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HODGKIN'S LYMPHOMA — FAVORABLE PROGNOSIS STAGE I AND II

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Summary of Literature Review

This topic addresses the treatment of newly diagnosed stage I and II favorable-prognosis Hodgkin's lymphoma. For most cases of favorable-prognosis stage I and II Hodgkin's lymphoma, combined-modality therapy (chemotherapy followed by involved-field radiotherapy [IFRT]) constitutes the current standard of care. Increasing information about the late effects of treatment has led to attempts to decrease toxicity by using less chemotherapy (decreased duration, intensity, agents) or less radiotherapy (RT) (reduced volume, dose).

Prognostic Factors

The definition of favorable prognosis for stage I and II Hodgkin's lymphoma varies among major cooperative groups. The German Hodgkin's Study Group (GHSG) defines favorable disease as no large mediastinal adenopathy (one-third of the maximum thoracic diameter), an erythrocyte sedimentation rate (ESR) of less than 50 and no "B" symptoms or an ESR of <30 with "B" symptoms, no extranodal disease and one to two sites of nodal involvement. In contrast, the European Organisation for Research and Treatment of Cancer (EORTC) criteria for favorable prognostic features include age 50 or younger, no large mediastinal adenopathy, an ESR of <50 and no "B" symptoms or an ESR of <30 with "B" symptoms, and lymphoma limited to one to three regions of involvement [1,2]. In interpreting trial results, it is important to pay attention to the risk group definition, as the results are applicable only to patients who fit the specific inclusion criteria.

Table 1: Criteria for Favorable Prognosis Hodgkin's Lymphoma

EORTC	GHSG
Age ≤50	No large mediastinal adenopathy
No large mediastinal adenopathy	ESR <50, no "B" symptoms
ESR <50, no "B" symptoms	ESR <30 if "B" symptoms present
ESR <30 if "B" symptoms present	No extranodal disease
1-3 sites of involvement	1-2 sites of involvement

Long-term Outcome of Treatment for Early-stage Hodgkin's Lymphoma

Much of the long-term follow-up data (15 years or longer) for early-stage Hodgkin's lymphoma is derived from laparotomy-staged patients treated mostly with large-field RT of 40-44 Gy. Large, single-institutional studies demonstrate >80% actuarial 10-15-year freedom from relapse and <10% mortality rates from Hodgkin's lymphoma following mantle and para-aortic irradiation for pathologically staged IA-IIA patients [3-5]. The treatment of early-stage Hodgkin's lymphoma has become so successful that at 15-20 years post-treatment, the overall mortality rate from causes other than Hodgkin's lymphoma appears to exceed that seen from Hodgkin's

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lymphoma [6-10]. Considering all causes of death, patients have approximately a 1% excess risk of mortality per year for the first 20 years after Hodgkin's lymphoma.

Deaths from Hodgkin's lymphoma occur most frequently in the first 5-10 years; deaths from causes other than Hodgkin's lymphoma are most common after 5-10 years [9,10]. The largest source of mortality from other causes is second malignant neoplasms [10-15]. Another important source of mortality from other causes is late cardiac toxicity [10,16]. RT has also been associated with a risk of cerebrovascular disease in Hodgkin's lymphoma survivors [17].

It is important to note that the data on late effects after Hodgkin's lymphoma are largely based on patients treated decades ago with outdated RT techniques, using much larger treatment fields to higher doses. There is ample evidence that risks of late complications are directly related to dose [18-23] and field size [17,24]. It is expected that with modern IFRT and the use of lower doses, these late effects will diminish [25,26]. Ongoing efforts to further reduce the radiation dose and radiation field to involved-node radiation therapy (INRT) will likely further reduce the risk of radiation-related late effects [27,28]. Similarly, modern chemotherapy with nonalkylating regimens is expected to reduce the risk of treatment-related late effects, including the risk of leukemia and infertility [29,30].

Reduction in Treatment: Ongoing and Completed Trials

Increasing concern for the long-term consequences of treatment has prompted many investigators to evaluate new approaches for early-stage Hodgkin's lymphoma. Many of the ongoing and recently completed studies were developed to reduce the long-term complications of treatment without increasing mortality from Hodgkin's lymphoma. These include studies that:

- Compare RT alone to combined RT and chemotherapy.
- Evaluate the optimal regimen and number of cycles of chemotherapy, and the optimal radiation dose and field size for combined-modality therapy.
- Evaluate chemotherapy alone.

Trials on Radiation Therapy Alone versus Combined-Modality Therapy

The GHSG HD7 trial was conducted on 650 patients with favorable-prognosis stage I and II Hodgkin's lymphoma [31]. Patients in this trial had none of the following risk factors: large mediastinal mass, extranodal lymphoma, massive splenic involvement, or high ESR. Patients were randomized to receive either extended-field radiotherapy (EFRT), or 2 cycles of ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) followed by EFRT. The RT dose was 30 Gy, followed by a 10 Gy boost to the involved field, in both arms. Patients in the combined-modality arm had a significantly higher rate of freedom from treatment failure than those in the EFRT-alone arm (7-year rates 88% vs 67%, P<0.0001). However, there was no significant difference in overall survival between the two arms (7-year rates 94% vs 92%, P=0.43). The Southwest Oncology Group (SWOG) and Cancer and Leukemia Group B (CALGB) conducted a similar study on 348 patients with stage IA or IIA supradiaphragmatic Hodgkin's lymphoma [32]. In this trial, patients were randomized to receive either subtotal lymphoid irradiation, or 3 cycles of AV (Adriamycin and vinblastine) followed by subtotal lymphoid irradiation. Patients in the combined-modality arm had a significantly higher failure-free survival rate than patients in the subtotal lymphoid irradiation arm (3-year rate 94% vs 81%, P<0.001). These two trials showed that the addition of chemotherapy improves outcomes in patients treated with extended-field or subtotal lymphoid RT.

The EORTC conducted a multi-institutional randomized trial, EORTC H7, in which patients with stage I or II Hodgkin's lymphoma were stratified into two groups, favorable and unfavorable, according to four prognostic factors: age, combination of ESR and "B" symptoms, number of involved sites, and bulky mediastinal lymphoma [33]. Three hundred thirty-three patients were enrolled in the favorable group, and they were randomized to receive either subtotal nodal irradiation alone (36-40 Gy) or 6 cycles of epirubicin, bleomycin, vinblastine, and prednisone (EBVP) followed by IFRT (36-40 Gy). Patients in the combined-modality arm had a significantly higher rate of event-free survival, compared to the RT-alone arm (10-year rates 88% vs 78%, P=0.01). However, there was no significant difference in overall survival between the two arms (10-year rates 92% vs 92%, P=0.79). This trial demonstrated that the previous standard of EFRT alone could be replaced by combined-modality therapy with IFRT in favorable-prognosis stage I or II Hodgkin's lymphoma patients, resulting in improved event-free survival and similar overall survival.

In a subsequent trial, EORTC H8F, 543 patients with supradiaphragmatic stage I or II Hodgkin's lymphoma and favorable prognostic features were randomized to receive either subtotal nodal irradiation or 3 cycles of mechlorethamine, vincristine, procarbazine, and prednisone (MOPP) combined with doxorubicin, bleomycin, and vinblastine (ABV) followed by IFRT [34]. Patients in the combined-modality arm had a significantly higher event-free survival rate than patients in the subtotal nodal irradiation arm (98% vs 74%, P<0.001). Patients in the combined-modality arm also had a significantly higher overall survival rate than patients in the subtotal nodal irradiation arm (10-year rates 97% vs 92%, P=0.001). This trial confirms the superiority of combined-modality therapy with IFRT over EFRT alone.

Trials on Optimal Chemotherapy Combination

The ABVD regimen has been used most commonly as part of combined-modality therapy for favorable prognosis stage I or II Hodgkin's lymphoma. Other chemotherapy regimens have also been used in efforts to reduce toxicity. One such modification of the ABVD regimen is EBVP, in which doxorubicin was replaced with epirubicin and dacarbazine was replaced with prednisone, in an attempt to reduce cardiac toxicity, nausea, and vomiting. In the EORTC H7 trial described above, EBVP followed by IFRT resulted in high rates of overall survival and event-free survival among favorable-prognosis patients [33]. However, EBVP was not found to be an acceptable regimen among unfavorable-prognosis patients [33]. Moreover, there has not been any randomized comparison of ABVD with EBVP.

The Stanford V regimen (nitrogen mustard, Adriamycin, vincristine, vinblastine, etoposide, bleomycin, and prednisone along with RT to bulky lymphoma sites) was initially developed for patients with locally extensive and advanced Hodgkin's lymphoma [35]. A modification of the regimen treated early stage I/II non-bulky HL patients with 8 weeks chemotherapy and 30 Gy IFRT. At a median follow up of 9 years the freedom from progression and overall survival rates were 94% and 96%, respectively [36]. A current study is evaluating a modified 8-week version, in which nitrogen mustard is replaced by cyclophosphamide, and the RT dose is reduced to 20 Gy INRT for non-bulky early-stage Hodgkin's lymphoma.

The GHSG 13 trial is currently investigating whether certain agents may be omitted from the ABVD regimen in patients treated with combined-modality therapy. In this four-arm randomized study, patients with stage I or II Hodgkin's lymphoma are being treated with either ABVD or AVD or ABV or AV, all followed by IFRT (30 Gy). In the most recent update, the ABV and AV arms were closed due to excessive relapses, suggesting the necessity of the dacarbazine agent in the regimen.

Trials on Optimal Number of Cycles of Chemotherapy

The use of fewer cycles of chemotherapy could potentially reduce long-term toxicity from combined-modality therapy. Results were published recently from the GHSG HD10 trial [28]. In this trial 1,371 stage I or II favorable prognosis Hodgkin's lymphoma patients were randomized to one of four arms: 4 cycles of ABVD followed by 30 Gy of IFRT, 4 cycles of ABVD followed by 20 Gy of IFRT, 2 cycles of ABVD followed by 30 Gy of IFRT, and 2 cycles of ABVD followed by 20 Gy of IFRT [37].

Trials on Optimal Radiation Dose

Two randomized trials have investigated the optimal radiation dose in favorable-prognosis stage I or II Hodgkin's lymphoma patients treated with combined-modality therapy.

In the GHSG HD10 trial, as discussed above, 1,371 patients were randomized to one of four arms: 4 cycles of ABVD followed by 30 Gy of IFRT, 4 cycles of ABVD followed by 20 Gy of IFRT, 2 cycles of ABVD followed by 30 Gy of IFRT, and 2 cycles of ABVD followed by 20 Gy of IFRT [28]. There was no significant difference in freedom from treatment failure (P=1.00), progression-free survival (P=0.98) or overall survival (P=0.61) between the groups treated with 20 Gy and 30 Gy of IFRT. The 5-year rate of freedom from treatment failure was 93% with 20 Gy or 30 Gy of IFRT. Again, radiation dose de-escalation to 20 Gy should be considered only in early-stage patients with favorable-risk disease as defined by the GHSG (ie, 2 sites or less of nodal disease), an ESR of <50 and no "B" symptoms, or an ESR of <30 with "B" symptoms, no extranodal disease, and no large mediastinal adenopathy.

In the EORTC H9F trial, patients were treated with 6 cycles of EBVP and those attaining a complete response were randomized to one of three arms: no radiation, 20 Gy IFRT, or 36 Gy IFRT [38]. The no-radiation arm was closed early, as discussed in a following section. The event-free survival rates of the 20 Gy and 30 Gy arms were

84% and 87%, respectively. Mature results of this trial will determine whether the lower dose of 20 Gy can be used in patients with favorable disease as per the EORTC criteria.

Trials on Optimal Radiation Field Size

Although no randomized trial has compared IFRT and EFRT in favorable-prognosis patients, multiple trials have addressed this issue in unfavorable-prognosis patients. In the GHSG HD8 trial, 1,204 early-stage, unfavorable-prognosis patients were randomized to receive 2 cycles of COPP (cyclophosphamide, vincristine, procarbazine, and prednisone) and ABVD, followed by either EFRT or IFRT [39]. There was no significant difference in the rates of freedom from treatment failure (5-year rates 86% vs 84%, P=0.56) or overall survival (5-year rates 91% vs 92%, P=0.24) between the two arms. In the EORTC H8U trial, 996 stage I or II unfavorable-prognosis patients were randomized to one of three arms: 6 cycles of MOPP/ABV followed by IFRT, 4 cycles of MOPP/ABV followed by IFRT, and 4 cycles of MOPP/ABV followed by EFRT [34]. There was no significant difference in the rates of overall survival or event-free survival between the three arms. A smaller Italian study enrolled 140 patients with stage I unfavorable and stage IIA favorable or unfavorable Hodgkin's lymphoma [40]. These patients were randomized to receive 4 cycles of ABVD and either subtotal nodal and splenic irradiation or IFRT. There was no significant difference in the 12-year freedom-from-progression rate (93% vs 94%) or overall survival rate (96% vs 94%) between the two arms. Based on these three trials on unfavorable-prognosis patients, it may be reasonably concluded that after chemotherapy, IFRT is adequate for favorable-prognosis patients. In selected cases, depending on the treatment site, modified IFRT could be acceptable (eg, excluding the upper neck in patients with supraclavicular disease only).

There has been growing interest in the role of INRT for Hodgkin's lymphoma [27]. Of note; the definition of INRT varies between different groups. For example the EORTC recommends the use of prechemotherapy positron emission tomography/computed tomography (PET/CT) in the radiation treatment planning position as well as the post-treatment scan in determining the clinical target volume. The expansion from clinical target volume to planning target volume is 1 cm isotropically [27]. In contrast, the GHSG does not require the use of pretreatment PET/CT. Their expansion is from the clinical target volume to the planning target volume by 1-3 cm depending on the anatomic location [41]. A retrospective study from Canada compared 96 patients treated with IFRT and 102 patients treated with INRT, all of whom received combined-modality therapy [42]. In this study, INRT was defined as prechemotherapy nodal volumes with margins ≤5 cm. Five relapses occurred in the IFRT group and three in the INRT group. There were no locoregional or marginal relapses in the INRT group. Moreover, there was no significant difference in overall or progression-free survival between the IFRT and INRT groups.

Further studies are needed to establish the role of INRT for favorable prognosis Hodgkin's lymphoma. The ongoing EORTC H10F trial, discussed later, has already incorporated INRT in both the standard and experimental arms. A new trial by the GHSG HD17 will be comparing IFRT versus INRT in early-stage patients.

Trials on Chemotherapy Alone

Since RT has been associated with long-term side effects such as second malignancies and cardiac toxicity, some studies have evaluated whether early-stage Hodgkin's lymphoma patients could be treated with chemotherapy alone, thereby excluding RT. In a study conducted by the Grupo Argentino de Tratamiento de la Leucemia Aguda (GATLA), 277 stage I or II favorable- or unfavorable-prognosis Hodgkin's lymphoma patients were randomized to receive either 6 cycles of cyclophosphamide, vinblastine, procarbazine, and prednisone (CVPP) or CVPP followed by IFRT [43]. Patients in the combined-modality arm had a significantly higher rate of lymphoma-free survival compared to the chemotherapy-alone arm (71% vs 62% at 84 months, P=0.01). However, subgroup analysis showed that there was no significant difference in lymphoma-free survival rate (77% vs 70%) or overall survival rate (92% vs 91%) between the two arms for favorable-prognosis patients. Since the CVPP regimen was used in this trial, it is unclear whether these results apply to patients treated with ABVD. Moreover, 45% of patients were younger than age 16, and the results may not necessarily be generalized to adults. This trial may also have been underpowered to detect a difference in lymphoma-free survival rate for favorable-prognosis patients.

In the Children's Cancer Group (CCG) 5942 trial, 501 patients younger than age 21 who achieved a complete response to combination chemotherapy were randomized to receive either low-dose IFRT (21 Gy) or no RT [44]. Among the randomized patients, 72% had stage I or II lymphoma. The 3-year event-free survival rate was 92% in the RT arm and 87% in the no-RT arm (P=0.057). Overall survival was similar in the two arms (98% vs 99%).

While the trial was designed to accrue 650 randomized patients, randomization was stopped early because of a high number of relapses in the no-RT arm. Since this trial was conducted only among pediatric patients, the results may not be applicable to adult patients.

Investigators at the Tata Memorial Hospital, India, conducted a randomized trial in which 179 patients who achieved a complete response to 6 cycles of ABVD were randomized to receive either IFRT or no RT [45]. Among the randomized patients, 55% had stage I-II lymphoma, 46% were younger than age 15, and 69% had mixed cellularity histology. Patients in the RT arm had a significantly higher rate of overall survival than those in the no-RT arm (8-year rates 100% vs 89%, P=0.002). Patients in the RT arm also had a significantly higher rate of event-free survival (8-year rates 88% vs 76%, P=0.01). The results of this study may not necessarily be pertinent for all favorable-prognosis early-stage Hodgkin's patients, given the high proportion of pediatric patients, stage III or IV patients, and mixed cellularity patients in this trial.

In a randomized trial at the Memorial Sloan Kettering Cancer Center, 152 patients with stage IA to IIIA nonbulky Hodgkin's lymphoma were treated with either 6 cycles of ABVD or 6 cycles of ABVD followed by RT (IFRT in 14%, modified extended field in the rest) [46]. This trial did not detect any significant difference between the chemotherapy and combined-modality arms for the 5-year rates of freedom from progression (81% vs 86%, P=0.61) or overall survival (90% vs 97%, P=0.08). However, this trial closed early because of poor accrual and was not powered to detect any difference less than 20%.

The National Cancer Institute of Canada (NCIC) and the Eastern Cooperative Oncology Group (ECOG) conducted a randomized trial on 405 patients with nonbulky stage I or IIA Hodgkin's lymphoma [47]. Favorable-risk patients were randomized to receive either 4-6 cycles of ABVD or subtotal nodal irradiation. Unfavorable-risk patients (age ≥40, or ESR ≥50 mm/hour, or mixed cellularity or lymphocyte-depleted histology, or four or more sites of lymphoma) were randomized to receive either 4-6 cycles of ABVD or combined-modality therapy with 2 cycles of ABVD followed by subtotal nodal irradiation. The rate of freedom from lymphoma progression was significantly lower in the chemotherapy-alone arm compared to the RT arm (5-year rates 87% vs 93%, P=0.006). There was a trend towards lower event-free survival in the chemotherapy-alone arm compared to the RT arm (5-year rates 86% vs 88%, P=0.06). However, there was no difference in overall survival between the two arms (5-year rates 96% vs 94%, P=0.4). Among the favorable-risk patients, there was no difference between the two arms for any of the outcome measures. This trial compared chemotherapy alone to RT alone in favorable-prognosis patients and did not evaluate combined-modality therapy. As discussed in a previous section, combined-modality therapy has been shown to be superior to RT alone. Moreover, the RT used in this trial, subtotal nodal irradiation, is no longer used because of concerns about late effects.

In the EORTC H9F trial, patients with favorable-prognosis stage I or II Hodgkin's lymphoma were treated with 6 cycles of EBVP, and those attaining a complete response were randomized to one of three arms: no RT, 20 Gy of IFRT, or 36 Gy of IFRT [38]. The no-RT arm of the trial had to be closed early since predefined stopping rules were met. The event-free survival rate was significantly lower in the no-RT arm (4-year rate 70%), compared to the 20 Gy (84%) and 36 Gy (87%) arms (P<0.001).

In a recent meta-analysis that included randomized trials on early-stage patients comparing chemotherapy alone versus the same chemotherapy and RT, combined-modality therapy was associated with a significantly improved tumor control rate (HR, 0.41, P=0.0003) which translated into a significant overall survival benefit (HR, 0.4, P<0.00001) [48]. (See Variant 1 and Variant 2.)

Response-Adapted Therapy Based on Early PET Results

PET scans are increasingly used in the initial staging and follow-up of patients with Hodgkin's lymphoma. Multiple studies have shown that interim and postchemotherapy PET results are highly predictive of treatment outcome [49-52]. Picardi et al [53] conducted a randomized trial addressing the question of whether RT can be omitted if a complete response by PET is achieved after chemotherapy in patients with Hodgkin's lymphoma. Patients with disease size of 5 cm or greater were included in this trial. One hundred sixty patients who had a complete response to induction chemotherapy but residual mass and PET-negative scan were randomized to undergo either observation or consolidative RT. Patients in the observation arm had a significantly inferior event-free survival rate (86%) compared to those in the RT arm (96%, P=0.03). These results suggest that negative PET scans cannot be used to exclude patients from RT.

Ongoing randomized trials are evaluating response-adapted therapy based on PET results. In the EORTC H10F trial, favorable-prognosis Hodgkin's lymphoma patients are being treated initially with 2 cycles of ABVD, followed by a PET scan. Patients are then randomized to receive either a third cycle of ABVD and INRT in the standard arm, or two additional cycles of ABVD in PET-negative patients and 2 cycles of dose-escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP) followed by INRT in PET-positive patients, in the experimental arm. Based on recent interim analysis, it was determined that the experimental arm of omitting RT in the setting of negative PET after 2 cycles of ABVD was unlikely to be non-inferior to the standard arm of combined-modality therapy. At the recommendation of an independent data-safety monitoring board, the experimental arm of no RT was closed and all patients on the trial are to receive INRT. The portion of the experimental arm of using dose-escalated BEACOPP in patients with PET positive disease after 2 cycles of ABVD is still ongoing.

The RAPID trial, a multicenter trial in the United Kingdom, is also exploring response-adapted therapy. Patients who are PET-negative after 3 cycles of ABVD will be randomized to receive either IFRT (arm A) or no further treatment (arm B). Individuals who are PET-positive will receive a further (fourth) cycle of ABVD followed by INRT. In the GHSG HD16 trial, favorable prognosis Hodgkin's lymphoma patients are being randomized to receive either 2 cycles of ABVD followed by 30 Gy IFRT in all patients in the control arm, or 2 cycles of ABVD in PET-negative patients and 2 cycles of ABVD followed by 30 Gy IFRT in PET-positive patients in the experimental arm. These trials will further clarify whether PET response can be used to guide treatment for Hodgkin's lymphoma. However, changes in therapy (either changing chemotherapy or omitting RT) based on PET response for early-stage patients are not supported by currently available data and should only be performed as part of a clinical trial. (See Variant 3.)

Nodular Lymphocyte-Predominant Hodgkin's Lymphoma

Nodular lymphocyte-predominant Hodgkin's lymphoma represents a distinct clinical entity that accounts for about 5% of Hodgkin's lymphomas. Patients with nodular lymphocyte-predominant Hodgkin's lymphoma typically present at earlier stages, compared to those with classical Hodgkin's lymphoma. Nodular lymphocyte-predominant Hodgkin's lymphoma typically presents more commonly at peripheral than at central sites. The GHSG reported a retrospective study on 131 patients with stage IA lymphocyte-predominant Hodgkin's lymphoma, of whom 45 were treated with IFRT to 30 Gy (on the LPHL IA trial), 45 with either EFRT to 30 Gy plus IFRT to 10 Gy or EFRT to 40 Gy, and 41 with 2-4 cycles of ABVD plus either IFRT to 20-30 Gy or EFRT to 30 Gy plus IFRT to 10 Gy [54]. There was no significant difference in the rates of complete remission between the IFRT, EFRT/IFRT, and combined-modality groups. One hundred percent of patients in the IFRT group, 98% in the EFRT/IFRT group, and 95% in the combined-modality group achieved complete remission. The 2-year overall survival rate was 100% in all three groups. A recent retrospective study reported outcomes in 113 patients with stage I-II lymphocyte-predominant Hodgkin's lymphoma, of whom, 93 were treated with RT alone, 13 were treated with combined-modality therapy, and 7 were treated with chemotherapy alone [55]. The addition of chemotherapy to RT did not appear to improve overall survival or progression-free survival. Most patients who received chemotherapy alone developed early relapse and required salvage. Among patients receiving RT alone, there was no difference in overall survival or progression-free survival among those treated with limited-field RT such as IFRT (median dose, 32 Gy), regional RT such as mantle (median dose, 36 Gy), or EFRT (median dose, 38 Gy). These studies indicate that IFRT to 30 Gy will likely provide excellent outcomes in patients with nodular lymphocyte-predominant Hodgkin's lymphoma, with less toxicity than EFRT or combined-modality therapy. (See Variant 4.)

Summary

- The standard of care for favorable stage I-II Hodgkin's lymphoma is combined-modality therapy, consisting of 2-4 cycles of ABVD chemotherapy followed by 20-30 Gy of IFRT. For patients with early-stage favorable disease who fit the GHSG favorable criteria, 2 cycles of ABVD followed by 20 Gy IFRT are adequate. For patients with early-stage favorable disease who fit the EORTC criteria but not the GHSG criteria, 3-4 cycles of ABVD followed by 30 Gy IFRT are recommended.
- The standard radiation treatment field is IFRT, although modified IFRT may be acceptable depending on the treatment site.
- Changing chemotherapy or omitting RT based on PET response for early-stage patients is not supported by currently available data and should only be performed as part of a clinical trial.
- The standard of care for stage I-II lymphocyte-predominant Hodgkin's lymphoma is IFRT to 30-36 Gy.

Supporting Documents

- ACR Appropriateness Criteria® Overview
- Evidence Table

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Clinical Condition: Hodgkin's Lymphoma — Favorable Prognosis Stage I and II

Variant 1: 25-year-old woman with stage IIA NSHL with left supraclavicular and mediastinal (3 cm in widest diameter) involvement; normal ESR.

Treatment	Rating	Comments
Chemotherapy and IFRT	8	
Chemotherapy alone	4	
Type of Chemotherapy		
ABVD	9	
Stanford V	7	Includes IFRT. Eight-week course.
Duration of ABVD (If Chemotherapy Given Alone)		Note: Chemotherapy alone is rated 4.
2 cycles	2	
4 cycles	4	
6 cycles	7	
Duration of ABVD (Combined-Modality)		
2 cycles	8	Patient needs to meet all GHSG HD10 eligibility criteria. See text.
4 cycles	8	
6 cycles	5	
Dose of Radiation Therapy (Combined-Modality)		
20 Gy	8	Patient needs to meet all GHSG HD10 eligibility criteria. See text.
30 Gy	6	
30 Gy + 6 Gy boost to mediastinum	3	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Hodgkin's Lymphoma — Favorable Prognosis Stage I and II**

Variant 2:   **25-year-old woman with stage IIA NSHL with bilateral supraclavicular and mediastinal (7 cm in widest diameter) involvement; normal ESR.**

Treatment	Rating	Comments
Chemotherapy and IFRT	9	
Chemotherapy alone	4	
Type of Chemotherapy		
ABVD	9	
Stanford V	7	Includes IFRT. Eight-week course.
Duration of ABVD **(If Chemotherapy Given Alone)**		Note: Chemotherapy alone is rated 4.
2 cycles	2	
4 cycles	3	
6 cycles	7	
Duration of ABVD (Combined-Modality)		
2 cycles	2	
4 cycles	8	
6 cycles	6	
Dose of Radiation Therapy (Combined-Modality) 20 Gy	2	
30 Gy	8	
30 Gy + 6 Gy boost to mediastinum	5	Consider if area remains PET positive after chemotherapy.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Hodgkin's Lymphoma — Favorable Prognosis Stage I and II**

Variant 3:   **25-year-old woman with stage IIA NSHL with left supraclavicular and mediastinal (3 cm in widest diameter) involvement; normal ESR. PET negative after 2 cycles of ABVD.**

Treatment	Rating	Comments
Chemotherapy and IFRT	8	
Chemotherapy alone	6	
Duration of ABVD (If Chemotherapy Given Alone)		Note: Chemotherapy alone is rated 6.
2 cycles	2	
4 cycles	6	
6 cycles	7	
Duration of ABVD (Combined-Modality)		
2 cycles	8	Patient needs to meet all GHSG HD10 eligibility criteria. See text.
4 cycles	7	
6 cycles	4	
Dose of Radiation Therapy (Combined-Modality)		
20 Gy	8	Patient needs to meet all GHSG HD10 eligibility criteria. See text.
30 Gy	5	
30 Gy + 6 Gy boost to mediastinum	3	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 4:   **30-year-old man with stage IA NLPHL with right upper cervical involvement.**

Treatment	Rating	Comments
Involved-field RT alone	8	
Chemotherapy and IFRT	6	
Mantle RT alone	3	
Chemotherapy alone	3	
Mantle-para-aortic and splenic RT alone	2	
Dose of Radiation Therapy (RT alone)		
20 Gy	3	
30-36 Gy	8	
>36 Gy	3	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		