PROTOCOL
# 1. ACUTE LEUKEMIA

## 1.1 Acute non-lymphoblastic leukemia (ANLL)

### A) Previously untreated case
- **Cytosine arabinoside**: 100 mg/m²
- **Adriamycin**: 45 mg/m²

### Consolidation therapy
- **Cytosine arabinoside**: 100 mg/m²
- **Adriamycin**: 60 mg/m²

### Maintenance therapy

#### Regimen A:
- (Follow Consolidation therapy)

#### Regimen B:
- **Cytosine arabinoside**: 20 mg/m²
- **6-Thioguanine**: 40 mg/m²

### B) Elderly case
- **Cytosine arabinoside**: 20 mg/m²

### C) Relapse or Refractory cases

#### Option 1:
- **Cytosine arabinoside**: 100 mg/m²
- **Adriamycin**: 45 mg/m²

#### Option 2:
- **Etoposide**: 100 mg/m²
- **Mitoxantrone**: 10 mg/m²

## 1.2 Acute lymphoblastic leukemia (ALL)

### Phase 1
- **Vincristine**: 1.4 mg/m²
  
  (maximal single dose 2 mg)
- **Adriamycin**: 15 mg/m²
- **Prednisolone**: 60 mg/m²
- **+ L-asparaginase**: 5,000 U/m²
<table>
<thead>
<tr>
<th>คัดแยก</th>
<th>ประเภท</th>
<th>จดหมาย</th>
<th>ขนาด</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 2</td>
<td>Cyclophosphamide</td>
<td>650 mg/m²</td>
<td></td>
</tr>
<tr>
<td>(maximal single dose 1,000 mg)</td>
<td></td>
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<tr>
<td>Ara-C</td>
<td>75 mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-Mercaptopurine</td>
<td>60 mg/m²</td>
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</tr>
<tr>
<td>Methotrexate</td>
<td>10 mg/m²</td>
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<tr>
<td>(maximum 15 mg)</td>
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</tr>
<tr>
<td>CNS irradiation</td>
<td>24 Gy</td>
<td></td>
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<tr>
<td>Consolidation :</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Phase 1</td>
<td>Vincristine</td>
<td>1.4 mg/m²</td>
<td></td>
</tr>
<tr>
<td>(maximal single dose 2 mg)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Adriamycin</td>
<td>25 mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>10 mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 2</td>
<td>Cyclophosphamide</td>
<td>650 mg/m²</td>
<td></td>
</tr>
<tr>
<td>Ara-C</td>
<td>75 mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-Thioguanine</td>
<td>60 mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance :</td>
<td>6-Mercaptopurine</td>
<td>60 mg/m²</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>20 mg/m²</td>
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</tr>
</tbody>
</table>
## 2. MALIGNANT LYMPHOMA

### 2.1 Non-Hodgkin Lymphoma (NHL)

**A) Low grade NHL**

**Protocol for treatment**

<table>
<thead>
<tr>
<th>Arm-I: COP without maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide 750 mg/m²</td>
</tr>
<tr>
<td>Vincristine 1.4 mg/m²</td>
</tr>
<tr>
<td>Prednisolone 100 mg/m²</td>
</tr>
</tbody>
</table>

**Arm-II: COP with IFN maintenance**

(COP as Arm-I regimen)

<table>
<thead>
<tr>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon alfa-2A 3 Mu</td>
</tr>
</tbody>
</table>

**Arm-III: I-COP with IFN maintenance**

<table>
<thead>
<tr>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon alfa-2A 6 Mu</td>
</tr>
</tbody>
</table>

**B) Intermediate grade (IG)**

and **High grade (HG) NHL**

**Arm-I: CHOP-I**

<table>
<thead>
<tr>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon alfa-2B 3 Mu</td>
</tr>
<tr>
<td>สัญลักษณ์</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Arm-II : CHOP with COP maintenance</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Arm-III : CHOP without maintenance</td>
</tr>
<tr>
<td>C) Other types of NHL</td>
</tr>
<tr>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>D) Failure, Progression, Relapse or Stable disease</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Option 2 : MINE regimen</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>
### Option 3: CMPP regimen

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>650 mg/m²</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>50 mg</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>100 mg/m²</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>100 mg</td>
</tr>
</tbody>
</table>

### 2.2 Hodgkin's disease (HD)

**A) Previously untreated case**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>750 mg/m²</td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.4 mg/m²</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>100 mg/m²</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>40 mg/m²</td>
</tr>
</tbody>
</table>

**B) Failure, Progression of disease, stable disease or Relapse**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adriamycin</td>
<td>50 mg/m²</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>6 mg/m²</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>10 mg/m²</td>
</tr>
</tbody>
</table>
### 3. MYELOPROLIFERATIVE DISEASES

#### 3.1 Chronic myelogenous leukemia (CML), chronic phase

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Busulphan</td>
<td>2-12 mg/day PO</td>
</tr>
</tbody>
</table>

#### 3.2 Interferon protocol in CML, chronic phase

**Phase I:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyurea</td>
<td>50 mg/kg/day PO</td>
</tr>
</tbody>
</table>

**Phase II:** Patients will be randomized into 2 groups

**Arm-1:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfa-2B</td>
<td>5 Mu</td>
</tr>
<tr>
<td>Hydroxyurea</td>
<td></td>
</tr>
<tr>
<td>If WBC &gt; 15 x 10^9/L, add hydroxyurea</td>
<td></td>
</tr>
</tbody>
</table>

**Arm-2:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon alfa-2B</td>
<td>5 Mu</td>
</tr>
<tr>
<td>Ara-C</td>
<td>20 mg/m²</td>
</tr>
</tbody>
</table>

**Option 1:** Palliative chemotherapy

| Cytosine arabinoside | 20 mg/m² |

**Option 2:** To assess the efficacy of combination of low dose cytosine arabinoside and IFN in treatment of CML patients with blastic crisis

| Interferon alfa-2B | 5 Mu |
| Ara-C              | 20 mg/m² |

#### 3.3 CML, blastic phase

**Option 1:** Palliative chemotherapy

| Cytosine arabinoside | 20 mg/m² |

**Option 2:**

| Interferon alfa-2B | 5 Mu |
| Ara-C              | 20 mg/m² |

#### 3.4 Other myeloproliferative diseases

**Option 1:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Busulphan</td>
<td>2-12 mg/day PO</td>
</tr>
</tbody>
</table>

**Option 2:**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Interferon alfa-2B</td>
<td>3 Mu</td>
</tr>
<tr>
<td>2</td>
<td>Maintain with interferon alfa-2B</td>
<td>5 Mu</td>
</tr>
</tbody>
</table>
# 4. MULTIPLE MYELOMA (MM)

## 4.1 Previously untreated cases

### A) Conventional therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melphalan</td>
<td>6 mg/m²</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>60 mg/day</td>
</tr>
</tbody>
</table>

### B) Interferon protocol for MM

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melphalan</td>
<td>6 mg/m²</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>60 mg/day</td>
</tr>
</tbody>
</table>

**Maintenance regimens:**

| Arm-I                  | Interferon alfa-2B | 3 Mu |
| Arm-II                 | Interferon alfa-2B | 3 Mu |
| Arm-III                | Interferon alfa-2B | 3 Mu |
| Dexamethasone          | 25 mg/m²            |

## 4.2 Failure, Progressing, Relapsing or Stable disease

### Option 1:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vincristine</td>
<td>0.4 mg</td>
</tr>
<tr>
<td>Adriamycin</td>
<td>9 mg/m²</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40 mg/day</td>
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</table>

### Option 2:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melphalan</td>
<td>6 mg/m²</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>60 mg/day</td>
</tr>
<tr>
<td>Repeat cycle every 6 weeks</td>
<td></td>
</tr>
<tr>
<td>plus Interferon alfa-2B 3 Mu SC thrice a week</td>
<td></td>
</tr>
</tbody>
</table>
## PROTOCOL FOR MANAGEMENT OF LUNG CANCER
(จากหนังสือแผนการรักษาโรคมะเร็ง โรงพยาบาลธัญบุรีศิริ 2587)

<table>
<thead>
<tr>
<th>ลำดับที่</th>
<th>ประทีป</th>
<th>ชื่อยา</th>
<th>ขนาด</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Cisplatin</td>
<td>25 mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Etoposide</td>
<td>100 mg/m²</td>
<td></td>
</tr>
<tr>
<td>A2</td>
<td>Carboplatin</td>
<td>25 mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Etoposide</td>
<td>100 mg/m²</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>Ifosfamide + A1 or A2</td>
<td>2 g/m²</td>
<td></td>
</tr>
<tr>
<td>3.1</td>
<td>Ifosfamide + Cisplatin + Etoposide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.2</td>
<td>Ifosfamide + Carboplatin + Etoposide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A4 (Etoposide, orally)</td>
<td>VP-16</td>
<td>50 mg</td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>Mitomycin</td>
<td>8 mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
<td>4.5 mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cisplatin</td>
<td>100 mg/m²</td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>Mitomycin</td>
<td>8 mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
<td>4.5 mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carboplatin</td>
<td>(ขนาดของยาแก้ไขยาร้าย)</td>
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</tr>
</tbody>
</table>

เพื่อป้องกันภาวะ severe neutropenia โดยให้ยา Neupogen (G-CSF) ร่วมกับ chemotherapy ทุกครั้ง
1. **ACUTE LEUKEMIA**

1.1 Acute non-lymphoblastic leukemia (ANLL)

A) Previously untreated case

**Eligibility criteria:**

- Adult patient, 15 to 60 years old
- Morphologic proof of ANLL, FAB types M1 through M7, as determined by morphology and cytochemistry
- No previous treatment with chemotherapy or radiation
- ECOG performance status of 0, 1, 2 and 3
- Adequate hepatic and renal function
- No evidence of infections

**Protocol for treatment**

**Induction:**

- Cytosine arabinoside 100 mg/m² continuous IV infusion days 1-7
- Adriamycin 45 mg/m² IV days 1-3

Repeat cycle every 4 weeks

**Criteria for evaluation**

**Complete remission (CR):**

- Normal physical status - normal spleen, liver and lymph node
- Normal peripheral blood - Hb > 11 gm/dL
  - Neutrophils > 1.5 x 10⁹/L
  - Platelet count > 100 x 10⁹/L
- M1 marrow status - < 5% blast
  - > 15% erythroid elements, > 25% normal granulocyte precursors, in a nonhypocellular marrow

**Failure:** Complete remission cannot be achieved within 2 induction courses
Postremission therapy:
Postremission chemotherapy began 4 weeks after CR. It consists of consolidation and maintenance therapy.

Consolidation therapy
- Cytosine arabinoside 100 mg/m² continuous IV infusion days 1-5
- Adriamycin 60 mg/m² IV days 1

Maintenance therapy
Maintenance chemotherapy began 4 weeks after consolidation therapy. They will be randomized into 2 regimens to assess their efficacy in terms of survival and disease-free duration.

Regimen A:
The intensification therapy with the same regimen as consolidation therapy should be given every 6 months.

Regimen B:
- Cytosine arabinoside 20 mg/m² SC days 1-7
- 6-Thioguanine 40 mg/m² PO days 1-7
  Repeat every 4 weeks
Maintenance therapy will be continued for at least 2 years or until relapse occurs.
Bone marrow aspiration to detect relapse should be performed routinely every 3 months for the first 2 years of follow-up period.

Drug Toxicity: Grading according to WHO criteria

Criteria for relapse:
- Appearance of circulating leukemic cells, or
- > 5% blasts in the bone marrow

B) Elderly case
Study objective:
To evaluate the efficacy of low-dose cytosine arabinoside in treatment of acute non-lymphoblastic leukemia in elderly patients in terms of response rate and survival.

Eligibility criteria:
- Adult patient > 60 years old
- Morphologic proof of ANLL, FAB-types M1 through M7,
as determined by morphology and cytochemistry
- No previous treatment with chemotherapy or radiation
- ECOG performance status of 0, 1, 2 and 3
- Adequate hepatic and renal function
- No evidence of infections

Protocol for treatment
Cytosine arabinoside 20 mg/m² SC days 1-7
Repeat every 4 weeks

C) Relapse or Refractory cases
Option 1: Relapse occurs after 6 months from CR
Cytosine arabinoside 100 mg/m² continuous IV infusion
Adriamycin 45 mg/m² IV days 1-3
Repeat cycle every 4 weeks

Option 2: Refractory case or Relapse within 6 months from CR
Etoposide 100 mg/m² IV infusion in 1 hr
Mitoxantrone 10 mg/m² IV day 1-3

Drug Toxicity: Grading according to WHO criteria

1.2 Acute lymphoblastic leukemia (ALL)
Open, prospective, multicenter study
Songklanagarind hospital
Chulalongkorn hospital
Maharaj Nakorn-Chiangmai hospital
Pramongkutkloa hospital
Rajavithi hospital
Ramathibodi hospital

Study objectives:
1. To determine the complete remission rate, survival and
disease-free survival of adult ALL treated with modified
Hoelzer's chemotherapy regimen
2. To determine the factors that are prognostic for the
achievement of complete remission and disease-free duration

Eligibility criteria:
- Adult patient, age ≥ 15 and ≤ 65 years old
Morphologic proof of ALL, FAB types L1, L2, L3 as determined by morphology and cytochemistry
- No previous treatment with chemotherapy or radiation
- ECOG performance status of 0, 1, 2 and 3
- Adequate hepatic and renal function
- Free of infections

Protocol for treatment
Induction:
Phase 1
Vincristine 1.4 mg/m² IV day 1, 8, 15, 22
(maximal single dose (2 mg))
Adriamycin 15 mg/m² IV day 1, 8, 15, 22
Prednisolone 60 mg/m² PO day 1-28
± L-asparaginase 5,000 U/m² IV day 1-14

Phase 2
Cyclophosphamide 650 mg/m² IV day 29, 43, 57
(maximal single dose 1,000 mg)
Ara-C 75 mg/m² IV day 31-34, 38-41, 45-48, 52-55
6-Mercaptopurine 60 mg/m² PO day 29-57
Methotrexate 10 mg/m² IT day 31, 38, 45, 52
(maximum 15 mg)
CNS irradiation 24 Gy day 29-57

Criteria for evaluation:
Complete remission (CR):
Normal physical status - normal spleen, liver and lymph node
Normal peripheral blood - Hb > 11 gm/dL
Neutrophils > 1.5 x 10⁹/L
Platelet count > 100 x 10⁹/L
M marrow status - < 5% blast
> 15% erythroid elements, > 25% normal granulocyte precursors, in a nonhypocellular marrow

Failure: complete remission cannot be achieved within 2 induction courses
Consolidation:

Phase 1

Vincristine 1.4 mg/m² IV day 1, 8, 15, 22
(maximal single dose 2 mg)
Adriamycin 25 mg/m² IV day 1, 8, 15, 22
Dexamethasone 10 mg/m² PO day 1-28

Phase 2

Cyclophosphamide 650 mg/m² IV day 29
Ara-C 75 mg/m² IV day 31-34, 38-41
6-Thioguanine 60 mg/m² PO day 29-42

Maintenance:

6-Mercaptopurine 60 mg/m² PO daily week 10-18
Methotrexate 20 mg/m² PO weekly and 29-130

The patient will be followed every months after completing chemotherapy. Bone marrow aspiration should be performed every 3 months.

Drug Toxicity: Grading according to WHO criteria

2. MALIGNANT LYMPHOMA
2.1 Non-Hodgkin Lymphoma (NHL)

A) Low grade NHL

Open, randomized, prospective, multicenter study

Songklanagarind hospital, Songkhla
Chulalongkorn hospital, Bangkok
Maharaj Nakorn-Chiangmai hospital, Chiangmai
Pramongkutkloa hospital, Bangkok
Rajavithi hospital, Bangkok
Ramathibodi hospital, Bangkok

Study objectives:

To evaluate the addition for combination alfa Interferon (IFN) to a three-drug chemotherapy regimen (COP) for low-grade NHL with respect to objective response rate, toxicity, duration of response and survival

Eligibility criteria:

- Biopsy proven diagnosis of malignant lymphoma of one of the following histologic subtypes as per the International Working Formulation
  - Diffuse lymphoma, small lymphocytic
  - Diffuse lymphoma, plasmacytoid lymphocytic

5
Follicular, predominantly small-cleaved
Follicular, mixed small cleaved and large-cell
Mantle zone lymphoma
Monocytoid B-cell lymphoma
- At least stage II (Ann Arbor's) disease
- At least one objective measurable disease parameter
- WBC count > 4.0 x 10^9/L and platelet count > 100 x 10^9/L, except for marrow invasion
- No previous treatment with chemotherapy or radiation
- ECOG performance status of 0, 1, 2 and 3
- Adequate hepatic and renal function
- No evidence of infections

Protocol for treatment
Arm-I: COP without maintenance
Induction
Cyclophosphamide 750 mg/m² IV day 1
Vincristine 1.4 mg/m² IV day 1
Prednisolone 100 mg PO day 1-5
Repeat cycle every 28 days x 8 courses

Arm-II: COP with IFN maintenance
Induction
COP as Arm-I regimen
Maintenance
Interferon alfa-2A 3 Mu SC thrice weekly for 12 months started from achievement of CR, PR or SD to disease progression/relapse or patient off study therapy

Arm-III: I-COP with IFN maintenance
Induction
Cyclophosphamide 750 mg/m² IV day 1
Vincristine 1.4 mg/m² IV day 1
Prednisolone 100 mg PO day 1-5
Interferon alfa-2A 6 Mu SC day 22-26
Repeat cycle every 28 days x 8 courses
Maintenance
IFN maintenance as Arm-II regimen
Criteria for evaluation

Complete response (CR) - Disappearance of all measurable or evaluable disease, symptoms, signs and biochemical change related tumor

Partial response (PR) - A reduction > 50% in the sum of products of two perpendicular diameters of all measurable lesions

Stable disease (SD) - A < 50% reduction and < 25% increase in the sum of products of two perpendicular diameters of all measurable lesions

Progression of disease (PD) - An increase in the products of two perpendicular diameters of a measured lesion by > 25% over the size present at entry of study and/or the appearance of new areas of disease

Drug Toxicity: Grading according to WHO criteria

B) Intermediate grade (IG) and High grade (HG) NHL

Open, randomized, prospective, multicenter study
(Asian Investigators Multi-center Studies, AIMS-Thaiand)
Songkla Narind hospital, Songkhla
Chulalongkorn hospital, Bangkok
Maharaj Nakorn-Chiangmai hospital, Chiangmai
Pramongkutkloa hospital, Bangkok
Rajavithi hospital, Bangkok
Ramathibodi hospital, Bangkok

Study objectives:

1. To compare and contrast the duration of survival of patients with IG/HG NHL treated with the study CHOP-I, CHOP with COP maintenance or CHOP regimens

2. To compare and contrast the rates and duration of objective response or stable disease in patients with IG/HG NHL treated with the study CHOP-I, CHOP with COP maintenance or CHOP regimens

Eligibility criteria:

- Biopsy proven diagnosis of malignant lymphoma of one of the following histologic subtypes as per the International Working Formulation (IWF)
Intermediate grade:
Follicular, predominantly large cell (IWF-D)
Diffuse small cleaved cell (IWF-E)
Diffuse mixed (IWF-F)
Diffuse large cell (IWF-G)

High grade:
Diffuse immunoblastic (IWF-H)

- At least stage II (Ann Arbor's) diseases
- At least one objective measurable diseases parameter
- WBC count > 4.0 x 10^9/L and platelet count > 100 x 10^9/L, except for marrow invasion
- No previous treatment with chemotherapy or radiation
- ECOG performance status of 0, 1, 2 and 3
- Adequate hepatic and renal function
- No evidence of infections

Protocol for treatment

Arm-I : CHOP-I

Induction
Cyclophosphamide 750 mg/m^2 IV day 1
Adriamycin 50 mg/m^2 IV day 1
Vincristine 1.4 mg/m^2 IV day 1
Prednisolone 60 mg/m^2 PO day 1-5
Interferon alfa-2B 5 Mu SC day 22-26
Repeat cycle every 28 days x 8 courses

Maintenance
Interferon alfa-2B 3 Mu three times a week for 52 weeks from achievement of CR, PR or SD or patient off study therapy.

Arm-II : CHOP with COP maintenance

Induction
Cyclophosphamide 750 mg/m^2 IV day 1
Adriamycin 50 mg/m^2 IV day 1
Vincristine 1.4 mg/m^2 IV day 1
Prednisolone 60 mg/m^2 PO day 1-5
Repeat cycle every 28 days x 8 courses

Maintenance
Cyclophosphamide 750 mg/m^2 IV day 1
Vincristine 1.4 mg/m^2 IV day 1
Prednisolone 60 mg/m² PO day 1-5
Repeat cycle every 28 days x 12 courses

Arm-III: CHOP without maintenance
Induction
CHOP regimen as Arm-II

Criteria for evaluation
Complete response (CR) - Disappearance of all measurable or evaluable disease, symptoms, signs and biochemical change related tumor
Partial response (PR) - A reduction > 50% in the sum of products of two perpendicular diameters of all measurable lesions
Stable disease (SD) - A < 50% reduction and < 25% increase in the sum of products of two perpendicular diameters of all measurable lesions
Progression of disease (PD) - An increase in the products of two perpendicular diameters of a measured lesion by > 25% over the size present at entry of study and/or the appearance of new areas of disease

Drug Toxicity: Grading according to WHO criteria

C) Other types of NHL
Cyclophosphamide 750 mg/m² IV day 1
Adriamycin 50 mg/m² IV day 1
Vincristine 1.4 mg/m² IV day 1
Prednisolone 60 mg/m² PO days 1-5
Repeat cycle every 28 days x 8 courses

D) Failure, Progression, Relapse or Stable disease
Option 1: ENAP regimen
Etoposide 100 mg/m² IV infusion days 1-3
Mitoxantrone 10 mg/m² IV infusion days 1-2
Cytosine arabinoside 100 mg IV infusion days 1-2
Prednisolone 100 mg PO days 1-3
Repeat cycle every 28 days
Option 2: MINE regimen
Mesna 400 mg IV every 4 hr days 1-3
Ifosfamide 1.33 g/m² IV days 1-3
Mitoxantrone 8 mg/m² IV day 1
Etoposide 65 mg/m² IV days 1-3
Repeat cycle every 28 days

Option 3: CMPP regimen
Cyclophosphamide 650 mg/m² IV day 1
Methotrexate 50 mg IV day 1
Procarbazine 100 mg/m² PO days 1-7
Prednisolone 100 mg PO days 1-7
Repeat cycle every 28 days

2.2 Hodgkin's disease
A) Previously untreated case
C-MOPP regimen:
Cyclophosphamide 750 mg/m² IV day 1, 8
Vincristine 1.4 mg/m² IV day 1, 8
Procarbazine 100 mg/m² PO day 1-14
Prednisolone 40 mg/m² PO day 1-14
Repeat cycle every 28 days x 8 courses

Criteria of evaluation: as NHL

B) Failure, Progression of disease, Stable disease or Relapse
ABV regimen :
Adriamycin 50 mg/m² IV day 1
Vinblastine 6 mg/m² IV day 1
Bleomycin 10 mg/m² IV day 1
Repeat cycle every 28 days x 8 courses

3. MYELOPROLIFERATIVE DISEASES
3.1 Chronic myelogenous leukemia (CML), chronic phase
Busulfan 2-12 mg/day PO, adjusted to WBC count

3.2 Interferon protocol in CML, chronic phase
Open, randomized, prospective, multicenter study
Songklanagarind hospital, Songkhla
Chulalongkorn hospital, Bangkok
Pramongkutkloa hospital, Bangkok
Rajavithi hospital, Bangkok
Ramathibodi hospital, Bangkok
Srinagarind hospital, Khon Kaen

Study objectives:
1. To compare and contrast the hematologic, cytogenetic responses and survival in CML patients treated with interferon alfa-2B or IFN with low dose cytosine arabinoside.
2. To assess the efficacy of combination of low dose cytosine arabinoside and IFN in those patients not achieving complete hematologic response (CHR) or cytogenetic response (CCR) by IFN treatment alone.
3. To study the side effect profiles of interferon alfa-2B in these study populations.

Eligibility criteria:
- All patients, age < 65 years, with chronic phase of Ph-positive CML.
- Previously untreated with cytotoxic drug (except in the case of busulfan if less than 7 days duration or hydroxyurea for less than 12 months).
- ECOG performance status 0-1.
- Adequate hepatic and renal function.
- No evidence of infections.

Protocol for treatment
Phase I:
Hydroxyurea 50 mg/kg/day PO
The dose should be adjusted until the WBC is < 15 x 10^9 per litre.

Phase II: Patients will be randomized into 2 groups
Arm-1:
Interferon alfa-2B 5 Mu SC thrice a week or that dose which will maintain the WBC around 4 x 10^9/L until CCR is produced and maintained for the duration of a minimum of 12 months.

If WBC > 15 x 10^9/L, add hydroxyurea.
Patients not achieving a CHR within 3 months or CCR at 6 months will be considered for the addition of Ara-C 20
mg/m²/day SC for 12 days each month until a CCR is obtained and then maintain for 12 months.

Arm-2:
- Interferon alfa-2B 5 Mu SC thrice a week
- Ara-C 20 mg/m² SC for 12 days each month

Hematologic response should be evaluated at the end of 3 months and cytogenetic response at the end of 6 months.

Criteria for response:

Hematological response:
- Complete hematologic remission (CHR): Normalization of peripheral WBC counts to levels < 10 x 10⁹ per litre with normal differential counts, normal platelet counts, and disappearance of all clinical symptoms and signs of disease including splenomegaly.
- Partial hematologic remission (PHR): Decrease in WBC to at least < 20 x 10⁹/L (> 50% from pre-treatment) and of platelet counts, and reduction by more than 50% of splenomegaly.

Cytogenetic response:
- Complete cytogenetic response (CR): Hematologic and clinical remission with Ph¹ chromosome in marrow metaphase < 1%.
- Partial cytogenetic response (PR): Ph¹ chromosome suppression was to levels of 1-34%.
- Minimal cytogenetic response (MR): Suppression was to levels of 35% to 95% of metaphases.
- No cytogenetic response (NR): Ph¹ chromosome persisted in > 95% of analyzable metaphases.

Drug Toxicity: Grading according to WHO criteria.

3.3 CML, blastic phase

Option 1: Palliative chemotherapy:

- Cytosine arabinoside 20 mg/m² SC days 1-10
- Repeat every 4 weeks

Option 2: To assess the efficacy of combination of low dose cytosine arabinoside and IFN In treatment of CML patients with...
blastic crisis

Interferon alfa-2B 5 Mu SC thrice a week
Ara-C 20 mg/m² SC for 10 days each month

Hematologic response should be evaluated at the end of 3 months and cytogenetic response at the end of 6 months.

Criteria for response
Complete remission:
Normal physical status,
Normal peripheral blood (Hb >11 g/dL, neutrophils > 1.5 x 10⁹/L, platelet count > 100 x 10⁹/L)
M marrow status: < 5% blast
> 15% erythroid elements, > 25% normal granulocytic precursors in a nonhypocellular marrow

Failure: complete remission cannot be obtained within 3 induction courses

Drug Toxicity: Grading according to WHO criteria

3.4 Other myeloproliferative diseases (Polycythemia vera, Essential thrombocythemia)

Option 1:
Busulfan 2-12 mg/day PO, adjusted to WBC count

Option 2:
Phase 1 - Interferon alfa-2B 3 Mu SC thrice a week

Criteria for response
Polycythemia vera
Complete response - A normalization of the hematocrit level (< 48%) in the absence of further phlebotomy, WBC count, platelet count within 16 weeks of treatment and maintained for at least 2 months, without clinical symptoms or palpable spleen

Partial response - Persistence of any the following: Hct > 48% or Hb > 16 g/dL, WBC > 10 x 10⁹/L, platelet > 400 x 10⁹/L, spleen 1-5 cm below left costal margin
No response - no change or disease progression

Essential thrombocythemia

Complete response - A reduction of platelet count to < 450 x 10^9/L within 16 week of treatment and maintained for at least 2 months, without clinical symptoms or palpable spleen

Partial response - A greater than 50% reduction in spleen and decrease in platelet count less than the levels for CR

No response - no change

Phase 2 - Maintain with interferon alfa-2B 5 Mu twice a week after CR till 12 months

4. MULTIPLE MYELOMA (MM)

4.1 Previously untreated cases

A) Conventional therapy

Melphalan 6 mg/m² PO days 1-4
Prednisolone 60 mg/day PO days 1-4
Repeat cycle every 6 weeks

B) Interferon protocol for MM

Open, randomized, prospective, multicenter study
(Asian Investigators Multi-center Studies, AIMS-Thailand)
Songklanagarind hospital, Songkhla
Chulalongkorn hospital, Bangkok
Maharaj Nakorn-Chiangmai hospital, Chiangmai
Pramongkutkloa hospital, Bangkok
Rajavithi hospital, Bangkok
Ramathibodi hospital, Bangkok

Study objectives:
1. To compare and contrast the durations of objective responses of patients with MM recieving the protocol maintenance regimens
2. To compare and contrast the durations of survival of patients with MM recieving the protocol maintenance regimens

Eligibility criteria:
- Durie-Salmon stage II or III MM
- ECOG performance status 0, 1, 2 and 3
- Patients may not have recieved any prior systemic
anti-MM therapy
- Adequate hepatic and renal function
- No evidence of infections

Protocol for treatment
Induction regimens:
- Melphalan 6 mg/m² PO days 1-7
- Prednisolone 60 mg/m² PO days 1-7
- Repeat cycle every 28 days for 6 cycles

Criteria for response
Complete response - all of the following: Disappearance of serum and/or urine M protein on two determinations at least 4 weeks apart.
- Normal marrow with < 5% plasma cells,
- Normal peripheral blood and no signs or symptoms,
- Normal calcium and resolution of all soft tissue plasmacytoma

Objective response - all of the following: Reduction of serum M protein levels to ≤ 50% of baseline levels on two determinations at least 4 weeks apart, decreased plasmacytoma by ≤ 50% the sum of the products of two perpendicular diameters, decrease in bone pain

Stable disease - Failure to meet response criteria of complete remission, objective response and disease progression

Relapse or Progression - any of the following:
- Increase in serum M protein level to > 50% above lowest remission level
- Increase in urinary M protein level to > 50% above lowest remission level
- Appearance of new plasmacytomas or increase in plasmacytomas by 50%
- Appearance of new lytic bone lesions or a > 50% increase in the size of any existing lesion

Failure or Resistance: When compared with baseline values, a > 50% in the serum or urinary M-protein levels,
measured on two determinations 2 weeks apart, having received 3 cycles of therapy.

Maintenance regimens: Patient randomization into 3 groups.

Arm-I
Interferon alfa-2B 3 Mu SC thrice a week from objective response to disease relapse.

Arm-II
Interferon alfa-2B 3 Mu SC thrice a week for 1 year from objective response.

Arm-III
Interferon alfa-2B 3 Mu SC thrice a week from objective response to disease relapse.
Dexamethasone 25 mg/m² PO for 4 days every 28 days from objective response to disease relapse.

Drug Toxicity: Grading according to WHO criteria.

4.2 Failure, Progressing, Relapsing or Stable disease

Option 1: Patients receiving either from 4.1 A) or 4.1 B)
Vincristine 0.4 mg IV continuous infusion days 1-4
Adriamycin 9 mg/m² IV continuous infusion days 1-4
Dexamethasone 40 mg/d PO days 1-4, 9-12, 17-20
Repeat cycle every 4 weeks x 6 courses.

Option 2: Patients receiving regimen 4.1 A)
Melphalan 6 mg/m² PO days 1-4
Prednisolone 60 mg/day PO days 1-4
Repeat cycle every 6 weeks plus interferon alfa-2B 3 Mu SC thrice a week.
# Protocol for Wilms' Tumor

## Favorable and Unfavorable Histology

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Actinomycin</th>
<th>Vincristine</th>
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</table>

**AMD + VCR 6 Mo.**

- **Actinomycin** = 15 mcg/kg/d (i.v.)
- **Vincristine** = 1.5 mg/m²/week (i.v.)

No further Rx
PROTOCOL FOR WILM'S TUMOR

st. II FAVORABLE HISTOLOGY

ACTINOMYCIN

VINCristINE

WEEKS 0 2 4 6 8 10 12 22 30 40 49 58 66

AMD + VCR 15 Mo.

- ACTINOMYCIN = 15 mcg/kg/d (i.v.)
- VINCristINE = 1.5 mg/m²/week (i.v.)
PROTOCOL FOR WILM'S TUMOR

st. III FAVORABLE HISTOLOGY

ADRIAMYCIN

ACTINOMYCIN

VINCRISTINE

WEEKS

0 2 4 6 8 10 12 19 26 32 39 45 52 58 65

AMD + VCR + ADR 15 Mo. + RT 1,000 cGy

- ACTINOMYCIN = 15 mcg/kg/d (i.v.)
- VINCristine = 1.5 mg/M²/week (i.v.)
- ADRIAMYCIN = 20 mg/M²/d (i.v.)
PROTOCOL FOR WILM'S TUMOR

st. IV FAVORABLE HISTOLOGY

WEAKS 0 2 4 6 8 10 12 19 26 32 39 45 52 58 65

ADOPIAMYCIN  +  ACTINOMYCIN  +  VINCristINE

ADOPIAMYCIN  3d
ACTINOMYCIN  5d
VINCristINE  VVVVVVVVV

AMD + VCR + ADR 15 Mo. + RT 2,000 cGy TU
+ DISTANT METASTASIS (PULMONARY) RT 1,200 cGy

* ACTINOMYCIN = 15 mcg/kg/d (i.v.)
* VINCristINE = 1.5 mg/m²/week (i.v.)
* ADRIAMYCIN = 20 mg/m²/d (i.v.)
PROTOCOL FOR WILM'S TUMOR

UNFAVORABLE HISTOLOGY st. II - IV

- Adriamycin
- Cyclophosphamide
- Actinomycin
- Vincristine

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<th>4</th>
<th>6</th>
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<td>AMD + VCR + ADR + CPM 15 Mo.</td>
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<td>ACTINOMYCIN</td>
<td>20 mg/M²/week (i.v.)</td>
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<td>VINCristine</td>
<td>1.5 mg/M²/week (i.v.)</td>
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<td>ADRIAMycin</td>
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<td>TOTAL TUMOR DOSE (cGy)</td>
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| 13 - 19 | 19 - 30 | 31 - 40 | 41↑ |   |   |   |   |    |    |    |    |    |    |    |    |
"Childhood Non-Hodgkin's Lymphoma"

Staging of NHL

<table>
<thead>
<tr>
<th>Stage</th>
<th>Extent of tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A single tumor (extranodal) or single anatomic area (nodal) with the exclusion of mediastinum or abdomen</td>
</tr>
<tr>
<td>II</td>
<td>A single tumor (extranodal) with regional LN involvement</td>
</tr>
<tr>
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<td>Two single (extranodal) tumors with or without regional LN involvement on the same side of the diaphragm</td>
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<tr>
<td></td>
<td>A resectable primary GI tract tumor, usually in the ileocecal area, with or without involvement of the associated mesenteric nodes only</td>
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<tr>
<td>III</td>
<td>Two single tumors (extranodal) on opposite sides of the diaphragm</td>
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<tr>
<td></td>
<td>Two or more nodal areas above or below the diaphragm</td>
</tr>
<tr>
<td></td>
<td>All the primary intrathoracic tumor (mediastinal, pleural, thymic)</td>
</tr>
<tr>
<td></td>
<td>All extensive primary intraabdominal disease</td>
</tr>
<tr>
<td></td>
<td>All para-spinal or epidural tumors, regardless of other tumors' site (or sites)</td>
</tr>
<tr>
<td>IV</td>
<td>Any of the above with initial involvement of CNS or bone marrow or both</td>
</tr>
</tbody>
</table>
**Chemotherapy**

**CONP Protocol**

**Induction of remission**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTX</td>
<td>1,200 mg/m²</td>
<td>I.V.</td>
<td>D₁</td>
</tr>
<tr>
<td>VCR</td>
<td>2 mg/d</td>
<td>I.V.</td>
<td>D₃, 10, 17, 24</td>
</tr>
<tr>
<td>MTX</td>
<td>6.25 mg/m²</td>
<td>I.T.</td>
<td>D₅, 31, 34</td>
</tr>
<tr>
<td>MTX</td>
<td>300 mg/m²</td>
<td>I.V.</td>
<td>D₁₂</td>
</tr>
</tbody>
</table>

(60% I.V. push, 40% I.V. drip in 4 hrs.)

**Pred**: 60 mg/m²/d P.O. D₃⁻₃₀ tapering off D₃₁⁻₃₇

**Maintenance**

Start 7⁻⁻⁻⁻1 after last dose of MTX I.T.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTX</td>
<td>1,000 mg/m²</td>
<td>I.V.</td>
<td>D₁ q 20 d.</td>
</tr>
<tr>
<td>VCR</td>
<td>1.5 mg/m²</td>
<td>I.V.</td>
<td>D₁ q 28 d.</td>
</tr>
<tr>
<td>MTX</td>
<td>6.25 mg/m²</td>
<td>I.T.</td>
<td>D₂₉ q 28 d.</td>
</tr>
<tr>
<td>MTX</td>
<td>300 mg/m²</td>
<td>I.V.</td>
<td>D₁₅ q 28 d.</td>
</tr>
<tr>
<td>Pred</td>
<td>60 mg/m²/d P.O. x 5 d. D₂₉ q 23 d.</td>
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</tbody>
</table>

"Total duration of therapy 18 months"

Keep WBC > 1,500/cu.mm.
PROTOCOL FOR TREATMENT OF LYMPHOMA IN CHILDREN

1. Non-Hodgkin's Lymphoma
   Acute lymphoblastic leukemia (ALL) with cytoxin 600 mg/m²/day, I.V. push twice. Induction of remission
   Intensive treatment, CNS prophylaxis and maintenance therapy
   Protocol 1

2. Hodgkin's Lymphoma
   a. Stage I - Radiotherapy or Deep X-ray locally.
   b. Stage II + III
      1. Deep X-ray to involved mantle's technique
         3,500 - 4,000 r in 10 weeks. Inverted Y technique 3,500 -
         4,000 r (maximum)
      2. Chemotherapy
         Deep X-ray and chemotherapy
         Modified HOPE treatment:
         Prednisolone: 2 mg/kg/day for 14 days. Tail off slowly.
         Procarbazine: 2 mg/kg/day for 14 days.
         Cytoxan: 600 mg/m² I.V. push daily 1 week.
         VCR: 1.5 mg/m² I.V. push daily 1 week.
         Repeat course every 4 weeks repeating every 2 - 3 weeks.
   c. Stage IV
      Chemotherapy with or without Modified HOPE treatment
      Palliative treatment with or without radiation
      Deep X-ray to involved Palliative treatment is not recommended
**PHASE I**

- **BM**
- **VCR 1.5 mg/m²** (V)
- **PRED 40 mg/m²/dPO.**
- **METHOTREXATE** T 10 mg Age 24-36 Mo T MTX T T T
- **12 mg Age >3 yrs**
- **6 MP 75 mg/m²/dPO.**

**PHASE II**

- **BM**
- **CRANIAL RADIATION 1800 cGy**
- **VCR 1.5 mg/m² (V)**
- **PRED 40 mg/m²/dPO.**
- **METHOTREXATE** T 10 mg Age 24-36 Mo T MTX T T T
- **12 mg Age >3 yrs**
- **6 MP 75 mg/m²/dPO.**

**PHASE III**

- **VCR 1.5 mg/m²**
- **T MTX T 8, 10 or 12 mg**
- **PRED 40 mg/m²/dPO. FOR 5 DAYS**
- **MTX 20 mg/M/wk PO.**
- **6 MP 75 mg/m²/dPO.**

**REPEAT CYCLE EVERY 12 WEEKS FOR 3 YEARS**