clinical trials. These DOE should be explored to better design clinical trials.

Objectives: To identify effect-modifiers of antipsychotic drugs, in schizophrenia treatment.

Methods: Data were retrieved from the CGS observational cohort study, including 1859 schizophrenia inpatients and outpatients aged 15-65 years old through 177 centres in France. Patients were followed-up at 3, 6, 9 and 12 months.

Patients who initiated or switched APD were identified and schizophrenia symptoms evolution was measured 3 to 6 months later, using the BPRS-18 scale (ΔBPRS).

First, potential DOE of APD were identified through a focused literature search, which was reviewed by 3 schizophrenia specialized psychiatrists. Five DOE were short-listed: (1) shorter duration of illness, (2) higher level of negative symptoms, (3) poor adherence, (4) cannabis/drug use and (5) tobacco use.

Effect modification was assessed using sub-group analyses, with comparisons of the ΔBPRS in the 2 strata of each DOE. Two-sided Welch t-tests were used with a "non-conservative" type-I error $\alpha = 0.2$. Multivariate analyses were not performed due to limited sample size.

Results: Out of 1859 schizophrenia patients, 116 patients initiated drug B, 272 patients initiated drug D and 204 patients initiated drug K. Other drugs were initiated by too few patients. The mean decreases in BPRS were: -7.2 points (SD = 16.3) in "drug B initiators", -7.5 points (SD = 15.3) in "drug D initiators" -3.9 points (SD = 14.1) in "drug K initiators". The level of symptoms improvement was higher in patients with a "higher level of negative symptoms" for all drugs ($p < 0.012$) and "poorer adherence", for drugs D and K ($p < 0.013$). The level of symptoms improvement was also better in patients who did not smoke, however not significantly. Cannabis use was not an effect-modifier, in all drugs.

Conclusions: Overall, "adherence", "tobacco smoking" and "negative symptoms" may be drivers of effectiveness. These factors should be adequately captured and explored in pre-launch clinical trials to avoid an efficacy-effectiveness gap.

289. A Systematic Literature Review on the Efficacy-Effectiveness Gap: Comparison of Randomized Controlled Trials and Observational Studies of Glucose-Lowering Drugs

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Background: Beneficial effects of drugs can be divided into efficacy and effectiveness. An understanding of the efficacy-effectiveness gap is important for patients, health care professionals, payers, regulators and the pharmaceutical industry to provide effective treatments.

Objectives: to identify a potential efficacy-effectiveness gap, and possible explanations (drivers of effectiveness) for differences between results of randomized, controlled trials (RCTs) and observational studies investigating anti-diabetic drugs.

Methods: A systematic literature review of studies comparing glucagon-like peptide-1 analogues (GLP-1) with insulin or comparing dipeptidyl peptidase-4 inhibitors (DPP-4i) with sulfonylurea, all with change in glycated haemoglobin (HbA1c) as outcome. Information on baseline characteristics of the study population, publication year, study duration, number of patients and quality of observational studies were extracted.

Results: Twelve RCTs and six observational studies comparing GLP-1 with insulin, and 19 RCTs and four observational studies comparing DPP-4i with sulfonylurea were finally included. No differences were observed in baseline characteristics of the study populations (age, sex, BMI, time since diagnosis, HbA1c) or effect sizes across study designs. No patterns were observed when plotting effect estimates against baseline characteristics of the study population, publication year, study duration or number of patients, neither within nor across RCTs and observational studies. The quality of the identified observational studies was generally low.

Conclusions: Neither potential drivers of effectiveness nor an efficacy-effectiveness gap were identified. However, the low quality of the identified observational studies may have hidden a true efficacy-effectiveness gap.

290. Interim Analyses in Prospective Observational Studies of Medical Product Safety

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