and/or conjunctivitis.

B. Infection prophylaxis:

Cytomegalovirus

***CMV negative** -patients get their antibodies checked again on admission to confirm negativity then get all CMV negative blood products (even if their donor is CMV positive!).

***CMV positive transplant recipients:** *Ganciclovir* is given to patients who are CMV antibody positive to protect them from developing active CMV infection while profoundly immunosuppressed.

*6 mg/kg iv over 1 hr q day, start at time of admission (Day-7) to Day -2 and then hold until after bone marrow has recovered because ganciclovir can be myelosuppressive and we want the stem cells to thrive in the marrow.

*Restart when ANC >1000 x 3 days, give 5 days a week IV thru D+100 (watch for recurrent neutropenia after starting ganciclovir). If ANC drops to <1000, decrease to 6 mg/kg/day x 3 days/week and start GCSF. If ANC persists <1000, decrease to 3 mg/kg/day x 3 days/week and start GCSF.

PCP

*Trimethoprim 160 mg/sulfamethoxazole 800 mg (2 amps iv) tid without leucovorin given on admission thru day -2.

*Stop D-1 because of concerns of myelosuppression.

*Posttransplant - start Bactrim DS po tid Qsat/sun with leucovorin 5 mg po qSat/Sun when ANC>1000 x 3 consecutive days and continue 2 wks after all immunosuppression has stopped.

*If Bactrim-allergic, give Dapsone (100 mg po q day), atovaquone (1500 mg or 10 ml susp q day) or pentamidine (300 mg aerosol. q month—arrange with RT)

Fungal

***Itraconazole:** Given iv q12 x 2 days then 200 mg iv q day starting D+1 post transplant until at least Day +100. Can switch to po when tolerating po's. Use suspension rather than pills (pills poorly absorbed). Given with coca cola if on PPI to ensure proper absorption. *If patient on special protocol/research study (voriconazole, etc), may not receive this.

C. GVHD Prophylaxis

Cyclosporine

- Given to **all** allogeneic patients (including non-myeloablative or “mini-allo”) as immunosuppression to prevent graft-versus-host disease.
- Start as loading dose 3mg/kg iv over 12 hours on Day -2, then as continuous 3mg/kg/day iv starting Day -1.
- Level to be checked Day +1, +4 then weekly

- Switch to po after 21 days if patient taking food and po meds. PO form is **Neoral**. Dose is two times the iv dose, divided into two doses a day (BID). (So if patient was on 250 mg iv q day, they would convert to Neoral 250 mg po q12h.)
- Once oral started levels should be checked days 2 and 7 after starting.
- Goal level is 150-350.
- Toxicity of cyclosporine includes renal toxicity, hypertension, tremor, liver toxicity, nausea, headache, diarrhea.
 - Less commonly but still significant: seizure and rash. There can also be drug-drug interactions, so check.
- Pts get cyclosporine 3-12 mos, depending on a variety of factors
 - If related 6/6 match, get 6 mos then taper weekly
 - If unrelated or mismatched, get one year then taper if no GVHD.
 - ****watch closely for GVHD when tapering****

IVIg

- Given to **all** allogeneic patients (including non-myeloablative or “mini-allo”)
- 0.5 gm/kg ivpb q week Day +100 starting on day of admission. Then will give monthly for 1 year. Infusion should be started at 50 cc/hr x 30 mins; then, if stable VS, increase to 75 cc/hr x 30 mins. If no problems, increase to 125 cc/hr until end (RNs on 10th floor know this, no need to write in order)
- This is for GVHD prophylaxis but theoretically also helps patients who will become hypogammaglobulinemic during transplant course...so might help with infection prophylaxis

Solumedrol

- Given to allogeneic patients who are **≥40** years old OR have **mismatched** donor (meaning less than 6/6 match) OR have **unrelated** donor OR **aplastic anemia patients**. Discuss with attending whether to use in non-myeloablative (mini-allo) transplant patients.
- To prevent severe graft-versus-host disease.
- Starts Day +3 (1mg/kg/d ivpb) and continues at same dose until Day+30. Tapered then if no GVHD - usually as follows:
 - Day +43 to +56, give 0.5mg/kg/d
 - D+57 to D+100 give 0.3 mg/kg/day then taper over 1 month
- If Grade II GVHD develops in a Matched Sibling transplant or if GVH worsens on one of the above steroid regimens give 2mg/kg q day Solumedrol until improvement.

Methotrexate

- Given to allogeneic patients who are **≥40** years old OR have **unmatched** donor (meaning less than 6/6 match) OR have **unrelated** donor OR **CML patients in chronic phase** or **aplastic anemia** Not used in non-myeloablative allogeneic (mini-allo's) patients.
- To prevent severe graft versus host disease.
- Starts 24 hours after last stem cell infusion. Given three times (D+1, +3, +6). Methotrexate 15 mg/m² on day +1 (given at least 24 hours after the completion of the stem cell infusion) and 10 mg/m² on days +3 and +6.

Prophylaxis for all J patients

A. Gut Sterilizers/Neutropenic Precautions

*Given routinely to allo and auto transplant patients starting day of admission

Norfloxacin 400 mg po bid

Clotrimazole troche 10mg dissolve in mouth QID

Nystatin tab 1 MU po QID

Nystatin pwdr to groin, axillae and skin folds TID

(see prewritten antibiotic order sheet).

*Exception: no Clotrimazole/Nystatin if on antifungal prophylaxis protocol (Dr. Winston's protocol).

Also, put patients on *low bacterial diet* and make sure *hepa-filter* is on in their rooms when neutropenic.

B. Blood products

*Patients need to be consented for blood products on day of admission.

*Should all be *irradiated* and *leukocyte-reduced*.

*If patient is CMV negative and has any chance of getting allogeneic transplant in the future, give only CMV negative blood products (even if donor is CMV+). If CMV status unknown, order CMV negative products and order CMV IgG.

*Patients exposed to IVIG may have +CMV Ab test even if they have not been exposed to CMV. Discuss use of CMV negative blood products in these patients with attending/fellow

*For allogeneic transplants, if patient and donor are not ABO-matched, discuss this on rounds with the attending and fellow to determine if special monitoring for hemolysis will need to occur. Patients who are ABO-mismatched should get type O blood for all RBC transfusions starting on admission.

*In general, transfuse 2U PRBCs when Hb <9.0

*In general, transfuse platelets when count is:

<10,000 always (except in cases of transfusion-refractoriness, then discuss with attending)

<20,000 and febrile

<50,000 and bleeding or undergoing invasive procedure

C. TPN

TPN is to be given to patients who cannot maintain 25% of necessary caloric intake for three consecutive days (excluding time period during chemo administration) and unlikely to resolve within 7 days. Decision should be made during rounds with attending.

D. Bleeding prophylaxis

Norlutate (norethindrone) 10 mg po q day starting with day of admission in all menstruating females to avoid bleeding during profound thrombocytopenia. Can be stopped when plts self-maintained over 50K. Patients who are already maintained on other hormonal suppression medication (non-cyclical) can be continued on that medication (i.e. Tamoxifen).

Vitamin K: 10 mg po once a week given; however, patients will usually be on antibiotics and likely will have poor po intake. Instead, vit K can be given subcutaneously or put in TPN if problem with po's. Once they start iv abx, the dosing should increase to three times a week.

E. Tumor lysis prophylaxis

Allopurinol 300 mg po qd given on day of admission if pt has active tumor and stop D-1. Also give in patients with large tumor burden who are starting induction chemotherapy (to be discussed with fellow/attending)

F. Growth Factors

• Refer to specific protocol for patient in chart.

• Generally, do not start until 24 hours after chemo

*Allogeneic patients do not receive routinely, but may be put on either GCSF if PMN<50 by Day+20 or <500 by Day +28.

*Auto lymphoma/myeloma patients will receive GCSF post transplant

*Auto AML will NOT routinely receive GCSF

*Acute lymphoblastic leukemia patients may receive GCSF as part of induction regimen

*Pre-autologous stem cell harvest patients will receive GCSF to stimulate the release of stem cells into peripheral blood. Will usually start GCSF as they are being discharged from hospital after consolidation chemo, and will take at home.

- Can be given IV or SQ

*GCSF (neupogen) 5 mcg/kg sq/ivpb over 30 mins q day (round to 300 or 480)

*GMCSF 250 mcg/m² sq/ivpb over 2 hours q day

*Neulasta 6 mg SQ 24 hr after chemo (not given in transplant pts, usually need to give in clinic as not approved for hospitalized pts.) Cannot give less than 14 days prior to next chemotherapy.

G. Mucositis

Cocktail:

Benadryl elixir 25 mg/10 ml

Maalox ES 10 ml

Lidocaine viscous 2% 10 ml

Mix together and have patient swish and spit OR swish and swallow q4hr prn mouth pain

PCA:

When mucositis becomes severe, patients might not be able to even swallow their own saliva. A PCA pump should be started using either dilaudid or morphine. See order forms.

Complications of Therapy

A. Hepatic Venous Occlusive Disease (VOD)

VOD is thought to begin with injury to the hepatic venous endothelium. Signs/symptoms include hepatomegaly, right upper quadrant pain, jaundice, and ascites, most often occurring in patients undergoing stem cell transplant; but, VOD can be seen after chemotherapy in non-transplant settings. It resembles the Budd-Chiari syndrome clinically; however, hepatic venous outflow obstruction in VOD is due to occlusion of the terminal hepatic venules and hepatic sinusoids rather than the hepatic veins and inferior vena cava.

Clinical and laboratory features of veno-occlusive disease usually begin within the first three weeks after transplant. Symptoms can be mild, moderate or severe (life-threatening). Increases in bilirubin usually occur after weight gain and hepatomegaly. Patients with severe disease often develop confusion, bleeding, and renal and cardiopulmonary failure. Liver tests in patients with VOD usually reveal an elevation in AST/ALT/DBili. In severe disease, an elevation in the INR may be present.

Possible risk factors for developing VOD:

- Preexisting liver disease (hepatitis, etc)
- Specific types of conditioning therapy prior to transplant (XRT>13 Gy, non fractionated XRT; drugs including busulfan, Ara-C, cytoxan)
- Use of certain abx during transplant (ampho, vanco, acyclovir)
- Allo transplant (compared to auto), mismatched/unrelated (compared to matched/related)
- Abnormal lung diffusing capacity (independent risk factor for VOD..might indicate preexisting systemic endothelial damage)
- Female gender (possibly due to use of progesterone)
- Other drugs: Cyclosporine/methotrexate

Treatments: Not a lot so far. Looked at Heparin and TPA but high risk of bleed. Also looked at Defibrotide, an adenosine receptor antagonist derived from mammalian tissue with multiple antithrombotic and fibrinolytic activities. Being tested and might have a therapeutic advantage over the use of tpa/heparin.

B. Acute Graft-Versus-Host Disease

Clinically significant acute graft-versus-host disease (GVHD) occurs in 9 to 50 percent of patients who receive an allo transplant from a 6/6 matched sibling, despite intensive prophylaxis with immunosuppressive agents. It is also common in matched unrelated donors. Risk factors include:

- HLA mismatch
- Increasing age
- Donor and recipient gender disparity
- Type and status of underlying disease
- Amount of radiation delivered
- Doses of methotrexate and cyclosporine or tacrolimus

Development of moderate (grade II) or severe (grade III or IV) acute GVHD after HCT is associated with a significant decrease in survival. Furthermore, once GVHD occurs, it may not be treatable.

The principal target organs in patients with acute GVHD are skin, liver, gastrointestinal tract, and the hematopoietic system.

- Usually **skin** is 1st sign of acute GVHD: a maculopapular rash, usually occurring at or near the time of the white blood cell engraftment (check nape of the neck, ears, shoulders, the palms of the hands, and the soles of the feet). It can be described as a sunburn and may be pruritic. In severe GVHD, the rash forms bullous lesions with toxic epidermal necrolysis.
- **Liver** is the second most commonly involved organ in acute GVHD. Rarely, patients have moderate to severe hepatic GVHD without evidence of cutaneous disease. Manifested by abnormal liver function tests (earliest and most common finding is rise in D bilirubin and alkaline phosphatase). Pathology associated

with liver GVHD is damage to the bile canaliculi, leading to cholestasis. Can be tough to distinguish btw this and VOD vs. hepatitis vs. chemo/drug toxicity. A biopsy is the most definitive method to diagnose GVHD of the liver. A transjugular hepatic biopsy usually preferred b/c of bleed risk. Pathology usually shows extensive bile duct damage with lymphocytic infiltration of small bile ducts, leading to occasionally severe cholestasis.

- Involvement of the **GI tract** with acute GVHD is often severe, and is characterized by diarrhea and abdominal cramping. The severity of gastrointestinal involvement is determined by the volume of diarrhea, which can occasionally exceed 10 liters per day. Maintenance of adequate fluid balance may be extremely difficult in such patients. The diarrhea may initially be watery, but frequently becomes bloody. Again, tough to distinguish diarrhea from chemo toxicity, abx reaction, C dif etc. Rectal bx might be helpful +/- colonoscopy. Upper GI GVHD can also occur, causing anorexia, dyspepsia, nausea, and vomiting. Distinguish from CMV and other infections/pathology by endoscopy.
- Although less common, acute GVHD can affect the **hematopoietic** system (lymphoid, plts,) leading to frequent and possibly fatal infectious complications.

Grading: Patients are graded I-IV based on severity and this helps assess response to prophylaxis/treatment and prognosticate.

Grade	Skin	Liver	GI
0	None	None	None
1	Maculopapular Rash < 25% BSA	Bilirubin 2-3 mg/dl	> 500 ml diarrhea/day
2	Maculopapular Rash 25-50% BSA	Bilirubin 3-6 mg/dl	> 1 L diarrhea/day
3	Generalized Erythroderma	Bilirubin 6-15 mg/dl	> 1.5 L diarrhea/day
4	Generalized Erythroderma with bullous formation and desquamation	Bilirubin > 15 mg /dl	Severe abdominal pain with or without ileus

Overall GVHD Staging

Stage

1	Grade 1-2 skin; no gut, no liver, no decr clinical performance
2	Grade 1-3 skin; grade 1 gut or grade 1 liver (or both); mild decr clin performance
3	Grade 2-3 skin; grade 2-3 gut or 2-4 liver (or both); marked decr clin performance
4	2-4 organ involvement and extreme decr in clinical performance

Therapy involves immunosuppression with agents such as intravenous solumedrol (2-2.5 mg/kg/d), ATG, Cellcept, Tacrolimus, Pentostatin. Therapy to be determined by attending(s).

C. Emergency: Neutropenic Fever

The quickest killer in the J service patients (especially in neutropenic patients) is **GRAM NEGATIVE SEPSIS**. It needs to be identified early and treated promptly!!! Make sure antibiotics are hung within the hour, not just ordered.

When a neutropenic patient spikes a fever over 38.5 (or if they are not yet febrile but are starting to look ill...chills, sweats, rigors, altered mental status, dropping blood pressure, tachycardia, or tachypnea) **examine** them and then get blood cultures for bacteria and fungus, UA, urine cultures, CXR and treat them with:

- **Imipenem** 500 mg ivpb q6hr
(if PCN allergy, can use **Aztreonam** 1 gm IV q 8 hrs)
- **Gentamicin** if patient looks very septic (call pharm for dosing: generally 1-2 mg/kg q8-12 hr, adjust if reduced Cr clearance) Check levels - goal is peak of 8 and trough<1
- **Vancomycin** 1 gm IVPB q12hr, if line is suspected as source of fever (d/c in 3 days if no evidence of gram + infection)

Empiric Antifungal Therapy: usually added if patient continues to spike after 5 days on Imipenem. Discuss with heme fellow/attending and/or Drew Winston (ID attending for transplant patients). Give Fluconazole, Voriconazole, Itraconazole, Caspofungin, ABLC according to patient's protocol and patient's particular situation

D. Emergency: Tumor Lysis Syndrome

Telltale Signs: Hyperphosphatemia, hypocalcemia (due to precipitation of calcium phosphate), hyperuricemia, hyperkalemia, and acute renal failure. LDH levels are used as a marker for the degree of tumor lysis. Acute uric acid nephropathy is almost always oligoanuric with no symptoms in urinary tract.

Tumor Types Associated: Poorly differentiated lymphomas (Burkitt's lymphoma) and leukemias (acute lymphoblastic leukemia and less often acute myeloid leukemia). Also described in multiple myeloma among other cancers.

Timing: May occur spontaneously, after beginning steroids or after combination chemotherapy started.

Differential Diagnosis: Other causes of acute renal failure, including tumor-related urinary tract obstruction, hypercalcemia, infection, drug reaction, etc.

Prophylaxis: Patients with tumors with rapid cell turnover should be *pretreated* for at least two days with allopurinol (300 mg bid to tid) plus fluid loading (with saline) to maintain a high urine output (greater than 2.5 L/day).

Treatment: Hydration, allopurinol and rapid dialysis. Renal fellow should be notified at the first sign of tumor lysis syndrome, as should heme/onc fellow on-call. The prognosis for complete recovery is excellent if treatment is initiated rapidly.

Solid Oncology: The Big Picture

The solid oncology service is essentially very much like general medicine for patients with cancer. Common reasons for patients to be admitted include: pain management, chemotherapy administration (that can't be given as an outpatient such as high dose therapies for CNS lymphoma and sarcomas and infusional regimens for lymphomas), post-procedure management of patients who have had radiofrequency ablation or chemoembolization for their liver tumors, monitoring of patients receiving high dose Il-2 for melanoma or renal cell carcinoma, palliation and end-of-life care with placement issues, neutropenic fever, DVT/PE, cord compression, hypercalcemia of malignancy and pre/post-operative cancer patients (for example, patient's who have had small bowel obstruction surgery as a complication of their GI malignancy).

In general, any patient with active cancer who has an oncology attending at UCLA (in the Dept of Med, Division of Heme/Onc) can and should be admitted to this service (unless they have acute leukemia or are a pre or post- transplant patient, in which case they go to J).

The following sections will review the management of patients who are receiving Il-2 (probably a dwindling population in the coming months and years, given newer therapies that are becoming available for patients with renal cell carcinoma) as well as patients who are admitted from the Neuro-oncology team for management of complications due to their brain tumors, or for high dose chemotherapy (CNS lymphoma).

Interleukin 2 Guidelines

IL2 cytokine therapy is used in the treatment of metastatic renal cell carcinoma and metastatic melanoma. This therapy is aimed at stimulating the patients immune system to destroy the malignancy by administering a large volume of interleukin 2

A course of high dose IL-2 consists of 2 cycles with 2 treatments in each cycle. Approximately 10 days of rest between each treatment. Each treatment has a potential of 14 doses of IL –2 (600,000 IU/kg) given over 15 minutes q 8 hours over 5 days. Patients will have 1 cycle of 2 treatments and be re-evaluated for response. If disease is stable or has responded, the patient will continue for the 2nd cycle (4-6 weeks after 1st cycle).

IL – 2 therapy has many expected toxicities or side effects that must be managed by the nursing staff and the solid oncology fellow. These guidelines will act as a resource when administering this therapy. In general, treatments become harder with later cycles/treatments. Doses may be skipped for lab abnormalities, vital sign abnormalities and symptoms as delineated below. No dose is made up.

INTERNS AND RESIDENTS ARE NOT RESPONSIBLE FOR (NOR ALLOWED TO) REPLETING ELECTROLYTES OR MANAGING FLUIDS. SOLID ONCOLOGY FELLOW MUST BE CONTACTED FOR ORDERS REGARDING ELECTROLYTE REPLACEMENT, ALTERATIONS IN VITALS, ETC. INTERNS MAY SEE PATIENT IN THE MORNING AND WRITE SOAP NOTE, BUT MAY NOT WRITE ORDERS.

Administration of IL – 2 procedure (for nurses and housestaff)

Prior to hospital admission

- Placement of tunneled catheter will be done.
- Cardiac (Dr Hamilton's group) and pulmonary (Dr. Levine) consultations will occur.
- Patients not allowed if brain mets, ECOG>1, seizure history, recent infections or steroids

On admission

- Nurse to determine if placement of a PICC is needed.
- Pt placed on cardiac monitor for whole hospitalization
- Baseline vital signs including pulse ox and weight checked. If a patient has a cardiac history, order a 12 lead baseline EKG.
- Procedure, monitoring equipment, and side effects explained to patient and family. Family member instructed regarding their role in assisting the patient (e.g.- For chills - call RN, apply warm blankets. For fevers – cooling measures using tepid water and washcloths).
- Prophylactic meds and antibiotics given.
- Fellow to sign order set for IL-2, review labs or order labs as appropriate

Monitoring while patient on IL – 2

- Continuous cardiac monitoring with VS q1 hr post initiation of IL – 2.
- Pulse ox q shift after initiation of IL – 2
- Daily weights (preferably at the same time of day) and Strict I/Os recorded q2 hours post initiation of IL – 2. Patient must maintain an hourly output of >25 cc hour. Patient is strongly encouraged to drink a minimum of 50 – 100 cc /hour/day (when aware) IV fluid is kept to a minimum. (IL-2 causes total body fluid overload, but pts are intravascularly depleted so can become hypotensive. Don't give IVF. Use neo/dopa.
- Daily labs include CBC, diff, plt, lytes, BUN, Cr, Tbili, AST/ALT, and Mg to be drawn in time to have the results for the 8 AM dose. Labs (Cr, Mg, K, and any other abnormal labs such as platelets or Na) will be drawn q 8 h.
- Procedure for the administration of IL – 2
 - Dosage calculation based on admission weight. Subsequent cy doses based on original wt
 - IL – 2 doses are given at 0800, 1600 and 2400. Fellow is contacted 2 hours prior to next dose to discuss lab values, I & O, VS. mental status.
- Pts premedicated with
 - Tylenol 650 mg 30 minutes prior to 1st dose then q4 hours ATC.
 - Benadryl 50 mg prior to each dose and prn pruritis
 - Start Neo 40 mcg/min & titrate to max of 200 mcg/min. Fellow contacted if tachy (>160)
 - If unable to sustain SBP \geq 90 mm/hg, start Dopa 2mcg/kg/min. Titrate to SBP > 90. Max 10 mcg/kg/min.
 - Trental 400 mg PO on admission then q4h. Consider premedication with anti-emetics.
 - Cipro 500 mg PO on admission then BID.

COMMON TOXICITIES / SIDE EFFECTS OF INTERLEUKIN-2 ADMINISTRATION

REACTION	ONSET	ROLE OF MEDS	INTERVENTION
Chills	Immediate or delayed	Stop rigors ↓ heart workload	Premedicate prior to each dose of IL-2 with Tylenol and Benadryl. For chills: Warm blankets 25-50 mg Demerol
Fevers	Approx 2 hours after dose	Antipyretic (Tylenol, Indocin)	T>38.5 use cooling measures, Tylenol continues q4h ATC
Pruritis Red Man syn. with hand/foot desquamation	May start as early as D 3, usually after D 7		Benadryl ATC as ordered
Diarrhea	After D 5 -7	Anti-diarrheal	Lomotil Tincture of Opium
Nausea Ataxia Taste Changes	Starts w/1 st dose getting worse with each treatment	Anti-emetic	Kytril 1 mg q 12 hr PO or 10 mcg/kg IV Ativan Compazine
Hypotension	2 – 4 hours post start of IL-2		Initiate Neosynephrine prior to first dose. If unable to maintain SBP ≥ 90, initiate Dopamine per order
Shortness of Breath O ₂ Desat 2° to fluid collection in the lungs	At any time		
Altered Mental Status/behavior		Anxiolytic	Ativan
Fluid Retention and weight gain			Weigh daily Accurate I & O
Laboratory Data: ↓WBC, ↓lymphos ↑eos, ↓Hb ↓plt, ↓Mg, ↑Cr/ BUN ↓HCO ₃ ↓Na TSH ↓ or ↑ ↑Glucose			Replace K if < 4.0 Replace Mg if < 1.0. No transfusions during IL-2 tx!

Guidelines for when to administer dose

Mental Status

- ✓ Patient is alert and easily arousable.
- ✓ Patient is oriented to person, place and reason for hospitalization.

Vital Signs

- ✓ EKG in normal sinus rhythm or sinus tachycardia
- ✓ HR >60 bpm and <135 bpm
- ✓ RR >12 and <24
- ✓ SBP >90 and DBP >40 with Dopamine <5mcg and/or Neo <100mcg
- ✓ O2 saturation WNL (can be on supplemental O2)
- ✓ Temperature <38C

Lab Values

- ✓ Cr. <3.5mg/dl if patient voiding 100cc/4hrs or <3.0 if not voiding
- ✓ Plts >50,000K
- ✓ K+ >3.8 & <5.5 meq/l
- ✓ Mg >0.8mg/dl
- ✓ T-bili <3.0mg/dl
- ✓ HCO3 >17

Output

- ✓ Urine output >100cc q4hrs
- ✓ Controlled nausea and vomiting
- ✓ Controlled diarrhea

Neuro

- ✓ Patient denies hand or digit nerve pain.

Judgment

- ✓ Is your clinical judgment to administer this dose?

Solid Oncology: Liver Procedures

A. Radiofrequency Ablation (RFA)

RFA is performed on patients with hepatocellular carcinoma usually with lesions ≤ 3 cm, but can be performed in lesions up to 5 cm in size. This procedure is performed at UCLA by either Dr. Steve Raman or Dr. David Lu. Patients are admitted to the Solid Oncology team with pre-printed orders, mostly for pain and nausea/vomiting monitoring. Otherwise patients are discharged home by interventional radiology 3 hrs post procedure if no symptoms. The typical orders are:

- Analgesia:
 - Mild Pain 1-4/10 Tylenol 650 mg q4hrs
 - Moderate Pain 5-6/10 Vicodin 5mg/500mg q4hrs
 - Severe Pain - team is called. Either try other orals or if necessary PCA
- Prophylactic Antibiotics to complete a 7 day course:
 - Cipro 500 mg IV q12, change to PO on D/C
 - Flagyl 500 mg PO TID

Prior to D/C, next day post procedure, patient needs a “CT Scan with IV contrast only, NO po contrast, Dual phase liver protocol.” This scan is to be reviewed by IR to assess appropriate ablation, no e/o residual tumor and no complications (e.i. hemorrhage).

If pain is controlled, patient is tolerating p.o. intake and afebrile, patient can be discharged home next day with follow-up typically with Dr. Finn, Britten or Sadeghi (whomever has seen the patient as an outpatient). Prior to discharge, you can touch base with the IR fellow or attending to make sure they concur with d/c home plan.

B. Chemoembolization

Management of patients is essentially the same as for patients with RFA (above). The main difference is that the patients' LFTs (ALT, AST, Alk phos, Bili) must be checked daily along with CBC (to rule out GI Bleed). The patient cannot be sent home until the LFTs are trending downward. Pain management is the same as above, and patients generally go home on antibiotics as above. The fellow who has performed the procedure will write admission orders to solid onc. You can touch base with that fellow or directly with the attending, Dr. Gomes prior to discharging the patient as sometimes they request that imaging be done (MRI of liver) prior to D/C home.

Neuro-oncology

- Attending Neuro-Oncologists
 - Tim Cloughesy, MD (Program Director)
 - Albert Lai, MD, PhD
 - Leia Nghiemphu, MD
- Neuro-Oncology NPs
 - Carrie Graham, MSN, NP (Follows clinical trial pts)
 - Mady Stovall, MSN, NP
 - Nanette Fong, MSN, NP
- Contact #s
 - Main Office 310-825-5321 (asst: Dan Gamboa)
 - Outpt Oncology Center Scheduling (Leo) 206-9260
- Common Referrals:
 - Radiation Oncology – Michael Selch sees majority of primary brain tumors (can page radiation oncology fellow & request that Dr. Selch consult on a patient)
 - Neurosurgeons
 - If patient has been previously seen by specific neurosurgeon, that neurosurgeon should be contacted for any surgical issues
 - Neurosurgeons that most commonly see brain tumor patients
 - Marvin Bergsneider, MD
 - Linda Liao, MD, PhD
 - Donald Becker, MD (on sabbatical)
 - Neil Martin, MD
 - Daniel Kelly, MD
- Most common reasons NeuroOnc patients present to ER/unscheduled admission
 - Acute change in mental status
 - Order MRI brain with & without gadolinium (CLOUGHESY PROTOCOL)
 - Initiate/increase dexamethasone to 10mg q6hrs until MRI done & evaluated
 - Also evaluate for other sources of MS changes:
 - Infection, electrolyte abnormalities, hyperglycemia, subclinical seizures, thrombotic event (PE/DVT)
 - DVT/PE
 - Venous thrombotic events seen in higher frequency in primary brain tumor population (>20%)
 - Order venous duplex ultrasound & spiral CT (as appropriate)
 - If positive, check recent brain imaging to assure no evidence of recent hemorrhage
 - Contraindications to anticoagulation: recent hemorrhage; less than 14 days postop
 - Otherwise, OKAY TO INITIATE ANTICOAGULATION in primary brain tumor pts
 - Preferred regimen: Initiate Lovenox & then convert to Coumadin (target INR 2-2.5)
 - NO HEPARIN BOLUSES
 - Notify Neuro-Oncology Team if need for follow-up on anticoagulation postdischarge/Instruct pt or arrange homecare to check PT/INR prior to discharge
 - Palliation
 - Evaluate sources of mental status change/neuro decline prior to automatically initiating palliative care/hospice
 - Preferred hospice agencies: Rozerom, Cedars Hospice, Trinity Hospice
- Most common scheduled admissions:
 - Admission for primary CNS lymphoma patients to receive high dose methotrexate
 - See attached sample chemo order
- General recommendations for seizure management
 - Acute management
 - Ativan 1mg IV. May repeat as necessary up to 8mg within 24 hours or onset of respiratory depression.
 - If seizures persist, can call neuro-onc attending or call a neuro consult for further assistance
 - Following seizure activity:
 - Check anticonvulsant levels if appropriate (dilantin, tegretol, phenobarb, valproic acid)
 - If subtherapeutic levels, increase dosages appropriately
 - If pt not previously on anticonvulsants, prefer to initiate Keppra 500mg PO BID for 3-5 days, then increase to 1000mg PO BID ongoing
 - Preferred prophylactic regimen: Keppra 500mg PO BID for 3-5 days, then increase to 1000mg PO BID ongoing

- We try to avoid traditional enzyme -inducing antiseizure meds (i.e. dilantin, phenobarb, tegretol) due to multiple drug interactions
 - YOU CAN ALWAYS PAGE NEURO-ONC TEAM FOR SPECIFIC CASES (these are general guidelines)
- Research study/Clinical Trial Patients
 - PLEASE PAGE CARRIE GRAHAM, NP #93294 OR DR. TIM CLOUGHESY #11422 ASAP IF PT ADMITTED TO HOSPITAL.
- Upfront treatment for GBM:
 - Tissue diagnosis (biopsy or resection)
 - Conformal radiation therapy (6000cGY)
 - Concurrent Temodar 75mg/m² daily while pt on radiation (need to give bactrim for PCP prophylaxis)
 - Post XRT: Adjuvant Temodar 150-200mg/m²/day, Days 1-5 of a 28 day cycle (repeated up to 24 cycles, MRI scans every 4-8 weeks)
- Upfront treatment for Grade 3 Gliomas (Anaplastic Astrocytoma, Anaplastic Oligo, Anaplastic Mixed Gliomas):
 - Tissue diagnosis (biopsy or resection)
 - Conformal radiation therapy (6000cGY)
 - NO concurrent Temodar during XRT
 - Post XRT: Adjuvant Temodar 150-200mg/m²/day, Days 1-5 of a 28 day cycle (repeated up to 24 cycles, MRI scans every 4-8 weeks)
- Call Schedule:
 - Weekends: 1 of the 3 attendings is on-call and available 24hrs
 - Weekdays: All 3 attendings available by pager

UCLA Medical Center
Chemotherapy Order Form

- All parenteral and oral antineoplastic agents must be ordered on this form.
- Orders for chemotherapeutic agents must be received in pharmacy at least four hours prior to first dose.

Addressograph

Section 1: Patient information – Complete all information requested

Diagnosis Primary Central Nervous System Lymphoma

Allergies _____

Cycle # _____

Regimen or HSPC # _____ ? HSPC signed consent is in patient chart

Height (cm) _____ cm Actual Weight _____ kg Ideal Weight _____ kg Dosing Weight (kg) _____ kg Dosing BSA (m²) _____ m²

Section 2: Hydration and premedications – Include doses, routes, and start times

A. Hydration	D5W + 10 mEq KCl/L + 50 mEq NaHCO₃ @ _____ ml/hr					
	Please start IVH within 1 hour of admission. Use Port-A-Cath for infusion of IVH and chemo. Initial IVH rate based on 2.5L / m ² / 24-hours					
	If urine pH < 7 after 4 hrs of hydration, notify HO to increase D5W+10mEq KCl/L+100mEq NaHCO ₃ @same rate.					
B. Premedications	Dose (mg)	Route	Frequency	Duration	Special instructions	Start time
Granisetron (Kytril)	1 mg PO 30 minutes prior to MTX and continue every 12 hours for a total of 6 doses _____ to _____					
Aprepitant (Emend)	125 mg PO on day 1 (_____) of chemotherapy only					
Aprepitant (Emend)	80 mg PO on day 2 (_____) and day 3 (_____) of chemotherapy only					
Prochlorperazine (Compazine)	10 mg PO every 4 hours PRN nausea or vomiting while hospitalized					
Lorazepam (Ativan)	1 mg PO / IV every 4 hours PRN nausea, vomiting, or anxiety while hospitalized					

Section 3: Antineoplastic agents

Chemotherapy Drug	Dosage = Dose mg/kg or	Administration guidelines	Route	Frequency, dates, duration of therapy	Start time:
METHOTREXATE	8 grams/ m² = _____ grams IV in D5W 500 ml to infuse over 4 hours on				Start time: _____
	Methotrexate to be reconstituted with preservative free water. Administer MTX when urine output >= 100 ml/hr and urine pH >7 for 4 consecutive hours.				Stop time: _____
	Record start and stop time of MTX.				

Section 4: Supportive Medications

Medication	Dose (mg)	Route	Frequency	Duration	Special instructions	Start time
NaHCO₃ tablets	3 grams PO every 4 hours (while awake) beginning on _____ to be continued until MTX levels are less than 0.05 uM/L. Take NaHCO₃ tablets with 10 oz water.					
Leucovorin Calcium	25 mg IV / PO every 6 hours to begin 24 hours after completion of MTX infusion.					
G-CSF (Neupogen)	300 mcg or 480 mcg SQ for 7 days, beginning _____ (at least 24 hours post completion of MTX)					

Section 5: Special instructions and treatment parameters

Draw CBC with PLT & Diff, AST, ALT, AlkPhos, Creatinine, BUN, T. Bili, potassium, magnesium on admit and with daily A.M. labs.

Draw MTX level DAILY with A.M. labs.

Maintain strict I&O and measure urine pH on ALL urine collections.

Avoid use of NSAIDs, aspirin, and aminoglycoside antibiotics.

Timothy Cloughesy 11422

UCLA Medical Center Chemotherapy Order Form
1. All parenteral and oral antineoplastic agents must be ordered on this form. 2. Orders for chemotherapeutic agents must be received in pharmacy at least four hours prior to first dose.

Addressograph

Diagnosis	<u>Primary Central Nervous System Lymphoma</u>
Allergies	_____
Cycle #	_____

Section 6: Treatment Parameters

Leucovorin Rescue Schedule

Methotrexate Level

Leucovorin Dosage

24 hrs post initiation of Leucovorin
(48 hrs post COMPLETION of MTX)

Date/Time: _____

MTX Level ≥ 10 uM/L - - - - - Give 100 mg IV every 6 hours until MTX level ≤ 0.1 uM/L

48 hrs post initiation of Leucovorin
(72 hrs post COMPLETION of MTX)

Date/Time: _____

MTX Level ≥ 1 uM/L - - - - - Give 100 mg IV every 6 hours until MTX level ≤ 0.1 uM/L
 MTX Level ≥ 2 uM/L - - - - - Give 200 mg IV every 6 hours until MTX level ≤ 0.1 uM/L

72 hrs post initiation of Leucovorin
(96 hrs post COMPLETION of MTX)

Date/Time: _____

MTX Level > 0.1 uM/L - - - - - Give 200 mg IV every 6 hours until MTX level ≤ 0.1 uM/L

**** Patient can be discharged when MTX level ≤ 0.2 uM/L.**

****Patient MUST continue to take supportive medications on schedule after discharge.**

****Supportive medications (Sodium Bicarbonate & Leucovorin) MUST be continued at home until MTX level ≤ 0.1 uM/L.**

Please contact the Neuro-Oncology Service prior to patient discharge (310.825.5321)

_____ Date/Time	Timothy Cloughesy Print Attending Physician Name	_____ Attending Physician Signature	11422 UCLA ID#
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Palliative Care: Communication

Palliative Care is the active total care of patients whose disease is not responsive to curative treatment (chronic progressive diseases or serious life-limiting illnesses). Our mission is to partner with patients and their families to help them define and achieve realistic goals to optimize quality of life. Palliative Care is related to hospice care, but is broader in concept. Unlike the usual paradigm of hospice care, Palliative care can occur alongside and in partnership with standard disease-directed treatment.

Palliative Care is NOT restricted to those who are dying or those enrolled in hospice programs, although palliative care does provide exemplary end-of-life care. Palliative care, because it can be given alongside standard medical management of disease, can reach patients earlier than hospice care, improving their quality of life.

If palliative care is consulted, please be as specific as possible regarding the reason for the consult. If goals of care are to be discussed, then communicating both the doctor's and the patient's understanding of the prognosis and current treatment plan is best included in a brief note.

COMMUNICATION - Bad news Conversations

1. PLAN – Gather specific data, include social work, spiritual care, and close family members
2. SIT – eye level – calm voice – unrushed speaking tempo
3. INTRODUCTION of all people present
4. PURPOSE of the meeting is explicitly stated:
 - Physical care – Prognosis, healthcare planning, Setting of care
 - Social care – Family and Financial issues
 - Emotional care - Support
 - Spiritual care – Meaning
5. PERMISSION to speak about this topic–Does the patient/family want others present for this discussion
6. INSIGHT - ASK the patient and family for their understanding of medical situation.
7. PAUSE to give opportunity to for a full response
8. PERMISSION How much do they want to know?
9. WARNING SHOT “Unfortunately, we need to discuss some bad news.”
10. PAUSE to give time for the shock to clear
11. DELIVERY speak briefly and non-medically “The MDs don’t believe that they can fix your cancer.”
12. PAUSE to allow time for pt and family emotional responses
13. NON-VERBAL COMMUNICATION AND SILENCE (usually acceptable to touch pt’s arm)
14. RESPOND to both
 - a. EMOTIONS use NURSE mnemonic
 - i. Name the emotion and Normalize the response
 - ii. Understanding “I can understand that you must feel…”
 - iii. Respect “I have such respect for …” Praise the patient/family
 - iv. Support “We are going to continue to care for you and will not abandon you”
 - v. Explore anticipate fears that the patient may want addressed
 - b. QUESTIONS be honest, thorough, and brief. –
 - i. Certain questions should be anticipated and specific responses may be planned prior to the meeting – eg. “How long do I have” – reasonable to give large time frames – eg. “Months, but not years” “Days probably not weeks”
15. PLAN- briefly state next steps
 - a. Medical – symptom management – (review EOL symptom management sheet)
 - b. Ancillary Support – social work and spiritual care
 - c. Introduce Advanced Care Planning – (confirm DPOAHC, Adult DNR sheet)
16. ASK “Do You have any questions?” before you end meeting, then stand.

Whenever possible, utilize a multidisciplinary approach. Often, patients will bond with certain individual team members. Social work can help patients and family to deal with their “business”, both personal and emotional through counseling and resource identification. Spiritual care helps patients and family to discuss what gives their life meaning and purpose, their visits are not the same as religious visits. Both can help the patient to identify areas of strength and provide support. These healthcare team members have the time and training to help medical staff to understand what is important to the patient and to address those issues. They can also spend time with patients after bad news conversations.

Palliative Care: Managing Pain

PAIN and DYSPNEA:

Morphine: ____mg PO qid ATC (start 5mg for opioid naïve 2.5 elderly)

Morphine: ____mg PO q 2 hours PRN (10-15% of 24 hour dose or 5mg to start)

Morphine: ____mg SQ/IV q 1 hour ATC (start 1mg/hr in opioid naïve 0.25-0.5mg/hr in elderly)

Morphine: ____mg SQ/IV q 10-15 mins PRN (start 0.5 -1mg in naïve patients)

Dialudid: ____mg SQ/IV (start 0.2 mg/h with 0.2mg q10-15mins pca lockout- 0.1 elderly)

PCA bolus dose is ½-1x hourly dose. Incident pain: may increase bolus dose above basal

Equianalgesic Dosing Conversion Table

Drug	PO dose	PO:SQ/IV ratio	SQ/IV dose
Morphine	30	3:1	10
Hydrocodone	30	n/a	n/a
Hydromorphone	7.5	5:1	1.5
oxycodone	20	n/a	n/a
Codeine	200		Not used
Fentanyl			0.05 mg

PO dilaudid to PO morphine 1:4

PO MS/4 = PO DIL

IV dilaudid to PO dilaudid is 1:5

PO DIL/5 = IV DIL

IV dilaudid to IV morphine 1:7

IV MS/7 = IV DIL

IV dilaudid to PO morphine 1:20

PO MS/20 = IV DIL

PO oxycodone to PO morphine 1: 1.5

PO MS/1.5 = PO OXY

Duragesic to PO morphine 24 hour 1:2

PO MS/2 = DUR

Morphine is opiate of choice and for all conversions use PO morphine as reference

*Begin transition to long acting medications 12-24 hours after pain control is achieved with short acting opiates. (to help get people transitioned to the home schedule quickly)

*Break-through pain dose 10-15% of 24 hour dose

* Start and continue PO route unless unable to swallow or dose finding with PCA

*For Fentanyl patch 25mcg (smallest patch) = 50mg 24 hour dose of po morphine.- never use fentanyl patch for opioid naïve patients - Only good for well controlled pain. Too hard to dose find with.

* Calculation for incomplete cross tolerance- reduce dose by 75% if pain well controlled, and 100% if pain poorly controlled.

BONE PAIN:

NSAIDS or Dexamethosone 4mg SQ or PO QD consider radiation therapy

NEUROPATHIC PAIN:

Gabapentin (Neurontin): 300mg po BID titrate q 3 days by 300mg to 3600mg or effect

Nortriptyline (Pamelor): 10-25 po qhs start increase q 5-7 days

CONSTIPATION:

Senna/Colace (Senokot-S): 2 tabs po QHS Bisacodyl (Dulcolax): 1-2 tabs po QD prn

NAUSEA:

Droperidol (Inapsine): 2.5mg IV Q4 prn , Prochlorperazine (Compazine): 10mg PO q6

Metoclopramide (Reglan): 5-15mg PO/SQ AC and HS

AGITATION/DELIRIUM: * Consider bladder/bowel/drug toxicities/dehydration.

Haloperidol (Haldol): 0.5-5mg PO/SQ Q6 Max 30mg/d

Risperidone (Risperidal): 0.5-1mg po QD incr by 0.5-1mg q2-7 days

Olanzapine (Zyprexa): 2.5-5mg po QD increase by 5mg q week

ANXIETY:

Lorazepam (Ativan): 0.5-2mg PO/IV Q 6 prn

Oxazepam (Serax): 10-30 mg PO TID/QID

INSOMNIA:

Temazepam (Restoril): 15-30 mg po qhs (7.5mg in elderly), Mirtazipine (Remeron): 15-30mg po qhs

GURGLING RESPIRATIONS/SECRETIONS/"DEATH RATTLE":

Glycopyrrolate (Robinul): 0.2-0.6mg SQ/IV q 4 hours PRN

Atropine: 1-3gtt or 0.4mg ODT tab SL q1 PRN

Interns: Electrolyte replacement

- Potassium:** Goal is 4.0
Give IV at rate of 10 meq/hr
General dose required: $(\text{Desired K} - \text{Current K})/\text{Cr} \times 100$
If on amphi/ABLC..will need aggressive replacement several times a day, even days to weeks after amphi discontinued.
- Magnesium:** Goal is 2.0
Give IV at rate of 2 gm/hr
For Mag of:
1.8-1.9 give 2 gm Mag Sulfate IV
1.6-1.7 give 3 gm “ “
1.4-1.5 give 4 gm “ “
1.2-1.3 give 5 gm “ “
Can give po as MagPlus 2 tabs po tid
- Phosphorus** DO NOT TX IF $\text{Ca} \times \text{PO}_4 > 70$ b/c of risk of calciphylaxis!
Oral repletion: $\text{Kphos} = 4 \text{ mmol PO}_4 / 4\text{-}14 \text{ meqK}$
 $\text{Neutraphos} = 8 \text{ mmol PO}_4, 6\text{-}13 \text{ meq Na}, 1\text{-}7 \text{ mEq K}$
For PO_4 of:
1.5-2.0, give 0.1-0.2 mmol/kg iv
1.0-1.5, give 0.2-0.3 mmol/kg iv
<1 give 0.3-0.4 mmol/kg iv
Replete iv at rate of 3 mmol/hr (there is 4.4 meq k in 3 mmol PO_4)
- Calcium** Use ionized calcium
Tx if $\text{iCa} < 1.00$ or if Sx
DO NOT TREAT IF $\text{Ca} \times \text{PO}_4 > 70$ or if in Tumor Lysis Syndrome
Tx with 1 amp (or 1 gm) CaGluc iv over 1 hr
Oral Tx Calcium Carbonate 1250 mg po tid (=500 mg elemental ca)

INTERNS: DISCHARGING PATIENT CHECKLIST

<u>PRIOR TO DISCHARGING A PATIENT – Oncology Services</u>		
<u>Responsibility</u>	<u>Physician</u>	<u>Managed Care</u>
HOME	Contact the case manager at least the day prior to discharge	Verify patient benefits and appropriate home care agency. Obtain information regarding appropriate pharmacy for discharge meds
Medications	Prepare discharge medication. Any prescriptions to be filled at an outside pharmacy must be completed by a physician with a personal furnishing license (fellow, attending or 3 rd year resident), Narcotics need exemption code and fellow or 3 rd yr res signature. Review complete list with fellow AND resident to make sure appropriate meds are given, including neupogen and infection prophylaxis, if appropriate.	Send prescriptions to pharmacy as appropriate
On the weekend	Call ext. 62770 for home care	
On holidays	Call ext 62770 for home care	
Follow-up Appt.	Inform case manager of date for appointment	Call Oncology Center for appropriate appt. and/or lab draws
HOSPICE	Request a social work consult with either J or Solid Onc	
DME	Contact Case Manager. Prescriptions must be placed in patient chart the day prior to discharge. Please indicate patient's private medical doctor on the form	Case Manager will arrange for DME
DIABETIC EDUCATOR	If patient is newly diagnosed diabetic or is in need of diabetic education, place order and inform case manager 2 days prior to discharge	Case Manager will inform Diabetic Educator
NUTRITION	If pt. Is to be discharged on parenteral or G-Tube feeds, notify the dietit prior to discharge	
DISABILITY FORMS	Complete these forms and return to patient ASAP	For further assistance page the charge nurse 90309

10/01/03

Interns: Differential Dx/Workup Common Problems on J/SO

1. Rising Bilirubin/Icterus

Hemolysis (Intravascular or Extravascular)
Microangiopathy
ABO Incompatibility
Delayed Transfusion Events
Immuno-hemolysis
Resorption of Hematoma
Intramedullary Hemolysis
Hepatic disease (see below)

Work-Up

Routine Urinalysis with Microscopic (looking for dipstick-positive for hemoglobin but few or no rbc's)
Direct and Indirect antiglobulin tests; D dimmers, fibrinogen, etc.
Haptoglobin, LDH (retic uninterpretable in these patients)

2. Hepatic Disease

Hepatitis
Infection
Drug-Induced
Veno-Occlusive Disease
Graft-Vs.-Host Disease
Right Ventricular Insufficiency
Intrahepatic or Extrahepatic Biliary Obstruction
Pancreatitis

Work-Up

Radiographic studies of hepatobiliary system including study of portal venous flow/pressure
Biochemical analysis of liver function (synthetic and inflammatory)
Amylase/Lipase
Liver Biopsy

3. Diarrhea

Impaired Absorption
Mucosal injury from chemo/radiotherapy
Inflammatory Disease
 Infectious enteritis (c dif)
 Graft-Vs.-Host Disease
Infiltrative Disease
 Lymphoma, leukemia
 Amyloidosis

Impaired Digestion

Pancreatic insufficiency
Hepatobiliary disease
Bacterial overgrowth

Work-Up:

Stool analysis/cultures:
 Bacterial, especially C. difficile
 Parasite examination
Systemic cultures
 CMV
 Radiographic studies
Computerized tomography
Biopsy

4. Constipation

Neurogenic disorders
 Anticholinergic drugs and opiates, tricyclics
 Vinca alkaloids (vincristine)
 Other drugs (thalidomide)
Electrolyte disorders
 Hypercalcemia, hypokalemia

Immobilization
Gastrointestinal disorders
 Bowel obstruction
 Extrinsic compression
Work-Up
 Electrolyte analysis
 Radiographic

5. Hyponatremia

Hypervolemic disorders
 Excessive intravascular fluids
 Nephrotic syndrome, cardiomyopathy, hepatic cirrhosis
Euvolemic states:
 Excessive ADH secretion
 Chemotherapy (Vincristine, Cyclophosphamide, morphine, diuretics)
 CNS lesion
 Pulmonary process
 Pain
 Hypothyroidism
Volume depletion
 Gastrointestinal (diarrhea, vomiting)
 Diuretics
 Adrenal insufficiency

Work-Up:
 Physical assessment of volume status
 Urine and serum electrolytes and osmolality
 Review of medication list
 Chest radiograph
 Laboratory assessment of thyroid and adrenal function
 Head CT
 Laboratory assessment of thyroid function

6. Hypernatremia

Water loss
 Diabetes insipidus
 (nephrogenic due to amphotericin B or vinblastine, hypokalemia, hypercalcemia)
 (central due to increased intravascular pressure, tumor)
 Gastrointestinal loss (vomiting, diarrhea)
 Renal loss (diuretics)
 Excessive sodium intake
 (intravascular fluid resuscitation)
 Mannitol
 Glucocorticoid excess
 Dialysis

Work-Up
 Review of medication list
 Serum and urine electrolytes and osmolality
 Urine specific gravity
 Laboratory assessment of gluco/mineralocorticoid activity

7. Dyspnea

Pulmonary causes
 Infections (bacterial, fungal, viral, mycobacterial)
 Pulmonary edema (think noncardiogenic first, then cardiogenic)
 Pulmonary embolism (regardless of platelet count)
 Chronic Graft-Vs.-Host disease
 Gastric aspiration
 Drug toxicity
Non-pulmonary
 Acidosis (think sepsis, ketoacidosis, renal tubular)
 Fever
 Shock
 Liver disease, ascites
 Psychogenic

Work-up

- Arterial Blood Gas (no substitution for this - pulse ox often misleading)
- Serum electrolytes
- Chest radiograph
- Chest CT (consider spiral)
- Radiographic venous imaging
- Tests for liver damage, intracranial hypertension (if ABG shows metabolic alkalosis)
- Work-up for sepsis, hyperglycemia (if ABG shows metabolic acidosis)

8. Rising Creatinine

Intrinsic Renal Disease

Drugs

- Tubular toxins, interstitial nephritis, vasculitis

- Hyperuricemia, hypercalcemia

Glomerulopathies

- lymphoma, t.t.p./h.u.s.

- post-infectious

- Pigment (hemoglobin/myoglobin)

- D.I.C.

Prerenal

- Intravascular volume depletion

- dehydration, hemorrhage, gastrointestinal, diuretics, hepatic insufficiency, cardiac tamponade, cardiomyopathy, sepsis, vascular

Obstructive

- Hemorrhagic/thrombotic ureteral/bladder/urethral inflammation (chemical cystitis)

Work-up

- Review medication list

- Physical assessment of volume status with careful attention to signs of tamponade, sepsis, cardiac insufficiency

- Routine urinalysis with microscopic

- Serum and urine electrolytes and osmolality

- Urinalysis for eosinophils

- CBC, platelet, and coagulation studies (D dimers, fibrinogen)

- Renal ultrasound

- Computerized tomography to assess for obstructive lesions

9. Fever

Infection

- Neutropenic fever or fever associated with granulocyte defects (Gram-negative bacteria, Gram-positive cutaneous organisms, hyphal fungal infection, Candida)

- Pathogens associated with cellular immune deficiency (CMV, HSV/VZV, mycobacterial, intracellular fungal, PCP, reactivation infections, defective bacterial infections, toxoplasmosis)

- Pathogens associated with humoral immune deficiency (encapsulated bacterial, esp. Legionella)

- Site specific causes:

- Central venous catheter, pneumonia, intra-abdominal, urothelial, sinus, intrahepatic

Drugs

- Neoplastic

- Lymphoma, leukemia

Pulmonary embolism

Work-up

- Cultures of the blood and urine for bacterial, mycobacterial, fungal, and viral pathogens, CMV specific DNA

- Routine urinalysis with microscopic

- Chest radiograph

- Biochemical studies of liver function

- Review medication list

- Computerized tomography of abdomen/pelvis

- Empiric withdrawal of medications/ central venous catheter

Common Chemotherapy Agents

Drug Class	Name	Mechanism	Important Side Effects Not to Miss
Antimetabolites	Methotrexate	<ul style="list-style-type: none"> Analog of Folic Acid blocking dihyrolyate reductase 	Neurotoxicity
Antimetabolites	Cytarabine (ara-C)	<ul style="list-style-type: none"> Pyrimidine Analog but arabinoside (not ribose) Incorporated into via deaminases becoming pharmacologically inactive metabolites (ara-U, ar-UMP) Via dinase becoming active (ara-CTP) incorporating into DNA, terminating DNA chain elongation, and inhibiting DNA polymerase 	
Antimetabolites	Cladribine (2-chlorodeoxyadenosine)	<ul style="list-style-type: none"> Purine Analog Not incorporated into DNA Inhibits ribonucleotide reductase (ADP to dADP) Blocks DNA repair 	
Antimetabolites	Fludarabine	<ul style="list-style-type: none"> Synthetic purine antagonist Converted by deoxycytidine kinase to the nucleotide, fludarabine triphosphate (FATP, 2-fluoroarabinofuranosyladenine triphosphate, 2-fluoro-ara-ATP) Inhibits a-DNA polymerase, ribonucleotide reductase, and DNA primase by competing with the physiologic substrate, deoxyadenosine triphosphate, resulting in inhibition of DNA synthesis Incorporated into growing DNA chains as a false nucleotide, thus interfering with chain elongation (prematurely terminating DNA synthesis) 	
Antimetabolites	5-Fluorouracil	<ul style="list-style-type: none"> Pyrimidine Analog 	
Antimetabolites	Mercaptopurine (6-MP)	<ul style="list-style-type: none"> Purine Analog 	
Antimetabolites	6-Thioguanine	<ul style="list-style-type: none"> Purine Analog 	
Anthracyclines	Doxorubicin Adriamycin	<ul style="list-style-type: none"> Topoisomerase II inhibitor blocking ligation of DNA strand maintaining DNA break 	Cardiotoxicity , mucosal ulcers, mucositis , venous sclerosis (burns)
Anthracenedione	Mitoxantrone	<ul style="list-style-type: none"> DNA-reactive agent Interferes with the function of topoisomerase II, thereby preventing religation of DNA strand breaks 	
Antibiotics	Etoposide (VP-16)	<ul style="list-style-type: none"> Possibly induced single-stranded DNA breaks indirectly, through endonuclease activation, inhibition of intranuclear type II topoisomerase, or formation of a free-radical metabolite 	Cardiomyopathy
Antibiotics	Bleomycin	<ul style="list-style-type: none"> Breaks in DNA by intercalating Forms superoxide that cleaves C3-C4 of G, C or T base 	Pulmonary Fibrosis , pneumonitis
Alkylating Agents	Cyclophosphamide (cytoxan)	<ul style="list-style-type: none"> Incorporates into molecules, activated by P450 Inactive metabolites and toxic metabolites 	Hemorrhagic Cystitis , pulmonary fibrosis
Alkylating Agents	Cis-Platin	<ul style="list-style-type: none"> Neutrophilic attack to purines/pyrimidines Does not put on alkyl group Does bind and prevent synthesis 	Ototoxicity and renal toxicity
Alkylating Agents	Carboplatin	<ul style="list-style-type: none"> Neutrophilic attack to purines/pyrimidines Does not put on alkyl group Does bind and prevent synthesis 	
Alkylating Agents	BCNU (Carmustine)	<ul style="list-style-type: none"> Inhibition of both DNA and RNA synthesis via the alkylation of DNA and RNA Mechanism not fully understood 	Pulmonary toxicity, including acute or delayed onset of pulmonary fibrosis; delayed hematologic toxicity

Common Chemotherapy Agents

Drug Class	Name	Mechanism	Important Side Effects Not to Miss
Alkylating Agents	Thiotepa	<ul style="list-style-type: none"> • Interferes with DNA replication and transcription of RNA, and ultimately results in the disruption of nucleic acid function • Possesses some immunosuppressive activity. 	
Alkylating Agent	Busulfan	<ul style="list-style-type: none"> • Interferes with DNA replication and transcription of RNA and ultimately results in the disruption of nucleic acid function • 2 labile methanesulfonate groups attached to opposite ends of a 4-carbon alkyl chain; when hydrolyzed the methanesulfonate groups are released, producing reactive carbonium ions capable of alkylating DNA 	Hepatic veno-occlusive disease
Plant Alkaloids	Vincristine	<ul style="list-style-type: none"> • Inhibit mitosis, M phase, promoting disassembly of microtubules by blocking assembly 	
Plant Alkaloids	Vinblastine	<ul style="list-style-type: none"> • Inhibit mitosis, M phase, promoting disassembly of microtubules by blocking assembly 	
Plant Alkaloids	Taxol	<ul style="list-style-type: none"> • Inhibit mitosis, M phase, promoting assembly of microtubules by blocking disassembly 	
Steroid Hormones	Tamoxifen	<ul style="list-style-type: none"> • Estrogen/Progesterone receptor inhibitor 	
Steroid Hormones	Prednisone	<ul style="list-style-type: none"> • Agonist of Glucocorticoid receptor • Activation of specific genes causing apoptosis 	Osteoporosis, hypertension, hyperglycemia, gynecomastia
Steroid Hormones	Flutamide	<ul style="list-style-type: none"> • Androgen receptor inhibitors 	
Miscellaneous	STI-571	<ul style="list-style-type: none"> • Tyrosine Kinase inhibitor 	
Differentiation	ATRA (all-trans-retinoic acid)	<ul style="list-style-type: none"> • Promote differentiation (PML/RAR t(15;17)) 	

Chemotherapy: Management of Nausea & Vomiting

	High-Moderate Risk Chemotherapy	Low Risk Chemotherapy	Minimal
<u>ACUTE (Day 1)</u> <i>Give prior to chemotherapy</i>	<p>*<u>Aprepitant (Emend) 125mg PO Day 1, 80mg PO day2-3 (All High Emetogenic and/or High Risk (young, female, history of poor control, tumor burden)</u></p> <p>and 5-HT3 antagonist such as: <i>Palonosetron (Aloxi)</i> 0.25mg IVP (given only ONCE, day 1 of each cycle, don't use more than qwk..preferred agent) or <i>Granisetron (Kytril)</i> 2mg po or 1 mg po bid or 1mg IV 30sec or <i>Ondansetron (Zofran)</i> 16-24 mg po or 8-12 mg IV can be used qd or bid)</p> <p>and Dexamethasone 12 mg po or IV, 8mg po or IV daily days 2-4</p> <p>and/or Lorazepam 0.5-2mg po or IV every 4-6 hours days 1-4</p>	<p>Dexamethasone 12 mg po or IV daily</p> <p align="center">OR</p> <p>Prochlorperazine 10 mg po or IV every 4 or every 6 h or 15 mg spansule</p> <p align="center">OR</p> <p>Metoclopramide 20-40 mg po every 4 h or every 6 h or 1-2mg/kg IV either every 4h or 6 h.±</p> <p>Diphenhydramine 25-50mg po or IV every 4-6 h</p> <p>± Lorazepam 0.5-2mg po or IV every 4-6 hours days 1-4</p>	<p>No routine prophylaxis but consider low risk treatment if patient has nausea/emesis within 24 hours of treatment</p>
<u>DELAYED (Days 2-4)</u>	<p>Aprepitant 80 mg po days 2-3 if used on Day 1</p> <p>and Dexamethasone 8 mg po or IV daily or 4 mg PO or IV BID (preferred)</p> <p>and/or *Granisetron 2mg po or 1 mg po bid or 1mg IV *Ondansetron 8 mg PO bid or 16mg PO daily or 8 mg (max 32mg) IV</p> <p><u>*NOT NECESSARY IF PATIENT RECEIVED PALONOSETRON (Aloxi)</u></p>		
<u>BREAKTHROUGH</u>	<p>Prochlorperazine 25mg supp pr every 12 h or 10 mg PO or 15 mg spansule PO every 8 or every 12 h</p> <p align="center">OR</p> <p>Reglan 20-40 mg PO q4h or q6h or 1-2mg/kg IV q4h or 6 h.</p> <p>OR Lorazepam 0.5-2mg PO every 4 or 6 hours OR Ondansetron 16 mg PO or 8 mg IV QD OR Granisetron 1-2 mg PO QD or 1 mg PO bid or 0.01 mg/kg IV OR Haloperidol 1-2 mg PO q 4-6 h or 1-3 mg IV every 4-6 h OR Dronabinol 5-10 mg PO every 3 or every 6 h OR Oplanzapine 2.5-5 mg PO bid prn OR Promethazine 12.5-25 mg PO ro IV every 4 h.</p>	<u>Same</u>	<u>Same</u>

Emetogenic Potential of Antineoplastics Agents

<u>Level: High Emetic Risk</u> (>90 % frequency of emesis)	<u>Level: Moderate emetic risk</u> (30-90 % frequency of emesis)	<u>Low emetic risk</u> (10-30% frequency of emesis)	<u>Minimal emetic risk</u> (<10 % frequency of emesis)
AC (doxorubicin or epirubicin + cytoxan) <u>Altretamine</u> Carmustine \leq 250mg/m ² Cisplatin >50mg/m ² Cyclophosphamide >1500 mg/m ² <u>Dacarbazine</u> Mechlorethamine Procarbazine (oral) Streptozocin	<ul style="list-style-type: none"> •Amifostine > 300 •Arsenic trioxide •5-Azacytidine •Busulfan >4 mg/d •Carboplatin •Carmustine \leq 250 mg/m² •Cisplatin < 50 mg/m² •Cyclophosphamide (oral) •Cyclophosphamide \leq 1,500 mg/m² •Cytarabine >1 g/m² •Dactinomycin •Daunorubicin •Doxorubicin •Epirubicin •Etoposide (oral) •Idarubicin •Ifosamide •Imatinib (oral) •Interleukin-2 >12-15 million units/m² •Irinotecan •Lomustine •Melphalan > 50 mg/m² •Methotrexate 250-> 1,000 mg/m² •Oxaliplatin > 75 mg/m² •Temozolomide (oral) •Vinorelbine (oral) 	Amifostine 200-300 mg/m ² Bortezomib (Velcade) Bexarotene (Targetin) Cytarabine 100-200 mg/m ² Capecitabine Cetuximab Docetaxel Doxorubicin (liposomal) Etoposide 5-Fluorouracil < 1000mg/m ² Fludarabine (oral) Gemcitabine Methotrexate >50 mg/m ² < 250 mg/m ² Mitomycin Mitoxantrone Paclitaxel Pemetrexed Temozolomide Transtuzumab Topotecan	Alemtuzumab (Campath) Alpha interferon Asparaginase Bevacizumab Bleomycin Busulfan Chlorambucil 2-Chlorodeoxyadenosine Cladribine Dexrazoxane Denileukin diftitox Erlotinib Fludarabine Gefitinib Gemtuzumab ozogamicin Hydroxyurea (oral) Melphalan (oral low-dose) Methotrexate \leq 50 mg/m ² Pentostatin Rituximab Thioguanine (oral) Valrubicin Vinblastine Vincristine Vinorelbine

Common Regimens used on J/SO

ATG (Aplastic Anemia)

- ATG Test Dose: ATG 1:1000 dilution in NS 0.1 cc intradermally. Control saline 0.1 cc intradermally.
- Premedication:
 - Tylenol 650 mg po 30 mins before;
 - Benadryl 50 mg po/iv 30 mins b4;
 - Hydrocortisone 50 mg IV 30 mins before
- ATG Dosing: ATG 40 mg/kg in 1 L NS IV over 8-12 hours QD days 1-4
- Concomitant Medications:
 - Prednisone 100 mg/M2 PO QD x 7days, start with ATG, taper over 7 days if no serum sickness;
 - Cyclosporine 5 mg/kg/d divided BID; taper by 1 mg/kg/month as tolerated. Start at 4 mg/kg/d if >50 yrs old.

Hyper-CVAD/Hi dose MTX-AraC (Mantle Cell lymphoma/ ALL)

- Alternate HyperCVAD (cy 1, 3, 5, 7) & MTX (cy 2, 4, 6, 8). Subsequent cycles given when WBC >3.0 & plt > 60K
- Hyper-CVAD (cycles 1, 3, 5, 7)
 - Cytoxan 300 mg/m2 IV over 3 hrs q12 hr days 1-3
 - Mesna 600 mg/m2/d CIV days 1-3 (start at same time as cytoxan and finish 6h after completion of cytoxan)
 - Vincristine 2 mg iv days 4, 11
 - Doxorubicin 50 mg/M2 IV day 4
 - Dexamethasone 40 mg PO days 1-4, days 11-14
- High dose Methotrexate and Cytarabine (Ara-C) (cycles 2, 4, 6, 8)
 - Methotrexate 200 mg/M2 IV (over 2 hr) day 1
 - Followed by Methotrexate 800 mg/M2 CIV (over 24 hr) day 1
 - Leucovorin 15 mg po q6h x 8 doses. Increase to 50 mg po q6h if MTX level is >20 umol at end of infusion or >1 umol/L 24 hr later or >0.1 umol/L 48 hr after end of infusion. Continue until MTX level is < 0.1 umol/L
 - Ara-C 3 gm/M2 IV over 2hr q12 hr x 4 doses (days 2 & 3)
 - Methylprednisolone 50 mg IV BID days 1-3
 - Dexamethasone eye drops: 2 gtt OU q3h during and for 48-72 h after completion of cytarabine
- Support Medications
 - Premeds: antiemetics (kytril, etc)
 - Antibiotics (for all cycles):
 - Levaquin 500 po qd; Fluconazole 200 mg po QD; Valacyclovir 500 mg po QD
 - Neupogen or Neulasta (after all cycles)
- CNS Treatment/Prophylaxis
 - Methotrexate 12 mg IT day 2
 - Ara-C 100 mg IT day 8
 - Known CNS disease-IT twice weekly until CNS negative then per prophylaxis protocol.
 - If pts are high risk (LDH>600, hi Ki67 or mature B cell ALL) above is repeated for each of the 8 cy of chemo
 - Low risk, above repeated only during the first two cycles of chemo.
 - Unknown risk, above repeated during 1st 4 cy of chemotherapy

7+3 (Induction chemo for AML)

Ara-C 100 mg/M2 continuous IV days 1-7

Idarubicin 12 mg/m2 IV days 1-3

Check echo pre-1st infusion with idarubicin

Note: many other centers use daunorubicin instead of ida; no difference

HiDAC (Consolidation or for Recurrent AML)

Ara-C 3 gm/m2 IV over 3 hrs q12hr days 1, 3, 5

Usually given with mitoxantrone 12 mg/m2 iv days 1-3 (check with attding)

Pred forte eye gtt: 2 gtt OU q3h days 1-6

Follow cerebellar toxicity: signature test, etc

For consolidation therapy, repeat q28 days (after wbc recovery) x 2-3 courses

ATRA/7+3 (Acute promyelocytic anemia induction)

IVF: NS 100 cc/hr with cytarabine and to continue 4 hrs after cytarabine infusion ends

ATRA 45 mg/m² PO (divide dose into BID) daily until CR or 90 days

Idarubicin 12 mg/m² iv qd days 3-5

Cytarabine 100 mg/m² continuous IV qd days 3-9

Pred forte eye gtt: 2 gtt OU q4h days 1-8

Watch for ATRA syndrome (discuss with attending)

Then give consolidation (Ida/Ara-C x 2 cycles, discuss with attending) and maintenance (ATRA only 15 days q3 mos to complete 2 years of tx)

MINE (Refractory ALL, occasionally Lymphoma)

IVF: D5-1/2NS with 1 amp bicarb 150 cc/hr to start 6 hrs pre chemo and continue til end of chemo

Mitoxantrone 8 mg/m² IV qd days 1-3

Etoposide 100 mg/m² IV qd days 1-5

Ifosfamide 1.5 gm/m² continuous IV qd days 1-5

Mesna 1.5 gm/m² CIV qd days 1-5 to finish 12 hours after ifos finishes

Echo prior to Mitoxantrone to check EF

ESHAP +/- R (Lymphoma)

Etoposide 40 mg/m² IV over 1 hr days 1-4

Solumedrol 500 mg IV over 15 min days 1-4

Cytarabine 2000 mg/m² IV over 2 hr day 5

Cisplatin 25 mg/m² CIV over 96 hr days 1-4

If give rituximab: 375 mg/m² iv x 1, usually day 1

IVF: vigorous hydration necessary for cisplatin; hold or reduce if Cr > 1.5

Cytarabine: watch for cerebellar toxicity

ICE +/- R (Lymphoma)

Ifosfamide 5000 mg/m² CIV x 24 hr day 2

Mesna 5000 mg/m² CIV x 24 hr day 2

Carboplatin AUC 5 IV day 2

Etoposide 100 mg/M² IV days 1-3

If give rituximab: 375 mg/m² iv x 1, usually day 1

SARCOMA REGIMENS

High dose Ifosfamide (Sarcoma)

- Anti-emetics with compazine, decadron, benadryl, kytril
- IVF: 500 cc bolus then D51/2NS with 1 amp bicarb at 250 cc/hr x 2hrs prechemo then 150 cc/hr
- Ifosfamide 2 gm/m² continuous IV over 24hr/day x 7days (total dose 14 gm/m²)
- Mesna 2 gm/m² CIV 24 hr/d x 7d with Ifosfamide. Total dose 14 gm/m²
- GCSF or Neulasta 24 hrs after last dose

High dose methotrexate

- Anti-emetics with Compazine, Decadron, Benadryl and Kytril d1-3
- IVF: See below
- Prior to infusion, check CrCl. If less than 80%, call Dr. Tap to reduce dose
- Methotrexate 12 gm/m²: give in 500 ml/m² D5W with 1 amp bicarb at 250 cc/hr x 4 hrs
- Leucovorin to begin 24 hours after infusion of MTX. 25 mg IV q6 hr x 24 hrs, then 20 mg po q6hrs until d/c.
- MTX level drawn qam (8am) to begin day after infusion.
- Daily urinalysis: keep pH>8.0
- D/C home with PO leucovorin and PO bicarbonate

Ifosfamide/Etoposide

- Anti-emetics with compazine, decadron, benadryl and kytril

- IVF: D5-1/2 NS with 1 amp bicarb at 150 cc/hr
- Ifosfamide 1800 mg/m² IV in 800 ml/m² D5-1/2NS over 4 hrs qd x 5 days
- Mesna 1800 mg/m² IV over 24 hrs qd x 5 days
- Etoposide 100 mg/m² IV qd x 5 days
- Neulasta or Neupogen 24 hours after chemo

Ifosfamide/Adriamycin (osteosarcoma)

- Anti-emetics with compazine, decadron, benadryl, kytril
- IVF: D5-1/2 NS with 1 amp bicarb at 150 cc/hr
- Ifosfamide 1800 mg/m² IV in 800 ml/m² D5-1/2NS over 4 hrs qd x 5 days
- Mesna 1800 mg/m² continuous IV over 24 hrs/day x 5 days
- Dexarazoxane 375 mg/m² on day 1 & 2 over 15 mins
- Doxorubicin 37.5 mg/m² iv on day 1 & 2 over 15 mins. Give 20 mins after dexarazoxane
- Check echo pre-doxorubicin 1st cycle
- Neupogen or Neulasta 24 hrs after chemo

