

## **Grupul Roman de Lucru pentru Studiul Leucemiilor acute la adult**

### **1.1. PROTOCOL CHIMIOTERAPIE LEUCEMII ACUTE LIMFOBLASTICE (LAL)**

#### **1.1.1 Protocol standard - sub 65 ani**

##### **1. Inductia I.**

Vincristin (iv) – 2mg, zilele 1, 8, 15, 22

Doxorubicin (iv, 30 min), 25 mg/m<sup>2</sup>, zilele 1, 8, 15, 22

L-Asparaginaza (iv, 30 min), 5 000 IU/m<sup>2</sup>, zilele 15,17,19,21,23,25,27

Prednison (po) 60 mg/m<sup>2</sup>, zilele 1-4, 8-12, 15-19, 28-32

Methotrexate (intratecal) - 15 mg, ziua 1

##### **2. Inductia II.**

Cyclophosphamide (iv) - 650 mg/m<sup>2</sup>, zilele 29, 43, 57

Cytarabine (iv, 1 h) - 75 mg/m<sup>2</sup>, zilele 31-34, 38-41, 45-48, 52-55

6-Mercaptopurine (po) - 60 mg/m<sup>2</sup>, zilele 29-57

Methotrexat (intratecal) – 15 mg, zilele 31, 38, 45, 52

##### **3. Consolidare I. (HDARAC+Doxo) + (HDMTX+Asp+6MP)**

Cytarabine (iv, 3 h, la 12 ore) - 1 000 mg/m<sup>2</sup>, zilele 1-4

Doxorubicin (iv, 30 min) – 30 mg/m<sup>2</sup>, zilele 3-5

- apoi, dupa recuperarea hematogica:

Methotrexat (iv, 24 h) - 1 500 mg/m<sup>2</sup>, zilele 1, 15 + Leucovorin (iv, la 24 ore de la inceperea MTX) – 6 doze la interval de 6 ore

L-Asparaginase (iv, 30 min) - 10 000 U/m<sup>2</sup>, zilele 2,16

6-Mercaptopurine (po) - 25 mg/m<sup>2</sup>, zilele 1-5, 15-19

#### **4. Reinductia I.**

Vincristin (iv) – 2mg, zilele 1, 8, 15, 22

Doxorubicin (iv, 30 min) - 25 mg/m<sup>2</sup>, zilele 1, 8, 15, 22

Prednison (po) 60 mg/m<sup>2</sup>, zilele 1-4, 8-12, 15-19, 28-32

MTX 15 mg + Cytarabina 50 mg + Dexametazona 4 mg (intratecal) – ziua 1

#### **5. Reinductia II.**

Cyclophosphamida (iv) - 650 mg/m<sup>2</sup>, ziua 29

Cytarabina (iv, 1 h) - 75 mg/m<sup>2</sup>, zilele 31-34, 38-41

6-Thioguanina (po) - 60 mg/m<sup>2</sup>, zilele 29-57

MTX 15 mg + Cytarabina 50 mg + Dexametazona 4 mg (intratecal) – ziua 29

#### **6. Consolidare II. (Etopozid + Ara-C) + (Ciclofosfamida + Ara-C)**

Etopozid (iv, 1 h) - 100 mg/m<sup>2</sup>, zilele 1-5

Cytarabine (iv, 1 h) - 150 mg/m<sup>2</sup>, zilele 1-5

- apoi, dupa revenirea hematologica

Cyclophosphamide (iv) - 1 000 mg/m<sup>2</sup>, ziua 1

Cytarabine (iv, 24 h) - 500 mg/m<sup>2</sup>, ziua 1

MTX 15 mg + Cytarabina 50 mg + Dexametazona 4 mg (intratecal) – ziua 1

#### **7. Intretinere – pana la 30 luni (2,5 ani) de la obtinerea remisiunii complete.**

- 6-Mercaptopurine (po) - 60 mg/m<sup>2</sup>, zilele 1-5

- Metotrexat (po) – 12,5 mg/m<sup>2</sup>, ziua 6

### **1.1.2. LAL - Resuta/boala refractara – sub 65 ani**

#### **- HyperCVAD**

##### **1. Ciclul A.**

Ciclofosfamida (iv, 3h, la 12 ore) – 300mg/m<sup>2</sup>, zilele 1,2,3 (in total 6 doze)

Metotrexat (it) – 15 mg, ziua 2

Doxorubicina (iv, 30min) – 50mg/m<sup>2</sup>, ziua 4

Vincristin (iv) – 2mg, zilele 4,11

Dexametazona (iv sau po) – 40mg zilele 1-4 si 11-14

Cytarabina (it) - 70mg, ziua 7

##### **2. Ciclul B**

Metotrexat (iv, 24h) – 1000mg/m<sup>2</sup>, ziua 1

Leucovorin (iv, la 24 ore de la inceperea MTX) – 6 doze la interval de 6 ore

Cytarabina (iv, 2 ore, la 12 ore) – 3000mg/m<sup>2</sup>, zilele 2,3 (in total 4 doze)

In total 8 cicluri (4A + 4B)

##### **3. Intretinere – POMP – pana la 2 ani**

Vincristin (iv) - 2mg, ziua 1

Prednison (po) – 60mg/m<sup>2</sup>, zilele 1-5

6-Mercaptopurina (po) – 60mg/m<sup>2</sup>, zilele 1-5, 8-12, 15-19, 22-26

Metotrexat (po) – 12,5mg/m<sup>2</sup>, zilele 6,13,20,27

Repetat la 28 zile, pana la 30 luni (2,5 ani) de la obtinerea remisiunii complete

**- Protocol alternativ – B-LAL, Burkitt**

**Prefaza :**

- Prednisolon 3 X 20mg zilele 1-5
- Ciclofosfamida 200mg/m<sup>2</sup> i.v. zilele 1-5

**Bloc A :**

- Vincristin 2 mg i.v. ziua 1
- Metotrexat 3000mg/m<sup>2</sup> perf. cont., ziua 1 + leucovorin 6 doze la 24 ore

de la inceperea MTX

- Ifosfamida 800mg/m<sup>2</sup> i.v. (1h) + Mesna, zilele 1-5
- Etopozid 100mg/m<sup>2</sup> i.v. (1h), zilele 4,5
- Cytarabina 150/m<sup>2</sup> la 12 ore, i.v. (1h), zilele 4,5
- Dexametazona 10mg/m<sup>2</sup>, zilele 1-5
- MTX 15mg + Ara-C 50mg + Dexametazona 8 mg, i.t., zilele 1,5

**Bloc B :**

- Vincristin 2 mg i.v. ziua 1
- Metotrexat 3000mg/m<sup>2</sup> perf. cont., ziua 1 + leucovorin 6 doze la 24 ore

de la inceperea MTX

- Ciclofosfamida 200mg/m<sup>2</sup> i.v. (1h), zilele 1-5
- Doxorubicin 25mg/m<sup>2</sup> i.v. zilele 4-5
- Dexametazona 10mg/m<sup>2</sup>, zilele 1-5
- MTX 15mg + Ara-C 50mg + Dexametazona 8 mg, i.t., zilele 1,5

**Bloc C :**

- Vindezina 3 mg i.v. ziua 1
- Cytarabina 2000mg/m<sup>2</sup> la 12 ore, i.v., (1h)
- Etopozid 150mg/m<sup>2</sup> i.v. (1h) zilele 3-5
- Dexametazona 10mg/m<sup>2</sup>, zilele 1-5

### **1.1.3. Protocol LAL-Philadelphia (BCR-ABL) pozitive**

#### 1. Inductie

- Vincristin 2mg i.v zilele 1,8,15,28
- Adriblastin 30mg/m<sup>2</sup>, perf i.v., zilele 1-3
- Ciclofosfamida 1200mg/m<sup>2</sup>, perf i.v. 3h, ziua 1
- Dexametazona 8mg/m<sup>2</sup> i.v/i.m, zilele 1-4, 8-12, 15-19, 28-32
- **Imatinib 600mg p.o. zilele 8-63**
- MTX 15mg, ARA-C 50mg, Dexa 8mg i.t. ziua 29

#### 2. Consolidare 1

- MTX 1g/m<sup>2</sup>, perf cont. 24 h, ziua 1
- Citozinarabinozid 2g/m<sup>2</sup>, perf i.v. 3 h la 12h zilele 2-3 (in total 4 doze)
- Dexametazona 8mg/m<sup>2</sup> zilele 1-3
- MTX 15mg, ARA-C 50mg, Dexa 8mg i.t. ziua 1

#### 3. Consolidare 2

- Imatinib 600 mg p.o. zilele 1-28
- MTX 15mg, ARA-C 50mg, Dexa 8mg i.t. ziua 1

**Curele consolidare 1 si consolidare 2 se administreaza alternativ, de 4 ori fiecare (in total 8 cure)**

#### 4. Intretinere – pana la 2 ani de la obtinerea RC

- Vincristin 2mg i.v. ziua 1
- Dexametazona 8mg/m<sup>2</sup> zilele 1-5
- Imatinib 600mg zilele 1-28

#### **1.1.4. LAL - Protocol tratament LAL la persoane in varsta - 65 ani**

##### 1. Inductie

- Vincristin 2mg i.v zilele 1,8,15,28
- Adriblastin 25mg/m<sup>2</sup>, perf i.v., zilele 1,8,15,28
- Dexametazona 8mg/m<sup>2</sup> i.v/i.m, zilele 1-4, 8-12, 15-19, 28-32
- MTX 15mg i.t. ziua 1

In caz de raspuns complet,

- Aceeasi schema repetata la 35-42 zile, inca 3-5 cicluri

##### 2. Intretinere cu Purinethol si MTX p.o. pana la 2 ani

In caz de IP-0,1,2, lipsa bolilor asociate, la cererea pacientului sau familiei (dupa explicarea amanuntita a riscurilor implicate)

- o protocol standard (vezi protocol LAL la persoane <65 ani)

#### **1.1.5. LAL – Criterii de remisiune completa**

- Pacient asimptomatic
- Fara adenopatii/organomegalii
- Neutrofile > 1500/mmc; Trombocite >100.000/mmc, Hgb>10g/dl
- Fara blasti in sangele periferic
- Blasti medulari <5%; daca intre acesti < 5% exista cellule cu aspect de blasti cu caractere morfologice sau citochimice de limfoblasti, nu este remisiune completa
- Fara anomalii citogenetice