

Case Nordic Lymphoma Group

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University Hospital Comprehensive Cancer Center
University of Helsinki, Research Program Unit
Nordic Lymphoma Group, LBCL working group

6th Conference on Clinical Trials in the Nordic Countries
25-26.10.2017 Helsinki

23.10.2017

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Aim of the Nordic Lymphoma group



- Promote research in treatment, biology and epidemiology of malignant lymphomas in the Nordic countries
- www.nordic-lymphoma.org

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Activities



- Own investigator initiated clinical trials
- Collaborative efforts with EORTC, European MCL network, GHLSG, HOVON, IESLG, SAKK
- Correlative studies -> PhDs
- Annual Plenary Meeting

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Nordic Lymphoma Group

www.nordic-lymphoma.org



- Coordinating Group

Peter de Nully Brown, *chairman, Denmark*

Sirkku Jyrkkiö, *vice chairman, Finland*

Elisa Pulczynski, *Denmark*

Mats Jerkeman, *Sweden*

Björn Wahlin, *Sweden*

Björn Östenstad, *Norway*

Arne Kolstad, *Norway*

Outi Kuittinen, *Finland*

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Nordic Lymphoma Group: Research Organization – Working groups



Para-clinical

- Epidemiology/staging
- Pathology

Clinical

- Large B-cell
- Peripheral T-cell
- Mantle cell
- CNS
- Low grade (indolent)
- Hodgkin's
- PTLD

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32 Study Centers



DK:	NO:	SE:
Copenhagen	Oslo	Stockholm ^{x2}
Herlev	Bergen	Halmstad
Aalborg	Trondheim	Lund
Odense	Stavanger	Linköping
Århus	Tromsø	Malmö
	Kristiansand	Sundsvall
FIN:		Uppsala
Helsinki		Umeå
Tampere		Göteborg
Turku		Luleå
Kuopio		Örebro
Oulu		Jönköping
Jyväskylä		Kalmar
Mikkeli		



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Epidemiology

Karin Ekstrøm Smedby (chair) and Mats Jerkeman, Sweden,
Martin Maisenholder and Knut Halvor Bjørø Smeland, Norway
Henrik Frederiksen and Tarec El-Galaly, Denmark

Pia Suonpää, Finland

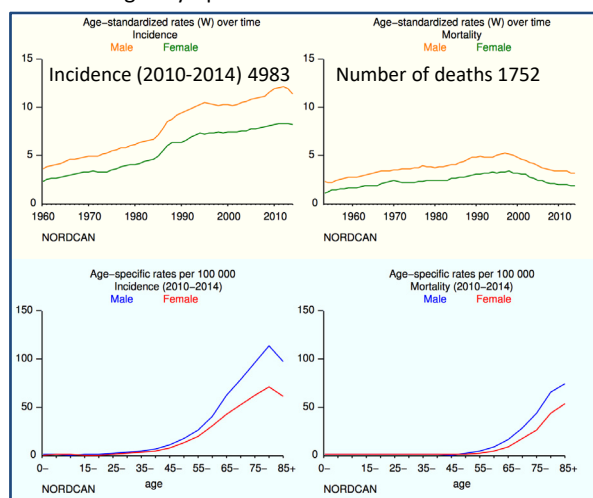
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Incidence and mortality of lymphomas in Nordic area



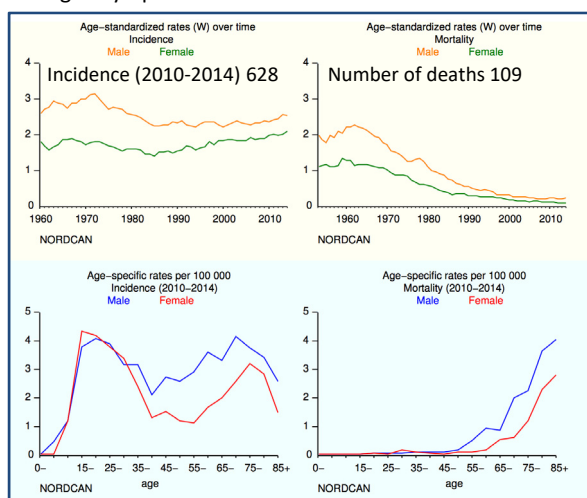
Non-Hodgkin lymphomas*



* Mature B, T, NK neoplasms and PTLDs >70 entities

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Hodgkin lymphomas**



** Five entities

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Lymphoma registries



Nation-wide population-based registration in Denmark and Sweden since 2000

- Collect data on diagnostics, histopathology, prognostic factors, therapy and outcome
- More than 95 % of lymphoma patients are included

www.swedishlymphoma.se/lymfomregistret
www.lymphoma.dk

blood 2014 124: 1288-1295
doi:10.1182/blood-2014-03-559690 originally published online May 21, 2014

Real world data on primary treatment for mantle cell lymphoma: a Nordic Lymphoma Group observational study
Anna Abrahamsson, Alexandra Albertsson-Lindblad, Peter N. Brown, Stefanie Baumgartner-Wormuth, Lars M. Pedersen, Francesco D'Amore, Herman Nilsson-Ehle, Paw Jørgensen, Michael Pedersen, Christian H. Gessler and Mats Jerkeman

R-CHOEP-14 improves overall survival in young high-risk patients with diffuse large B-cell lymphoma compared with R-CHOP-14. A population-based investigation from the Danish Lymphoma Group
A. O. Gang¹, C. Strøm², M. Pedersen³, F. d'Amore⁴, L. M. Pedersen⁵, A. Blak⁶, B. B. Pedersen⁷, M. B. Mosler⁸, L. S. Mortensen⁹, O. V. Gadsberg¹⁰, S. Ingeberg¹¹, T. Mourids-Andersen¹², S. Pulczynski¹³ & P. d. Nully Brown¹⁴

Impact of chemotherapy regimen and rituximab in adult Burkitt lymphoma: a retrospective population-based study from the Nordic Lymphoma Group
T. Wälstedt¹, P.N. Brown², O. Hagberg³, H. Hagberg⁴, L.M. Pedersen⁵, F. D'Amore⁶ & M. Jerkeman⁷

Leukemia (25 August 2014) | doi:10.1038/leu.2014.251

Follicular lymphoma in Sweden: nationwide improved survival in the rituximab era, particularly in elderly women: a Swedish Lymphoma Registry Study
H R Junlén, S Peterson, E Kimby, S Lockmer, O Lindén, H Nilsson-Ehle, M Erlanson, H Hagberg, A Rådlund, O Hagberg and B E Wahlén

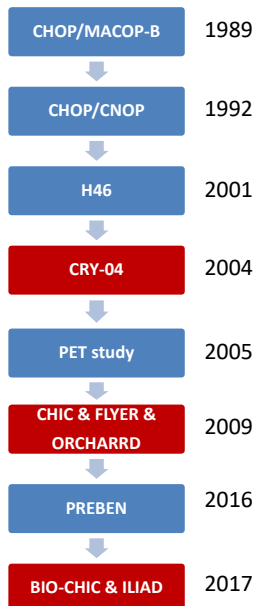


Large B-cell Lymphoma Group

Sirpa Leppä (chair) & Sirkku Jyrkkiö, Finland
Harald Holte & Øystein Fluge, Norway
Kristina Drott & Per-Ola Andersson, Sweden
Judith Jørgensen & Peter Brown, Denmark



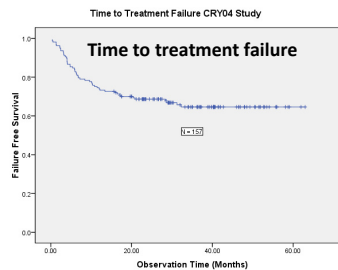
DLBCL trial activities



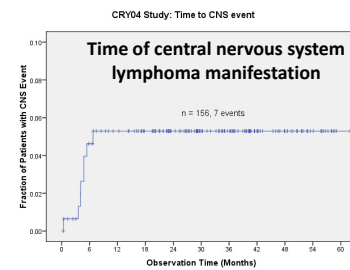
How to improve the outcome of high risk DLBCL patients and prevent CNS progression?

- Dose dense immunochemotherapy followed by systemic CNS prophylaxis

CRY-04 trial (Chemotherapy-Rituximab-Young)



Median F-up 5.4 years (2-6.3)
5-year OS rate 77%
5-year PFS rate 63%
CNS progression rate 4.6%

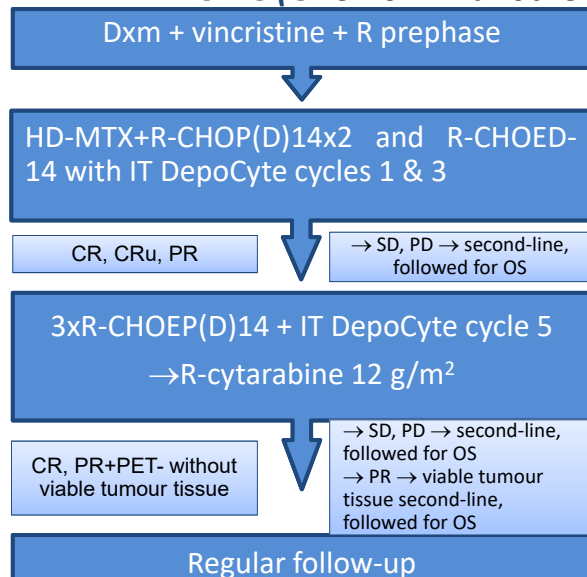


Holte et al., Ann Oncol 2013, update 10/2014

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CHIC (CHemoImmunotherapy with early CNS prophylaxis)

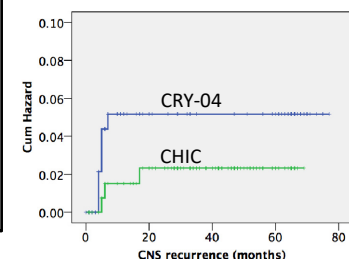
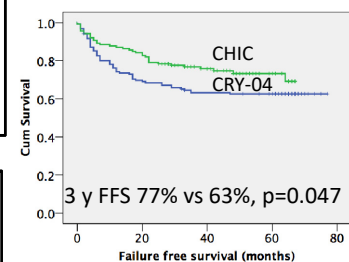


Co-Primary endpoints

FFS at 3 years
CNS relapse rate at 1.5 years

Secondary endpoints

Toxicity
Clinical response rate
Incidence of CNS relapse in CSF cytology neg/FCM posit cases
PFS (3 years)
OS (3 years)
Molecular predictors

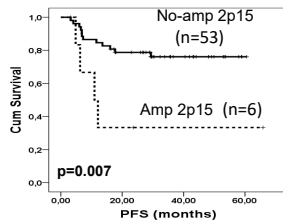


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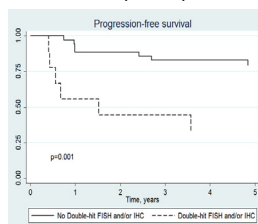
Biological risk factors in DLBCL

Prognostic significance of copy number alterations and gene expression



• *B3GNT1*, *FAM161A*, *CCT4*, *COMMD1*, and *XPO1*

Taskinen et al., 2014
Leivonen et al., 2017

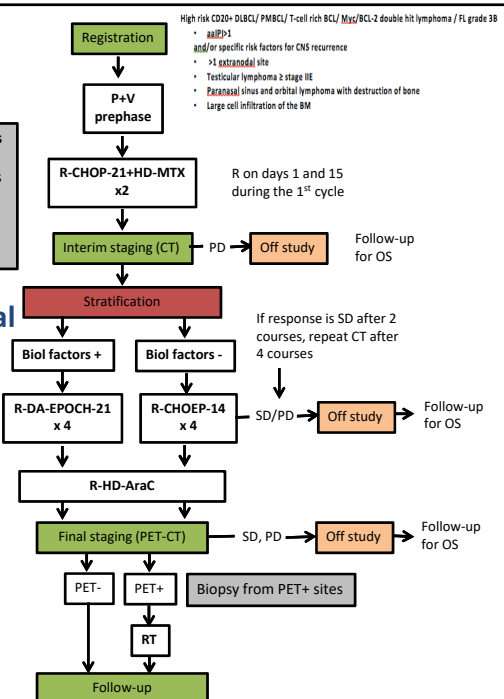


Prognostic significance of BCL2/Myc double hits

Fiskvik et al., 2014

Biological risk factors
Single MYC
Double MYC/bcl2 hits
P53 del (FISH)
P53 + (IHC)
MYC+and bcl2+ (IHC)
CD5 +

Bio-CHIC trial (ongoing)



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T-cell lymphoma group

Francesco d'Amore (chair), Peter Nørgaard & Helle Erbs Toldbod, Denmark

Thomas Relander & Fredrik Ellin, Sweden

Grete Lauritzsen & Peter Meyer, Norway

Esa Jantunen, Susanna Mannisto & Martine Vornanen, Finland

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Nordic NLG-T-01 study: 2001-2007



CHOEP-14 x 6



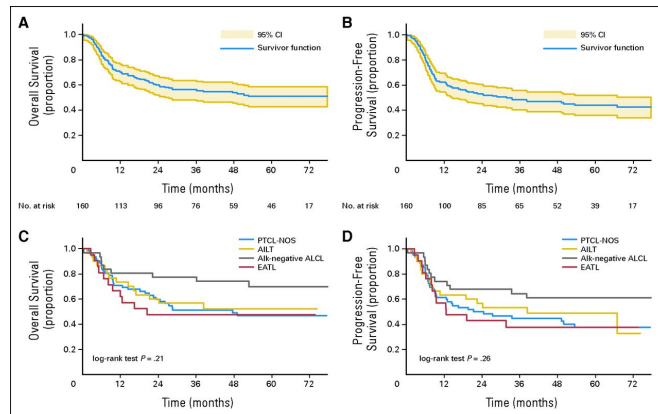
ASCT



Follow-up

Excluded:

- 1) ALK-1 pos ALCL
- 2) CTCL
- 3) Leukemic T-NHL



N=160, median age 57 y (18-67), 115 underwent HDT/ASCT with 90 in CR 3 months post ASCT, TRM rate 4%

d'Amore F et al. JCO 2012;30:3093-3099

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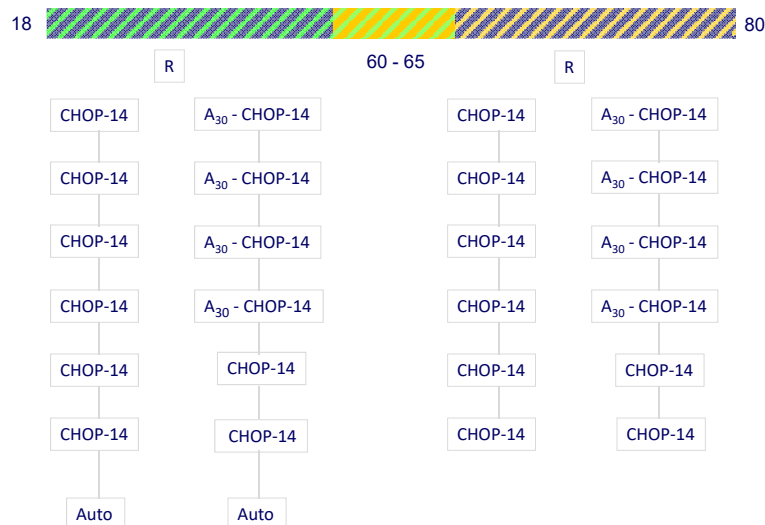
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The ACT trials for PTCL:2008-2013

AFTER the dose/age amendments



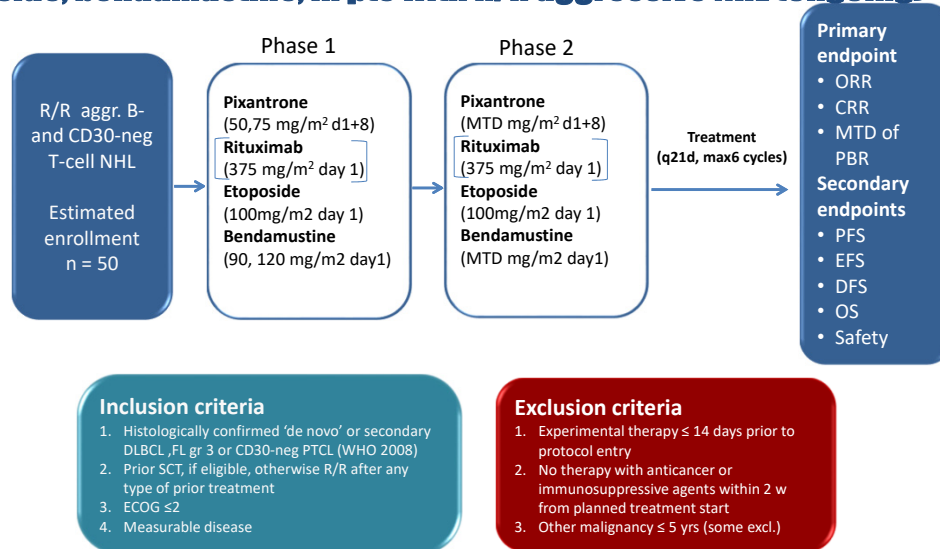
GERMAN HIGH-GRADE NON-HODGKIN'S LYMPHOMA STUDY GROUP



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PREBen -Phase I/II trial of pixantrone, rituximab only in CD20+ tumors, etoposide, bendamustine, in pts with R/R aggressive NHL (ongoing)



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Mantle cell lymphoma group

Christian Geisler, Denmark; Riikka Rätty, Finland; Anna Laurell & Mats Jerkeman, Sweden; Arne Kolstad & Karin Wader, Norway

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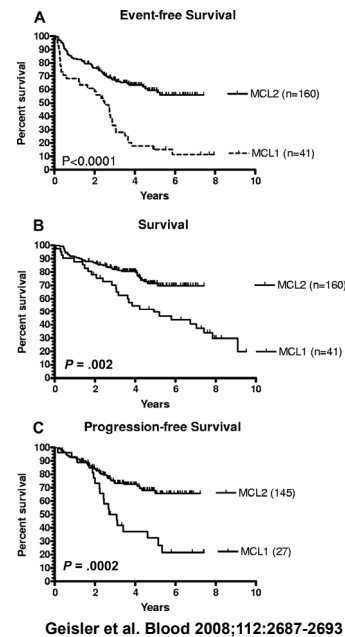
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Nordic MCL1-2 Studies

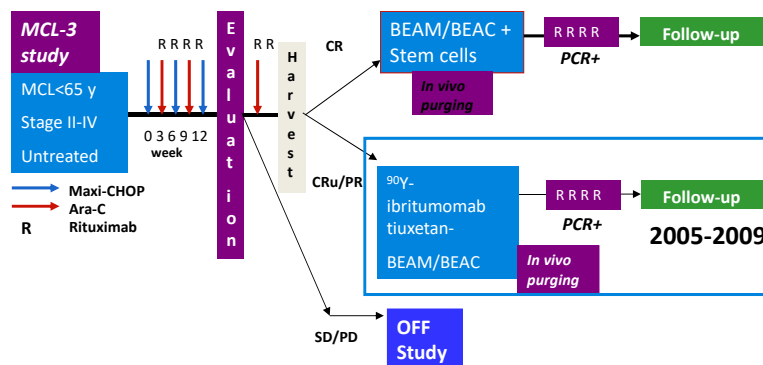
Regimens	MCL1: 1996-2000	MCL2: 2000-2006
Induction	Maxi-CHOP21 × 3	Maxi-CHOP21 × 3 alternating with HD-Ara-C × 2, Rituximab from cycle 4
Stem cell mobilization	Maxi-CHOP	HD-cytarabine
Stem cell purging	In vitro: CD34+ cell selection when possible	In vivo: rituximab × 2 (days 1 and 9 of the HD-cytarabine)
Consolidation	Allowed (1-2 series)	Allowed (1-2 series)
High-dose therapy	BEAM/BEAC	BEAM/BEAC
Preemptive treatment at molecular relapse	No	Rituximab 375 mg/m ² weekly × 4

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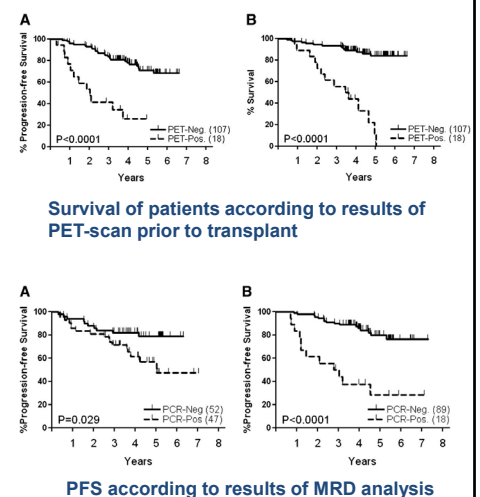


Nordic MCL3 study 2005-2009



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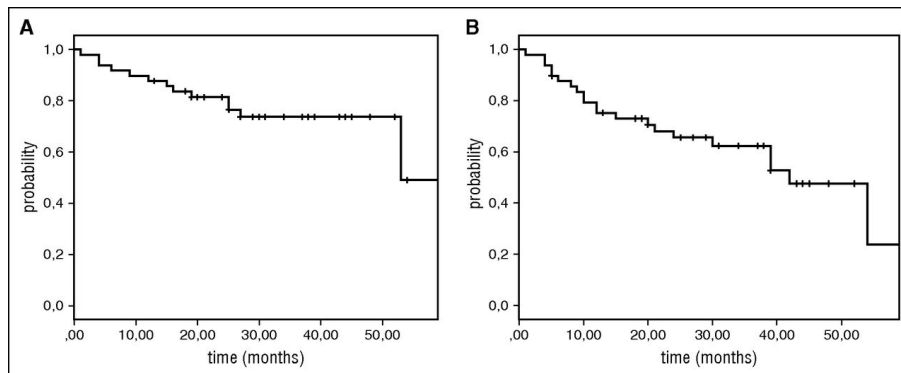
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Kolstad et al., Blood 2014

Nordic MCL4 Study

*LENAlidomide-BEndamustine-Rltuximab
in patients older than 65 years with
untreated mantle cell lymphoma*



Alexandra Albertsson-Lindblad et al. *Blood* 2016;128:1814-1820

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Hodgkin lymphoma group

Alexander Fosså & Unn-Merete Fagerli, Norway, Daniel Molin, Sweden; Lena Specht & Peter Kamper, Denmark; Kaija Vasala, Finland



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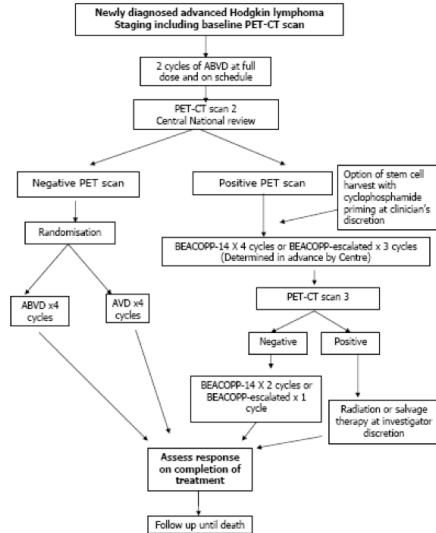
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RATHL study

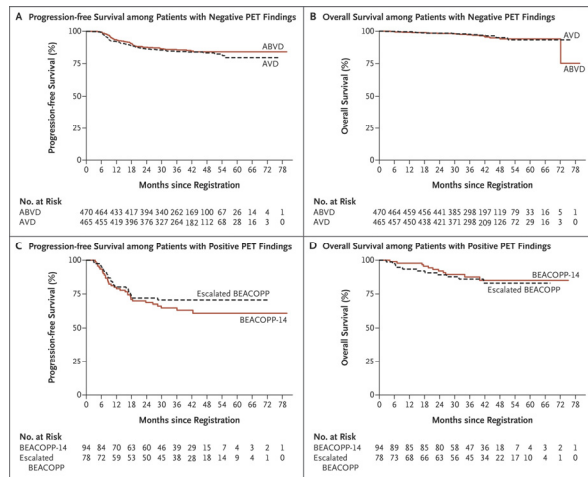
A randomized phase III trial to assess Response Adapted Therapy using FDG-PET imaging in patients with newly diagnosed, advanced HL



1.4 Trial Outline



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Johnson P et al. N Engl J Med 2016;374:2419-2429

B-CAP study (ongoing)

Hodgkin Lymphoma
Age ≥ 60 years

Patients eligible for poly-chemotherapy?*

YES
advanced stage

2 x
B-CAP

NO
any stage

2 x
Brentuximab

INTERIM-STAGING*
CR, PR, NC → continue study treatment
PD → contact trial center for rescue treatment

4 x
B-CAP

4 x
Brentuximab

RESTAGING*

PR, NC: 30 Gy RT on PET+ lesions
→ final staging
FOLLOW UP
CR: →

RT at investigators discretion
PD/Tox: STOP
CR/PR/SD: continue ≤ + 10 cycles

Brentuximab vedotin or B-CAP in the treatment of older patients with newly diagnosed classical Hodgkin lymphoma
GHSG-NLG Intergroup phase II trial

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*Refer to study protocol for details
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Clinical trial office (CTO)



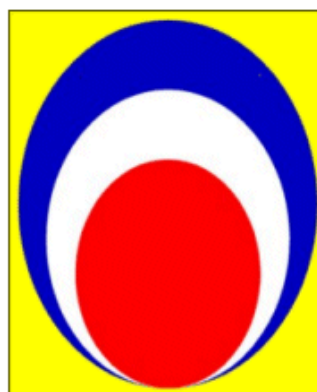
- Coordination of trial activities
- eCRF setup
- Registration of patients at inclusion
- Pharmacovigilance
- Query management
- Data management
- Monitoring (Nordic Monitoring network; NORM)

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Thank you for good collaboration

- **All NLG working groups, study centers and CTO:** Harald Holte, Mats Jerkeman, Arne Kolstad, Björn Östenstad, Francesco d'Amore, Alexander Fosså, Elisa Jacobsen, Helle Erbs Toldbod, Marja-Liisa Karjalainen-Lindsberg, Karin Ekstrøm Smedby, Peter Brown and many others...
- **For financial support:** Nordic Cancer Union, Abbvie, Amgen, Bayer, Celgene, CTI, Gilead, Janssen-Cilag, Mundipharma, Roche, Takeda



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