Nordic Lymphoma Group

Newsletter June 2020

www.nordic-lymphoma.org

Dear members of the NLG society,

All members of NLG and representatives of collaborating companies are welcome to the next NLG Plenary meeting November 5, 2020. This year, the meeting will be different. Instead of a physical meeting, we will arrange a webinar, by Zoom. The preliminary program is enclosed. However, som things will remain the same. Scientific papers and case presentations will be presented from all countries as in previous years, and invited speakers will inspire, by highlighting current topics on both clinical and translational research on lymphomas.

NLG is hereby also inviting representatives from the pharmaceutical companies, representing relevant products used for diagnosing and treatment of malignant hematological diseases, to participate in our annual plenary meeting, free of charge.

Wish you all warmly welcome to attend the meeting. Links for participation will be published on our homepage before the meeting.

Looking forward seeing you online in November, and in real life 2021!

Best,

Mats

Mats Jerkeman, chairperson of NLG
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NLG Plenary meeting

Working group meetings may be arranged on either physically or virtually in advance of the plenary meeting.

Information on links for participation for the NLG plenary meeting is found at our web-site www.Nordic-lymphoma.org

There will be 500 available links.

Abstract submission

Please send your abstract and case presentation before October 1st to your national member of the NLG coordination group.

Free papers session

Scientific papers on on-going lymphoma research form each country are appreciated and will be presented in this session.

Interesting cases session

As previous years, we have one session on interesting and difficult cases. One patient from each country can be presented and we welcome especially younger delegates to present challenging cases.

Young scientists and PhD-students are encouraged to send abstracts in these sessions to their national representatives.

NLG Plenary Meeting 2020 – *online*

5 November 2020

0900-0910	Welcome – *Mats Jerkeman*	
0910-0930	Indolent group – *Björn Östenstad*	Moderator: *Mats Jerkeman*
0930-0950	T-cell group – *Francesco D'Amore*	
0950-1010	Large cell group – *Sirpa Leppä*	
1010-1020	Pathology group - TBD	
1020-1040	Coffee break	
1040-1140	Invited speaker – *Catherine Thieblemont* – Real world data on CAR-T cell therapy	Moderator: *Sirpa Leppä*
1140-1230	Lunch break	
1230-1250	CNS group – *Marjukka Pollari*	Moderator: *Arne Kolstad*
1250-1430	Free papers Moderator: *Arne Kolstad*	Parallell CTO session (research nurses/coordinators) *Helle Toldbod, Rikke Lundqvist, Emelie Skou*
1430-1445	Coffee break	
1445-1515	Invited speaker – *Akmal Safwat* – Proton therapy in lymphoma	Moderator: *Daniel Molin*
1515-1545	Invited speaker – *Stefan James* – Randomized registry trials	
1545-1605	Epidemiology group – *Karin E Smedby*	Moderator: *Judit Jörgensen*
1605-1615	PTLD group – *Harald Holte*	
1605-1625	Hodgkin group – *Alexander Fosså*	
1625-1645	Mantle cell group – *Mats Jerkeman*	

Update on working group activities

Indolent group

The second collaborative SAKK/NLG project (35/14), is a randomized phase II study comparing Rituximab with or without Ibrutinib for untreated patients with advanced follicular lymphoma. The study has been put on hold for 3 months, but will reach the target accrual number of 190 patients in June 2020.

Correlative studies based on previous trial patient material have been published with focus on predictors of prognosis and transformation. We also collected data on Health related Quality of Life from 100 previous trial patients, and analysis is ongoing.

The study group is currently working on the development of different new clinical studies.
In follicular lymphoma (FL) a new first line study may include all patients, but treated according to a risk-based algorithm introducing innovative drugs and randomized comparison to standard therapy. Another study will focus on the poor prognostic group of rituximab refractory/early recurrent (R/R) patients. The design is not yet determined.

Marginal zone lymphoma (MZL) is another subgroup of interest. We are in close dialogue with the IELSG group, who are planning a randomized phase III study on untreated symptomatic MZL comparing rituximab combined with zanubrutinib vs rituximab alone. For patients with relapsed or refractory MZL, a phase II NLG study of Betalutin in combination with rituximab has been proposed.

Large cell group

Clinical studies –Previous NLG-LBC-05 (CHIC) trial demonstrated favourable impact of dose dense chemoimmunotherapy with early systemic CNS prophylaxis on FFS and lower number of CNS recurrences rates in high risk DLBCL patients less than 65 years. Based on the previous trial experiences, the ongoing phase II trial, NLG-LBC-06 (BIO-CHIC), is testing whether stratification of the patients according to biological risk factors for different treatment groups, can further improve the outcome of the patients with clinically rich risk DLBCL. By the end of May 2020, 99 of the planned 120 patients have been recruited.

Phase II trial, NLG-LBC-07 (ILIAD), testing the safety and efficacy of oral PI3K inhibitor idelalisib as a monotherapy in the frail patients with relapsed or refractory DLBCL enrolled 36 patients and was closed for recruitment in March 2020.

In q2 2020, a novel randomized phase III POLAR BEAR trial for the elderly patients with DLBCL (>80 years, or frail >75 years) will start enrolment. This trial will compare standard treatment, R-mini-CHOP to a regimen where vincristine has been substituted by the anti-CD79b immunoconjugate polatuzumab vedotin. The trial is planned to include 200 patients from the Nordic area, and from Italy.

When Bio-CHIC trial has been concluded, we plan to launch a risk factor and PET-response adapted phase III trial, where we will determine if interim FDG-PET scan can be used to guide therapy, The patients will be stratified according to clinical and biological risk factors for different treatment groups, and based on early metabolic response evaluation by FDG-PET, either de-escalate the treatment or change to experimental therapy.

Correlative studies on the basis of trial material - Several trial-related molecular projects are ongoing. To date, the studies have demonstrated for example survival association of tumour infiltrating immune cells, and MYC, BCL2, and TP53 alterations.

CNS-lymphoma group

The working group has been involved in establishing a European network with different teams interested in PCNSL across Europe. Through this network, a possible European H2020 collaboration is planned and will be conducted if the study is granted with financial support. The aim is to create a retrospective and a prospective cohort for every center and gather the data to create a multi-modal analysis in order to better stratify the prognosis and identify potential new therapeutic targets in PCNSL.

IELSG43 (MATRix) was a phase III study designed to compare two consolidation policies in younger PCNSL patients with randomization between high-dose chemotherapy followed by ASCT and conventional dose chemotherapy after the induction therapy (MATRix). The study was closed for inclusion in Aug 2019 with 342 patients enrolled, including patients from Denmark and Norway, and the data analysis will be performed during 2020.

A randomized phase II IELSG45 study (FIORELLA) is evaluating the efficacy of fitness- and comorbidity -tailored treatment in elderly PCNSL patients and is ongoing in Italy, Switzerland, Denmark, and Finland. Sweden is also planning to join the study.

Updated results of the former Nordic PCNSL study, after a median follow up of 76 months, as well as retrospective analysis of the application of temozolomide maintenance treatment in PCNSL are under preparation for publication.

A Nordic phase ll study in refractory/relapsed PCNSL is being planned and financial support has been applied for. The study will be activated as soon as financial funding is provided, but so far, financial support as not been confirmed. Once the study begins, translational studies will be performed before and during treatment as well as during the follow-up.

MCL group

Younger patients (<65 years): The Nordic MCL group has joined the European MCL Net TRIANGLE phase III three-arm trial, testing intensive therapy + ibrutinib in younger untreated patients. The trial started in the Nordic area in q4 2016, and is open for centres in Sweden, Denmark, Finland and Norway. At this point, 720 of the planned 870 patients have been randomized (83%), and enrollment is likely to end by Q1 2021. 90 patients have been enrolled by NLG.

Elderly patients: Since December 2017, NLG has joined the ENRICH trial, with Simon Rule, Plymouth, as sponsor. This is a randomized phase III trial, comparing rituximab+ibrutinib with rituximab-chemo (either R-bendamustine or R-CHOP). As in TRIANGLE, more than 80% (325) of the 400 patients have been enrolled, of which 95 are from NLG centres.

A new NLG trial, NLG-MCL7 (Valeria), exploring the combination of venetoclax, lenalidomide and rituximab, started in June 2019. This is a phase I-II trial, for patients with relapsed MCL, and a population of untreated MCL, ineligible for combination chemotherapy. This trial will also explore a novel treatment strategy for MCL, an MRD-driven approach, where treatment will be stopped following molecular remission. The phase 1 part of the study has been concluded, and the recommended phase 2 dose of venetoclax has been established as 600 mg, in combination with 15 mg of lenalidomide. In total, 20 patients have been enrolled to date, and an abstract is planned to be submitted to ASH, where we are able to show the feasibility of stopping treatment in MRD-negative patients.

When ENRICH has been concluded, we will launch a new trial for elderly patients first line, with the novel combination of another BTK-inhibitor, acalabrutinib, and rituximab. This is a phase II trial with a maximum treatment duration of 1 year, except for patients with biological high risk features. This trial, NLG-MCL8, Altamira, will start recruitment in Q1 2021.

Several translational studies based on the MCL2/3 biobank are ongoing, including mutational profiling and gene expression profiling.

T cell group

ACT trial:

The final analysis of the ACT-2 trial (elderly patients; >60 yrs) has just been published in Leukemia (april 2020) and can be found on PubMed (Wulf G et al). The final analysis paper of the ACT-1 trial is in preparation and still waits for the final details regarding the gene expression data characterizing the "predictor of alemtuzumab response (PAR)", which will be included in the paper. The ACT-1 final analysis data were presented, with a preliminary version of PAR, as an oral paper at ASH in December 2018.

Additional translational studies based on the ACT-1 trial biospecimens are ongoing.

NLG-T-01 trial:

A manuscript with late follow-up (median 10 years) data from the NLG-T-01 study, including those patients, whose tissue samples have been analyzed for DUSP-22 and TP63 rearrangements, has been drafted and will be circulated among working group members shortly. The data set will be presented for the single PTCL subtypes, including ALK-negative ALCL (ALK-positive ALCL patients were excluded from the study due to an expected better prognosis, which did not justify upfront ASCT). Long-term outcome data from NLG-T-01 will be useful for the coming national and European (ESMO) guidelines since they will allow us to compare outcomes with what reported for ALK-negative ALCL in the ECHELON-2 trial.

Additional translational studies based on the NLG-T-01 trial biospecimens are ongoing. .

P[R]EBEN trial

The phase 1b/2a P[R]EBEN protocol in relapsed aggressive B- and T-cell lymphomas is approaching its completion. The target accrual is 60 patients and the present recruitment status is: 57 patients.

It seems therefore realistic to successfully reach end of accrual within the current calendar year. The manuscript with the final analysis of the study will combine the results of the phase 1b part of the trial with the results of the phase 2 part. Patients have been accrued in various centers from the 4 Nordic countries and from HOVON centers in the Netherlands. Results from correlative biological data regarding per protocol gene expression profile analyses performed at Helsinki University Hospital were presented at the 4th Nordic Meeting on Tumor Microenvironment in Lymphoma and at ASH 2019. This data will also be included in the final analysis paper.
Additional translational studies based on the P[R]EBEN trial biospecimens are ongoing.

PANTHEON trial:
The latest trial proposal from the NLGs Working Group on T-cell lymphomas, the PANTHEON trial (**PAN T**-**H**istological **E**ntities trial **O**f the **N**ordic lymphoma group), has evolved in design and infrastructural planning within the last year. Two applications for academic funding of the trial are currently submitted. Further funding will be negotiated with potential partners from the pharmaceutical industry. The new PANTHEON trial will address three main questions: (i) does a pre-induction antiviral pre-phase (steroid+rituximab) improve performance score and disease status prior to induction start along with schedule adherence during induction, in patients who are EBV viremic at diagnosis?; (ii) does measurement of minimal residual disease by means of liquid biopsies (ctDNA) improve response assessment compared to the current standard-of-care (PET/CT)?; (iii) does a biofeature-driven post-induction consolidation (6 months) reduce the occurrence of post-induction relapses as compared to current standard-of care (observation only)? The PANTHEON trial is designed to include all PTCL subtypes ('PAN T-Histological entities') in the context of a full spectrum of clinical fitness categories, i.e. 'fit', 'frail' and 'very frail'. The induction treatment in the trial aims at being as flexible as possible in order to optimize inclusion of most of the PTCL patients throughout the Nordic countries. Possible collaborations with other countries in Europe and Asia are under discussion.
There will be one group meeting in September/October 2020 (date not yet specified) in order to discuss the new trial proposal prior to the next plenary meeting.

Hodgkin group

The BVB trial on the use of Brentuximab vedotin as first line treatment in elderly patients with HL started in 2015 as a joint German and Nordic study. The study is completed and abstracts covering early results were presented in Cologne in in the fall of 2018 and at ASH in 2018. The publication is planned for late 2020. Discussions have started for a new trial in the elderly population, resulting in a plan to explore the BrECADD regimen from the HD21 study in an elderly population.

The Nordic countries are collectively joining the German Hodgkin Study Group in the HD21 trial for newly diagnosed advanced stage Hodgkin lymphoma comparing escalated BEACOPP to a Brentuximab vedotin based variant called BrECADD. The study in currently estimated to continue recruitment through 2020.

A subanalysis of the 50-60 year old patients receiving BrECADD in HD21 showed a favorable toxicity profile. To evaluate BrECADD for elderly patients 61-75 years, the trial has been amended and allows for elderly patients to be enrolled in the BrECADD arm without randomization. This part of the study opens in 2020 and will go one for one year.

The “Nordic trial” on stage I-IIA Hodgkin lymphoma was initiated as a treatment recommendation in 1997. The patients treated in the first decade after initiation of the recommendation have been evaluated for relative survival and mortality rates. The final publication has published in 2020.

PTLD group

The group was formally initiated during the NLG meeting in Stockholm 2014. Initial work has mainly been focused on joining the German PTLD-2 trial. Due to issues with funding this will not be possible, and the group will examine the possibility of a Nordic PTLD trial in the relapsed setting.

Epidemiology group

The group is working with several projects using data from the national lymphoma registers in Denmark, Sweden and Norway as well as clinical data being assembled in Finland. Apart from regular phone calls, the group also has one separate meeting per year. This year, the meeting will be hold on zoom the 2nd of September.

If you have a lymphoma epi project idea or wishes to get epidemiological input, get on touch with the group chair Karin E Smedby (Karin.ekstrom.smedby@ki.se).

Ongoing or recently completed projects include:
1) Evaluation of long-term survival in Hodgkin lymphoma (published 2019).
2) Life after lymphoma – survivorship aspects including childbearing, second malignancies and infections
3) Treatment and survival among very elderly lymphoma patients