Russian experience of using perampanel in daily clinical practice.
Preliminary report

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SUMMARY

Introduction. Perampanel (PER) (Fycompa) 5'- (2-cyanophenyl)-1'-phenyl-2,3'-bipyridinyl-6'(1'H)-on is the newest antiepileptic drug and is the first-in-class selective non-competitive antagonist of ionotropic AMPA glutamate receptors of the postsynaptic neuronal membrane.

The aim was to summarize Russian experience in using PER in daily clinical practice, and for this purpose the results of its use as an add-on treatment for focal epilepsy were assessed retrospectively.

Material and Method. The results of the study of PER efficacy and safety in 52 patients with refractory focal epilepsy are presented. Mean age was 28.9 ± 14.0 years; proportion of male patients was 56%, duration of the disease over 10 years – 69.2%, symptomatic epilepsy – 76.9%, with frontal – 46.2% and temporal – 44.2% localization of epileptic lesion. Majority of patients – 71.2% started PER treatment after 3 preceding lines of therapy.

Results. The baseline seizure frequency of all types was 127.3 ± 82.3 per month; secondary generalized seizures – 6.7 ± 1.9 per month. After PER was added, a significant decrease in seizure frequency was observed.
already during the first month, to 52.1 ± 29.3 seizures per month (Sign test, p = 0.00001) for seizures of all types and to 3.7 ± 1.7 (Sign test, p = 0.00001) for secondary generalized seizures. In an overwhelming majority of cases, duration of PER treatment was more than 6 months. In 58% of patients, seizure frequency decreased by more than 50% (responders). Seizure-free status for all seizure types was observed in 9% of cases at 12 month, and absence of secondary generalized seizures only was achieved in 31% of patients. Adverse events were observed in 30.1% of patients: aggression – 11.5% and drowsiness – 9.6%, with all other AEs observed more rarely. PER dose was reduced due to side effects in 7 patients (13.5%), and in 4 patients (7.7%) PER was discontinued. Average PER dose in adult patients was as low as 6 mg.

**Conclusions.** PER was effective in the treatment of refractory forms of focal epilepsy, reducing seizure frequency on average by 76% by the second month of treatment. In addition to a good clinical effect, PER demonstrated a rather acceptable and predictable safety profile.

**Key words:** perampanel • refractory focal/partial epilepsy • efficacy • tolerability • safety • adverse events • side effects

**INTRODUCTION**

The introduction of about 15 new antiepileptic drugs (AEDs) in clinical practice over the last 25 years has significantly expanded our therapeutic possibilities for effective pharmacotherapy of epilepsy (Karlov, 2010; Avakyan, 2014). However, the majority of new-generation drugs represents a chemical modification of the initial AED molecule with enhanced properties: brivaracetam (a derivative of levetiracetam), eslicarbazepine (a derivative of carbamazepine), ganaxolone (analogue of pregnenolone), valnoctamide and sec-butyl-propylacetamide (derivatives of valproate). However, being the derivatives of already existing AEDs, the latest AEDs are qualitatively quite different. Hence, new and the newest developments based on newly synthesized AED molecules, such as perampanel (PER) and retigabine, are of particular interest. PER (Fycompa, 2015) 5’-(2-cyanophenyl)-1’-phenyl-2,3’-bipyridinyl-6(1H)-on is the newest AED and is the first-in-class selective non-competitive antagonist of ionotropic AMPA glutamate receptors of the postsynaptic neuronal membrane, which makes its mechanism of action unique (Rogawski, 2011; Hanada et al., 2011). The drug demonstrated its efficacy in the treatment of both primary (French et al., 2015) and secondary generalized and partial seizures (Steinhoff et al., 2013). The additional advantages of PER include administration once per day, which significantly simplifies its use and improves compliance (Fycompa, 2015). Due to the qualitatively new mechanism of PER, different from any previously existing mechanisms, clinical effect can be expected when the drug is added to any initial treatment. Previously published data on the use of PER in patients in the Russian Federation were a part of an international study (Belousova, 2014; Vlasov, 2014).

**AIM**

The goal of the study is to present summarized Russian experience in using PER in daily clinical practice.

**MATERIAL AND METHODS**

Patients with refractory focal epilepsy, who received PER as an add-on AED, were enrolled in the study. The study was designed as a multi-center retrospective study. Epileptologists from various Russian cities (Moscow, Volgograd, Kazan, Krasnoyarsk, Novosibirsk, Saratov, Tomsk, Cheboksary, Chelyabinsk), many of whom participated in international clinical studies (Krauss et al., 2012; Krauss et al., 2014; French et al., 2012), completed a special questionnaire that included data on the types of epileptic seizures, their frequency, type of epilepsy; duration of disease, previous therapy, reasons for switching therapy, current AED treatment regimen, including doses, individual PER titration scheme, efficacy, PER dose, tolerability of combination therapy, general health status assessment and a comment by the healthcare professional who completed the questionnaire. Quality of life was assessed by use of a self-rating questionnaire. The analysis included all materials provided by the co-authors, irrespective of any age restrictions (the drug is approved for use in patients above 12 years of age). In total, 52 patients were included in the study. There were no symptomatic epilepsy due to progressive diseases (tumor, etc.). Most of these forms of epilepsy were associated with focal cortical dysplasia.

**Ethics Committee**

The design of the study was approved by the Local Ethics Committee of Moscow State Medical and Dental University named after A.I. Evdokimov.
The key characteristics of the patients are presented on Table 1. Preceding and concomitant therapies are summarized in Table 2.

The presented data highlight the severe course of the disease, with all preceding attempts of drug therapy being unsuccessful. Mean age was 28.9 ± 14.0 years, with absolute prevalence of patients above 12 years of age – 83% (n = 43). Female patients accounted for 44.2% (n = 23), and male patients accounted for 55.8% (n = 29). Prevailing disease duration was >10 years 69.2% (n = 36); the most frequent type was symptomatic epilepsy 76.9% (n = 40) with temporal 44.2% (n = 23) and frontal 46.2% (n = 24) localizations of epileptic lesion. Median frequency demonstrated a high activity of the disease, in particular median frequency for secondary generalized seizures was 3.5 over the initial 4 weeks before initiation of PER. In most cases, initial therapy included 3–5 AEDs (52%), with the maximum number of concomitant AEDs (other than PER) being 2 (44.2%) or 3 (38.5%) AEDs. In 50% of patients, the preceding therapy was ineffective, with 44.2% of patients experiencing both treatment ineffectiveness and side effects that resulted in AED discontinuation. The main concomitant drugs included valproate (57.7%), lamotrigine (25%) and levetiracetam (25%). The baseline frequency of seizures of all types was 127.3 ± 82.3 seizures per month; secondary generalized seizures – 6.7 ± 1.9 seizures per month. Median baseline frequency values are presented in Table 1.

An extremely sever course of the disease was observed in every tenth patients from the analyzed subgroup – 11.5% (n = 6). Out of them, 3 patients underwent medical investigations for further surgical treatment, with surgical treatment denied to 2 female patients due to the multifocal nature of their disease, and surgical treatment was scheduled for 1 patient. This subgroup of patients with an extremely sever course of the disease also included 3 patients with a severe form
of Infantile cerebral palsy, who previously had received 4–7 AED regimens.

**RESULTS**

**Seizure control**

After PER was added to the treatment regimen, a significant seizure frequency decrease was observed already during the first month, to 52.1 ± 29.3 per month (Sign test, p = 0.00001) for seizures of all types and to 3.7 ± 1.7 (Sign test, p = 0.00001) per month for secondary generalized seizures. After the second month of drug use, seizure frequency further decreased: to 30.4 ± 12.4 seizures per month without differentiation by types of seizures (Sign test, p = 0.003) and to 2.6 ± 1.2 secondary generalized seizures (Sign test, p = 0.04). Subsequently, decrease in seizure frequency was observed for up to 12 months, but it did not achieve statistical significant (Figure 1). The seizure free rate was 9% at 12 months. Analysis of PER efficacy demonstrated that within 6 months of treatment, seizures of all types completely disappeared in 8% of patients in the sample group (n = 52), while secondary generalized seizures completely disappeared in 31% of patients in the sample group (n = 36).

**Adverse events**

Adverse events (AEs) included a rather high percentage of aggression (11.5%) that was transient and in all cases required reduction of daily dose of PER (Table 3); however, in the group, there were no cases of PER discontinuation. Aggression was observed only in a case of symptomatic epilepsy (Table 4), in an overwhelming majority of cases on an 8-mg daily dose of PER, and dose reduction to 6 mg made it possible to control the AE. No correlation between aggression and age or administration of concomitant AEDs was found.

Other AEs were observed with an insignificant frequency (drowsiness 9.6%, unsteady walk 5.8%, tearfulness 5.8%; all other AEs, such as dizziness, appetite decrease, irritability, lethargy, were reported with a less than 5% frequency (Table 3). Median last effective dose of PER for the whole sample group (n = 52) was 6 mg/day. Daily dose was reduced due to AEs in 13.5% (n = 7). In 4 patients (7.7%) PER was discontinued, since they developed lethargy (n = 2), appetite decrease (n = 1) and drowsiness (n = 1).

**Quality of life**

During treatment quality of life improved in 73% of patients and remained unchanged in 15.4% of cases (significant difference, p < 0.05). Based on the patient health self-concept questionnaire data, the greatest effect was achieved in terms of well-being, mood, and energy.

**DISCUSSION**

The interim results obtained in this study demonstrate that the use of PER for epilepsy is highly prom-

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**Table 2. Preceding and concomitant antiepileptic drug (AED) therapy**

| The number of preceding therapies | n = 52, n (%) |
|-----------------------------------|--------------|
| 1                                 | 6 (11.5%)    |
| 2                                 | 9 (17.3%)    |
| 3-5                               | 27 (52.0%)   |
| > 5                               | 10 (19.2%)   |

| The number of concomitant AEDs | n (%) |
|--------------------------------|-------|
| 1                              | 4 (7.7%) |
| 2                              | 23 (44.2%) |
| 3                              | 20 (38.5%) |
| 4                              | 5 (9.6%) |

| Concomitant administered AEDs | n (%) |
|------------------------------|-------|
| Valproates                   | 30 (57.7%) |
| Lamotrigine                  | 13 (25.0%) |
| Levetiracetam                | 13 (25.0%) |
| Topiramate                   | 10 (19.0%) |
| Carbamazepine                | 8 (15.0%) |
| Oxcarbazepine                | 8 (15.0%) |
| Lacosamide                   | 4 (7.7%) |
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Table 3. Adverse events

| Nature of adverse event          | n (%)   |
|----------------------------------|---------|
| Total patients with adverse events* | 16 (30.1%) |
| Aggression                       | 6 (11.5%) |
| Drowsiness                       | 5 (9.6%)  |
| Unsteady walk                    | 3 (5.8%)  |
| Tearfulness                      | 3 (5.8%)  |
| Appetite decrease                | 2 (3.8%)  |
| Irritability                     | 2 (3.8%)  |
| Lethargy                         | 2 (3.8%)  |
| Dizziness                        | 2 (3.8%)  |
| Nervousness                      | 1 (1.9%)  |
| Fever                            | 1 (1.9%)  |
| Fears                            | 1 (1.9%)  |
| Headache                         | 1 (1.9%)  |

* One patient could experience several adverse events that developed successively or simultaneously.

Table 4. Characteristics of patient group that demonstrated aggression during treatment with perampanel

| Diagnosis                      | Age | Sex | Therapy (mg/day)                  |
|--------------------------------|-----|-----|----------------------------------|
| Symptomatic frontal            | 13  | M   | VPA 1050, LEV 4500, LCM 300, PER 6 – not changed |
| Symptomatic frontal            | 20  | F   | LEV 2000, LTG 200, PER 8 – 2 = 6  |
| Symptomatic frontal            | 36  | M   | VPA 1500, LTG 200, PER 8 – 2 = 6  |
| Symptomatic frontal-temporal   | 27  | M   | VPA 1500, PER 8 – 2 = 6           |
| Symptomatic temporal           | 50  | F   | VPA 1500, TPM 100, PER 8 – 2 = 6 |
| Symptomatic temporal           | 31  | M   | VPA 600, LCM 200, PB 100, PER 8 – 2 = 6 |

VPA – valproate, LEV – levetiracetam, LCM – lacosamide, LTG – lamotrigine, TPM – topiramate, PB – phenobarbital

Figure 1. Dynamic of seizure frequency after perampanel administration.
ising. In the group with refractory focal epilepsy within 6 months, complete absence of seizures was achieved in 8% (n = 4) and absence of secondary generalized seizures (SGS) was achieved in 31% (11 out of 36 patients with SGS). In this study, seizure-free rates are almost identical to those published earlier: remission for seizures of all types for a one-year period was achieved in 5.3% (Krauss et al., 2014), and in a study conducted by Steinhoff et al. (2014a) no seizures were reported in 14% and the maximum effect of PER was confirmed for SGS. In the open phase of a study conducted by Krauss et al. (2014), patients with focal epilepsy achieved a more than 90% decrease in SGS frequency by the end of the second year of use of PER as an add-on treatment. PER turned out to be effective for the treatment of primary generalized tonic-clonic seizures: during the period of support therapy (from study week 23 to study week 159), generalized seizure-free status was achieved in 30% of cases (French, 2015). In our study, median effective daily dose of PER was 6 mg, which is close to the previously published 7.7 mg dose (4–15 mg) (Steinhoff et al., 2014b). A targeted analysis did not identify the most effective combination with PER, as the drug demonstrated its therapeutic effects irrespectively of any concomitant AED.

PER was discontinued only in 4 cases (7.7%) due to the development of AEs (lethargy (n = 2), appetite decrease (n = 1), drowsiness (n = 1).

This study confirmed good tolerability of PER: AEs were registered only in 30.1% of cases (n = 16). Only one AE, aggression, was observed in 11.5% of cases (n = 6), while all other AEs were reported with a frequency below 10%, with drowsiness (9.6%), unsteady walk (5.8%), tearfulness (5.8%) being the most frequent. In general, AE percentage rates in this study were lower than those in previously published studies; which is probably due to the lack of strict protocol, and in case of any minimal signs of AEs the physician immediately took required actions: explained to the patient why it was important to take the drug late in the evening, reduced PER dose in some cases or even changed PER treatment regimen for several days, with PER administered every other day. Aggression observed in every tenth patient was transient and occurred at a daily dose of 8 mg, and no patient required PER discontinuation to correct aggression. In an overwhelming majority of cases, aggression regressed following daily dose reduction to 6 mg. In previous studies, aggression was reported as an AE during the use of PER mostly in teenagers (Renroe et al., 2013), unlike the results obtained in the Russian Federation – only 1 out of 6 patients was a teenager (possibly, it is connected with the fact that there were few teenagers in the sample group). This subgroup was characterized by symptomatic epilepsy with the epileptic lesion localized in the frontal or temporal lobe and also by lack of correlation with the use of any AED. Five out of 6 patients with aggression received valproate as a part of polytherapy; however mental side effects, such as depression, psychosis, irritability/emotional lability, are not typical for patients using valproate (Mula et al., 2013). Taking into account the high percentage rates for this AE, it is recommended to purposefully interview patients to find out whether they had mental/behavioral problems in the past and pay more attention to them: also actively monitor possible manifestations of aggression.

In general, patients very positively assessed the use of PER as a part of combination therapy: quality of life improved in 73% of patients and remained unchanged in 15.4%. In the questionnaires, epileptic patients outlined their improved mood, a feeling of well-being, and burst of energy. Patients did not point out any impact of PER on cognitive functions, which is consistent with the results of the study conducted by Meador et al. (2016), which demonstrated that PER had a minimal impact on cognitive functions vs placebo (Meador et al., 2016).

Recommendation of PER administration and its pharmacokinetics

A practicing physician should stress that a PER tablet should be swallowed whole and should not be divided or chewed. PER should be administered per os once daily, regardless of meals. The starting dose is 2 mg/day, and weekly dose increase is 2 mg. When a 4-mg dose is achieved, it is necessary to wait for some time, since a 4-mg dose possibly may be sufficient, as it was repeatedly observed. If necessary, the dose may be increased at a slower rate – once every 2 weeks. In some cases, we practice PER administration every other day, as its average half-life (T1/2) is 105 h. The maximum dose of PER as a part of combination therapy is 12 mg/day. It is necessary to know the specifics of concomitant use of PER with AEDs-inducers of the cytochrome P450, which may decrease its average T1/2 to 25 h. As PER is metabolized by CYP3A4 isoenzyme, its pharmacokinetics will be affected by carbamazepine (CBZ), oxcarbazepine (OXC), phenytoin and topiramate. However, classic enzyme inducers, such as phenobarbital and
primidone, while used concomitantly with PER, do not reduce its blood concentrations (Patsalos, 2013a, b). Sera PER concentrations were determined using liquid chromatography/mass spectroscopy in research by Patsalos et al. (2016). In total, 160 sera from 107 patients were prescribed a median PER dose of 6 mg/d and were concomitantly prescribed a variety of AEDs, including enzyme-inducing [carbamazepine (CBZ) and oxcarbazepine (OXC)] and enzyme-inhibiting (valproic acid) AEDs. A linear relationship was observed between PER dose and serum concentrations. Sex and age were found not to influence PER serum concentration. Enzyme-inducing AEDs dose-dependently decreased PER concentrations, with CBZ and OXC decreasing mean values by 69% and 37%, respectively. In contrast, although topiramate and phenytoin also decreased mean PER concentrations by 18% and 13%, respectively, these changes did not achieve statistical significance (Patsalos et al., 2016). So, PER exhibits a linear dose-concentration relationship, and therapeutic drug monitoring is not necessary for it as a matter of routine.

The presently known pharmacokinetic interactions of PER are summarized in Table 5.

CONCLUSION
PER was effective in the treatment of refractory forms of focal epilepsy, reducing seizure frequency on average by 76% by the second month of treatment. The drug demonstrated its therapeutic effect for all types of partial seizures, with maximum effect achieved for secondary generalized seizures. In addition to a good clinical effect, PER demonstrated a rather acceptable and predictable safety profile. It is known that a combination therapy is usually required in case of drug resistance and potentially increases the risk of AEs, in particular neurotoxicity in case of AEDs with a similar mechanism of action. The use of the latest AEDs in such case, which have mechanisms of action that are qualitatively different from those used previously, makes it possible to personalize drug therapy and have great prospects of being used in special patient populations (based on age, gender, concomitant somatic pathology, etc.). The use of PER in real clinical practice demonstrated that its efficacy should be evaluated after a 4-mg dose and further dose titration rate can be slowed down by 2-fold or more. This study demonstrated that in a situation when a physician was free to select the dose and titration rates, PER efficacy was comparable to previously published study results, while tolerability was significantly better. Average PER dose in adult patients was as low as 6 mg.

CONFLICT OF INTEREST DISCLOSURE
The author has no conflict of interest to declare.
REFERENCES

Avakyan G.N.: Epidemiology of epilepsy and optimization of treatment of focal epilepsies. Epilepsia and paroxysmal states, 2014, 1: 3–5.

Belousova Y.D.: Effectiveness and tolerability of perampanel in patients with refractory partial-onset seizures: results of randomized double-blind, placebo-controlled study conducted in the Russian Federation. Epilepsia, 2014, 55: 1058–1068.

French J.A., Krauss G.L., Biton V., Squillacote D., Yang H., Laurens A. et al.: Adjunctive perampanel for refractory partial-onset seizures: randomized phase III study 304. Neurology, 2012, 79: 589–596.

French J.A., Krauss G.L., Steinhoff B.J., Squillacote D., Yang H., Kumar D., Laurens A. et al.: Evaluation of adjunctive perampanel in patients with refractory partial-onset seizures: results of randomized global phase III study 305. Epilepsia, 2013, 54: 117–125.

French J.A., Krauss G.L., Wechsler R.T., Wang X.F., DiVentura B., Brandt C. et al.: Perampanel for tonic-clonic seizures in idiopathic generalized epilepsy: A randomized trial. Neurology, 2015, 85: 1–8.

Fycompa®. Package leaflet of the medicinal product for human use dated 29.06.2015. Registration number: LIII-002200. International nonproprietary name: Perampanel.

Hanada T., Hashizume Y., Tokuhara N., Takenaka O., Kohmura N., Ogasawara A. et al.: Perampanel: a novel, orally active, noncompetitive AMPA-receptor antagonist that reduces seizure activity in rodent models of epilepsy. Epilepsy, 2011, 52: 1331–1340.

Karlov V.A.: Farmakorezistentnost i tolerantnost (Pharmacoresistance and tolerance). In the book “Epilepsiya u detey i vzroslykh: zhenshchin i muzhchin. Rukovodstvo dlja vrachev”. [Epilepsy in children and adult women and men. Guide for doctors]. M., Meditsina, 2010, 667–676.

Krauss G.L., Perucca E., Ben-Menachem E., Kwan P., Shih J.J., Clément J.F. et al.: Long-term safety of perampanel and seizure outcomes in refractory partial-onset seizures and secondarily generalized seizures: Results from phase III extension study 307. Epilepsia, 2014, 55: 1058–1068.

Krauss G.L., Serratos J.M., Villanueva V., Endziniene M., Hong Z., French J. et al.: Randomized phase III study 306: adjunctive perampanel for refractory partial-onset seizures. Neurology, 2012, 78: 1408–1415.

Meador K.J., Yang H., Pina-Garza J.E., Laurens A., Kumar D., Wesnes K.A.: Cognitive effects of adjunctive perampanel for partial-onset seizures: A randomized trial. Epilepsia, 2016, 57: 243–251.

Mula M., Kanner A.M., Schmitz B., Schacht S.: Antiepileptic drugs and suicidality. An expert consensus statement from the Task Force on Therapeutic Strategies of the ILAE Commission on Neuropsychobiology. Epilepsia, 2013, 54: 199–203.

Patsalos P.N.: Drug Interactions With the Newer Antiepileptic Drugs (AEDs) – Part 1: Pharmacokinetic and Pharmacodynamic Interactions Between AEDs. Clinical Pharmacokinetics, 2013a, 52: 927–966.

Patsalos P.N.: Drug Interactions With the Newer antiepileptic drugs (AEDs) – Part 2: Pharmacokinetic and Pharmacodynamic Interactions Between AEDs and Drugs Used to Treat Non-epilepsy Disorders. Clinical Pharmacokinetics, 2013b, 52: 1045–1061.

Patsalos P.N., Gougoulaki M., Sander J.W.: Perampanel Serum Concentrations in Adults With Epilepsy: Effect of Dose, Age, Sex, and Concomitant Anti-Epileptic Drugs. Ther Drug Monit., 2016, Jun 38 (3): 358–364. doi: 10.1097/FTD.0000000000000274.

Renroe B., Yang H., Williams B.: Interim efficacy and safety analysis of adjunctive perampanel in the adolescent population from the extension phase of 3 double-blind, placebo-controlled phase 3 (core) studies in patients with refractory partial-onset seizures. 42nd Annual Meeting of the Child Neurology Society; 30 Oct.–2 Nov. 2013, Austin, TX, USA, 2013.

Rogawski M.A.: Revisiting AMPA receptors as an antiepileptic drug target. Epilepsy Currents, 2011, 11: 56–63.

Steinhoff B.J., Bacher M., Bast T., Kornmeier R., Kurth C., Scholly J. et al.: First clinical experiences with perampanel – the Kork experience in 74 patients. Epilepsia, 2014a, 55 (Suppl. 1): 16–18.

Steinhoff B.J., Hamer H., Trinka E., Schulze-Bonhage A., Bien C., Mayer T. et al.: A multicenter survey of clinical experiences with perampanel in real life in Germany and Austria. Epilepsy Res., 2014b, 108: 986–988.

Vlasov P.N.: Efficacy and tolerability of perampanel in the Russian Federation. Epilepsy and paroxysmal states, 2014, 1: 10–12.