Best Practices: Outpatient Conditioning for Autologous and Allogeneic Hematopoietic Cell Transplantation (HCT)

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HCT Conditioning Regimens

- Goals of conditioning
- Autologous
- Allogeneic
  - Myeloablative
  - Nonmyeloablative
  - Reduced-intensity
- Inpatient vs. outpatient

ARS Question
How many institutions do outpatient conditioning regimens?

- Autologous?
  - Myeloma
  - Other?
- Allogeneic?
  - What regimens?
  - PK targeting?

Outpatient Conditioning

- What makes a regimen attractive for outpatient conditioning?
- Supportive care mechanisms needed?
- Additional patient education required?
- Services from pharmacy, nursing, others?

Best Practices: Outpatient Conditioning for Autologous and Allogeneic HCT: The Panel

- Joseph Bubalo
  - Oregon Health and Science University Hospital
- Angela Hsieh
  - Seattle Cancer Care Alliance
- Vicky Brown
  - The Johns Hopkins Hospital

Objectives

- Review elements of an outpatient hematopoietic cell transplant (HCT) conditioning regimen
- Discuss patient attributes associated with success when using outpatient conditioning regimens
- Compare and contrast the elements of supportive care and immune suppression between centers that perform outpatient HCT conditioning
- Describe and discuss the logistics and associated procedures involved in managing patients undergoing outpatient HCT conditioning

Best Practices: Outpatient Conditioning for Autologous and Allogeneic (HCT):

NORTHWEST MARROW TRANSPLANT PROGRAM

OREGON HEALTH & SCIENCE UNIVERSITY

LEGACY HEALTH

DOERNBECHER CHILDREN'S HOSPITAL

Oregon Health & Science University

ASBMT CIBMTR

Joseph Bubalo PharmD, BCPS, BCOP

OHSU Campus: Portland, Oregon

OREGON HEALTH & SCIENCE UNIVERSITY

HCT Program at OHSU

- Established 1990 with first allogeneic HCT in 1994
- Serves Oregon, Idaho, Washington, and Alaska
- Approximately 200 transplants annually
  - ~50% autologous/50% allogeneic
- Primarily inpatient program with a 30 bed ward and one overflow unit (general oncology)
- With the advent of non-ablative regimens we designed one specifically for outpatient care

ASBMT CIBMTR

Outpatient Regimens

- Autologous
  - Melphalan – myeloma
  - BuMelTT (busulfan melphalan, thiotepa)
- Allogeneic
  - BuFluTBI (RIT)
  - For 2012 - 20% (n=10) of our RIT regimens were this outpatient regimen

RIT – reduced intensity transplant

Decision Points in Outpatient Regimen Design

- Daily dosing?
- Supportive care
  - Continuous infusion required?
  - Multiple vs. single IV infusions daily
  - Emesis or mucositis a problem?
  - Pharmacokinetic monitoring required?
- Logistics
  - Caregiver available?
  - Patient reliable?
  - Local housing secured?

Patient Attributes for Outpatient HCT

- Meets general physical and financial requirements for HCT, critical among them are:
- Karnofsky > 50%
- Reliable patient
- Consistent caregiver
- Ability to stay locally for 3 months
- Completed education

- *Outpatient transplant donor types*
- MRD, URD(including mismatches), cord blood

MRD – matched related donor, URD – unrelated donor

Outpatient Care Team

- MD – available in clinic daily if needed, currently <10% see an MD for the first 60 days
- Midlevels – see patient 3 times per week, available daily
- Clinic pharmacist: Monday – Friday, weekend covered by inpatient pharmacist
  - see patient intermittently to follow up on medication issues, questions, etc
- Clinic nurses
- Social worker, transplant coordinator

- Goal: coordinated care, smooth transitions, timely assessments, and interventions to meet patient needs and minimize morbidity

Patient Elements of Care

- Pre-transplant education
  - Includes social, dietary, medication, self care, and other important life adaptations
- Medication sheet and organizer
- Pre-conditioning: All medications prescribed and acquired.
- Communication plan with medical team
- Process overview and expectations understood

Nonmyeloablative Allogeneic HCT

- BuFluTBI
  - Busulfan 3.2 mg/kg IV on Day -5
    - Adjusted body weight (IBW + 0.25(TBW-IBW))
  - Fludarabine 30 mg/m2/day on Day-4 thru -2
    - BSA based on TBW
  - TBI 200 cGy on day -1
- Admitted for cell infusion day 0 then discharged the next day or same evening back to clinic.
- Seen in clinic until day +100 or when stable enough for management at home

IBW – ideal body weight TBW- total body weight

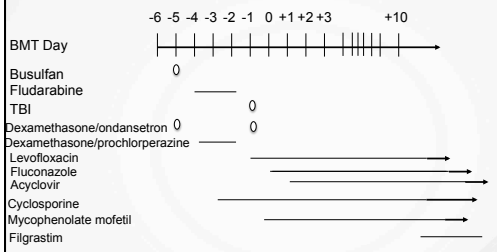
GVHD Prophylaxis

- Oral cyclosporine(modified) starting Day -3, 4 mg/kg PO Q 12H - targeting 300-400 ng/mL
  - Day +28 target reduced to 250-350 ng/mL
  - Day +56 begin taper to off by Day +180 if GVHD controlled
- Oral mycophenolate 15 mg/kg PO Q 12 (Q 8 for URD) – round to the nearest 250 mg
  - Starts Day 0
  - Related donor stops Day +28
  - URD decrease to BID dosing Day +28 and stops on Day +56

Supportive Care

- Hydration, daily during conditioning and when neutropenic
- Filgrastim x 6 days (+10 - +15)
- Antiemetics – Targeted on emetogenicity during conditioning then PRN
- Anti-infectives – acyclovir, begins Day +1, fluconazole, begins day 0, levofloxacin begins day -1
- Admitted to inpatient if febrile neutropenia
  - Direct admission to the inpatient unit

Regimen Medications



What I wish I knew when we started outpatient HCT regimens

- Older patients/RIT are different from ablative allogeneic HCT
  - A fib
- The need for good communications
  - RN coordinators with pharmacy and RN clinic staff especially
  - Pharmacist to pharmacist coordination: inpatient-outpatient
- The amount of time and number or repetitions needed for medication teaching

ARS Question

- The person patients see in the clinic most frequently is:
- A. the transplant physician
- B. the midlevel practitioner
- C. the pharmacist
- D. the clinic nurse

Best Practices: Outpatient Conditioning for Autologous and Allogeneic HCT

Includes UW Medicine, Seattle Children's Hospital, and Fred Hutchinson Cancer Research Center

Total beds:
- 38 beds at Seattle Children's
- 100 beds at UW Medical Center
- 55 infusion chairs and beds at SCCA

In 2011:
- 5500 patient visits
- 550 HCT's

SEATTLE CANCER CARE ALLIANCE

Fred Hutchinson Cancer Research Center
UW Medicine
Seattle Children's

Working together to cure cancer

Angela Hsieh, PharmD, BCOP

Outpatient Care Team
Structure

- Attending physician
- Advanced practice practitioners, fellows, visiting physicians
- Team nurse
- Team pharmacist
- Team schedulers
- Team dietitian
- Team social worker
- Clinical coordinator/ Transplant intake
- Patient financial service
- Specialty consult services

Outpatient Care Team
Responsibilities

Pre-transplant

- Perform medical evaluation for transplant eligibility
- Identify appropriate transplant regimen and intensity
- Provide medical management to optimize therapy for co-morbidities prior to transplant
- Provide patient and family education
- Obtain insurance clearance and provide necessary documentation

Outpatient Care Team
Responsibilities

Conditioning to Day +100

- Coordinate outpatient conditioning and supportive care
- Monitor for and manage post-transplant complications
- Disease restaging
- Coordinate transition of care for hospital admission and discharge
- All-system chronic GVHD screening
- Coordinate transition of care to local physicians and long-term follow up clinic

GVHD- graft-versus-host disease

All outpatient but…

- Regimen related
  - IV busulfan
  - Anti-thymocyte globulin
  - Consecutive days of high dose cyclophosphamide
  - High dose cyclophosphamide on weekends
  - Q12 hour administration of BEAM
  - Radiolabeled monoclonal antibodies requiring radiation isolation
- Cellular therapy related
  - Cord blood infusion
  - Duration of stem cell infusion likely to exceed outpatient infusion operating hours
- Patient risk factors
  - Patients receiving transplant for amyloidosis
  - Patients require monitoring and caregiving beyond the ability of outpatient care team
  - Pediatric transplant

BEAM- carmustine, etoposide, cytarabine, melphalan conditioning

Common Outpatient Immunosuppressive Regimens

- Cyclosporine
  - PO or IV infusion over 1-2 hours every 12 hours
  - Start on day -3
  - Primarily self-administered at home
- Sirolimus
  - PO daily
  - start on day -3
- Tacrolimus
  - 0.03 mg/kg/day IV divided into twice daily dosing
  - 1 mg IV over 2 hours once daily in haploidentical HCT
  - May convert to twice daily oral dosing as soon as first therapeutic level obtained
  - Primarily self-administered at home
- Mycophenolate mofetil
  - PO or IV infusion over 2 hours every 8 or 12 hours starting on day 0 after HCT
  - IV therapy initiated at the hospital after cord blood infusion
  - May convert to oral therapy on day +8

Elements of Outpatient Conditioning

- Infusion service
- Home infusion service
- Daily HCT nursing check
- Medication calendar
- Patient and caregiver education
- 24-hour triage
- Direct admission
- Local housing

Infusion Services

- Operating hours
  - 7 am to 10 pm on weekdays
  - 7:30 am to 5 pm on weekends and holidays
- Infusion nurses trained to administer common conditioning regimens, e.g.,
  - Oral busulfan blood sampling
  - High dose etoposide, cyclophosphamide, or melphalan
- Direct communication between infusion nurses and outpatient care team

Home Infusion Service

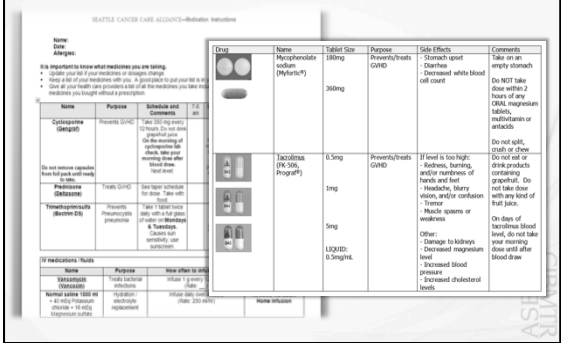
- Case rate or private agency
  - Training provided by agency nurses
  - Group and individual infusion pump class
  - Continuously assessing patients and caregivers' ability in operating pumps and performing line care
- Immunosuppressants, antimicrobials, fluid and electrolyte management and TDM
  - Coordinating refill and lab draws
- Outpatient enteral and parenteral nutrition
  - Team dietitians assess the need and coordinate orders
- Finance and billing
  - PFS and private agency obtain documentation from outpatient care team

TDM- Therapeutic drug monitoring
PFS- Patient financial service

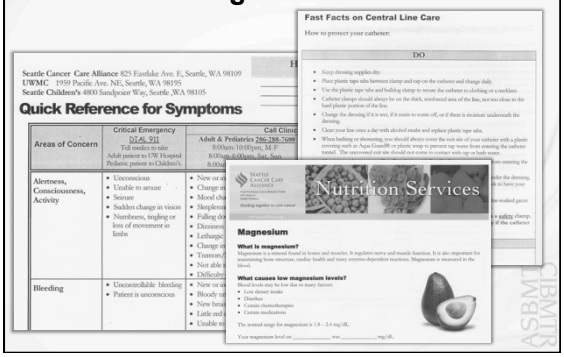
Patient and Caregiver Education

- Daily HCT nursing check during conditioning
- Pre-transplant education
  - Clinic orientation
  - Managing care at home
  - Pharmacy arrival, medication history, medication adherence and barrier assessment
  - Dietitian arrival and food safety class
  - Social work assessment
- Pre-conditioning education
  - Central line care
  - Chemotherapy teaching
  - Radiotherapy teaching
  - Radiation isolation self-care guidelines

Medication Calendar and Reference



Patient & Caregiver Resource Manual



Triage and Emergency Care

- Wallet contact card and quick reference for symptoms and monitoring parameters
- 24-hour triage by HCT providers
  - 8 am – 5 pm triaged by clinic provider
  - 5 pm – 10 pm triaged by HCT moonlighter at outpatient clinic
  - 10 pm – 8 am triaged by HCT nocturnist inpatient
- Direct admission to HCT inpatient

Neutropenic Precautions

- Common infection control guidelines
- Broad-spectrum antibiotics prophylaxis
  - Oral: fluoroquinolones, e.g. levofloxacin 750mg daily
  - IV: Ceftriaxone. Ceftazidime in some cases
- Self-monitoring of body temperature every 6 hours
- Septic bundle
  - Meropenem/linezolid/tobramycin
  - Aztreonam/linezolid/tobramycin for penicillin allergic
  - Administered at outpatient triage prior to transporting to hospital
- Direct admission to UWMC if at home

UWMC- University of Washington Medical Center

Patient Characteristics

- Able to comprehend instructions on how to manage care at home
- Able to contact care team and after-hour triage for emergency
- Able to maintain communication with care team on timely manner
- Patient are required to stay within 30 minutes of car ride to UWMC and SCCA
- Must have 24-hour caregiver that is committed and involved in patient's care

SCCA- Seattle Cancer Care Alliance
UWMC- University of Washington Medical Center

Responsibilities of Caregivers

- Providing physical care
  - Identify changes in patient's condition
  - Report patient's symptoms
  - Obtain medical care
  - Monitor patient's adherence to medications and instructions
  - Acquire and maintain medical supplies
  - Assist in central line care
  - Assist in administering parenteral medications and fluid
- Providing emotional support
  - Physical presence
  - Encouragement
- Maintain home environment
  - Cleaning
  - Food preparation
  - Shopping
- Patient advocacy
- Making arrangements
  - Transportation
  - Financial assistance
  - Tracking appointments
- Communication to family, friends and children

Pre-transplant Screening

- Caregiver plan
- Transportation
- Local housing
- Financial coverage
  - Prescription
  - Home Infusion
  - Housing and transportation
  - Caregiver
- Performance status and comorbidity
- ? Neurocognitive assessment ?

Audience Response Question

- Which of the following is a key element for successful outpatient conditioning?
  - A. Committed caregivers actively involved in patient's care
  - B. Availability of around-the-clock triage and emergency care
  - C. Experienced HCT staff to provide outpatient infusion and patient/caregiver education
  - D. All of the above

Best Practices: Outpatient Conditioning for Autologous and Allogeneic (HCT)

JOHNS HOPKINS MEDICINE
THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

Vicky Brown, Pharm.D., BCOP

Bone marrow transplant at SKCCC

- Established in 1968 by George Santos
- Greater than 300 transplants in 2013
  - Adult ~270, pediatric ~40
  - Donor Sources:
    - Allogeneic: MRD, MUD, and Haploidentical; Cords
    - Autologous
- Inpatient/Outpatient (IPOP) program launched in 1995

MA: Myeloablative; MRD: Matched related donor; MUD: Matched unrelated donor

Types of allogeneic transplant by donor source and patient location

Donor source and preparative regimen intensity	IPOP	In-patient
Haploidentical - RIC	106	0
Haploidentical – MA	0	24
MRD – RIC	22	0
MRD – MA	0	15
MUD – RIC	13	0
MUD – MA	0	6
Cord – RIC	8	0
Total	**149**	**45**

RIC: Reduced-intensity conditioning; MA: Myeloablative; MRD: Matched related donor; MUD: Matched unrelated donor

- **130 related haploidentical transplants in 2013**
  - **2/3's of all allotransplants**

Acknowledgement: Rick Jones, MD and Rebekah M. Zonozy, RN, MSN, CRNP

Inpatient/Outpatient Program (IPOP)

- Day hospital operating 7 days per week from 7:00 AM to 7:00 PM
- Available transplant treatment modalities:
  - Autologous transplant
  - Allogeneic reduced intensity conditioning transplants
  - Allogeneic myeloablative transplants following count recovery until day +60
- Patients spend an average of less than 10 days admitted to the in-patient unit
- Approximate census of 50 patients
- IPOP providers:
  - 1 to 2 attending physicians
  - 3 to 4 Nurse practitioners
  - Clinical pharmacy specialist and student pharmacists

Outpatient HCT reduced intensity conditioning regimen for allogeneic transplants

- Standard conditioning
  - Fludarabine 30 mg/m2 days -6 to -2
    - Body surface area using actual body weight
    - Dose adjusted for renal dysfunction
  - Cyclophosphamide 14.5 mg/kg days -6 and -5
    - Dose based on ideal body weight unless actual is less than ideal
  - Total body irradiation day -1

Outpatient HCT conditioning regimen for non-myeloablative allogeneic transplants

- Standard GVHD prophylaxis
  - Cyclophosphamide 50 mg/kg days +3 and +4
    - Dose based on ideal body weight unless actual is less than ideal
  - Tacrolimus 1 mg IV over 4 hours every 24 hours day +5
    - Can convert to oral as early as Day +8
    - Goal: 10 – 15 ng/ml
  - Mycophenolate mofetil (MMF) 15 mg/kg by mouth every 8 hours days +5 to +35
    - Max dose of 3 grams per day
    - Administer 1 hour before a meal or 2 hours after a meal
      - 6:00 AM / 2:00 PM / 10:00 PM

Outpatient HCT conditioning regimen for autologous stem cell transplants

- Multiple myeloma patient population
- Melphalan 100 mg/m^2 on days -2 and -1
  - Dose reduced to 70 mg/m^2 if:
    - Age > 70 years
    - CrCl < 30 ml/min
    - ECOG of 2

Patient attributes associated with success in outpatient transplants

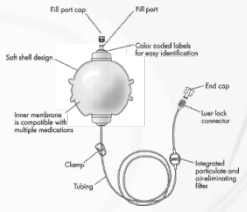
- Eligibility Criteria:
  - Diagnosis
  - Type of treatment
  - Pre-existing conditions
  - Functional status
  - Ability to communicate and follow instructions
  - Availability of a consistent caregiver
- IPOP eligibility included as part of initial screen for transplant

Supportive Care

- Anti-emetics
  - Intravenous: Clinic provided
  - Oral: Patient provided
- Treatment of GVHD
  - Initiation of oral prednisone taper
  - Initiation of tacrolimus 1 mg IV over 4 hours daily

Supportive Care

- Treatment of febrile neutropenia in IPOP
  - Hemodynamically stable
  - Non-Medicare insurance
  - Eclipse Ambulatory Infusion Systems
    - One dose administered in IPOP and remaining doses self-administered
      - Example: Piperacillin/Tazobactam 4.5 mg IV every 6 hours
        - One dose every 24 hours in IPOP
        - Three "take-home" doses



Immunosuppression

- Post-transplant cyclophosphamide
  - Mesna doses administered:
    - 15 minutes prior
    - 3 hours post, 6 hours post and 8 hours post
- Tacrolimus therapeutic drug monitoring
  - Initial level drawn following 2 to 3 days of therapy
  - May be transitioned to oral at day +8
    - Typically delayed until patient achieves therapeutic IV dose
  - Attempt to have patients always scheduled in morning or afternoon

Logistics involved in managing patients undergoing outpatient HCT conditioning

- Availability of housing within one hour drive
- Temporary housing
  - Hackerman-Patz Patient and Family Pavilion
- Insurance and Financial counselors
  - Outpatient IV antibiotics (Medicare patients)
  - Prescriptions for oral medications

Other populations seen in IPOP

- AML patients
  - Status post induction therapy with impending count recovery
  - HiDAc patients awaiting count recovery between cycles
- ALL patients
  - Count recovery between chemotherapy cycles
- APL patients
  - Arsenic chemotherapy
- Highly aggressive and aggressive lymphoma patients
  - Example: NK-cell patients receiving SMiLE chemotherapy

HiDAc: High-dose cytarabine
SMiLE: steriod=dexamethasone, methotrexate, ifosfamide, pegylated-L-asparaginase, etoposide

Wish I had known…

- Initially start with a limited patient population based on:
  - Type of transplant
  - Single-provider, etc. etc.
- Establish program for student pharmacist involvement
  - Patient counseling
  - Therapeutic drug monitoring
- Get an "arts and craft box" for student-pharmacist led patient counseling
  - Stickers
  - Label maker
  - Markers

Audience-response question

- What is the maximum driving time for a patient to be eligible to undergo HCT in the an outpatient clinic?

A. 15 minutes
B. 30-60 minutes
C. 120 minutes
D. 240 minutes

Audience Response Question

- The most common type of outpatient HCT is

- A. Allogeneic ablative
- B. Autologous for Myeloma
- C. Autologous for Lymphoma
- D. Allogeneic reduced intensity

Conclusions

- Outpatient HCT can work in very different settings and volumes
- Success relies on multidisciplinary collaboration
- We have many things in common
  - Financial issues (medical costs, housing, transportation)
  - Logistic issues
  - Reliable caregivers and communications
- Continuing challenges with the ever changing reimbursement landscapes