XXN-I Semiconductor Laser Treatment Instrument Clinical Trial Report

Product: Semiconductor Laser Treatment Instrument

Type: XXN-I

Applicant: Thinkman (Beijing) Technology Co., Ltd.

Clinical Trial Institution:

Beijing Chao-Yang Hospital, Capital Medical University

The Military General Hospital of Beijing PLA

Class of clinical trial: Clinical validation class II

1. General clinical data (selection of disease category, total number of cases, cases)

1. Indications

Hyperlipidemia and the accompanying sub-health symptoms such as dizziness, weariness, insomnia, amnesia, and chest pain

2. Contraindications

(1) Cancer and coagulation disorders

(2) Severe cardiac diseases and pregnant women

(3) Bleeding tendency

3. Case selection

(1) Inclusion criteria

(1) Voluntary signing of informed consent form

(2) Age >18 years, female or male

(3) Diagnostic basis of hyperlipidemia by detection of total cholesterol, triglyceride and low-density lipoprotein in blood

(4) No intake of lipid-lowering drugs 2 weeks before the experiment

(5) Ability to achieve good communication with the researchers and comply with the experimental requirements

(2) Exclusion criteria

(1) Refusal to sign informed consent form

(2) Photosensitivity, platelet and coagulation disorder, or patients taking oral anticoagulants and antiplatelet agents

(3) Patients in acute stage of bleeding disorder (systematic, local or intracranial hemorrhage)

(4) Severe cardiac, hepatic, lung and renal failure

(5) Systemic failure or low immune functions

(6) Cancer, angina, or women in pregnancy

(7) Neurological and psychiatric disorders that prevent collaboration with researchers

(8) Other situations considered to prevent participation in the research

4. Selection of the number of cases and justification

The security and efficacy of the tested device are verified. The detection results are compared by self-control study (before and after treatment). The assessment indices are qualitative, and the non-inferiority test is performed. According to the efficacy of the approved devices of the similar type and statistical requirements, assume α=0.05, β=0.2; equivalent standard δ=0.15, and mean efficacy P=0.95.

The calculation formula is $N = 12.365 \times P \times (1–P) \div \delta 2$.

Then $N = 12.365 \times P \times (1–P) \div \delta 2 = 26.10389 \approx 27$

N: Number of cases in each group N1=N2; N1 and N2 are the numbers of cases treated by the test and control devices, respectively.

P: Mean efficacy

δ: Equivalent standard

α: Significance level, or false positive rate

β: 1–β is the power of test

According to the calculation with the above formula, 27 cases need to be recruited. Under the 10% dropout rate, the experimental and control groups need to include 30 cases each. Thus, for each of the two institutions undertaking the clinical trial, the experimental and control groups should include 15 cases. Thus, there will be a total of 60 valid cases recruited to meet the design requirements.

2. Methods of clinical trial (including the setting of the control groups when necessary)

(1) Overall design

In accordance with the decree No. 5 of the China Food and Drug Administration, 60 patients will be recruited, and two hospitals undertake the clinical trials. The clinical validation is performed using parallel control and non-inferiority tests. For each hospital, the experimental and control groups include 15 patients. The researchers should record the main complaints and the results of special and auxiliary examinations. The patients will be treated by the test and control devices, respectively. The assessment indicators are recorded, and the complications and adverse events during treatment are observed. The recruited patients should meet the inclusion conditions and sign the informed consent form.

2. Test device and control device

(1) Test device

Manufacturer: TinkM (Beijing) Technology Co. Ltd.

Product: XXN-I Semiconductor Laser Treatment Instrument

Type: XXN-I

Product standard: YZB/Beijing 0741-2010

(2) Control product

Manufacturer:

Product name: Semiconductor Laser Treatment Instrument

Type: see attachment

Registration No.:

3. Statistical method and evaluation method used

The statistical analysis is performed using SPSS version16.0. The data of all patients satisfying the scheme requirements are used for statistical analysis.

The conclusion is derived by statistical inference. $P \leq 0.05$ is considered to be a statistically significant difference; the confidence interval is selected as 95%.

The quantitative indicators include the number of cases, mean, standard deviation (SD), median, minimum value and maximum value. Depending on data distribution, the *t* test, *t′* test or signed rank sum test is used to draw statistical inference.

The classification indices are described by the number of cases and percentage for each category. For the classification indices, the χ^2 test or Fisher's exact test is used to draw the statistical inference.

Class indices are described using the number of cases and percentage for each category. The rank sum test or regression analysis of the repeated measurements is performed to draw the statistical inference.

4. Standards for clinical assessment

1. Standards for security assessment

(1) Routine examination: respiratory rate, blood pressure, heart rate, pulse

(2) Allergic reaction: pruritus, skin rash, skin rupture

(3) Adverse event: adverse event and severe adverse event

2. Standards for efficacy assessment

Laboratory blood lipid indicators: serum cholesterol, triglyceride, low-density lipoprotein

Diagnostic standards: diagnostic basis for hyperlipidemia accords with the standards of the Microcirculation Branch, Chinese Association of Pathophysiology, 1989.

Total cholesterol >6.5 mmol/L, triglyceride >1.7 mmol/L, low-density lipoprotein >3.1 mmol/L. Any of the indicators above exceeding the normal level indicates hyperlipidemia.

Standards for efficacy assessment

Marked effect: After two courses of treatment, the abnormal indicators of blood lipids restore to normal or decrease considerably (decrease ≥50%).

Effective: After two courses of treatment, the abnormal indicators of blood lipids decrease (decrease <50% or subjective symptoms alleviated without obvious decrease in abnormal indicators).

No effect: After two courses of treatment, the abnormal indicators of blood lipids have no change, and the subjective symptoms are not alleviated.

According to the above standards for efficacy assessment, the efficacy classes of the experimental group are compared. The proportion of the patients showing a marked effect plus that showing improvement is the total efficacy.

3. Standards for operational assessment

Assessment items	Semiconductor laser treatment instrument	Assessment	
Appearance	Logo	Clear and accurate □	Obscure □
	Product appearance	No mechanical damage, scratching or cracks; the surface is neat and attractive. □	Poor □
Application performance	Laser output	Stable output □	Stable output □
	Mode adjustment	Easy operation □	Inconvenient operation □
	Timing	Easy operation □	Inconvenient operation □
		Accurate timing □	Inaccurate timing □
	Intensity tuning	Easy operation □	Inconvenient operation

			□
		Accurate adjustment □	Inaccurate adjustment □
Patients′ satisfaction degree		Satisfied □	Unsatisfied □
Note	Mark “×” in “□”		

Excellent: performance indicators completely satisfy the standards; assessment indicators are described as ready or convenient; no problem occurring during the operation.

Qualified: Minor problems occur during the operation, but do not affect efficacy. An inconvenient operation or poor accuracy does not harm the patients.

Unqualified: Due to the poor quality of the sample, faults occur during the operation, which terminates the experiment, without causing damage to the patients′ health.

5. Results of clinical trials

1. Inclusion of the cases and completion of the trial

Table 1 Case inclusion and trial completion

Center	Group	Inclusion	Completed	Dropout	Eliminated
Center 01	Experimental group	15（100.0%）	15（100.0%）	0（0.0%）	0（0.0%）
	Control group	15（100.0%）	15（100.0%）	0（0.0%）	0（0.0%）
Center 02	Experiment group	15（100.0%）	14（93.3%）	1（6.7%）	0（0.0%）
	Control group	15（100.0%）	13（100.0%）	2（13.3%）	0（0.0%）
Total	Experiment group	30（100.0%）	29（96.7%）	1（3.3%）	0（0.0%）
	Control group	30（100.0%）	28（93.3%）	2（6.7%）	0（0.0%）

Center 01, Military General Hospital of Beijing PLA; Center 02, Beijing Chao-Yang Hospital, Capital Medical University

In the clinical trial, a total of 60 patients are included in two hospitals. The experimental and control groups include 30 cases each; there are three dropout cases, and the dropout rate is 5.0%<10.0%. 0 cases are eliminated. Thus, a total of 57 cases are included for the statistical analysis, which meets the design requirements.

Table 2 List of dropout cases

Center	Name abbreviation	Group	Reason	Whether included in the statistical analysis
Center 02	QCHU	Experimental group	Poor compliance, not completing two courses of treatment, not receiving the last laboratory examination	No
Center 02	LIYU	Control group	Poor compliance, not completing two courses of treatment, not receiving the last laboratory examination	No
Center 02	WYLO	Control group	Poor compliance, not completing two courses of treatment, not receiving the last laboratory examination	No

Center 02, Beijing Chao-Yang Hospital, Capital Medical University

2. Baseline analysis

Table 3 Age of patients (years)

Group	Number of cases	Mean±SD	Minimum value	Maximum value	Median
Experimental group	29	48.14±12.343	26	73	48.00
Control group	28	49.57±10.549	28	69	51.50
Lower-upper 95% CI	–7.538 to 4.671				
Statistics: t= –0.471, P=0.640					

Note: *t* test performed for age.

As seen from the combined data analysis from the two hospitals, the mean age of the experimental group is 48.14 years, with a minimum of 26 and maximum of 73 years; the mean age of the control group is 49.57 years, with a minimum of 28 and maximum of 69 years. The inter-group difference is not significant.

Table 4 Patient sex

Group	Number of cases	Male	Female	Statistics	*P* value
Experimental group	29	15（51.7%）	14（48.3%）	0.169	0.681
Control group	28	16（57.1%）	12（42.9%）		
Total	57	31（54.4%）	26（45.6%）		

Note: Pearson χ^2 test is performed for sex.

As seen from the combined data analysis from the two hospitals, there are 31 males (15 in the experimental group, 16 in the control group) and 26 females (14 in the experimental group, 12 in the control group). The inter-group difference is not statistically significant.

Table 5 Combined use of drug

Group	Number of cases	Yes	No	Statistics	*P* value
Experimental group	29	0（0.0%）	29（100.0%）	--	--
Control group	28	0（0.0%）	28（100.0%）		
Total	57	0（0.0%）	57（100.0%）		

Note: Fisher's exact test is performed by the combined use of drugs (the count in the 2 cells is 0, no statistics).

As seen from the combined data analysis from the two hospitals, there is no combined use of drug in the experimental or control group.

Table 6 Vital signs of patients before treatment

Vital signs	Indicator	Experimental group	Control group	Statistics	P value
Body temperature	Mean(SD)	36.372(0.2389)	36.364(0.2164)	0.134	0.894
	Min,Max	35.6,36.8	36.0,36.8		
	Median	36.50	36.50		
Pulse	Mean(SD)	72.86(6.507)	71.50(6.557)	0.787	0.435
	Min,Max	60,84	60,83		
	Median	72.00	70.50		
Respiratory rate	Mean(SD)	18.24(1.504)	17.89(1.397)	0.906	0.369
	Min,Max	16,21	16,20		
	Median	18.00	18.00		
Systolic blood pressure	Mean(SD)	128.17(13.763)	126.82(11.972)	0.395	0.695
	Min,Max	100,178	110,160		
	Median	125.00	125.50		
Diastolic blood pressure	Mean(SD)	81.41(8.139)	81.00(7.343)	0.201	0.841
	Min,Max	70,100	70,100		
	Median	80.00	80.00		

Table 7 Vital signs of patients after two courses of treatment

Vital signs	Indicator	Experimental group	Control group	Statistics	P value
Body temperature	Mean(SD)	36.321(0.2513)	36.318(0.2144)	0.046	0.964
	Min,Max	35.8,36.8	36.0,36.7		
	Median	36.40	36.40		
Pulse	Mean(SD)	72.66(7.052)	71.82(5.389)	0.500	0.619
	Min,Max	60,100	60,80		
	Median	72.00	72.00		
Respiratory rate	Mean(SD)	18.52(1.184)	18.07(1.152)	1.440	0.156

	Min,Max	16,20	16,20		
	Median	18.00	18.00		
Systolic blood pressure	Mean(SD)	127.45(11.513)	125.57(11.727)	0.610	0.545
	Min,Max	110,167	108,150		
	Median	125.00	125.50		
Diastolic blood pressure	Mean(SD)	80.86(6.374)	80.46(8.435)	0.201	0.841
	Min,Max	70,90	64,110		
	Median	80.00	80.00		

As seen from the combined data analysis from the two hospitals, the vital signs of the patients in both the experimental and control groups are stable. The difference between the two groups is not significant.

3. Clinical security assessment

Table 8 Allergic reactions of patients

Group	Number of cases	Yes	No	Statistics	*P value*
Experimental group	29	0（0.0%）	29（100.0%）	--	--
Control group	28	0（0.0%）	28（100.0%）		
Total	57	0（0.0%）	57（100.0%）		

Note: Fisher’s exact test is performed for the concomitant diseases (the count in 2 cells is zero, no statistics)

As can be seen from the combined data analysis from the two hospitals, no laser-induced allergy occurs in the experimental or control group.

Table 9 Abnormal vital signs of the patients

Group	Number of cases	Yes	No	Statistics	*P value*
Experimental group	29	0（0.0%）	29（100.0%）	--	--

Control group	28	0（0.0%）	28（100.0%）		
Total	57	0（0.0%）	57（100.0%）		

Note: Fisher's exact test is performed for the concomitant diseases (the count in 2 cells is zero, no statistics).

As seen from the combined data analysis from the two hospitals, there is no concomitant disease occurring in the experimental or control group.

4. Clinical efficacy assessment

Table 10 Efficacy assessment

Group	Number of cases	Marked effect	Effective	No effect	Statistics	*P value*
Experimental group	29	3（10.3%）	23（79.3%）	3（10.3%）	-0.584	0.559
Control group	28	2（7.1%）	22（78.6%）	4（14.3%）		
Total	57	5（8.8%）	45（78.9%）	4（12.3%）		

Note: The efficacy assessment is performed using the Wilcoxon rank sum test.

As seen from the combined data analysis from the two hospitals, the rates of marked effect, effective and total efficacy in the experimental group are 10.3%, 79.3% and 89.6%, respectively. In the control group, the rates are 7.1%, 78.6% and 85.7%, respectively. P=0.559>0.05, the inter-group difference is not significant.

5. Performance assessment of the device

Table 11 Performance of the device

Group	Number of cases	Excellent	Qualified	Unqualified	Statistics	*P value*
Experimental group	29	18（62.1%）	11（37.9%）	0（0.0%）	--	1.000
Control group	28	16（57.1%）	12（42.9%）	0（0.0%）		
Total	57	34（59.6%）	23（40.4%）	0（0.0%）		

Note: Pearson χ^2 test is performed for the device performance.

As seen from the combined data analysis from the two hospitals, the excellent rate of the test group is 62.1%, the qualified rate is 37.9%, and the total qualified rate is 100.0%; for the control group, the rates are 57.1%, 42.9% and 100.0%, respectively.

6. Adverse events occurring in clinical trial, the side effects and handling

Table 12 Adverse events

Group	Number of cases	Yes	No	Statistics	*P value*
Experimental group	29	0（0.0%）	29（100.0%）	--	--
Control group	28	0（0.0%）	28（100.0%）		
Total	57	0（0.0%）	57（100.0%）		

Note: Fisher's exact test is performed for the adverse events (the count in 2 cells is zero, no statistics)

As seen from the combined data analysis from the two hospitals, no adverse events occur in the experimental or control groups. The inter-group difference is not significant.

7. Analysis of clinical trial results

(1) There are no significant differences in age, sex, disease course, concomitant diseases and combined use of drugs in patients compared with baseline.

(2) There is no laser-induced allergy in any patients. The vital signs are stable before and after treatment. There is no significant difference between the experimental and control groups.

(3) Efficacy assessment: rates of marked effect, effective and total efficacy of the experimental group are 10.3%, 79.3% and 89.6%, respectively. The corresponding rates in the control group are 7.1%, 78.6% and 85.7%, respectively. P=0.559>0.05, the inter-group difference is not significant.

4. The excellent rate, qualified rate and total qualified rate of the test device are 62.1%, 37.9% and 100.0%, respectively; for the control group, the rates are 57.1%, 42.9% and 100.0%, respectively.

5. No adverse events occur in the clinical trial. Both the experimental and control groups have high security.

8. Conclusions of clinical trial

1. Security of the test device

In the clinical trial, no allergy is induced by the test or control devices. The vital signs of the patients are stable. The non-occurrence of adverse events in the clinical trial indicates good security of the test device and satisfactory design requirements.

2. Efficacy of the test device

In the clinical trial, the rates of marked effect, effective and total efficacy are 10.3%, 79.3% and 89.6% for the test device, respectively. The corresponding rates in the control group are 7.1%, 78.6% and 85.7%, respectively. Compared with the control group, $P=0.559>0.05$. The inter-group difference is not significant. Some of the patients in the two groups suffer from disease-induced insomnia, amnesia, weariness and dizziness. All these symptoms are alleviated after two courses of treatment. The symptom of dizziness is most significantly improved. Thus, it is considered that the test device has good clinical efficacy, and can satisfy the needs for clinical application and family healthcare.

3. Performance of the test device

In the clinical trial, the excellent rate, qualified rate and total qualified rate for the experimental group are 62.1%, 37.9% and 100.0%, respectively. The corresponding rates for the control group are 57.1%, 42.9% and 100.0%, respectively. The test device has better performance than the control device.

9. Indications, application scope, contraindications and cautions

1. Indications

Hyperlipidemia and accompanying sub-health symptoms such as dizziness, weariness, insomnia, amnesia and chest pain

2. Contraindications

(1) Cancer and coagulation disorders

(2) Severe cardiac diseases and women in pregnancy

(3) Bleeding tendency