Provincial Clinical Knowledge Topic

Flubup Cyclophosphamide TBI for Haploidentical, Adult BMT - Inpatient

V 1.0

Revision History

Version	Date of Revision	Description of Revision	Revised By
1.0	December 27, 2018	Topic Completed	See Acknowledgments

Important Information Before you Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these recommendations should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements such as the Required Organizational Practices. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Healthcare Now campaign etc.

Guidelines

This topic is based on the following guideline(s): Alberta Blood and Marrow Transplant Program (ABMTP) Standard Practice Manual

Please refer to ABMTP Standard Practice Manual for more information and recommendations about this topic.

Keywords

Topic Name: Flubup Cyclophosphamide TBI for Haploidentical, Adult BMT - Inpatient

- Alberta Blood and Marrow Transplant Program (ABMTP)
- Blood and Marrow Transplant (BMT)
- Total Body Irradiation (TBI)
- Stem Cell Transplant
- Haploidentical Transplant
- Conditioning

Clinical Decision Support

Guides:

- Order set should include access to the ABMTP Standard Practice Manual

References:

- Reference in other order groups as indicated in each protocol once developed
    - Stem Cell Infusion - Allogeneic

Alerts:

- If a corticosteroid is ordered, alert ordering clinician steroids are not to be used in any form from Day 0 to Day 5
- If acetaminophen, metoclopramide, metronidazole, or prochlorperazine are ordered, alert ordering clinician these medications are not recommended starting 3 days (Day -10) prior to Day -7 busulfan and continuing until after last busulfan infusion is complete on Day -2 (Can be removed if attached to drug order)

Flubup Cyclophosphamide TBI for Haploidentical, Adult BMT Inpatient Order Set

Order Set Keywords: bone marrow transplant, blood and marrow transplant, BMT, allogeneic, Haplo, conditioning, total body irradiation, fludarabine, busulfan, cyclophosphamide, tacrolimus, mycophenolate mofetil

Order Set Requirements

Most recent:

- Height ______ cm
- Weight
  - actual ______ kg
  - ideal _____ kg
- BSA ______ m^2
- Estimated Creatinine Clearance (CrCl) ______
- Bilirubin and creatinine lab results

Link patient weight with recommended dose of ursodiol

- For patient weighing less than 75 kg: ursodiol 250 mg PO TID
- For patient weighing 75 – 100 kg: ursodiol 500 mg PO BID
- For patient weighing more than 100 kg: ursodiol 500 mg PO TID

~~~~~~

Indication

Conditioning for Haploidentical Allogeneic Stem Cell Transplant

Treatment Cycle and Dates

Stem Cell Infusion date: Day 0 ____________ (*dd-Mon-yyyy*)

Protocol Summary:

Protocol Day -7

busulfan (test dose) 0.8 mg/kg/dose

Protocol Day -5, -4, -3, -2

fludarabine 50 mg/m^2/dose

busulfan 3.2 mg/kg/dose (With TBI: Target 3750 umol x min/L)

Protocol Day -1 or 0

Total Body Irradiation 200 cGy

Protocol Day 0

Haploidentical Stem Cell Infusion

Protocol Day 2, 3, 4, 5

GVHD Prophylaxis: Cyclophosphamide / Tacrolimus / Mycophenolate Mofetil
~~~~~~

~*Start of Order Panel~ BMT Laboratory Investigation – ONCE - Inpatient*

**BMT Laboratory Investigation – ONCE - Inpatient

Keywords: Admission, labs, one time

ONCE – Day of Admission/Pre-Treatment - STAT

☐ Unit to Collect ☐ Lab to Collect

Hematology

☑ Complete Blood Count (CBC) with Differential
☑ PTT
☑ PT (INR)
☐ Retic count

Chemistry

☑ Electrolytes (Na, K, Cl, CO2)
☑ Creatinine
☑ Glucose Random
☑ Calcium (Ca)
☑ Magnesium (Mg)
☑ Phosphate
☑ Albumin
☑ ALP
☑ ALT
☑ Bilirubin Total
☑ Bilirubin Direct
☑ GGT
☐ LD
☑ Protein Total
☑ Urea
☑ Urate (uric acid)

Other Labs

Order for ALL women of childbearing age

☐ HCG Beta - serum

Urine Tests

☐ Urinalysis

~*End*~

~*Start of Order Panel~ BMT Laboratory Investigation – REPEATING - Inpatient*

**BMT Laboratory Investigation – REPEATING - Inpatient

Keywords: labs, repeat, Day 2

REPEATING - Starting on second day of protocol

☐ Unit to Collect ☐ Lab to Collect

Draw the following labs daily for 35 occurrences:

☑ Complete Blood Count (CBC) with Differential
☑ Electrolytes (Na, K, Cl, CO2)
☑ Creatinine
☑ Magnesium (Mg)

Draw the following labs every Mon/Thurs for 5 weeks:

Hematology

☑ PTT
☑ PT (INR)
☑ Retic Count

Chemistry

☑ Glucose Random
☑ Calcium (Ca)
☑ Phosphate
☑ Albumin
☑ ALP
☑ ALT
☑ Bilirubin Total
☑ Bilirubin Direct
☐ GGT
☐ LD
☐ Protein Total
☑ Urea
☐ Urate (uric acid)

~End~

Day -7

~Start of Smart Group~ Busulfan Pharmacokinetic Testing - Inpatient

*Busulfan Pharmacokinetic Testing - Inpatient

☐ **Busulfan PK Levels:** Draw first sample within 5 minutes after completion of sodium chloride 0.9% 25 mL IV flush and then at 1, 3, 5, and 7 hour intervals post busulfan infusion: Level must be drawn from a non-Busulfan infusion lumen of central venous access device (CVAD)
- Busulfan – End of Infusion LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 1 Hour LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 3 Hour LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 5 Hour LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 7 Hour LEVEL**:** Label sample with time. Place on ice and send to lab

~End~

Day -5

~Start of Smart Group~ Busulfan Pharmacokinetic Testing - Inpatient

*Busulfan Pharmacokinetic Testing - Inpatient

☐ **Busulfan PK Levels:** Draw first sample within 5 minutes after completion of sodium chloride 0.9% 25 mL IV flush and then at 1, 3, 5, and 7 hour intervals post busulfan infusion: Level must be drawn from a non-Busulfan infusion lumen of central venous access device (CVAD)
- Busulfan – End of Infusion LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 1 Hour LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 3 Hour LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 5 Hour LEVEL**:** Label sample with time. Place on ice and send to lab
- Busulfan – 7 Hour LEVEL**:** Label sample with time. Place on ice and send to lab

~End~

Provider Communication

☐ Provider Communication: Busulfan exposure should be kept below an AUC of 3750 umol x min/L

Nurse Communication

☐ Nurse Communication: Initiate mouth care protocol
☐ Nurse Communication: Irradiated Blood Products only

☐ Nurse Communication: Ensure central venous access device is insitu and patent prior to initiating treatment protocol
☐ Nurse Communication: Do Not Order/ Do Not Give: Avoid use of acetaminophen, metoclopramide, metronidazole, prochlorperazine or other medications that may lower seizure threshold or interfere with busulfan clearance starting 3 days (Day -10) prior busulfan on Day -7 and continuing until after last busulfan infusion is complete
☐ Nurse Communication: May also filter fludarabine if using 0.2 micron filter for busulfan

Pre-Medications

☐ ondansetron 8 mg PO/IV TID starting on Day -7 for a total of 8 days; Give morning dose pre-chemotherapy and pre-TBI

Busulfan Seizure Prophylaxis

Choose one of the following:

☐ LORazepam 0.5 mg SUBLING tab QID starting on Day -5 for a total of 5 days; Continue until 24 hours post final busulfan infusion

OR

☐ LORazepam 1 mg SUBLING tab QID starting on Day -5 for a total of 5 days; Continue until 24 hours post final busulfan infusion

Intravenous Fluids

Busulfan Hydration DAY -7, -5, -4, -3, -2

☐ 0.9% NaCl IV at 100 mL/hour once on Days -7, -5, -4, -3, -2; Infuse concurrently with busulfan and continue until busulfan infusion complete each day, **OR** on days with busulfan LEVEL draws, continue until busulfan LEVEL draws are complete

Systemic Therapy

Use ideal body weight if less than actual body weight for dosing calculations
Seizure prophylaxis with BMT doses

☐ busulfan test dose (0.8 mg/kg) _____mg IV once on Day -7 for a total of 1 dose; **Infuse at a rate of 160 mL/hr**; Requires 0.2 to 1.2 micron filter on primary line

Use ideal body weight if less than actual body weight for dosing calculations

☐ fludarabine (50 mg/m^2) _____ mg IV daily starting 0800 hours on Day - 5, -4, -3, -2 for a total of 4 doses; Infuse each dose over 1 hour
  ❖ *Dosing adjustments: Dosage reduction may be required for renal impairment*

Use ideal body weight if less than actual body weight for dosing calculations
Seizure prophylaxis with BMT doses

☐ busulfan (3.2 mg/kg) _____ mg IV daily starting 0900 hours on Day -5, -4, -3, -2 for a total of 4 doses; **Infuse at a rate of 160 mL/hr**; Requires 0.2 micron filter on primary line
  ❖ *Dosing adjustments: Dosage adjustment may be required as a result of pharmacokinetic analysis*

Day -1 or 0

~Start of Smart Group~ Total Body Irradiation (TBI) - Inpatient

*Total Body Irradiation (TBI) – Inpatient

Nurse Communication

☐ Nurse Communication: Total Body Irradiation must be completed **PRIOR** to hematopoietic progenitor cell (HPC) infusion

☐ Nurse Communication: Ensure patient has only **ONE** corticosteroid scheduled prior to morning Total Body Irradiation (i.e. methylPREDNISolone sodium succinate or dexamethasone)

Pre-medication (first fraction)

☐ LORazepam 1 mg PO/SUBLING once immediately prior to first fraction Total Body Irradiation

***DO NOT** order if corticosteroid already ordered in protocol*

☐ methylPREDNISolone sodium succinate 40 mg IV once immediately prior to second fraction Total Body Irradiation

Pre-medication (second fraction)

☐ LORazepam 1 mg PO/SUBLING once immediately prior to second fraction Total Body Irradiation

***DO NOT** order if corticosteroid already ordered in protocol*

☐ methylPREDNISolone sodium succinate 40 mg IV once immediately prior to second fraction Total Body Irradiation

TBI

☐ Total Body Irradiation First Fraction

☐ Total Body Irradiation Second Fraction

~end~

Day 0

***Required order set** (Currently under development; to be referenced in upon completion)*

- **Stem Cell Infusion – Allogeneic**

~Start of Smart Group~ GVHD Prophylaxis: Cyclophosphamide / Tacrolimus / Mycophenolate Mofetil Adult Cancer - Inpatient

*GVHD Prophylaxis: Cyclophosphamide / Tacrolimus / Mycophenolate Mofetil Adult Cancer - Inpatient

Tacrolimus Level

☐ Unit to Collect ☐ Lab to Collect

☐ Tacrolimus LEVEL: every Mon/Wed/Fri X 35 occurrences starting on Day 7; **Target LEVEL 5.0 – 15.0 mcg/L**; Draw trough level PRIOR to AM dose of tacrolimus from a non-tacrolimus infusion line

Patient Care

☐ Weight – BID at 0800 hours and 1600 hours starting on Day 2 to 5; Notify physician of weight as may require furosemide PRN for fluid overload

Nurse Communication

☐ Nurse Communication: No exposure to corticosteroids in any form from Day 0 to 5

Pre-Cyclophosphamide Hydration

☐ 0.9% NaCl IV at 150 mL/hour starting at 2200 hours on Day 2 for a total of 3 days; Stop infusion 24 hours post last dose of cyclophosphamide on Day 5

Pre-Cyclophosphamide Medications

☐ ondansetron 8 mg PO/IV TID on Day 3 and 4 for a total of 6 doses; Give morning dose pre-chemotherapy

☐ aprepitant 125 mg PO once on Day 3 **AND THEN** aprepitant 80 mg PO daily on Day 4 and 5 for a total of 2 doses; Give dose pre-chemotherapy

Cyclophosphamide

☐ mesna (12.5 mg/kg/dose) _____ mg IV daily starting 0930 hours on Day 3 and 4 for a total of 2 doses. Start 30 minutes prior to cyclophosphamide infusion; Infuse dose over 15 minutes
- ❖ *Dosing adjustments: Dosage adjustments may be required for body weight*

☐ cyclophosphamide (50 mg/kg/dose) _____ mg IV daily starting 1000 hours on Day 3 and 4 for a total of 2 doses; Infuse each dose over 2 hours
- ❖ *Dosing adjustments: Dosage adjustments may be required for renal impairment and body weight*

☐ mesna (12.5 mg/kg/dose) _____ mg IV starting 1500 hours, 1800 hours, and 2000 hours on Day 3 and 4 for a total of 6 doses; Infuse each dose over 15 minutes
- ❖ *Dosing adjustments: Dosage adjustments may be required for body weight*

Tacrolimus

*Choose **ONE** of the following options:*

☐ tacrolimus (0.12 to 0.15 mg/kg-ideal/day) _____ mg PO divided every 12 hours starting on Day 5 to Day 100; If administering tacrolimus by this route, suspend any other scheduled routes ordered for this drug

OR

☐ tacrolimus (0.03 mg/kg-ideal/day) _____ mg IV divided every 12 hours starting on Day 5 to Day 100; Infuse each dose over 2 to 4 hours; Use non-DEHP tubing for administration; If administering tacrolimus by this route, suspend any other scheduled routes ordered for this drug
- ❖ *Dosing adjustments: Dosage reduction may be required for renal and hepatic impairment*

Mycophenolate Mofetil

☐ mycophenolate mofetil 1000 mg PO/IV BID starting on Day 5 to Day 35

~End~

~Start of Order Panel~ BMT Electrolyte Imbalance - Inpatient

** BMT Electrolyte Imbalance - Inpatient

Order Set Keywords: potassium, K, KCl, magnesium, Mg

Nurse Communication:

☐ Nurse Communication: Ensure patient has no other IV potassium infusing while receiving PRN IV potassium doses

Potassium:

*Choose **ONE** option based on site availability of product*

☐ KCl 20 mmol in 100 mL sterile water IV bolus daily PRN if potassium level 3.0 to 3.3 mmol/L; Infuse as per provincial parenteral monograph

OR

☐ KCl 10 mmol in 100 mL sterile water IV bolus daily PRN; Give 2 boluses for a total of 20 mmol if potassium level 3.0 to 3.3 mmol/L; Infuse as per provincial parenteral monograph

Magnesium:

☐ magnesium sulfate 4 grams IV daily PRN if magnesium level is LESS than 0.55 mmol/L; Infuse as per provincial parenteral monograph

~End~

***~Start of Smart Group~ Allogeneic Prophylactic/Supportive Medication** - Inpatient*

*Allogeneic Prophylactic/Supportive Medication - Inpatient

Prophylactic Medications

☐ valACYclovir 500 mg PO daily starting on day of admission

☐ fluCONazole 400 mg PO daily starting on Day 1 for a total of 30 days

Start Protocol Day 21 if neutrophils are greater than $1x10E^9/L$

☐ sulfamethoxazole - trimethoprim 400 mg - 80 mg 1 tab PO daily starting on Day 21

OR

If patient has allergy to sulfa or sulfamethoxazole/trimethoprim order both:

Start Protocol Day 21 if neutrophils are greater than $1x10E^9/L$

☐ dapsone 50 mg PO daily starting on Day 21

☐ penicillin V potassium 300 mg PO BID starting on Day 21

Supportive Medications

Only order for menstruating women

☐ norethindrone - ethinyl estradiol (Ortho 1/35®) 1 tab PO daily starting on day of admission

For patient weighing less than 75 kg

☐ ursodiol 250 mg PO TID with meals starting on day of admission

OR *for patient weighing 75 – 100 kg*
☐ ursodiol 500 mg PO BID with meals starting on day of admission
OR *for patient weighing more than 100 kg*
☐ ursodiol 500 mg PO TID with meals starting on day of admission

~End~

Transition Planning

Patient and Family Education

MyHealth.Alberta.ca

- Cancer Resources
- Allogeneic Stem Cell Transplant
- Conditioning Phase When Having an Allogeneic Stem Cell Transplant
- Radiation Treatment: Video Series (includes Total Body Irradiation)
- Other Allogeneic Stem Cell Transplant Resources

YouTube: AHS Channel

- CancerControl Alberta Playlist

Transitions to Primary Care

Alberta Health Services Website (External)

- Provider and Patient Resources

Patient Medication Teaching Sheets

MyHealth.Alberta.ca

- Fludarabine
- Busulfan
- Cyclophosphamide
- Mesna
- Tacrolimus
- Mycophenolate mofetil
- Ondansetron
- Dapsone
- Sulfamethoxazole/Trimethoprim
- Penicillin V Potassium
- Fluconazole
- Valacyclovir
- Ursodiol
- Norethindrone/ethinyl estradiol

Alberta Health Services Website (Internal)

- Total Body Irradiation: Please see Patient and Family Education Resources – Radiation Treatment on the CancerControl Alberta AHS Internal website

References

1. Cancer Control Alberta: Guideline Resource Unit: Alberta Blood and Marrow Transplant Program (ABMTP) Standard Practice Manual. Alberta, Canada. https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-bmt-manual.pdf. Updated January 16, 2017. Accessed November 1, 2017.

Acknowledgements

We would like to acknowledge the contributions of the clinicians who participated in the development of this topic. Your expertise and time spent are appreciated.

Name	Title	Zone
Knowledge Lead		
Elizabeth Kurien	Physician, Oncology	Provincial
Topic Lead		
Andrew Daly	Director of Alberta Blood and Marrow Transplant Program (ABMTP)/Physician Hematology - FMC/TBCC/PLC	Calgary
Working Group Members		
Doug Pankoski	CKCM Foundation Team	Provincial
Jennifer Jupp	Provincial Pharmacy (SPOC)	Provincial
Irwindeep Sandhu	Physician, Hematology/BMT - UAH	Edmonton
Ahsan Chaudhry	Physician, BMT – FMC/TBCC	Calgary
Lynn Savoie	Physician, Hematology/BMT - FMC/TBCC	Calgary
Chris Venner	Physician, Hematology/BMT - CCI	Edmonton
Nanette Cox-Kennett	Nurse Practitioner - CCI	Edmonton
Nadia Kloc	Inpatient Manager - CCI	Edmonton
Michelle Gardecki	Unit Charge Nurse – Unit 31 CCI	Edmonton
Michelle Blue	Inpatient Unit Manager - CCI	Edmonton
Laura Spilchen	Unit Manager - Unit 5F4 UAH	Edmonton
Benjamin Dowell	Clinical Nurse Educator - Unit 57 FMC	Calgary
Carla Hornberger	Clinical Nurse Educator - Unit 57 FMC	Calgary
Clinical Support Services		
Lesley Beique	on behalf of Pharmacy Information Management Governance Committee (PIM-GC) - Pharmacy Services	Provincial
James Wesenberg	on behalf of Laboratory Services - Provincial Networks	Provincial
Carlota Basualdo	on behalf of Nutrition & Food Services	Provincial
Bernice Lau	on behalf of Diagnostic Imaging Services	Provincial
SCN or Provincial Committee		
Provincial Hematology Tumor Team		Provincial
Clinical Informatics Lead		
Alexis Desautels RNBN		Provincial

Additional Contributors

Thank you to the clinicians who participated in the colleague review process.
Your time spent reviewing the knowledge topics and providing valuable feedback is appreciated.

For questions or feedback related to this knowledge topic please contact Clinical Knowledge Topics by emailing ClinicalKnowledgeTopics@albertahealthservices.ca