

reported as AEs of special interest (AESIs). Most common AESIs ( $\geq 5\%$ ) included arthralgia/arthritis (60.7%), soft tissue swelling (35.7%), headache (32.1%), hyperhidrosis (25%), carpal tunnel (14.3%), musculoskeletal pain (14.3%), weight increased (7.1%) and tongue disorders (7.1%). The 5 patients receiving placebo with controlled IGF-I at 36 weeks received active medical treatment in the open label extension by decision of their study PIs, as they were deemed to have either lost their response during the study or had continuing active acromegaly symptoms. 93% of patients receiving placebo lost response following withdrawal of injectable SRLs, with a median duration of 16 weeks. All 5 patients receiving placebo who met the primary endpoint criteria at the end of the study were assessed clinically to have active disease and were continued on oral SRL treatment in the open label extension.

## Adrenal

### ADRENAL PHYSIOLOGY AND DISEASE

#### *High Salt Intake May Paradoxically Drive Autonomous Aldosterone Production*

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Many modifiable factors contribute to the high prevalence rates of hypertension, among them is the consumption of too much salt (sodium). Another curable cause of hypertension is the excess of the hormone aldosterone. Aldosterone is normally produced by the zona glomerulosa (ZG) of the adrenal glands in response to a lack of salt and conversely suppressed by salt excess. We hypothesize that [i] suppression of aldosterone production induces apoptosis of ZG cells, as occurs following genetic deletion<sup>1</sup>; [ii] this sets up a maladaptive response to chronic salt overload by conferring a survival advantage to cells in which mutations drive autonomous aldosterone production. To address [i], we measured apoptosis of cells in which aldosterone synthesis was inhibited; to address [ii] we undertook a cross-sectional clinical study of aldosterone and sodium excretion, hypothesising that aldosterone excretion will be highest in the outside quartiles of sodium excretion. Aldosterone was inhibited by modification, in human adrenocortical H295R cells, of either *CADM1* expression (mutated in aldosterone-producing adenomas<sup>2</sup>) or intracellular calcium concentration<sup>3</sup>. Apoptosis was measured by flow cytometric analysis of annexin V conjugates. 24-hour urinary aldosterone excretion (24h-Ualdo) was correlated

with 24-hour urinary sodium (24h-Usodium) in 24h-urine samples collected for a Malaysian population-based salt intake study (MyCoSS). The prevalence of autonomous aldosterone production was estimated from the proportion of subjects with serum measurement whose "SUSSPUP" ratio (= serum sodium to urinary sodium)/(serum potassium<sup>2</sup> to urinary potassium) was  $>5.3^4$ . Modification of *CADM1* in human adrenocortical H295R cells decreased aldosterone production by half compared to vector control, and this was associated with a 3 to 5-fold increase of apoptotic cells ( $p<0.05$ ;  $n>3$ ). Pilot investigation of a Cav1.3 inhibitor decreased aldosterone production by 70%, and increased apoptosis by 7-fold ( $p<0.10$ ;  $n=2$ ). In 767 subjects, 24h-urine samples from the high urinary sodium quartile ( $>150\text{mmol/d}$ ) had higher urinary aldosterone ( $4+0.18\text{ ug/d}$ ) than other quartiles ( $p=0.00001$ ). Overall, the estimated prevalence of autonomous aldosterone production using SUSSPUP ratio was 4.5% (8 of 179 subjects). In 63 subjects with 24h-Usodium $>200\text{ mmol/day}$ , autonomous aldosterone secretion (conventionally  $>10\mu\text{g/d}$ ) was found in 9.5%. Our results support the hypothesis that initial suppression of aldosterone production by salt excess may create a selective advantage for cells which autonomously produce aldosterone, and hence an inappropriate long-term increase in aldosterone production.

<sup>1</sup>Lee et al., *Endocrinology*. 2005;146:2650-6.

<sup>2</sup>Wu et al., 21st European Congress of Endocrinology. Vol. 63. BioScientifica, 2019.

<sup>3</sup>Xie et al., *Sci Rep*. 2016;6:24697.

<sup>4</sup>Willenberg et al., *Eur J Clin Invest*. 2009;39:43-50.

## Thyroid

### BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

#### *Rural India Embracing Advanced Techniques in MIS:- A Series of 20 Cases of Thyroid Surgeries by Transoral Endoscopic Thyroidectomy-Vestibular Approach (TOETVA) Technique with Respect to Acceptance of Progressive Surgeries Using Advanced Technologies, Techniques by Rural Patients and it's Safety & Feasibility in Small Setup Hospital in Rural India.*

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Title

Rural India embracing Advanced Techniques in MIS: - A Series of 20 Cases of Thyroid Surgeries by Transoral Endoscopic Thyroidectomy-Vestibular Approach (TOETVA) Technique with Respect to an Acceptance of progressive surgeries using Advanced Technologies, Techniques by Rural patients and it's Safety & Feasibility in Small setup Hospital in Rural India.

Aims & Objectives

Transoral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) an alternative surgical technique for thyroid surgery is slowly gaining widespread popularity.

Majority of TOETVA surgeries are performed in Tertiary Care institutes. It's safety & Feasibility in small setup