Reference Population

Experimental Population

Participants

Non Participants

Random Allocation to Treatment (or Study) and Control Group

Treatment (or Study) Group

Control Group

Treated

Refused Treatment

Followed

Followed

Outcome Known

Outcome Unknown

Outcome Known

Outcome Unknown

Outcome Known

Outcome Unknown

Outcome Known

Outcome Unknown

Outcome Known

Outcome Unknown
AN IMPORTANT MESSAGE
TREATING CANCER

Clinical studies indicate that Ativan® (lorazepam) Injection can play a significant role in enhancing patient tolerance for and acceptance of chemotherapy.1-5 In studies comparing Ativan Injection to other adjunctive agents, patients expressed a strong preference for the regimen including Ativan Injection because of its anxiolytic, amnesic and sedative effects.1-4

NEW ADJUNCTIVE AGENTS NEEDED
A study of 52 mastectomy patients on regimens of cyclophosphamide, methotrexate and 5-FU (CMF) revealed that over one fourth of patients failed to even complete a treatment course of 12 to 18 months, mostly because of the side effects associated with these agents.6 A recent survey of 56 oncology centers found up to 10% of patients refused further chemotherapy because of actual or feared side effects.7 Statistics such as these have spurred researchers to seek new adjunctive agents or combinations of existing agents that would increase the tolerability of chemotherapy.

ATIVAN® INJECTION:
A SUPPORTIVE ADJUNCT
In a study involving 18 patients receiving 36 courses of cis-platinum therapy, Ativan Injection was administered prior to therapy. Lack of recall for the chemotherapy infusion, and for the subsequent 8 hours, was reported in 33 of 36 courses of therapy studied. Furthermore, amnesia for the day of chemotherapy was reported in 29 courses. All 18 patients believed the lack of recall was highly desirable.5

Dr. John Laszlo and colleagues from Duke Comprehensive Cancer Center, Durham, NC, and Memorial Sloan-Kettering Institute, New York, reported a pilot study involving 32 patients receiving cisplatin with or without other cytotoxic chemotherapy and adjunctive use of Ativan Injection.3 Thirty patients were evaluated over 45 courses of treatment (two were eliminated for protocol violations).

Dr. Laszlo observed that following lorazepam, recall of the day’s events was reduced for most patients. Post-treatment anxiety was also reduced. Almost all of the patients in the study requested lorazepam (Ativan Injection) pretreatment again for subsequent chemotherapy courses, regardless of incidence or intensity of emetic episodes. From this study, Dr. Laszlo concluded that lorazepam can be an effective agent for these patients.

The reduction of recall following administration of Ativan Injection was considered by most patients to be not only acceptable, but also desirable.1-5 Furthermore, due to its anxiolytic action, Ativan Injection was helpful in relieving the anxiety associated with the stresses of chemotherapy.1-4
A SIGNIFICANT ROLE IN ENHANCING COMPLIANCE IN CHEMOTHERAPY

Clearly, Ativan® (lorazepam) Injection represents an important supportive adjunct in chemotherapy. Patients' ability to tolerate the experience is usually enhanced. Their acceptance of a regimen incorporating Ativan Injection has been excellent. Thus, it is felt that many patients who might otherwise abandon treatment may now be more willing to proceed with Ativan Injection as an adjunct in their chemotherapy regimen.

If outpatients are treated with lorazepam injection, care must be taken on the day of treatment to prevent their undertaking any activity requiring full awareness or coordination.

REFERENCES:

Please see important information on the following page.
DESCRIPTION: Ativan® (lorazepam) injection, a benzodiazepine with anxiolytic and sedative effects, is intended for IM or IV use. It has the chemical formula C17H13ClFN2O2 and is 1,3-dihydro-3-phenyl-2H-1,4-benzo-

Lorazepam is a white powder almost insoluble in water. Each ml of sterile injection contains either 2.0 or 4.0 mg lorazepam, 0.18 mg polyethylene glycol 400 and 0.2% benzyl alcohol as preservative.

CLINICAL PHARMACOLOGY: Administration of a single dose of 2-4 mg lorazepam to adult patients is followed by dose related effects of sedation (sleepiness) and drowsiness, relief of preparatory anxiety and lack of recall of events related to day of surgery in most patients. The clinical sedation (sleepiness or drowsiness) is not so marked that most patients are able to drive and operate machinery safely within 2-3 hours of receiving the injection. Lorazepam in delirious or brain damaged patients may produce profound sedation and delirium.

Pediatric Use: There are insufficient data to support efficacy or make dosage recommendations for injectable lorazepam for children under 12 years of age.

ADVERSE REACTIONS: CNS: Most frequent adverse effects with injectable lorazepam are extensions of drug's CNS depressant effects. Incidence varied from study to study depending on dosage, route, use of other CNS depressants, and investigator's opinion concerning degree and duration of sedation desired.

DRUG INTERACTIONS: Lorazepam, like other benzodiazepines, produces CNS depression when given concomitantly with alcohol, barbiturates, MAO inhibitors and other anxiolytics. When scopolamine is used concurrently with injectable lorazepam, hallucinations, disorientation and irrational behavior was observed.

Benzodiazepine Reactivation: No laboratory test abnormalities were identified when lorazepam was given alone or concomitantly with another drug, e.g. narcotic analgesics, inhalation anesthesia, scopolamine, atropine, and various tranquilizers. The injection was followed by dose related effects of sedation and drowsiness, relief of preparatory anxiety and recall of events related to day of surgery in most patients. The clinical sedation was not so marked that most patients were able to drive and operate machinery safely within 2-3 hours of receiving the injection. Lorazepam in delirious or brain damaged patients may produce profound sedation and delirium.

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General acceptance of biometrically designed, monitored, and analyzed clinical trials was accelerated by the organization of multiinstitutional investigations of anticancer agents that arose during the 1950s (K. M. Endicott, J. Natl. Cancer Inst., 19: 275, 1957).

As Peter Armitage (Statistics in Med., 1: 305, 1982) stated, random assignment of individuals to the tested and to the control (or contraste) groups is the essential feature in the design of such trials.


Among the many historical figures who have contributed to the evolution of randomized clinical trials, three are selected for especial note:

James Lind (1716–1794), a British naval surgeon, in 1747 showed the curative effect of citrus fruit on scurvy. He made his observations on 12 scorbutic sailors, two of whom “ate with greediness” two oranges and one lemon given to them every day as their therapy.

C. P. A. Louis (1787–1872), a Parisian clinician, in 1835 introduced his “Numerical Method” to medicine. He compared patients “taken indiscriminately,” who were and who were not bled, and showed that bleeding had no beneficial effect upon the course of their inflammatory diseases.

Ronald A. Fisher (1890–1962), a British statistician, in 1923 formally introduced randomization into the design of experiments. His initial subject of investigations was agricultural, from whence it eventually spread to clinical trials.


M. B. S.