BC Cancer Protocol Summary for Therapy of Acute Myeloid Leukemia using DAUNOrubicin Liposomal-Cytarabine Liposomal

Protocol Code	*LKAMLDCYT*
Tumour Group	*Leukemia/BMT*
Contact Physician	*Dr. David Sanford*

ELIGIBILITY:

- Adult patients with newly diagnosed therapy-related AML (t-AML) or AML with myelodysplasia-related changes (AML-MRC)
- Suitable for intensive induction chemotherapy
- ECOG performance status 0-2
- Prescribed by Leukemia/BMT Program physicians

Patients should have:

- CrCl greater than or equal to 30 mL/min
- Total bilirubin less than or equal to 50 micromol/L
- LVEF greater than 50%

EXCLUSIONS:

- Presence of t(8;21), inv(16)/t(16;16) or t(15;17) in t-AML

TESTS:

- **Baseline:** CBC and differential, platelets, bilirubin (total and direct), GGT, ALT, alkaline phosphatase, LDH, INR, creatinine, urea, electrolyte panel, calcium, phosphate, magnesium, albumin, uric acid, pregnancy test (if child-bearing potential), HIV, HBsAg, HBsAb, HBcAb, HCAb, HSV1 and 2 Ab, VZV
- **Baseline:** MUGA or ECHO, ECG
- **Prior to each cycle:** CBC and differential, platelets, bilirubin (total and direct), GGT, ALT, alkaline phosphatase, LDH, creatinine, urea, electrolyte panel, calcium, phosphate, magnesium, albumin, INR, MUGA or ECHO, ECG
- **Before each treatment:** CBC and differential, platelets, electrolyte panel, creatinine, urea, GGT, ALT, alkaline phosphatase, LDH, bilirubin (total and direct)
- **Bone marrow biopsy** day 28 to 35 post induction to assess response

PREMEDICATIONS:

- Antiemetic protocol for moderately emetogenic chemotherapy (see SCNAUSEA)
- Refer to current Leukemia/BMT program recommendations for antiviral, antifungal and antibiotic prophylaxis related to induction and consolidation chemotherapy

TREATMENT:

First induction:

Drug	Dose	BC Cancer Administration Guideline
DAUNOrubicin liposomal-cytarabine liposomal	44* mg/m^2 on Days 1, 3 and 5	IV in 500 mL D5W over 90 minutes

Second induction:
To be given 2 to 5 weeks after the start of first induction if patient failed to achieve remission with the first induction and show no unacceptable toxicity.

Drug	Dose	BC Cancer Administration Guideline
DAUNOrubicin liposomal-cytarabine liposomal	44* mg/m^2 on Days 1 and 3	IV in 500 mL D5W over 90 minutes

Consolidation:
To be given 5 to 8 weeks after the start of last induction, if remission was achieved, no unacceptable toxicity, and recovered hematologically (ANC greater than 0.5 x 10^9/L and platelets greater than 50 x 10^9/L).

Drug	Dose	BC Cancer Administration Guideline
DAUNOrubicin liposomal-cytarabine liposomal	29* mg/m^2 on Days 1 and 3	IV in 500 mL D5W over 90 minutes

- Repeat 5 to 8 weeks after the start of the first consolidation for 2 total cycles of consolidation.

*DAUNOrubicin liposomal-cytarabine liposomal is prescribed based on the DAUNOrubicin component. Each 44 mg/m^2 DAUNOrubicin component will deliver cytarabine 100 mg/m^2 in combination.

DOSE MODIFICATIONS:

1. **Renal:** No adjustment required for mild to moderate renal impairment. There is no information for use in severe renal impairment (CrCl 15 to 29 mL/min).

2. **Hepatic:** No adjustment required for bilirubin less than or equal to 50 micromol/L. There is no information for use in patients with bilirubin greater than 50 micromol/L.

PRECAUTIONS:

1. **DAUNOrubicin liposomal-cytarabine liposomal** has a different posology than DAUNOrubicin injection and cytarabine injection and **must not be substituted or interchanged** with other DAUNOrubicin and/or cytarabine containing products.
2. **Tumour Lysis Syndrome (TLS):** DAUNOrubicin liposomal-cytarabine liposomal may induce hyperuricemia. Patients should receive adequate hydration, prophylaxis with antihyperuricemic agents and close monitoring during induction.
3. **Neutropenia:** DAUNOrubicin liposomal-cytarabine liposomal has been associated with severe and prolonged myelosuppression, with a longer time to neutrophil and platelet count recovery compared to 7+3 treatment. Close monitoring of blood counts and supportive measures (e.g. transfusions, antimicrobial prophylaxis) is warranted. Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BMT/Leukemia Febrile Neutropenia Guidelines.
4. **Hypersensitivity**: Non-serious reactions are commonly reported. Monitor for symptoms (rash, flushing, dyspnea, chest discomfort). Refer to BC Cancer Hypersensitivity Guidelines. For subsequent doses, prophylaxis with antihistamines and/or corticosteroids should be considered.
5. **Cardiac Toxicity**: DAUNOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. The lifetime cumulative anthracycline exposure should be calculated prior to treatment. Previous radiotherapy to the mediastinum and pre-existing cardiac disease may increase risk of cardiac toxicity. Regular cardiac assessment is recommended during treatment.
6. **Extravasation**: DAUNOrubicin causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.

Call any member of the Leukemia/BMT Program of BC at (604) 875-4863 or (604-875-5000 24 hours via Vancouver General Hospital paging) with any problems or questions regarding this treatment program.

References:

1. Lancet JE, Uy GL, Cortes JE, et al. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. J Clin Oncol 2018;36(26):2684-2692.
2. Lancet JE, Uy GL, Newell LF, et al. CPX-351 versus 7+3 cytarabine and daunorubicin chemotherapy in older adults with newly diagnosed high-risk or secondary acute myeloid leukaemia: 5-year results of a randomised, open-label, multicentre, phase 3 trial. Lancet Haematol. 2021;8(7):e481-e491.
3. Jazz Pharmaceuticals Inc. VYXEOS (daunorubicin and cytarabine liposome) Product Monograph. Mississauga, Ontario; 28 April 2021.