# Induction Therapy for Advancedstage Hodgkin Lymphoma

Late Intensification (ABVD Chemotherapy Followed by High-dose Chemotherapy and Autologous Stem Cell Transplant Only for Those Who Relapse)

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#### **KEYWORDS**

- Hodgkin lymphoma
  ABVD chemotherapy
  Escalated BEACOPP
  Response rate
- Toxicity Failure-free survival (FFS) Event-free survival (EFS) Overall survival (OS)

#### **KEY POINTS**

- Approximately 65% to 75% of advanced-stage Hodgkin lymphoma patients have a complete response to initial therapy with ABVD chemotherapy.
- The 5-year failure-free survival for advanced-stage Hodgkin lymphoma patients treated with ABVD is 70% to 75%.
- ABVD can be given to patients less than 60 years and patients with a poorer performance score.
- Although more intensive combinations, such as escalated BEACOPP, result in higher response rates and improved failure-free survival, the short- and long-term complications are greater.
- When all therapy including salvage therapy after initial treatment is considered, the outcomes of patients initially treated with ABVD or escalated BEACOPP were similar in a randomized trial. A network meta-analysis however showed a survival benefit with escalated BEACOPP.
- Because many patients are cured, exposing all patients to early intensive therapy increases the long-term complication risk in everyone. Reserving intensification for only those patients who need it decreases complications without clearly compromising overall outcome.

### INTRODUCTION: NATURE OF THE PROBLEM

Hodgkin lymphoma is a B-cell malignancy that has been shown to be highly sensitive to chemotherapy. 1,2 The overall response rates to combination chemotherapy are in

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excess of 70% and most patients are cured with standard therapy.<sup>3</sup> Patients with advanced-stage disease commonly have a higher risk of disease relapse than limited stage patients and often present with more poor prognostic features. Despite this, the percentage of patients who are cured by initial therapy is typically 70% to 75%.

ABVD chemotherapy (Adriamycin, Bleomycin, Vinblastine, and Dacarbazine) is a standard therapy for patients with Hodgkin lymphoma and is often used in North America to treat patients with advanced-stage disease. Typically patients receive 6 to 8 cycles of therapy, and provided they have had a complete response to the treatment that is PET negative, they will then be observed without further therapy. Some patients may have disease that proves to be resistant to this initial therapy and may require further treatment intensification. Other patients may subsequently relapse and then will receive salvage chemotherapy followed by high-dose chemotherapy with an autologous stem cell transplant.

A difference in opinion regarding optimal management of patients with advanced-stage Hodgkin lymphoma has developed over time. Some physicians think that an intensive approach as early as possible should be considered. Groups advocating this position commonly administer escalated BEACOPP (Bleomycin, Etoposide, Adriamycin, Cyclophosphamide, vincristine, Procarbazine, and Prednisone) chemotherapy for 6 cycles of treatment. They argue that an intensive approach will decrease the number of patients having an inadequate response to initial treatment and result in a greater percentage of patients who remain in remission and do not require further salvage chemotherapy. However, the more intensive escalated BEACOPP approach may be associated with a greater frequency of initial toxicities and treatment-related mortality, and a greater prevalence of long-term toxicities.

Those advocating for initially treating patients with less intense ABVD chemotherapy reason that the response rates are high with ABVD chemotherapy and the combination is substantially less toxic. ABVD chemotherapy can also be administered to older patients as well as those with a poor performance score at diagnosis, many of whom do not tolerate the more intensive approach. The minority of patients who fail this less intense initial treatment approach would then proceed to be treated in an intensive fashion with salvage chemotherapy followed by high-dose chemotherapy and an autologous stem cell transplant. Those physicians favoring the limited late intensification approach argue that most patients are not exposed to more intense chemotherapy and therefore the short-term and long-term complications are substantially less for most patients.

This concern about exposing all patients who generally have a very favorable prognosis to intensive therapy is illustrated by a study by Biasoli and colleagues<sup>4</sup> that looked at a Groupe d'Etudes des Lymphomes de l'Adulte/European Organisation for Research and Treatment of Cancer clinical trial randomizing patients between ABVD chemotherapy and escalated BEACOPP. They found that only one-half of the patients that were considered for the study at one of the participating centers were enrolled. The remaining patients chose not to participate. The choice not to participate was due to both patient and physician concerns. The main reason for patient's refusal was that they preferred the standard treatment (ABVD chemotherapy) and were concerned about toxicity in the experimental arm (escalated BEACOPP). When questioned further, the patient's main concern was the high incidence of anticipated infertility in the BEACOPP arm. Similarly, physicians chose not to enroll patients in the study because of their concerns with increased toxicity in the escalated BEACOPP arm. Subsequent studies by this group however have used escalated BEACOPP as initial therapy, suggesting that these attitudes may have changed over time.

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