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PILOT CLINICAL TRIAL OF PROBIOTIC BACTERIA (KIBOW BIOTICS®) IN CHRONIC KIDNEY DISEASE (CKD)

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1. INTRODUCTION

Probiotics, prebiotics and synbiotics are increasingly utilized clinically. As their safety and health benefits are established, it is reasonable to anticipate that probiotic bacteria will be incorporated into a growing number of clinical regimens.

Following exploratory testing of orally administered probiotic bacteria in rats and miniature pigs with surgically induced chronic kidney disease (CKD), a trial is now in progress to determine whether daily treatment with gastrointestinal (GI) probiotic bacteria will delay the onset of and/or improve established signs and symptoms of human CKD.

2. PRIOR STUDIES

To assess the potential benefit in devising a gut-based probiotic formulation (Kibow Biotics®) as therapy in CKD:

- extensive *in vitro* R&D investigations in Kibow laboratories
- Simulated Human Intestinal Microbial Ecosystem (SHIME, Ghent University, Belgium) utilized in a computer-controlled *in vitro* system validated the concept that the chosen microbial formulation would metabolize and reduce concentration of nitrogenous components including urea, creatinine, and uric acid. Bacterial strains studied were *Streptococcus thermophilus* (KB19), *Lactobacillus acidophilus* (KB27) and *Bifidobacterium longum* (KB31).
- Oral administration of these bacterial formulations, tested in the 5/6th nephrectomized rat model (at Thomas Jefferson University, Phila., PA) and minipig model (at Indiana University, Indianapolis, IN), decreased both blood urea nitrogen (BUN) and serum creatinine (Scr) levels.
- Two independent veterinarians investigated the effect of Kibow Biotics® on clinically manifested renal failure in uremic cats and dogs of both genders and varying body weights. Based on positive results, this formulation, marketed and distributed as AzodylTM, is currently licensed for veterinary applications to Vetoquinol SA..

3. CURRENT STUDY: HYPOTHESIS

- The bowel can serve as a complement to kidneys' excretory function
- A specifically formulated probiotic product comprised of defined and tested microbial trains may afford renoprotection in what has been called "enteric dialysis"®

4. GOALS

- Confirm the alleviation of uremic syndrome hypothesis
- Determine the outcome of probiotics treatment
- Confirm U.S. FDA's Generally Recognized As Safe (GRAS) status

5. INCLUSION CRITERIA

- CKD patients Stage III and IV
- At least 18 y.o., able and willing to give an informed consent
- Baseline serum creatinine >2.5 mg/dL

6. TREATMENT REGIMEN AND STUDY DESIGN

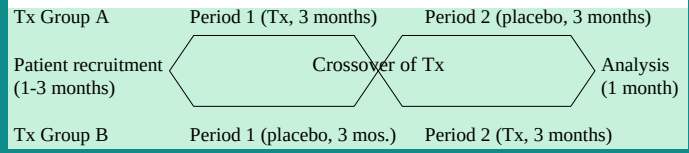
Treatment Regimen

- Patient recruitment – 1-3 months
- 1st treatment period – 3 months
- Crossover after 3 months
- 2nd treatment period – 3 months
- Data analysis – 1 month

As soon as recruitment period begins, the participants will be randomized and treated on a rolling basis according to thedate of enrollment

Study Design

Multi-site, randomized, double blind, placebo controlled crossover study in an outpatient setting. Each patient will act as their own placebo control. Minimal enrollment at each site is 30 patients.



7. MONITORING PARAMETERS

Control and treated cohorts will be monitored and compared by following parameters known to vary and correlate with progressive CKD:

PRIMARY: Body weight or body mass index (BMI), blood pressure (BP), complete blood count (CBC).

SECONDARY: Blood chemistry determinations (including blood urea nitrogen (BUN), serum creatinine, phosphorus, uric acid) and a standardized metabolic profile in CKD. Additionally, alanine aminotransferase (ALT), C-reactive protein (CRP), serum ammonia, random urine collection for measurement of creatinine and urinary protein concentrations and fecal nitrogen content will be assayed.

TERTIARY: Quality of life (QOL) will be assessed on a scale of 1 to 5.

8. CLINICAL SITES

1. Downstate Medical Center, Brooklyn, NY, U.S.A.
2. VA Medical Center, New York, NY, U.S.
3. Nephrology Associates, Scarborough, ON, Canada
4. Hospital Juarez de Mexico, Madero, Mexico
5. Hospital Italiano de Buenos Aires, Argentina
6. National Hospital, Abuja, Nigeria

9. CONCLUSIONS

This clinical trial is a critical step in further validating the oral formulation, Kibow Biotics®, for probiotic therapy of CKD and ESRD. In addition, trial results will provide a basis for further investigations into probiotic therapy applications in other conditions related to immunity and metabolism.

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