Nordic Lymphoma Group

Newsletter June 2022

Dear members of the NLG society,

All members of NLG and representatives of collaborating companies are welcome to the next NLG Plenary meeting November 9-10, 2022, at the Scandic Strandpark Hotel, close to Copenhagen Airport, same as last year. The preliminary program is enclosed. Recent lymphoma research 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.

Wish you all warmly welcome to attend the meeting. Link for participation is found on our homepage, www.Nordic-lymphoma.org and here: https://na.eventscloud.com/nlg2022

Looking forward to seeing you in November!

All the best,

Mats

Mats Jerkeman, Chairman of NLG
Skane University Hospital, Lund, Sweden
e-mail: mats.jerkeman@med.lu.se phone: +46 46 177520

NLG Plenary meeting – working groups

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

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 from each country are appreciated and will be presented in this session.

Young scientists and PhD-students are encouraged to submit abstracts to their national representatives.

NLG Plenary Meeting 2022

9-10 November 2022

09.11.2022		
1000-1200	CTO session (research nurses/coordinators)	
1200-1300	Registration and lunch	
1300-1330	Indolent group	Moderator: Judit Jørgensen
1330-1400	T-cell group	
1400-1430	Large cell group	
1430-1500	Coffee break	
1500-1600	Invited speaker **Daniel Hodson** Molecular profiling in diffuse large B-cell lymphoma – does it matter?	Moderator: Peter Brown
1600-1800	Free papers	Moderator: Daniel Molin
1800-1830	Business meeting	

10.11.2022		
0900-1000	Invited speaker **Martin Hutchings** Bispecific antibodies – where do they fit into the treatment algorithms?	Moderator: Alexander Fosså
1000-1030	Coffee	
1030-1100	Pathology Group	
1100-1130	CNS group	
1130-1200	Epidemiology group	
1200-1300	Lunch	
1300-1330	Hodgkin group	Moderator: Susanna Mannisto
1330-1400	Mantle cell group	
1330-1500	Controversies in indolent lymphomas	

Update on working group activities

Indolent group

The SAKK-NLG 35/14 phase II study comparing Rituximab with or without Ibrutinib for untreated patients with advanced follicular lymphoma reached the target accrual of 190 patients in 2020. Last patient last treatment happened in March 2022 and primary analysis is ongoing. The primary endpoint is CR at 24 months and hopefully we can present preliminary data in November.

The study group will open two new academic studies for follicular lymphoma (FL) in the fall.
A new 1st line study (FLAME) may enroll all new patients and the treatment is determined according to a risk-based algorithm. The investigational drug is zandelisib, a new PI3K inhibitor, will be tested in different combinations.

MERLIN is a 2nd line study for FL patients with early progression (POD24) or primary refractory (R/R) disease. This is a selected group of patients with a poor prognosis. All included patients will be treated with mosunetuzumab, a new bispecific antibody, in a non-randomized fashion.

We have been approached by the IELSG (international extranodal lymphoma study group) and invited to participate in a randomized phase III trial for 1st line treatment of splenic marginal zone lymphoma. Patients will be randomized between rituximab alone or in combination with zanubrutinib.

Large cell group

Clinical studies
NLG-LBC-06 (BIO-CHIC) phase II trial, which 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 high risk DLBCL enrolled the planned 120 patients in Feb 2021. Results from the first efficacy analysis were presented at ICML in June 2021 and final results are expected to be presented at ASH 2022.

After Bio-CHIC trial, we plan to conduct a ctDNA-guided phase III trial, where we will determine if ctDNA levels can be used to guide treatment decisions. The patients will be stratified according to their ctDNA levels to different treatment groups, and based on high, intermediate, or low ctDNA levels either de-escalate, continue, or change to experimental therapy.

The ongoing randomized phase III POLAR BEAR trial for elderly patients with DLBCL (>80 years, or frail >75 years) is comparing standard treatment, R-mini-CHOP with a regimen where vincristine has been substituted by the anti-CD79b immunoconjugate polatuzumab vedotin. By the end of May 2022, 90 of the planned 200 patients have been included from the Nordic area and from Italy. The trial DSMB reviewed safety data from the first 50 patients in January 2022, and recommended continuous enrolment according to protocol.

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, MYC, BCL2, and TP53 alterations, soluble CD163, soluble PD1 and circulating tumor DNA levels.

CNS-lymphoma group

The working group has had a great pleasure of welcoming two new members from Denmark, as Martin Bjerregård Pedersen and Tarec El-Galaly have joined the working group.

The randomized phase II IELSG45 study (FIORELLA) is still ongoing in Denmark, Finland, Israel, Italy, and Switzerland, and evaluates the efficacy of fitness- and comorbidity -tailored treatment in elderly patients with newly diagnosed PCNSL. The NLG working group has continued its efforts in commencing a clinical trial for patients with relapsed/refractory PCNSL, and a new collaboration with the French network for oculo-cerebral lymphoma (LOC) has been established. Negotiations are ongoing with industry, and the aim is to start a R/R PCNSL trial in the Nordics in 2022-2023.

A retrospective epidemiologic study evaluating the treatments and outcomes for patients with PCNSL in the Nordic countries in the period 2010-2020 is planned. Applications for funding to conduct correlative studies are also ongoing. In addition, an update on the previous NLG phase II first line PCNSL study, published in 2015, with a median follow-up of 76 months is under preparation for publication.

MCL group

Younger patients (<65 years): The Nordic MCL group has participated in 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 was closed for enrolment in January 2021. 870 patients were randomized, making this the largest clinical trial in MCL so far. 111 patients have been enrolled from NLG centres.

Elderly patients: Since December 2017, NLG has participated in the ENRICH trial, with University of Plymouth as sponsor. This is a randomized phase III trial, comparing rituximab+ibrutinib with rituximab-chemo (either R-bendamustine or R-CHOP). Enrolment was finalized in June 2021, and results are expected in 2024.

In Q4 2021, a new trial for elderly patients, NLG-MCL8, ALTAMIRA, started recruitment.
This includes patients >60 years with untreated MCL, using a 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. By the end of April, 2022, 10 of 80 patients have been enrolled, and is open for centres in Sweden and Norway. Soon, centres in Denmark, Finland and South Korea will be able to enroll patients.

The NLG trial for relapsed MCL, NLG-MCL7, VALERIA, exploring the combination of venetoclax, lenalidomide and rituximab, was concluded in April 2021, with 59 patients. This is a phase I-II trial,

for patients with relapsed MCL, and a population of untreated MCL, ineligible for combination chemotherapy. This trial also explores 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 was presented at ASH 2020, where we were able to show the feasibility of stopping treatment in MRD-negative patients. Final results are expected to be presented at ASH 2022.

T cell group

ACT trial:
The final analysis of the ACT-2 trial (elderly patients; >60 yrs) has recently 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. A combined analysis of long-term outcome of the ACT-1 and ACT-2 trials is in progress.

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 has been completed, after accrual of 60 patients. 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. An application for academic funding of the trial is planned for August 2022. Further funding will be negotiated with potential partners from the pharmaceutical industry (consolidation part). The PANTHEON trial will address two main questions:

(i) does measurement of minimal residual disease by means of liquid biopsies (ctDNA) improve response assessment compared to the current standard-of-care (PET/CT)?; (ii) 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 will be given as per national guidelines 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 consideration. Collaborations with labs within Denmark regarding analysis of ctDNA have been initiated.
There have been virtual working group meetings during Q1 and Q2 2022 regarding ongoing and planned projects and additional meetings will take place during the fall.

Hodgkin group

The B-CAP 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 postponed due to work load from the Covid-19 pandemic.

The Nordic countries have collectively joined 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 has completed recruitment and the results are awaited.

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 opened in 2020 and is still ongoing.

The "Nordic trial" on stage I-IIA Hodgkin lymphoma was initiated as a treatment recommendation in 1997. The patients treated 1999-2005 have been evaluated for relative survival and mortality rates. The final publication has been published in 2020. Data on late toxicity has been published in 2022.

Results in elderly patients treated in Sweden, Denmark and Norway, comparing different chemotherapy regimens will be submitted to the ISHL-12 conference in Cologne.

Interim results of the PRO-Hodgkin study with proton therapy for early stages will be submitted to the ISHL-12 conference in Cologne.

Epidemiology group

The group is working with several projects using data from the national lymphoma registers in Denmark, Sweden, and Norway. Clinical data being assembled in Finland. The group has regular digital meetings 3-4 times a year. A seminar is planned for November 2022, before the NLG

meeting. This has been sponsored by NCU. The group is working on both clinical and statistical research. Exchange of PhD students has been done in 2022 already. Funding has been granted by NCO and cover salaries in three Nordic countries. We have had external lectures (Zoom) this year and plan to have more.

Several projects are ongoing, and some have been completed. Among projects, we are currently working on outcomes of rare lymphomas, fertility, gender differences, and elderly patients.

If you have a lymphoma epi project idea or wishes to get epidemiological input, get on touch with the group chair Tarec El-Galaly (tceg@rn.dk).