NIVEAU DSHNHL 2015-1

Improvement of Outcome in Elderly Patients or Patients not eligible for high-dose chemotherapy with Aggressive Non-Hodgkin Lymphoma in first Relapse or Progression by adding Nivolumab to Gemcitabine, Oxaliplatin plus Rituximab in case of of B-cell lymphoma

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Protocol Synopsis

Indication: Aggressive Non-Hodgkin Lymphoma in first R/P

Study design: International, multicentre, randomised, open-label, treatment optimisation study

Planned sample size: 310 with B-cell, 78 with T-cell (international)

Number of Patients: 388 (international)
- 310 patients with B-Cell Lymphoma
- 78 patients with T-Cell Lymphoma

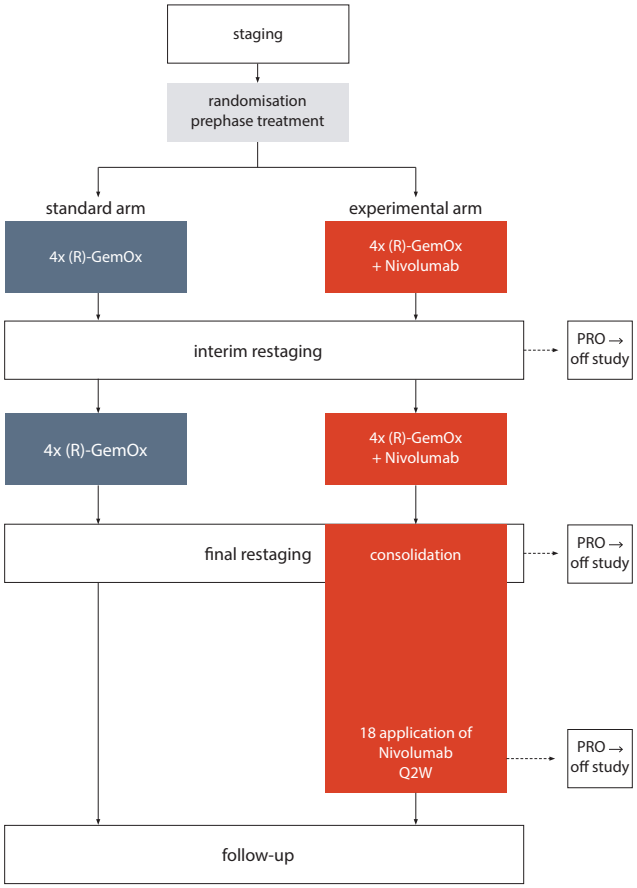
Number of sites: 77 sites in 9 countries

Duration: First patient in (FPI): Jan 2018 (run-in phase)
Last patient in (LPI): Q4 2022 (expected)
Last patient out (LPO): Q4 2024 (expected)

Study medication: Nivolumab

Status: Run-in phase completed
Study in submission (Austria)
First patient in Q2 2019 (Austria)

Study Design



This trial is designed as an international, multicentre, randomised, open-label, treatment optimisation study, preceded by safety run-in phases conducted for B-cell and T-cell lymphoma separately. A Safety analysis was done after inclusion of 15 patients. In addition a safety analysis after the randomisation of thirty patients with Nivolumab is planned.

Aim of the phase-III trial is to test whether prognosis of patients with relapsed or refractory aggressive Non-Hodgkin Lymphoma not eligible for neither autologous nor allogeneic stem cell transplantation can be improved by combining nivolumab with (R)-GemOx.

All patients with first relapse or progression of an aggressive Non-Hodgkin's lymphoma aged older than 65 years or older than 18 years with HCT-CI score > 2 are eligible for this study irrespective of their gender or stage of disease. There is no upper limit of age. Also patients not eligible neither autologous nor allogeneic stem cell transplantation are eligible for this study.

The duration of therapy according to study protocol ranges between 16 and 52 weeks. Patients randomised to receive eight 2-week cycles of (R)-GemOx are 16 weeks on therapy. Patients randomised to receive eight 2-week cycles nivolumab plus (R)-GemOx followed by 18 2-week applications of nivolumab are 52 weeks on treatment.

Follow-up observation within the study will end for all patients presumably in Q4/2024, which is 2 years after inclusion of the last patient. Thus duration within the clinical study will last at least 2 years for the individual patient.

Primary endpoint:
- 1-year Progression free survival (PFS)

Secondary endpoints (selected):
- complete response rate after eight cycles of (R)-GemOx
- partial response rate after eight cycles of (R)-GemOx
- overall response rate after eight cycles of (R)-GemOx
- duration of response
- progression rate, relapse rate
- EFS, OS, Toxicity

Inclusion Criteria (selected)

- Histologically proven aggressive Non-Hodgkin's lymphoma
- Ineligibility for neither autologous nor allogeneic stem cell transplantation
- Patients must have only one prior chemotherapy regimen including an anthracycline
- all patient >65 years of age or older than 18 years if HCT-CI score > 2
- All risk groups (IPI 0 to 5)
- Performance status ECOG 0 – 2

Exclusion Criteria (selected)

- Already initiated lymphoma therapy after first relapse or progression
- Serious accompanying disorder or impaired organ function
- Previous therapy with Gemcitabine or Oxaliplatin
- Patients with an active, known or suspected autoimmune disease
- Prior chemo- or radiotherapy, long-term use of corticosteroids or anti-neoplastic drugs for previous disorder (except for first-line therapy of lymphoma)
- CNS involvement of lymphoma or primary CNS lymphoma

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An academic clinical trial of DSHNHL (Deutsche Studiengruppe für Hochmaligne Non-Hodgkin-Lymphome), in cooperation with LYSARC (Lymphoma Academic Research Organisation) and Arbeitsgemeinschaft medikamentöse Tumortherapie gemeinnützige GmbH, Clinical-Scientific Director: R. Greil