Acute lymphocytic leukemia survival in children under 20
1956-1980

CANCER AND LEUKEMIA GROUP B

PERCENT SURVIVING

YEARS FROM ONSET OF PROTOCOL

556: N = 59 Med = 6 yrs
560: N = 92 Med = 33 yrs
570: N = 101 Med = 8 yrs
605: N = 51 Med = 13 yrs
631: N = 193 Med = 16 yrs
661: N = 265 Med = 28 yrs

— 74: N = 482 Med = 65 yrs
— 76: N = 584 Med = 74 yrs

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**DESCRIPTION:** Lorazepam injection, a benzodiazepine with anxiolytic and sedative effects, is intended for IM or IV use. It has the chemical formula 7-chloro-5-(4-chlorophenyl)-1,3-dihydro-5H-3,4-endo-diazepine-5-one.

**CLINICAL PHARMACOLOGY:** IV or IM administration of recommended dose of 2.5 mg lorazepam injection to adult patients is followed by dose related effects of sedation (sleepiness or drowsiness), relief of paroxysmal anxiety, relief of muscle spasms and inhibition of convulsive seizures. This is due to its ability to increase the inhibitory actions of the neurotransmitter gamma-aminobutyric acid (GABA) by increasing GABA inhibition by promoting GABA receptor binding. This increase in GABA activity is associated with anxiolytic, sedative, and anticonvulsant effects.

**ADVERSE REACTIONS:**

INJECTORS: In adults (for anesthetic and surgical purposes) lorazepam injection has not been found to interfere with anesthetic and surgical procedures, and the patient could be made to undergo surgery more safely, as evidenced by change in patient behavior and cardiovascular reactions. Cases of laryngospasm, hypotension, bradycardia, apnea, and cardiorespiratory arrest have been reported. A patient with anaphylaxis from injection of lorazepam injection is a potential risk. There have been reports of anaphylactoid reactions following lorazepam injection. Lorazepam injection may cause anaphylactoid reactions, including laryngospasm, hypotension, bradycardia, apnea, and cardiorespiratory arrest. Lorazepam injection may be associated with the following adverse reactions:

- **Allergic Reactions**: Rash, urticaria, angioedema, respiratory distress, anaphylaxis, aphthous stomatitis, and facial swelling have been reported with lorazepam injection. Some of these reactions have been associated with anaphylactoid reactions.

- **Central Nervous System Affects**: Sedation, drowsiness, confusion, memory impairment, amnesia, somnolence, ataxia, depression, emotional lability, fatigue, fatigue, insomnia, and nightmares have been reported with lorazepam injection. Lorazepam injection may cause drowsiness, confusion, memory impairment, amnesia, somnolence, ataxia, depression, emotional lability, fatigue, and insomnia.

- **Respiratory Affects**: Respiratory depression, hypoxia, apnea, and bradypnea have been reported with lorazepam injection. Lorazepam injection may cause respiratory depression, hypoxia, apnea, and bradypnea.

- **Cardiovascular Affects**: Hypotension, orthostatic hypotension, tachycardia, bradycardia, and arrhythmias have been reported with lorazepam injection. Lorazepam injection may cause hypotension, orthostatic hypotension, tachycardia, bradycardia, and arrhythmias.

- **Gastrointestinal Affects**: Nausea, vomiting, and diarrhea have been reported with lorazepam injection. Lorazepam injection may cause nausea, vomiting, and diarrhea.

- **Miscellaneous Affects**: Rash, urticaria, angioedema, respiratory distress, anaphylaxis, aphthous stomatitis, and facial swelling have been reported with lorazepam injection. Some of these reactions have been associated with anaphylactoid reactions.

**PRECAUTIONS:**

- **General**: Lorazepam injection should be used with caution in patients with a history of drug dependence, respiratory depression, or alcoholism. Lorazepam injection should be used with caution in patients with a history of drug dependence, respiratory depression, or alcoholism.

- **Geriatric Patients**: In elderly patients, lorazepam injection may cause drowsiness, confusion, memory impairment, amnesia, somnolence, ataxia, depression, emotional lability, fatigue, and insomnia.

- **Pediatric Patients**: Lorazepam injection is generally safe and effective in pediatric patients. However, pediatric patients may be more sensitive to the sedative effects of lorazepam injection. Lorazepam injection should be used with caution in pediatric patients.

- **Pregnancy and Lactation**: Lorazepam injection is generally safe and effective in pregnant and lactating women. However, pediatric patients may be more sensitive to the sedative effects of lorazepam injection.

**INTERACTIONS:**

Lorazepam injection is generally safe and effective in patients with liver or kidney disease. However, pediatric patients may be more sensitive to the sedative effects of lorazepam injection.

**DRUG/LABORATORY TEST INTERACTIONS:** Lorazepam injection is generally safe and effective in patients with liver or kidney disease. However, pediatric patients may be more sensitive to the sedative effects of lorazepam injection.

**OVERDOSAGE:** Lorazepam injection is generally safe and effective in patients with liver or kidney disease. However, pediatric patients may be more sensitive to the sedative effects of lorazepam injection.

**CONTRAINDICATIONS:** Lorazepam injection is generally safe and effective in patients with liver or kidney disease. However, pediatric patients may be more sensitive to the sedative effects of lorazepam injection.
This month’s cover of Cancer Research deals with curative cancer chemotherapy, the subject of the second position paper of the American Association for Cancer Research. Commissioned by the Association’s Committee on Scientific and Public Affairs, the article details the progress made since the 1950s in the treatment of cancer by chemotherapy. The integrated efforts of clinicians and basic researchers have developed various strategies of chemotherapy which have proved effective in providing long-term disease-free survival and cures of a number of forms of cancer.

The photographs on the cover illustrate two such cases: J. C. G., the woman in the family portrait on the right, reported to the Clinical Center of the National Cancer Institute (NCI) in 1962 with a diagnosis of acute lymphocytic leukemia. She was 7 years old at the time and she was treated with a new combination chemotherapy treatment strategy called VAMP (vincristine, amethopterin, mercaptopurine, and prednisone). With the institution of this therapy, all evidence of her disease promptly disappeared, and she remains disease free 23 years later. She has three wonderful children and a devoted husband.

The photograph on the left is of L. W., who presented in 1969 at M. D. Anderson Hospital with Hodgkin’s disease, after having had extensive prior treatment which included radiotherapy and chemotherapy. While some response to treatment had been achieved earlier, he was considered refractory to further therapy. He became one of the first patients with extensive prior treatment to be treated with the MOPP program (mustargen, oncovin, procarbazine, and prednisone), which had been developed at the NCI in 1963 to 1964 and was found to be curative when used as initial chemotherapy for patients with disseminated Hodgkin’s disease. The patient entered complete remission promptly; he received a total of six courses of treatment, which he tolerated well, and, at the age of 61, he remains disease free with excellent quality of life.

The graph (lower left) depicts data on successive controlled clinical trials involving 3072 children with acute lymphocytic leukemia. It shows the improved survival of these children from 1956 to 1980. (The year for individual curves can be obtained from the first two numbers of the key.) Note that in 1956 the median survival was approximately 6 months and all patients died within the first 1 to 2 years. There was a progressive improvement in survival over the next 10 years, and by 1966 to 1971 the survival curves leveled off at 20 to 40%. In subsequent studies, where the follow-up is not as long, there is a leveling off of the curves ranging from 50 to 75%. Patients who survive in a disease-free state for 4 or 5 years after diagnosis rarely relapse thereafter. These results have been confirmed and extended by studies from numerous other groups and institutes, including (in alphabetical order) the Children’s Cancer Oncology Group, Los Angeles, CA; Dana-Farber Cancer Institute, Boston, MA; Memorial Sloan-Kettering Cancer Center, New York, NY; NCI, Bethesda, MD; and St. Jude Children’s Research Hospital, Memphis, TN.

* Reprinted with permission from Holland, J. F. and Frei, E., III (eds.). Cancer Medicine, Ed. 2, p. 1403. Philadelphia: Lea and Febiger, 1982. Also, we are indebted to the patients and their families for supplying us with their photographs for use on the cover to illustrate their brief medical histories.