Provincial Clinical Knowledge Topic
Flubup ATG TBI, Adult BMT – Inpatient
V 1.0

Revision History

Version	Date of Revision	Description of Revision	Revised By
1.0	December 26, 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 ATG TBI, Adult BMT - Inpatient

- Alberta Blood and Marrow Transplant Program (ABMTP)
- Blood and Marrow Transplant (BMT)
- Anti-thymocyte Globulin (ATG)
- Total Body Irradiation (TBI)
- Stem Cell Transplant
- Allogeneic 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 acetaminophen, metoclopramide, metronidazole, or prochlorperazine are ordered, alert ordering clinician these medications are not recommended starting 3 days (Day -11) prior to Day -8 busulfan and continuing until after last busulfan infusion is complete on Day -2 (Can be removed if attached to drug order)
- Methotrexate drug orders within the *GVHD Prophylaxis: Methotrexate/Leucovorin Adult Cancer – Inpatient* are not to be signed until the day each dose is to be administered. If possible, prefer configuration of a hard stop preventing methotrexate from being signed prior to the day each dose is to be administered

Flubup ATG +/- TBI, Adult BMT Inpatient Order Set

Order Set Keywords: allogeneic, bone marrow transplant, blood and marrow transplant, BMT, conditioning, fludarabine, busulfan, anti-thymocyte globulin (RABBIT), total body irradiation, methotrexate, leucovorin calcium, cyclosporine

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

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Indication

Conditioning for Allogeneic Stem Cell Transplant

Treatment Cycle and Dates

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

Protocol Summary:

Protocol Day -8 (or -7)

busulfan (test dose) 0.8 mg/kg/dose

Protocol Day -6, -5, -4, -3, -2

fludarabine 50 mg/m^2/dose

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

busulfan 3.2 mg/kg/dose (TBI: Target 3750 umol x min/L) (No TBI: Target 4500 umol x min/L)

Protocol Day -2

GVHD Prophylaxis: Anti-thymocyte globulin (RABBIT) 0.5 mg/kg/dose

Protocol Day -1, 0

GVHD Prophylaxis: Anti-thymocyte globulin (RABBIT) 2 mg/kg/dose

Protocol Day -1

GVHD Prophylaxis: Cyclosporine
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Protocol DAY -1 or 0
Total Body Irradiation (TBI) 400 cGy (if not previously received)
Allogeneic Stem Cell Infusion
Protocol Day 1 to 12
GVHD Prophylaxis: Methotrexate/Leucovorin

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

~End~

Day -8 or -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 if TBI is ordered or below an AUC of 4500 umol x min/L if TBI is NOT ordered

☐ Provider Communication: TBI would not be ordered for recipients who have received TBI previously

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 starting 3 days (Day -11) prior busulfan on Day -8 and continuing until after last busulfan infusion is complete as they may lower seizure threshold or interfere with busulfan clearance
☐ Nurse Communication: May also filter fludarabine if using 0.2 micron filter for busulfan

Pre-Medication

☐ ondansetron 8 mg IV/PO TID starting on Day -8 for a total of 9 days; Give first dose 30 to 60 minutes pre-chemotherapy

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 -8, -5, -4, -3, -2

☐ 0.9% NaCl IV at 100 mL/hour once on Days -8, -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 -8 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 -6, -5, -4, -3, -2 for a total of 5 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 to 1.2 micron filter on primary line
- ❖ *Dosing adjustments: Dosage adjustment may be required as a result of pharmacokinetic analysis*

Start of Order Panel~ GVHD Prophylaxis: Anti-Thymocyte Globulin (RABBIT) Adult Cancer - Inpatient

****GVHD Prophylaxis: Anti-Thymocyte Globulin (RABBIT) Adult Cancer - Inpatient**

Order Set Keywords: ATG, BMT, graft vs host disease

Order Set Requirements:

- Weight
  - actual _____ kg

Patient Care

☐ Vital Signs: For each anti-thymocyte globulin (RABBIT) infusion
- Pre-ATG infusion initiation
- Then every 15 minutes x 4
- Then every hour for 3 hours and with rate changes
- Then 15 minutes post end of infusion

Pre-Medications

☐ methylPREDNISolone sodium succinate 40 mg IV BID on Days -2, -1, 0 for a total of 6 doses; Give morning dose 30 minutes pre-anti-thymocyte globulin (RABBIT) at the following times:
- To be given at 1130 hours on Day -2
- To be given at 0830 hours on Day -1
- To be given at 0430 hours on Day 0

☐ diphenhydrAMINE 50 mg IV daily on Days -2, -1, 0 for a total of 3 doses; Give dose 15 minutes pre-anti-thymocyte globulin (RABBIT):
- To be given at 1145 hours on Day -2
- To be given at 0845 hours on Day -1
- To be given at 0445 hours on Day 0

☐ acetaminophen 1000 mg PO daily on Days -2, -1, 0 for a total of 3 doses; Give immediately pre-anti-thymocyte globulin (RABBIT):
- To be given at 1200 hours on Day -2
- To be given at 0900 hours on Day -1
- To be given at 0500 hours on Day 0

Emergency Medications

☐ meperidine 25 mg IV every 4 hours PRN on Days -2, -1 and 0 for rigors with anti-thymocyte globulin (RABBIT) infusion

☐ meperidine 50 mg IV every 4 hours PRN on Days -2, -1 and 0 for rigors with anti-thymocyte globulin (RABBIT) infusion

Anti-thymocyte globulin (RABBIT)

Pre-medication is recommended

☐ anti-thymocyte globulin (RABBIT) (0.5 mg/kg) _____mg IV once starting 1200 hours on Day -2 for a total of 1 dose; Infuse over 4 to 6 hours as per provincial parenteral monograph; Requires 0.2 to 1.2 micron filter on primary line
☐ anti-thymocyte globulin (RABBIT) (2 mg/kg) _____mg IV once starting 0900 hours on Day -1 and 0500 hours on Day 0 for a total of 2 doses; Infuse over 4 to 6 hours as per provincial parenteral monograph; Requires 0.2 to 0.22 micron filter on primary line

~End~

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 first 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: Cyclosporine Adult Cancer - Inpatient*

*GVHD Prophylaxis: Cyclosporine Adult Cancer - Inpatient

Cyclosporine LEVEL

☐ Unit to Collect ☐ Lab to Collect

☐ cyclosporin LEVEL, pre-dose: every Mon/Wed/Fri X 35 occurrences starting on Day 0; **Target LEVEL 200 – 400 mcg/L**; Draw trough level PRIOR to AM dose of cyclosporine from a non-cyclosporine infusion line

Cyclosporine

Choose ONE of the following options:

Round PO cyclosporine dose to nearest 25 mg. If actual body weight is less than ideal body weight, use actual body weight for all dosing calculations

☐ cycloSPORINE (6.25 mg/kg-ideal/dose) _____ mg PO every 12 hours starting on Day -1; If administering cycloSPORINE by this route, suspend any other scheduled routes ordered for this drug

- ❖ *Dosing adjustments: Dosage reduction may be required for renal and hepatic impairment*

OR

If actual body weight is less than ideal body weight, use actual body weight for all dosing calculations

☐ cycloSPORINE (2.5 mg/kg-ideal/dose) _____ mg IV every 12 hours starting on Day -1; Infuse over 2 to 6 hours; If administering cycloSPORINE by this route, suspend any other scheduled routes ordered for this drug

- ❖ *Dosing adjustments: Dosage reduction may be required for renal and hepatic impairment*

~*End*~

~*Start of Smart Group*~ *GVHD Prophylaxis: Methotrexate / Leucovorin Adult Cancer - Inpatient*

*GVHD Prophylaxis: Methotrexate / Leucovorin Adult Cancer - Inpatient

Methotrexate Monitoring

☐ Unit to Collect ☐ Lab to Collect

☐ Bilirubin Total daily on Day 1, 3, 6, and 11

☐ Bilirubin Direct daily on Day 1, 3, 6, and 11

Nurse Communication

☐ Nurse Communication: If creatinine rising or abnormal, ascites, effusions, mucositis, or increasing direct bilirubin, consult physician regarding holding/reducing methotrexate dose

☐ Nurse Communication: Methotrexate orders to be signed by ordering clinician individually on each day of administration after patient has been assessed

Provider Communication

☐ Provider Communication: methotrexate orders are not to be signed until after patient has been assessed on each day of administration

Methotrexate (Held Orders: to be signed each day of dose administration)

Order both of the following methotrexate orders:

☐ methotrexate (15 mg/m^2-ideal) _____ mg IV once on Day 1 for a total of one dose; Give dose 24 hours post **END** of stem cell infusion; Administer IV direct push over 2 to 5 minutes

- ❖ *Dosing adjustments: Dosage reduction may be required for renal impairment, ascites, mucositis and elevated direct bilirubin*

☐ methotrexate (10 mg/m^2-ideal) _____ mg IV once at 1200 hours on Day 3, 6, 11 for a total of 3 doses; Administer IV direct push over 2 to 5 minutes

- ❖ *Dosing adjustments: Dosage reduction may be required for renal impairment, ascites, mucositis and elevated direct bilirubin*

Leucovorin Calcium

☐ leucovorin calcium 5 mg IV every 6 hours starting on Days 2, 4, 7, 12:

- Start Day 2 dose 24 hours post last methotrexate dose for a total of 3 doses; Not to be given within 12 hours prior to next methotrexate dose; Due to timing of stem cell transplant and methotrexate dose, third leucovorin dose may need to be held
- Start Day 4 at 1200h for a total of 7 doses; Not to be given within 12 hours prior to next methotrexate dose
- Start Day 7 at 1200h for a total of 15 doses; Not to be given within 12 hours prior to next methotrexate dose
- Start Day 12 dose at 1200h; MD to reassess when absolute neutrophil count (ANC) greater than or equal to 0.5x10^9/L

~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
- Anti-thymocyte Globulin (ATG)
- lorazepam
- Methotrexate
- Leucovorin Calcium
- Cyclosporine
- Ondansetron
- Dexamethasone
- 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

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Your time spent reviewing the knowledge topics and providing valuable feedback is appreciated.

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