



Clinical trial results:

KPL-716-C201: A Phase 2a/b, Randomized, Double-Blind, Placebo Controlled Study to Investigate the Efficacy, Safety, Tolerability and Pharmacokinetics of KPL-716 in Reducing Pruritus in Subjects with Prurigo Nodularis

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2020-004198-38 |
| Trial protocol | CZ DE FR BE IT AT |
| Global end of trial date | 24 August 2023 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 07 July 2024 |
| First version publication date | 07 July 2024 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | KPL-716-C201 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03816891 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | IND: 132912 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Kiniksa Pharmaceuticals, Ltd |
| Sponsor organisation address | 100 Hayden Avenue, Lexington, Massachusetts, United States, 02421 |
| Public contact | Chrissy Lundquist, Kiniksa Pharmaceuticals, Ltd. , +1 7813170276, clundquist@kiniksa.com |
| Scientific contact | Chrissy Lundquist, Kiniksa Pharmaceuticals, Ltd. , +1 7813170276, clundquist@kiniksa.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 | 26 March 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 December 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 August 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of subcutaneous (SC) KPL-716 vs. placebo in reducing pruritus in Prurigo Nodularis (PN) subjects experiencing severe pruritus

Protection of trial subjects:

(1) Independent Ethics Committee (IEC) or Institutional Review Board (IRB): The core study documents (Protocol and subsequent amendments, Investigator's Brochure (IB), Patient facing materials [Informed Consent Form (ICF), Subject recruitment procedures (e.g. advertisements), any other written information provided to subjects] were reviewed and approved by the IRB/ IEC before implementation. Additionally, the IRBs/IECs were informed by the Investigator of serious and unexpected SAEs in accordance with the reporting requirements.

(2) Ethical Conduct: The study was conducted (a) in accordance with the protocol (b) per consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines (c) per applicable International Council for/Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines (d) per applicable country and local laws and regulations.

(3) ICF: The investigator or their representative explained the nature of the study to the participants or their legally authorized representative before signing the ICF. Participants were re-consented to the most current version of the ICF(s) during their participation in the study. A copy of the ICF(s) was provided to the participant or the participant's legally authorized representative.

Background therapy:

There are no approved therapies for PN. Topical therapies such as topical corticosteroids, calcineurin inhibitors, calcipotriol, and capsaicin, systemic corticosteroids, thalidomide, systemic immunomodulatory drugs such as methotrexate and cyclosporin, antiepileptics and antidepressants, phototherapy and photochemotherapy are often tried with limited success.

Evidence for comparator:

-

| | |
|---|------------------|
| Actual start date of recruitment | 01 December 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Poland: 7 |
| Country: Number of subjects enrolled | Austria: 7 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Country: Number of subjects enrolled | Czechia: 4 |
| Country: Number of subjects enrolled | France: 3 |

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Germany: 28 |
| Country: Number of subjects enrolled | Italy: 5 |
| Country: Number of subjects enrolled | United States: 72 |
| Country: Number of subjects enrolled | Canada: 28 |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | Australia: 5 |
| Country: Number of subjects enrolled | Korea, Republic of: 6 |
| Country: Number of subjects enrolled | Taiwan: 16 |
| Worldwide total number of subjects | 190 |
| EEA total number of subjects | 57 |

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) | 137 |
| From 65 to 84 years | 53 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 443 participants were screened and 190 participants enrolled subjects were randomized at 1:1:1:1 ratio into one of the 4 arms to receive different dosing regimens of or placebo. At the end of the Double-Blind Period, all participants had the option to enter the Open Label Extension Period to receive KPL-716.

Pre-assignment

Screening details:

After ICF was signed, 443 participants entered the Screening Period for assessment of eligibility. A full physical examination was performed to assess the following systems: head/neck/thyroid; eyes/ears/nose/throat (EENT); respiratory; cardiovascular; lymph nodes; abdomen; skin; musculoskeletal; and neurological.

Period 1

| | |
|------------------------------|------------------------------|
| Period 1 title | Double Blind |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

Blinding implementation details:

An Interact Web Response System issued a unique treatment code to each subject, which assigned the treatment for the subject. The investigator, the sponsor study team, and remaining clinical site staff (other than the unblinded pharmacist or unblinded designee) were blinded to treatment assignment. The unblinded treatment assignment for individual participant was made available to the investigator only in the event of a medical emergency or or an adverse reaction.

Arms

| | |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm A |

Arm description:

KPL-716 was administered subcutaneously at the dose of 540 mg every 4 weeks for 16 weeks during double blind period.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | KPL-716 |
| Investigational medicinal product code | |
| Other name | Vixarelimab |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Cutaneous use |

Dosage and administration details:

KPL-716 is provided as a sterile liquid formulation and supplied as a single-use vial for SC injection.

| | |
|------------------|-------|
| Arm title | Arm B |
|------------------|-------|

Arm description:

KPL-716 was administered subcutaneously at the dose of 360 mg every 4 weeks for 16 weeks during the double-blind period.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | KPL-716 |
| Investigational medicinal product code | |
| Other name | Vixarelimab |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Cutaneous use |

Dosage and administration details:

KPL-716 is provided as a sterile liquid formulation and supplied as a single-use vial for SC injection.

| | |
|--|--------------------|
| Arm title | Arm C |
| Arm description: KPL-716 was administered subcutaneously at the dose of 120 mg every 4 weeks for 16 weeks during double blind period. | |
| Arm type | Experimental |
| Investigational medicinal product name | KPL-716 |
| Investigational medicinal product code | |
| Other name | Vixarelimab |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Cutaneous use |

Dosage and administration details:
KPL-716 was provided as a sterile liquid formulation and supplied as a single-use vial for SC injection.

| | |
|--|--------------------|
| Arm title | Arm D |
| Arm description: Placebo was administered subcutaneously every 4 weeks for 16 weeks during the double-blind period. | |
| Arm type | Placebo |
| Investigational medicinal product name | Matching Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Cutaneous use |

Dosage and administration details:
Placebo matching to KPL-716 excipients was provided as a sterile liquid formulation and supplied for SC injection

| Number of subjects in period 1 | Arm A | Arm B | Arm C |
|---------------------------------------|-------|-------|-------|
| Started | 47 | 47 | 47 |
| Completed | 45 | 44 | 47 |
| Not completed | 2 | 3 | 0 |
| Physician decision | - | 1 | - |
| Consent withdrawn by subject | - | 1 | - |
| Adverse event, non-fatal | 2 | 1 | - |
| Lost to follow-up | - | - | - |
| Early discontinuation | - | - | - |

| Number of subjects in period 1 | Arm D |
|---------------------------------------|-------|
| Started | 49 |
| Completed | 47 |
| Not completed | 2 |
| Physician decision | - |
| Consent withdrawn by subject | - |
| Adverse event, non-fatal | - |
| Lost to follow-up | 1 |
| Early discontinuation | 1 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Open Label Extension |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-----------|
| Arm title | Treatment |
|------------------|-----------|

Arm description:

Open label extension participants who previously received KPL-716 during Double-Blind period. KPL-716 was administered subcutaneously at the dose of 360 mg every 2 weeks for 36 weeks (starting at week 16 and with the last dosing at the week 48 visit).

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | KPL-716 |
| Investigational medicinal product code | |
| Other name | Vixarelimab |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Cutaneous use |

Dosage and administration details:

KPL-716 is provided as a sterile liquid formulation and supplied as a single-use vial for SC injection.

| Number of subjects in period 2^[1] | Treatment |
|---|-----------|
| Started | 181 |
| Completed | 157 |
| Not completed | 24 |
| Consent withdrawn by subject | 9 |
| Adverse event, non-fatal | 8 |
| Lost to follow-up | 3 |
| Lack of efficacy | 4 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Per study design, all subjects in double blind period (DB) had an option of receive KPL-716 360 mg SC, Q2W during the Open Label Extension (OLE) Period to evaluate the long-term safety and PK. Out of 190

subjects randomized in DB period, 181 consented to OLE.

Baseline characteristics

Reporting groups

| | |
|--|-------|
| Reporting group title | Arm A |
| Reporting group description: KPL-716 was administered subcutaneously at the dose of 540 mg every 4 weeks for 16 weeks during double blind period. | |
| Reporting group title | Arm B |
| Reporting group description: KPL-716 was administered subcutaneously at the dose of 360 mg every 4 weeks for 16 weeks during the double-blind period. | |
| Reporting group title | Arm C |
| Reporting group description: KPL-716 was administered subcutaneously at the dose of 120 mg every 4 weeks for 16 weeks during double blind period. | |
| Reporting group title | Arm D |
| Reporting group description: Placebo was administered subcutaneously every 4 weeks for 16 weeks during the double-blind period. | |

| Reporting group values | Arm A | Arm B | Arm C |
|---|---------|---------|---------|
| Number of subjects | 47 | 47 | 47 |
| Age categorical | | | |
| KPL-716 was administered subcutaneously at the dose of 360 mg every 2 weeks for 36 weeks (starting at week 16 and with the last dosing at the week 48 visit). | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 31 | 35 | 35 |
| From 65-84 years | 16 | 12 | 12 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 56.7 | 55.9 | 54.4 |
| standard deviation | ± 12.18 | ± 13.73 | ± 16.11 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 29 | 28 | 28 |
| Male | 18 | 19 | 19 |

| Reporting group values | Arm D | Total | |
|---|-------|-------|--|
| Number of subjects | 49 | 190 | |
| Age categorical | | | |
| KPL-716 was administered subcutaneously at the dose of 360 mg every 2 weeks for 36 weeks (starting at week 16 and with the last dosing at the week 48 visit). | | | |
| Units: Subjects | | | |

| | | | |
|--|---------|-----|--|
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 36 | 137 | |
| From 65-84 years | 13 | 53 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54.8 | | |
| standard deviation | ± 13.35 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 29 | 114 | |
| Male | 20 | 76 | |

Subject analysis sets

| | |
|----------------------------|------------------------|
| Subject analysis set title | mITT efficacy analysis |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All randomized subjects who receive at least 1 dose of KPL-716 or placebo and have at least 1 post-baseline efficacy assessment in the double-blind treatment period were included in the modified intent-to-treat (mITT) analysis set.

| Reporting group values | mITT efficacy analysis | | |
|---|------------------------|--|--|
| Number of subjects | 189 | | |
| Age categorical | | | |
| KPL-716 was administered subcutaneously at the dose of 360 mg every 2 weeks for 36 weeks (starting at week 16 and with the last dosing at the week 48 visit). | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 136 | | |
| From 65-84 years | 53 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 55.4 | | |
| standard deviation | ± 13.83 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 114 | | |

| | | | |
|------|----|--|--|
| Male | 75 | | |
|------|----|--|--|

End points

End points reporting groups

| | |
|---|------------------------|
| Reporting group title | Arm A |
| Reporting group description: KPL-716 was administered subcutaneously at the dose of 540 mg every 4 weeks for 16 weeks during double blind period. | |
| Reporting group title | Arm B |
| Reporting group description: KPL-716 was administered subcutaneously at the dose of 360 mg every 4 weeks for 16 weeks during the double-blind period. | |
| Reporting group title | Arm C |
| Reporting group description: KPL-716 was administered subcutaneously at the dose of 120 mg every 4 weeks for 16 weeks during double blind period. | |
| Reporting group title | Arm D |
| Reporting group description: Placebo was administered subcutaneously every 4 weeks for 16 weeks during the double-blind period. | |
| Reporting group title | Treatment |
| Reporting group description: Open label extension participants who previously received KPL-716 during Double-Blind period. KPL-716 was administered subcutaneously at the dose of 360 mg every 2 weeks for 36 weeks (starting at week 16 and with the last dosing at the week 48 visit). | |
| Subject analysis set title | mITT efficacy analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All randomized subjects who receive at least 1 dose of KPL-716 or placebo and have at least 1 post-baseline efficacy assessment in the double-blind treatment period were included in the modified intent-to-treat (mITT) analysis set. | |

Primary: 1. Percent change from baseline in weekly average Worst Itch-Numeric Rating Scale (WI-NRS) at Week 16

| | |
|---|---|
| End point title | 1. Percent change from baseline in weekly average Worst Itch-Numeric Rating Scale (WI-NRS) at Week 16 |
| End point description: All efficacy analyses were performed in the mITT analysis set. | |
| End point type | Primary |
| End point timeframe: Percent change from baseline in weekly average WI-NRS was measured at week 16 using mITT analysis set | |

| End point values | Arm A | Arm B | Arm C | Arm D |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45 | 45 | 47 | 47 |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | -56.2 (± 35.7) | -51.2 (± 31.91) | -33 (± 34.31) | -14.8 (± 25.86) |

Statistical analyses

| | |
|--|------------------------|
| Statistical analysis title | Analysis of covariance |
| Statistical analysis description: The primary efficacy endpoint (percentage change from baseline of WI-NRS at Week 16) was analyzed with ANCOVA with treatment and randomization stratification factors of sex and years since the first nodule observed (i.e., ≥ 10 versus < 10 years) as fixed effect factors, baseline as covariates. | |
| Comparison groups | Arm A v Arm D |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| | |
|---|------------------------|
| Statistical analysis title | Analysis of covariance |
| Statistical analysis description: The primary efficacy endpoint (percentage change from baseline of WI-NRS at Week 16) was analyzed with ANCOVA with treatment and randomization stratification factors of sex and years since the first nodule observed (i.e., ≥ 10 versus < 10 years) as fixed effect factors, baseline as covariates | |
| Comparison groups | Arm B v Arm D |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| | |
|--|------------------------|
| Statistical analysis title | Analysis of covariance |
| Statistical analysis description: The primary efficacy endpoint (percentage change from baseline of WI-NRS at Week 16) was analyzed with ANCOVA with treatment and randomization stratification factors of sex and years since the first nodule observed (i.e., ≥ 10 versus < 10 years) as fixed effect factors, baseline as covariates. | |
| Comparison groups | Arm C v Arm D |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | $= 0.0061$ |
| Method | ANCOVA |

Secondary: 2.1 Proportion of subjects achieving at least a 6-point reduction from baseline in weekly average WI-NRS at Week 16

| | |
|-----------------|---|
| End point title | 2.1 Proportion of subjects achieving at least a 6-point reduction from baseline in weekly average WI-NRS at Week 16 |
|-----------------|---|

End point description:

All efficacy analyses were performed in the mITT analysis set.

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

End point timeframe:

Baseline up to week 16

| End point values | Arm A | Arm B | Arm C | Arm D |
|----------------------------------|---------------------|-------------------|--------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 47 | 47 | 46 | 48 |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 42.6 (28.3 to 57.8) | 23.4 (12.3 to 38) | 17.4 (7.8 to 31.4) | 2.1 (0.1 to 11.1) |

Statistical analyses

No statistical analyses for this end point

Secondary: 2.2 Proportion of subjects achieving at least a 4-point reduction from baseline in weekly average WI-NRS at Week 16

| | |
|-----------------|---|
| End point title | 2.2 Proportion of subjects achieving at least a 4-point reduction from baseline in weekly average WI-NRS at Week 16 |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline up to week 16

| End point values | Arm A | Arm B | Arm C | Arm D |
|----------------------------------|-------------------|---------------------|---------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 47 | 47 | 47 | 48 |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 66 (50.7 to 79.1) | 61.7 (46.4 to 75.5) | 29.8 (17.3 to 44.9) | 16.7 (7.5 to 30.2) |

Statistical analyses

No statistical analyses for this end point

Secondary: 2.3 Proportion of subjects achieving 0 or 1 in Prurigo Nodularis - Investigator Global Assessment at week 16

| | |
|-----------------|--|
| End point title | 2.3 Proportion of subjects achieving 0 or 1 in Prurigo Nodularis - Investigator Global Assessment at week 16 |
|-----------------|--|

End point description:

Proportion of subjects achieving clear (0) or almost Clear (1) in PN-IGA score at week 16 (mITT Analysis Set)

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

End point timeframe:

At week 16

| End point values | Arm A | Arm B | Arm C | Arm D |
|----------------------------------|---------------------|---------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 47 | 47 | 47 | 48 |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 38.3 (24.5 to 53.6) | 29.8 (17.3 to 44.9) | 14.9 (6.2 to 28.3) | 10.4 (3.5 to 22.7) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were observed or reported during the study from the time the subject signs the ICF through the EOS Visit. Serious Adverse Event and Adverse Event of Special Interest were reported to the Sponsor or designee within 24 hours of occurrence.

Adverse event reporting additional description:

Data presented here reports Treatment-Emergent Adverse Events of Any Grade Occurring in $\geq 5\%$ of the Subjects During the Double-Blind and Open-Label Extension Period (Safety Analysis Set)

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 26.0 |

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Double Blind-Arm A |
|-----------------------|--------------------|

Reporting group description:

KPL-716 was administered subcutaneously at the dose of 540 mg every 4 weeks for 16 weeks during double blind period.

| | |
|-----------------------|--------------------|
| Reporting group title | Double Blind-Arm B |
|-----------------------|--------------------|

Reporting group description:

KPL-716 was administered subcutaneously at the dose of 360 mg every 4 weeks for 16 weeks during the double-blind period.

| | |
|-----------------------|--------------------|
| Reporting group title | Double Blind-Arm C |
|-----------------------|--------------------|

Reporting group description:

KPL-716 was administered subcutaneously at the dose of 120 mg every 4 weeks for 16 weeks during double blind period.

| | |
|-----------------------|--------------------|
| Reporting group title | Double Blind-Arm D |
|-----------------------|--------------------|

Reporting group description:

Placebo was administered subcutaneously every 4 weeks during the double-blind period.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Open-Label Extension Period |
|-----------------------|-----------------------------|

Reporting group description:

Data presented here reports Treatment-Related Adverse Events of Any Grade Occurring in $\geq 5\%$ of the Subjects During the Open-Label Extension Period (Safety Analysis Set)

| Serious adverse events | Double Blind-Arm A | Double Blind-Arm B | Double Blind-Arm C |
|---|--------------------|--------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 0 / 47 (0.00%) | 1 / 47 (2.13%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Injury, poisoning and procedural complications | | | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fusion fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial Paralysis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |

| | | | |
|--|---------------------------|------------------------------------|----------------|
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal Ulcer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 1 / 47 (2.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Eczema nummular | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 0 / 47 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serious adverse events | Double Blind-Arm D | Open-Label Extension Period | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 48 (6.25%) | 8 / 181 (4.42%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|----------------|-----------------|--|
| Colon cancer | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 181 (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 | | | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 181 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fusion fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 181 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 181 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 181 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 181 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial Paralysis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 181 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |

| | | | |
|--|----------------|-----------------|--|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 181 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 181 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal Ulcer | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 181 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 181 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Eczema nummular | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 2 / 181 (1.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 181 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 181 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 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 | Double Blind-Arm A | Double Blind-Arm B | Double Blind-Arm C |
|--|----------------------|----------------------|---------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 35 / 47 (74.47%) | 29 / 47 (61.70%) | 21 / 47 (44.68%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Neoplasms benign, malignant and unspecified (incl cysts and polyps) subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 0 / 47 (0.00%) 0 | 1 / 47 (2.13%) 1 |
| Vascular disorders Vascular disorders subjects affected / exposed occurrences (all) | 3 / 47 (6.38%) 3 | 0 / 47 (0.00%) 0 | 2 / 47 (4.26%) 2 |
| General disorders and administration site conditions General disorders and administration site conditions subjects affected / exposed occurrences (all) | 7 / 47 (14.89%) 7 | 7 / 47 (14.89%) 7 | 4 / 47 (8.51%) 4 |
| Immune system disorders Immune system disorders subjects affected / exposed occurrences (all) | 2 / 47 (4.26%) 2 | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 |
| Reproductive system and breast disorders Reproductive system and breast disorders subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 0 / 47 (0.00%) 0 | 1 / 47 (2.13%) 1 |
| Respiratory, thoracic and mediastinal disorders Respiratory, thoracic and mediastinal disorders subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 2 / 47 (4.26%) 2 | 2 / 47 (4.26%) 2 |
| Psychiatric disorders Psychiatric disorders subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 1 / 47 (2.13%) 1 | 1 / 47 (2.13%) 1 |
| Investigations Investigations subjects affected / exposed occurrences (all) | 4 / 47 (8.51%) 4 | 5 / 47 (10.64%) 5 | 3 / 47 (6.38%) 3 |

| | | | |
|--|------------------------|------------------------|----------------------|
| Injury, poisoning and procedural complications Injury, poisoning and procedural complications subjects affected / exposed occurrences (all) | 6 / 47 (12.77%) 6 | 4 / 47 (8.51%) 4 | 5 / 47 (10.64%) 5 |
| Cardiac disorders Cardiac disorders subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 | 1 / 47 (2.13%) 1 |
| Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all) | 7 / 47 (14.89%) 7 | 3 / 47 (6.38%) 3 | 5 / 47 (10.64%) 5 |
| Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 0 / 47 (0.00%) 0 | 1 / 47 (2.13%) 1 |
| Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 |
| Eye disorders Eye disorders subjects affected / exposed occurrences (all) | 4 / 47 (8.51%) 4 | 1 / 47 (2.13%) 1 | 0 / 47 (0.00%) 0 |
| Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all) | 6 / 47 (12.77%) 6 | 5 / 47 (10.64%) 5 | 5 / 47 (10.64%) 5 |
| Hepatobiliary disorders Hepatobiliary disorders subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 | 1 / 47 (2.13%) 1 |
| Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all) | 10 / 47 (21.28%) 10 | 13 / 47 (27.66%) 13 | 5 / 47 (10.64%) 5 |
| Renal and urinary disorders | | | |

| | | | |
|--|------------------------|------------------------|------------------------|
| Renal and urinary disorders subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 |
| Endocrine disorders Endocrine disorders subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 | 0 / 47 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all) | 3 / 47 (6.38%) 3 | 1 / 47 (2.13%) 1 | 0 / 47 (0.00%) 0 |
| Infections and infestations Infections and infestations subjects affected / exposed occurrences (all) | 14 / 47 (29.79%) 14 | 11 / 47 (23.40%) 11 | 11 / 47 (23.40%) 11 |
| Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 4 / 47 (8.51%) 4 | 0 / 47 (0.00%) 0 |

| Non-serious adverse events | Double Blind-Arm D | Open-Label Extension Period | |
|--|----------------------|-----------------------------|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 26 / 48 (54.17%) | 135 / 181 (74.59%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Neoplasms benign, malignant and unspecified (incl cysts and polyps) subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 1 / 181 (0.55%) 1 | |
| Vascular disorders Vascular disorders subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 4 | 9 / 181 (4.97%) 9 | |
| General disorders and administration site conditions General disorders and administration site conditions subjects affected / exposed occurrences (all) | 7 / 48 (14.58%) 7 | 17 / 181 (9.39%) 17 | |
| Immune system disorders | | | |

| | | | |
|--|---------------------|------------------------|--|
| Immune system disorders subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 1 / 181 (0.55%) 1 | |
| Reproductive system and breast disorders Reproductive system and breast disorders subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 1 / 181 (0.55%) 1 | |
| Respiratory, thoracic and mediastinal disorders Respiratory, thoracic and mediastinal disorders subjects affected / exposed occurrences (all) | 2 / 48 (4.17%) 2 | 16 / 181 (8.84%) 16 | |
| Psychiatric disorders Psychiatric disorders subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 8 / 181 (4.42%) 8 | |
| Investigations Investigations subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 4 | 18 / 181 (9.94%) 18 | |
| Injury, poisoning and procedural complications Injury, poisoning and procedural complications subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 15 / 181 (8.29%) 15 | |
| Cardiac disorders Cardiac disorders subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 1 / 181 (0.55%) 1 | |
| Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 13 / 181 (7.18%) 13 | |
| Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 5 / 181 (2.76%) 5 | |

| | | | |
|--|------------------------|-------------------------|--|
| Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 3 / 181 (1.66%) 3 | |
| Eye disorders Eye disorders subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 5 / 181 (2.76%) 5 | |
| Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 4 | 22 / 181 (12.15%) 22 | |
| Hepatobiliary disorders Hepatobiliary disorders subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 1 / 181 (0.55%) 1 | |
| Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 49 / 181 (27.07%) 49 | |
| Renal and urinary disorders Renal and urinary disorders subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 2 / 181 (1.10%) 2 | |
| Endocrine disorders Endocrine disorders subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 1 / 181 (0.55%) 1 | |
| Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 25 / 181 (13.81%) 25 | |
| Infections and infestations Infections and infestations subjects affected / exposed occurrences (all) | 14 / 48 (29.17%) 14 | 87 / 181 (48.07%) 87 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|---------------------|------------------------|--|
| Metabolism and nutrition disorders subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 11 / 181 (6.08%) 11 | |
|--|---------------------|------------------------|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 06 August 2021 | EU specific Protocol Amendment v1.0_06Aug2021: Global Protocol v5.0, dated 21 December 2020, was updated to a European Union Regional Protocol, v1.0, dated 06 August 2021, to incorporate comments and changes requested by European Regulatory Authorities during the initial clinical trial application review process. In summary the following important updates were made: (1) Clarified that the PN-IGA measures the overall assessment at Week 16 (2) Clarifications on sexually active female subjects, methods of contraception, and pregnancy test sections were included (3) Exclusion criteria were revised to reduce screen failures (4) Subject withdrawal and replacement section was updated per Germany regulatory authority (5) A new subsection "Suspected Unexpected Serious Adverse Reactions" was added to Safety and Tolerability Assessments. |

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.

None

Notes: