



Clinical trial results:

A Phase 2, Open-label, Multicenter Study to Evaluate the Safety and Clinical Activity of Durvalumab in Combination with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone (R-CHOP) or with Lenalidomide plus R-CHOP (R2-CHOP) in Subjects With Previously Untreated, High-Risk Diffuse Large B-Cell Lymphoma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-005173-20 |
| Trial protocol | AT DK EE SK PL |
| Global end of trial date | 24 April 2022 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 10 May 2023 |
| First version publication date | 10 May 2023 |

Trial information

Trial identification

| | |
|-----------------------|--------------------|
| Sponsor protocol code | MEDI4736-DLBCL-001 |
|-----------------------|--------------------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 09 November 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 April 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to explore the clinical activity of durvalumab (MEDI4736) in combination with R-CHOP or R2-CHOP followed by durvalumab consolidation therapy in previously untreated subjects diagnosed with high-risk DLBCL.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 28 February 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 22 |
| Country: Number of subjects enrolled | Denmark: 8 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Austria: 15 |
| Worldwide total number of subjects | 46 |
| EEA total number of subjects | 23 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 24 |

| | |
|---------------------|----|
| From 65 to 84 years | 22 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

46 participants were enrolled and treated.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | DUR + R-CHOP |

Arm description:

Participants receive Induction Therapy (21-day cycles): Durvalumab 1125 mg intravenously (IV) on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5). Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Vincristine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at 1.4 mg/m² BSA (recommended capping at 2 mg absolute dose) on Day 1 of each 21-day cycle for 6-8 cycles as part of the R-CHOP treatment regimen.

| | |
|--|--------------------------------------|
| Investigational medicinal product name | Prednisone / Prednisolone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion, Oral solution |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

a 100 mg

| | |
|--|-----------------------|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at 50 mg/m² BSA on Day 1 of each 21-day cycle for 6 to 8 cycles as part of the R-CHOP treatment regimen.

| | |
|--|--|
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion, Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at 375 mg/m² BSA on Day 1 of each 21-day cycle for 6 to 8 cycles as part of the R-CHOP treatment regimen.

| | |
|--|-----------------------|
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at 750 mg/m² BSA on Day 1 of each 21-day cycle for 6 to 8 cycles as part of the R-CHOP treatment regimen.

| | |
|--|-----------------------|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1125 and 1500 mg administered intravenously (IV)

| | |
|------------------|---------------|
| Arm title | DUR + R2-CHOP |
|------------------|---------------|

Arm description:

Participants receive Induction Therapy (21-day cycles): Cycle 1 - induction therapy of durvalumab in combination with R-CHOP (as described in DUR + R-CHOP arm). Starting at cycle 2 - Durvalumab 1125 mg IV on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R2-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5; daily oral lenalidomide 15 mg from Day 1 to 14) from the cycle following COO determination until end of induction therapy (Cycle 6 or Cycle 8) or starting Cycle 1 if ABC subtype is identified prior to C1D1. Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1125 and 1500 mg administered intravenously (IV)

| | |
|--|--|
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion, Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at 375 mg/m² BSA on Day 1 of each 21-day cycle for 6 to 8 cycles as part of the R-CHOP treatment regimen.

| | |
|--|-----------------------|
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at 750 mg/m² BSA on Day 1 of each 21-day cycle for 6 to 8 cycles as part of the R-CHOP treatment regimen.

| | |
|--|-------------|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |

| | |
|---|--------------------------------------|
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Administered at 50 mg/m ² BSA on Day 1 of each 21-day cycle for 6 to 8 cycles as part of the R-CHOP treatment regimen. | |
| Investigational medicinal product name | Vincristine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Administered at 1.4 mg/m ² BSA (recommended capping at 2 mg absolute dose) on Day 1 of each 21-day cycle for 6-8 cycles as part of the R-CHOP treatment regimen. | |
| Investigational medicinal product name | Prednisone / Prednisolone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| a 100 mg | |
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion, Oral solution |
| Routes of administration | Intravenous use, Oral use |
| Dosage and administration details: | |
| 15 mg | |

| Number of subjects in period 1 | DUR + R-CHOP | DUR + R2-CHOP |
|---------------------------------------|---------------------|----------------------|
| Started | 43 | 3 |
| Completed Induction Treatment | 31 | 3 |
| Completed Consolidation Treatment | 14 | 2 |
| Completed | 14 | 2 |
| Not completed | 29 | 1 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 6 | - |
| Adverse event, non-fatal | 9 | - |
| Other reasons | 4 | - |
| Progressive disease | 9 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | DUR + R-CHOP |
|-----------------------|--------------|

Reporting group description:

Participants receive Induction Therapy (21-day cycles): Durvalumab 1125 mg intravenously (IV) on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5). Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy.

| | |
|-----------------------|---------------|
| Reporting group title | DUR + R2-CHOP |
|-----------------------|---------------|

Reporting group description:

Participants receive Induction Therapy (21-day cycles): Cycle 1 - induction therapy of durvalumab in combination with R-CHOP (as described in DUR + R-CHOP arm). Starting at cycle 2 - Durvalumab 1125 mg IV on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R2-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5; daily oral lenalidomide 15 mg from Day 1 to 14) from the cycle following COO determination until end of induction therapy (Cycle 6 or Cycle 8) or starting Cycle 1 if ABC subtype is identified prior to C1D1. Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy.

| Reporting group values | DUR + R-CHOP | DUR + R2-CHOP | Total |
|---|--------------|---------------|-------|
| Number of subjects | 43 | 3 | 46 |
| Age Categorical Units: participants | | | |
| <65 years | 23 | 1 | 24 |
| >=65 years | 20 | 2 | 22 |
| Age Continuous Units: years | | | |
| arithmetic mean | 61.1 | 67.7 | |
| standard deviation | ± 12.77 | ± 8.62 | - |
| Sex: Female, Male Units: participants | | | |
| Female | 17 | 1 | 18 |
| Male | 26 | 2 | 28 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 43 | 3 | 46 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| White | 42 | 3 | 45 |
| Not Collected or Reported | 0 | 0 | 0 |
| Other | 1 | 0 | 1 |
| Eastern Cooperative Oncology Group | | | |
| ECOG performance status is used by doctors and researchers to assess how a participant's disease is | | | |

| | | | |
|---|----|---|----|
| progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. - 0 = Fully Active (most favorable status); - 1 = Restricted activity but ambulatory; - 2 = Ambulatory but unable to carry out work activities; - 3 = Limited Self-Care; - 4 = Completely Disabled, No self-care (least favorable status) | | | |
| Units: Subjects | | | |
| 0 = Fully Active | 16 | 2 | 18 |
| 1 = Restricted activity but ambulatory | 19 | 0 | 19 |
| 2 = Ambulatory but unable to work | 8 | 1 | 9 |
| 3 = Limited Self-Care | 0 | 0 | 0 |
| 4 = Completely Disabled, No self-care | 0 | 0 | 0 |
| Ann Arbor Stage at Diagnosis | | | |
| The criteria for Clinical Stage (Ann Arbor staging) are as below: - I: involvement of a single nodal region. - II: involvement of 2 or more lymph node regions on the same side of the diaphragm. - III: involvement of lymph node regions on both sides of the diaphragm. - IV: disseminated involvement of 1 or more extra-lymphatic sites with or without associated lymph node involvement. | | | |
| Units: Subjects | | | |
| Stage I | 0 | 0 | 0 |
| Stage II | 0 | 0 | 0 |
| Stage III | 9 | 2 | 11 |
| Stage IV | 34 | 1 | 35 |
| Presence of Bulky Disease (Baseline) | | | |
| Bulky disease refers to the size of the tumor. | | | |
| Units: Subjects | | | |
| Yes = tumor diameter ≥ 7.0 cm | 21 | 2 | 23 |
| No = tumor diameter < 7.0 cm | 22 | 1 | 23 |
| International Prognostic Index (IPSS) Score | | | |
| The IPI assesses risk of central nervous system disease according to the following scale: - 0-1: Low risk - 2: Low-Intermediate risk - 3: High-Intermediate risk - 4-5: High risk | | | |
| Units: Subjects | | | |
| 0-1: Low risk | 0 | 0 | 0 |
| 2: Low-Intermediate risk | 9 | 0 | 9 |
| 3: High-Intermediate risk | 21 | 0 | 21 |
| 4-5: High risk | 9 | 2 | 11 |
| Missing | 4 | 1 | 5 |

Subject analysis sets

| | |
|--|--------------------------------------|
| Subject analysis set title | High Group for CD8 Density |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their CD8 density evaluation was above threshold, defined as the median of 774 cells/mm ² found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders. | |
| Subject analysis set title | Low Group for CD8 Density |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their CD8 density evaluation was below threshold, defined as the median of 774 cells/mm ² found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders. | |
| Subject analysis set title | High Group for PDL1 % of total cells |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PDL1 % of total cell evaluation was above threshold, defined as the median of 13.8% found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders.

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | Low Group for PDL1 % of total cells |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PDL1 % of total cell evaluation was below threshold, defined as the median of 13.8% found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders.

| | |
|----------------------------|--------------------------------------|
| Subject analysis set title | High Group for PDL1 % of tumor cells |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PD-1 % of tumor cell evaluation was above threshold, defined as the median of 6.2% found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders.

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | Low Group for PDL1 % of tumor cells |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PDL1 % of tumor cell evaluation was below threshold, defined as the median of 6.2% found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | High Group for RNA IFN Gamma Score |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had RNA IFN Gamma Score calculated based on a biopsy sample collected before treatment on this protocol. The result of their RNA IFN Gamma Score was above threshold, defined as the median of 3.28 found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Low Group for RNA IFN Gamma Score |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had RNA IFN Gamma Score calculated based on a biopsy sample collected before treatment on this protocol. The result of their RNA IFN Gamma Score was below threshold, defined as the median of 3.28 found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders.

| Reporting group values | High Group for CD8 Density | Low Group for CD8 Density | High Group for PDL1 % of total cells |
|--|----------------------------|---------------------------|--------------------------------------|
| Number of subjects | 15 | 11 | 20 |
| Age Categorical Units: participants | | | |
| <65 years | | | |
| >=65 years | | | |
| Age Continuous Units: years | | | |
| arithmetic mean | 67 | 64 | 75 |
| standard deviation | ± | ± | ± |
| Sex: Female, Male Units: participants | | | |
| Female | | | |
| Male | | | |

| | | | |
|---|--|--|--|
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | | | |
| Not Hispanic or Latino | | | |
| Unknown or Not Reported | | | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | | | |
| Asian | | | |
| Black or African American | | | |
| Native Hawaiian or Other Pacific Islander | | | |
| White | | | |
| Not Collected or Reported | | | |
| Other | | | |
| Eastern Cooperative Oncology Group | | | |
| ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. - 0 = Fully Active (most favorable status); - 1 = Restricted activity but ambulatory; - 2 = Ambulatory but unable to carry out work activities; - 3 = Limited Self-Care; - 4 = Completely Disabled, No self-care (least favorable status) | | | |
| Units: Subjects | | | |
| 0 = Fully Active | | | |
| 1 = Restricted activity but ambulatory | | | |
| 2 = Ambulatory but unable to work | | | |
| 3 = Limited Self-Care | | | |
| 4 = Completely Disabled, No self-care | | | |
| Ann Arbor Stage at Diagnosis | | | |
| The criteria for Clinical Stage (Ann Arbor staging) are as below: - I: involvement of a single nodal region. - II: involvement of 2 or more lymph node regions on the same side of the diaphragm. - III: involvement of lymph node regions on both sides of the diaphragm. - IV: disseminated involvement of 1 or more extra-lymphatic sites with or without associated lymph node involvement. | | | |
| Units: Subjects | | | |
| Stage I | | | |
| Stage II | | | |
| Stage III | | | |
| Stage IV | | | |
| Presence of Bulky Disease (Baseline) | | | |
| Bulky disease refers to the size of the tumor. | | | |
| Units: Subjects | | | |
| Yes = tumor diameter \geq 7.0 cm | | | |
| No = tumor diameter $<$ 7.0 cm | | | |
| International Prognostic Index (IPSS) Score | | | |
| The IPI assesses risk of central nervous system disease according to the following scale: - 0-1: Low risk - 2: Low-Intermediate risk - 3: High-Intermediate risk - 4-5: High risk | | | |
| Units: Subjects | | | |
| 0-1: Low risk | | | |
| 2: Low-Intermediate risk | | | |
| 3: High-Intermediate risk | | | |
| 4-5: High risk | | | |
| Missing | | | |

| Reporting group values | Low Group for PDL1 % of total cells | High Group for PDL1 % of tumor cells | Low Group for PDL1 % of tumor cells |
|---|--|---|--|
| Number of subjects | 5 | 11 | 9 |
| Age Categorical Units: participants | | | |
| <65 years >=65 years | | | |
| Age Continuous Units: years arithmetic mean standard deviation | 20 ± | 64 ± | 56 ± |
| Sex: Female, Male Units: participants | | | |
| Female Male | | | |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported | | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| American Indian or Alaska Native Asian Black or African American Native Hawaiian or Other Pacific Islander White Not Collected or Reported Other | | | |
| Eastern Cooperative Oncology Group | | | |
| ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. - 0 = Fully Active (most favorable status); - 1 = Restricted activity but ambulatory; - 2 = Ambulatory but unable to carry out work activities; - 3 = Limited Self-Care; - 4 = Completely Disabled, No self-care (least favorable status) | | | |
| Units: Subjects | | | |
| 0 = Fully Active 1 = Restricted activity but ambulatory 2 = Ambulatory but unable to work 3 = Limited Self-Care 4 = Completely Disabled, No self-care | | | |
| Ann Arbor Stage at Diagnosis | | | |
| The criteria for Clinical Stage (Ann Arbor staging) are as below: - I: involvement of a single nodal region. - II: involvement of 2 or more lymph node regions on the same side of the diaphragm. - III: involvement of lymph node regions on both sides of the diaphragm. - IV: disseminated involvement of 1 or more extra-lymphatic sites with or without associated lymph node involvement. | | | |
| Units: Subjects | | | |
| Stage I Stage II Stage III Stage IV | | | |
| Presence of Bulky Disease (Baseline) | | | |

| | | | |
|---|--|--|--|
| Bulky disease refers to the size of the tumor. | | | |
| Units: Subjects | | | |
| Yes = tumor diameter ≥ 7.0 cm No = tumor diameter < 7.0 cm | | | |
| International Prognostic Index (IPSS) Score | | | |
| The IPI assesses risk of central nervous system disease according to the following scale: - 0-1: Low risk - 2: Low-Intermediate risk - 3: High-Intermediate risk - 4-5: High risk | | | |
| Units: Subjects | | | |
| 0-1: Low risk 2: Low-Intermediate risk 3: High-Intermediate risk 4-5: High risk Missing | | | |

| Reporting group values | High Group for RNA IFN Gamma Score | Low Group for RNA IFN Gamma Score | |
|---|------------------------------------|-----------------------------------|--|
| Number of subjects | 7 | 20 | |
| Age Categorical | | | |
| Units: participants | | | |
| <65 years ≥65 years | | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 43 | 60 | |
| standard deviation | ± | ± | |
| Sex: Female, Male | | | |
| Units: participants | | | |
| Female Male | | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported | | | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native Asian Black or African American Native Hawaiian or Other Pacific Islander White Not Collected or Reported Other | | | |
| Eastern Cooperative Oncology Group | | | |
| ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. - 0 = Fully Active (most favorable status); - 1 = Restricted activity but ambulatory; - 2 = Ambulatory but unable to carry out work activities; - 3 = Limited Self-Care; - 4 = Completely Disabled, No self-care (least favorable status) | | | |
| Units: Subjects | | | |
| 0 = Fully Active | | | |

| | | | |
|---|--|--|--|
| 1 = Restricted activity but ambulatory 2 = Ambulatory but unable to work 3 = Limited Self-Care 4 = Completely Disabled, No self-care | | | |
| Ann Arbor Stage at Diagnosis | | | |
| The criteria for Clinical Stage (Ann Arbor staging) are as below: - I: involvement of a single nodal region. - II: involvement of 2 or more lymph node regions on the same side of the diaphragm. - III: involvement of lymph node regions on both sides of the diaphragm. - IV: disseminated involvement of 1 or more extra-lymphatic sites with or without associated lymph node involvement. | | | |
| Units: Subjects | | | |
| Stage I Stage II Stage III Stage IV | | | |
| Presence of Bulky Disease (Baseline) | | | |
| Bulky disease refers to the size of the tumor. | | | |
| Units: Subjects | | | |
| Yes = tumor diameter ≥ 7.0 cm No = tumor diameter < 7.0 cm | | | |
| International Prognostic Index (IPSS) Score | | | |
| The IPI assesses risk of central nervous system disease according to the following scale: - 0-1: Low risk - 2: Low-Intermediate risk - 3: High-Intermediate risk - 4-5: High risk | | | |
| Units: Subjects | | | |
| 0-1: Low risk 2: Low-Intermediate risk 3: High-Intermediate risk 4-5: High risk Missing | | | |

End points

End points reporting groups

| | |
|---|--------------------------------------|
| Reporting group title | DUR + R-CHOP |
| Reporting group description: | |
| Participants receive Induction Therapy (21-day cycles): Durvalumab 1125 mg intravenously (IV) on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5). Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy. | |
| Reporting group title | DUR + R2-CHOP |
| Reporting group description: | |
| Participants receive Induction Therapy (21-day cycles): Cycle 1 - induction therapy of durvalumab in combination with R-CHOP (as described in DUR + R-CHOP arm). Starting at cycle 2 - Durvalumab 1125 mg IV on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R2-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5; daily oral lenalidomide 15 mg from Day 1 to 14) from the cycle following COO determination until end of induction therapy (Cycle 6 or Cycle 8) or starting Cycle 1 if ABC subtype is identified prior to C1D1. Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy. | |
| Subject analysis set title | High Group for CD8 Density |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their CD8 density evaluation was above threshold, defined as the median of 774 cells/mm ² found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders. | |
| Subject analysis set title | Low Group for CD8 Density |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their CD8 density evaluation was below threshold, defined as the median of 774 cells/mm ² found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders. | |
| Subject analysis set title | High Group for PDL1 % of total cells |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PDL1 % of total cell evaluation was above threshold, defined as the median of 13.8% found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders. | |
| Subject analysis set title | Low Group for PDL1 % of total cells |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PDL1 % of total cell evaluation was below threshold, defined as the median of 13.8% found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders. | |
| Subject analysis set title | High Group for PDL1 % of tumor cells |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PD-1 % of tumor cell evaluation was above threshold, defined as the median of 6.2% found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders. | |
| Subject analysis set title | Low Group for PDL1 % of tumor cells |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had IHC analysis performed on a biopsy sample collected before treatment on this protocol. The result of their PDL1 % of tumor cell evaluation was below threshold, defined as the median of 6.2% found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | High Group for RNA IFN Gamma Score |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had RNA IFN Gamma Score calculated based on a biopsy sample collected before treatment on this protocol. The result of their RNA IFN Gamma Score was above threshold, defined as the median of 3.28 found in commercial DLBCL samples using matched analytical methods. Participants with values above threshold were predicted to be responders.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Low Group for RNA IFN Gamma Score |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants had RNA IFN Gamma Score calculated based on a biopsy sample collected before treatment on this protocol. The result of their RNA IFN Gamma Score was below threshold, defined as the median of 3.28 found in commercial DLBCL samples using matched analytical methods. Participants with values below threshold were predicted to be non-responders.

Primary: Percentage of Participants Who Achieved a Complete Response (CR) at the End of Induction Therapy

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved a Complete Response (CR) at the End of Induction Therapy ^[1] |
|-----------------|---|

End point description:

The primary efficacy analysis evaluated the complete response rate (CRR) at the end of the induction therapy in the efficacy evaluable population in a comparative manner against historical control. The response to treatment was assessed according to the 2014 International Working Group (IWG) Response Criteria for Non-Hodgkin's Lymphoma (NHL) (Cheson, 2014). CR was defined as a complete metabolic response and radiographic evidence showing target nodes/nodal masses regressed to ≤ 1.5 cm in longest diameter, no new lesions, regression of lymph nodes to normal size, absence of splenomegaly, and absence of bone marrow involvement. Clopper-Pearson two-sided 95% confidence interval is reported. Null hypothesis for the primary endpoint was rejected if the lower limit of the confidence interval for the complete response rate at the completion of the induction therapy in the efficacy evaluable population is above 55%.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From first dose of study drug to end of Induction therapy (Day 1 up to Week 26 – maximum duration of Induction Period).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics were planned for this endpoint.

| End point values | DUR + R-CHOP | DUR + R2-CHOP | | |
|-----------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 37 | 3 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 54.1 (36.9 to 70.5) | 66.7 (9.4 to 99.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for Immunohistochemistry (IHC) CD8 T-Cell Density

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for Immunohistochemistry (IHC) CD8 T-Cell Density |
|-----------------|--|

End point description:

Data in the analysis include all participants who received durvalumab, irrespective of the study arm in which they enrolled, because the selected biomarkers have been associated with response in other anti-PD1 or anti-PDL1 studies, such as durvalumab. IHC analysis was performed on the baseline tumor biopsy to quantify CD8 T-cell density. Participants with 'high' values, i.e. above the threshold defined as the median value of 774 cells/mm² found in commercial DLBCL samples using matched analytical methods, were predicted to be responders to treatment with durvalumab. The definition of a complete response was that used in the primary outcome.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Biomarker biopsies: Days -28 to Day -1. Clinical response: From first dose of study drug to end of Induction therapy (Day 1 up to Week 26 – maximum duration of Induction Period).

| End point values | High Group for CD8 Density | Low Group for CD8 Density | | |
|-----------------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 15 | 11 | | |
| Units: percentage of participants | 67 | 64 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | CD8 T-cell density |
| Comparison groups | High Group for CD8 Density v Low Group for CD8 Density |
| Number of subjects included in analysis | 26 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | > 0.99 [2] |
| Method | Fisher exact |

Notes:

[2] - Significance defined as 0.05.

| | |
|----------------------------|--------------------|
| Statistical analysis title | CD8 T-cell density |
|----------------------------|--------------------|

Statistical analysis description:

The Area Under the Receiver Operator Characteristic Curve (AUC-ROC) is the estimated parameter. Responders were compared to non-responders by ranking them according to their CD8 density.

| | |
|---|--|
| Comparison groups | High Group for CD8 Density v Low Group for CD8 Density |
| Number of subjects included in analysis | 26 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.872 [3] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[3] - Significance defined as 0.05.

Secondary: Percentage of Participants Who Responded During Induction and Continued into Consolidation Therapy (Database cutoff date: 02-Aug-2018)

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Responded During Induction and Continued into Consolidation Therapy (Database cutoff date: 02-Aug-2018) |
|-----------------|--|

End point description:

The percentage of participants who achieved a partial response (PR) or complete response (CR) at the end of Induction and continued into consolidation period in the efficacy evaluable population in a comparative manner against historical control. The response to treatment was assessed according to the 2014 International Working Group (IWG) Response Criteria for Non-Hodgkin's Lymphoma (NHL) (Cheson, 2014). CR was defined in outcome #1. PR was defined as a partial metabolic response and radiographic evidence showing $\geq 50\%$ decrease in sum of perpendicular diameters (SPD) of up to 6 target measurable nodes and extranodal sites, no new lesions, spleen must have regressed $> 50\%$ in length beyond normal, and residual bone marrow involvement improved from baseline. Clopper-Pearson two-sided 95% confidence interval is reported. Null hypothesis was rejected if the lower limit of the confidence interval for the rate of subjects who continue consolidation therapy out of all subjects.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose of study drug to completion of at least one cycle in the Consolidation Period (Day 1 up to Week 52)

| End point values | DUR + R-CHOP | DUR + R2-CHOP | | |
|-----------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 37 | 3 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 67.6 (50.2 to 82.0) | 66.7 (9.4 to 99.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for Immunohistochemistry (IHC) Programmed Death Ligand – 1 (PDL1) Total Percentage

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for Immunohistochemistry (IHC) Programmed Death Ligand – 1 (PDL1) Total Percentage |
|-----------------|---|

End point description:

Data in the analysis include all participants who received durvalumab, irrespective of the study arm in which they enrolled, because the selected biomarkers have been associated with response in other anti-PD1 or anti-PDL1 studies, such as durvalumab. IHC analysis was performed on the baseline tumor biopsy to quantify CD8 T-cell density. Participants with 'high' values, i.e. above the threshold defined as the median value of 774 cells/mm² found in commercial DLBCL samples using matched analytical methods, were predicted to be responders to treatment with durvalumab. The definition of a complete response was that used in the primary outcome.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Biomarker biopsies: Days -28 to Day -1. Clinical response: From first dose of study drug to end of Induction therapy (Day 1 up to Week 26 – maximum duration of Induction Period).

| End point values | High Group for PDL1 % of total cells | Low Group for PDL1 % of total cells | | |
|-----------------------------------|--------------------------------------|-------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 5 | | |
| Units: percentage of participants | 75 | 20 | | |

Statistical analyses

| Statistical analysis title | PDL1 (Total Percentage) |
|----------------------------|-------------------------|
|----------------------------|-------------------------|

Statistical analysis description:

The Area Under the Receiver Operator Characteristic Curve (AUC-ROC) is the estimated parameter. Responders were compared to non-responders by ranking them according to their PDL1 % of total cells.

| | |
|---|--|
| Comparison groups | High Group for PDL1 % of total cells v Low Group for PDL1 % of total cells |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.523 ^[4] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[4] - Significance defined as 0.05.

| Statistical analysis title | PDL1 (Total Percentage) |
|---|--|
| Comparison groups | High Group for PDL1 % of total cells v Low Group for PDL1 % of total cells |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0403 ^[5] |
| Method | Fisher exact |

Notes:

[5] - Significance defined as 0.05.

Secondary: Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for Immunohistochemistry (IHC) Programmed Death Ligand – 1 (PDL1) Percentage of Tumor Cells

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for Immunohistochemistry (IHC) Programmed Death Ligand – 1 (PDL1) Percentage of Tumor Cells |
|-----------------|--|

End point description:

Data in the analysis include all participants who received durvalumab, irrespective of the study arm in which they enrolled, because the selected biomarkers have been associated with response in other anti-PD1 or anti-PDL1 studies, such as durvalumab. IHC analysis was performed on the baseline tumor biopsy to quantify CD8 T-cell density. Participants with 'high' values, i.e. above the threshold defined as the median value of 774 cells/mm² found in commercial DLBCL samples using matched analytical methods, were predicted to be responders to treatment with durvalumab. The definition of a complete response was that used in the primary outcome.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Biomarker biopsies: Days -28 to Day -1. Clinical response: From first dose of study drug to end of Induction therapy (Day 1 up to Week 26 – maximum duration of Induction Period). | |

| End point values | High Group for PDL1 % of tumor cells | Low Group for PDL1 % of tumor cells | | |
|-----------------------------------|--------------------------------------|-------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 11 | 9 | | |
| Units: percentage of participants | 64 | 56 | | |

Statistical analyses

| Statistical analysis title | PDL1 (Percentage of tumor cells) |
|----------------------------|----------------------------------|
|----------------------------|----------------------------------|

Statistical analysis description:

The Area Under the Receiver Operator Characteristic Curve (AUC-ROC) is the estimated parameter. Responders were compared to non-responders by ranking them according to their PDL1 % of tumor cells.

| | |
|---|--|
| Comparison groups | High Group for PDL1 % of tumor cells v Low Group for PDL1 % of tumor cells |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.557 ^[6] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[6] - Significance defined as 0.05.

| Statistical analysis title | PDL1 (Percentage of tumor cells) |
|---|--|
| Comparison groups | High Group for PDL1 % of tumor cells v Low Group for PDL1 % of tumor cells |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | > 0.99 ^[7] |
| Method | Fisher exact |

Notes:

[7] - Significance defined as 0.05.

Secondary: Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for the Interferon Gamma Score (IFNG-Score) from Ribonucleic Acid (RNA)-Sequencing Data

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved a Clinical Response in the Biomarker Subpopulation for the Interferon Gamma Score (IFNG-Score) from Ribonucleic Acid (RNA)-Sequencing Data |
|-----------------|--|

End point description:

Data in the analysis include all participants who received durvalumab, irrespective of the study arm in which they enrolled, because the selected biomarkers have been associated with response in other anti-

PD1 or anti-PDL1 studies, such as durvalumab. IHC analysis was performed on the baseline tumor biopsy to quantify CD8 T-cell density. Participants with 'high' values, i.e. above the threshold defined as the median value of 774 cells/mm² found in commercial DLBCL samples using matched analytical methods, were predicted to be responders to treatment with durvalumab. The definition of a complete response was that used in the primary outcome.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Biomarker biopsies: Days -28 to Day -1. Clinical response: From first dose of study drug to end of Induction therapy (Day 1 up to Week 26 – maximum duration of Induction Period). | |

| End point values | High Group for RNA IFN Gamma Score | Low Group for RNA IFN Gamma Score | | |
|-----------------------------------|------------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 7 | 20 | | |
| Units: percentage of participants | 43 | 60 | | |

Statistical analyses

| | |
|-----------------------------------|----------------|
| Statistical analysis title | RNA Sequencing |
|-----------------------------------|----------------|

Statistical analysis description:

The Area Under the Receiver Operator Characteristic Curve (AUC-ROC) is the estimated parameter. Responders were compared to non-responders by ranking them according to their IFNG-Score.

| | |
|---|--|
| Comparison groups | High Group for RNA IFN Gamma Score v Low Group for RNA IFN Gamma Score |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.399 ^[8] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[8] - Significance defined as 0.05.

| | |
|---|--|
| Statistical analysis title | RNA Sequencing |
| Comparison groups | High Group for RNA IFN Gamma Score v Low Group for RNA IFN Gamma Score |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.662 ^[9] |
| Method | Fisher exact |

Notes:

[9] - Significance defined as 0.05.

Secondary: Participants with Treatment Emergent Adverse Events (TEAE)

| | |
|-----------------|--|
| End point title | Participants with Treatment Emergent Adverse Events (TEAE) |
|-----------------|--|

End point description:

An AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen during a

study. A serious AE is any AE occurring at any dose that: • Results in death; • Is life-threatening; • Requires or prolongs existing inpatient hospitalization; • Results in persistent or significant disability/incapacity; • Is a congenital anomaly/birth defect; • Constitutes an important medical event. The Investigator assessed the relationship of each AE to study drug and graded the severity according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE, Version 4.03): - Grade 1 = Mild (no limitation in activity or intervention); - Grade 2 = Moderate (some limitation in activity; no/minimal medical intervention required); - Grade 3 = Severe (marked limitation in activity; medical intervention required, hospitalization possible); - Grade 4 = Life-threatening; - Grade 5 = Death. Relation to IP is determined by the investigator. 99999= N/A

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of the first dose of study drug to within 90 days after the last dose of durvalumab or 28 days after the last dose of any investigational product (IP) whichever is greater. (Up to approximately 72 weeks)

| End point values | DUR + R-CHOP | DUR + R2-CHOP | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 3 | | |
| Units: participants | | | | |
| >= 1 Treatment-emergent adverse event (TEAE) | 43 | 3 | | |
| >=1 TEAE related to durvalumab | 33 | 3 | | |
| >=1 TEAE related to R-CHOP | 40 | 3 | | |
| >=1 TEAE related to lenalidomide | 99999 | 3 | | |
| >=1 TEAE related to durvalumab or any other IP | 41 | 3 | | |
| >=1 TEAE severity grade 3-4 | 37 | 3 | | |
| >=1 TEAE severity grade 3-4 related to durvalumab | 18 | 1 | | |
| >=1 TEAE severity grade 3-4 related to R-CHOP | 27 | 3 | | |
| >=1 TEAE severity grade 3-4 related to lenalidomide | 99999 | 2 | | |
| >=1 TEAE severity grade 3-4 related to any IP | 31 | 3 | | |
| >=1 TEAE severity grade 5 | 3 | 0 | | |
| >=1 TEAE severity grade 5 related to any IP | 0 | 0 | | |
| >=1 serious TEAE | 23 | 1 | | |
| >=1 serious TEAE related to durvalumab | 10 | 1 | | |
| >=1 serious TEAE related to R-CHOP | 10 | 1 | | |
| >=1 serious TEAE related to lenalidomide | 99999 | 1 | | |
| >=1 serious TEAE related to any IP | 14 | 1 | | |
| >=1 leading to discontinuation of durvalumab | 13 | 0 | | |
| >=1 leading to discontinuation of R-CHOP | 4 | 0 | | |
| >=1 leading to discontinuation of lenalidomide | 99999 | 0 | | |
| >=1 leading to discontinuation of any IP | 13 | 0 | | |
| >=1 leading to interruption of durvalumab | 15 | 2 | | |
| >=1 leading to interruption of R-CHOP | 12 | 1 | | |

| | | | | |
|--|-------|---|--|--|
| >=1 leading to interruption of lenalidomide | 99999 | 2 | | |
| >=1 leading to interruption of any IP | 18 | 3 | | |
| >=1 leading to infusion interruption of durvalumab | 2 | 0 | | |
| >=1 leading to dose reduction of vincristine | 4 | 1 | | |
| >=1 leading to dose reduction of lenalidomide | 99999 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessed from first dose to 90 days after the last dose of durvalumab or 28 days after other IP and up to 5 years after C1D1 of the last lenalidomide dose. All-Cause Mortality was assessed in participants from first dose to study completion.

Adverse event reporting additional description:

Participants treated with lenalidomide during any stage of the study will be continued to be followed for Second Primary Malignancies (SPM) for up to 5 years after enrollment (C1D1) of the last Participant to receive lenalidomide as part of their study treatment.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | DUR + R-CHOP |
|-----------------------|--------------|

Reporting group description:

Participants receive Induction Therapy (21-day cycles): Durvalumab 1125 mg intravenously (IV) on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5). Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy.

| | |
|-----------------------|---------------|
| Reporting group title | DUR + R2-CHOP |
|-----------------------|---------------|

Reporting group description:

Participants receive Induction Therapy (21-day cycles): Cycle 1 - induction therapy of durvalumab in combination with R-CHOP (as described in DUR + R-CHOP arm). Starting at cycle 2 - Durvalumab 1125 mg IV on Day 1 of each 21-day cycle in combination with 6 to 8 cycles R2-CHOP (IV rituximab, doxorubicin, vincristine and cyclophosphamide on Day 1; daily oral/IV prednisone/prednisolone from Day 1 to 5; daily oral lenalidomide 15 mg from Day 1 to 14) from the cycle following COO determination until end of induction therapy (Cycle 6 or Cycle 8) or starting Cycle 1 if ABC subtype is identified prior to C1D1. Participants then receive Consolidation Therapy (28-day cycles): Durvalumab 1500 mg IV on Day 1 of each 28-day cycle for up to a total of 12 months from C1D1 of induction therapy.

| Serious adverse events | DUR + R-CHOP | DUR + R2-CHOP | |
|---|------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 23 / 43 (53.49%) | 1 / 3 (33.33%) | |
| number of deaths (all causes) | 5 | 1 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Diffuse large B-cell lymphoma recurrent | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clear cell renal cell carcinoma | | | |

| | | | |
|--|----------------|---------------|--|
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoma | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour pain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|---------------|--|
| Immune system disorders | | | |
| Haemophagocytic lymphohistiocytosis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | 1 / 3 (33.33%) | |
| occurrences causally related to treatment / all | 5 / 6 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|---------------|--|
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral diarrhoea | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis bacterial | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Perirectal abscess | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 3 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | DUR + R-CHOP | DUR + R2-CHOP | |
|---|-------------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 43 / 43 (100.00%) | 3 / 3 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Histiocytic necrotising lymphadenitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 3 (33.33%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 0 / 3 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Hot flush | | | |

| | | | |
|---|------------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 3 (0.00%) 0 | |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 | 0 / 3 (0.00%) 0 | |
| Fatigue | | | |
| subjects affected / exposed occurrences (all) | 26 / 43 (60.47%) 29 | 2 / 3 (66.67%) 3 | |
| Mucosal inflammation | | | |
| subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 | 0 / 3 (0.00%) 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed occurrences (all) | 6 / 43 (13.95%) 6 | 1 / 3 (33.33%) 1 | |
| Pyrexia | | | |
| subjects affected / exposed occurrences (all) | 9 / 43 (20.93%) 9 | 0 / 3 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed occurrences (all) | 9 / 43 (20.93%) 13 | 0 / 3 (0.00%) 0 | |
| Dyspnoea | | | |
| subjects affected / exposed occurrences (all) | 10 / 43 (23.26%) 10 | 0 / 3 (0.00%) 0 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed occurrences (all) | 6 / 43 (13.95%) 6 | 0 / 3 (0.00%) 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 1 / 3 (33.33%) 1 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 3 (0.00%) 0 | |
| Insomnia | | | |

| | | | |
|---|------------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 11 / 43 (25.58%) 18 | 0 / 3 (0.00%) 0 | |
| Investigations | | | |
| Blood pressure increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 3 (33.33%) 1 | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 3 (33.33%) 2 | |
| Weight decreased subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 7 | 0 / 3 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 | 0 / 3 (0.00%) 0 | |
| Infusion related reaction subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 6 | 1 / 3 (33.33%) 1 | |
| Nervous system disorders | | | |
| Cognitive disorder subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 3 (33.33%) 1 | |
| Dizziness subjects affected / exposed occurrences (all) | 9 / 43 (20.93%) 10 | 1 / 3 (33.33%) 1 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 6 / 43 (13.95%) 8 | 0 / 3 (0.00%) 0 | |
| Headache subjects affected / exposed occurrences (all) | 11 / 43 (25.58%) 11 | 0 / 3 (0.00%) 0 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 23 / 43 (53.49%) 24 | 2 / 3 (66.67%) 2 | |
| Restless legs syndrome | | | |

| | | | |
|--|------------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 1 / 3 (33.33%) 1 | |
| Sensory disturbance subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 3 (33.33%) 1 | |
| Taste disorder subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 | 0 / 3 (0.00%) 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 8 | 1 / 3 (33.33%) 3 | |
| Neutropenia subjects affected / exposed occurrences (all) | 21 / 43 (48.84%) 39 | 3 / 3 (100.00%) 5 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 | 1 / 3 (33.33%) 2 | |
| Leukopenia subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 10 | 1 / 3 (33.33%) 1 | |
| Ear and labyrinth disorders | | | |
| Hypoacusis subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 3 (33.33%) 1 | |
| Eye disorders | | | |
| Vision blurred subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 5 | 0 / 3 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 | 0 / 3 (0.00%) 0 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 7 | 0 / 3 (0.00%) 0 | |
| Constipation | | | |

| | | | |
|--|------------------|----------------|--|
| subjects affected / exposed | 9 / 43 (20.93%) | 2 / 3 (66.67%) | |
| occurrences (all) | 9 | 2 | |
| Diarrhoea | | | |
| subjects affected / exposed | 13 / 43 (30.23%) | 1 / 3 (33.33%) | |
| occurrences (all) | 18 | 1 | |
| Dry mouth | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | 0 / 3 (0.00%) | |
| occurrences (all) | 9 | 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 1 / 3 (33.33%) | |
| occurrences (all) | 1 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 18 / 43 (41.86%) | 2 / 3 (66.67%) | |
| occurrences (all) | 24 | 2 | |
| Stomatitis | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | 2 / 3 (66.67%) | |
| occurrences (all) | 12 | 2 | |
| Vomiting | | | |
| subjects affected / exposed | 10 / 43 (23.26%) | 0 / 3 (0.00%) | |
| occurrences (all) | 17 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 0 / 3 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Erythema | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 1 / 3 (33.33%) | |
| occurrences (all) | 1 | 2 | |
| Generalised erythema | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 3 (33.33%) | |
| occurrences (all) | 0 | 1 | |
| Pruritus | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 0 / 3 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Rash | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | 1 / 3 (33.33%) | |
| occurrences (all) | 11 | 1 | |

| | | | |
|--|--|--|--|
| Alopecia subjects affected / exposed occurrences (all) | 10 / 43 (23.26%) 10 | 0 / 3 (0.00%) 0 | |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 1 / 3 (33.33%) 1 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Spinal pain subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 7 / 43 (16.28%) 8 4 / 43 (9.30%) 4 7 / 43 (16.28%) 8 4 / 43 (9.30%) 4 1 / 43 (2.33%) 1 | 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 | |
| Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Lung infection subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 5 3 / 43 (6.98%) 3 4 / 43 (9.30%) 7 | 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 | |

| | | | |
|---|------------------------|---------------------|--|
| Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 3 (0.00%) 0 | |
| Oral herpes subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 1 / 3 (33.33%) 1 | |
| Pneumonia subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 3 (33.33%) 1 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 3 (0.00%) 0 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 4 | 0 / 3 (0.00%) 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 12 / 43 (27.91%) 13 | 0 / 3 (0.00%) 0 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 8 / 43 (18.60%) 8 | 1 / 3 (33.33%) 1 | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 3 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 25 October 2019 | Discontinuation of Follow-up Period, assessments and data collection. Second Primary Malignancies (SPMs) data collection. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

After the US FDA Partial Clinical Hold, enrollment of new subjects into Arm B was discontinued.

Notes: