# Combination chemotherapy for Hodgkin lymphoma

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"It appears that combinations of effective drugs that act by different mechanisms and manifest different toxicities can be used effectively to increase the response rate and probably the survival of patients with sensitive tumors such as Hodgkin's disease."[1]

This is a concept that we now take for granted, but in 1970 it changed the trajectory for patients with Hodgkin lymphoma (HL). Before the use of combination chemotherapy, HL was primarily incurable and fatal. A portion of patients with early-stage disease achieved cure with radiation, but it was not until combination chemotherapy was introduced, in the form of MOPP (nitrogen mustard, vincristine, procarbazine, prednisone), that HL became a highly curable disease. MOPP was developed based on the premise that different classes of independently active antitumor agents had significant activity in HL. These classes included alkylating agents, vinca alkaloids, the methylhydrazine derivative (procarbazine), and corticosteroids. When administered alone, each drug often produced short-lived responses; however, patients who developed resistance to one type of drug often responded to a drug in a different class. Preclinical studies revealed that manipulation of doses and schedules, along with the use of effective drugs in combination, reduced rates of drug resistance and allowed for higher rates of tumor cell killing. This led to the development of the MOPP regimen (Figure 1) which initially demonstrated promising efficacy in 43 patients with advanced stage disease.[1] A 20-year follow-up of a series of MOPP studies that enrolled 188 patients (including the 43 patients from the initial study) demonstrated that MOPP produced complete responses in 84% of patients, leading to 66% of patients being disease-free for over 10 years.[2]

MOPP is associated with significant hematologic toxicity, infertility, and the risk of secondary leukemia, however given the great strides made with this regimen at the time,

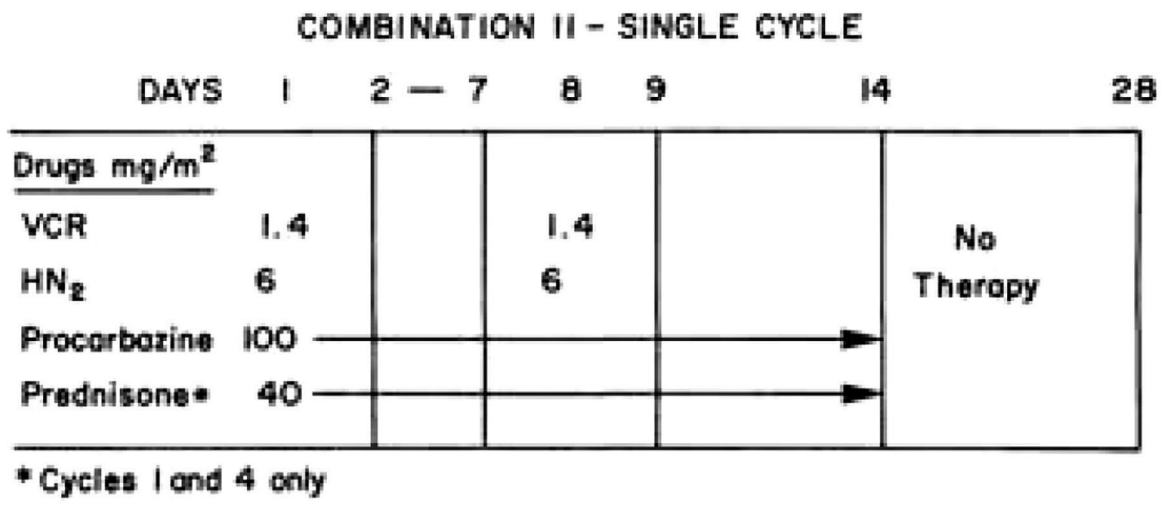


Figure 1. A single cycle of therapy with drug combination 2. VCR = vincristine sulfate; $HN_2$ = nitrogen mustard.

**Figure 1. The MOPP regimen.** Figure reproduced, with permission, from Ann Intern Med. 1970;73(6):881-895.

the toxicity was justified. It was initially the most widely used regimen for advanced stage HL. Thankfully, it is rare that MOPP is needed today. The Milan Cancer Institute developed ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) with the intent to design a non-cross-resistant regimen that could be given as salvage after MOPP. ABVD was eventually proven to be more effective than MOPP in a Cancer and Leukemia Group B study, which compared front-line treatment with ABVD, MOPP, and ABVD alternating with MOPP (ABVD/MOPP hybrid).[3] While both the ABVD and ABVD/MOPP hybrid regimens were superior to MOPP alone, ABVD was also associated with reduced myelotoxicity, secondary leukemia, and infertility compared to MOPP. Therefore, ABVD was substituted for MOPP and is now the major backbone of modern HL regimens.

Since the introduction of MOPP in 1970, there has been a major shift in HL research. The high efficacy of modern HL therapy has enabled investigators to focus not only on cure, but on balancing efficacy with short- and long-term toxicity. Although combination chemotherapy was one of the first major breakthroughs for HL, current studies are investigating ways to chip away at exposure to traditional chemotherapy through integration of novel agents and biomarker-driven therapy.

## References

1. Devita VT Jr, Serpick AA, Carbone PP. Combination chemotherapy in the treatment of advanced Hodgkin's disease. Ann Intern Med. 1970;73(6):881-895.
2. Longo DL, Young RC, Wesley M, et al. Twenty years of MOPP therapy for Hodgkin's disease. J Clin Oncol. 1986;4(9):1295-1306.
3. Canellos GP, Anderson JR, Propert KJ, et al. Chemotherapy of advanced Hodgkin's disease with MOPP, ABVD, or MOPP alternating with ABVD. N Engl J Med. 1992;327(21):1478-1484.