OC.06 Miscellaneous

OC.06.1
ANALYSIS OF THE EFFICACY OF OCA IN PRIMARY BILIARY CIRRHOSIS BY VARYING PATIENT DISEASE SEVERITY ACROSS THREE RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIALS
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Background and aim: Obeticholic acid (OCA), a selective and potent farnesoid X receptor (FXR) agonist, produced significant liver biochemistry improvements, including alkaline phosphatase (ALP) and total bilirubin (bili) in 3 randomized, double-blind (DB) placebo-(PBO)-controlled trials in primary biliary cirrhosis (PBC). This pooled analysis from the 3 trials evaluates efficacy of OCA across a range of disease severity based on baseline (BL) ALP tertile and total bili. (≤ULN/≥ULN).

Material and methods: Key inclusion criteria: ALP 1.5 to 10x ULN and conjugated bili ≤2x ULN for the two 3 month trials and ALP ≥1.67x ULN or total bili >ULN but <2x ULN for the 12 month trial. Data were pooled based on end of DB treatment (EOT). Treatment arms were PBO (n=134) and ≤OCA 10 mg (n=201). Endpoints were LS mean (SE) change from BL to EOT for ALP and percent of patients achieving a composite endpoint (ALP <1.67 ULN, total bili ≤ULN and ALP decrease ≥15%), shown to be correlated with long-term survival in PBC. Safety and tolerability by disease severity were also assessed.

Results: Significant differences for OCA compared with PBO for both efficacy endpoints were achieved irrespective of PBC disease severity. The magnitude of ALP reduction was proportional to ALP and total bilirubin (bili) in 3 randomized, double-blind (DB) placebo-(PBO)-controlled trials in primary biliary cirrhosis (PBC). This pooled analysis from the 3 trials evaluates efficacy of OCA across a range of disease severity based on baseline (BL) ALP tertile and total bili. (≤ULN/≥ULN).

ANCova model for p-value (PBO vs active OCA)

OC.06.2
PANCREATIC CANCER IN WOMEN: LATE ONSET OF MENOPAUSE, USE OF HORMONE REPLACEMENT THERAPY AND TWO-PARITY ARE PROTECTIVE FACTORS
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Background and aim: The incidence of Pancreatic ductal adenocarcinoma (PDAC) is slightly higher in men than in women, although the difference in smoking and alcohol consumption between the two genders does not explain this disparity completely. Reproductive and hormonal factors might have an influence, but the few published data are inconsistent. The aim of this study is to investigate the role of reproductive and hormonal factors on PDAC occurrence in women.

Material and methods: We conducted a uncenter case-control study on women; risk factors were screened through questionnaires about gynecologic and medical history. Cases were matched to controls for age with a 1:2 ratio.

Results: 160 PDAC and 320 matched controls (mean age 70 in both groups) were enrolled. Age of onset of menopause was significantly lower in cases (48.9 vs. 50; p=0.02). At a logistic regression multivariate analysis adjusted for smoking, older age at menopause (OR:0.9 per year; 95% CI:0.92-1), use of hormonal replacement therapy (HRT) (OR:0.14; 95% CI:0.04-0.49) and having given birth to two children (OR:0.62; 95% CI:0.39-0.98) were significant, independent protective factors. No difference among cases and controls was found on age of onset of menarche, nulliparity or parity different from two, use of birth control pill or number of abortions.

Conclusions: The results of this study provide support for the hypothesis that PDAC is related to reproductive or hormonal factors. In our cohort of patients, late onset of menopause, use of HRT and having given birth to two children are protective factors for the occurrence of PDAC. Conversely, age at menarche, history of abortions, multiple abortions, use of OC, years of use of HRT or OC were not related to risk. These data confirm some previous findings on menopause age and number of births while, to our knowledge, this is the first study to show a protective effect of Hormonal Replacement Therapy.

OC.06.3
PROTECTIVE ACTIVITY OF LACTOBACILLUS RHAMNOSUS GG-DERIVED FACTORS ON PATHOGEN LIPOPOLYSACCHARIDE (LPS)-INDUCED DAMAGE OF HUMAN COLONIC SMOOTH MUSCLE CELLS
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Background and aim: Some of the beneficial effects of probiotics result to be determined by secreted probiotic-derived factors, identified as “postbiotic” mediators. The identification of these soluble factors may represent an opportunity not only to understand their fine mechanisms of action but also to develop new therapeutic strategies, that would avoid risks associated with the administration of live bacteria. Aim of this study was to evaluate if supernatants harvested from LGG cultures protect human smooth muscle cells (SMC) from persistent LPS-induced myogenic damage.