Clinical Trials in Retinitis Pigmentosa Treatment

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If disposing of this product, please recycle the paper.

For the patients that have allowed us the privilege to serve.

Preface

This book is a compendium of the worldwide ocular stem cell, gene therapy, opto-genetic, and other miscellaneous studies treating Retinitis Pigmentosa registered with Clinicaltrials.gov. Clinicaltrials.gov is the largest website listing of registered clinical research studies in the world. The information presented is accurate as of September 2023. I have divided the studies into multiple categories: Completed, Active/Recruiting, Active/Not-Recruiting, Not Yet Recruiting, and Enrolling by Invitation. Regarding study location, United States locations are listed first, followed by other countries in alphabetical order.

I have corrected the mischaracterization of studies, to only include those that truly belong within each category, and to correct spelling and grammar, while maintaining the original spirit and intent of the researchers, so as to produce a consistent and easy-to-read format. The Study title and the clinical trial number are provided in order to make it easier for the reader to obtain further information.

I hope that by providing this reference, the field of retinitis pigmentosa treatment will be advanced.

Parkland, FL, USA   Jeffrey N. Weiss

Contents

Chapter 1
Introduction to Retinitis Pigmentosa

The term "retinitis pigmentosa" is generally attributed to Donders in 1855 and 1857, though evidence for its existence presumably dates back earlier to 1744 when Ovelgun reported cases of familial night blindness. The ophthalmoscope was invented by Helmholtz in 1851, and shortly thereafter, van Trigt (1853) and Ruete (1853) described cases of presumed retinitis pigmentosa (RP). The term is actually a misnomer, as inflammation is not a significant part of the condition.

RP is a spectrum, or a group of genetically determined degenerations characterized by rod dysfunction leading to cone loss. Depending on the severity of genetic expression, the patient may experience no significant symptoms, as in sector RP, or significant symptoms, such as night blindness (nyctalopia), visual field loss, loss of central vision, and blindness. The age of onset varies, depending on the type of RP, from infancy to adulthood.

Other terms have been used to describe the condition, including rod-cone dystrophy, pigmentary retinopathy, primary pigmentary retinal degeneration, and tapeto-retinal degeneration. RP is the inclusive term, but subtypes such as sector RP, inverse RP, and adult-onset RP have been described.

The prevalence of RP is 1 in 3500 (US), 1 in 4016 (China), 1 in 4500 (Israel), and 1 in 7000 (Switzerland). Though RP is a genetic condition, inherited as an autosomal recessive, autosomal dominant, or as an X-linked recessive trait, from 15% to 63% of cases has no family history of the condition. An estimated two million individuals worldwide are estimated to suffer from the disease. It is the leading cause of inherited blindness.

Nyctalopia is a common symptom of this condition. In autosomal recessive RP, the median age for developing nyctalopia is 10.7 years and, in the autosomal dominant condition, 23.4 years. Dark adaptometry may demonstrate elevation of the cone segment, the rod segment, or both. There may be a delay in reaching final dark adaptation.

Progressive visual field loss, initially manifested with smaller and dimmer test objects, is noted. The earliest visual field defects are frequently relative

midperipheral scotomas that enlarge over time forming ring scotomas. The visual field loss corresponds closely to the fundus appearance with greater field loss in the eye with more pigmentary abnormality.

RP patients have reported photopsias in their midperipheral visual field adjacent to the areas of relative or absolute scotomas. This is presumably caused by abnormal signals from the degenerating retina. The symptoms may be confused with ophthalmic migraine but differ in that the photopsias may be continuous and are generally stationary within the field. As the scotomas increase in density, the photopsias will diminish and disappear.

The earliest funduscopic abnormalities of RP are retinal vessel attenuation and fine retinal pigment epithelial mottling in the mid and far periphery. Retinal pigment epithelial disintegration migrates into the interstitial spaces at retinal vessels producing bone-spicules and perivascular pigment cuffing. Vessel attenuation may become severe over time. Fluorescein angiography may demonstrate RPE transmission defects, diffuse leakage, and cystoid macular edema. The prevalence of cataracts in patients with RP is dependent on the genetic defect and the patient age. Posterior subcapsular cataracts are the most common type of lenticular opacity.

There are multiple syndromes associated with RP:

1. Usher's Syndrome—The most common condition consisting of RP and deafness accounting for 50% of the patients who are both deaf and blind. Usher's syndrome may be divided into Type I, Type II, and Type III. Type I is the prepubertal onset of RP and profound prelingual deafness, and Type II with more a more variable expression of RP, possibly milder, and partial deafness. Type III (Hallgren's syndrome) is characterized by congenital deafness, RP, and vestibular ataxia. There is controversy whether this is a truly separate entity from Type I. A Type IV has also been described, associated with mental retardation, but this too may not be a separate entity from the more recognized Types I and II.

Other syndromes associated with RP include:

1. Abetalipoproteinemia (Bassen–Kornzweig syndrome)
2. Alstrom's disease
3. Arteriohepatic dysplasia (Alagille syndrome, cholestasis with peripheral pulmonary stenosis)
4. Bardet–Biedl syndrome
5. Cockayne's syndrome (Neill–Dingwall syndrome)
6. Flynn–Aird syndrome
7. Hallervorden–Spatz syndrome (Neuroaxonal dystrophy, late infantile)
8. Infantile Refsum's disease (infantile phytanic acid storage disease)
9. Refsum's disease (phytanic acid oxidase deficiency)
10. Jeune's syndrome (asphyxiating thoracic dystrophy; thoracic pelvic-phalangeal dystrophy)
11. Kearns–Sayre syndrome (chronic progressive external ophthalmoplegia (CPEO) plus)
12. Laurence–Moon Hutchinson syndrome

13. Mucopolysaccharidoses
14. Neuronal ceroid lipofuscinosis (Batten's disease)
15. Late infantile form (Jansky–Bielschowsky form)
16. Juvenile (Batten–Mayou disease, Vogt–Spielmeyer disease)
17. Adult (Kufs' disease)

Differential Diagnosis of RP

Rubella retinopathy may mistakenly be diagnosed as RP, as it can cause a similar panretinal pattern. This is more likely to occur in the presence of deafness, as the child is mistakenly diagnosed with rubella retinopathy and deafness, and not RP and deafness (Usher's syndrome). A distinguishing feature is the electroretinogram (ERG) which is normal or just mildly abnormal in rubella retinopathy, but is severely abnormal in Usher's syndrome.

Syphilis, congenital or acquired, may demonstrate a pigmentary retinopathy that is similar in appearance to advanced RP. Careful examination will distinguish between the two conditions. Congenital syphilis generally includes interstitial keratitis with patchy, post-inflammatory appearing pigmentary clumps involving the posterior pole as well as the posterior fundus with a possible overlying vitreous reaction. Acquired syphilis may resemble an advanced retinal degeneration.

Infections, such as toxoplasmosis, herpes, and cytomegalovirus, may produce a retinal appearance similar to RP. However, unless the entire retina is severely damaged, the ERG will be normal or mildly abnormal. A random and patchy lesion distribution may also serve to distinguish the correct cause.

Cancer-associated retinopathy may produce extensive panretinal degeneration as a remote effect of cancer, generally small-cell undifferentiated cervical carcinoma, or oat cell carcinoma of the lung. This is an immunologically mediated retinopathy presumably caused by a cross-reactive antigenicity between certain carcinomas and the retina. Loss of vision and retinopathy may be rapid or slow. With severe loss of vision, the ERG will be severely abnormal, even in the presence of a normal fundus examination.

Thioridazine is a phenothiazine that has been demonstrated to cause severe retinal toxicity and a pigmentary retinopathy similar to that seen with RP or choroideremia. ERG testing may demonstrate subnormal a and b wave responses.

Chlorpromazine, when taken for long duration at a high dose, has also caused a pigmentary retinopathy. Retinal function is not significantly affected. The retinopathy may regress when the drug is discontinued.

Chloroquine, when taken for a prolonged duration at high dose, may also cause a pigmentary retinopathy. Unlike in RP, dark adaptometry may be normal, or just mildly abnormal. Bone-spicules may be seen in the mid and far periphery and a bulls-eye maculopathy may be noted.

Pigmented paravenous retinochoroidal atrophy has been reported in association with a family history of tuberculosis, syphilis, rubella, or in association with

tuberculosis or meningoencephalitis. The pigment clumping is in association with the retinal veins and is generally stable over time. The ERG may be mildly to moderately abnormal, but the EOG can be severely abnormal.

A traumatic injury may lead to a unilateral pigmentary retinopathy simulating unilateral RP.

Diffuse unilateral subacute neuroretinitis is a panretinal pigmentary retinopathy resulting from an infection with various kinds of worms. The patient has normal vision until a certain age when a visual disturbance develops. The retina may appear normal or show evidence of early retinal degeneration. A living nematode is sometimes observed. The funduscopic picture may eventually resemble that seen in advanced RP. The fellow eye remains normal. The course is as expected for an acquired parasitic infection.

Retinal pigment hypertrophy, or grouped pigmentation of the retina, also known as "bear track pigmentation" is a benign and congenital condition. Areas of pigment hypertrophy are scattered throughout the retina. Retinal function tests are normal.

Stem Cells

Human mesenchymal stem cells (hMSCs) are able to differentiate into different tissues in vitro, are multipotent, and are capable of renewing themselves. However, a major difference between the in vivo hMSCs and the manufactured pharmaceutical product is that in vivo hMSCs also provide trophic factors which induce intrinsic stem cells to repair tissue and to modulate the immune system.

The original premise was that stem cells would migrate to the site of injury and stimulate tissue repair. It now appears that the original theory was incorrect. hMSCs have been determined to be perivascular cells. They express cellular markers CD10, CD13, CD44, CD73, CD90, CD105, and CD146. hMSCs do not differentiate into the damaged tissue, but provide the signaling immunomodulatory and trophic factors that stimulate other tissue-specific progenitor cells to regenerate the injured tissue. Rather than the term "stem cells," the new proposed term is "Medicinal Signaling Cells." hMSCs have high immunomodulatory potential. They alter antigen-presenting maturation, inhibit T-cell expansion and recognition, and promote lymphocyte T helper (Th2) response by increasing interleukin 10 (IL-10) and inhibiting tumor necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ).

There are two main types of mesenchymal stem cells (MSCs) used in clinical studies. Adult MSCs include those derived from bone marrow, peripheral blood, adipose tissue, and dental pulp and neonatal-derived MSCs from umbilical cord, amnion, and placenta. Bone-marrow-derived MSCs are the most popularly used cells in clinical trials and have been shown to be beneficial in clinically relevant models.

Induced pluripotent stem cells or iPSC are pluripotent stem cells that can be derived from a somatic cell, such as skin or blood cells. In 2006, Yamanaka and

Takahashi demonstrated that the introduction of four specific genes could change somatic into pluripotent cells. As such, they bypass the ethical dilemma of destroying an embryo to produce embryonic stem cells. Like embryonic stem cells, there is the risk of tumor formation. In addition, the efficiency of reprogramming a somatic cell to an iPS cell is low.

Chapter 2
Treatments for Retinitis Pigmentosa

From an historical perspective, it was once thought that limited light exposure might slow the progression of retinitis pigmentosa (RP), but no effect was found. Likewise, there was no benefit of an increased intake of vitamin A, although vitamin E intake was found to be deleterious.

Gene-independent, neuroprotective strategies are under study, including: rod-derived cone viability factor, N-acetyl cysteine, and NFE2-like bZIP transcription factor 2 (previously known as *NRF2*). Gene-specific therapies are progressing, along with strategies for end-stage disease in which there are no rods or cones (e.g., optogenetics).

At the present time, the only FDA approved treatment is Luxturna® (voretigene neparvovec) for a small sub-population of patients that have the RPE65 mutation, which represents 0.3–1% of total RP cases. Luxturna is an adeno-associated virus vector-based gene therapy.

Twelve patients (mean age 13.5 years ±7.9 years) were treated with Luxturna with 1 year of follow-up. They reported an improvement in best corrected visual acuity (BCVA) of −0.21 (±0.14; $P < 0.001$) an improvement on a full-field stimulus threshold (FST) test white light sensitivity thresholds of −26.3 (±10.7, $P < 0.001$), and using chromatic pupillometry, an improvement in maximum pupillary constriction in response to blue and white stimulus at 10 lux level ($P < 0.05$). There was an enlargement of the semi-automated kinetic visual field (SKVF) using I4e ($1921.7 \pm 3247.3^{\circ 2}$; $P = 0.011$) and III4e ($2478 \pm 3659.7^{\circ 2}$; $P < 0.001$).

Bilateral retinal atrophy was observed in 4/12 patients at 6 months of follow-up, but this adverse event was not associated with worse outcomes on the efficacy measures, except in the SKVF using I4e stimulus size, in which patients with retinal atrophy showed significantly less improvement in their eyes ($159.9 \pm 1309.9^{\circ}$) compared to the eyes of patients who were not experiencing retinal atrophy ($2802.6 \pm 3589.6^{\circ}$; $P = 0.033$).

Luxturna costs $425,000 per eye, for one treatment.

However, Oxford Eye Hospital reported a retrospective study of 5 Luxturna treated patients which did not find significant improvement in BCVA. The BCVA for treated patients (19–51 years, mean 35.6) was similar at the last follow-up (1.17 LogMAR; ±0.38) to the mean BCVA at baseline (1.15 LogMAR; ±0.47; $P = 0.93$). Improvements were observed in FST testing.

Ghent University Hospital reported that a study of eight treated Belgian patients (6–54 years, mean 27.5) did not demonstrate a statistically significant improvement in BCVA, but an improvement in FST testing was noted.

A potential treatment for RP is the use of optogenetics to control neuron activity with light. Genes for light sensitive proteins are introduced into cells, so they may be controlled using light. Spatial selectivity is important, that is, there needs to be a spectral separation, where channels are activated by different wavelengths of light.

The RESTORE clinical trial, conducted by Nanoscope Therapeutics Inc., is a Phase 2b multicenter, randomized, double-masked, sham-controlled clinical trial (clinical trials NCT04945772) of their product, multi-characteristic opsin (MCO)-010 (sonpiretigene isteparvovec), and an ambient-light activatable MCO optogenetic therapy. Eighteen patients with severe vision impairment due to RP received a single intravitreal injection of MCO-010, and nine received a sham intravitreal injection.

Twelve-month results:

- 18 of 18 (100%) MCO-010-treated patients showed vision improvement in the multi-luminance Y-mobility test (MLYMT), multi-luminance shape discrimination test (MLSDT) or BCVA compared to 5 of 9 (55.6%) receiving placebo ($P = 0.007$).
- 17 of 18 (94.4%) MCO-010-treated patients showed vision improvement in the MLYMT or BCVA compared to 4 of 9 (44.4%) receiving placebo ($P = 0.008$).
- 16 of 18 (88.9%) MCO-010-treated patients demonstrated a 2 or more luminance-level improvement in the MLYMT or MLSDT compared to 4 of 9 (44.4%) receiving placebo ($P = 0.02$).
- 14 of 18 (77.8%) MCO-010-treated patients showed vision improvement in the MLSDT or BCVA compared to 3 of 9 (33.3%) receiving placebo ($P = 0.04$).

The most common ocular treatment emergent adverse events reported across treatment arms were anterior chamber cells, ocular hypertension, and conjunctival hemorrhage.

Chapter 3
Notes

The rationale for proprietary stem cell products has been to replace the damaged retinal tissue. However, this basic premise may be incorrect if the new cells do not engraft, but purely serve to stimulate other already present cells to heal. In addition, when the proprietary cells alone are injected, in the absence of the platelet-rich plasma, as occurs when autologous bone-marrow-derived stem cells (BMDsc) are used, there is an absence of the other beneficial growth factors.

Could this be the reason why no proprietary product used in retinal or optic nerve "stem cell" trials have proven more successful than the autologous bone marrow we use in the stem cell ophthalmology study (SCOTS)?

I am the Principal Investigator of the SCOTS I and II studies. SCOTS I began in 2012 and continues to the present time as SCOTS 2 (ClinicalTrials.gov ID NCT03011541). The original SCOTS1 had three arms. Arm 1 is the retrobulbar, subtenon, and intravenous injections of the autologous BMDsc, Arm 2 is the intra-vitreal and intravenous injections of BMDsc, and Arm 3 is the placement of the BMDsc in the subretinal space for retinal conditions, or directly into the optic nerve, for optic nerve conditions.

Arm 3 was discontinued in mid-2017, as in the absence of an anchor or scaffold, subretinal cell placement dissipates over time. Figures 3.1, 3.2, and 3.3 the visual results were similar to Arm 2. Arm 2 was discontinued later that same year, as the results were similar to those obtained in Arm 1. We have been exclusively been performing Arm I since that time.

Retinal detachment has been a significant complication of the subretinal place-ment of cells. Cells migrate to the point of instrument insertion and produce mem-branes, opening the hole in the retina and producing a retinal detachment. I developed a shelved, self-sealing needle and there have been no retinal detachments when I was still performing Arm 3 of SCOTS. No laser or gas was needed after cell insertion.

However, is direct placement of cells even necessary? As you can see, the major-ity of cells disappear over time. Sometimes, pigment remains (see below) (Fig. 3.4).

Fig. 3.1 One-week postoperative subretinal cell placement. At the time of surgery, the entire area of atrophy was covered with cells. Despite instructions to the contrary, the patient reported sleeping on their right side. Note that the cells have migrated to the right
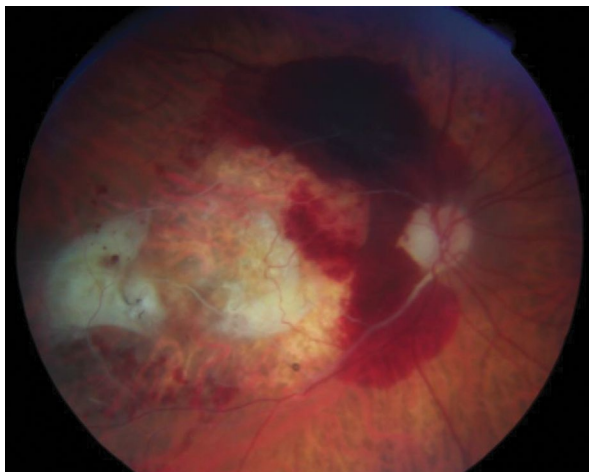
Fig. 3.2 Three weeks postoperatively. The cells continue to dissipate

In addition, what is the rationale for intravitreal injections? If there is no engraftment, but a stimulation of already present cells, might subtenon and retrobulbar injections work equally as well? That is what we found in SCOTS. Sometimes, what seems the most obvious, isn't.

Years ago, I was an investigator in the early treatment diabetes retinopathy study. The diabetic retinopathy study proved that laser photocoagulation in the presence of significant proliferative diabetic retinopathy, as defined in the study, was effective in reducing blindness. It seemed obvious that earlier treatment would result in better results. And yet it didn't. That's why I say what seems "obvious" isn't always, which is why we do studies, and not just accept a theory without proof. Hypothesis must fit facts, not the other way around.

As the injected cells are opaque, patients who received an intravitreal injection in Arm 2 of SCOTS complained of seeing a "glob" or a "cloud" in their vision. In a

Fig. 3.3 Ten weeks postoperatively. The surgically implanted cells have disappeared
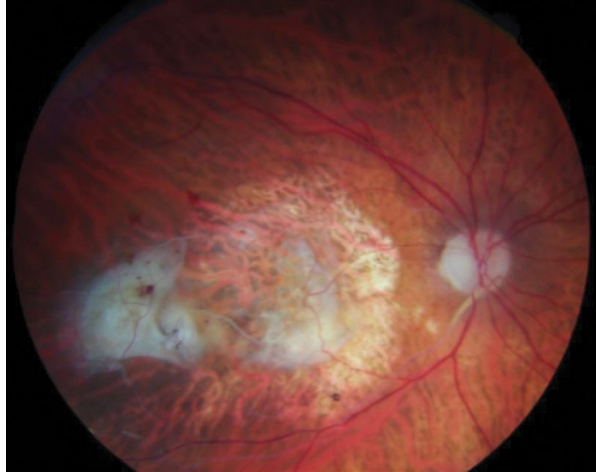
Fig. 3.4 Five months postoperatively

vitrectomized eye, the cells dissipated with a more severe decrease in the patient's vision after the procedure. However, we found that the visual results of the intravitreal injection were similar to those undergoing the retrobulbar and subtenon injections. As a result, we no longer perform intravitreal injections. Patients are happy and there is a lower potential risk of a complication.

Part I
Stem Cell Studies

Chapter 4
Completed Stem Cell Studies

Completed Studies

United States

Safety of Repeat Intravitreal Injection of Human Retinal Progenitor Cells (jCell) in Adult Subjects with Retinitis Pigmentosa

ClinicalTrials.gov ID NCT04604899

Sponsor jCyte, Inc
Information provided by jCyte, Inc (Responsible Party)
Last Update Posted 2022-08-10

Brief Summary

The primary objective of the study is to assess the safety of repeat injection of human retinal progenitor cells (jCell) in adult subjects with retinitis pigmentosa (RP) that have previously been treated with jCell.

Detailed Description

This is a prospective, multi-center, single arm, Phase 2 study of human retinal progenitor cells (jCell) for the treatment of RP. The study will include only subjects previously treated with jCell.

To assess reinjection of a previously treated eye, subjects who have previously been treated with jCell and desire a second treatment in the same eye will be enrolled. Subjects must have completed at least 12 months of follow-up since the prior injection of jCell. Subjects who have had both eyes previously treated with jCell will only have one eye retreated; the eye to be retreated will preferably be the better seeing eye, but exceptions may be made by the study investigator, taking into consideration best corrected visual acuity (BCVA), prior response to treatment, and

any other medical conditions that may indicate which eye is the best candidate for retreatment. Subjects will be followed for 12 months for safety and efficacy.

Official Title

A Phase 2 Study of the Safety of Repeat Intravitreal Injection of Human Retinal Progenitor Cells (jCell) in Adult Subjects with Retinitis Pigmentosa (RP)

Conditions

Retinitis Pigmentosa

Intervention/Treatment

Biological: human retinal progenitor cells
Interventional Model: Single Group Assignment
Masking: None (Open Label)

Arms and interventions

Participant group/arm	Intervention/treatment
Experimental: Retreated subjects Subjects receiving human retinal progenitor cells (jCell) who have previously received jCell is a jCyte study	Biological: human retinal progenitor cells • Single intravitreal injection of 6.0 million human retinal progenitor cells (hRPC) • Other Names: – jCell

Primary outcome measures

Outcome measure	Measure description	Time frame
Safety of intravitreal injection of hRPC	Assessed by proportion of subjects with treatment emergent adverse events	12 months

Secondary outcome measures

Outcome measure	Measure description	Time frame
Best corrected visual acuity	Assessed by E-ETDRS	12 months
Visual fields	The Octopus 900 will be used for kinetic visual field testing using a specified target of V4e for more severe subjects and a target of III4e and V4e for better seeing subjects	12 months
Contrast sensitivity	The Beethoven System will be used to capture the peak mean contrast sensitivity threshold value at any given spatial frequency	12 months
Mobility	Maze testing	12 months

Results

Arm/Group Title	Retreated Subjects
Arm/Group Description	Subjects receiving human retinal progenitor cells (jCell) who have previously received jCell is a jCyte study Human retinal progenitor cells: single intravitreal injection of 6.0 million human retinal progenitor cells (hRPC)

Quality Control Review Comment provided by the National Library of Medicine:
  1. The Enrollment number appears inconsistent with information in other parts of the record

Period Title: Overall Study	
Started	30[a]
Completed	23
Not Completed	7

[a] 31 total subjects were enrolled but only 30 were treated; one was determined to have met the exclusion criteria after enrollment but prior to treatment

1. Primary Outcome:	
Title	Safety of Intravitreal Injection of hRPC
Description	Assessed by proportion of subjects with treatment emergent adverse events (TEAE)
Time Frame	12 months
Outcome Measure Data	
Analysis Population Description	
Safety population: all subjects who receive any study treatment	
Overall Number of Participants Analyzed	30
Measure Type: Number Unit of Measure: Subjects	
Subjects with any TEAEs	15 50%
Subjects with any TEAEs related/ possibly related to study drug	6 20%
Subjects with any serious TEAEs	6 20%
Subjects with any serious TEAEs related/possibly related to study drug	2 6.7%
Subjects with any severe TEAEs related/possibly related to study drug	1 3.3%
2. Secondary Outcome:	
Title	Best Corrected Visual Acuity
Description	Assessed by E-ETDRS
Time Frame	12 months
Outcome Measure Data Not Reported	
3. Secondary Outcome:	
Title	Visual Fields
Description	The Octopus 900 will be used for kinetic visual field testing using a specified target of V4e for more severe subjects and a target of III4e and V4e for better seeing subjects
Time Frame	12 months
Outcome Measure Data Not Reported	
4. Secondary Outcome:	
Title	Contrast Sensitivity
Description	The Beethoven System will be used to capture the peak mean contrast sensitivity threshold value at any given spatial frequency
Time Frame	12 months

Outcome Measure Data Not Reported	
5. Secondary Outcome:	
Title	Mobility
Description	Maze testing
Time Frame	12 months
Outcome Measure Data Not Reported	
▼ Adverse Events	
Time Frame	12 months
Adverse Event Reporting Description	[Not specified]
All-Cause Mortality	
	Retreated Subjects
	Affected/At Risk (%)
Total	2/30 (6.67%)
Serious Adverse Events	
	Retreated Subjects
	Affected/At Risk (%)
Total	6/30 (20%)
Cardiac disorders	
Acute left ventricular failure[a]	1/30 (3.33%)
Ear and labyrinth disorders	
Vertigo positional[a]	1/30 (3.33%)
Eye disorders	
Tractional retinal detachment[a]	1/30 (3.33%)
Vitreoretinal traction syndrome[a]	1/30 (3.33%)
Infections and infestations	
COVID-19[a]	1/30 (3.33%)
COVID-19 pneumonia[a]	1/30 (3.33%)
Pneumonia[a]	1/30 (3.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Non-small cell lung cancer[a]	1/30 (3.33%)
Nervous system disorders	
Cerebrovascular accident[a]	1/30 (3.33%)
Psychiatric disorders	
Hallucination[a]	1/30 (3.33%)
Respiratory, thoracic and mediastinal disorders	
Chronic obstructive pulmonary disease[a]	1/30 (3.33%)
Pleural effusion[a]	1/30 (3.33%)
Pulmonary embolism[a]	1/30 (3.33%)
Quality Control Review Comment provided by the National Library of Medicine: 1. Required information appears to be missing	
Other (Not Including Serious) Adverse Events	
Frequency Threshold for Reporting Other Adverse Events	5%
	Retreated Subjects
	Affected/At Risk (%)

Total	8/30 (26.67%)
Eye disorders	
Conjunctival hemorrhage[a]	6/30 (20%)
Infections and infestations	
COVID-19[a]	2/30 (6.67%)

Quality Control Review Comment provided by the National Library of Medicine:
    1. Required information appears to be missing

[a] Indicates events were collected by systematic assessment

Completed

United States

Safety and Efficacy of Intravitreal Injection of Human Retinal Progenitor Cells in Adults with Retinitis Pigmentosa

ClinicalTrials.gov ID NCT03073733

Sponsor jCyte, Inc
Information provided by jCyte, Inc (Responsible Party)
Last Update Posted 2022-04-04

Brief Summary
This study evaluates the changes in visual function at 12 months following a single injection of human retinal progenitor cells compared to sham-treated controls in a cohort of adult subjects with RP.

Detailed Description
There is no effective treatment for RP; once photoreceptors are lost, they do not regenerate. The rate of deterioration of vision varies from person to person, with most people with RP legally blind by age 40. Preclinical studies demonstrated that transplantation of retinal progenitor cells into the eye can result in both photoreceptor replacement and significant slowing of host photoreceptor loss. Thus, the primary goal of this therapy is to preserve, and potentially improve, vision by intervening in the disease at a time when dystrophic host photoreceptors can be protected and reactivated. Based on the demonstration of acceptable safety and tolerability in a phase 1/2a study, this phase 2b study is designed as a controlled comparison of the changes in visual function and functional vision in subjects who receive a single jCell injection in comparison with a comparable sham-treated control group of subjects with RP.

Official Title
A Prospective, Multicenter, Randomized, Study of the Safety and Efficacy of Intravitreal Injection of Human Retinal Progenitor Cells (jCell) in Adult Subjects with Retinitis Pigmentosa (RP)

Conditions
Retinitis Pigmentosa

Study Type
Interventional

Enrollment (Actual)
84

Intervention/Treatment
Biological: human retinal progenitor cells
Other: Mock injection

Phase
Phase 2

Study Start (Actual)
2017-03-01

Primary Completion (Actual)
2020-11-13

Study Completion (Actual)
2020-11-13

Primary Purpose: Treatment
Allocation: Randomized
Interventional Model: Parallel Assignment
Masking: Double

Arms and interventions

Participant group/arm	Intervention/treatment
Experimental: Test (jCell injection) dose level 1 single intravitreal injection of $3.0 \times 10e6$ human retinal progenitor cells into the eye with the poorest visual acuity or, if vision is comparable in both eyes, the non-dominant eye	Biological: human retinal progenitor cells • Live suspension of 3.0 or $6.0 \times 10e6$ human retinal progenitor cells (hRPC) suspended in clinical grade medium injected intravitreally under local anesthesia • Other Names: – jCell
Other: Sham-treated Control a mock injection will be performed on the eye with the poorest vision in each Control subject (designated as the "study eye")	Other: Mock injection • Pressing the hub of a syringe with no needle against the eye to mimic intravitreal injection
Experimental: test (jCell injection) dose level 2 single intravitreal injection of $6.0 \times 10e6$ human retinal progenitor cells into the eye with the poorest visual acuity or, if vision is comparable in both eyes, the non-dominant eye	Biological: human retinal progenitor cells • Live suspension of 3.0 or $6.0 \times 10e6$ human retinal progenitor cells (hRPC) suspended in clinical grade medium injected intravitreally under local anesthesia • Other Names: – jCell

Primary outcome measures

Outcome measure	Measure description	Time frame
Best Corrected Visual Acuity (BCVA)	Mean change in BCVA in study eye from baseline to month 12 as assessed by E-ETDRS in ITT population. A letter score is used to compare change over time, with a higher number of letters representing better visual function, and a lower number of letters representing worse visual function. For example, 85 letters is equivalent to 20/20 visual acuity and 5 letters is equivalent to 20/800 visual acuity. A change value is derived for each subject by taking the letter score at 12 months and subtracting the letter score at baseline. A mean of all change values is then calculated for each arm	12 months

Secondary outcome measures

Outcome measure	Measure description	Time frame
Contrast Sensitivity (CS) at 1.0 CPD	Assessment of the ability to detect changes in shades of grey, as measured with a vertical striped pattern that varies in width (cycles per degree or CPD); CS thresholds are created by taking the mean of multiple trials at each pattern width. A CS curve is created using a minimum of three pattern widths, one at the subject's peak or highest sensitivity, and then one larger and smaller pattern width on either side of the peak. For example, if a subject's CS peak appears to be at 2.0 CPD, then additional testing occurs at 1.0 and 4.0 CPD. RP patients have suppressed CS curves and the most common pattern widths are at 0.5, 1.0, 2.0, and 4.0 CPD. Severely impaired subjects (e.g., BCVA <20/400) usually have flat curves with low values (e.g., 1.28), while in mildly impaired RP subjects the values can be higher (e.g., 7.12), but are rarely near normal. These data represent mean change in CS from baseline to 12 months, with greater values representing greater improvement in visual function	12 months
Kinetic Visual Field (KVF)	Mean change in total area (degrees squared) of all islands of vision from baseline to 12 months	12 months
Low Luminance Mobility Test (LLMT)	The LLMT identifies the performance of RP patients as they walk along an indoor pathway of arrows and obstacles at varying lighting levels. The Critical Illumination Level (CIL) is the light level below which the patient has a markedly slower pace and more errors than all light levels above (brighter than) that point. The LLMT uses light levels that go from very dim (0.12 lux) to a bright indoor room (500 lux), with evenly spaced increments that increase light by doubling the brightness of the room from the prior level. These evenly spaced light levels have been converted to a scale score to enable easier calculation of change scores. The dimmest light level of 0 lux (completely dark room) corresponds to a scale score of 13, whereas the brightest light level of 500 lux corresponds to a scale score of 0. A positive scale score change from baseline to 12 months represents improvement in low light vision, whereas a negative scale score change represents a decline in low light vision	12 months