NODULER LENFOSİT PREDOMİNANT HL TEDAVİ YAKLAŞIMI

DR. ELİFCAN ALADAĞ KARAKULAK

GÜLHANE EĞİTİM VE ARAŞTIRMA HASTANESİ HEMATOLOJİ KLİNİĞİ

19.12.2021

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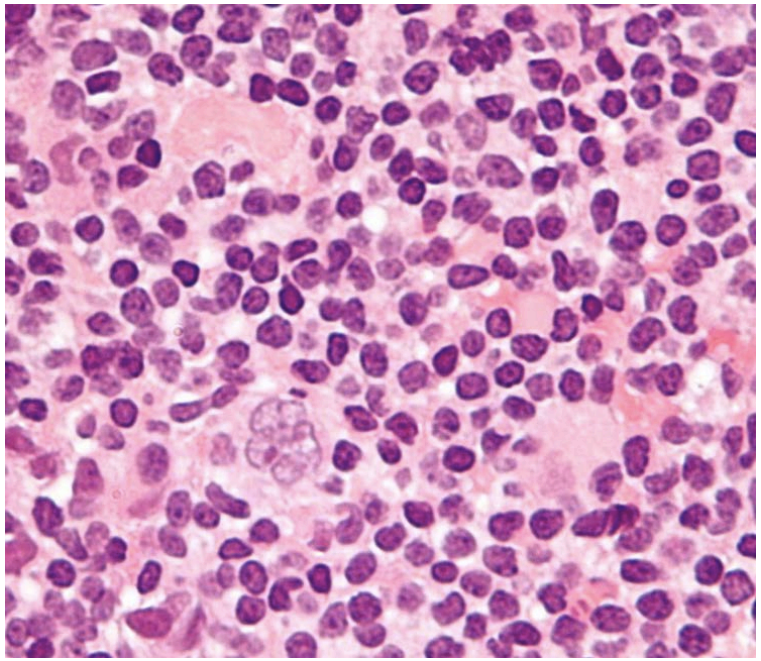
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

İNSİDANS

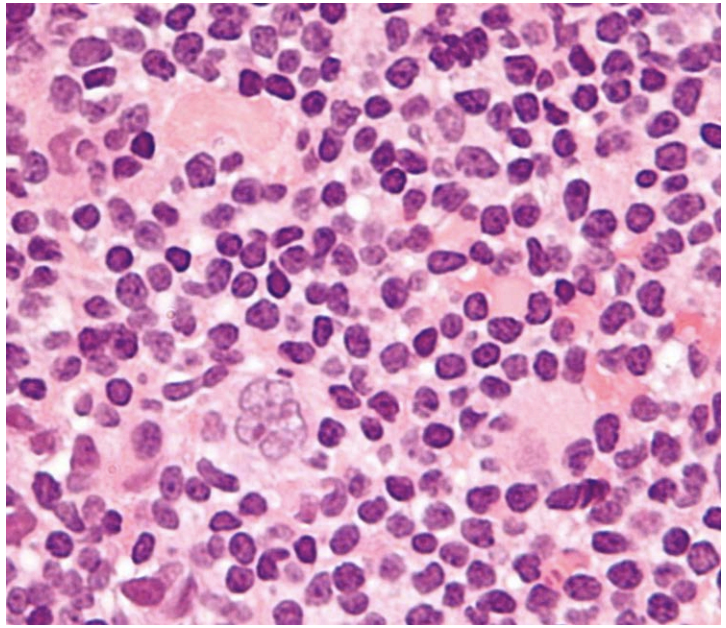


- ✓ 1.5 / 1.000.000
- ✓ Tüm HL'ların yaklaşık %5'ini oluşturur.
- ✓ Birinci derece akrabalarda görülme sıklığı cHL'ye göre daha fazla (SIR 19 vs 5.3)

doi:10.1182/blood-2013-07-453241

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

PATOLOJİK ÖZELLİKLER



Popcorn cells

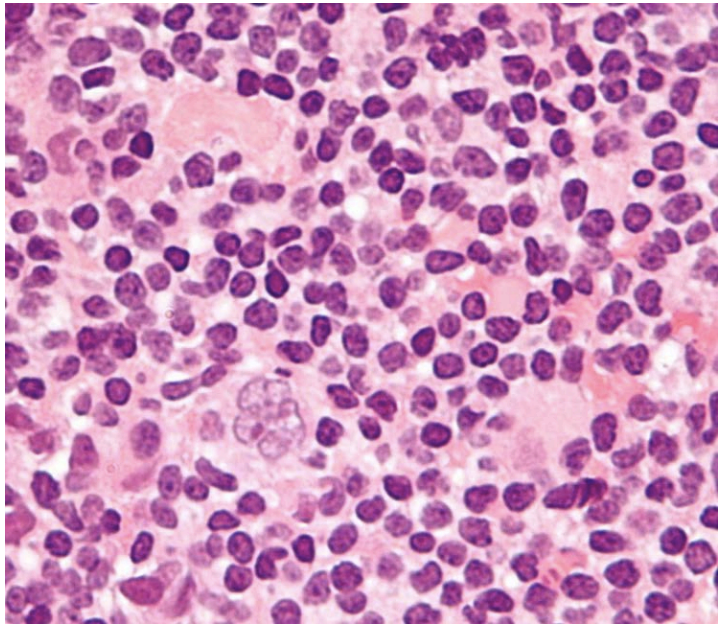
↓

bcl-6 (+)
CD 19, CD 20, CD 45 ve CD 79a (+)
PAX-5 ve OCT-2 (+)
CD 30 ve CD15 (-)

doi:10.1182/blood-2013-07-453241

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

KLİNİK

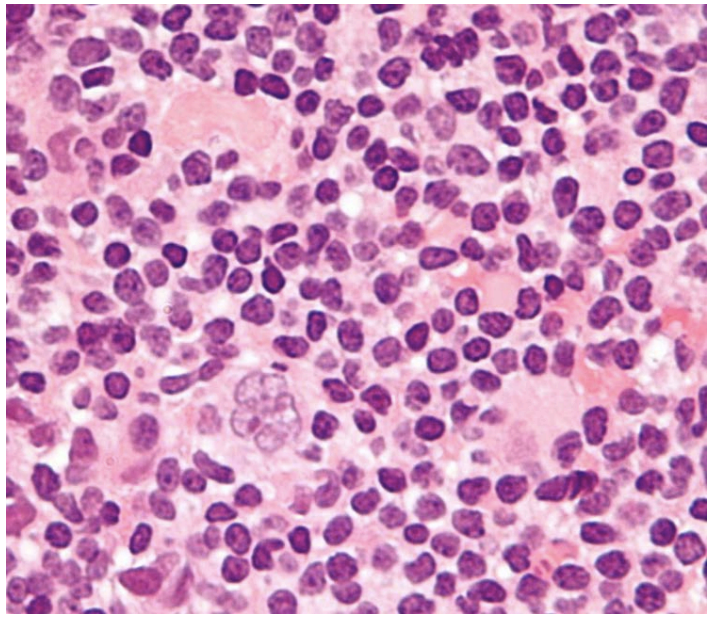


- ✓ Median tanı yaşı 37
- ✓ Hastaların %75 i erkek
- ✓ B semptomları <%10 vakada
- ✓ Indolen seyir, geç relaps.
- ✓ Relaps oranı cHL'ye göre yüksek (>1 yıl relaps %7.4 vs %4.7)

doi:10.1182/blood-2013-07-453241

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TANI



- ✓ FDG aviditesi vardır, ancak tek başına BT ye PET BT eklenmesi hastaların sadece %10'unda tedavi değişimine yol açmaktadır
- ✓ Tanıda Anında; %63 erken evre - iyi risk
  %21 ileri evre

doi:10.1182/blood-2013-07-453241

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

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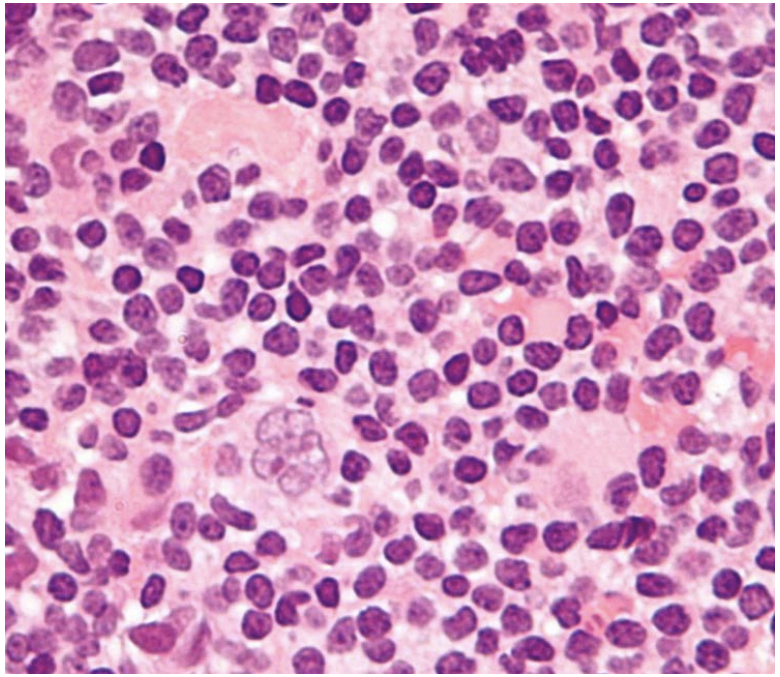


Klasik olarak servikal tutulum

Median hastalık sadece %7.

Dalak tutulumu

- ✓ 10 yıllık PFS / %48 vs %71 p:0.049
- ✓ Sekonder agresif lenfoma insidansı yüksek (p:0.014)

Bulky hastalık

Dalak tutulumu

Subdiafragmatik tutulum

} Kötü Prognoz

doi:10.1182/blood-2013-07-453241

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

PROGRESYON- TRANSFORMASYON

Transformation to Aggressive Lymphoma in Nodular Lymphocyte-Predominant Hodgkin's Lymphoma

Mubarak Al-Mansour, Joseph M. Connors, Randy D. Gascoyne, Brian Skinnider, and Kerry J. Savage

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

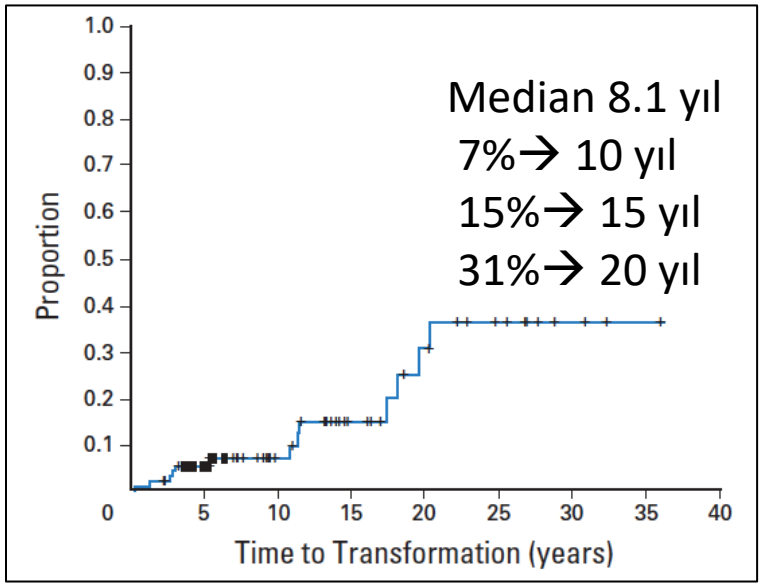


Table 4. Univariate Analysis of Risk Factors for Transformation at Diagnosis of NLPHL

Clinical Feature	*P*
Age ≥ 40 years	.556
Male sex	.625
Performance status ≥ 2	.522
Stage III or IV disease	.057
Splenic disease	.006
B symptoms	.913
LDH elevated	.526
Bulk ≥ 5 cm	.331

Al-Mansour M, Connors JM, Gascoyne RD, Skinnider B, Savage KJ. Transformation to aggressive lymphoma in nodular lymphocytepredominant Hodgkin's lymphoma. J Clin Oncol. 2010;28(5):793-799.

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

EVRELEME

GHSG Evreleme Sistemi	
Erken evre	Evre 1-2 (risk faktörü yok)
Orta evre	Evre 1-2A (≥1 risk faktörü) Evre 2B (C/D risk faktörleri)
İleri evre	Evre 2B (A/B risk faktörleri) Evre 3-4

EORTC Age >50 yıl

EORTC ≥ 4 Nodal alan

Risk Faktörleri	
A	Geniş mediastinal kitle
B	Ekstranodal hastalık
C	ESR >50 mm/h B semptomu yoksa ESR >30 mm/h B semptomu varsa
D	≥ 3 Nodal alan

Dennis A. Eichenauer, Andreas Engert; How I treat nodular lymphocyte-predominant Hodgkin lymphoma. *Blood* 2020; 136 (26): 2987–2993. doi: https://doi.org/10.1182/blood.2019004044

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ

Initial diagnosis of NLPHL

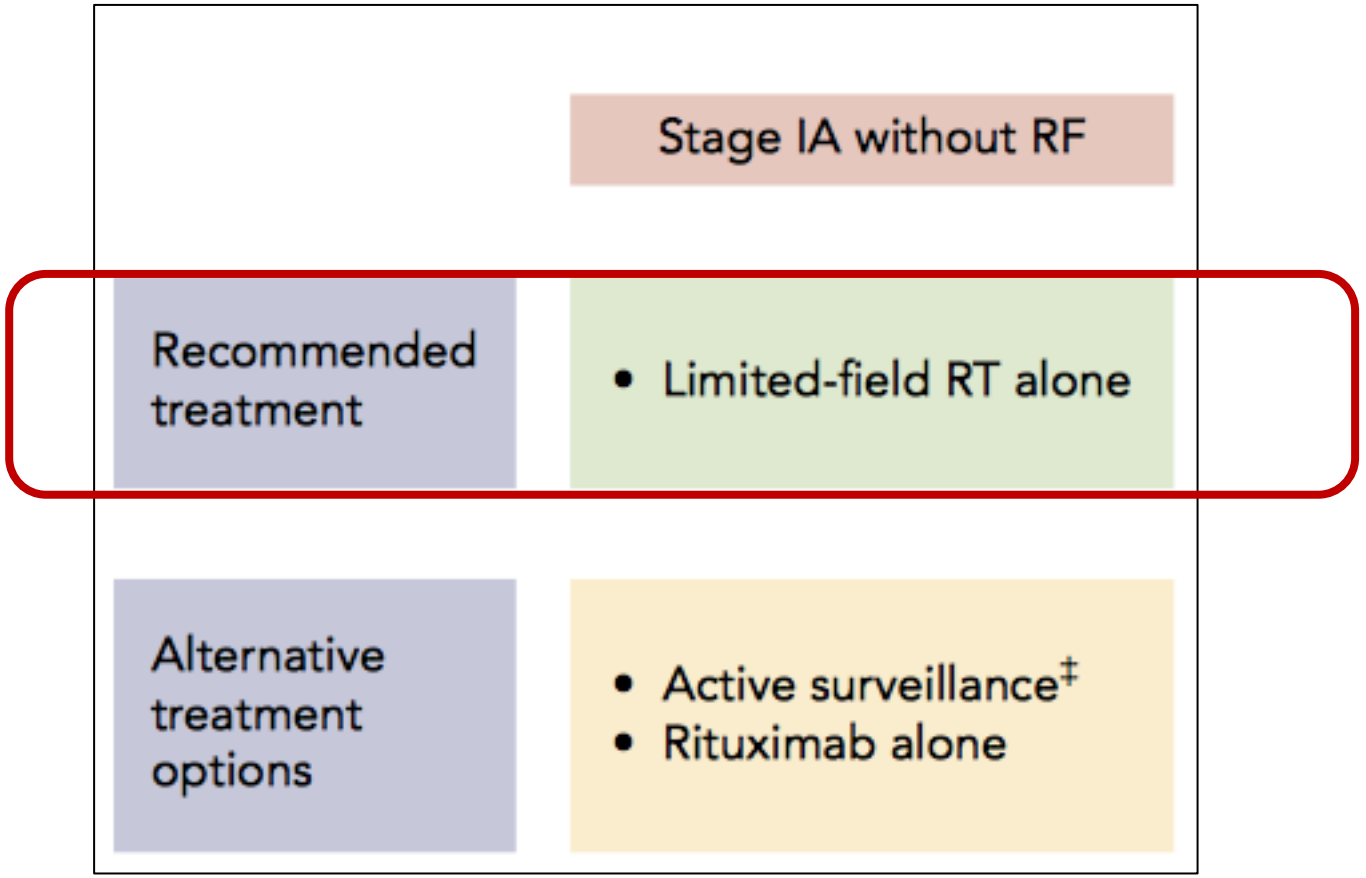
	Stage IA without RF	Early stages[1]	Intermediate stages	Advanced stages
Recommended treatment	• Limited-field RT alone	• 2 x (R-)ABVD + limited-field RT	• 4 x (R-)ABVD + limited-field RT	• 4 or 6 x BEACOPPesc +/-RT (PET-2-guided)[2] • 6 x R-CHOP +/-RT
Alternative treatment options	• Active surveillance[3] • Rituximab alone	• BR +/- RT[4] • R-CVP +/- RT[4] • Rituximab +/-RT • RT alone	• BR +/- RT[4] • R-CVP +/- RT[4] • Rituximab +/-RT • RT alone	• BR +/-RT[4] • R-CVP +/- RT[4] • Active surveillance • (R-)ABVD +/-RT

[1]:Patients with early-stage NLPHL except for stage IA without clinical risk factors
[2]:4 cycles of escalated BEACOPP in case of PET-2 negativity, 6 cycles of escalated BEACOPP in case of PET-2 positivity
[3]:Can be considered in patients with a complete remission according to PET and CT after lymph node resection
[4]:Can be considered in patients with conditions precluding the use of anthracyclines

Dennis A. Eichenauer, Andreas Engert; How I treat nodular lymphocyte-predominant Hodgkin lymphoma. *Blood* 2020; 136 (26): 2987–2993. doi: https://doi.org/10.1182/blood.2019004044

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- EVRE 1A



Dennis A. Eichenauer, Andreas Engert; How I treat nodular lymphocyte-predominant Hodgkin lymphoma. *Blood* 2020; 136 (26): 2987–2993. doi: https://doi.org/10.1182/blood.2019004044

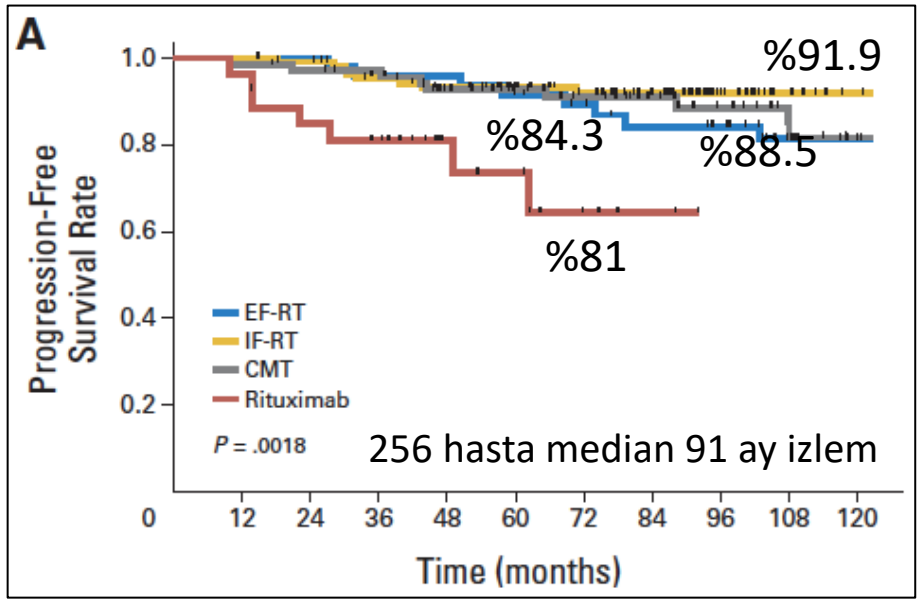
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

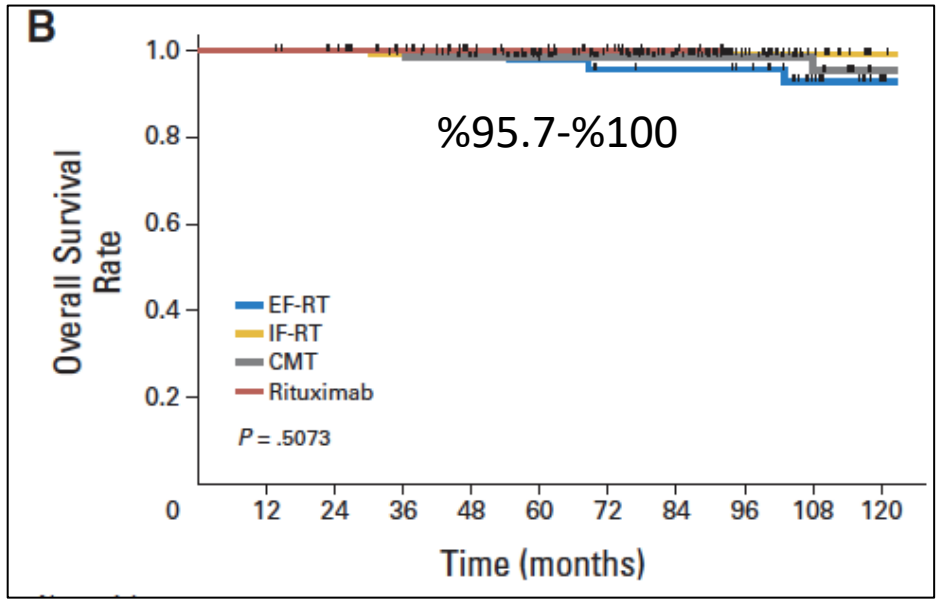
TEDAVİ- EVRE 1A - Radyoterapi

Long-Term Course of Patients With Stage IA Nodular Lymphocyte-Predominant Hodgkin Lymphoma: A Report From the German Hodgkin Study Group

Dennis A. Eichenauer, Annette Plütschow, Michael Fuchs, Bastian von Tresckow, Boris Böll, Karolin Behringer, Volker Diehl, Hans Theodor Eich, Peter Borchmann, and Andreas Engert

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

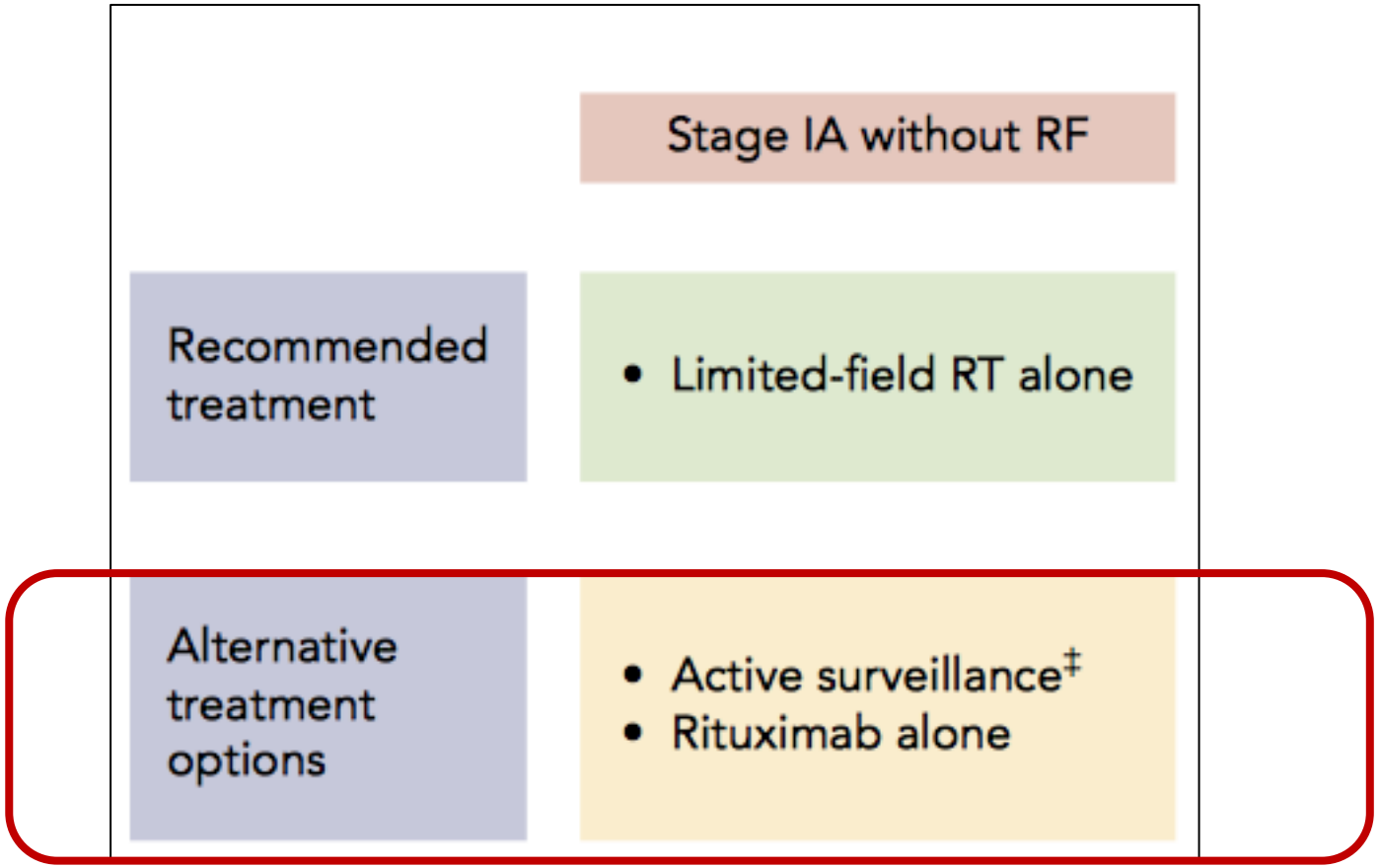




J Clin Oncol 2015 Sep 10;33(26):2857-62. doi: 10.1200/JCO.2014.60.4363. Epub 2015 Aug 3.

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- EVRE 1A



Dennis A. Eichenauer, Andreas Engert; How I treat nodular lymphocyte-predominant Hodgkin lymphoma. *Blood* 2020; 136 (26): 2987–2993. doi: https://doi.org/10.1182/blood.2019004044

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- EVRE 1A– Tedavisiz izlem

Minimal Treatment of Low-Risk, Pediatric Lymphocyte-Predominant Hodgkin Lymphoma: A Report From the Children's Oncology Group

Burton E. Appel, Lu Chen, Allen B. Buxton, Robert E. Hutchison, David C. Hodgson, Peter F. Ehrlich, Louis S. Constine, and Cindy L. Schwartz

Journal of Clinical Oncology®
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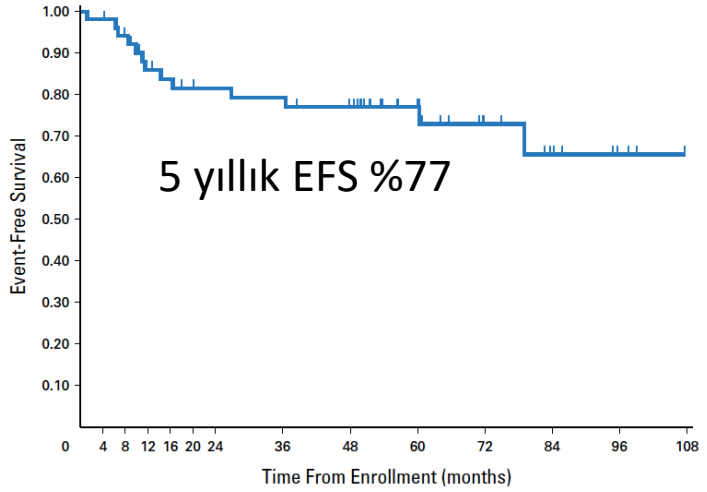
52 pediatrik NLPDHL Evre 1A hastası
Tam rezeksiyon sonrası tedavisizi izlem

13 hasta median 11.5 ayda relaps olmuş.



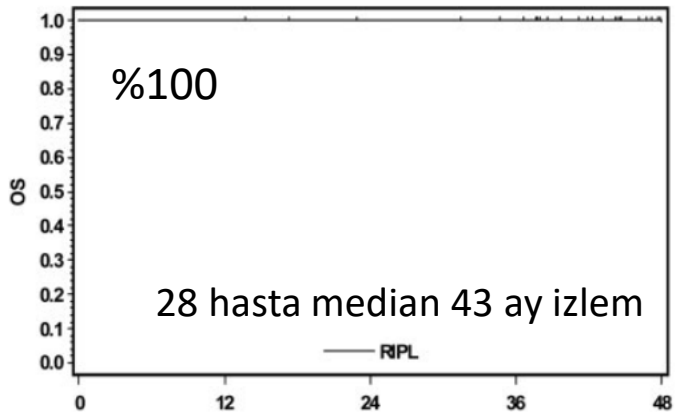
DOI: 10.1200/JCO.2015.65.3469 *Journal of Clinical Oncology* 34, no. 20 (July 10, 2016) 2372-2379

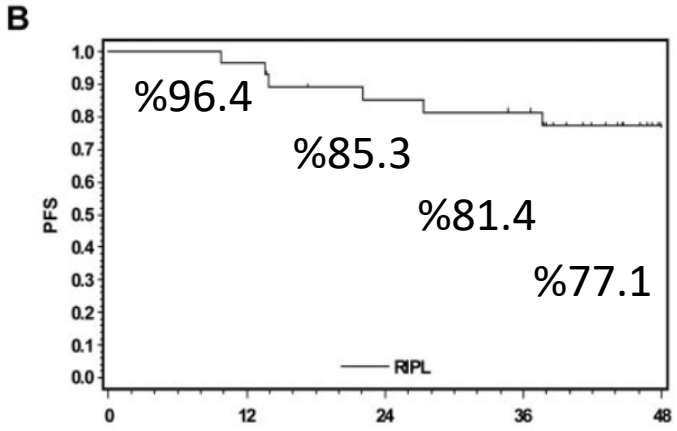
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- EVRE 1A– Rituximab Monoterapi

Phase 2 study of rituximab in newly diagnosed stage IA nodular lymphocyte-predominant Hodgkin lymphoma: a report from the German Hodgkin Study Group

Dennis A Eichenauer [1], Michael Fuchs, Annette Pluetschow, Beate Klimm, Teresa Halbsguth, Boris Böll, Bastian von Tresckow, Lucia Nogová, Peter Borchmann, Andreas Engert





Blood 2011 Oct 20;118(16):4363-5. doi: 10.1182/blood-2011-06-361055.Epub 2011 Aug 9.

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- ERKEN/ORTA EVRE

	Early stages*	Intermediate stages
Recommended treatment	• 2 × (R-)ABVD + limited-field RT	• 4 × (R-)ABVD + limited-field RT
Alternative treatment options	• BR ± RT§ • R-CVP ± RT§ • Rituximab ± RT • RT alone	• BR ± RT§ • R-CVP ± RT§ • Rituximab ± RT • RT alone

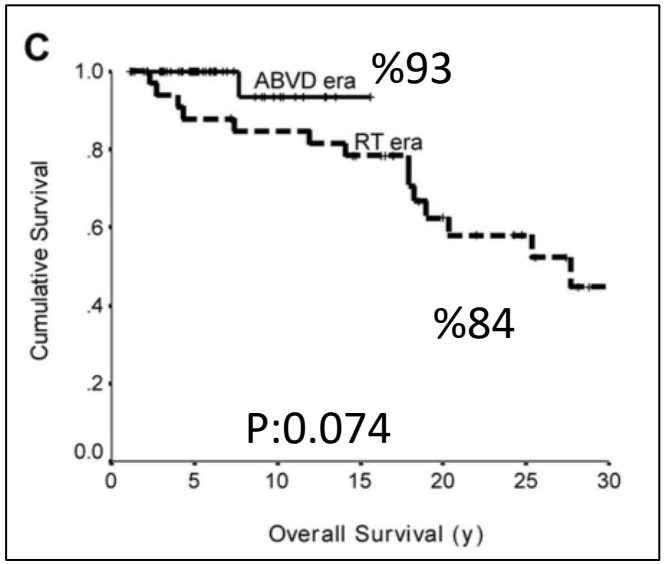
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

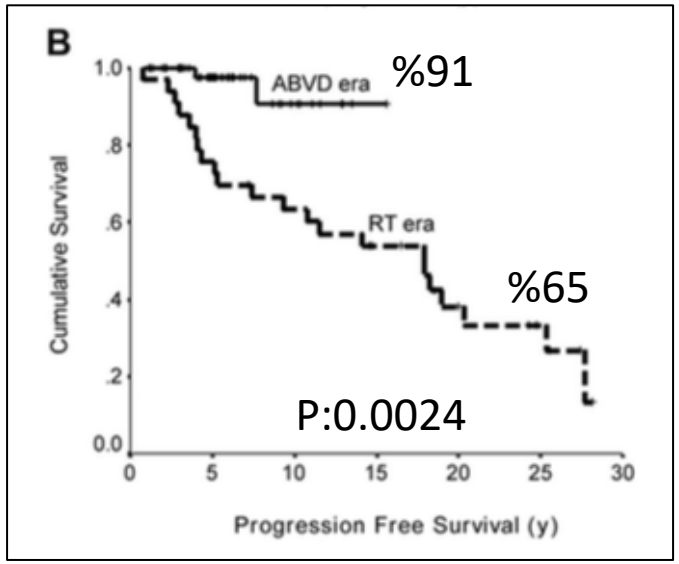
TEDAVİ- ERKEN/ORTA EVRE

Treating limited-stage nodular lymphocyte predominant Hodgkin lymphoma similarly to classical Hodgkin lymphoma with ABVD may improve outcome

Kerry J. Savage,[1] Brian Skinnider,[2] Mubarak Al-Mansour,[1] Laurie H. Sehn,[1] Randy D. Gascoyne,[2] and Joseph M. Connors[1]

[1]Centre for Lymphoid Cancer and Department of Medical Oncology, British Columbia Cancer Agency and the University of British Columbia, Vancouver, BC; and
[2]Centre for Lymphoid Cancer and Department of Pathology, British Columbia Cancer Agency, Vancouver, BC





Evre 1A- 1B ve 2A
RT (n:32) vs 2xABVD -/+ RT(n:56-16)

Blood 2011 Oct 27;118(17):4585-90. doi: 10.1182/blood-2011-07-365932. Epub 2011 Aug 26

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- ERKEN/ORTA EVRE

	Early stages*	Intermediate stages
Recommended treatment	• 2 × (R-)ABVD + limited-field RT **20 Gy**	• 4 × (R-)ABVD + limited-field RT **30 Gy**
Alternative treatment options	• BR ± RT§ • R-CVP ± RT§ • Rituximab ± RT • RT alone	• BR ± RT§ • R-CVP ± RT§ • Rituximab ± RT • RT alone

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

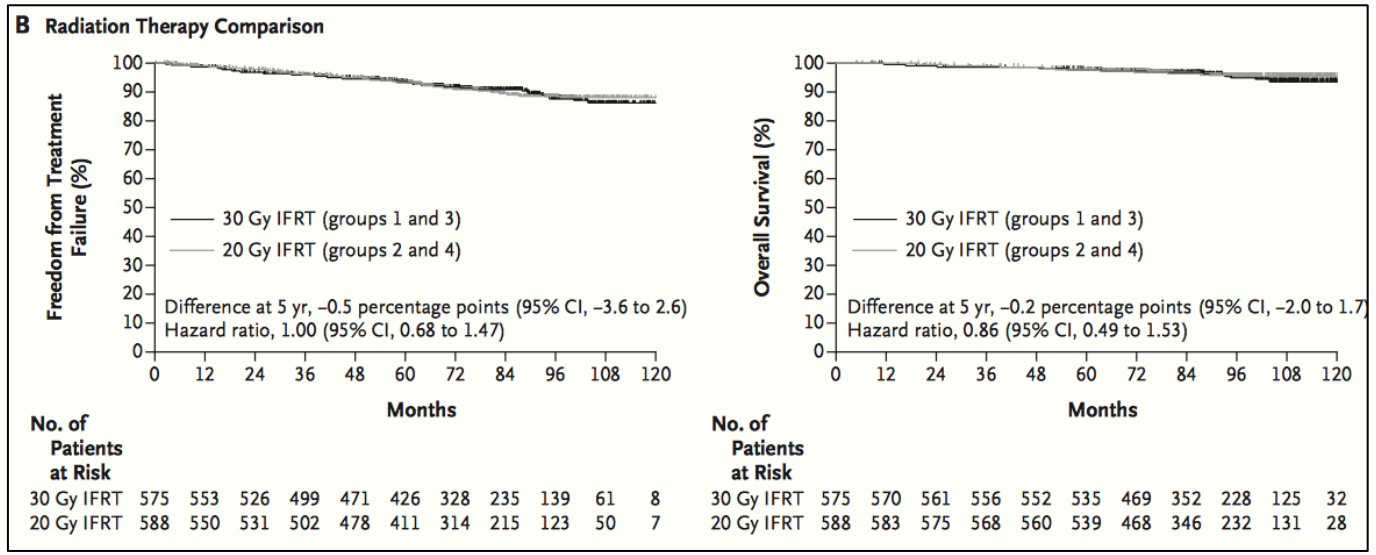
TEDAVİ- ERKEN/ORTA EVRE

ORIGINAL ARTICLE

Reduced Treatment Intensity in Patients with Early-Stage Hodgkin's Lymphoma

Andreas Engert, M.D., Annette Plütschow, Ph.D., Hans Theodor Eich, M.D., Andreas Lohri, M.D., Bernd Dörken, M.D., Peter Borchmann, M.D., Bernhard Berger, M.D., Richard Greil, M.D., Kay C. Willborn, M.D., Martin Wilhelm, M.D., Jürgen Debus, M.D., Michael J. Eble, M.D., et al.

The NEW ENGLAND JOURNAL of MEDICINE



1370 yeni tanı HL hastası (81 NLPHL)

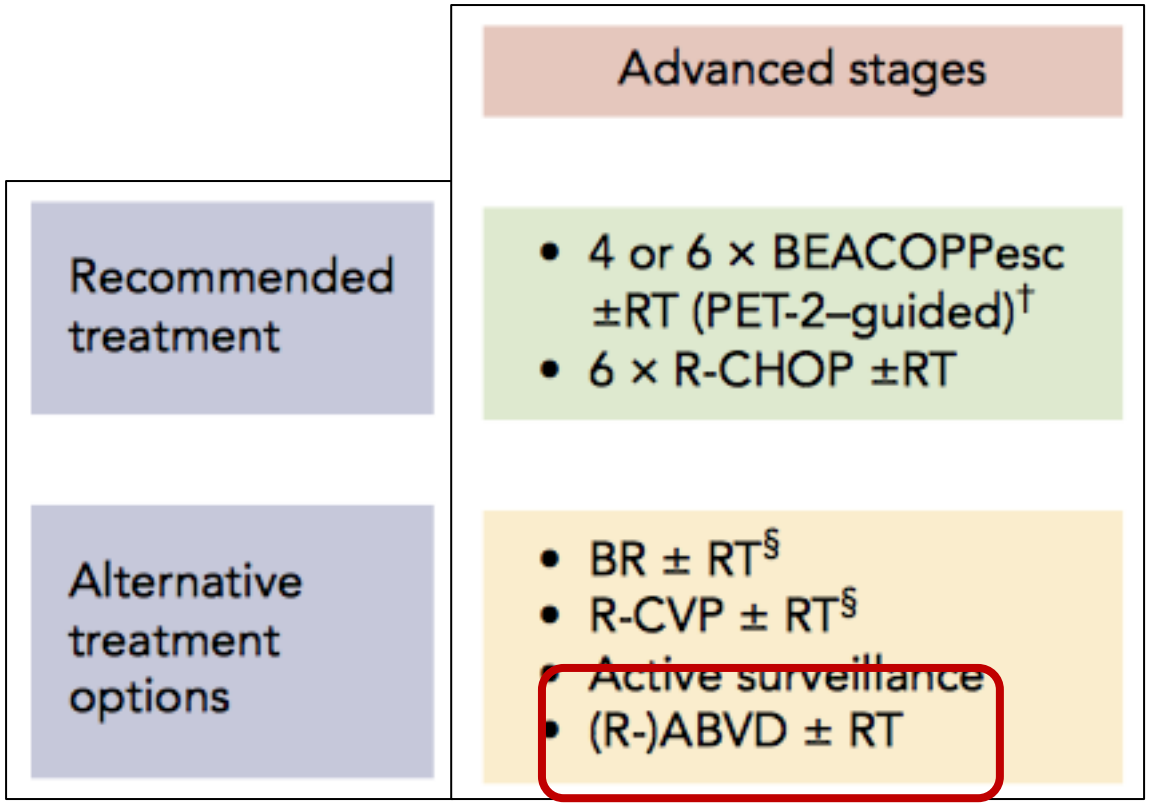
20 Gy ile 30 Gy arası OS ve PFS farkı yok.

Toksisite 30 Gy >20 Gy

N Engl J Med 2010; 363:640-652 DOI: 10.1056/NEJMoa1000067

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- İLERİ EVRE



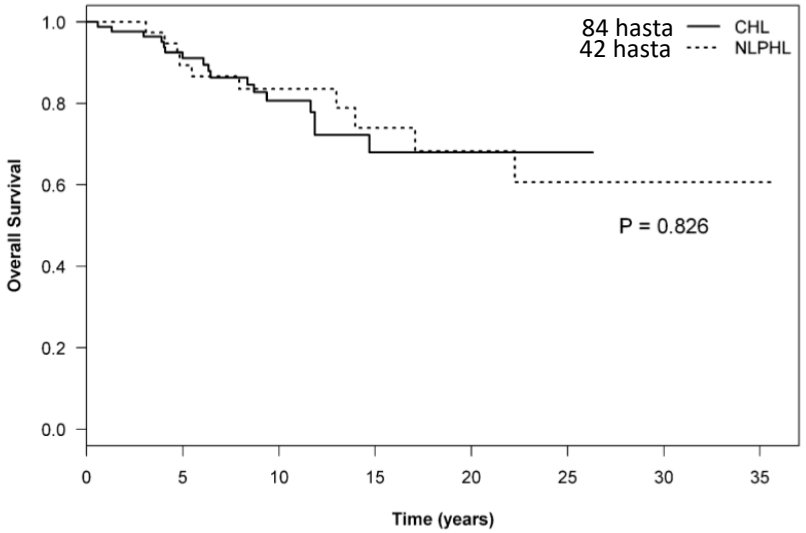
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

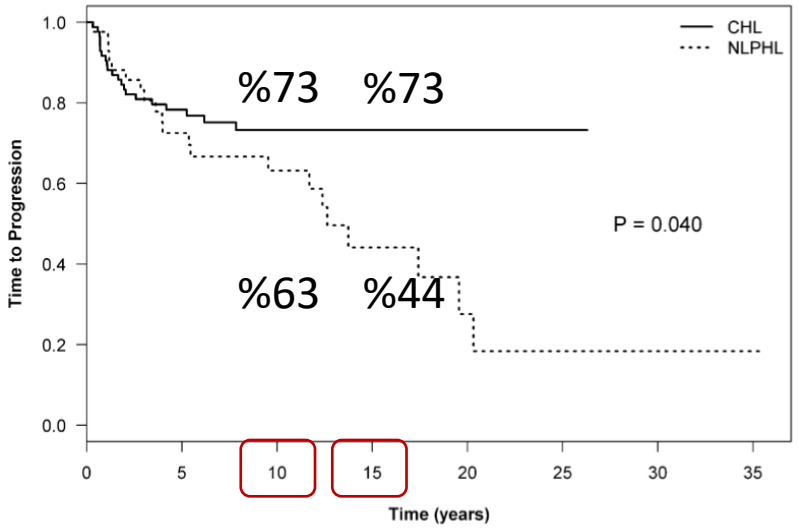
TEDAVİ- İLERİ EVRE – ABVD

Advanced-stage nodular lymphocyte predominant Hodgkin lymphoma compared with classical Hodgkin lymphoma: a matched pair outcome analysis

Katharine H. Xing,[1] Joseph M. Connors,[1] Anky Lai,[2] Mubarak Al-Mansour,[3] Laurie H. Sehn,[1] Diego Villa,[1] Richard Klasa,[1] Tamara Shenkier,[1] Randy D. Gascoyne,[4] Brian Skinnider,[4] and Kerry J. Savage[1]

[1]Centre for Lymphoid Cancer and Department of Medical Oncology, British Columbia Cancer Agency and the University of British Columbia, Vancouver, BC, Canada; [2]Cancer Surveillance and Outcomes, Population Oncology, British Columbia Cancer Agency, Vancouver, BC, Canada; [3]Oncology Department, King Abdulaziz Medical City, Riyadh, Saudi Arabia; and [4]Centre for Lymphoid Cancer and Department of Pathology, British Columbia Cancer Agency, Vancouver, BC, Canada





NLPHL hastalarında agresif lenfomaya transformasyon

%24

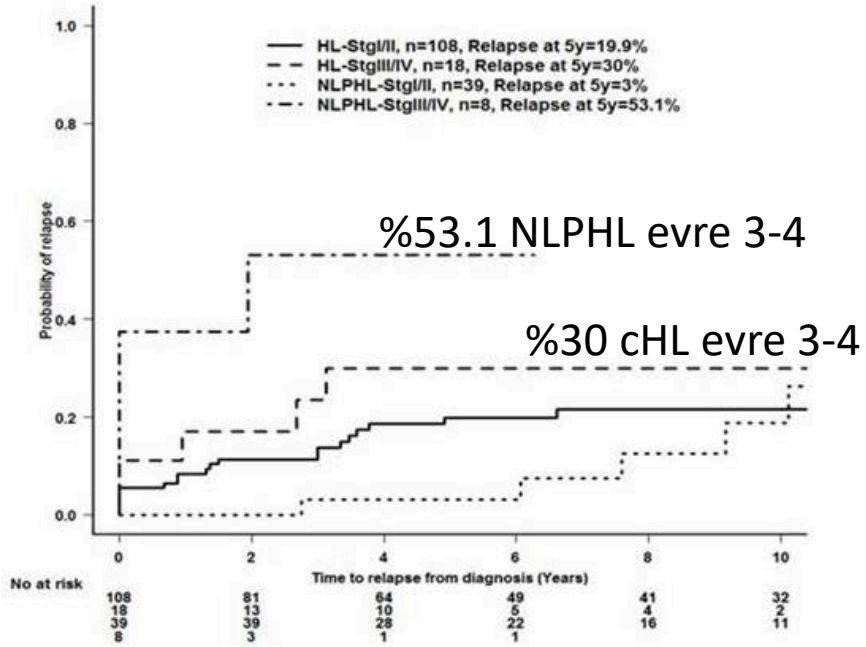
Blood 2014 Jun 5;123(23):3567-73. doi: 10.1182/blood-2013-12-541078. Epub 2014 Apr 8.

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- İLERİ EVRE – ABVD

Outcomes of Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL) Vs. Classical Hodgkin Lymphoma (cHL) at Princess Margaret Cancer Centre

Jeffery Ames, MD, Manjula Maganti, MSc, Bethany E Monteith, MD, David C. Hodgson, MD, Vishal Kukreti, MD, John G. Kuruvilla, MD, Anca Prica, MD, Richard Tsang, MD, Alex Sun, MD, Mary Gospodarowicz, MD, Melania Pintilie, MSc, Michael Crump, MD



%53.1 NLPHL evre 3-4

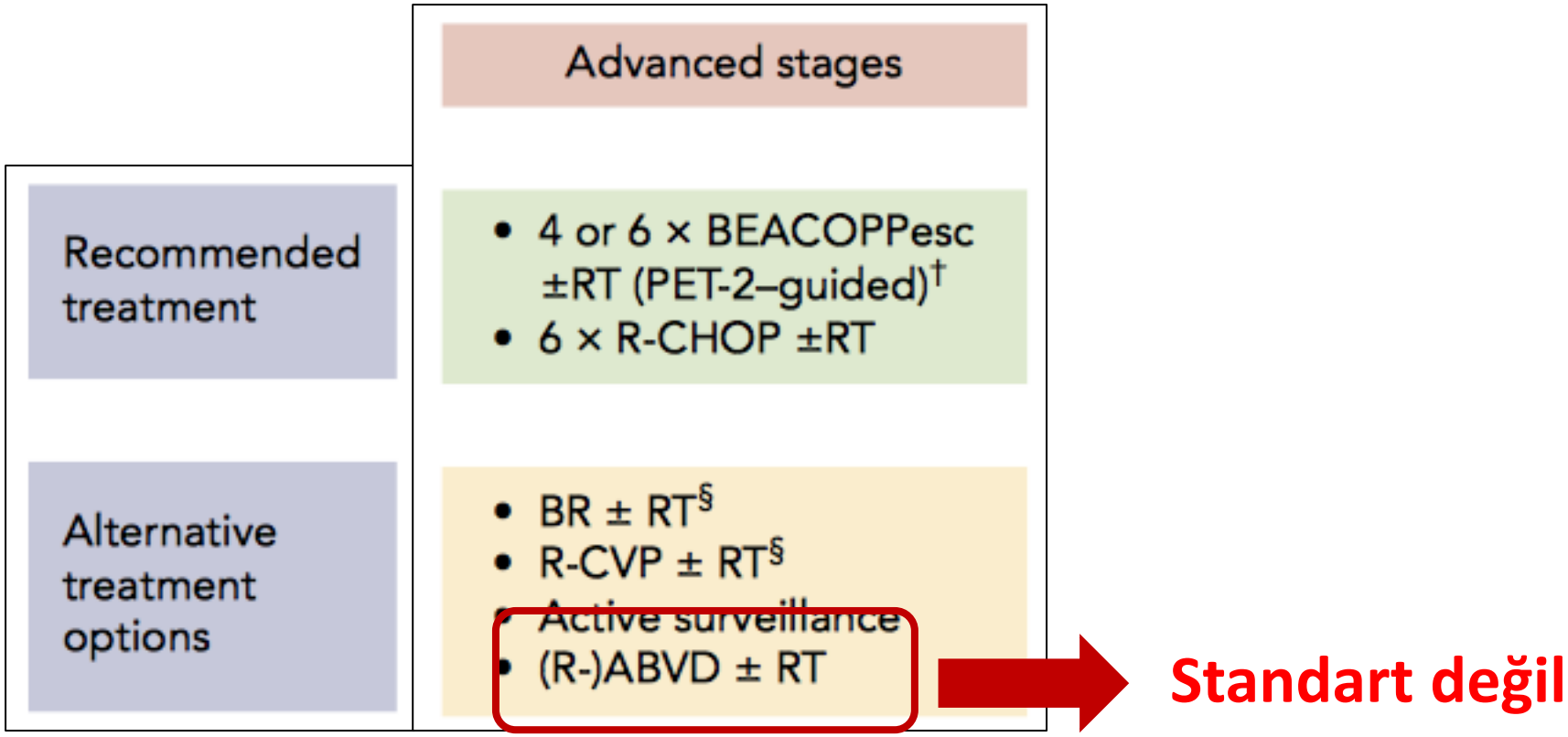
%30 cHL evre 3-4

47 NLPHL (8 ileri evre) vs 126 cHL (18 ileri evre)
5-yıllık DFS NLPHL < cHL

https://doi.org/10.1182/blood.V126.23.3863.3863

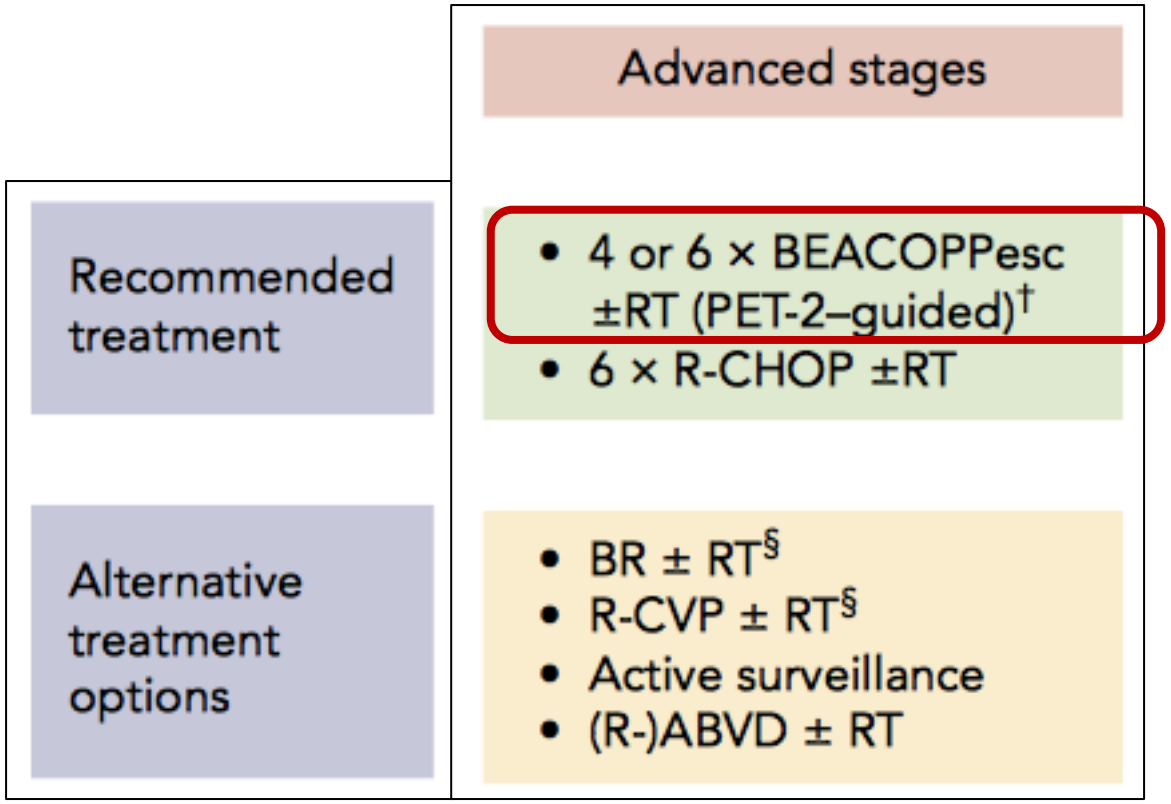
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- İLERİ EVRE



NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- İLERİ EVRE



NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- İLERİ EVRE- BEACOPP

ORIGINAL REPORTS | Hematologic Malignancies

Long-Term Follow-Up of Patients With Nodular Lymphocyte-Predominant Hodgkin Lymphoma Treated in the HD7 to HD15 Trials: A Report From the German Hodgkin Study Group

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

HD 9 – HD 12 – HD 15 çalışmaları

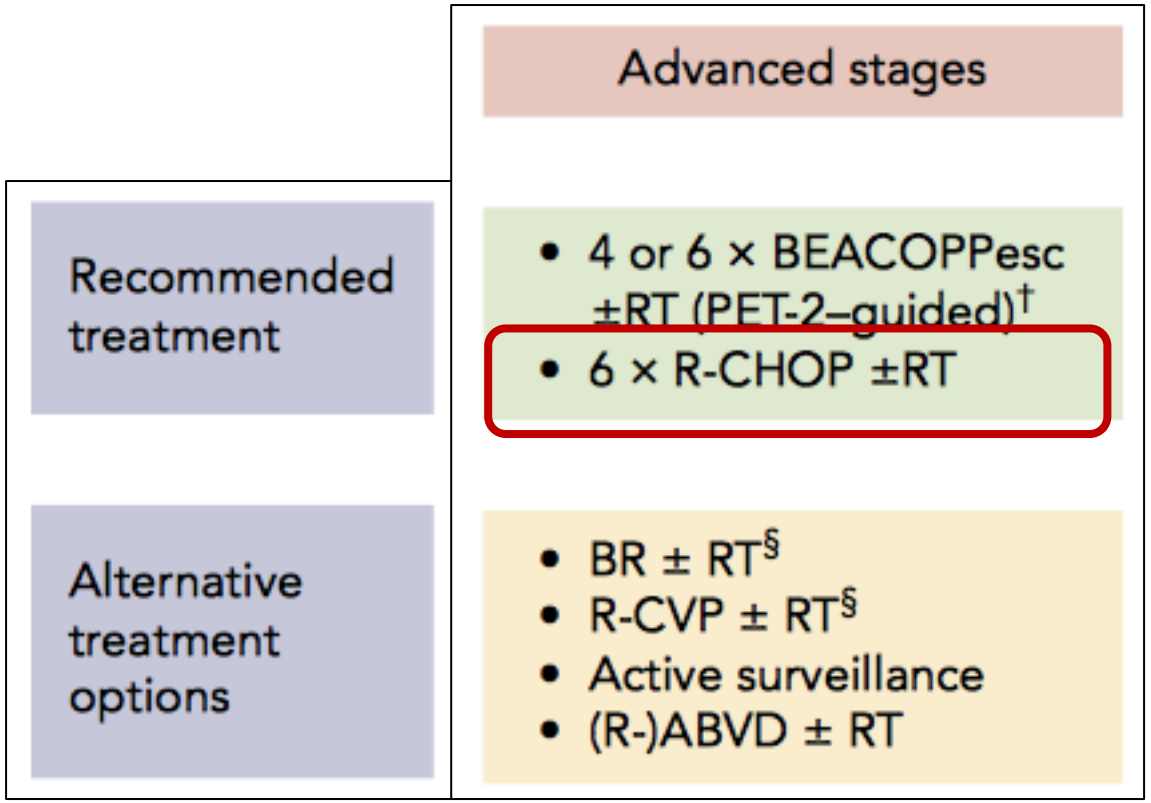
133 Hasta → esc. BEACOPP
11 Hasta → esc. BEACOPP + RT

8 yıllık PFS %76.2 **8 yıllık OS %87.4**

J Clin Oncol 2020 Mar 1;38(7):698-705. doi: 10.1200/JCO.19.00986. Epub 2019 Oct 18

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- İLERİ EVRE



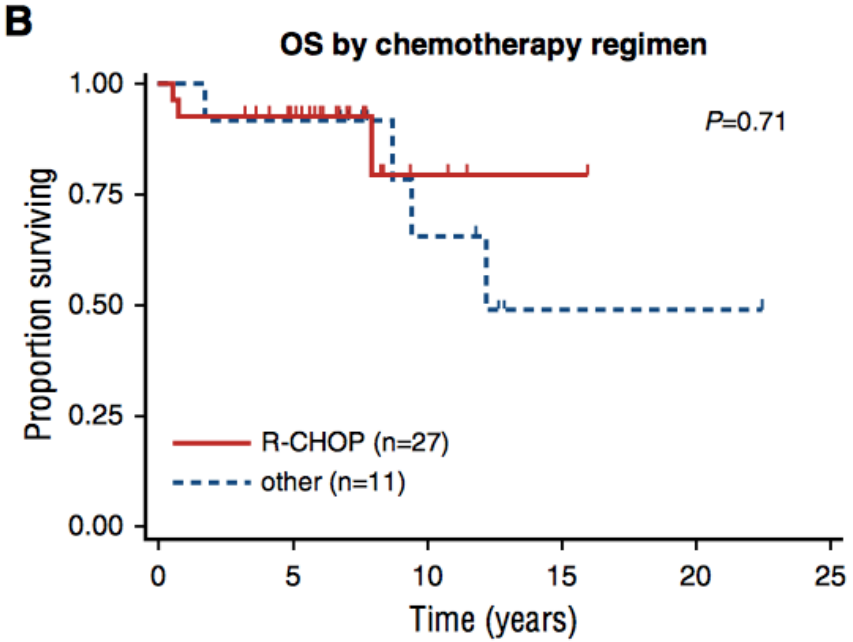
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

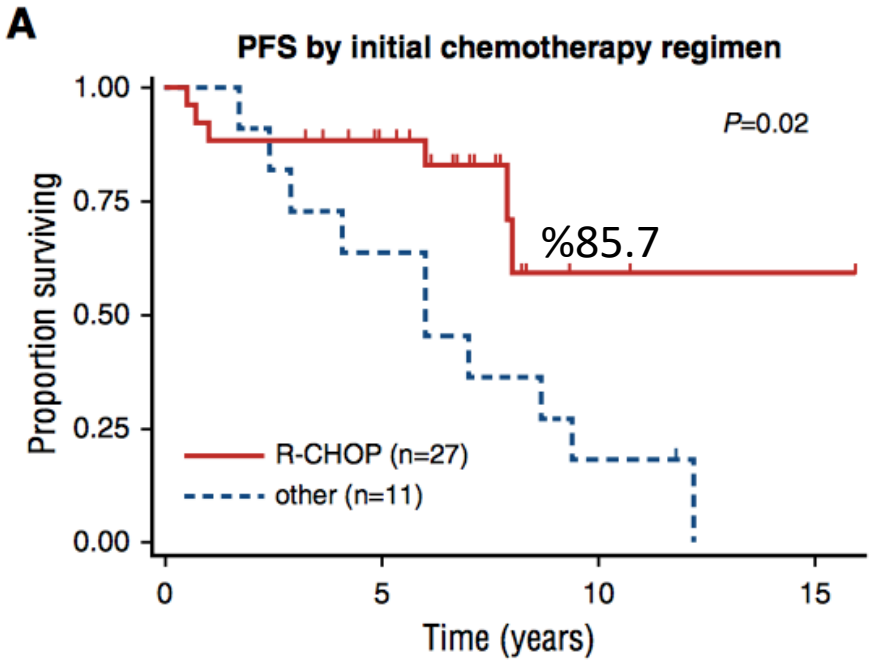
TEDAVİ- İLERİ EVRE – R-CHOP

Encouraging activity for R-CHOP in advanced stage nodular lymphocyte–predominant Hodgkin lymphoma

Michelle A. Fanale,[1,*] Chan Yoon Cheah,[1-4,*] Amy Rich,[5] L. Jeffrey Medeiros,[5] Chao-Ming Lai,[1] Yasuhiro Oki,[1] Jorge E. Romaguera,[1] Luis E. Fayad,[1] F. B. Hagemeister,[1] Felipe Samaniego,[1] Maria A. Rodriguez,[1] Sattva S. Neelapu,[1] Hun J. Lee,[1] Loretta Nastoupil,[1] Nathan H. Fowler,[1] Francesco Turturro,[1] Jason R. Westin,[1] Michael L. Wang,[1] Peter McLaughlin,[6] Chelsea C. Pinnix,[7] Sarah A. Milgrom,[7] Bouthaina Dabaja,[7] Sandra B. Horowitz,[8] and Anas Younes[9]

[1]Department of Lymphoma and Myeloma, University of Texas MD Anderson Cancer Center, Houston, TX; [2]Department of Haematology, Sir Charles Gairdner Hospital, Nedlands, WA, Australia; [3]Department of Haematology, Pathwest Laboratory Medicine, Nedlands, WA, Australia; [4]Medical School, University of Western Australia, Crawley, WA, Australia; [5]Department of Hematopathology, [6]Physicians Network, [7]Department of Radiation Oncology, and [8]Department of Pharmacy Clinical Programs, University of Texas MD Anderson Cancer Center, Houston, TX; and [9]Lymphoma Department, Memorial Sloan Kettering Cancer Center, New York, NY





14 NLPHL hastası
Median 6.6 yıl izlem

↓

Tedavi ilişkili mortalite yok
Agresif lenfomaya dönüşüm yok

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- İLERİ EVRE

even in patients with advanced NLPHL, a relevant proportion of this patient group likely was overtreated with the current GHSG standard of care for advanced cHL consisting of 6 cycles of escalated BEACOPP.

Despite limited available data, R-CHOP appears to represent the treatment approach with the most favorable risk-benefit ratio for patients with advanced NLPHL. Only selected patients presenting with poor-risk features, such as large lymphoma masses, extranodal disease, or bone marrow involvement, may benefit from more aggressive BEACOPP-based treatment.

J Clin Oncol 2020 Mar 1;38(7):698-705. doi: 10.1200/JCO.19.00986. Epub 2019 Oct 18

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- RELAPS HASTALIK

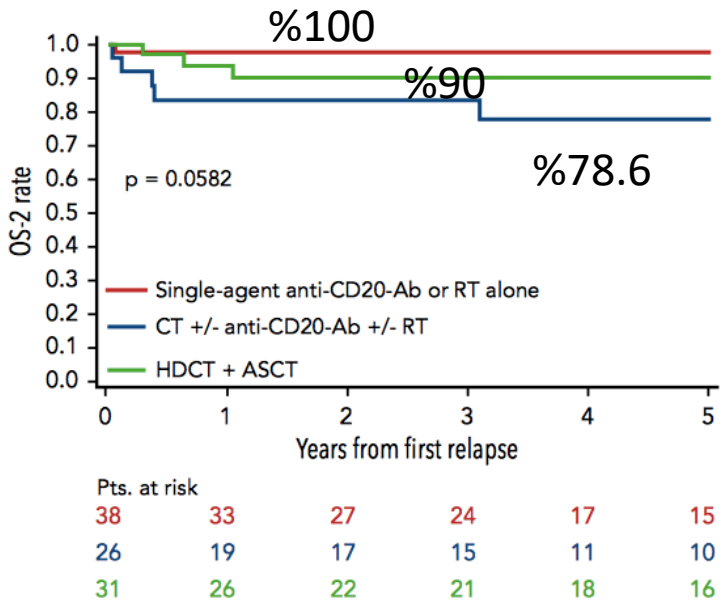
	Early relapse	Late relapse
Recommended treatment	• High-dose chemotherapy and ASCT • Stage-adapted conventional therapy*	• Rituximab alone • RT alone • Conventional chemotherapy ± rituximab ± RT • Active surveillance
Alternative treatment options	• Rituximab alone • RT alone • Conventional chemotherapy ± rituximab ± RT	• High-dose chemotherapy and ASCT†

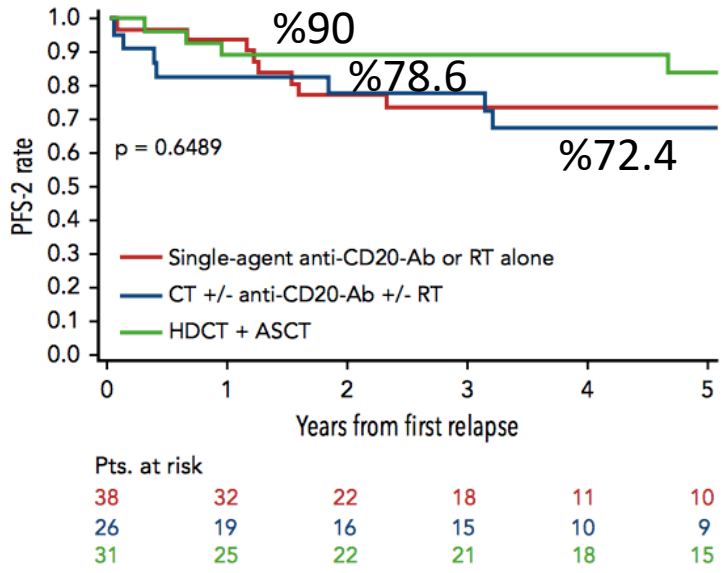
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

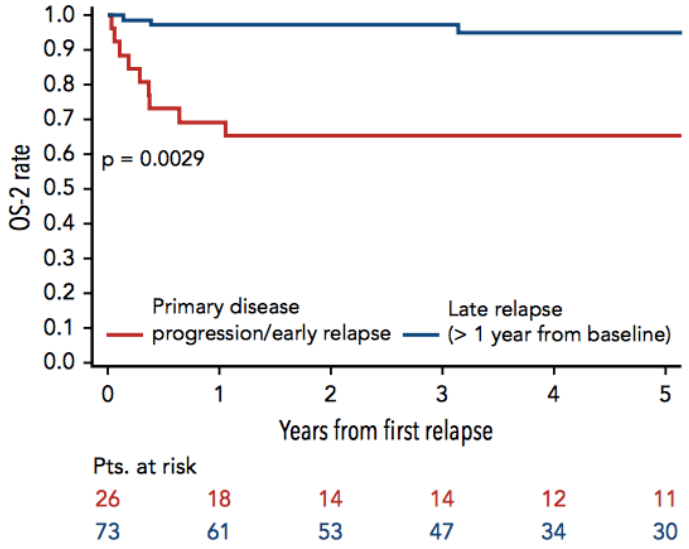
TEDAVİ- RELAPS HASTALIK- Kemoterapi/OKIT

Relapsed and refractory nodular lymphocyte-predominant Hodgkin lymphoma: an analysis from the German Hodgkin Study Group

Dennis A. Eichenauer,[1,2] Annette Plütschow,[1,2] Lena Schröder,[2] Michael Fuchs,[1,2] Boris Böll,[1,2] Bastian von Tresckow,[1,2] Volker Diehl,[2] Peter Borchmann,[1,2] and Andreas Engert[1,2]







Blood 2018 Oct 4;132(14):1519-1525 doi: 10.1182/blood-2018-02-836437. Epub 2018 Jul 31.

NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- RELAPS HASTALIK

	Early relapse	Late relapse
Recommended treatment	• High-dose chemotherapy and ASCT • Stage-adapted conventional therapy*	• Rituximab alone • RT alone • Conventional chemotherapy ± rituximab ± RT • Active surveillance
Alternative treatment options	• Rituximab alone • RT alone • Conventional chemotherapy ± rituximab ± RT	• High-dose chemotherapy and ASCT†

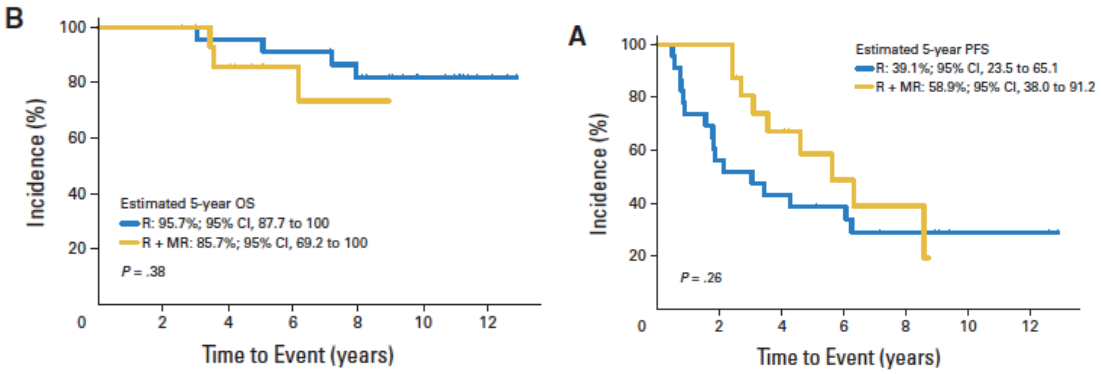
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ- RELAPS HASTALIK- Anti CD 20

Journal of Clinical Oncology®

Mature Results of a Phase II Study of Rituximab Therapy for Nodular Lymphocyte–Predominant Hodgkin Lymphoma

Ranjana H. Advani, Sandra J. Horning, Richard T. Hoppe, Sarah Daadi, John Allen, Yasodha Natkunam, and Nancy L. Bartlett

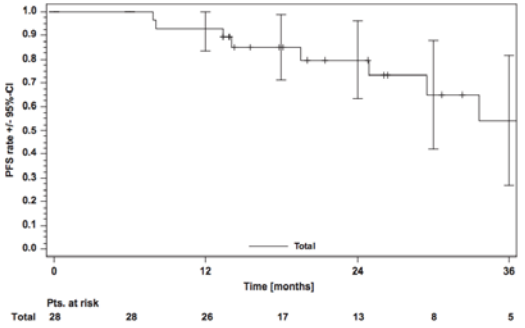


Overall Response Rate→ %94
Median izlem süresi→ 63 ay
Median time to progresyon→ 33 ay
5 yıllık PFS / OS rituximab monoterapisi→ %36.4 / %90
5 yıllık PFS / OS rituximab + idame→ %71.4 / %71.4

Leukemia

Ofatumumab in relapsed nodular lymphocyte-predominant Hodgkin lymphoma: results of a phase II study from the German Hodgkin study group

D A Eichenauer [1 2], H Goergen [1 2], A Plütschow [1 2], D Wongso [2], K Behringer [1 2], S Kreissl [1 2], I Thielen [2], T Halbsguth [2], P J Bröckelmann [1 2], M Fuchs [1 2], B Böll [1 2], B von Tresckow [1 2], P Borchmann [1 2], A Engert [1 2]



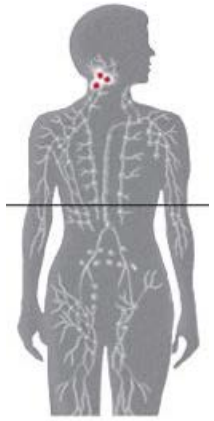
Overall Response Rate→ %96
Median izlem süresi→ 26 ay

1 yıllık PFS→ %93
2 yıllık PFS→ %80

J Clin Oncol 2014 Mar 20;32(9):912-8. doi: 10.1200/JCO.2013.53.2069.Epub 2014 Feb 10.
Leukemia 2016 Jun;30(6):1425-7. doi: 10.1038/leu.2015.321.Epub 2015 Nov 20.

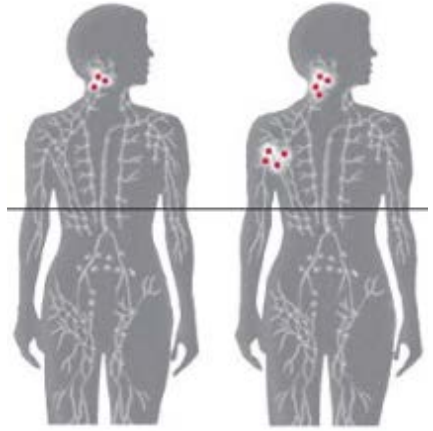
NODULER LENFOSİT PREDOMİNANT HODGKIN LENFOMA

TEDAVİ ÖZETİ



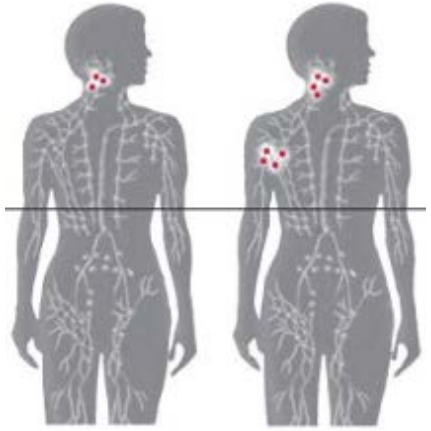
STAGE 1A

30 Gy IS-RT



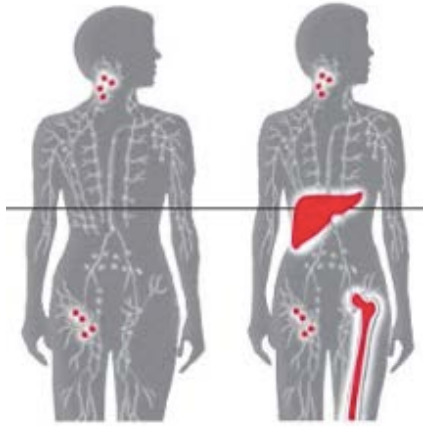
ERKEN EVRE

2 X (R) ABVD
+ 20 Gy IS-RT



ORTA EVRE

4 X (R) ABVD
+ 30 Gy IS-RT



İLERİ EVRE

6 X R-CHOP
+/- 30 Gy RT

TEŞEKKÜRLER

elifcan.aladag@gmail.com

Hematolojik Onkoloji Derneği

www.hod.org.tr