on PK was assessed. Exposure-response relationship was evaluated in TED studies for key efficacy endpoints (proptosis response rate, % patients with a clinical activity score value of 0 or 1, and diplopia responder rate) and selected safety variables (hyperglycemia and muscle spasms).

Results: Teprotumumab PK was linear in TED patients and consistent with other immunoglobulin G1 monoclonal antibodies (IgG1 mAbs), with low systemic clearance (0.334 L/day), low volume of distribution (3.9 L for central compartment and 4.2 L for peripheral compartment), and long elimination half-life (19.9 days). [4,5] Model-predicted mean (± standard deviation) steady-state area under the concentration curve (AUC_{ss}), peak ($C_{max,ss}$), and trough ($C_{min,ss}$) concentrations in TED patients were 131 (± 30.9) mg·hr/mL, 643 (± 130) µg/mL and 157 (± 50.6) µg/mL, respectively, suggesting low inter-subject variability.

Population PK analysis indicated no significant impact of baseline age, gender, race, weight, smoking status, renal impairment (mild/moderate), and hepatic function (total bilirubin, aspartate and alanine aminotransferases) on teprotumumab PK. Female patients had 15% higher $C_{max,ss}$ but similar AUC compared to male patients, which is not considered clinically relevant.

Exposure-response analysis from the TED dose regimen indicated no meaningful correlations between exposures (AUC_{ss}, $C_{max,ss}$ and $C_{min,ss}$) and key efficacy endpoints or selected safety variables, supporting the demonstrated, favorable benefit-risk profile of the TED dose regimen.[2]

Conclusion: Teprotumumab PK was characterized in TED patients by long elimination half-life, low systemic clearance and low volume of distribution, consistent with other IgG1 mAbs. There was no meaningful exposure-response relationship at the selected TED dose regimen for both efficacy and safety endpoints, supporting the teprotumumab dose regimen used in TED patients.

Reference: (1) Smith TJ, et al. *N Engl J Med* 2017;376:1748-1761. (2) Douglas RS, et al. AACE 2019 late-breaking abstract. (3) ClinicalTrials.gov: NCT00400361. (4) Dirks NL et al. *Clin Pharmacokinet*. 2010;49(10):633-59. (5) Ryman JT et al. *CPT Pharmacometrics Syst Pharmacol*. 2017;6(9):576-88.

Diabetes Mellitus and Glucose Metabolism

DIABETES DIAGNOSIS, TREATMENT AND COMPLICATIONS

Gender Difference in the Outcome of Patients with Diabetes Admitted for Hyperosmolar Hyperglycemia. from the National Inpatient Sample.

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SUN-620

Objective: There is paucity of literature on the impact of gender on outcomes of hyperosmolar hyperglycemic state (HHS) among adult patients with diabetes. The aim of this study was to evaluate the effect of gender on the outcome of these patients. Methodology: The National Inpatient Sample (NIS) was queried for all patients who were admitted with a diagnosis of hyperosmolar hyperglycemic state (HHS) during the years 2005-2014. The primary outcomes of the study were all-cause mortality, acute myocardial infarction (MI), and acute stroke. The secondary outcomes were acute kidney injury (AKI), rhabdomyolysis, acute respiratory failure (ARF), need for mechanical ventilation (MV), length of stay (LOS), and total cost of stay. Results: Overall, 188,725 patients were admitted for HHS. Mean age of males was 53.7, standard error of the mean (SEM: 0.13), and of females was 58.5 (SEM: 0.15), p<0.001. Females were (43.9%), Caucasians were 37.4% while African Americans were 35.2%. Total mortality was 1.1%, MI was 1.3% and stroke was 1.1%. Most common secondary outcome was AKI seen in 31.3% followed by ARF seen in 2.9% of total. The mean cost was 7887 $ (SEM: 84.6) and mean LOS was 4.1 days (SEM: 0.03). Both males and females had equivalent rates of mortality, stroke, ARF and need for mechanical ventilation. Compared to males, females had significantly higher risk for MI 1.6% vs 1.1%, p<0.001, lower risk for AKI 29.3% vs 32.9%, p<0.001, lower risk for rhabdomyolysis 1.1% vs 2%, p<0.001 and higher LOS 4.3 vs 3.9 days, p<0..01 and higher total costs 8165.6 $ vs 7669.3 $, p < 0.001. On multivariable analysis, female gender was independently predictive for higher risk for MI with adjusted odds ratio (aOR) 1.34 [95%CI: 1.08-1.67] p=0.01 and lower risk for rhabdomyolysis with aOR 0.52 [95%CI: 0.42-0.63] p<0.001 and lower risk for AKI with aOR 0.74 [95%CI: 0.7-0.78] p<0.001. In addition, female gender correlated with higher cost and length of stay. Conclusion: Females with hyperosmolar hyperglycemic state are at higher risk for MI and lower risk for AKI and rhabdomyolysis.

Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Coordination of Care: National Survey of Endocrinologists' Experience with PCPs

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MON-138

Introduction:

Coordination of care between primary care physicians (PCPs) and specialists is crucial in providing safe, efficient specialty care for referred patients, but shortcomings in coordination are common.

Objective:

Examine endocrinologists' experience of coordination with PCPs and examine the relationship of a shared EHR to coordination.

Methods:

We surveyed a national sample of US endocrinologist members of the Endocrine Society (ES) or American Association of Clinical Endocrinologists (AACE), using a previously-developed online survey for specialists about care coordination[1]. ES and AACE included a link in a web-based newsletter and dedicated email. Four multi-item scales included 18 items measuring aspects of coordination with PCPs in the past 3 months: Communication (timeliness and helpfulness), Data Transfer (timeliness and usability), Relationships (mutually respectful), and Roles and Responsibilities (referral clarity, sufficiency, and appropriateness). Item responses and scale scores were on a 7-point frequency scale. A single-item measure of overall coordination with PCPs was measured on a 10-point scale (0 worst possible to 10 best possible). We asked "With about how many referring PCPs do you share an EHR?". We examined frequencies of individual item responses (≤30%, about 50%, or ≥ 70% of the time) and extent of shared EHR with PCPs (None, Some, All), calculated mean scale scores (range 1-7) and used ANOVA to examine the relationship of a shared EHR to coordination scales and overall coordination.
Results:
Of 236 respondents: 35% age ≥ 60, 44% female, 80% ≥ 75% clinical effort. The highest frequency of good coordination (≥70% of the time) was reported for: aligned expectations of roles (84%), feeling valued by PCPs (80%) and clear division of responsibilities (70%). The lowest frequency of good coordination was for: kept informed by PCP about relevant issues (14%), and PCPs adequately evaluated prior to referring (18%). Mean (SD) for scale scores were: Communication 4.2 (1.0), Data Transfer 4.2 (1.1), Relationships 4.9 (0.8), Roles and Responsibilities 4.2 (0.9). The score for overall coordination with PCPs was 6.0 (1.9). Sharing an EHR with more PCPs was associated with higher Data Transfer scores (None, N=59, 3.9 (1.0), Some, N=126, 4.1 (0.9), All, N=26, 5.4 (0.8), P for trend <0.001). The effect size (Cohen's *d*) for the difference between None and All EHR sharing was 1.6, well over the threshold for "large" effect size (d = 0.8).
Conclusions:
There are opportunities for improvement across all aspects of inter-clinician coordination for endocrinology referrals. Use of a shared EHR improves data transfer, but not other aspects of coordination.
1. Vimalananda VG, Fincke BG, Qian S, et al. Development and psychometric assessment of a novel survey to measure care coordination from the specialist's perspective. *Health Serv Res*. 2019;54(3):689-699.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING II

Crude Protein Extract of Pyropia Yezoensis Protects Against Tumor Necrosis Factor-á-Induced Apoptosis and Atrophy in C2C12 Myotubes

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MON-724

Proinflammatory cytokines such as tumor necrosis factor (TNF)-α play an important role in the development of skeletal muscle atrophy, and TNF-α-induced apoptosis may mediate skeletal muscle atrophy. Therefore, we evaluated the effect of *Pyropia yezoensis* crude protein (PYCP) on TNF-α-induced apoptosis and identified the involved signaling pathways. For this purpose, C2C12 myotubes were treated with 20 ng/mL TNF-α in the presence or absence of 25-100 μg/mL PYCP for 48 h. Treatment with TNF-α markedly increased the protein level of TNF-receptor 1 (TNF-R1). In contrast, treatment with PYCP downregulated the TNF-α-induced increase in the TNF-R1 protein level. Also, the expression of Bax, Bcl-2, cytochrome C, and apoptosis-inducing factor, markers of apoptosis in myofibers, was increased by TNF-α, but this effect was inhibited by PYCP in a concentration-dependent manner. In addition, exposure of C2C12 myotubes to TNF-α for 48 h enhanced the activity of caspase-3, which was significantly inhibited by PYCP. Furthermore, poly[ADP-ribose] polymerase cleavage and histone-associated DNA fragmentation were markedly increased by TNF-α and attenuated by PYCP in a concentration-dependent manner. In conclusion, the ability of PYCP to inhibit the apoptosis induced by TNF-α suggests that it has therapeutic potential for skeletal muscle atrophy.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

T2 MRI Signal Analysis of The Pituitary Gland Is Efficient in the Diagnosis of Acromegaly Due to GHRH Ectopic Secretion

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MON-294

Less than 1% of cases of acromegaly are secondary to ectopic secretion of Growth Hormone Releasing Hormone (GHRH), usually from a neuroendocrine tumor. Symptoms of ectopic acromegaly did not differ from classical acromegaly from pituitary origin. GH and IGF 1 values are in the same range. GHRH measurement only could make the correct diagnosis but is not routinely proposed in acromegaly. MRI of the pituitary gland is considered not very effective in ectopic acromegaly. In the literature (1), different patterns are described: pituitary enlargement (46%), adenoma (30%), empty sella (2%) or normal (20%). But T2MRI signal of the pituitary is never mentioned nor illustrated. Finally, in about 30 % of published cases, pituitary surgery, of course inefficient, was performed.
These data enhance the poor contribution of imaging studies in the published cases of ectopic acromegaly.
We have been able to obtain and read MRIs and particularly T2WI of 27 acromegalic patients- 20 female, 7 male- due to GHRH hypersecretion from a neuroendocrine tumor –principally bronchial carcinoid and pancreatic NET- which have been published or not. Remarquably, T2 sequences were available in only 27/61 cases we have collected. In all these 27 cases but two, the T2 signal was clearly hypointense if compared