

## Acute Myelogenous (AML)

## Cytarabine and Idarubicin (7 + 3)

Idarubicin and Cytarabine (7 + 3) <sup>1,2,4-8</sup>																								
Drug	Dose	Route	Administered on day(s)																		Total dose/ cycle			
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Idarubicin	12 to 13 mg/m <sup>2</sup>	IV	X	X	X																			36 to 39 mg/m <sup>2</sup>
Cytarabine	80 to 200 mg/m <sup>2</sup>	CIVI	X	X	X	X	X	X	X															560 to 1400 mg/m <sup>2</sup>
Cycle does not repeat. If the bone marrow does not show complete remission by day 28, reinduction with 5 or 7 days of cytarabine and 2 or 3 days of idarubicin is usually used.																								
<b>Alternatives:</b>																								
1. Idarubicin 12 mg/m <sup>2</sup> on days 1 through 3, cytarabine 25 mg/m <sup>2</sup> IV bolus on day 1, then 200 mg/m <sup>2</sup> CIVI on days 1 through 5. <sup>8</sup>																								
2. Idarubicin 8 mg/m <sup>2</sup> daily for 5 days, and cytarabine 100 or 200 mg/m <sup>2</sup> daily for 7 days. <sup>9,10</sup>																								
3. Idarubicin 5 mg/m <sup>2</sup> and cytarabine 1000 mg/m <sup>2</sup> daily for 6 days <sup>9,11</sup> (also used in pediatric patients).																								
4. Idarubicin 12 mg/m <sup>2</sup> daily for 3 days, and cytarabine 1000 or 2000 mg/m <sup>2</sup> daily for 4 days. <sup>12,13</sup>																								
5. Idarubicin 12 mg/m <sup>2</sup> , and cytarabine 3000 mg/m <sup>2</sup> every 12 hours daily for 3 days. <sup>19</sup>																								
6. Idarubicin 10 mg/m <sup>2</sup> daily for 3 days, and cytarabine 1000 mg/m <sup>2</sup> daily for 4 days. <sup>15</sup>																								
7. Idarubicin 12 mg/m <sup>2</sup> daily for 3 days, and cytarabine 1500 to 3000 mg/m <sup>2</sup> every 12 hours daily for 6 days. <sup>16</sup>																								
8. Cytarabine 100 mg/m <sup>2</sup> every 12 hours daily for 7 days, and idarubicin 12 mg/m <sup>2</sup> daily on days 5, 6, and 7. <sup>17</sup>																								
9. Idarubicin 6 to 12 mg/m <sup>2</sup> daily for 3 days, and cytarabine 200 to 1000 mg/m <sup>2</sup> every 12 hours daily for 5 days. <sup>18,19</sup>																								

**CONSTITUENT DRUGS**

- Cytarabine
- Idarubicin

**SYNONYMS**

- 7 + 3

**USES**

- Induction regimen for acute myelogenous leukemias (AML)<sup>1-19</sup>
- Current guidelines recommend idarubicin and cytarabine (7 + 3) as initial induction therapy for AML.<sup>20</sup>

**SUPPORTIVE CARE****Emetogenicity**

- Predicted: > 90% (high) (see p. 520)

**Hydration**

- No special precautions required

**Hypersensitivity Precautions**

- No special precautions required

**Myeloid Growth Factors**

- Prophylactic use recommended (see p. 522)
- Neutropenia
  - Febrile: 92%<sup>4</sup>

**Extravasation**

- Idarubicin (see p. 522)

**TOXICITIES****Common (> 50%)**

- *Dermatologic*<sup>1,2,5,6</sup>
  - Alopecia
    - ♦ Grade 1 to 4: 37% to 100%
    - ♦ Grade 3 or 4: 7% to 40%
- *Gastrointestinal*
  - Diarrhea: 46% to 78%<sup>1,2,4</sup>
    - ♦ Grade 3 or 4: 16%<sup>1</sup>

- Nausea and vomiting<sup>1,2,4-6</sup>
  - ◆ Grade 1 to 4: 57% to 87%
  - ◆ Grade 3 or 4: ≤ 9%
- Mucositis<sup>1,4-6</sup>
  - ◆ Grade 1 or 2: 43% to 65%
  - ◆ Grade 3 or 4: 3% to 18%
- Anorexia<sup>5</sup>
  - ◆ Grade 1 to 4: 81%
  - ◆ Grade 3 or 4: 34%
- Infection<sup>1,2,4,5,8</sup>
  - ◆ Grade 1 to 4: 66% to 92%
  - ◆ Grade 3 or 4: 25% to 66%
- Fever occurred in the majority of these patients.
- Hematologic
  - Hemorrhage<sup>2,5,8</sup>
    - ◆ Grade 1 to 4: 10% to 56%
    - ◆ Grade 3 or 4: 1%
  - Febrile neutropenia: 92%<sup>4</sup>
- Hepatic
  - Hyperbilirubinemia
    - ◆ Grade 1 or 2: 13% to 45%<sup>1,5-7</sup>
    - ◆ Grade 3 or 4: 8% to 9%<sup>1,5-7</sup>
    - ◆ Mild (> 1.25 times ULN): 59%<sup>2</sup>
  - Increased AST or alkaline phosphatase<sup>1,5</sup>
    - ◆ Grades 1 and 2: 47% and 52%, respectively
    - ◆ Grade 3 or 4: 5%

### Frequent (20% to 50%)

- Dermatologic
  - Rash
    - ◆ Grade 1 to 4: 4% to 41%<sup>1,5</sup>
    - ◆ Grade 3 or 4: ≤ 5% of patients<sup>1,5,6</sup>
- Hepatic
  - Increased serum transaminases<sup>5,7</sup>
    - ◆ Grade 1 or 2: 16% to 41%
    - ◆ Grade 3 or 4: 3% to 9%
- Treatment-related mortality
  - Hypoplasia: 29%<sup>7</sup>
  - Cardiogenic shock and ventricular fibrillation: 2%<sup>7</sup>
  - Cardiac toxicity: 2%<sup>7</sup>
  - Infections: 4%<sup>8</sup>
  - Neutropenic infection: 4%<sup>4</sup>

### Infrequent (5% to 19%)

- Gastrointestinal
  - Esophagitis: 13%<sup>2</sup>
- Cardiovascular
  - Congestive heart failure: 3% to 16%<sup>6,7</sup>
  - Phlebitis: 7%<sup>2</sup>
  - Unspecified clinical cardiac dysfunction (grades 1 to 4): 2% to 11%<sup>1,5,6,8</sup>

## RECOMMENDED LABORATORY TESTS

### Baseline

- AST/ALT
- Total bilirubin
- Serum creatinine
- CBC with differential

### Prior to Each Treatment

- CBC with differential
- An ANC of 1,000 cells/mcL and platelets of 75,000 cells/mcL are usually considered acceptable for treatment.

## DOSAGE MODIFICATIONS

### Renal Function (see p. 526)

### Liver Function (see p. 531)

- Bilirubin<sup>1</sup>
  - > 2.5 mg/dL: Reduce idarubicin dose by 50%.
  - > 5 mg/dL: Do not administer the drug.

## REFERENCES

1. Vogler WR, Velez-Garcia E, Weiner RS, et al. A phase III trial comparing idarubicin and daunorubicin in combination with cytarabine in acute myelogenous leukemia: a Southeastern Cancer Study Group Study. *J Clin Oncol.* 1992;10(7):1103-1111.
2. Wiernik PH, Banks PL, Case DC Jr, et al. Cytarabine plus idarubicin or daunorubicin as induction and consolidation therapy for previously untreated adult patients with acute myeloid leukemia. *Blood.* 1992;79(2):313-319.
3. Berman E, Heller G, Santorsa J, et al. Results of a randomized trial comparing idarubicin and cytosine arabinoside with daunorubicin and cytosine arabinoside in adult patients with newly diagnosed acute myelogenous leukemia. *Blood.* 1991;77(8):1666-1674.
4. Chen YC, Lin SF, Yao M, Chen TY, Tsao CJ, Chen TP. Induction therapy of newly diagnosed acute non-lymphocytic leukemia with idarubicin and cytosine arabinoside—the Taiwan experience. *Semin Hematol.* 1996;33(4 suppl 3):30-34.
5. Masaoka T, Ogawa M, Yamada K, Kimura K, Ohashi Y. A phase II comparative study of idarubicin plus cytarabine versus daunorubicin plus cytarabine in adult acute myeloid leukemia. *Semin Hematol.* 1996;33(4 suppl 3):12-17.
6. Vogler WR, Velez-Garcia E, Omura G, Raney M. A phase-three trial comparing daunorubicin or idarubicin combined with cytosine arabinoside in acute myelogenous leukemia. *Semin Oncol.* 1989;16(1 suppl 2):21-24.
7. Mandelli F, Petti MC, Ardia A, et al. A randomized clinical trial comparing idarubicin and cytarabine to daunorubicin and cytarabine in the treatment of acute

- non-lymphoid leukaemia. A multicentric study from the Italian Co-operative Group GIMEMA. *Eur J Cancer*. 1991;27(6):750-775.
8. de Witte T, Suci S, Peetermans M, et al. Intensive chemotherapy for poor prognosis myelodysplasia (MDS) and secondary acute myeloid leukemia (sAML) following MDS of more than 6 months duration. A pilot study by the Leukemia Cooperative Group of the European Organisation for Research and Treatment in Cancer (EORTC-LCG). *Leukemia*. 1995;9(11):1805-1811.
  9. Reiffers J, Huguet F, Stoppa AM, et al. A prospective randomized trial of idarubicin vs daunorubicin in combination chemotherapy for acute myelogenous leukemia of the age group 55 to 75. *Leukemia*. 1996;10(3):389-395.
  10. Harousseau JL, Cahn JY, Pignon B, et al. Comparison of autologous bone marrow transplantation and intensive chemotherapy as postremission therapy in adult acute myeloid leukemia. The Groupe Ouest Est Leucémies Aiguës Myéloblastiques (GOELAM). *Blood*. 1997;90(8):2978-2986.
  11. Bernstein ML, Abshire TC, Pollock BH, et al. Idarubicin and cytosine arabinoside reinduction therapy for children with multiple recurrent or refractory acute lymphoblastic leukemia: a Pediatric Oncology Group study. *J Pediatr Hematol Oncol*. 1997;19(1):68-72.
  12. Estey EH, Kantarjian H, Keating M. Idarubicin plus continuous-infusion high-dose cytarabine as treatment for patients with acute myelogenous leukemia or myelodysplastic syndrome. *Semin Oncol*. 1993;20(6 suppl 8):1-5.
  13. De La Serna J, Francisco Tomás J, Solano C, et al. Idarubicin and intermediate dose ARA-C followed by consolidation chemotherapy or bone marrow transplantation in relapsed or refractory acute myeloid leukemia. *Leuk Lymphoma*. 1997;25(3-4):365-372.
  14. Petti MC, Mandelli F. Idarubicin in acute leukemias: experience of the Italian Cooperative Group GIMEMA. *Semin Oncol*. 1989;16(1 suppl 2):10-15.
  15. Invernizzi R, Pecci A, Rossi G, et al. Idarubicin and cytosine arabinoside in the induction and maintenance therapy of high-risk myelodysplastic syndromes. *Hematologica*. 1997;82(5 suppl):9-12.
  16. Barone S, Baer MR, Sait SN, Lawrence D, Block AW, Wetzel M. High-dose cytosine arabinoside and idarubicin treatment of chronic myeloid leukemia in myeloid blast crisis. *Am J Hematol*. 2001;67(2):119-124.
  17. Ruutu T, Hänninen A, Järventie G, et al. Intensive chemotherapy of poor prognosis myelodysplastic syndromes (MDS) and acute myeloid leukemia following MDS with idarubicin and cytarabine. *Leuk Res*. 1997;21(2):133-138.
  18. Economopoulos T, Papageorgiou E, Stathakis N, et al. Treatment of high-risk myelodysplastic syndromes with idarubicin and cytosine arabinoside supported by granulocyte-macrophage colony-stimulating factor (GM-CSF). *Leuk Res*. 1996;20(5):385-390.
  19. Gardin C, Chaibi T, de Revel T, et al. Intensive chemotherapy with idarubicin, cytosine arabinoside, and granulocyte colony-stimulating factor (G-CSF) in patients with secondary and therapy-related acute myelogenous leukemia. Club de Réflexion en Hématologie. *Leukemia*. 1997;11(1):16-21.
  20. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology. Acute myeloid leukemia. v.2.2011. NCCN web site. <http://www.nccn.org>. Accessed October 26, 2010.