TOPSPIN Study Summary

TITLE: Treatment **O**ptimisation for blood **P**ressure with **S**ingle-**P**ill combinations in **In**dia (TOPSPIN)

Hypertension is also a leading cause of death and disability in India, with a prevalence of 30%. More importantly, hypertension control rates in India are low at 11% and 20% among rural and urban patients, respectively. Reducing BP to target levels is a major priority in preventing cardiovascular events in patients with hypertension, and typically, this requires more than one BP-lowering medication in the majority of patients. Since no randomized trial data are available to inform optimal combinations of antihypertensive agents in patients of South Asian origin, current guidelines on drug choices and sequencing in India are based on international guidelines, which may or may not be applicable to Indian patients.
In view of this lack of critical information, we propose to compare the efficacy of three different single-pill combinations of antihypertensive therapies (Amlodipine/Perindopril, Perindopril/Indapamide, and Amlodipine/Indapamide) on 24-hour ambulatory BP levels in Indians, as representative of South Asians who constitute one-sixth of the world population.

OBJECTIVES: To compare the efficacy of three single pill combinations (SPCs) of two anti-hypertensive agents on 24-hour ambulatory systolic blood pressure (ASBP) among individuals with hypertension in India.

DESIGN: A multi-centre, individual randomized, single-blind, parallel-group, three-armed superiority trial.

SAMPLE SIZE: 1968 patients in total and 656 patients per arm.

INCLUSION CRITERIA: Male or female patients aged 30-79 years with a sitting systolic blood pressure (SBP) ≥140 mmHg and <160 mmHg on one antihypertensive agent or sitting clinic SBP ≥150 mmHg and <180 mmHg on no antihypertensive treatment.

EXCLUSION CRITERIA: History or evidence of congestive heart failure, renal impairment, coronary heart disease, cerebrovascular disease, contraindications to the SPCs of investigational product studied, secondary hypertension or other significant illness likely to interfere with the effective conduct of the study, pregnancy or women of childbearing age not taking reliable contraception.

TREATMENT:
Arm 1: SPC of Amlodipine and Perindopril
Arm 2: SPC of Perindopril and Indapamide
Aim 3: SPC of Amlodipine and Indapamide

PRIMARY ENDPOINT:

ASBP at 6 months adjusted for baseline ASBP

SECONDARY ENDPOINTS:

1. 24-hour ambulatory diastolic blood pressure (ADBP) at 6 months adjusted for baseline ADBP
2. Clinic SBP and diastolic blood pressure (DBP) at two, four, and six months adjusted for baseline values
3. Daytime and nighttime blood pressure (BP) at six months adjusted for baseline values
4. BP variability measured by ABPM and within-visit clinic BPs
5. The proportion of patients who achieve BP control (primarily defined as clinic BP <140/90 mmHg) at two, four, and six months and ABPM measured control (<130/80 mmHg) at six months. In addition to reflecting more contemporary guidelines, control of clinic BPs will also be evaluated as <130/80 mmHg.
6. The proportion of “responders” (defined as clinic BP reduction ≥20mmHg SBP and ≥10 mmHg DBP) at any of the clinic visits (two, four, and six months).
7. Micro- and macro-albuminuria at six months adjusted for baseline values
8. Fasting blood glucose at six months adjusted for baseline values
9. Fasting blood lipid profile at six months adjusted for baseline values
10. Serum sodium, potassium, urea, creatinine, and estimated glomerular filtration rate at six months adjusted for baseline values
11. Adverse events causing trial withdrawal

Significance of the Study:

The results of this study will provide evidence-based information to treat hypertension patients in the South Asian region effectively.

TOPSPIN Trial Screening and Recruitment Steps