
**Non-Interventional Study (NIS) Report
Synopsis**

NIS Name/Code NIS-NRU-ATC-2011/1

Edition Number Final

Date 16 Nov 2012

RECONNECT-S ALPHA: A non-interventional study to observe real-life allocation of atypical antipsychotics in the acute inpatient management of schizophrenia

Study dates:

First subject in: 01 AUG 2011

Last subject out: 23 DEC 2011

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NIS REPORT SYNOPSIS

RECONNECT-S ALPHA: A non-interventional study to observe real-life allocation of atypical antipsychotics in the acute inpatient management of schizophrenia

Study sites:	8 study sites in Russia
Publications:	---
Study dates:	01 AUG 2011 (first subject in) – 23 DEC 2011 (last subject out) (Period covered by chart reviews: 20 JUL 2010 – 23 DEC 2011)
Primary objective:	To describe the use of atypical antipsychotics (AAPs) in schizophrenic patients during hospitalization due to an acute psychotic episode
Secondary objectives:	To investigate <ul style="list-style-type: none"> • the use of only one antipsychotic during the whole period of the hospitalization • how efficacy of antipsychotics is evaluated in current practice • whether different antipsychotics are used to treat different types of patients • the number of antipsychotics used in the clinical practice • the use of concomitant medication • the relationships between antipsychotics used during and after hospitalization
Methodology:	This was a non-interventional study (NIS). The patients were managed according to normal clinical practice until discharge from hospital. On the day of discharge, an extra "visit" was added to collect data on patient characteristics and treatment after discharge. Data on treatment during hospitalization were obtained by chart review.
Number of subjects:	Planned: 600 subjects (10 study sites) Analyzed: 600 subjects (8 study sites)
Main inclusion/exclusion criteria:	Men and women \geq 18 years of age diagnosed with schizophrenia according to the DSM-IV criteria, who were hospitalized due to an acute psychotic episode. Patients who were in an acutely agitated state upon discharge from the hospital were not eligible.

Criteria for evaluation:	Primary: % patients using AAPs; daily dose and mode of administration of AAP(s) Secondary: number, type, dose and mode of administration of antipsychotics used during and after hospitalization; concomitant medication used during hospitalization; reasons for antipsychotic and concomitant treatment; methods used for evaluation of efficacy
Statistical methods:	Descriptive statistics

Results:

Study population:

In total, 600 patients with schizophrenia were enrolled (315 (52.5%) men; 285 (47.5%) women). Their ages ranged from 18 to 82 years (mean \pm SD: 41.1 \pm 13.1 years). All subjects were Caucasians except for 10 Asians (1.7%). The time since the first schizophrenia diagnosis was \geq 11 years in about 50% of the patients.

The duration of the hospitalization period prior to Visit 1, i.e. the period covered by chart review, ranged from 5 to 454 days (median: 76 days; mean \pm SD: 84.8 \pm 63.61 days).

Primary analyses:

Approximately 2 out of 3 patients used AAPs during hospitalization, most of them in combination with typical antipsychotics. Only 74 of 600 patients (12.3%) received an AAP as mono-therapy.

	Antipsychotic treatment <u>during</u> hospitalization				Total
	AAP	AP	AAP+AP	None	
N _{subj} (%)	91 (15.2)	188 (31.3)	319 (53.2)	2 (0.3)	600 (100.0)

AAP = atypical antipsychotic(s); AP = typical antipsychotic(s)

The AAPs most frequently prescribed – either alone or in combination with another antipsychotic – were clozapine, risperidone and quetiapine. The following table gives an overview of the highest daily doses [mg] prescribed for these drugs.

Drug	Mode of admin.	Antipsychotic treatment <u>during</u> hospitalization					
		AAP (N=91)			AAP+AP (N=319)		
		Mean	Min - Max	N	Mean	Min - Max	N
Clozapine	p.o.	179.8	(25 - 450)	31	150.2	(15 - 650)	153
Risperidone	p.o.	5.8	(2 - 10)	24	6.0	(2 - 10)	105
Quetiapine	p.o.	761.9	(400 - 1200)	21	630.0	(50 - 1000)	45

Source: Section 14.3.1.1.2

AAP = atypical antipsychotic drug(s); AP = typical antipsychotic drug(s)

p.o. = per os (by mouth); i.v. = intravenous

The above mean daily dose of risperidone in the "AAP group" is at the upper limit of the therapeutic dose range recommended in the summary of product characteristics for "standard" patients (4 – 6 mg). The median dose of clozapine is slightly lower than the recommended dose (200 - 450 mg). The mean dose of quetiapine is within the therapeutic dose interval recommended for the treatment of schizophrenia (400 – 800 mg).¹

¹ Dose recommendations taken from <http://grls.rosminzdrav.ru/> (accessed on the internet on 06 NOV 2012).

Secondary analyses:

- All patients except two received antipsychotics during hospitalization.
- The most common drugs – each of which was used by $\geq 20\%$ of the patients – were haloperidol, chlorpromazine, clozapine and risperidone, i.e. two typical and two atypical antipsychotic compounds; see table below.

Preferred term	Antipsychotic treatment during hospitalization			
	AAP (N=91) N (%)	AP (N=188) N (%)	AAP+AP (N=319) N (%)	Total (N=600) N (%)
Haloperidol	0 (0.0)	150 (79.8)	213 (66.8)	363 (60.5)
Chlorpromazine	0 (0.0)	98 (52.1)	107 (33.5)	205 (34.2)
<u>Clozapine</u>	31 (34.1)	0 (0.0)	153 (48.0)	184 (30.7)
<u>Risperidone</u>	24 (26.4)	0 (0.0)	107 (33.5)	131 (21.8)
Zuclopenthixol	0 (0.0)	34 (18.1)	51 (16.0)	85 (14.2)
Chlorprothixene	0 (0.0)	34 (18.1)	36 (11.3)	70 (11.7)
<u>Quetiapine</u>	21 (23.1)	0 (0.0)	45 (14.1)	66 (11.0)
Trifluoperazine	0 (0.0)	35 (18.6)	25 (7.8)	60 (10.0)

Only medications prescribed to $\geq 10\%$ of the patients are listed in this table. For further details, see **Error!**

Reference source not found..

AAPs are underlined.

- In most cases, antipsychotics were prescribed for the treatment of medical conditions and symptoms belonging to the system organ class (SOC)² of *psychiatric disorders* (563 of 600 patients (93.8%)). The most common preferred terms (PTs) in this class were *agitation, delirium, insomnia, hallucinations (general and auditory), paranoia, schizophrenia, and aggression*. Each of these PTs was documented for $\geq 10\%$ of the patients.
- Most patients were treated with more than one antipsychotic drug during hospitalization (500 of 600 patients (83.3%)). Only approximately every sixth patient received mono-therapy: 74 patients (12.3%) received an AAP as mono-therapy and 24 patients (4.0%) received a typical antipsychotic as mono-therapy.
- The percentage of males, singles, and individuals without sick leave appeared to be higher and the percentage of individuals living alone appeared to be lower in the group of patients who received AAPs during hospitalization than in patients who received APs or AAPs+APs during hospitalization.
The picture was somewhat more complex when the patients were classified according to their antipsychotic maintenance treatment after discharge from hospital. The patients in the AAP group appeared to be slightly younger on average than the patients in the other treatment groups. The categorical variables analyzed did not reveal any obvious prescribing pattern.

² The 'reasons for treatment' were coded using the medical dictionary for regulatory activities (MedDRA) and tabulated by MedDRA system organ class (SOC) and preferred term (PT).

- Most patients received concomitant (other than antipsychotic) central nervous system-active medication during hospitalization (543 of 600 patients (90.5%)).
The most common reasons (MedDRA PTs) for using these medications were *agitation* (209 of 600 patients (34.8%)), *extrapyramidal disorder*³ (200 patients (33.3%)), and *insomnia* (164 patients (27.3%)). In line with this, psycholeptics (372 of 600 patients (62.0%)) and anti-Parkinson drugs (321 patients (53.5%)) were the most frequently documented central nervous system-active drug classes.
- Concomitant medication for somatic conditions was used by every other patient (308 of 600 patients (51.3%)). The most common disorders requiring medication were *vascular disorders*, *cardiac disorders*, *nervous system disorders*, *gastrointestinal disorders* and *infections and infestations* (13.3%, 11.0%, 9.7%, 9.3% and 8.7%, respectively). The medications most frequently used for treating somatic medical conditions were *psychoanaleptics* (51 of 600 patients (8.5%)) – in particular piracetam (40 of 600 subjects (6.7%)) – followed by *agents acting on the renin-angiotensin system* and *antibacterials for systemic use* (both in 48 of 600 patients (8.0%)).
- Antipsychotic maintenance treatment after hospitalization was prescribed for the majority of patients (458 of 600 patients (76.3%)).
Approximately 40% of the patients received AAPs after hospitalization, most of them as monotherapy or in combination with another atypical antipsychotic. The four most frequently prescribed drugs were haloperidol, clozapine, risperidone, and chlorpromazine (153, 98, 73 and 60 patients respectively). (For about every fourth patient, no information regarding antipsychotic treatment after discharge from the hospital was provided.)

(N _{total} = 600)	Antipsychotic maintenance treatment			
	AAP	AP	AAP+AP	None or unknown
	N (%)	N (%)	N (%)	N (%)
... before hospitalization	53 (8.8)	94 (15.7)	18 (3.0)	435 (72.5)*
... after hospitalization	160 (26.7)	208 (34.7)	90 (15.0)	142 (23.7)**

AAP = atypical antipsychotic drug(s); AP = typical antipsychotic drug(s)

*: "unknown" for 22 patients; **: "unknown" for 137 patients

- The efficacy of antipsychotic treatment during hospitalization was evaluated in 550 of 600 patients (91.7%). This evaluation was in almost all cases based on the responsible physician's clinical experience (549 of 550 patients (99.8%)).

Summary:

In Russian psychiatric hospitals, allocation of atypical antipsychotics in the acute inpatient management of schizophrenia is generally frequent, but rather in combination with typical antipsychotics than as single agents. Among other AAPs, clozapine, risperidone and quetiapine are most frequently prescribed in the hospital. When an AAP is prescribed to a patient, such factors, as relatively short time from schizophrenia offset and strong support by family members, can play a feasible role. Continuity of maintenance therapy with AAPs after discharge from hospital is confirmed only with regard to 2 drugs: clozapine and risperidone.

³ (including extrapyramidal symptoms possibly induced by antipsychotics)