

signaling is important to aid the development of new tissue-specific treatments. We hypothesized that the posttranslational modification phosphorylation in estrogen receptor alpha (ER α) may modulate ER α transcriptional activity in a tissue-dependent manner. Phosphorylation of site S122 in ER α has been shown *in vitro* to affect ER α activity, but the tissue-specific role *in vivo* is unknown. We herein developed and phenotyped a novel mouse model with a point mutation at the phosphorylation site 122 in ER α (S122A). Female S122A mice had increased fat mass and serum insulin levels but unchanged serum sex steroid levels, uterus weight, bone mass, thymus weight, and lymphocyte maturation compared to WT mice. In conclusion, phosphorylation of ER α S122 has a tissue-dependent role with an impact specifically on fat mass in female mice. This study is the first to demonstrate *in vivo* that phosphorylation of a transactivation domain in a nuclear steroid receptor modulates its activity in a tissue-dependent manner.

Reproductive Endocrinology

TRANSGENDER MEDICINE AND RESEARCH

Estradiol Dose and Concentrations in Transfeminine Individuals

Brendan J. Nolan, MBBS, FRACP¹, Adam Brownhill, MBBS, MRCP (UK), FRACGP, FARGP², Ingrid Bretherton, MBBS, FRACP¹, Peggy Wong, MBBS, FRACGP², Susan Fox, MBBS, FRACGP², Peter Locke,² Nicholas D. Russell, MBBS, FRACP¹, Mathis Grossmann, MD, PhD, FRACP¹, Jeffrey D. Zajac, MBBS, FRACP, PhD¹, Ada S. Cheung, MBBS, FRACP, PhD¹.

¹University of Melbourne (Austin Health), Melbourne, Australia,

²Equinox Gender Diverse Clinic, Melbourne, Australia.

SUN-039

Background: Feminizing hormone therapy with estradiol is used to align an individual's physical characteristics with their gender identity. Australian expert consensus guidelines (1) recommend targeting estradiol concentrations of 250-600 pmol/L (68-163 pg/mL) based on local cross-sectional data (2). We aimed to establish the proportion of individuals achieving estradiol concentrations in consensus guidelines.

Methods: A retrospective cross-sectional analysis was performed of transfeminine individuals attending a primary or secondary care clinic in Melbourne, Australia who were prescribed oral estradiol valerate for at least 6 months and had estradiol dose and concentration available. Estradiol concentration was measured by immunoassay. Outcomes were (1) proportion of individuals achieving target estradiol concentrations and (2) influence of estradiol dose and BMI on estradiol concentrations.

Results: 259 individuals (median age 25.8(IQR 21.9,33.5) years) had data available for analysis. Median duration of estradiol therapy was 24(15,33) months. Median estradiol concentration was 328(238,434) pmol/L (89(65, 118) pg/mL) on 6(4,8) mg estradiol valerate. 172 (66%) individuals had estradiol concentrations within the target range recommended in consensus guidelines. 70 (27%) individuals had estradiol concentrations below target, and 17 (7%) above target. There was a weak positive correlation between estradiol dose and estradiol concentration ($r=0.156$,

$p=0.012$). There was no correlation between BMI and estradiol concentration achieved ($r=-0.063$, $p=0.413$).

Conclusions: 66% of individuals achieved estradiol concentration recommended in consensus guidelines with a relatively high oral estradiol dose. There was significant interindividual variability. Estradiol concentration should be interpreted in conjunction with clinical features of feminization and weighed against potential risks of escalating estradiol dose.

References

1. Cheung AS, Wynne K, Erasmus J, Murray S, Zajac JD. Position statement on the hormonal management of adult transgender and gender diverse individuals. *Med J Aust* 2019; 211:127-133

2. Angus L, Leemaqz SY, Ooi O, Cundill P, Silberstein N, Locke P, Zajac JD, Cheung AS. Cyproterone acetate or spironolactone in lowering testosterone concentrations for transgender individuals receiving estradiol therapy. *Endocr Connect* 2019

Thyroid

THYROID DISORDERS CASE REPORTS III

A Case of Inoperable Substernal Goiter

Garyfallia Papaioannou, MD, PhD¹, Erick Perez Sifontes, MD¹, Gnanambal Manivel, MD¹, Manivel Kumaran Eswaran, MD, MS².

¹University of Central Florida College of Medicine, North Florida Regional Medical Center Internal Medicine Residency Program, Gainesville, FL, USA, ²University of Central Florida College of Medicine, North Florida Regional Medical Center Internal Medicine Residency Program, Accent Physician Specialists, Endocrinology, Gainesville, FL, USA.

MON-467

Introduction: Goiter is abnormal growth of the thyroid gland. When goiter extends into the mediastinum it is called retrosternal or substernal. Substernal goiter can cause compression of the great vessels, trachea, and esophagus. When it compresses trachea it can result in airway obstruction. In that case treatment of choice is thyroidectomy and Radio Iodine Ablation (RIA). But some patients are considered to be high risk for operation due to multiple comorbidities. We are presenting this case where we tried experimental therapy with airway stent and external beam radiation. **Case:** An 81 year old female presented to the hospital complaining of chest pain. She also reported dysphagia to solids and liquids and weight loss during one month. Past medical history included congestive heart failure, atrial fibrillation, chronic obstructive pulmonary disease with home oxygen support. On physical exam thyroid was palpable to the level of sternal notch. Arterial blood gases showed hypoxemia (PO₂ 63), thyroid function tests showed an abnormally suppressed TSH (<0.005 IU/ml), elevated free T₄ (2.48 ng/dl) and normal T₃. Thyroid stimulating immunoglobulin, IgG, IgM and IgA levels were normal. Thyroglobulin and thyroid peroxidase antibodies were negative. Chest X-ray revealed an upper mediastinal mass. Chest CTA showed a very large substernal goiter with left thyroid lobe of 7.4 x 3.4 x 7.8 cm that extended to the level of the carina causing compression of the