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Background: High drug use in older adults is associated with adverse outcomes. The association between medication use as a risk factor for mortality is investigated in a Belgian community-dwelling cohort of oldest old (80+).

Methods: Data was collected between November 2008 and July 2011 of the Belfrail-med cohort. Baseline predictors included medication data, and personal, clinical, and functional characteristics. Medications were coded by the Anatomic Therapeutic Chemical classification. Survival analysis included Kaplan-Meier and Cox regression analysis.

Results: Participants' (n = 503) mean age was 84.4 years (range 80 – 102) and 61.2% was female. The mean medication use was 5.4 (range 0 – 16). Mortality rate after 18 months was 8.9% (n = 45). The mortality group was significantly older (85.7 vs 84.3 years), received more nursing care (53.3% vs 35.2%), had a higher multimorbidity (CIRS 4.6 vs 3.7), and used more medications (6.4 vs. 5.3). Usage of antidepressants (Hazard Ratio 2.0, 95% CI 1.0 – 3.9), loop diuretics (HR 2.6, 95% CI 1.4 – 4.9), verapamil/diltiazem (HR 3.5, 95% CI 1.4 – 8.9), or anticholinergics (HR 2.4, 95% CI 1.3 – 4.4) were independent risk factors for mortality. Corrected for gender and age, loop diuretics (HR 2.8, 95% CI 1.2 – 4.3), anticholinergics (HR 2.05, 95% CI 1.1 – 3.8), and verapamil/diltiazem (HR 2.7, 95% CI 1.0 – 7.1) proved risk factors for mortality in a multivariate model.

Conclusions: Medication use is a risk factor for mortality in the oldest old. Usage of loop diuretics, verapamil/diltiazem, or anticholinergics by the oldest old requires close follow-up and further analysis for comorbidities.

PHASE I, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED CLINICAL TRIAL WITH THE PROBIOTIC NYADITUM RESAE® IN ADULTS WITH OR WITHOUT LATENT TUBERCULOSIS INFECTION

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Background or Introduction: Tuberculosis could be induced by an exaggerated inflammatory response against *Mycobacterium tuberculosis* (Mtb) in people with Latent Tuberculosis Infection. A probiotic containing heat-killed environmental *Mycobacterium manresensis* (Nyaditum resae®) (NR) was developed to induce a Treg-cells-mediated tolerance process, generating cross-immunity with Mtb. To evaluate its safety and immunogenicity a phase I clinical trial was conducted.

Material and Methods: A double-blind placebo-controlled, randomized trial stratified by tuberculosis skin test (TST) response was performed. Inclusion criteria: ≥18 years. Main exclusion criteria: active tuberculosis, immunodeficiency and pregnancy. Primary endpoints were adverse events (AE) and immunogenicity.

Volunteers received either placebo, NR low [104 Colony Forming Units (CFU)] or high [105 CFU] dose vials, orally daily during 14 days. Four control visits including physical exploration, blood analysis and a volunteer's log register were performed in a 6 weeks period.

Results: Of 76 volunteers screened, 51 were enrolled (18 received placebo, 16 low dose NR, and 17 high dose NR). They were mainly female (62%) with a mean (SD) age of 31.8 years (12). No loss to follow-up or discontinued intervention occurred.

A total of 322 AE were reported in 49 volunteers (96%), and 46.3% (149) considered possibly or probably related to the treatment. Most of AE were gastrointestinal (82%) and mild. None of them were severe. There were no significant statistical differences when comparing safety between groups.

A statistically significant increase on the Treg response (effector CD25+CD39– and memory cells CD25+CD39+) was observed in those groups treated with NR, higher in TST positive volunteers and in the high dose NR group.

Conclusions: Data support that NR administration has a good safety profile, and is able to induce an immunologic response through increasing Treg cell population. Future clinical trials are needed to assess the efficacy of NR in lowering the risk of the progression from latent infection to tuberculosis.

LIVER INJURY WITH DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS (GLIPTINS): SIGNALS EMERGING FROM THE US-FDA ADVERSE EVENT REPORTING SYSTEM

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Background: The recent debate on alogliptin hepatotoxicity has aroused interest on liver injury as a class effect of dipeptidyl peptidase-4 (DPP-4) inhibitors, known as gliptins. Considering that drug-induced liver injury (DILI) is unpredictable and clinical trials underpowered, we analysed the largest publicly available database of spontaneous reports, the US-FDA Adverse Event Reporting System (FAERS).

Material and Methods: We extracted FAERS reports (up to December 2013) where DDP-4 inhibitors were recorded as suspect and performed a *case/non case* study by calculating the Reporting Odds Ratio (ROR) with 95% CI, as a measure of disproportionality. A list of Preferred Terms (PTs) was compiled according to the Medical Dictionary for Regulatory Activities terminology to identify the following clinical events (i.e., cases): (a) Overall Liver Injuries (OLI, including acute and chronic damage); (b) Acute Liver Failure (ALF, a subcategory including only acute severe hepatic injuries). Non cases were all other reports without pre-specified PTs of interest. A signal was defined by statistical significant ROR (lower limit of the 95% CI >1).

Results: During the study period, no signal of DILI emerged for alogliptin (no ALF cases; number of OLI cases=100; ROR = 1.73; 95% CI = 0.55-4.20) and linagliptin (no ALF cases; OLI cases = 18; ROR = 1.20; 95% CI = 0.71-1.92). Conversely, statistically significant associations were found for OLI with the first-in-class DDP-4 inhibitor sitagliptin (234; 1.33; 1.16–1.52), and also for saxagliptin (38; 1.47; 1.03–2.03) and vildagliptin (22; 6.51; 3.92–10.35).

Conclusions: The heterogeneous marketing life, penetration and utilization of DDP-4 inhibitors may explain signals originated from FAERS, and justify population-based studies to assess actual class effect of gliptins. Notably, while the European label does not address DILI risk, the US label recommends mandatory hepatic monitoring before and during alogliptin (the latest DDP-4 inhibitors receiving US approval): this mandatory recommendation may have contributed to minimize DILI risk by excluding diabetic patients with baseline hepatic enzyme elevation.

H1 ANTIHISTAMINES' EFFECT ON PRO-INFLAMMATORY CYTOKINES IN ALLERGIC RHINITIS TO HOUSE DUST MITES

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