supported by translational models of this disease, even if the antipsychotics derived from this conceptual framework are not yet available on the market. However, the need for new pathogenesis models for schizophrenia and new generations of antipsychotics is acute, therefore, an exploration of the antipsychotics in the pipeline could be helpful in understanding the current stage of research in schizophrenia.
**Objectives:** To assess the evidence supporting the potential benefits of new antipsychotics in the pipeline.
**Methods:** A literature review was performed through the main electronic databases PubMed, Cochrane, Clarivate/Web Of Science, and EMBASE) and clinical trials repositories (US National Library of Medicine and World Health Organization Clinical Trials Registry Platform) using the search paradigm "antipsychotics" AND "schizophrenia" AND "non-dopaminergic" AND "non-glutamatergic". All papers published between January 2010 and September 2022 were included.
**Results:** Xanomeline/trospium (xanomeline is a muscarinic M1/M4 receptor agonist at the central nervous system, while trospium limits its peripheral effects) was efficient for schizophrenia in one phase III clinical trial. Pimavanserin (a selective 5HT2A inverse agonist and antagonist) was efficient in improving negative symptoms of schizophrenia in a phase II trial. Roluperidone (a 5HT2A and σ2 receptor antagonist) has been associated with favorable results in phase III clinical trials, mainly on negative symptoms of schizophrenia. SEP-363856 is a TAAR-1 agonist and 5HT1A agonist, currently explored in phase III clinical trials for schizophrenia. MK-8189 is a phosphodiesterase 10A inhibitor, investigated in phase III clinical trials for schizophrenia.
**Conclusions:** Based on the retrieved data in the literature, multiple mechanisms, other than glutamatergic and dopaminergic pathways, are currently being investigated, and many of the antipsychotics based on these mechanisms are in the advanced stage of research. This is important not only for the clinical need to find more efficient and tolerable drugs for patients with schizophrenia but also because they may shed new light on the pathogenesis of this disease.

**Disclosure of Interest:** None Declared

## EPP0896

## Defining the therapeutic reference range for cariprazine

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**Introduction:** According to the Consensus Guideline, the "therapeutic reference range" (TRR) defines ranges of drug blood concentrations that specify a lower limit below which a drug-induced therapeutic response is unlikely to occur and an upper limit above which tolerability decreases or the therapeutic improvement ceases. The TRR can be obtained from concentration measurements (trough (pre-dose) plasma concentration under steady-state conditions) in studies at therapeutically effective doses.
**Objectives:** The aim is to examine the TRR for cariprazine (CAR: 1.5 mg/day to 6 mg/day) in schizophrenia studies.
**Methods:** The population based TRR for CAR is derived by PK/PD evaluation from phase 2/3 schizophrenia efficacy studies with sparse PK sampling. The population PK simulated TRR is compared to the actually measured values obtained from two PK studies. As the two active metabolites of cariprazine also contribute to the drug effect, plasma exposure is given for Total cariprazine (CAR + DCAR + DDCAR) and the parent drug (CAR).
**Results:** PK/PD analyses demonstrated an increase in efficacy with increasing exposure. These efficacy results are related to Total cariprazine trough concentrations of ca. 30 nM and 100 nM that determine the lower and upper TRR limits. For the parent drug, the pre-dose mean plasma concentration at 6 mg/day was between 5.7-10 ng/mL in different studies, while at 1.5 mg/day it was 1.9 ng/mL.
**Conclusions:** The TRR of the trough plasma levels at steady state is ca. 30 – 100 nM for Total cariprazine and ca. 2-10 ng/mL for the parent drug (unchanged drug) for schizophrenia treatment.

**Disclosure of Interest:** M. Kapás Employee of: Gedeon Richter Plc., A. Horváth Employee of: Gedeon Richter Plc., D. Djuric Employee of: Gedeon Richter Plc., R. Csehi Employee of: Gedeon Richter Plc., Á. Barabássy Employee of: Gedeon Richter Plc.

# Suicidology and suicide prevention 03

## EPP0897

## Efficacy of a regional systems intervention for suicide prevention (SUPREMOCOL) in Noord-Brabant, the Netherlands

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**Introduction:** Worldwide, annually more than 800,000 suicides occur. In the Netherlands, suicide rates rose from 8.6 per 100,000 in 2007 to 11.4 per 100,000 in 2016. Rates in the province of Noord-Brabant were consistently higher than the national average. Noord-Brabant is a province in the south of the Netherlands covering an area of over 4700 km2 with 2.5 million inhabitants. Although Noord-Brabant has five specialised mental healthcare institutions (SMHIs), and 90% of suicides are deemed related to mental disorders, 60% of those who died by suicide did not receive mental health treatment. However, with good access to treatment, suicide could be preventable.
**Objectives:** To evaluate whether the systems intervention compared to the regular care approach led to a reduction in suicides in Noord-Brabant. We aimed to attain a reduction in suicides of at least 20%.
**Methods:** Co-design and development of a digital monitoring system and decision aid. Stepwise implementation per subregion of the systems intervention by the five specialized mental healthcare institutions (SMHIs) and their chain partners. Pre-post analysis for the whole province (Exact Rate Ratio Test, Poisson count).
**Results:** The SUPREMOCOL systems intervention consisted of four pillars, which were all supported by a digital decision aid