BIOTECH DIVISION
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SAFETY SUMMARY FOR THE OPEN–LABEL PHASE OF A DOUBLE–BLIND, PLACEBO–CONTROLLED STUDY TO DETERMINE THE SAFETY AND EFFICACY OF SUBCUTANEOUS DOSES OF r–HuEPO (RWJ 22512–000) IN AIDS PATIENTS WITH ANEMIA INDUCED BY THEIR DISEASE AND AZT THERAPY (PROTOCOL I88–009)[1]

SYNOPSIS

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STUDY DATES:
July 20, 1988 – April 27, 1990

OBJECTIVE:
The objective of the open–label phase of this study was to determine the safety of r–HuEPO administered subcutaneously to AIDS patients with anemia secondary to their disease and/or concomitant AZT therapy.

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[1] Interim (MR #002410) and final safety (MR #002701) analyses of the data from the double-blind phase of this protocol have been presented.

STUDY DESIGN:
This was the open–label phase of a multicenter, double–blind, parallel group, placebo–controlled, randomized study of the safety and efficacy of SC administration of r–HuEPO in the treatment of anemia of AIDS and/or concomitant AZT therapy. Eighty–nine patients who completed the double–blind phase of the study entered the six month open–label phase during which all patients were to receive SC or IV injections of r–HuEPO for at least an additional six months with the dose titrated to maintain the hematocrit between 38–40%.

Safety was evaluated on the basis of reasons for premature discontinuation, the incidence and severity of adverse or unusual experiences, deaths, the incidence of AIDS–defining opportunistic infections and development of r-HuEPO–specific antibodies.

PATIENT POPULATION:
A total of 89 patients were enrolled in the open–label phase of this study. Thirty–eight (43%) of the patients completed the 24 week course of therapy. Fifty–one patients (57%) discontinued open–label therapy prematurely: nine for adverse experiences, 11 due to death, 19 for protocol violations, four for personal reasons, 13 for other reasons and one was lost to follow–up. Six patients had both Adverse Experience and Death given as reasons for discontinuation and are counted in both categories.

SAFETY RESULTS:

Adverse experiences. Eighty–eight (99%) of the patients reported adverse experiences during the open–label phase of the study. Adverse experiences which occurred in 10% or more of patients were fatigue (41.6%), diarrhea (41.6%), pyrexia (39.3%), nausea (37.1%), oral candidiasis (28.1%), cough (25.8%), asthenia (24.7%), headache (23.6%), pneumonia (22.5%), shortness of breath (22.5%), rash (21.4%), vomiting (20.2%), abdominal pain (16.9%), trunk pain (15.7%), decreased appetite (15.7%), constipation (14.6%), herpes (14.6%), diaphoresis (14.6%), depression (13.5%), upper respiratory infection (13.5%), skin malignancy (13.5%), bacterial infection (12.4%), dizziness (12.4%), respiratory congestion (12.4%), gastrointestinal pain (12.4%), viral infection (11.2%), edema (11.2%), pain in the extremities (10.1%), and retinitis (10.1%).

Discontinuations due to adverse experiences. Nine patients discontinued open–label therapy due to adverse experiences. The investigators characterized these experiences as being unrelated to study medication.

Deaths. Eleven patients died while participating in or within one month of discontinuation from the open–label phase of this study.

Serious and unexpected adverse experiences. Four patients had adverse experiences during the open–label phase of the study that required filing an IND Safety Report to the FDA.

Incidence of AIDS–defining opportunistic infections. Thirty patients experienced AIDS–defining opportunistic infections during the open–label phase of this study. The incidence of opportunistic infections is consistent with the progression of HIV infection.

Antibody titers. No patients participating in the open–label phase of this study developed r–HuEPO antibodies during the course of therapy.

CONCLUSION:
The data from the open–label phase of this study demonstrate that r–HuEPO is safe for the treatment of anemia in AZT–treated, AIDS patients.

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