BC Cancer Protocol Summary for Treatment of Relapsed or Refractory Hodgkin Lymphoma with Gemcitabine, Vinorelbine and DOXOrubicin Pegylated Liposomal

Protocol Code	*LYGVLD*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Kerry Savage*

ELIGIBILITY:

Patients must have:
- Relapsed or refractory Hodgkin lymphoma, and
- Eligible for stem cell transplant

Patients should have:
- ECOG performance status 0-3,
- Adequate renal, hepatic, and bone marrow function, and
- LVEF ≥45% in patients with lifetime cumulative dose of doxorubicin >400 mg/m^2

TESTS:

- Baseline: CBC & Diff, creatinine, total bilirubin, ALT, alkaline phosphatase, LDH, GGT.
  - If clinically indicated: MUGA or echocardiogram
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): HBsAg, HBsAb, HBcoreAb
- Before each treatment (on day 1 and 8): CBC & Diff
- If clinically indicated: total bilirubin, ALT, alkaline phosphatase, GGT, LDH, creatinine, MUGA or echocardiogram
- If clinically indicated: HBV viral load (see protocol SCHBV)

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy (see SCNAUSEA)
- If prior infusion reaction to DOXOrubicin pegylated liposomal:
  - 45 minutes prior to treatment: dexamethasone 20 mg IV in NS 50 mL over 15 minutes
  - 30 minutes prior to treatment: diphenhydrAMINE 50 mg IV in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)

SUPPORTIVE MEDICATIONS

High risk of hepatitis B reactivation. If HBsAg or HBcoreAb positive, follow hepatitis B prophylaxis as per SCHBV.

TREATMENT:

Drug	Dose†	BC Cancer Administration Guideline
vinorelbine	20 mg/m^2 on day 1 and 8	IV in 50 mL NS over 6 minutes Flush line with 75 to 125 mL NS following infusion
gemcitabine	1000 mg/m^2 on day 1 and 8	IV in 250 mL NS over 30 minutes
DOXOrubicin pegylated liposomal	15 mg/m^2 on day 1 and 8	IV in 250 mL D5W over 1 hour *Initial dose:* at rate of 1 mg/min *Subsequent doses, if no prior infusion reaction:* infuse over 1 hour

† Doses for transplant-naïve patients.

For post-transplant patients, use doses below:

Drug	Dose
vinorelbine	15 mg/m^2 on day 1 and 8
gemcitabine	800 mg/m^2 on day 1 and 8
DOXOrubicin pegylated liposomal	10 mg/m^2 on day 1 and 8

Repeat every 21 days for a maximum of 6 cycles.

DOSE MODIFICATIONS:

1. Hematological on Day 1

ANC (x10^9/L)		Platelets (x10^9/L)	Dose (all drugs)
greater than or equal to 1.0	and	greater than or equal to 75	100%
Less than 1.0	or	Less than 75	Delay until recovery

Hematological on Day 8:

ANC (x10^9/L)		Platelets (x10^9/L)	Dose (all drugs)
greater than or equal to 1.0	and	greater than or equal to 75	100%
0.5 to less than 1.0	and	50 to less than 75	Reduce gemcitabine and vinorelbine dose to 75% of current cycle's day 1 dose; give 100% dose of DOXOrubicin pegylated liposomal
less than 0.5	or	less than 50	Omit

2. Hepatic

For vinorelbine:

Total bilirubin (micromol/L)	Vinorelbine dose
Less than 35	100%
36 to 50	50%
Greater than 50	25%

For DOXOrubicin pegylated liposomal:

Total bilirubin (micromol/L)	DOXOrubicin pegylated liposomal dose
Less than 21	100%
21 to 51	75%
Greater than 51	50%

3. Stomatitis: (for DOXOrubicin pegylated liposomal)

For Grades 2 to 3 toxicity, delay until recovery to Grade 1, then consider dose reduction.
For Grade 4 toxicity, discontinue DOXOrubicin pegylated liposomal.

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Cardiac toxicity**: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction.
3. **Extravasation**: **Vinorelbine** causes pain and tissue necrosis if extravasated. It is recommended to flush thoroughly with 75 to 125 mL NS after infusing vinorelbine. **DOXOrubicin pegylated liposomal** is considered an irritant. Refer to BC Cancer Extravasation Guidelines.

4. **Acute infusion reaction**: may occur with first infusion of **DOXOrubicin pegylated liposomal**, usually within minute of starting. Refer to BC Cancer Hypersensitivity Guidelines. Note: the first step is to stop the infusion. In subsequent cycles, reactions are rare, but prophylaxis with dexamethasone, diphenhydrAMINE, and famotidine may be used.
5. **Palmar-Plantar Erythrodysesthesia (PPE) (Hand-Foot Skin Reaction): DOXOrubicin pegylated liposomal** dose delay and reduction should be considered. See BC Cancer Drug Manual **DOXOrubicin pegylated liposomal** monograph for suggested strategies for preventing or minimizing PPE.
6. **Renal Toxicity**: Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with **gemcitabine**. Use caution with pre-existing renal dysfunction.
7. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue **gemcitabine** treatment if drug-induced pneumonitis is suspected.
8. **Hepatitis B Reactivation:** See SCHBV protocol for more details.

Call Dr. Kerry Savage or tumor group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Barlett N.L, Niedzwiecki D, Johnson J.L et al. Gemcitabiine, vinorelbine, and pegylated liposomal doxorubicin (GVD), a salvage regimen in relapsed Hodgkin's lymphoma: CALGB 59804. Ann Oncol. 2007; 18(6): 1071-9.
2. Queriroz LV, Fidalgo P, Moreira C et al. Gemcitabine, vinorelbine and pegylated liposomal doxorubicin (GVD) in the treatment of relapsed or refractory Hodgkin's lymphoma - Experience of a Portuguese Center. Blood 2012; 120(21): Abstract 4861.