Androgen Society

2022 ABSTRACT BOOK

#1

HIGHER RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS AFTER ANDROGEN DEPRIVATION THERAPY IN OLDER PATIENTS

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Introduction: Patients with prostate cancer (PCa) treated with androgen deprivation therapy (ADT) may experience major adverse cardiovascular events (MACE).1,2 A previous study found CV disease rate was approximately 15% higher in individuals >80 years compared to those 60- 79 (90%,91% vs. 78%,75% for men and women, respectively) in the general population.3 Th current study evaluated real-world data to evaluate impact of age on MACE risk.
Methods: US electronic medical records (2010 to 2020) of PCa patients (n=45,059) receiving ADT were evaluated for MACE events by age: <60, 60 to <70, 70 to <80, and ≥80. 178,388 ADT injections and 965 MACE events were identified. Exclusion criteria included MACE within 6 months before ADT initiation. MACE was defined as myocardial infarction, stroke, and death from any cause.4 Event-free survival curves with log-rank tests for significance compared the MACE risk between ages.
Results: Overall MACE risk on ADT was 2.4% and 6.0% at one year and seven years respectively. 6%, 24%, 39%, and 31% of patients were <60, 60 to <70, 70 to <80, and ≥80 years old, respectively. MACE risk increased with increasing age. All comparisons were $p<0.001$ except for 60 to <70 years vs. <60 years ($p<0.05$).
Conclusion: MACE risk was higher for older patients on ADT. This could be due to increased prevalence of co-morbidities such as diabetes,5 obesity,6 and frailty.7 Clinicians should recognize that age is a predisposing risk factor for CV disease in patients with PCa undergoing ADT, and consider risk-reduction strategies. Future studies evaluating co-morbidities on CV risk during ADT may be helpful.
Conflict of Interest: E. David Crawford is a consultant for Tolmar Pharmaceuticals, Inc.

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#2

ANALYSES OF REAL-WORLD MAJOR ADVERSE CARDIOVASCULAR EVENT RISK BY ANDROGEN DEPRIVATIONTHERAPY DRUG CLASS

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Disclosure: E. David Crawford and Lucio N. Gordan are consultants of Tolmar Pharmaceuticals, Inc., Stuart N. Atkinson and Deborah M. Boldt-Houle are employees of TolmarPharmaceuticals, Inc.

Background: Literature suggests an association between androgen deprivation therapy (ADT) and increased cardiovascular (CV) risk in prostate cancer (PCa) patients.[1, 2] 1-year incidence of major adverse CV events (MACE) in patients ≥45 years old was 1.4%,[3] and a recent study of PCa patients on ADT reported MACE in 2.9% of patients on an LHRH antagonist (relugolix) and6.2% of patients on an LHRH agonist (leuprolide acetate) over 48 weeks.[4] Current study evaluated MACE risk of LHRH agonists vs. antagonists using real-world data.

Methods: US electronic medical records (2010 to 2020) of PCa patients (n=45,059) receiving LHRH agonist and antagonist injections were evaluated for rate of MACE-free survival by drug class. 178,388 LHRH agonist and antagonist injection entries and 965 MACE events were identified. Exclusion criteria included taking more than one class of ADT and MACE within 6 months prior to ADT initiation. MACE was defined as myocardial infarction, stroke, and death from any cause.[4] Kaplan-Meier event-free survival curves compared the risk of MACE betweenpatients on agonists vs. antagonist, with statistical significant differences evaluated by log-ranktest.

Results: Overall MACE risk for all patients was 1.0% at one year. MACE risk was significantlyhigher on LHRH antagonist compared to agonists over the first seven years.

Conclusion: Risk of MACE was lower than previously reported and showed lower MACE riskfor LHRH agonists vs. antagonists. Future analyses will evaluate variations in baseline comorbidities, demographics and other potential additional causes. A study with >50,000 patients for approximately 2 years showed similar CV risk for GnRH agonists and antagonists.[5]Future studies evaluating the impact of ADT class and comorbidities on MACE risk for PCa patients during ADT may be helpful to identify CV predictors and further evaluate whether thereare differences between LHRH pharmacology on CV events.

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#3

REDUCED MORTALITY AND DIFFERENT CAUSES OF DEATH IN MEN WITH FUNCTIONAL HYPOGONADISM, COMPARED TO AN UNTREATED CONTROLGROUP IN A REAL-WORLD REGISTRY STUDY

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Introduction and Objectives: Several studies suggest an association between testosterone therapy (TTh)and a reduction in mortality. We investigated 8,190 patient-years observed over up to 15 years.
Methods: In a registry of 796 men with symptomatic functional hypogonadism, 394 men(49.5%) received testosterone therapy (TTh) by testosterone undecanoate (TU) injections 1000mg/12weeks following an initial 6-week interval (T-group). 402 men opted against TTh and served as controls (CTRL).
Results: Mean age at baseline: 60.9±6.0 years (T-group: 58.5±6.3, CTRL: 63.2±4.8).Mean (median) follow-up: T-group 10.1±3.0(11), CTRL 10.5±3.0(12) years.
During the observation time, 37 patients in the T-group (9.4%) and 111 inCTRL (27.6%) died (p<0.0001).
Causes of deaths fell into 15 classifications:

Classification	T-Group (n)	%	CTRL (n)	%
Post-surgical complications	18	4.6%	6	1.5%
Accident	10	2.5%	1	0.2%
Covid-19	2	0.5%	7	1.7%
Sepsis	4	1.0%		
Aortic aneurysm	1	0.3%		
Brain aneurysm	1	0.3%		
Food poisoning	1	0.3%		
Lung embolism			4	1.0%
Myocardial infarction			47	11.7%
Stroke			20	5.0%
Heart failure			19	4.7%
Stroke and myocardial infarction			2	0.5%
Pneumonia			1	0.2%
Thromboembolism			3	0.7%
Renal failure			1	0.2%

Adherence to testosterone was 100% as injections were administered in theoffice and documented.
Conclusion: During a median follow-up of 11 years, all-cause mortality was approximatelythree times higher in the untreated control group of men with functional hypogonadism compared to men receiving TTh. While the majority of deathsin the T-group was caused by post-surgical complications and accidents, more than three out of four deaths in CTRL were of cardiovascular nature.

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Curriculum Vitae

1954 born in Neirab, Syria; 1972 – 1978 studies of human medicine; 1978 specialization in Laboratory medicine; 1978 – 1984 specialization in surgery;1984 – 1988 specialization as a Urologist; 1988 German board of Urology; 1990 start of Praxis Dr. Haider medical office for Urology; since 1995 start ofhormonal therapies in Praxis Dr. Haider; 2004 start of study on long-term testosterone therapies with TU; 2006 specialization for Andrology.
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#4

TESTOSTERONE THERAPY IN BREAST CANCER SURVIVORS

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Introduction: Testosterone (T) or 'testosterone combined with an aromatase inhibitor' (T+AI) subcutaneous implants have been used to treat symptoms of hormone deficiency in breast cancer survivors since 1/2006. T has a direct effect at the androgen receptor – decreasing breast proliferation and tumor growth. However, the long-term effect of T therapy (TT) on disease recurrence and survival has not been documented.

Objective: To prospectively follow breast cancer patients treated with T/T+AI for disease recurrence and breast cancer specific survival (BCSS).

Methods: An IRB study was approved in March 2013. Patient demographics, disease state, and therapy were tracked. Person-years (P-Y) of therapy (active) are calculated from first implant to evaluation date (2/2/22) or 240 days following last pellet implant, the maximum length of clinical efficacy. Patients are evaluated at each appointment. Patients with stage 2, 3 or 4 disease, not seen for 240 days, were contacted for status.

Results: Since 3/2013, 238 women have been treated with a total of 3591 T/T+AI insertions at an average interval of 106.7 days. 79 study patients received therapy prior to 3/2013 (data included).

There have been seven local (breast) recurrences in 215 patients with stage 0-3 disease in 920 P-Y of therapy, mean length of therapy 4.3 $\pm$ 3.9 y, mean years since diagnosis 10.5 $\pm$ 8.4 y. All seven patients continued TT.

BCSS is shown below.

Stage (N of patients)	Length of TT, years Mean $\pm$ SD (Person-years therapy)	Years since diagnosis Mean $\pm$ SD (Person-years survival)	BCSS percent
0 (44)	5.0 $\pm$ 4.4 (221.9)	11.4 $\pm$ 9.2 (502.8)	100
1 (84)	4.2 $\pm$ 3.7 (352.4)	10.8 $\pm$ 8.8 (907.3)	99
2 (64)	4.3 $\pm$ 4.0 (277.1)	9.7 $\pm$ 7.6 (619.9)	100
3 (23)	3.0 + 3.2 (68.6)	10.0 $\pm$ 7.3 (229.5)	100
4 (20)	2.4 $\pm$ 3.1 (47.6)	5.6 $\pm$ 5.5 (112.0)	70

There was one systemic recurrence in 171 patients with stage 1-3 invasive disease. This patient discontinued TT and eventually died 15 months later. Six of 20 patients with metastatic disease died within 240 days of T/T+AI therapy. Our results compare favorably to current survival data.

Conclusion: T or T+A implant therapy does not increase breast cancer recurrence and may have a beneficial effect on BCSS.

#5

TESTOSTERONE REPLACEMENT THERAPY IN PATIENTS WITH CACHEXIA: A CONTEMPORARYREVIEW OF THE LITERATURE

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Introduction: Prevalence of adult-onset hypogonadism (AOH) is increasing and is currently estimated to be 6-12% in the general population. AOH is often associated with cachexia, a progressively debilitating loss of skeletal muscle often seen in late-stage chronic medicaldiseases such as malignancies, chronic obstructive pulmonary disease (COPD), and HIV. Cachexia contributes to mortality and morbidity with reduced quality-of-life (QoL) and disease treatment options.
Objectives: This comprehensive review highlights Testosterone Replacement Therapy (TRT) for management of AOH in patients with cachexia, with an emphasis on clinical outcomesand side effects.
Methods: A comprehensive PubMed literature review was performed to identify articles publishedbetween 2000-2021 on TRT and cachexia-related chronic medical diseases such as malignancies, COPD, and HIV. Search terms included 'TRT', 'cachexia', and 'muscle wasting'. Relevant English articles were included.
Results: Ten studies were included in our review out of 364 initial search results. In three studies of TRT in cancer patients, there were mixed results on the effects of TRT on quality of life (QoL) assessment (Table 1). While one study reported an improvement in QoL and lean body mass with adjunct testosterone, two others reported no improvement of QoL from testosterone therapy. Across three studies of TRT in COPD patients, there was consistent improvement in exercise capacity and disease condition with TRT, suggestingthat TRT is a promising therapy for improving patient condition. Lastly, across four studies of TRT in HIV patients, TRT resulted in notable improvement in body weight, muscle mass, function and QoL in HIV-infected men.
Conclusion: Based on recent studies, there is robust data for the clinical benefits of TRT for the management of certain subgroups of cachexic patients, specifically those with COPD and HIV. Because there are mixed results in cancer cachexia patients, further 0 investigation of its long-term efficacy is warranted.

Table 1. Breakdown of literature review findings, by study

Cachexia Etiology	Reference	Study Link	Study Type	*N*	Intervention	Outcomes of Interest	Study Findings
Cancer	Wright et al., 2018	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5989774/	Prospective	21	100 mg testosterone enanthate/placebo weekly for 7 weeks	% change in LBM; assessment of QoL, tests of physical performance, muscle strength, daily activity levels, resting energy expenditure, nutritional intake, overall survival	Adjunct testosterone increased lean body mass by3.2% whereas those receiving placebo lost 3.3%. Testosterone-treated patients maintained more favorable body condition, sustained daily activity levels, and showed meaningful improvements in quality of life and physical performance. Overall survival was similar in both treatment groups.
Cancer	Izumi et al., 2021	https://pubmed.ncbi.nlm.nih.gov/34029455/	Prospective	81	250 mg testosterone enanthate injected into the muscle tissue every 4 weeks	Differences in quality-of-life questionnaires, cachexia-related serum protein levels	Testosterone enanthate did not improve most of theitems in health-related quality of life questionnaires.But it induced a significantly better change in the 'unhappiness' item at week 12 compared with the control.
Cancer	Fabbro et al., 2013	https://pubmed.ncbi.nlm.nih.gov/23653013/	Prospective	29	Gluteal injections of 150or 200 mg testosterone enanthate or placebo were administered every14 days to achieve BT levels 70-270 ng/dL	FACIT-fatigue scores, Sexual Desire Inventory score, performance status, fatigue subscale scores	Four weeks of intramuscular testosterone replacement in hypogonadal male patients with advanced cancer did not significantly improve qualityof life (FACIT-fatigue scores).

COPD	Baillargeon et al., 2018	https://pubmed.ncbi.nlm.nih.gov/30205698/	Retrospective	703	Comparison of TRT usersvs. TRT nonusers	Difference-in-differences (DID) statistical modeling: pre- vs. post-respiratory hospitalization rates in TRT users vs matchedTRT nonusers	TRT can reduce hospitalizations related to COPD, asTRT users had a 4-9% decrease in respiratory hospitalizations compared to nonusers.
COPD	Atlantis et al., 2013	https://pubmed.ncbi.nlm.nih.gov/23943774/	Review/meta-analysis	287	Comparison of TRT usersvs. TRT nonusers (placebo)	Peak muscle strength, peak cardiorespiratory fitness outcomes (peak oxygen uptake VO2 and workload), health-related quality of life (HRQoL)	Testosterone therapy is associated with improved exercise capacity outcomes, namely peak musclestrength and peak workload.
COPD	Daga et al., 2014	https://pubmed.ncbi.nlm.nih.gov/24552826/	Prospective	32	25 mg of nandrolone decanoate intramuscularly in glutealmuscle vs. placebo (injections every 7 days)x 6 weeks	Anthropometric and spirometric measurements, peak respiratory flow rate, partial pressure of O2 in arterial blood, 6-minute walk test (6MWT), hand grip test, HRQL index scores at baseline and end of treatment (6 weeks)	Weekly administration of anabolic steroids for 6 weeks increased exercise capacity and quality of lifein patients with COPD.
HIV	Blick et al., 2013	https://pubmed.ncbi.nlm.nih.gov/23816768/	Prospective	849	Prescribed either 5 mg or10 mg of 1% testosteronegel per day to be applied topically x 12 months, in cohorts with and without HIV	Total testosterone (TT), free testosterone levels, symptoms of depression, sexual function, body composition profiles, and prostate-specific antigen levels	Both men with and without HIV experienced elevations in TT and free testosterone levels to within normal ranges. For both cohorts, sexual function and depression scores improved and antidepressant medication use decreased. Body composition profiles improved significantly in men without HIV/AIDS and remained stable in men with HIV/AIDS during the 12 months of follow-up.
HIV	Bhasin etal., 2000	https://pubmed.ncbi.nlm.nih.gov/10683055/	ProspectiveRCT	61	2x2 factorial design: testosterone enanthate(100 mg/wk intramuscularly) + exercise for 16 weeks	Changes in muscle strength, body weight, thigh muscle volume, and lean body mass	Testosterone and resistance exercise increased body weight, muscle mass, muscle strength, and lean body mass. Testosterone and exercise togetherdid not produce greater gains than either interventionalone.
HIV	Grinspoon et al., 2000	https://pubmed.ncbi.nlm.nih.gov/10979879/	ProspectiveRCT	54	2x2 factorial design: testosterone enanthate (200 mg/wk) or placebo injections and progressive resistance training (three times weekly) or no training for12 weeks	Cross-sectional muscle areaand other indices of muscle mass	Cross-sectional muscle area increased in responseto training compared with non training and in response to testosterone therapy compared with placebo
HIV	Kong and Edmonds, 2002	https://pubmed.ncbi.nlm.nih.gov/12409050/	Review/meta-analysis	417	Review of randomized, placebo-controlled trials that compared the effectsof testosterone therapy with placebo	lean body mass, total body weight, over-all exercise functional capacity, and perceived quality of life	The meta-analysis of the six trials showed a difference in the lean body mass between the testosterone group and placebo group of 1.22kg inthe random effect model, 0.51kg in the fixed effectmodel, and 3.34kg for trials that used the intramuscular route.

#6

LONG-TERM TESTOSTERONE TREATMENT IMPROVES LIVER FUNCTION PARAMETERS IN MEN WITH FUNCTIONAL HYPOGONADISM: REAL-WORLD DATA FROM A REGISTRY

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Introduction and Objectives: The prevalence of non-alcoholic fatty liver disease (NAFLD) in patients with hypogonadism is high. Most of these patients are overweight or obese.
Methods: In a registry of 796 men with symptomatic functional hypogonadism, 394 men (49.5%) received testosterone therapy (TTh) by testosterone undecanoate (TU) injections 1000mg/12weeks following an initial 6-week interval (T-group). 402 men opted against TTh and served as controls (CTRL). 13-year data are presented. Means and standard deviations of absolute measures over 13 years are reported.
Fatty liver index (FLI) was calculated using the formula by Bedogni.
Results: Mean age at baseline: 60.9±6.0 years (T-group: 58.5±6.3, CTRL: 63.2±4.8). Mean (median) follow-up: T-group 10.1±3.0(11), CTRL 10.5±3.0(12) years.
γ-GT (U/L) decreased from 45.3±26.2 to 21.1±6.8 in the T-group and increased from 34.8±11.3 to 62.0±6.9 in CTRL ($p<0.0001$ for both).
Triglycerides decreased from 3.2±0.6 to 2.2±0.1 in T-group and increased from 3.0±0.5 to 3.7±0.6 in CTRL ($p<0.0001$ for both).
Waist circumference (cm) decreased from 110.9±13.7 to 96.1±5.1 in the T- group ($p<0.0001$) and increased in CTRL from 111.0±11.8 to 114.3±8.3 ($p<0.0001$).
BMI (kg/m²) decreased from 34.2±5.4 to 27.5±2.4 in the T-group ($p<0.0001$) and increased in CTRL from 30.5±4.4 to 31.6±3.4 ($p<0.0001$).
AST (U/L) decreased from 39.7±15.1 to 20.7±2.0 in the T-group and increased from 26.9±8.3 to 52.7±9.8 in CTRL ($p<0.0001$ for both).
ALT (U/L) decreased from 42.7±14.9 to 24.6±2.3 in the T-group and increased from 31.1±8.6 to 58.6±12.0 in CTRL ($p<0.0001$ for both).
FLI decreased from 89.9±11.0 to 57.0±13.0 in the T-group and increased from 84.3±13.4 to 94.2±5.2 in CTRL ($p<0.0001$ for both).
Adherence to testosterone was 100% as injections were administered in the office and documented.
Conclusion: Long-term testosterone therapy in men with functional hypogonadism improved surrogate parameters of liver function indicating an improvement in NAFLD. All parameters deteriorated in untreated controls.

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Curriculum Vitae
1954 born in Neirab, Syria; 1972 – 1978 studies of human medicine; 1978 specialization in Laboratory medicine; 1978 – 1984 specialization in surgery; 1984 – 1988 specialization as a Urologist; 1988 German board of Urology; 1990 start of Praxis Dr. Haider medical office for Urology; since 1995 start of hormonal therapies in Praxis Dr. Haider; 2004 start of study on long-term testosterone therapies with TU; 2006 specialization for Andrology.
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#7

RELATIONSHIP BETWEEN TIME OF TESTING AND 24-HOUR AVERAGE CONCENTRATION OF TOTAL TESTOSTERONE IN HYPOGOANDAL MEN TREATED WITH AN ORAL TESTOSTERONE UNDECANOATE CAPSULE (JATENZO®)

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Introduction and Objective: In 2019, a novel, first-in-class testosterone (T) replacement therapy (TRT), oral testosterone undecanoate (TU) was approved by the US FDA for the treatment of male hypogonadism. Concordance studies have shown that total T at 6 hrs after the morning TU dose best corresponds to the total T 24-hr average concentration (Cavg). Unfortunately, testing at 6 hrs poses scheduling difficulties. The relationship between other assay time points and Cavg were examined to determine if a conversion factor could be derived.

Subjects and Methods: Hypogonadal men, age 18 – 65 y/o, were recruited into a randomized, open- label, multicenter, dose-titration trial. Dose titration was based on Cavg calculated from serial pharmacokinetic (PK) samples. There were three different PK visits, two potential doses adjustments and the final study Cavg. Ratio between the different timepoints and Cavg were determined for the PK samples following morning drug administration.

Results: With the pooled values from all PK days, there was a linear relationship between T concentrations at 4, 6, and 9 hrs and Cavg (r2= 0.35). A factor was derived to enable conversion of T values assessed at a times other than 6 hrs (i.e., time of blood draw) into an approximation of Cavg: 1.730 x (hours after AM dose). Table 1 summarizes the conversion factors to normalize T to Cavg at various time points. Hence, for a serum T value drawn at either 4 or 8 hrs after the morning oral TU dose, the approximate Cavg would be approximately 75% or 133% of the drawn value, respectively.

Conclusion: While Cavg is best approximated on a serum T level drawn at 6 hours after the AM dose, the Cavg can be estimated from samples obtained at other timepoints using a conversion factor.

Hours after Dose Oral TU Administration	Conversion Factor to Normalize T Value to Cavg
4	**0.76**
4.5	**0.81**
5	**0.85**
5.5	**0.91**
6	**0.97**
6.5	**1.04**
7	**1.12**
7.5	**1.22**
8	**1.33**
8.5	**1.47**
9	**1.64**

#8

COMPARISON BETWEEN ORAL TESTOSTERONE UNDECANOATE (JATENZO®) AND A TRANSDERMAL TESTOSTERONE GEL (ANDROGEL® 1%) IN TOTAL TESTOSTERONE, FREE TESTOSTERONE AND SHBG AFTER ONE-YEAR OF THERAPY

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Objective: A novel oral testosterone undecanoate formulation (TU, JATENZO) is now available for testosterone (T) replacement therapy (TRT) in appropriate men. The purpose of this analysis was to compare the effects of oral TU to those of a transdermal TRT (T-Gel, AndroGel 1%) on circulating total T, measured free T, and sex-hormone binding globulin (SHBG) concentrations.
Methods: Hypogonadal men, age 18-75 y/o, were enrolled into a one-year, open-label, multicenter, dose-titration trial. Subjects were randomized 1:1 between 2 treatment groups: oral TU or T-Gel. Total and free T concentrations were assayed at pre-designated time-points. Standard safety measures, including prostate and cardiovascular biomarkers, have been previously described (Swerdloff and Dudley, Ther Adv Urol 2020;12:1-16).
Results: After one-year of treatment, total and free T significantly increased in both groups. Total T concentrations went from 209.9 ± 8.52 ng/dL to 524.0 ± 19.1 ng/dL (BL to d365, mean ± SEM) and 218.9
± 8.20 ng/dL to 424.7 ± 15.51 ng/dL, for the TU and T-Gel groups, respectively. There was a marked decrease in SHBG for the TU group (-46%; 35.08 ± 2.08 to 18.85 ± 1.02 nmol/L) compared to a significantly smaller decrease (-9%; 34.45± 2.70 to 31.32 ± 2.72 nmol/L) in the T-Gel group. The difference in SHBG response contributed to a significantly higher increase in free T concentrations from baseline to d365 in oral TU group [3.07 ± 1.84 to 12.42 ± 5.08 ng/dL] versus T-Gel [3.20 ± 1.81 to 7.62 ±
3.92 ng/dL].
Conclusion: In addition to normalized total T levels, like T-Gel, oral TU also significantly reduced SHBG and increased free T – both being of higher magnitude than seen with T-Gel.

#9

LONG-TERM TESTOSTERONE THERAPY IMPROVES RENAL FUNCTION IN MEN WITH FUNCTIONAL HYPOGONADISM: EXPERIENCE FROM AN OBSERVATIONAL REGISTRY STUDY

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Introduction: Reduced estimated glomerular filtration rate (eGFR) is associated with increased risk of cardiovascular disease and mortality.
Methods: In a registry of 796 men with symptomatic functional hypogonadism, 394 men (49.5%) received testosterone therapy (TTh) by testosterone undecanoate (TU) injections 1000mg/12weeks following an initial 6-week interval (T-group). 402 men opted against TTh and served as controls (CTRL). 13-year data are presented. Means and standard deviations of absolute measures over 13 years are reported.
eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulae.
Results: Mean age at baseline: 60.9±6.0 years (T-group: 58.5±6.3, CTRL: 63.2±4.8). Mean (median) follow-up: T-group 10.1±3.0(11), CTRL 10.5±3.0(12) years.
Creatinine (mg/dL) decreased from 0.92±0.14 to 0.80±0.06 in the T-group and increased from 1.00±0.14 to 1.25±0.37 in CTRL ($p<0.0001$ for both).
Systolic blood pressure (mmHg) decreased in the T-group from 155.8±16.4 to 129.5±5.9 and increased in CTRL from 142.2±13.9 to 157.2±12.2 ($p<0.0001$ for both).
Diastolic blood pressure decreased in the T-group from 92.9±11.7 to 75.0±3.5 and increased in CTRL from 81.6±8.9 to 93.6±7.0 ($p<0.0001$ for both).
T-group: eGFR (MDRD) (mL/min/1.73 m²) increased from 85.9±11.8 to 95.6±7.7. CTRL: eGFR decreased from 77.4±12.0 to 59.1±10.9) ($p<0.0001$
for both).
T-group: eGFR (CKD-EPI) (mL/min/1.73 m²) increased from 88.6±14.0 to 89.5±4.4 ($p<0.05$). CTRL: eGFR decreased from 77.3±13.8 to 52.5±12.6) ($p<0.0001$).
37 deaths (9.4%), 1 myocardial infarction (MI) and no stroke occurred in the T-group. In CTRL, 111 deaths (27.6%), 86 MIs (21.4%) and 73 strokes (18.2%) were recorded ($p<0.0001$ for all).
Adherence to testosterone was 100% as injections were administered in the office and documented.
Conclusion: Long-term testosterone therapy in men with hypogonadism and T2DM prevents age-related deterioration in GFR.

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1992 born in Bremerhaven, Germany; 2019 – est. 2025 residency in urology, 2012 – 2019 studies of human medicine; 2004 start of study on longterm Testosterone Therapies with TU.
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#10

CHANGES IN METABOLIC PARAMETERS AND BONE MARKERS WITH ORAL VERSUS TOPICAL TESTOSTERONE

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Background: Oral testosterone undecanoate (TU) was recently evaluated for safety and efficacy in an open-label study in comparison with topical testosterone (T).
Methods: Hypogonadal men 18-65 yrs were randomized to oral TU or topical T for approximately 4 months. The starting dose was 237 mg TU twice daily and 60 mg topical T daily. Doses were titrated on Days 21 and 56. P1NP, CTX, and fasting insulin levels from baseline and the last visit (mean 142 days) were analyzed using stored samples in a subset of participants without diabetes. Hematocrit, systolic blood pressure (average of 3 measurements), HDL-C, LDL-C, and fasting glucose were previously assayed and the data now assessed for changes from baseline and differences between the two drugs using linear mixed model analyses. Outliers (>3 IQR from 25th or 75th percentile) were excluded from the analyses.
Results: 203 of 222 participants completed the study (154 oral, 49 topical). Total T increased in both groups with treatment (oral, baseline 207 to 489 ng/dL; topical, baseline 204 to 383 ng/dL). SBP (oral, 2.61 ± 11.86; topical, 1.88 ± 9.81 mmHg) and hematocrit increased (oral, 6.0 ± 7.5%; topical, 4.6 ± 6.4%). HDL-C (oral, -14.2 ± 15.5%; topical, -2.4 ± 16.2%) and total cholesterol decreased (oral, -4.3 ± 16.5%; topical, -4.6 ± 12.0%) (all $p<0.001$). HDL-C decreased to a greater extent with oral TU ($p<0.001$). LDL-C increased with oral TU but decreased with topical T (oral, 6.3 ± 26.5%; topical, -1.5 ± 18.0%; $p = 0.014$); this result was not significant after Bonferroni correction. There were no significant changes in triglycerides, glucose, insulin, P1NP, and CTX.
Conclusion: Both formulations decreased HDL-C and total cholesterol and increased SBP and hematocrit. HDL-C decreased to a greater extent with oral TU. Metabolic changes should be assessed for longer durations in larger studies.

#11

USE OF CLOMIPHENE CITRATE IN OLIGOSPERMIC OBESE MEN WITH HYPOGONADISM: RETROSPECTIVE PILOT STUDY

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Introduction: Obesity a significant risk factor for hypogonadism, and is also associated with reduced semen quality. Clomiphene citrate (CC) is recommended by the AUA in the management of testosterone deficiency and reported to increase testosterone levels in male obesity-related secondary hypogonadism (MOSH). The aim of this study was to evaluate the effect of CC on serum testosterone and semen parameters, particularly in oligospermic obese men.
Methods: A retrospective analysis of data (patient characteristics, semen parameters, hormonal profile) related to men (n=80) who underwent CC treatment for infertility and hypogonadism (testosterone <300 ng/dL) was performed. Patients with obesity (BMI
≥30 kg/m2) and sperm concentration ≤15 x 106/mL were included for analysis. Non- parametric Wilcoxon test was used to compare continuous variables (reported as mean±SD) with a p-value <.05, which was considered statistically significant.
Results: The overall results showed that in oligospermic obese men (n=33), treatment with CC significantly improved baseline serum testosterone (305±184.4 ng/dL vs. 395.4 ±
189.4 ng/dL, p = 0.02) as well as sperm concentration (2.8 ± 3.5 x106/mL vs. 8.2 ± 13.3 x106/mL, p = 0.0001) and motility (29.0% ± 23.1% vs 37.2% ± 19.9%, p = 0.0063).
Furthermore, subsequent examination of oligospermic obese men with hypogonadism (serum testosterone ≤300 ng/dl) treated with CC (n=14) revealed substantial improvements of baseline serum testosterone levels (162.2 ± 43.1ng/dL vs. 341.6 ±
204.7 ng/dL, p = 0.0039) as well as sperm concentration (0.8 ± 1.2 x106/mL vs 4.7 ± 8.5 x106/mL, p = 0.0098) and motility (16.9% ± 18.5% vs 31.3% ± 20.4 %, p = 0.0078).
Conclusion: The results of this pilot study suggest that CC treatment substantially improves total serum testosterone and sperm parameters in oligospermic obese men.

#12

PROFOUND, SUSTAINED WEIGHT LOSS IN MEN WITH FUNCTIONAL HYPOGONADISM RECEIVING 13 YEARS OF LONG-TERM TESTOSTERONE THERAPY - CLINICAL EXPERIENCE OF 8,190 PATIENT-YEARS

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Introduction and Objectives: Testosterone therapy (TTh) is addressed in AACE Guidelines as an approach to treating obesity in hypogonadal men. No other guidelines followed their recommendations. We investigated effects of TTh over 13 years and updated our study results.
Methods: In a registry of 796 men with symptomatic functional hypogonadism, 394 men (49.5%) received testosterone therapy (TTh) by testosterone undecanoate (TU) injections 1000mg/12weeks following an initial 6-week interval (T-group). 402 men opted against TTh and served as controls (CTRL). 13-year data are presented. Means and standard deviations of absolute measures over 13 years are reported.
Results: Mean age at baseline: 60.9±6.0 years (T-group: 58.5±6.3, CTRL: 63.2±4.8). Mean (median) follow-up: T-group 10.1±3.0(11), CTRL 10.5±3.0(12) years.
Waist circumference (cm) decreased from 110.9±13.7 to 96.1±5.1 in the T- group ($p<0.0001$) and increased in CTRL from 111.0±11.8 to 114.3±8.3 ($p<0.0001$). Difference between groups at 13 years: 20.2 ($p<0.0001$).
Weight (kg) decreased from 106.6±17.1 to 84.7±7.7 (T-group) ($p<0.0001$) and increased (CTRL) from 95.3±13.4 to 98.5±9.8 ($p<0.0001$). Difference between groups: 18.2 ($p<0.0001$).
BMI (kg/m²) decreased from 34.2±5.4 to 27.5±2.4 in the T-group ($p<0.0001$) and increased in CTRL from 30.5±4.4 to 31.6±3.4 ($p<0.0001$). Difference between groups: 5.7 ($p<0.0001$).
Weight change from baseline was -19.3±8.0% in the T-group and 9.6±3.5% in CTRL ($p<0.0001$ for both). Difference between groups: -28.5% ($p<0.0001$).
Waist:height ratio decreased from 0.63±0.08 to 0.55±0.03 in the T-group and increased from 0.63±0.07 to 0.65±0.05) in CTRL ($p<0.0001$ for both).
Difference between groups: 0.11 ($p<0.0001$).
Visceral adiposity index (VAI) decreased from 5.1±2.5 to 1.9±0.4 in the T- group and increased from 4.3±2.2 to 7.6±3.6 in CTRL ($p<0.0001$ for both). Difference between groups: 6.2 ($p<0.0001$).
Adherence to testosterone was 100% as injections were administered in the office and documented.
Conclusion: Men with hypogonadism receiving TTh had profound, sustained improvements in anthropometric parameters over 13 years. Untreated men gained weight.

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Curriculum Vitae

1992 born in Bremerhaven, Germany; 2019 – est. 2025 residency in urology, 2012 – 2019 studies of human medicine; 2004 start of study on longterm Testosterone Therapies with TU.
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#13

OPTIMIZING BODY COMPOSITION IN MEN WITH ANDROGEN DEFICIENCY SECONDARY TO HYPOGONADOTROPIC HYPOGONADISM

Florence Comite, Madeleine Heard, Emma Bednarski, Aalin Izhar

Objective: Precision Medicine utilizing N-of-1 can detect, predict, stop, and reverse aging and disease to optimize the health span. Testosterone, a key biomarker related to disorders of aging, declines in men in the thirties, correlating with increased fat mass and decreased muscle mass. Conventional medicine treats this condition with synthetic steroid testosterone replacement therapy (TRT), suppressing physiological testosterone production and undermining the hypothalamic-pituitary-testicular signaling pathway. In contrast, human chorionic gonadotropin (hCG) is a peptide hormone that stimulates Leydig cells to produce testosterone. In this study, hCG's impact on various body composition markers was analyzed.

Methods: Inclusion criteria for this retrospective cohort study were males age ≥29 years who underwent DXA scans prior to hCG and at 10-25 months (except for one 4-month follow-up). The three primary outcomes were subtotal fat mass (SFM), subtotal lean mass (SLM), and percent body fat (PBF), measured at baseline and follow-up DXA scans. P-values were generated using Wilcoxon signed-rank tests on R Studio (v3.6.1).

Results: The 33-patient cohort was 85% Caucasian and ranged in age from 29-75 years (mean=55 years). The mean follow-up period was 14 months. Overall, the median of SFM and PBF decreased from baseline by 2480.2g ($p<.001$) and 2.5% ($p<.0001$), respectively. SLM increased by 1313.3g ($p=.012$).

Discussion: These findings demonstrate hCG's efficacy in optimizing body composition in males presenting with hypogonadotropic hypogonadism. In conjunction, precision biomarkers with N-of-1 analysis allows for personalized actionable interventions. Therapy with hCG should be considered in men with a diagnosis of hypogonadotropic hypogonadism independent of age.

These preliminary findings will also address hCG dosing regimens and key biomarkers, currently undergoing analysis. Assessment of a larger, more ethnically diverse cohort treated with hCG for 5 to 10 years is underway to report short and long-term impact on body composition, as well as other variables.

#14

SUBCUTANEOUS TESTOSTERONE INJECTIONS IN HYPOGONADAL MEN

Rodney L Dennis MD

Testosterone Therapy may be administered in various ways. But, one delivery route not often considered is subcutaneous injection. Some reasons for this may include a lack of familiarity with the technique, a lack of understanding of the benefits or a particular preference for other techniques.

Based mainly on prior use in transgender (female to male) patients, our presumption was that use of subcutaneous testosterone therapy in hypogonadal patients might provide greater patient satisfaction based on the ease of self-administration, less pain with smaller needles, less need for interruption of therapy or therapeutic blood donations for elevated Testosterone or Hematocrit (Hct.) levels and, less Estradiol elevations, compared to reported statistics of intramuscular Testosterone therapy.

Methods:

A total of 60 patients using subcutaneous Testosterone Cypionate therapy were chosen randomly from a larger population of patients based mainly on their time for prescription renewal or lab review. Each patient had to have been on Subcutaneous therapy for more than three months for consideration. Primary lab values evaluated were total Testosterone, Estradiol and Hematocrit. Most patients use 100mg/week, self-delivered.

Results:

The mean Testosterone level in these 60 patients was 576.45 ng/dl. The mean Estradiol level was 26.7 pg/ml. The mean Hematocrit level was 48.95%.

Seventeen patients, 31%, had Hematocrit levels greater than 50%, compared to published data of 66.7% of men on Intramuscular Testosterone therapy. Eleven patients (18%), had Hct greater than 52%, compared to 43.8% of IM patients. Four patients, 6.% , had Hct greater than 54%.

Only four patients (6%) had Estradiol levels greater than 42.6 pg/ml , compared to 20.2% of patients on IM injections.

Conclusion:

Subcutaneous Testosterone replacement therapy in hypogonadal men seems to be well tolerated, more physiologic and potentially less costly for patients who qualify, compared to intramuscular testosterone therapy.

#15

SUSTAINED IMPROVEMENT OF LIPID PATTERN AS A RESULT OF LONG-TERM TESTOSTERONE THERAPY (TTH) OVER 13 YEARS IN MEN WITH FUNCTIONAL HYPOGONADISM

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Introduction: Studies reported inconsistent effects of TTh on the lipid profile in men with hypogonadism.
Methods: In a registry of 797 men with symptomatic functional hypogonadism, 394 men (49.5%) received TTh by testosterone undecanoate (TU) injections 1000mg/12weeks following an initial 6-week interval (T-group). 402 men opted against TTh and served as controls (CTRL). 13-year data are presented. Means and standard deviations of absolute measures over 13 years are reported.
Results: Mean age at baseline: 58.5±6.3 (T-group), 63.2±4.8 (CTRL). Mean (median) follow-up: T-group 10.1±3.0(11), CTRL 10.5±3.0(12) years.
Total cholesterol (TC) (mmol/L for all lipids) decreased from 8.0±1.1 to 5.1±0.3 (T-group) and increased from 6.6±1.3 to 8.0±1.3 (CTRL) ($p<0.0001$ for both).
HDL increased from 1.0±0.3 to 1.6±0.3 (T-group) and decreased from 1.2±0.5 to 0.9±0.4 (CTRL) ($p<0.0001$ for both).
The TC:HDL ratio decreased from 9.1±3.6 to 3.3±0.6 (T-group) and increased from 6.5±3.4 to 11.4±5.6 (CTRL) ($p<0.0001$ for both).
LDL decreased from 4.4±0.9 to 2.5±0.3 (T-group) and increased from 3.5±1.3 to 4.6±1.5 (CTRL) ($p<0.0001$ for both).
Triglycerides (TG) decreased from 3.2±0.6 to 2.2±0.1 (T-group) and increased from 3.0±0.5 to 3.7±0.6 (CTRL) ($p<0.0001$ for both).
The LDL:HDL ratio decreased from 5.1±2.5 to 1.7±0.4 (T-group) and increased from 3.6±2.6 to 6.8±4.5 (CTRL) ($p<0.0001$ for both).
The HDL:LDL ratio increased from 0.24±0.10 to 0.64±0.13 (T-group) and decreased from 0.41±0.22 to 0.22±0.13 (CTRL) ($p<0.0001$ for both).
Non-HDL decreased from 7.0±1.0 to 3.5±0.3 (T-group) and increased from 5.4±1.4 to 7.2±1.4 (CTRL) ($p<0.0001$ for both).
Remnant cholesterol decreased from 2.6±0.9 to 1.0±0.3 (T-group) and increased from 1.9±0.9 to 2.6±0.8 (CTRL) ($p<0.0001$ for both).
The TG:HDL ratio decreased from 8.4±3.7 to 3.2±0.6 (T-group) and increased from 6.7±3.5 to 11.7±5.7 (CTRL) ($p<0.0001$ for both).
Conclusion: Long-term treatment with TU in men with functional hypogonadism improved the lipid profile, which worsened in controls.

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Curriculum vitae
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#16

BENEFICIAL EFFECTS OF TESTOSTERONE THERAPY IN WOMEN: THE PROOF IS IN THE PUDDING CASE PRESENTATIONS AND TESTIMONIALS

Glaser, Rebecca

Introduction: Continuous testosterone delivered by subcutaneous implant has been shown to significantly relieve symptoms of hormone deficiency in women with and without breast cancer.1-4 Androgen receptors are present in every organ system. Testosterone has a dose dependent direct effect at the AR throughout the body including the brain and nervous system. In addition, testosterone is aromatized locally to estradiol and has a secondary effect at the estrogen receptor. Testosterone is anti-inflammatory, which has a beneficial effect in inflammatory related diseases. Serum testosterone accounts for 10-20 percent of bioavailable testosterone. Aging is associated with a decline of all androgens including the adrenal precursors, DHEA(S) and androstenedione, which produce the majority of local bioavailable testosterone.

Methods: Adequate doses of continuous testosterone delivered by subcutaneous implants have significant beneficial effects on age-related diseases/conditions.

Case 1: Urinary Incontinence (case presentation, testimonial) – 79 y/o with complete resolution of incontinence and other symptoms

Case 2: Essential tremor (case presentation) – documented marked improvement of tremor 2h post testosterone implant, significant impact on quality of life

Case 3: Memory loss, dementia (case presentation) – 75 y/o with dose dependent improvement in memory and eye hand coordination

Case 4: Vertigo (testimonial) – Resolution of severe vertigo after 8 years

Case 5: Aromatase induced arthralgia (case presentation, testimonial) – 59 y/o breast cancer survivor with incapacitating pain completely resolved on testosterone + anastrozole therapy

Case 6: Breast cancer survivor, disease control and quality of life (case presentation) – 65 y/o with metastatic disease, weight loss, weakness, bone pain, muscle loss, anemia. Documented tumor response and symptom control on therapy

Conclusion: Adequate doses of testosterone (with or without an aromatase inhibitor) – providing adequate amounts of bioavailable testosterone locally at the androgen receptor – can significantly affect age and inflammatory related diseases.

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#17

HYPOGONADISM AND INTRACRANIAL HYPERTENSION, A CASE REPORT AND BRIEF REVIEW

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Introduction: Primary hypogonadism, or hypergonadotropic hypogonadism, occurs when total testosterone levels are decreased but gonadotropins are increased. This condition reflects a derangement in the hypothalamus-pituitary-gonadal axis. Comorbidities such as obesity, diabetes, chronic obstructive pulmonary disease, and prostate disease have been studied in association with hypogonadism. However, there are fewer studies that have shown an association between primary hypogonadism and intracranial hypertension in men.
Case Presentation: We present a case in which a 40-year-old obese male presented for evaluation and treatment of adult-onset primary hypogonadism. Prior to starting testosterone replacement therapy, he underwent workup to rule out other causes of his low total testosterone, including a brain MRI. He was found to have increased tortuosity of the optic nerves bilaterally and thinning of the pituitary parenchyma concerning for intracranial hypertension. At presentation, he did not endorse any clinical symptoms of intracranial hypertension, such as visual changes, papilledema, gait changes, or headaches. However, he had yet to undergo a lumbar puncture for definitive diagnosis or exclusion of intracranial hypertension.
Conclusion: Although this patient with primary hypogonadism did not undergo a lumbar puncture to demonstrate increased intracranial pressure, his MRI findings and normal neurologic exam support a diagnosis of intracranial hypertension. His case supports an association between intracranial hypertension and primary hypogonadism that may affect how clinicians should evaluate patients presenting with low testosterone.

#18

EFFECT OF BULBOSPONGIOSUS MUSCLES CUTTING WITH FRENULAR DELTA EXCISION FOR TREATMENT PREMATURE EJACULATION (ALAA AGLAN OPERATION)

Alla Aglan

Introduction: Alaa aglan operation consists of two parts. Cutting bulbospongiosus muscles bilaterally, And excision of elliptical part of frenular delta. The operation has its own prediction test It is easy just spraying local anesthesia (procomail 10%®) at coronal ridge (inhibits glans-bulbospongiosus reflex) and at frenular delta (temporary excision) 30 minutes before having sex. The operation could be reversed by repairing the muscles again.
Methods: 1050 Cases were operated between 1/1/2015 and 3/10/2015 follow up was done at 1,3,6,12 months intervals then yearly (5 years duration).
Results: Satisfaction rate 99.6% due to prediction test application, in our early trials beyond this study Satisfaction rate was 71% (without prediction test). Side effects were minimal, No regression in results in any patient during the following up period. Only 4 patients were not satisfied although the operation was successful. 1st patient complained from neuroma due to adhesions post operative, Adhesiolysis was done, total relief of pain reported by patient immediately post operative, 2nd patient reported that the distance of expulsion of semen from penile orifice decreased in comparison to that before surgery. 3rd patient reported hematoma, Evacuation was done without complications. 4th patient reported that he lost the sensation of repetitive contraction of muscles at peno-scrotal area during ejaculation. Many patients reported absence or decrease in number of wet dreams post operative.
Conclusion: Alaa aglan operation is safe, Immediate, Curative technique for premature ejaculation treatment provided that prediction test shows good response.

#19

EFFECT OF BULBOSPONGIOSUS MUSCLES CUTTING WITH FRENULAR DELTA EXCISION AND VENTRAL NEURECTOMY FOR TREATMENT OF PREMATURE EJACULATION (ALAA AGLAN2 OPERATION)

Alla Aglan

Introduction: In our study (Alaa Aglan operation) we reported a case of penile skin loss at anterior third of ventral aspect of penis and we cut the bulbospongiosus and skin graft (split thickness) was applied, this patient reported improvement in ejaculation time from 2 minutes to 20 minutes. another patient came to us with penile abscess due to neglected wound after penile filler injection, the skin was lost at anterior third of ventral aspect of penis. Skin graft (split thickness) was applied. That patient reported that the time of ejaculation improved from 2 minutes to 25 minutes although we didn`t cut the bulbospongiosus muscles. Procomail%10® (prediction test) was applied at anterior third of ventral aspect of penis plus injection of local anesthesia xylocaine%10® at para-urethral area bilaterally (perineal nerves). 30 minutes before intercourse.

Methods: The study was done between 15/10/2011 and 17/2/2016, 218 patients were involved, follow up was done at 1, 3,6,12 months then yearly. Bulbospongiosus muscles were cut bilaterally, elliptical part of frenular delta were excised, ventral neurectomy were done including perineal nerves and dorsi-lateral branches of dorsal nerves.

Results: Satisfaction rate 98% it was 67% beyond this study (without prediction test). The side effects were minimal. Infection, wound dehesience and oedema were treated medically. 4 patients reported numbness disappeared within 3 months, 2 patients reported neuroma responded to single Botox injection (40 units).

Conclusion: Alaa Aglan(2) is modification to Alaa Aglan operation more potent, effective and is indicated if prediction test is promising.