# AERN study: Abscopal Effect of Radiotherapy and Nivolumab in anti-PD1 Pretreated Relapsed or Refractory classical Hodgkin Lymphoma - An international multicenter Phase II trial

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Lymphomas Hodgkin's disease |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON54697

**Source**
ToetsingOnline

**Brief title**
AERN study

### Condition

- Lymphomas Hodgkin's disease
- Lymphomas Hodgkin's disease

**Synonym**
Hodgkin Lymphoma; Hodgkin's disease; mallignant lymphoma

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** University of Cologne
**Source(s) of monetary or material Support:** Bristol-Myers Squibb,Universiteit van Keulen

## Intervention

**Keyword:** Hodgkin Lymphoma, Nivolumab, Refractory, Relapsed

## Outcome measures

### Primary outcome

Abscopal response rate (ARR-6) with abscopal response centrally confirmed as

restaging result after RT to a single lesion and at least four but not more

than six nivolumab infusions (RE-6 result)

### Secondary outcome

Overall abscopal response rate (OARR)

Overall response rate (ORR)

Duration of response (DOR)

Progression-free survival (PFS)

Overall survival (OS)

Adverse events (AE)

Feasibility aspects

Quality of life (QoL) and life situation (LS) aspects

Correlative studies

# Study description

### Background summary

Nivolumab is highly effective and well tolerated in relapsed / refractory HL, nevertheless CR-rates are low and a considerable proportion of patients suffers from progressive disease. Localized RT induces an immunogenic effect which might work synergistically and facilitate augmented systemic (i.e. abscopal) responses in combination with nivolumab.

### Study objective

The aim of the trial is to improve efficacy of nivolumab in patients with relapsed or refractory HL previously treated with an anti-PD1 antibody.

Primary objective of the trial is to show efficacy of the experimental treatment strategy.

Secondary objectives are to further evaluate efficacy, show safety and feasibility and perform correlative studies.

### Study design

Single-arm two-stage phase II study

### Intervention

Nivolumab 240 mg i.v. at 2-weekly intervals combined with 20Gy radiotherapy (RT) to a preferably recently progressive and not pre-irradiated single lesion. Nivolumab will be continued for a maximum of 18 months or until disease progression or unacceptable toxicity.

### Study burden and risks

All patients enrolled into the AERN trial will have previously received an anti-PD1 antibody as the last preceeding line of therapy, either until PD or for at least six months. Individual tolerability to the systemic checkpoint

blockade is hence already established outside the AERN trial. RT with 20 Gy to a single HL lesion is a well established treatment for localized r/r cHL and rarely associated with relevant toxicity.

Various previously described preclinical studies indicate synergistic systemic effects of local RT and checkpoint inhibition and currently available case report and a larger case series indicate feasibility, with no relevant treatment-related morbidity or mortality reported, and remarkable efficacy of such approaches.

Other treatment options in this setting are limited to palliative individualized approaches, which are often conventional chemotherapies and carry relevant toxicity, or best supportive care.

In summary, the benefit-risk ratio for the combination of localized RT and continued anti-PD1 therapy in the setting of the AERN trial is considered favorable.

Quality of Life is part of this trial and could be experienced as a burden.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

- Relapsed/refractory cHL with progression while treated with an anti-PD1 antibody or
Relapsed/refractory cHL with stable disease for > 6 months as best response to ongoing anti-PD1 antibody therapy
- At least two distinct FDG-avid HL-lesions with at least 5 cm distance between them, and one of them considered eligible for irradiation with 20Gy
- One but the irradiated lesion has to be outside the 10% isodose in RT planning confirmed by the Central Response Evaluation Panel (CREP)
- Age 18 years and older, all sexes

## Exclusion criteria

- Nodular lymphocyte-predominant HL or grey-zone lymphoma
- Evidence of active, non-infectious lung disorder with DLCOc < 50%
- History of long-term or ongoing ingestion of immunosuppressive agents >10mg prednisone/d
- Any other serious disease or organ dysfunction which might impair protocol treatment
Note: Patients on antiretroviral therapy (ART) with controlled HIV infection (defined as sufficient ART compliance, non-measurable HIV and CD4+ T helper cells > 200/µL) may be enrolled, if considered eligible for study treatment by the investigator.
- Prior allogeneic stem-cell transplantation (alloSCT), if one or more of the following conditions are met:
a. AlloSCT conducted <12 months prior to registration for the screening phase
b. Requiring continued immunosuppression beyond 7d) at registration for the screening phase
c. History of acute graft-versus-host disease >= grade3
d. History of chronic graft-versus-host disease >= grade3

# Study design

## Design

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|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 19-10-2020 |
| Enrollment: | 3 |
| Type: | Actual |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Opdivo |
| Generic name: | Nivolumab |
| Registration: | Yes - NL intended use |

# Ethics review

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| Approved WMO Date: | 07-04-2020 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-08-2020 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 07-06-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO | |

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| Date: | 02-07-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 08-08-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 21-12-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-03-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 25-04-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 18-11-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 10-02-2023 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 17-03-2023 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-04-2023 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO | |

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|---|---|
| Date: | 16-11-2023 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-12-2023 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-04-2024 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2017-003334-82-NL |
| ClinicalTrials.gov | NCT03480334 |
| CCMO | NL71853.029.20 |