**Participants flow**

**Excluded**

* Did not meet study criteria (n=6)
* Declined to participate n=1)

**Recruited and randomized (n=63)**

**Patients invited to participate (n=82)**

**Patients assessed for eligibility at preoperative visit (n=70)**

**Surgery (n=15)**

* Unexpected adverse effects (n=0)

**Surgery (n=16)**

* Unexpected adverse effects (n=0)

**Surgery (n=16)**

* Unexpected adverse effects (n=0)

**Surgery (n=16)**

* Unexpected adverse effects (n=0)

**3 months + 1 week (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**3 months + 1 week (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**1 week follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**1 week follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months + 3 months (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months + 3 months (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months + 3 months (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**3 months + 1 week (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**FIL618 group (n=15)**

**FIL611PV group (n=16)**

**SN6AD3 group (n=16)**

**SN6AD1 group (n=16)**

**1 week follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**6-months + 3 months (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**3 months + 1 week (other eye) follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up (controlateral eye)**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**1 week follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**First day follow-up**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**1month follow-up followed by Surgery in controlateral eye**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**1 month follow-up followed by Surgery in controlateral eye**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**1 month follow-up followed by Surgery in controlateral eye**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**1 month follow-up followed by Surgery in controlateral eye**

* Withdrawals (n=0)
* Unexpected adverse effects (n=0)

**Baseline characteristics**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **SN6AD1** | **SN6AD3** | **FIL611PV** | **FIL618** |
| **Total subjects** | 16 | 16 | 16 | 15 |
| **Male** | 10 | 7 | 7 | 9 |
| **Female** | 6 | 9 | 9 | 6 |
| **Mean age** | 72.9 | 71.8 | 70.87 | 70.8 |
| **Diabetes** | 5 | 3 | 3 | 2 |
| **Glaucoma (controlled)** | 1 | 2 | 1 | 1 |
| **Mean UCDVA (OD) (LogMAR)** | 0.61 | 0.58 | 0.75 | 0.66 |
| **Mean UCDVA (OS) (LogMAR)** | 0.74 | 0.49 | 0.71 | 0.75 |
| **Mean UCIVA (OD) (Jaeger)** | 7.2 | 8.9 | 7.57 | 9.2 |
| **Mean UCIVA (OS) (Jaeger)** | 5.1 | 10.8 | 6.50 | 12.41 |
| **Mean UCNVA (OD) (Jaeger)** | 8.02 | 8.06 | 8.00 | 10 |
| **Mean UCNVA (OS) (Jaeger)** | 7.20 | 9.10 | 7.50 | 13.33 |
| **Mean BCDVA (OD) (LogMAR)** | 0.52 | 0.39 | 0.30 | 0.27 |
| **Mean BCDVA (OS) (LogMAR)** | 0.45 | 0.48 | 0.37 | 0.37 |
| **Mean BCIVA (OD) (Jaeger)** | 3.8 | 4.2 | 3.67 | 4 |
| **Mean BCIVA (OS) (Jaeger)** | 4 | 4 | 3.44 | 4 |
| **Mean BCNVA (OD) (Jaeger)** | 3.24 | 3.58 | 3.9 | 4.25 |
| **Mean BCNVA (OS) (Jaeger)** | 3.9 | 3.5 | 3.54 | 3.14 |
| **UCDVA: uncorrected distance visual acuity; UCIVA: uncorrected intermediate visual acuity; UCNVA: uncorrected near visual acuity; BCDVA: best-corrected distance visual acuity; BCIVA: best-corrected intermediate visual acuity; BCNVA: best-corrected near visual acuity; OD: right eye; OS: left eye** | | | | |

**Outcome Measures**

Visual Acuity Outcome Measures – SN6AD1 group

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Mean Values (Standard Deviation) | | | | | |
|  | 1 day | 1 week | 1 month | 3 months | 6 months |
| UCDVA OD | 0.65 (0.42) | 0.40 (0.23) | 0.20 (0.28) | 0.14 (0.16) | 0.08 (0.10) |
| UCDVA OS | 0.65 (0.54) | 0.38 (0.47) | 0.24 (0.29) | 0.15 (0.17) | 0.10 (0.08) |
| UCIVA OD | 4.89 (0.42) | 4.24 (0.35) | 1.4 (0.10) | 1.01 (0.09) | 1 (0.01) |
| UCIVA OS | 5.12 (0.24) | 4.64 (0.24) | 1.6 (0.22) | 1.4 (0.08) | 1.01 (0.05) |
| UCNVA OD | 5.67 (0.34) | 4.48 (0.26) | 1.78 (0.14) | 1.03 (0.08) | 1.02 (0.03) |
| UCNVA OS | 6.14 (0.27) | 4.35 (0.38) | 2.01 (0.15) | 1.04 (0.05) | 1.04 (0.03) |
| BCDVA OD | 0,52 (0,48) | 0,25 (0.50) | 0.13 (0.30) | 0.07 (0.15) | 0,03 (0,06) |
| BCDVA OS | 0,53 (0,44) | 0,30 (0.42) | 0.13 (0.30) | 0.09 (0.11) | 0,04 (0,07) |
| BCIVA OD | 4.01 (0.45) | 2 (0.29) | 1.37 (0.66) | 1.03 (0.37) | 1.01 (0.44) |
| BCIVA OS | 4.01 (0.15) | 2 (0.35) | 1.57 (0.49) | 1.05 (0.08) | 1.02 (0.01) |
| BCNVA OD | 4.89 (0.79) | 2 (1.35) | 1.05 (0.16) | 1.01 (0.88) | 1.01 (0,01) |
| BCNVA OS | 4.86 (1.08) | 2 (0.99) | 1.06 (0.29) | 1.03 (0.02) | 1.02 (0,05) |
| UCDVA: Uncorrected Distance Visual Acuity (LogMAR); UCIVA: Uncorrected Intermediate Visual Acuity (Jaeger); UCNVA: Uncorrected Near Visual Acuity (Jaeger); BCDVA: Best-Corrected Distance Visual Acuity (LogMAR); BCIVA: Best-Corrected Intermediate Visual Acuity (Jaeger); BCNVA: Best-Corrected Near Visual Acuity (Jaeger); OD: Right Eye; OS: Left Eye | | | | | |

Visual Acuity Outcome Measures– SN6AD3 group

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Mean Values (Standard Deviation) | | | | | |
|  | 1 day | 1 week | 1 month | 3 months | 6 months |
| UCDVA OD | 0.65 (0.37) | 0.36 (0.20) | 0.16 (0.10) | 0.18 (0.24) | 0.14 (0.11) |
| UCDVA OS | 0.69 (0.48) | 0.32 (0.25) | 0.19 (0.13) | 0.17 (0.05) | 0.17 (0.12) |
| UCIVA OD | 5.23 (0.29) | 2.51 (0.13) | 1.86 (0.08) | 1.04 (0.04) | 1.08 (0.05) |
| UCIVA OS | 5.21 (0.26) | 2.52 (0.09) | 1.98 (0.04) | 1.08 (0.09) | 1.05 (0.07) |
| UCNVA OD | 5.68 (0.30) | 2.10 (0.20) | 1.05 (0.03) | 1.02 (0.08) | 1.03 (0.03) |
| UCNVA OS | 5.67 (0.33) | 2.79 (0.05) | 1.03 (0.09) | 1.04 (0.03) | 1.02 (0.03) |
| BCDVA OD | 0.49 (0.35) | 0.20 (0.78) | 0.07 (0.6) | 0.08 (0.05) | 0.07 (0.05) |
| BCDVA OS | 0.41 (0.33) | 0.19 (0.51) | 0.10 (0.6) | 0.07 (0.09) | 0.08 (0.09) |
| BCIVA OD | 3.78 (0.12) | 1.89 (0.08) | 1.35 (0.05) | 1.04 (0.04) | 1.03 (0.04) |
| BCIVA OS | 3.84 (0.17) | 2.02 (0.07) | 1.35 (0.04) | 1.09 (0.03) | 1.04 (0.05) |
| BCNVA OD | 4.73 (0.33) | 1.89 (0.30) | 1.01 (0.02) | 1.01 (0.02) | 1.01 (0.10) |
| BCNVA OS | 4.78 (0.35) | 1.99 (0.02) | 1 (0.05) | 1.01 (0.03) | 1.01 (0.02) |
| UCDVA: Uncorrected Distance Visual Acuity (LogMAR); UCIVA: Uncorrected Intermediate Visual Acuity (Jaeger); UCNVA: Uncorrected Near Visual Acuity (Jaeger); BCDVA: Best-Corrected Distance Visual Acuity (LogMAR); BCIVA: Best-Corrected Intermediate Visual Acuity (Jaeger); BCNVA: Best-Corrected Near Visual Acuity (Jaeger); OD: Right Eye; OS: Left Eye | | | | | |

Visual Acuity Outcome Measures – FIL611PV group

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Mean Values (Standard Deviation) | | | | | |
|  | 1 day | 1 week | 1 month | 3 months | 6 months |
| UCDVA OD | 0.66 (0.99) | 0.36 (0.14) | 0.15 (0.33) | 0.39 (1.01) | 0.39 (0.96) |
| UCDVA OS | 0.74 (1.53) | 0.36 (0.45) | 0.26 (0.11) | 0.34 (0.88) | 0.32 (0.79) |
| UCIVA OD | 4 (3.52) | 3.82 (1.56) | 3.45 (1.01) | 3.29 (1.16) | 3.27 (4.64) |
| UCIVA OS | 4.55 (3.86) | 3.77 (2.06) | 3.29 (1.12) | 3.30 (0.94) | 3.31 (1.05) |
| UCNVA OD | 4.40 (5.07) | 4.24 (2.26) | 3.56 (1.61) | 3.55 (0.07) | 3.53 (1.82) |
| UCNVA OS | 4.62 (3.31) | 4.56 (1.75) | 3.50 (2.02) | 3.57 (0.07) | 3.56 (0.06) |
| BCDVA OD | 0,56 (0,18) | 0,21 (0.62) | 0.12 (0.09) | 0.10 (0.08) | 0.10 (0.04) |
| BCDVA OS | 0,49 (0,73) | 0,28 (1.88) | 0.09 (0.12) | 0.09 (0.10) | 0.07 (0.09) |
| BCIVA OD | 3.04 (1,48) | 2.35 (1.77) | 1.68 (0.89) | 1 (0) | 1 (0) |
| BCIVA OS | 3.96 (2.16) | 2.55 (2.41) | 1.54 (1.07) | 1.01 (0.01) | 1 (0) |
| BCNVA OD | 3.92 (2,40) | 3.64 (0.84) | 3.20 (0.91) | 3 (0.06) | 3 (0.02) |
| BCNVA OS | 3.87 (1,99) | 3.33 (1.45) | 3.07 (1.00) | 3 (1.02) | 3 (0.46) |
| UCDVA: Uncorrected Distance Visual Acuity (LogMAR); UCIVA: Uncorrected Intermediate Visual Acuity (Jaeger); UCNVA: Uncorrected Near Visual Acuity (Jaeger); BCDVA: Best-Corrected Distance Visual Acuity (LogMAR); BCIVA: Best-Corrected Intermediate Visual Acuity (Jaeger); BCNVA: Best-Corrected Near Visual Acuity (Jaeger); OD: Right Eye; OS: Left Eye | | | | | |

Visual Acuity Outcome Measures – FIL618 group

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Mean Values (Standard Deviation) | | | | | |
|  | | 1 day | 1 week | 1 month | 3 months | 6 months |
| UCDVA OD | | 0.49 (0.31) | 0.44 (0.17) | 0.24 (0.21) | 0.23 (0.14) | 0.24 (0.24) |
| UCDVA OS | | 0.65 (0.31) | 0.56 (0.33) | 0.17 (0.24) | 0.18 (0.31) | 0.17 (0.19) |
| UCIVA OD | | 7.16 (10.2) | 6.42 (2.39) | 6.70 (2.85) | 6.70 (1.01) | 6.1 (3.69) |
| UCIVA OS | | 7.50 (8.16) | 7.33 (4.07) | 7.34 (2.49) | 7.05 (3.62) | 6.66 (4.37) |
| UCNVA OD | | 7.24 (6.04) | 7.01 (3.43) | 6.34 (2.75) | 6.82 (4.85) | 6.8 (3.82) |
| UCNVA OS | | 7.80 (3.49) | 7.80 (3.82) | 7.79 (4.16) | 7.71 (0.85) | 7.66 (4.81) |
| BCDVA OD | | 0,27 (0,17) | 0,42 (0.22) | 0.12 (0.18) | 0.04 (0.10) | 0,04 (0,06) |
| BCDVA OS | | 0,37 (0,33) | 0,39 (0.43) | 0.24 (0.08) | 0.09 (0.06) | 0,07 (0,07) |
| BCIVA OD | | 4 (1,51) | 4 (1.5) | 3.5 (1) | 3.2 (0.84) | 3,4 (0,89) |
| BCIVA OS | | 4 (1,51) | 4 (1.51) | 3.01 (1.8) | 3 (0.06) | 3 (0) |
| BCNVA OD | | 4,25 (1,48) | 3.89 (1.42) | 3.20 (0.81) | 3.20 (0.88) | 3,14 (0,89) |
| BCNVA OS | | 4 (1,51) | 4 (1.54) | 3.09 (0.84) | 3.10 (0.42) | 2,89 (0,33) |
| UCDVA: Uncorrected Distance Visual Acuity (LogMAR); UCIVA: Uncorrected Intermediate Visual Acuity (Jaeger); UCNVA: Uncorrected Near Visual Acuity (Jaeger); BCDVA: Best-Corrected Distance Visual Acuity (LogMAR); BCIVA: Best-Corrected Intermediate Visual Acuity (Jaeger); BCNVA: Best-Corrected Near Visual Acuity (Jaeger); OD: Right Eye; OS: Left Eye | | | | | | |

SN6AD1 group - Preoperative and 6-months follow-up additional correction (diopters) for intermediate and close-up distances, in order to achieve best-corrected binocular visual acuity at the relative range. SD = standard deviation.

|  |  |  |
| --- | --- | --- |
|  | **Pre-operative evaluation (t0). Mean value (SD)** | **6-months follow-up (t5). Mean value (SD)** |
|
| Additional for intermediate distances (D) | 2.84 (0,73) | 0.92 (0,48) |
| Additional for close-up distances (D) | 2,95 (0,67) | 1.01 (0,68) |

SN6AD3 group - Preoperative and 6-months follow-up additional correction (diopters) for intermediate and close-up distances, in order to achieve best-corrected binocular visual acuity at the relative range. SD = standard deviation.

|  |  |  |
| --- | --- | --- |
|  | **Pre-operative evaluation (t0). Mean value (SD)** | **6-months follow-up (t5). Mean value (SD)** |
|
| Additional for intermediate distances (D) | 2,75 (1.02) | 1,24 (0.44) |
| Additional for close-up distances (D) | 2,95 (0.71) | 0.99 (0.89) |

FIL611PV group - Preoperative and 6-months follow-up additional correction (diopters) for intermediate and close-up distances, in order to achieve best-corrected binocular visual acuity at the relative range. SD = standard deviation.

|  |  |  |
| --- | --- | --- |
|  | **Pre-operative evaluation (t0). Mean value (SD)** | **6-months follow-up (t5). Mean value (SD)** |
|
| Additional for intermediate distances (D) | 2,12 (1.68) | 0,9 (0.17) |
| Additional for close-up distances (D) | 2,75 (0.31) | 0,91 (0.51) |

FIL618 group - Preoperative and 6-months follow-up additional correction (diopters) for intermediate and close-up distances, in order to achieve best-corrected binocular visual acuity at the relative range. SD = standard deviation.

|  |  |  |
| --- | --- | --- |
|  | **Pre-operative evaluation (t0). Mean value (SD)** | **6-months follow-up (t5). Mean value (SD)** |
|
| Additional for intermediate distances (D) | 2,15 (0,38) | 1,41 (0,84) |
| Additional for close-up distances (D) | 2,95 (0,37) | 1,78 (0,89) |

**Adverse Events**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | SN6AD1 | SN6AD3 | FIL611PV | FIL618 |
| Transient/Expected Ocular Adverse Effects related to surgical procedure (Lasting < 7 Days) | Corneal edema | 4 | 5 | 1 | 2 |
| Subconjunctival hemorrhage | 0 | 1 | 0 | 1 |
| Mild ocular anterior segment inflammation | 1 | 0 | 1 | 0 |
| Transient ocular hypertension | 4 | 4 | 2 | 2 |
| Severe/Persistent Ocular Adverse Effects | n. a. | 0 | 0 | 0 | 0 |
| Extraocular adverse effects | n. a. | 0 | 0 | 0 | 0 |
| Life-Threatening Adverse Effects | n. a. | 0 | 0 | 0 | 0 |