Provincial Clinical Knowledge Topic
Acute Promyelocytic Leukemia, Adult Cancer – Inpatient
V 1.0

Revision History

Version	Date of Revision	Description of Revision	Revised By
1.0	November 21, 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): LYHE-008 ACUTE PROMYELOCYTIC LEUKEMIA Guidelines Resource Unit (GURU) Clinical Practice Guideline

Please refer to Acute Promyelocytic Leukemia Clinical Practice Guideline for more information and recommendations about this topic.

Keywords

Topic Name: Acute Promyelocytic Leukemia, Adult Cancer – Inpatient

- Acute Promyelocytic Leukemia
- APL
- APML
- AML M3
- ATRA+ATO
- LoCoCo
- Australian Protocol
- Induction
- Consolidation
- low risk
- moderate risk
- high risk

Clinical Decision Support

Guides:

- Each order set should include access to the LYHE-008 ACUTE PROMYELOCYTIC LEUKEMIA Guidelines Resource Unit (GURU) Clinical Practice Guideline

References:

- Cumulative doxorubicin-equivalent doses of anthracyclines and anthracenediones should be calculated and available on patient's chart at time of ordering these drugs

Alerts:

- Alert ordering clinician if cumulative doxorubicin-equivalent dose thresholds of anthracyclines and anthracenediones have been reached for patient at time of ordering these drugs
- If induction or re-induction is chosen as treatment phase, alert ordering clinician that patient is at risk for tumor lysis and, therefore, Tumor Lysis Prophylaxis should be ordered along with treatment protocol
- If induction or re-induction is chosen as treatment phase, alert ordering clinician that patient is at risk for disseminated intravascular coagulation (DIC) and, therefore, Disseminated Intravascular Coagulation (DIC) Laboratory Investigations should be ordered along with treatment protocol

All-Trans Retinoic Acid and Arsenic Trioxide (LoCoCo) - Low Risk Induction: APL, Adult Cancer Inpatient Order Set

Order Set Keywords: ATRA+ATO, LoCoCo, induction, low risk, moderate risk, APL, Acute Promyelocytic Leukemia, APML, AML M3

Order Set Requirements

Most recent:

- Height _____ cm
- Weight
  - actual _____ kg
- BSA _____ m^2
- Estimated Creatinine Clearance (CrCl) _____
- Baseline ECG

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Indication

Induction therapy for low to intermediate risk Acute Promyelocytic Leukemia (APL)

- Low Risk: Baseline WBC < 10 x 10^9/L

Treatment Phase:

Induction

Treatment Goal:

_____

Treatment Cycle and Dates

Cycle __1__ *(current cycle number)* of __1__ *(total number of cycles to be administered)*

Cycle length __2 - 4 weeks post remission__ *(~~days~~/weeks)*

Day 1 _____ *(dd-Mon-yyyy)*

Protocol Description:

Protocol DAY 1 to 60

tretinoin (All-trans-retinoic acid (ATRA)) 45 mg/m^2/day

predniSONE 0.5 mg/kg/dose

arsenic trioxide 0.15 mg/kg/dose

hydroxyurea 500 mg QID (if required for leukocytosis: WBC 10 - 50 x10^9/L)

hydroxyurea 1000 mg QID (if required for leukocytosis: WBC > 50 x10^9/L)
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~*Start of Order Panel*~ *Hematology Laboratory Investigations – ONCE - Inpatient*

**Hematology Laboratory Investigations – ONCE – Inpatient

ONCE - Day of admission or start of therapy

☐ Unit to Collect ☐ Lab to Collect

Hematology

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

Transfusion Medicine

☑ Type and Screen

Chemistry

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

Other Labs

Order for ALL women of childbearing age

☐ HCG Beta - serum

~*End*~

~*Start of Order Panel*~ *Hematology Laboratory Investigations – REPEATING - Inpatient*

**Hematology Laboratory Investigations – REPEATING – Inpatient

REPEATING - Start on Day 2

☐ Unit to Collect ☐ Lab to Collect

Draw the following labs daily for 5 weeks

☑ Complete Blood Count (CBC) with Differential
☑ Creatinine
☑ Electrolytes (Na, K, Cl, CO_2)
☑ Glucose (Random)

Draw the following labs every Monday and Thursday for 5 weeks

Hematology

☑ PT (INR)
☑ PTT
☑ Fibrinogen
☐ Retic Count

Chemistry

☑ Calcium (Ca)
☑ Magnesium (Mg)
☑ Phosphate
☑ Albumin
☐ AST
☑ ALT
☑ ALP
☐ GGT
☑ Bilirubin Total
☐ Bilirubin Direct
☑ LD
☐ Lipase
☑ Protein Total
☐ Urea
☑ Urate (Uric Acid)

~*End*~

Protocol Specific Laboratory Investigations

☐ Unit to Collect ☐ Lab to Collect

ONCE Pre-Chemotherapy Bloodwork on Day 1

☐ HLA ABC – DR Typing; Draw PRIOR to Day 1 chemotherapy if not previously collected

~Start of Order Panel~ Tumor Lysis Syndrome (TLS) Management - Inpatient

**Tumor Lysis Syndrome (TLS) Management – Inpatient

Day 1 of protocol if ordered within a protocol or on day of ordering if ordered independent of a protocol

Laboratory Investigations
REPEATING

☐ Unit to Collect ☐ Lab to Collect

Draw the following labs every 8 hours for 4 days

☑ Calcium (Ca)
☑ Creatinine
☑ LD
☑ Magnesium (Mg)
☑ Phosphate
☑ Potassium
☑ Urate (Uric Acid)

Tumor Lysis Syndrome Prophylaxis

Ensure patient is receiving tumor lysis prophylaxis prior to starting induction chemotherapy

☐ allopurinol 300 mg PO daily starting on Day 1; Authorized prescriber to reassess on Day 8

Intravenous Fluid (if required for tumor lysis or renal risk)

☐ 0.9% NaCl infusion at _____ mL/hour; Authorized prescriber to assess daily
☐ Other: _____ *(fluid)* with _____ *(electrolyte)* at _____ mL/hour; Authorized prescriber to assess daily

Provider Communication

☐ Provider Communication: Reassess need for further TLS management after 4 days of order panel

~End~

~Start of Order Panel~ Disseminated Intravascular Coagulation (DIC) Laboratory Investigations - Inpatient

**Disseminated Intravascular Coagulation (DIC) Laboratory Investigations – Inpatient

ONCE
Day 1 of protocol if ordered within a protocol or STAT if ordering independent of protocol

☐ Unit to Collect ☐ Lab to Collect

Hematology

☑ Complete Blood Count (CBC) with Differential ☑ PTT

☑ D-Dimer (DVT/PE and DIC)
☑ PT (INR)
☑ Fibrinogen

Use the following scoring results if appropriate:

Platelet Count
greater than 100 = 0
50 - 100 = 1
less than 50 = 2

D-Dimer
no increase = 0
increase less than 10 x ULN = 2
increase greater than 10 x ULN = 3

INR
less than 1.3 = 0
1.4 - 1.6 = 1
greater than 1.6 = 2

Fibrinogen
greater than 1 gm/L = 0
less than 1 gm/L = 1

A total score of greater than or equal to 5 has a sensitivity of 93% and a specificity of 98% for overt DIC; therefore, recommended to order further DIC monitoring.

REPEATING

Draw the following labs 6 hours after initial labs and continue every 6 hours for 4 days

☐ Unit to Collect
☐ Lab to Collect

Hematology

☐ Complete Blood Count (CBC) with Differential
☐ PT (INR)
☐ PTT
☐ Fibrinogen

Provider Communication

☐ Provider Communication: Reassess need for further DIC monitoring on Day 4 of order panel

~End~

~Start of Order Panel~ Hemostatic Support for Disseminated Intravascular Coagulation (DIC): Standing Orders - Inpatient

**Hemostatic Support for Disseminated Intravascular Coagulation (DIC): Standing Orders – Inpatient

Day 1 of protocol if ordered within a protocol or on day of ordering if ordered independent of a protocol; AND continuing for 4 days

Provider Communication

☐ Provider Communication: Reassess need for further hemostatic support for DIC on Day 4 of order panel

Nurse Communication

☐ Nurse Communication: Ensure a signed consent to transfuse is present in patient's chart
☐ Nurse Communication: Refer to Laboratory Services: Transfusion Medicine for information regarding:
- Blood Components and Products Information/Monographs
- Irradiated Blood Component Use
- Transfusion of Blood Components and Products Policy and Procedures
- Informed consent
- Transfusion Reactions

☐ Nurse Communication: Notify provider if patient experiences a transfusion/hypersensitivity reaction

Pre-Medication

Order the following pre-medications if patient has documented history of a transfusion reaction:

☐ diphenhydrAMINE _____ mg IV once pre-blood component transfusion; If history of previous reaction

☐ acetaminophen _____ mg PO once pre-blood component transfusion; If history of previous reaction

☐ hydrocortisone sodium succinate _____ mg IV once pre-blood component transfusion; If history of previous reaction

Emergency Medications

☐ diphenhydrAMINE _____ mg IV every 4 hours PRN if patient experiences hives or pruritis during infusion

Blood Components/Laboratory Investigations

☐ If serum **fibrinogen is less than 1.5 gm/L** order the following:

- Fibrinogen Concentrate - 1000 mg STAT; Indication: hemostatic support for DIC in APL; Reason for activation: fibrinogen less than 1.5 gm/L
- Fibrinogen - draw 30 minutes post fibrinogen concentrate infusion
  ☐ Unit to Collect ☐ Lab to Collect

☐ If serum **platelet is less than 30 x10^{9}/L** order the following:

- Platelets – Quantity: 1 dose STAT; Indication: hemostatic support for DIC in APL; Reason for activation: platelets less than 30 x109/L
- Complete Blood Count (CBC) – draw 30 minutes post platelet transfusion
  ☐ Unit to Collect ☐ Lab to Collect

☐ If serum **INR is greater than 1.5** order the following:

- Fresh Frozen Plasma - 2 units STAT; Indication: hemostatic support for DIC in APL; Reason for activation: INR greater than 1.5 gm/L
- PT (INR) - 30 minutes post FFP infusion
  ☐ Unit to Collect ☐ Lab to Collect

~End~

Diagnostic Investigations

☐ Chest X-ray, 2 Projections (GR Chest, 2 Projections): Once prior to starting chemotherapy

☐ Electrocardiogram – 12 Lead: Once prior to starting chemotherapy

☐ Electrocardiogram – 12 Lead: Monday, Wednesday, Friday for duration of arsenic trioxide

Provider Communication

☐ Provider Communication: Consider a dose reduction or holding of arsenic dose if ECG results report a QTc greater than 480 or if the QTc increases more than 25% over prior ECG, even if QTc is within normal limits

☐ Provider Communication: If WBC is greater than 10 x 10^{9}/L at the time of ordering or if rises to after treatment initiation, consider adding hydroxyurea. Recommended dosing for

hydroxyurea:

- WBC count greater than 50 x 10^9/L: hydroxyurea 1000 mg QID
- WBC count 10 to 50 x 10^9/L: hydroxyurea 500 mg QID
- WBC count less than 10 x 10^9/L: hydroxyurea not required if, or to be discontinued if previously ordered

Nurse Communication

☐ Nurse Communication: Ensure HLA typing has been drawn prior to initiating treatment
☐ Clinical Communication: Ensure central venous access device (CVAD) is insitu and patent prior to initiating treatment protocol
☐ Nurse Communication: Ensure clinician has reviewed and approved ECG results prior to initiating arsenic infusion

Supportive Medications

☐ multiple vitamins with minerals 1 tab PO daily starting on Day 1

Only order for menstruating women
☐ norethindrone - ethinyl estradiol (Ortho 1/35®) 1 tab PO daily starting Day 1

Prophylactic Medications

☐ valACYclovir 500 mg PO daily starting on Day 1
☐ micafungin 50 mg IV daily starting on Day 1

☐ sulfamethoxazole - trimethoprim 400 mg - 80 mg 1 tab PO daily starting on Day 1
OR
If patient has allergy to sulfa or sulfamethoxazole-trimethoprim order:
Consider sulfa desensitization
☐ dapsone 50 mg PO daily starting on Day 1

Differentiation Syndrome Prophylaxis

Round dose to nearest 5 mg. Consider ordering Blood Glucose monitoring
☐ predniSONE (0.5 mg/kg/dose) _____ mg PO daily starting on Day 1; Reassess at 28 days with possible taper initiation if appropriate and safely past differentiation syndrome risk

Pre-Medication

Substitution to ondansetron is not recommended due to higher potential for QT prolongation
☐ granisetron 2 mg PO daily PRN starting on Day 1
OR
☐ granisetron 1 mg IV daily PRN starting on Day 1

☐ metoclopramide 10 to 20 mg PO/IV every 6 hours PRN starting on Day 1

Oral Chemotherapy

All-trans retinoic acid Instructions: Round the total dose to the nearest 10 mg. The dose is then divided BID and each dose must be a multiple of 10 mg. Note: the morning and evening dose might not be the same.

☐ tretinoin (all-trans retinoic acid) (45 mg/m^2/day) _____ mg PO divided every 12 hours starting on Day 1 and continuing until hematological remission or maximum of 60 days
- morning dose _____ mg
- evening dose _____ mg

❖ *Dosing adjustments: For APL differentiation syndrome consider interrupting tretinoin until resolution of hypoxia; Dosage reduction may be required for renal and hepatic impairment*

Systemic Therapy

☐ arsenic trioxide (0.15 mg/kg/dose) _____ mg IV daily starting on Day 1 and continuing until hematological remission or maximum of 60 days; Infuse over 2 hours; On days when ECG is ordered, do not administer arsenic until ECG has been read and assessed by physician for QTc prolongation
❖ *Dosing adjustments: Dosage reduction may be required for severe renal or hepatic impairment*
❖ *Dosing adjustments: Dose may need to be held for QTc prolongation and restarted at reduced dose*

~start of Smart Group~ APL Potassium and Magnesium Replacement

*APL Potassium and Magnesium Replacement

Nurse Communication:

☐ Nurse Communication: Ensure patient has no other IV potassium ordered or infusing while receiving PRN IV potassium doses
☐ Nurse Communication: On days arsenic trioxide is administered ensure potassium level maintained at greater than 4.0 mmol/L
☐ Nurse Communication: On days arsenic trioxide is administered ensure magnesium level maintained at greater than 0.75 mmol/L

Potassium:

☐ KCl 20 mmol in 100 mL sterile water IV bolus daily PRN; Infuse as per provincial parenteral monograph; May give equivalent dosing using KCl 10 mmol in 100 mL sterile water IV boluses:
- Give a total of 20 mmol KCl if potassium level 3.6 to 4.0 mmol/L; To be infused prior to starting arsenic
- Give a total of 40 mmol KCl if potassium level is 3.0 to 3.5 mmol/L; To be infused prior to starting arsenic

- Give a total of 40 mmol KCl if potassium LEVEL is less than 3.0 mmol/L then draw post potassium level and notify authorized prescriber if level remains less than 4.0 mmol/L

☐ potassium SR _____ mg (1500 mg = 20 mmol) PO every _____ hours starting on Day _____ *(Protocol day)*

Magnesium:

☐ magnesium sulfate 4 grams IV daily PRN if magnesium level is 0.65 to 0.75 mmol/L; Infuse as per provincial parenteral monograph prior to starting arsenic

☐ magnesium sulfate 4 grams IV daily PRN if magnesium level is **LESS than** 0.65 mmol/L; Infuse as per provincial parenteral monograph prior to starting arsenic; Then draw post magnesium level and notify authorized prescriber if level remains less than 0.75 mmol/L

☐ magnesium gluconate _____ mg PO every _____ hours starting on Day _____ *(Protocol day)*

~end~

All-Trans Retinoic Acid, IDArubicin and Arsenic Trioxide (APML4) - High Risk Induction: APL, Adult Cancer Inpatient Order Set

Order Set Keywords: APML4 Induction, Australian Protocol, high risk, APL, Acute Promyelocytic Leukemia, APML, AML M3

Order Set Requirements

Most recent:

- Height _____ cm
- Weight
  - actual _____ kg
- BSA _____ m^2
- Estimated Creatinine Clearance (CrCl) _____
- Baseline ECG
- Baseline MUGA/ECHO/cardiac MRI: left ventricular ejection fraction displayed

Link patient age with recommended dose of chemotherapy:

- For adults age 60 or under: IDArubicin (12 mg/m^2/dose)
- For adults age 61 to 70 years of age: IDArubicin (9 mg/m^2/dose)
- For adults age 71 or greater: IDArubicin (6 mg/m^2/dose)

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Indication:

Induction therapy for high risk Acute Promyelocytic Leukemia (APL)

- High Risk: Baseline WBC > 10 x 10^9/L

Treatment Phase:

Induction

Treatment Goal:

_____

Treatment Cycle and Dates:

Cycle __1__ *(current cycle number)* of __1__ *(total number of cycles to be administered)*

Cycle length __36__ *(days/~~weeks~~)*

Day 1 _____ *(dd-Mon-yyyy)*

Protocol Description:

Protocol DAY 1 to 10

predniSONE 1 mg/kg/dose

Protocol DAY 1 to 36

tretinoin (All-trans-retinoic acid (ATRA)) 45 mg/m^2/day

Protocol DAY 2, 4, 6, 8
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IDArubicin 12 mg/m^2/dose - For patients LESS than 61 years old
IDArubicin 9 mg/m^2/dose - For patients 61-70 years old
IDArubicin 6 mg/m^2/dose - For patients GREATER than 70 years old
Protocol DAY 9 to 36
arsenic trioxide 0.15 mg/kg/dose

~Start of Order Panel~ Hematology Laboratory Investigations – ONCE - Inpatient

**Hematology Laboratory Investigations – ONCE – Inpatient

ONCE - Day of admission or start of therapy

☐ Unit to Collect ☐ Lab to Collect

Hematology

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

Transfusion Medicine

☑ Type and Screen

Chemistry

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

Other Labs

Order for ALL women of childbearing age

☐ HCG Beta - serum

~End~

~Start of Order Panel~ Hematology Laboratory Investigations – REPEATING - Inpatient

**Hematology Laboratory Investigations – REPEATING – Inpatient

REPEATING - Start on Day 2

☐ Unit to Collect ☐ Lab to Collect

Draw the following labs daily for 5 weeks

☑ Complete Blood Count (CBC) with Differential
☑ Creatinine
☑ Electrolytes (Na, K, Cl, CO_2)
☑ Glucose (Random)

Draw the following labs every Monday and Thursday for 5 weeks

Hematology

☑ PT (INR)
☑ PTT
☑ Fibrinogen
☐ Retic Count

Chemistry

☑ Calcium (Ca)	☑ ALT	☑ LD
☑ Magnesium (Mg)	☑ ALP	☐ Lipase
☑ Phosphate	☐ GGT	☑ Protein Total
☑ Albumin	☑ Bilirubin Total	☐ Urea
☐ AST	☐ Bilirubin Direct	☑ Urate (Uric Acid)

~End~

Protocol Specific Laboratory Investigations

☐ Unit to Collect ☐ Lab to Collect

ONCE Pre-Chemotherapy Bloodwork on Day 1

☐ HLA ABC – DR Typing; Draw PRIOR to Day 1 chemotherapy if not previously collected

~Start of Order Panel~ Tumor Lysis Syndrome (TLS) Management - Inpatient

****Tumor Lysis Syndrome (TLS) Management – Inpatient**

Day 1 of protocol if ordered within a protocol or on day of ordering if ordered independent of a protocol

Laboratory Investigations
REPEATING

☐ Unit to Collect ☐ Lab to Collect

Draw the following labs every 8 hours for 4 days

☑ Calcium (Ca)	☑ Phosphate
☑ Creatinine	☑ Potassium
☑ LD	☑ Urate (Uric Acid)
☑ Magnesium (Mg)	

Tumor Lysis Syndrome Prophylaxis

Ensure patient is receiving tumor lysis prophylaxis prior to starting induction chemotherapy

☐ allopurinol 300 mg PO daily starting on Day 1; Authorized prescriber to reassess on Day 8

Intravenous Fluid (if required for tumor lysis or renal risk)

☐ 0.9% NaCl infusion at _____ mL/hour; Authorized prescriber to assess daily

☐ Other: _____ *(fluid)* with _____ *(electrolyte)* at _____ mL/hour; Authorized prescriber to assess daily

Provider Communication

☐ Provider Communication: Reassess need for further TLS management after 4 days of order panel

~End~

~*Start of Order Panel~ Disseminated Intravascular Coagulation (DIC) Laboratory Investigations - Inpatient*

**Disseminated Intravascular Coagulation (DIC) Laboratory Investigations – Inpatient

ONCE

Day 1 of protocol if ordered within a protocol or STAT if ordering independent of protocol

☐ Unit to Collect ☐ Lab to Collect

Hematology

☑ Complete Blood Count (CBC) with Differential ☑ PTT
☑ D-Dimer (DVT/PE and DIC) ☑ Fibrinogen
☑ PT (INR)

Use the following scoring results if appropriate:

Platelet Count
- *greater than 100 = 0*
- *50 - 100 = 1*
- *less than 50 = 2*

D-Dimer
- *no increase = 0*
- *increase less than 10 x ULN = 2*
- *increase greater than 10 x ULN = 3*

INR
- *less than 1.3 = 0*
- *1.4 - 1.6 = 1*
- *greater than 1.6 = 2*

Fibrinogen
- *greater than 1 gm/L = 0*
- *less than 1 gm/L = 1*

A total score of greater than or equal to 5 has a sensitivity of 93% and a specificity of 98% for overt DIC; therefore, recommended to order further DIC monitoring.

REPEATING

Draw the following labs 6 hours after initial labs and continue every 6 hours for 4 days

☐ Unit to Collect ☐ Lab to Collect

Hematology

☐ Complete Blood Count (CBC) with Differential ☐ PTT
☐ PT (INR) ☐ Fibrinogen

Provider Communication

☐ Provider Communication: Reassess need for further DIC monitoring on Day 4 of order panel

~*End~*

~*Start of Order Panel~ Hemostatic Support for Disseminated Intravascular Coagulation (DIC): Standing Orders - Inpatient*

Hemostatic Support for Disseminated Intravascular Coagulation (DIC): Standing Orders - Inpatient

Day 1 of protocol if ordered within a protocol or on day of ordering if ordered independent of a protocol; AND continuing for 4 days

Provider Communication

☐ Provider Communication: Reassess need for further hemostatic support for DIC on Day 4 of order panel

Nurse Communication

☐ Nurse Communication: Ensure a signed consent to transfuse is present in patient's chart

☐ Nurse Communication: Refer to Laboratory Services: Transfusion Medicine for information regarding:

- Blood Components and Products Information/Monographs
- Irradiated Blood Component Use
- Transfusion of Blood Components and Products Policy and Procedures
- Informed consent
- Transfusion Reactions

☐ Nurse Communication: Notify provider if patient experiences a transfusion/hypersensitivity reaction

Pre-Medication

Order the following pre-medications if patient has documented history of a transfusion reaction:

☐ diphenhydrAMINE _____ mg IV once pre-blood component transfusion; If history of previous reaction

☐ acetaminophen _____ mg PO once pre-blood component transfusion; If history of previous reaction

☐ hydrocortisone sodium succinate _____ mg IV once pre-blood component transfusion; If history of previous reaction

Emergency Medications

☐ diphenhydrAMINE _____ mg IV every 4 hours PRN if patient experiences hives or pruritis during infusion

Blood Components/Laboratory Investigations

☐ If serum **fibrinogen is less than 1.5 gm/L** order the following:

- Fibrinogen Concentrate - 1000 unit STAT; Indication: hemostatic support for DIC in APL; Reason for activation: fibrinogen less than 1.5 gm/L
- Fibrinogen - draw 30 minutes post fibrinogen concentrate infusion
  - ☐ Unit to Collect ☐ Lab to Collect

☐ If serum **platelet is less than 30 x10^9/L** order the following:

- Platelets – Quantity: 1 dose STAT; Indication: hemostatic support for DIC in APL; Reason for activation: platelets less than 30 x109/L
- Complete Blood Count (CBC) with Differential – draw 30 minutes post platelet transfusion
  - ☐ Unit to Collect ☐ Lab to Collect

☐ If serum **INR is greater than 1.5** order the following:

- Fresh Frozen Plasma - 2 units STAT; Indication: hemostatic support for DIC in APL; Reason for activation: INR greater than 1.5 gm/L
- PT (INR) - 30 minutes post FFP infusion

☐ Unit to Collect ☐ Lab to Collect

~*End*~

Diagnostic Investigations

☐ Chest X-ray, 2 Projections (GR Chest, 2 Projections): once prior to starting chemotherapy
☐ Electrocardiogram – 12 Lead: once prior to starting chemotherapy
☐ Electrocardiogram – 12 Lead: Monday, Wednesday, Friday for duration of arsenic trioxide

*Complete **ONE** of the following tests prior to starting chemotherapy:*

☐ MUGA (NM Rest Gated Blood Pool +Lab): Pre-Anthracycline Therapy; once prior to starting chemotherapy
☐ Echo Transthoracic Complete (ECHO): Pre-Anthracycline Therapy; once prior to starting chemotherapy
☐ MR Cardiac: Pre-Anthracycline Therapy; once prior to starting chemotherapy

Provider Communication

☐ Provider Communication: Consider a dose reduction or holding of arsenic dose if ECG results report a QTc greater than 480 or if the QTc increases more than 25% over prior ECG, even if QTc is within normal limits
☐ Provider Communication: If WBC is greater than 10 x 10^9/L at the time of ordering or if rises to after treatment initiation, consider adding hydroxyurea. Recommended dosing for hydroxyurea:
- WBC count greater than 50 x 10^9/L: hydroxyurea 1000 mg QID
- WBC count 10 to 50 x 10^9/L: hydroxyurea 500 mg QID
- WBC count less than 10 x 10^9/L: hydroxyurea not required if, or to be discontinued if previously ordered

Nurse Communication

☐ Nurse Communication: Ensure HLA typing has been drawn prior to initiating treatment
☐ Nurse Communication: Ensure central venous access device (CVAD) is insitu and patent prior to initiating treatment protocol
☐ Nurse Communication: Ensure clinician has reviewed and approved ECG results prior to initiating arsenic infusion

Supportive Medications

☐ vitamins multiple with minerals 1 tab PO daily starting on Day 1

Only order for menstruating women

☐ Norethindrone - ethinyl estradiol (Ortho 1/35®) 1 tab PO daily starting Day 1

Prophylactic Medications

☐ valACYclovir 500 mg PO daily starting on Day 1
☐ micafungin 50 mg IV daily starting on Day 1

Differentiation Syndrome Prophylaxis

Round dose to the nearest 5 mg

☐ predniSONE (1 mg/kg/dose) _____ mg PO daily on Days 1 to 10 for a total of 10 doses

Pre-Medication

Substitution to ondansetron is not recommended due to higher potential for QT prolongation

☐ granisetron 2 mg PO daily on Days 2, 4, 6 and 8 for a total of 4 doses; first dose to be given 30 to 60 minutes pre-chemotherapy

OR

☐ granisetron 1 mg IV daily on Days 2, 4, 6 and 8 for a total of 4 doses; first dose to be given 30 to 60 minutes pre-chemotherapy on Day 2

AND

☐ granisetron 2 mg PO daily PRN starting on Day 1

OR

☐ granisetron 1 mg IV daily PRN starting on Day 1

☐ metoclopramide 10 to 20 mg PO/IV every 6 hours PRN starting on Day 1

Oral Chemotherapy

ATRA: Round the total dose to the nearest 10 mg. The dose is then divided BID and each dose must be a multiple of 10 mg. Note: the morning and evening dose might not be the same.

☐ tretinoin (All-trans retinoic acid) (45 mg/m^2/day) _____ mg PO divided every 12 hours daily Days 1 to 36 for a total of 72 doses

- **morning** dose _____ mg
- **evening** dose _____ mg

❖ *Dosing adjustments: For APL differentiation syndrome consider interrupting tretinoin until resolution of hypoxia; Dosage reduction may be required for renal and hepatic impairment*

Systemic Therapy

Choose ONE:

For adults age 60 or under

☐ IDArubicin (12 mg/m^2/dose) _____ mg IV once every 2 days on Days 2, 4, 6, and 8 for a total of 4 doses; infuse IV over 10 to 15 minutes or give direct IV push over 5 to 10 minutes

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

OR for adults age 61 to 70 years of age

☐ IDArubicin (9 mg/m^2/dose) _____ mg IV once every 2 days on Days 2, 4, 6, and 8 for a total of 4 doses; infuse IV over 10 to 15 minutes or give direct IV push over 5 to 10 minutes

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

OR for adults age 71 or greater

☐ IDArubicin (6 mg/m^2/dose) _____ mg IV once every 2 days on Days 2, 4, 6, and 8 for a total of 4 doses; infuse IV over 10 to 15 minutes or give direct IV push over 5 to 10 minutes
- ❖ *Dosing adjustments: Dosage reduction may be required for renal and hepatic impairment*

☐ arsenic trioxide (0.15 mg/kg/dose) _____ mg IV daily on Days 9 to 36 for a total of 28 doses; infuse over 2 hours; On days when ECG is ordered, do not administer arsenic until ECG has been read and assessed by physician for QTc prolongation
- ❖ *Dosing adjustments: Dosage reduction may be required for severe renal or hepatic impairment*
- ❖ *Dosing adjustments: Dose may need to be held for QTc prolongation and restarted at reduced dose*

~start of Smart Group~ APL Potassium and Magnesium Replacement

*APL Potassium and Magnesium Replacement

Nurse Communication:

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

☐ Nurse Communication: On days arsenic trioxide is administered ensure potassium level maintained at greater than 4.0 mmol/L

☐ Nurse Communication: On days arsenic trioxide is administered ensure magnesium level maintained at greater than 0.75 mmol/L

Potassium:

☐ KCl 20 mmol in 100 mL sterile water IV bolus daily PRN; Infuse as per provincial parenteral monograph; May give equivalent dosing using KCl 10 mmol in 100 mL sterile water IV boluses:
- Give a total of 20 mmol KCl if potassium level 3.6 to 4.0 mmol/L; To be infused prior to starting arsenic
- Give a total of 40 mmol KCl if potassium level is 3.0 to 3.5 mmol/L; To be infused prior to starting arsenic
- Give a total of 40 mmol KCl if potassium LEVEL is less than 3.0 mmol/L then draw post potassium level and notify authorized prescriber if level remains less than 4.0 mmol/L

☐ potassium SR _____ mg (1500 mg = 20 mmol) PO every _____ hours starting on Day _____ *(Protocol day)*

Magnesium:

☐ magnesium sulfate 4 grams IV daily PRN if magnesium level is 0.65 to 0.75 mmol/L; Infuse as per provincial parenteral monograph prior to starting arsenic

☐ magnesium sulfate 4 grams IV daily PRN if magnesium level is **LESS than** 0.65 mmol/L; Infuse as per provincial parenteral monograph prior to starting arsenic; Then draw post magnesium level and notify authorized prescriber if level remains less than 0.75 mmol/L

☐ magnesium gluconate _____ mg PO every _____ hours starting on Day _____ *(Protocol day)*

~end~

All-Trans Retinoic Acid and Arsenic Trioxide (APML4) - High Risk Consolidation Cycle 1: APL, Adult Cancer Inpatient Order Set

Order Set Keywords: ATRA+ATO, high risk, Australian Protocol, Acute Promyelocytic Leukemia, APML4 Consolidation Cycle 1, APL, APML, AML M3

Order Set Requirements

Most recent:

- Height _____ cm
- Weight
  - actual _____ kg
- BSA _____ m^2
- Estimated Creatinine Clearance (CrCl) _____
- Baseline ECG

~~~~~~

Indication

Consolidation cycle 1 therapy for high risk Acute Promyelocytic Leukemia (APL)

- High Risk: Baseline WBC > 10 x 10^9/L

Treatment Phase:

Consolidation

Treatment Goal:

_____

Treatment Cycle and Dates

Cycle __1__ *(current cycle number)* of __1__ *(total number of cycles to be administered)*
Cycle length __3 – 4__ *(~~days~~/weeks)*
Day 1 _____ *(dd-Mon-yyyy)*

Protocol Description:

Protocol DAY 1 to 28

tretinoin (All-trans-retinoic acid (ATRA)) 45 mg/m^2/day
arsenic trioxide 0.15 mg/kg/dose

~Start of Order Panel~ Hematology Laboratory Investigations – ONCE - Inpatient

**Hematology Laboratory Investigations – ONCE – Inpatient

ONCE - Day of admission or start of therapy

☐ Unit to Collect ☐ Lab to Collect

Hematology

☑ Complete Blood Count (CBC) with Differential ☑ Fibrinogen
~~~~~~

☑ PT (INR)
☑ PTT
☑ Retic Count

Transfusion Medicine
☑ Type and Screen

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

Other Labs
Order for ALL women of childbearing age
☐ HCG Beta - serum

~End~

~Start of Order Panel~ Hematology Laboratory Investigations – REPEATING - Inpatient

**Hematology Laboratory Investigations – REPEATING – Inpatient

REPEATING - Start on Day 2
☐ Unit to Collect ☐ Lab to Collect

Draw the following labs daily for 5 weeks
☑ Complete Blood Count (CBC) with Differential
☑ Creatinine
☑ Electrolytes (Na, K, Cl, CO_2)
☑ Glucose (Random)

Draw the following labs every Monday and Thursday for 5 weeks

Hematology
☑ PT (INR)
☑ PTT
☑ Fibrinogen
☐ Retic Count

Chemistry
☑ Calcium (Ca)
☑ Magnesium (Mg)
☑ Phosphate
☑ Albumin
☐ AST
☑ ALT
☑ ALP
☐ GGT
☑ Bilirubin Total
☐ Bilirubin Direct
☑ LD
☐ Lipase
☑ Protein Total
☐ Urea
☑ Urate (Uric Acid)

~End~

Protocol Specific Laboratory Investigations

☐ Unit to Collect ☐ Lab to Collect

ONCE Pre-Chemotherapy Bloodwork on Day 1
☐ HLA ABC – DR Typing; Draw PRIOR to Day 1 chemotherapy if not previously collected

Diagnostic Investigations

☐ Chest X-ray, 2 Projections (GR Chest, 2 Projections): once prior to starting chemotherapy

☐ Electrocardiogram – 12 Lead: once prior to starting chemotherapy
☐ Electrocardiogram – 12 Lead: Monday, Wednesday, Friday for duration of arsenic trioxide

Provider Communication

☐ Provider Communication: Consider a dose reduction or holding of arsenic dose if ECG results report a QTc greater than 480 or if the QTc increases more than 25% over prior ECG, even if QTc is within normal limits

Nurse Communication

☐ Nurse Communication: Ensure central venous access device (CVAD) is insitu and patent prior to initiating treatment protocol
☐ Nurse Communication: Ensure clinician has reviewed and approved ECG results prior to initiating arsenic infusion

Supportive Medications

☐ vitamins multiple with minerals 1 tab PO daily starting on Day 1

Only order for menstruating women
☐ norethindrone - ethinyl estradiol (Ortho 1/35®) 1 tab PO daily starting Day 1

Prophylactic Medications

☐ valACYclovir 500 mg PO daily starting on Day 1
☐ micafungin 50 mg IV daily starting on Day 1

Pre-Medication

Substitution to ondansetron is not recommended due to higher potential for QT prolongation
☐ granisetron 2 mg PO daily PRN starting on Day 1
OR
☐ granisetron 1 mg IV daily PRN starting on Day 1

☐ metoclopramide 10 to 20 mg PO/IV every 6 hours PRN starting on Day 1

Oral Chemotherapy

All-trans retinoic acid instructions: Round the total dose to the nearest 10 mg. The dose is then divided BID and each dose must be a multiple of 10 mg. Note: the morning and evening dose might not be the same.
☐ tretinoin (All-trans retinoic acid) (45 mg/m^2/day) _____ mg PO divided every 12 hours daily on Days 1 to 28 for a total of 56 doses
- **morning** dose _____ mg
- **evening** dose _____ mg

- ❖ *Dosing adjustments: For APL differentiation syndrome consider interrupting tretinoin until resolution of hypoxia; Dosage reduction may be required for renal and hepatic impairment*

Systemic Therapy

☐ arsenic trioxide (0.15 mg/kg/dose) _____ mg IV daily on Days 1 to 28 for a total of 28 doses; Infuse over 2 hours; On days when ECG is ordered, do not administer arsenic until ECG has been read and assessed by physician for QTc prolongation

- ❖ *Dosing adjustments: Dosage reduction may be required for severe renal or hepatic impairment*
- ❖ *Dosing adjustments: Dose may need to be held for QTc prolongation and restarted at reduced dose*

~start of Smart Group~ APL Potassium and Magnesium Replacement

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☐ potassium SR _____ mg (1500 mg = 20 mmol) PO every _____ hours starting on Day _____ *(Protocol day)*

Magnesium:

☐ magnesium sulfate 4 grams IV daily PRN if magnesium level is 0.65 to 0.75 mmol/L; Infuse as per provincial parenteral monograph prior to starting arsenic

☐ magnesium sulfate 4 grams IV daily PRN if magnesium level is **LESS than** 0.65 mmol/L; Infuse as per provincial parenteral monograph prior to starting arsenic; Then draw post magnesium level and notify authorized prescriber if level remains less than 0.75 mmol/L

☐ magnesium gluconate _____ mg PO every _____ hours starting on Day _____ *(Protocol day)*

~end~

Transition Planning

Patient and Family Education

MyHealth.Alberta.ca

- Cancer Resources
- Leukemia

Alberta Health Services Website (Internal)

- Leukemia Resources - Please see *Patient and Family Education Resources: Disease Specific* on the CancerControl Alberta: Alberta Health Services Internal website

YouTube: AHS Channel

- CancerControl Alberta Playlist

Transitions to Primary Care

Alberta Health Services Website (External)

- Cancer: Provider and Patient Resources

Patient Medication Teaching Sheets

MyHealth.Alberta.ca

- Idarubicin
- Arsenic Trioxide
- Tretinoin ATRA
- Granisetron
- Prednisone
- Valacyclovir
- Micafungin
- Norethindrone - Ethinyl Estradiol
- Sulfamethoxazole - Trimethoprim
- Dapsone

Alberta Health Services Website (Internal)

- Metoclopramide - Please see *Patient Medication Teaching Sheets* on the CancerControl Alberta AHS Internal website

References

1. Clinical Practice Guideline LYHE-008: Acute Promyelocytic Leukemia; Version 1. Cancer Control Alberta: Guideline Resource Unit. https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-lyhe008-apl.pdf. Created May 2015. Accessed Nov 17, 2017.

Additional Readings and General References

Kharkhanis P, Bolds S, Debragga S, Caprara CR, Simon KS, Arellano ML, Jillella A, & Kota V. Acute Promyelocytic Leukemia (APL) Induction Therapy and Incidence of Renal Insufficiency. *Blood*. 2017; 130 (Suppl 1), 5020. Retrieved from http://www.bloodjournal.org/content/130/Suppl_1/5020. Accessed September 19, 2018.

Falanga A. Predicting APL lethal bleeding in the ATRA era. *Blood*. 2017; 129(13), 1739-1740. https://doi.org/10.1182/blood-2017-02-763490. Accessed September 19, 2018.

Caprara CR, Kharkhanis P, Simon KS, Debragga S, Bolds S, Arellano ML, Jillella A, & Kota V. Utility of D-Dimer LEVEL As a Marker for Differentiation Syndrome, Infection, and Death in ACUTE Promyelocytic Leukemia (APL). *Blood*. 2017; 130(Suppl 1), 5071. Retrieved from http://www.bloodjournal.org/content/130/Suppl_1/5071. Accessed September 19, 2018.

Levi M, & Scully M. How I treat disseminated intravascular coagulation. *Blood*. 2018; 131(8), 845-854. https://doi.org/10.1182/blood-2017-10-804096. Accessed September 18, 2018.

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Name	Title	Zone
Knowledge Lead		
Elizabeth Kurien	Physician, Oncology	Provincial
Topic Lead		
Joseph Brandwein	Physician, Hematology	Edmonton
Working Group Members		
Doug Pankoski	CKCM Foundation Team	Provincial
Jennifer Jupp	Provincial Pharmacy (SPOC)	Provincial
Andrew Daly	Director of ABMTP / Physician Hematology - FMC/TBCC/PLC	Calgary
Lynn Savoie	Physician, Hematology/BMT - FMC/TBCC	Calgary
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
Karen Raymaakers	Clinical Nurse Specialist - Unit 38 PLC	Calgary
Dawn Marie Lawrence	Clinical Nurse Educator – Unit 38 PLC	Calgary
Benjamin Dowell	Clinical Nurse Educator - Unit 57 FMC	Calgary
Carla Hornberger	Clinical Nurse Educator - Unit 57 FMC	Calgary
Etienne Mahe	Hematopathologist, Calgary Lab Services	Calgary
Clinical Support Services		
Carole Chambers	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		
Sarah Searle RNBN		Provincial
Alexis Desautels RNBN		Provincial

Additional Contributors

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