

## TREATMENT OF ADVANCED HODGKIN'S DISEASE

Hodgkin's disease is a lymphoma that was once considered a fatal disease, but is now often - but not always - curable. There are a variety of treatment options available including chemotherapy and radiation. Dating back decades, advances in radiation as well as in chemotherapy were shown to help control and often cure this previously fatal disease.

One of the first chemotherapies used for Hodgkin's was MOPP. It had a high rate of remission and cure. MOPP included Mechlorethamine, Vincristine, Procarbazine and Prednisone. Subsequent treatments including ABVD or Doxorubicin, Bleomycin, Vinblastine and Dacarbazine were shown to have potential curative power for people who relapsed after MOPP.

In the 1990's a study comparing MOPP/ABVD and combination of the two, for advanced Hodgkin's disease was undertaken. The response rate for ABVD and MOPP/ABVD was 81% versus 82% for complete responses and failure free survival was 64% for both at three years. The ABVD regimens however were superior to MOPP with 69% complete response at three years. Overall survival was not different.

A subsequent development of MOPP/ABV hybrid produced an 83% complete response rate and 73% five-year freedom from recurrence rates. This included people who received adjuvant or additional radiation as part of the treatment. Other studies looked at MOPP/ABV versus sequential MOPP followed by ABVD and alternating MOPP and ABVD treatment. MOPP/ABV was equally effective to MOPP/ABVD and more effective than sequential MOPP followed by ABVD. The trial reported, currently evaluated MOPP/ABV and ABVD. Doxorubicin and Bleomycin are known to cause potential damage to the heart and lungs. These two drugs were part of ABVD. MOPP/ABV was considered a less toxic regimen.

Patients evaluated for this study had stage III<sub>2</sub>A, III<sub>2</sub>B, or IV Hodgkin's disease or who had relapse after radiation. Certain blood tests were required as well as reasonable cardiac and pulmonary function. CT scans of the chest, abdomen and pelvis were required and bone marrow evaluation was required. A gallium scan was recommended but not required. People who had prior chemotherapy or history of other malignancies were excluded. All people gave informed consent.

Patients were randomly allocated to ABVD versus MOPP/ABV. Major end points were failure free and overall survival, life threatening acute toxicities and serious long-term toxicities, including damage to the heart, lung and bone marrow as well as secondary malignancies. The complete response rate was 78% in all patients and 76% in ABVD versus 80% in MOPP/ABV. Nine patients on ABVD and eight patients on MOPP/ABV had progression of cancer while on treatment. Failure free survival was 63% after ABVD and 66% after MOPP/ABV. Overall survival at five years was 81% for all patients with 82% after ABVD and 81% after MOPP/ABV. There was felt to be no difference between treatment arms. Eighty-one percent of patients younger than forty years old had a complete response versus 74% of patients older than forty. There were fifteen deaths during initial treatment on MOPP/ABV arm and nine on ABVD arm. Patients who had a combination of the two arms had an increased incidence of malaise, fatigue, anorexia and hypotension with statistical analysis showing a significant difference. The MOPP/ABV also had a greater chance of hematologic toxicity including life-threatening or lethal lowering of the white blood count, anemia, thrombocytopenia, lowering of platelet counts or infection. This was statistically significant.

After six years follow-up 46% secondary cancers were seen including eighteen in those having ABVD and twenty-eight in those having MOPP/ABV. Eleven patients had acute leukemia in the MOPP/ABV arm with two in the ABVD arm. There was no relationship to the use of radiation in these secondary tumors.

The authors concluded, “This trial compared ABVD and the MOPP/ABV high-bred regimen as initial therapy for advanced Hodgkin’s disease. The data demonstrated a striking similarity in overall survival and failure free survival of patients on either arm after six years of follow-up. Given the low relapse rates for Hodgkin’s disease after five years of remission in previous trials of ABVD or MOPP/ABV, it seems unlikely that significant failure free survival or overall survival advantages will emerge within the next several years of observation.”

“However, there are statistically significant and clinically important differences in both the toxicity and secondary malignancies observed with these two therapies. The MOPP/ABV hybrid caused significantly more acute hematologic and pulmonary toxicity. MOPP/ABV also caused significantly more fatigue, anorexia, and nausea. The MOPP/ABV hybrid was associated with a higher rate of treatment-related deaths, but this was not statistically significant. Many of the toxic deaths on the MOPP/ABV arm were due to pulmonary failure, and it is difficult to determine whether infection or drug toxicity was the primary insult; in many patients, both likely contributed to death. Moreover, many patients were neutropenic at the time they developed pulmonary infiltrates. Nevertheless, although the exact pathophysiology may be uncertain, the direct attribution of death to treatment-related toxicity is clear. It is not clear why there is increased pulmonary toxicity on the MOPP/ABV arm, which delivered a lower total dose of Bleomycin than did ABVD. There were significantly more patients receiving MOPP/ABV who experience pulmonary toxicity that necessitated dose adjustment or elimination of Bleomycin.”

Thus this study is important to show that more treatment may not be better for the patient. In fact, more treatment may be toxic. Certain chemotherapy agents, when used in combination, have toxicities that may well be undesirable. It is important for each patient and their family to speak with their physicians about all treatment options as well as risks and alternatives before proceeding.

We have seminars open to the public to discuss treatment options. We also have multi-disciplinary panels of physicians to review films, reports and medical history. We have a cancer hot line to answer questions: 212-CHOICES and as well have an e-mail address: [gil.lederman@rsny.org](mailto:gil.lederman@rsny.org).