

## Clinical Trial Details (PDF Generation Date :- Tue, 15 Jun 2021 12:32:32 GMT)

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|---|---|
| **CTRI Number** | CTRI/2021/04/032987 [Registered on: 21/04/2021] - **Trial Registered Prospectively** |
| **Last Modified On** | 15/06/2021 |
| **Post Graduate Thesis** | No |
| **Type of Trial** | Interventional |
| **Type of Study** | Drug |
| **Study Design** | Randomized, Parallel Group Trial |
| **Public Title of Study** | A Prospective Trial of Renochlor Formulation as an add on to the Standard of care for the Management of Chronic Renal Failure (CRF) |
| **Scientific Title of Study** | A Prospective, Observational, Randomized, Open labeled, Multi Center, Parallel-Group, Two arm, Clinical trial Study to Evaluate the Efficacy, Safety and Tolerability of Renochlor Formulation as an add on to the Standard of care for the Management of Chronic Renal Failure (CRF) |

**Secondary IDs if Any**

| Secondary ID | Identifier |
|---|---|
| NIL | NIL |

**Details of Principal Investigator or overall Trial Coordinator (multi-center study)**

| Details of Principal Investigator | |
|---|---|
| **Name** | Dr Aniruddha Gokhale |
| **Designation** | Principal Investigator |
| **Affiliation** | Dr.Gokhales Urology & Gynaecology Clinic |
| **Address** | Next Cafe Coffee Day, Dr.Gokhales Urology & Gynaecology Clinic, GREENWOODS CHD,Link road, off, Shimpoli Rd, Borivali West, Mumbai, Maharashtra 400092 Next Cafe Coffee Day, Dr.Gokhales Urology & Gynaecology Clinic, GREENWOODS CHD,Link road, off, Shimpoli Rd, Borivali West, Mumbai, Maharashtra 400092<br>Thane<br>MAHARASHTRA<br>400092<br>India |
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**Details Contact Person (Scientific Query)**

| Details Contact Person (Scientific Query) | |
|---|---|
| **Name** | Dr Ravindra Mote |
| **Designation** | Director |
| **Affiliation** | Mediclin Clinical Research |
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**Details Contact Person (Public Query)**

| Details Contact Person (Public Query) | |
|---|---|
| **Name** | Dr Milind Gharpure |
| **Designation** | Senior General Manager |
| **Affiliation** | THINQ Pharma CRO Limited |
| **Address** | A30, Rd Number 10, Wagle Estate, MIDC, Thane West, Thane, Maharashtra 400604 A30, Rd Number 10, Wagle Estate, MIDC, |



| | |
|---|---|
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| **Email** | milind@thinqcro.com |

**Source of Monetary or Material Support**

| Source of Monetary or Material Support |
|---|
| > THINQ Pharma CRO Limited, A30, Rd Number 10, Wagle Estate, MIDC, Thane West, Thane, Maharashtra 400604 |

**Primary Sponsor**

| Primary Sponsor Details | |
|---|---|
| **Name** | Thinq Pharma CRO Limited |
| **Address** | A30, Rd Number 10, Wagle Estate, MIDC, Thane West, Thane, Maharashtra 400604 |
| **Type of Sponsor** | Pharmaceutical industry-Indian |

**Details of Secondary Sponsor**

| Name | Address |
|---|---|
| NIL | NIL |

**Countries of Recruitment**

| List of Countries |
|---|
| India |

**Sites of Study**

| Name of Principal Investigator | Name of Site | Site Address | Phone/Fax/Email |
|---|---|---|---|
| Dr Aniruddha Gokhale | Dr.Gokhales Urology & Gynaecology Clinic | Next Cafe Coffee Day, Dr.Gokhales Urology & Gynaecology Clinic, GREENWOODS CHD,Link road, off, Shimpoli Rd, Borivali West, Mumbai, Maharashtra 400092<br>Thane<br>MAHARASHTRA | 9820271476<br><br>draniruddhagokhale10@gmail.com |
| Dr Anurag Shukla | Mother Teresa Multispeciality Hospital | Satpala Naka, Pipri Dontalav, Virar West, Vasai-Virar, Maharashtra 401301<br>Thane<br>MAHARASHTRA | 9764718377<br><br>dranuragshuklamth@gmail.com |
| Dr B R Ramesh Rao | Sanjeevani Kidney Care | 20, Plot No-51/52, Next to Sanjeevani Hospital, Nityapriya Society, Nityanandan, Andheri East, Mumbai, Maharashtra 400069<br>Thane<br>MAHARASHTRA | 9820075652<br><br>drrameshrao10@gmail.com |
| Dr Chaitanya Sawant | Vijay Vallabh Hospital | Tirupati Nagar Rd, beside Banjara Hotel, Phase 1, Tirupati Nagar, Virar West, Virar, Maharashtra 401303<br>Thane<br>MAHARASHTRA | 9082805199<br><br>drchaitanyasawantvvh@gmail.com |



**Details of Ethics Committee**

| Name of Committee | Approval Status | Date of Approval | Is Independent Ethics Committee? |
|---|---|---|---|
| Ethicare Ethics Committee | Approved | 04/04/2021 | Yes |
| Ethicare Ethics Committee | Approved | 04/04/2021 | Yes |
| Ethicare Ethics Committee | Approved | 06/06/2021 | Yes |
| Ethicare Ethics Committee | Approved | 06/06/2021 | Yes |

**Regulatory Clearance Status from DCGI**

| Status | Date |
|---|---|
| Not Applicable | No Date Specified |

**Health Condition / Problems Studied**

| Health Type | Condition |
|---|---|
| Patients | Chronic kidney disease, stage 3 (moderate) |

**Intervention / Comparator Agent**

| Type | Name | Details |
|---|---|---|
| Intervention | Renochlor Tablet 40 mg active Sodium Copper Chlorophyllin | 1 tablet of 40 mg active Sodium Copper Chlorophyllin, 3 times in a day (Oral route, for 90 days) |
| Comparator Agent | Renochlor Syrup (Each 10 ml contains 40 mg of Sodium Copper Chlorophyllin) | 10 ml three times a day, Each 10 ml contains 40 mg of Sodium Copper Chlorophyllin (Oral route, for 90 days) |

**Inclusion Criteria**

| Inclusion Criteria | |
|---|---|
| **Age From** | 18.00 Year(s) |
| **Age To** | 75.00 Year(s) |
| **Gender** | Both |
| **Details** | Subjects must meet all of the following criteria: <br/> 1. Male or female subjects aged between 18-75 years (both inclusive).<br/> 2. Subject with clinically diagnosed with chronic kidney disease (CKD) (an eGFR of 30 to 60 ml/min/1.73 m2 <br/> 3. Subject voluntarily provides written informed consent and comes for regular follow up. |

**Exclusion Criteria**

| Exclusion Criteria | |
|---|---|
| **Details** | Subjects will be excluded if ANY of the following conditions apply:<br>1. Subjects with life expectancy less than one year<br>2. Subjects who have had renal replacement therapy in the prior 3 months<br>3. Subjects who had renal transplants or planning for renal transplantation during the study period<br>4. Evidence of recent acute kidney injury (>50% increase in serum creatinine in the preceding 30 days)<br>5. Subjects on chronic dialysis therapy or had episode(s) of dialysis in the past 3 months<br>6. Subject having any disease/ abnormalities as follow,<br>Cardiovascular system:<br>7. Subject with unstable angina pectoris, myocardial infarction, percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) surgery and any clinically significant cardiac arrhythmias.<br>8. Subjects with known case of Secondary or Malignant Hypertension.<br>9. Subjects with known case of symptomatic congestive heart failure, severe aortic stenosis<br>Endocrine system:<br>10. Subjects with uncontrolled Type 1 and Type 2 Diabetes Mellitus |



| | |
|---|---|
| | whose diabetes has not been stable and controlled for the previous three months and with HbA1c value greater than 8%.<br>Hepatic system:<br>11. Subjects with abnormal Liver Function Test with values more than 3 times the upper limit of normal.<br>12. Female subjects who are pregnant, lactating or planning to become pregnant during the study period.<br>13. Subjects who is chronic smoker, alcoholic or drug abuse suspected.<br>14. Subjects with known case of HIV, Hepatitis B or C.<br>15. Subjects with medical history of oncological conditions since last 2 years.<br>16. Subjects who have participated in other clinical trials within 3 months prior to the screening examination.<br>17. Subject with hypersensitivity to any of the ingredients of the study products. |

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|---|---|
| **Method of Generating Random Sequence** | Computer generated randomization |
| **Method of Concealment** | An Open list of random numbers |
| **Blinding/Masking** | Open Label |

**Primary Outcome**

| Outcome | Timepoints |
|---|---|
| Change from baseline of eGFR | Day -3, Day 30, 60 and 90 |

**Secondary Outcome**

| Outcome | Timepoints |
|---|---|
| Change in Albumin-to-creatinine ratio (ACR) | Day -3, Day 30, 60 and 90 |
| Change in TGF-?1 from baseline visit to end of study visit | Day -3 and day 90 |
| Change in Serum Creatinine | Day -3, Day 30, 60 and 90 |
| Change in BUN and electrolytes as compared to baseline. | Day -3, Day 30, 60 and 90 |
| Incidence rates of AE/ SAE including changes in vital signs and laboratory parameters | Day -3, Day 1, Day 30, 60 and 90 |
| Kidney Disease Quality of Life (KDQOL-SFTM) Version 1.3 | Day -3 and Day 90 |

| | |
|---|---|
| **Target Sample Size** | **Total Sample Size=**44<br>**Sample Size from India=**44<br>**Final Enrollment numbers achieved (Total)=**Applicable only for Completed/Terminated trials<br>**Final Enrollment numbers achieved (India)=**Applicable only for Completed/Terminated trials |
| **Phase of Trial** | Phase 3 |
| **Date of First Enrollment (India)** | 26/04/2021 |
| **Date of First Enrollment (Global)** | No Date Specified |
| **Estimated Duration of Trial** | **Years=**0<br>**Months=**6<br>**Days=**0 |
| **Recruitment Status of Trial (Global)** | Not Applicable |
| **Recruitment Status of Trial (India)** | Not Yet Recruiting |
| **Publication Details** | No |
| **Brief Summary** | A Prospective, Observational, Randomized, Open labelled, Multi Center, P arallel-Group, Two arm, Clinical trial Study to Evaluate the Efficacy, Safety |



and Tolerability of Renochlor Formulation as an add on to the Standard of care for the Management of Chronic Renal Failure (CRF).

## STUDY DESIGN

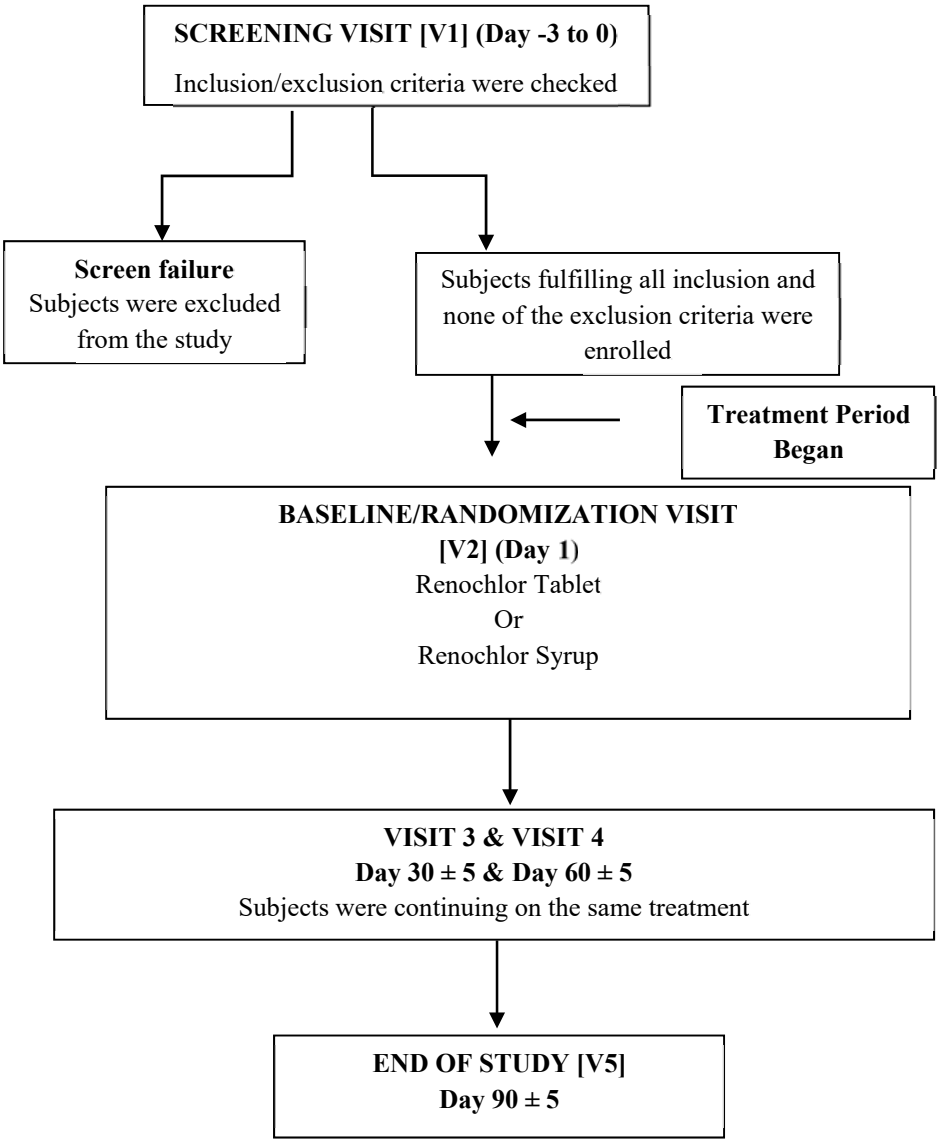


**Figure 1: Study Flow Chart**

## EFFICACY CONCLUSIONS

1. **eGFR** –

   The primary efficacy endpoint of the study was change in eGFR from baseline to Day 30, 60 and 90. Glomerular filtration rate (GFR) is defined as the volume of plasma that is filtered by the glomeruli per unit of time. In healthy individuals, eGFR ranges from **90 – 120**

**mL/min/1.73m$^2$**. In presence of CKD, eGFR is significantly reduced, with values below 60 mL/min/1.73m$^2$.

The eGFR increased by **12.45 %, 13.53 % and 27.33 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Syrup. The eGFR increased by **11.27 %, 23.64 % and 36.04 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Tablets. A significant ($p < 0.01$ and $p < 0.001$) increase was observed in eGFR of patients administered with both Renochlor Formulations.

## 2. Serum Creatinine –

An indirect relationship was observed between eGFR values and levels of Serum Creatinine, Creatinine is a nonprotein nitrogenous compound that is produced by the breakdown of creatine in muscle. Creatinine is found in serum, plasma, and urine and is excreted by glomerular filtration at a constant rate and in the same concentration as in plasma. Elevated serum creatinine level signifies impaired kidney function or kidney disease. The serum creatinine level is an insensitive marker of GFR early in the course of CKD.

In healthy individuals, Serum Creatinine levels range from **0.5 – 1.4 mg/dL**.

The results of present study depict a high Serum Creatinine level in patients at baseline, which is indicative of compromised renal function and subsequently reduced eGFR. The Serum Creatinine level decreased by **9.44 %, 8.89 % and 17.78 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Syrup. The Serum Creatinine level decreased by **8.82 %, 16.47 % and 23.52 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Tablets. A significant ($p < 0.05$ and $p < 0.001$) decrease was observed in Serum Creatinine levels of patients administered with both Renochlor Formulations.

## 3. Albumin-to-Creatinine ratio (ACR) -

Another secondary efficacy parameter was Change in from baseline to Day 30, 60 and 90, which was found to exhibit a direct relationship with levels of Serum Creatinine and an indirect relationship with eGFR.

Albuminuria is characterized by increased excretion of urinary albumin, and is a marker of kidney damage. Healthy individuals excrete very small amounts of protein in the urine. Albuminto-creatinine ratio (ACR) is the first method of preference to detect elevated urinary protein.

- Normal < 30 mg/g ,
- Microalbuminuria 30.0 – 299.0 mg/g
- Clinical Albuminuria > 300 mg/g

The results of present study depict a very high Urinary ACR in patients at baseline, which is indicative of compromised renal function. The Urinary ACR decreased by **22.48 %, 26.27 % and 30.76 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Syrup. The Urinary ACR decreased by **20.08 %, 26.09 % and 29.91 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Tablets. A significant ($p < 0.05$ and $p < 0.001$) decrease was observed in Urinary ACR of patients administered with both Renochlor Formulations.

However, due to the multi-factorial nature of Chronic Renal Failure, these relationships may not be considered as definitive indicators of disease condition or its effect on individual parameters.

## 4. Blood Urea Nitrogen (BUN)

From Baseline to Day 30, 60 and 90 was measured as another secondary efficacy endpoint. Blood Urea Nitrogen (BUN) test measures the amount of urea nitrogen in your blood. Urea nitrogen is one of the waste products removed from your blood by your kidneys. Higher than normal BUN levels may be a sign of CKD. Blood urea nitrogen (BUN) is a serum byproduct of protein metabolism. Urea is formed by the liver and carried by the blood to the kidneys for excretion. Diseased or damaged kidneys cause BUN to accumulate in the blood as glomerular filtration rate (GFR) drops. BUN indicates the urea nitrogen produced in the body during protein breakdown. It is removed from the body through urine. A decline

in kidney function due to a disease or kidney damage can cause an increase in BUN. In healthy individuals, BUN levels range from **6 - 24 mg/dL**.

Results of present study depict a high BUN level in patients at baseline, which is indicative of compromised renal function. The BUN level decreased by **10.99 %, 11.06 % and 14.51 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Syrup. The BUN level decreased by **10.38 %, 21.27 % and 22.40 %** respectively from baseline to Day 30, 60 and 90 in patients treated with Renochlor Tablets. A significant ($p < 0.05$ and $p < 0.001$) decrease was observed in BUN levels of patients administered with both Renochlor Formulations.

## 5. Transforming growth factor beta (TGF-$\beta_1$) -

has been recognized as an important mediator in the genesis of chronic kidney diseases (CKD), which are characterized by the accumulation of extracellular matrix (ECM) components in the glomeruli (glomerular fibrosis,

glomerulosclerosis) and the tubular interstitium (tubulointerstitial fibrosis). Glomerulosclerosis is a major cause of glomerular filtration rate reduction in CKD and all three major glomerular cell types (podocytes or visceral epithelial cells, mesangial cells and endothelial cells) participate in the fibrotic process.

In healthy individuals, the levels of TGF-β1 range from **1 – 33 ng/mL**. The levels of TGF-β1 decreased by **10.57 % and 14.56 %** respectively, in patients treated with Renochlor Syrup and Renochlor Tablets. This depicts a significant ($p < 0.001$) reduction in levels of TGF-β1 from baseline to end of study. However, there was no significant ($p > 0.05$) difference in its levels within groups.

Furthermore, levels of all the serum electrolytes (Ca, P, Na, K, and Cl) were found to be within their respective reference ranges from baseline throughout the study period.

## 6. KDQOL-SF™

Highlighted an overall improvement in patient's health and quality of life. This study describes that Renochlor Tablet (Sodium Copper Chlorophyllin) + Standard Care of Treatment was observed to be statistically non-inferior in treatment of Chronic Renal

Failure (CRF) when compared with Renochlor Syrup (Sodium Copper Chlorophyllin) + Standard Care of Treatment.

## ADVERSE EVENTS

| Analysis of Adverse Events | | | | |
|---|---|---|---|---|
| **Adverse Events** | **Renochlor Tablet (Sodium Copper Chlorophyllin) (N=22)** | | **Renochlor Syrup (Sodium Copper Chlorophyllin) (N=22)** | |
| | **Number of Adverse Events** | **Number of Subjects N%** | **Number of Adverse Events** | **Number of Subjects N%** |
| Dark Green Stool | 02 | 9.09 | 02 | 9.09 |
| Suppressed Appetite | 00 | 0.00 | 01 | 4.55 |
| Dry Lips | 00 | 0.00 | 02 | 9.09 |
| Headache | 00 | 0.00 | 01 | 4.55 |
| Diarrhea | 01 | 4.55 | 00 | 0.00 |
| GI Cramping | 01 | 4.55 | 00 | 0.00 |

## SAFETY CONCLUSIONS

Renochlor Tablet (Sodium Copper Chlorophyllin) + Standard Care of Treatment was well tolerated and observed to have comparable safety in subjects with Chronic Renal Failure (CRF) as per clinical evaluation when compared with Renochlor Syrup (Sodium Copper Chlorophyllin) + Standard Care of Treatment. Both, Renochlor Tablet (Sodium Copper Chlorophyllin) + Standard Care of Treatment and Renochlor Syrup (Sodium Copper Chlorophyllin) + Standard Care of Treatment have no hepatic and hematological effects.

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|---|---|
| **Conclusion** | Renochlor Tablet (Sodium Copper Chlorophyllin) + Standard Care of Treatment has observed to be Non-inferior efficacy and comparable safety profile to Renochlor Syrup (Sodium Copper Chlorophyllin) + Standard Care of Treatment of patients with Chronic Renal Failure (CRF). There were no deaths or SAEs reported in overall conduct of the study. |

- A significant ($p < 0.01$ and $p < 0.001$) increase was observed in **eGFR** of patients administered with both Renochlor Formulations.
- A significant ($p < 0.05$ and $p < 0.001$) decrease was observed in **S Creatinine , BUN & ACR** levels of patients administered with both Renochlor Formulations.
- A significant ($p < 0.001$) reduction in levels of **TGF-β1** from baseline to end of study.