Nordic Lymphoma Group

Newsletter June 2017

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 7-8, 2017, at the Bella Sky Hotel, Copenhagen. The preliminary program of the meeting and information on the venue of the meeting are enclosed. Scientific papers and case presentations will be presented from all countries as in previous years. Invited lecturers will highlight the 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.

Looking forward seeing you in Copenhagen

Sincerely,

Peter

Peter Brown, chairperson of NLG
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NLG Plenary meeting

The venue of the meeting will be in Copenhagen, Bella Sky Hotel overlooking the central Copenhagen, for more details:

www.bellasky.com

Distance from the Copenhagen City centre is 10 km and from the Kastrup airport 5 km. A shuttle bus between the airport and the hotel is available every 30 minutes. There are trains from the airport to Örestad Station (1 stop), change to the metro and after one stop you are at the hotel.

Collaborative companies are welcome to send one representative to attend the meeting including in the sponsorship. Additional participants from collaborative companies can participate on special conditions, please contact Peter Brown for further information:

Working group meetings may be arranged on Monday evening Nov 6th, 2017, and Tuesday morning Nov 7th.

All members of the working groups have a possibility to participate the meeting, and at least one delegate from every NLG study centre.

The procedure for registration of the NLG plenary meeting was changed last year and we continue this concept, that also includes a fee for accommodation. Details are found at our web-site www.Nordic-lymphoma.org

Recommended max number of delegates from each country:

- DK 20
- N 20
- FIN 20
- Sweden 35
- 5 seats for colleagues presenting interesting case and free papers

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. Active participants will have their travel expenses paid by NLG.

NLG Plenary meeting program
Tuesday 7.11.2017

12.00-13.00 Registration and lunch

Session I (Chaired by (t.b.a.))

13.00-14.30 Free papers
14.30-15.30 Invited speaker: Matthew S. Davids from Dana-Farber Cancer Institute. "Optimizing BCL2 inhibition in lymphoma."

15.30-16.00 Coffee

Session II (Chaired by (t.b.a.))

16.00-16.30 Large Cell Group, Sirpa Leppä, Helsinki:
16.30-17.00 T-Cell group, Francesco d'Amore, Århus
17.00-17.30 Mantle cell group, Mats Jerkeman, Lund
17.30-18.00 CNS-Group, Elisa Jacobsen-Pulczynski, Århus:

18.00-18.30 Business meeting

19.30 Dinner

Wednesday 8.11.2017

Session III (Chaired by (t.b.a.))

9.00-10.00 Interesting cases

10.00-10.30 Coffee

Session IV (Chaired by (t.b.a.))

10.30 - 12.00 Educational session "Controversies in treatment of lymphoma"

12.00 - 13.00 lunch

Session V (Chaired by (t.b.a.))

13.00 - 13.30 Indolent group, Bjørn Østenstad, Oslo
13.30 - 13.50 Hodgkin group, Alexander Fosså, Oslo
13.50 - 14.15 Epidemiology Group, Karin Ekström-Smedby, Stockholm
14.15 - 14.30 PTLD Group, Maja Vase, Århus
14.30 - 15.00 Pathology group, Marja-Liisa Karjalainen-Lindsberg, Helsinki:
15.00 Farewell

Update on working group activities

Indolent group

The SAKK/NLG randomized phase II study (35/10) treating follicular lymphoma with rituximab with or without lenalidomid enrolled 152 patients, showing a significantly higher CR at week 23 in the experimental arm as compared to rituximab alone (primary endpoint) (Lugano 2015). The improved response translated into significantly prolonged progression free survival (PFS) and time to new treatment (TNT) (secondary endpoints) (ASH 2016). A manuscript is being prepared.

The SAKK/NLG collaboration will be prolonged in the 35/14-study. The design is similar to the previous studies and is a randomized phase II study on Rituximab with or without Ibrutinib for untreated patients with advanced follicular lymphoma. The study is open for inclusion both in the SAKK group and in the Nordic countries and the accrual is good.

A long-term follow-up study of patients treated in previous clinical trials (M39035 and ML16865) is ongoing. Median follow-up is 8-10 years and we will look at efficacy (OS, PFS), transformation rates, late toxicities, Health related Quality of Life and exploratory outcomes. Data collection has been completed and analysis ongoing

Large cell group

Correlative studies on the basis of CRY-04 trial material - Several CRY-04 trial-related molecular projects are ongoing. To date, the studies have demonstrated survival association of tumor associated macrophages, MYC, BCL2, TP53 and DTX1 alterations, impact of differentially expressed genes and alternative splicing on survival, and described plasma protein specific for high risk DLBCL.

Clinical studies – The CHIC study testing the impact of dose dense chemoimmunotherapy with early CNS prophylaxis on the outcome of high risk DLBCL patients <65 years was closed for recruitment on Dec 2014. Total of 143 patients were included, and the results from the final analyses presented at ASH 2016. Overall, the CRY-04 and CHIC trials have demonstrated favorable FFS and OS and lower CNS recurrence rates as compared to previous studies. They also underscore the importance of giving systemic CNS targeted therapy early during the course of treatment. The results from the comparison of the CRY-04 and CHIC trials will be presented at ICML-14, Lugano in June 2017.

On the basis of the CRY and CHIC trial experiences, a new biomarker-driven and risk-adapted phase II trial, BIO-CHIC, will start in Q2. In the trial, we test whether stratification of the patients according to biological risk factors for different treatment groups, including DA-EPOCH-R and R-CHOEP for the patients with and without biological risk factors, respectively, can further improve the outcome of the patients with clinically rich risk DLBCL. In both cohorts, the patients will receive HD-MTX as a CNS prophylaxis in the beginning of the therapy. Planned target size is 120.

Another phase II trial, ILIAD, testing the safety and efficacy of oral PI3K inhibitor idelalisib in the frail patients with relapsed or refractory DLBCL will be opened in Q3 2017.

The ORCHARRD study for relapsed and refractory DLBCL patients was closed for recruitment on Q3 2013. The final data has been published. No benefit of ofatumumab was found in comparison to rituximab salvage chemoimmunotherapy.

CNS-lymphoma group

Three centers in Denmark participated in the IELSG32 trial which was closed after completed accrual. The results of the first randomization have been published (Lancet Haematology 2016). The results of the second randomization were presented at ASH 2016 and a manuscript is submitted for publication. The next IELSG study in younger PCNSL patients (IELSG43) is ongoing in Germany and activated in Denmark. Some centers in Finland and Norway are expected to join this study as well. An upcoming study in elderly patients has been delayed, but is expected to be activated later this year. Updated results of the former Nordic PCNSL study after a median follow up of 76 months are prepared for publication. A Nordic phase ll study in refractory/relapsed PCNSL will be activated as soon as financial funding is provided. The study treatment includes Lenalidomide, Ibrutinib and Rituximab induction, high-dose chemotherapy followed by autologous stem cell transplantation as consolidation and Ibrutinib as maintenance therapy. Translational studies will be performed before and during treatment as well as during 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.

Elderly patients: MCL4 1st-line trial “Lena-BeRit” trial was completed in 2013 with 51 patients, and results have been published in Blood 2016. After summer 2017, NLG will join 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).

Relapsed MCL: A second line phase-II trial, NLG-MCL6, “Philemon” opened in May 2015 also with a chemotherapy-free approach: Ibrutinib, rituximab and lenalidomide, followed by ibrutinib+rituximab maintenance. This trial completed enrollment of 50 patients very rapidly, after one year, and results were presented at ASH 2016 as an oral presentation. A new NLG trial, NLG-MCL7 (Valeria), exploring the combination of venetoclax, lenalidomide and rituximab, is scheduled to start in q4 2017. This is a phase I-II trial, for patients with relapsed MCL, and a population of untreated MCL, ineligible for combination chemotherapy.

Several translational studies based on the MCL2/3 biobank are ongoing, including mutational profiling and gene expression profiling. Data on mutational profiling were presented as an oral presentation at ASH 2016, showing a dismal prognosis in patients with a TP53 mutation at diagnosis. A manuscript has recently been submitted to Blood. A long term follow-up study of MRD and pre-emptive rituximab treatment in the MCL2+3 trials was also presented at ASH 2016, and has recently been published.

T cell group

With regard to the ACT trials (ACT-1 and ACT-2), the final analysis of the ACT-2 part (coordinated by the German High-Grade Lymphoma Group) was presented as an oral paper at the 2016 ASCO meeting. The analysis was presented unsupervised, i.e. without information on the CD52-status of the tumor samples, and showed no significant outcome difference (Event-Free Survival as primary end-point). In agreement between the trial coordinators of the ACT-1 and ACT-2 trials, the final analysis of the ACT-1 trial (coordinated by the Nordic Lymphoma Group) is currently ongoing with a median follow-up of 48 months. In connection with the analysis it included the last patient on December 1 2013.

A manuscript with late follow-up (median 9.5 years) data from the NLG-T-01 study is in preparation. The NLG-T-01 specific tissue micro-array is completed and correlative studies initiated. In collaboration with the Mayo Clinic (dr. Andrew Feldman), we are currently analyzing the samples for rearrangement of the DUSP22 and TP63 genes and will correlate the findings with outcome. The aim is to establish whether the DUSP22 and TP63 rearrangements and the 'triple negative' status (no ALK, no DUSP22, and no TP63 rearrangement) can be used as biomarkers for therapeutic decisions in general and upfront SCT in particular.

A proposal for a randomized phase II trial for relapsed/refractory CD30+ PTCL was discussed with global Takeda representatives at ASH 2016. Despite a previous encouraging response (negotiation meeting at Lugano 2015), no agreement on support was reached due to an apparently very similar study proposal submitted by the French LYSA group. Discussions are currently ongoing in the working group with regard to the design of a new NLG front-line trial in PTCL, also in the light of the upcoming ACT-1 results.

The phase 1b/2a P[R]EBEN protocol in relapsed aggressive B- and T-cell lymphomas was activated in Q3 2016 and has presently accrued 17 patients (12 in the phase 2 'frail' and 5 in the phase 1 'fit' part of the trial). Per May 2017, 7 centers have been activated (in chronological order: Aarhus, Helsinki, Copenhagen, Odense, Lund, Oslo, and Trondheim). Additional Nordic and European centers, including 10 HOVON centers, are expected to be opened later this year. Preliminary results on the first included patients were sent in abstract form to the 14th ICML in Lugano, June 2017.

Hodgkin group

The RATHL trial (Response adapted therapy in advanced Hodgkin lymphoma) was published in NEJM in June 2016. An updated analysis of the outcome is presented in Lugano 2017. The basic assumption that Bleomycin can be safely omitted after 2 courses of ABVD in interim PET-CT negative patients is substantiated with longer follow up. Subgroup analyses will also be presented.

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 open for inclusion in all Nordic countries. As of June 2017, 45 patients of the planned 70 are included, 5 in Sweden, 9 in Denmark, 5 in Norway and 5 in Finland. The inclusion period has been extended.

The Nordic countries are all planning to join 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 will soon open in Norway; the other countries are on their way.

The “Nordic trail” on stage I-IIA Hodgkin lymphoma was imitated as a treatment recommendation in 1997. The patients treated in the first decade after initiation of the recommendation are now being evaluated in a joint Swedish-Norwegian study. A final publication is expected shortly.

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 had a separate meeting in Copenhagen June 7, 2017.
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 projects include:
1) Evaluation of the addition of radiotherapy in DLBCL.
2) Development of a web-based prognostic tool for DLBCL based on register data.
3) Evaluation of long-term survival in Hodgkin lymphoma.
4) Survival of lymphoplasmacytic lymphoma/Waldenström.