Eisai sponsored satellite symposium
35th International Epilepsy Congress, Dublin, Ireland
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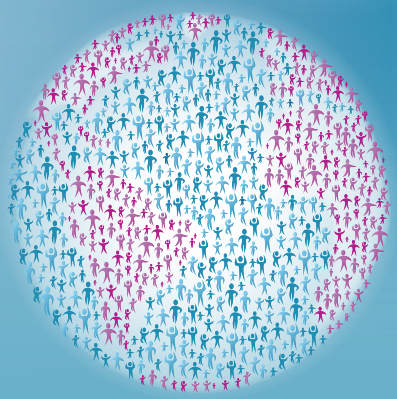
Early use of adjunctive antiseizure medications and potential impact on quality of life



A satellite symposium presented at the
35th International Epilepsy Congress (IEC) 2023
Sunday 3rd September 2023, 08:00–09:30

Introduction

This symposium, chaired by Professor Norman Delanty from the Beaumont Hospital in Dublin, Ireland, discussed the impact of epilepsy and antiseizure medications (ASMs) on the quality of life (QoL) of people with epilepsy (PWE), the challenges faced by clinicians on when to switch from monotherapy to polytherapy and how to select appropriate adjunctive therapies. In addition, real-world data on the use of Fycompa® (perampanel) as an early or late adjunctive therapy in PWE with focal and generalised seizures were presented.

Impact of epilepsy and antiseizure medications on the quality of life in people with epilepsy

Dr Adam Strzelczyk from the Epilepsy Centre Frankfurt Rhine-Main at the Goethe University in Frankfurt am Main, Germany, opened the symposium by providing a general overview of the epidemiology of epilepsy, noting that, in industrialised countries, there is a peak of incidence of focal epilepsy in the elderly and of generalised epilepsy in young children.[1–3] He added that the aetiology of epilepsy, which needs to be taken into account when selecting a treatment strategy, differs in these age groups: underlying congenital causes are more commonly found in the early ages while cerebrovascular and degenerative aetiologies are more common in the elderly.[2]

Epilepsy is a burdensome condition for the individuals affected, their carers and society due to its high direct and indirect costs.[4] As the high direct costs are mostly driven by hospitalisations, reducing hospital visits through therapy does not only improve the QoL of PWE but also reduces costs. The indirect costs of epilepsy are linked to unemployment, days off work and early retirement, with refractory seizures being associated with higher costs than other types of seizures, as they tend to have a more severe impact on PWE's ability to work and on their QoL.[4] Studies have shown that, across their adult lifespan, PWE suffer from a poorer QoL and higher levels of depression and anxiety compared to people without the condition.[5]

Dr Strzelczyk summarised the key factors that can affect the QoL of PWE and need to be considered carefully when managing the disease, such as the time of onset of the condition, how it changes and evolves during an individual's life, changes in the response to ASMs, development of comorbidities in previously healthy individuals, polypharmacy and specific epilepsy aetiologies. He then went on to describe two recent studies that investigated two key questions regarding QoL in PWE: *'What is important and matters most to the patients?'* and *'What affects patients' QoL?'*

The first study was a qualitative netnographic study of epilepsy conversations posted on public social media sites between November 2018 and 2019, which had originated in different countries in Europe, with the aim of identifying key themes and issues for PWE. The findings demonstrated that PWE are particularly concerned about disease awareness among the general public, the psychological and physical impact of seizures, the importance of ensuring proper sleep, understanding disease burden through time, finding treatment and managing side effects, and dealing with depression and anxiety.[6] PWE live in a cycle of anxiety, seizures, and limitations, significantly impacting their mental health, overall QoL, and well-being.[6] The key determinants of PWE's QoL are ASM-related adverse effects and depression, but not seizure frequency, suggesting that, in PWE who cannot achieve seizure freedom, it is critical to address their depression and the side effects of ASMs, in order to improve their QoL.[7]

The second study presented by Dr Strzelczyk was a European survey of 500 PWE and 500 matched controls, that aimed to understand the impact and burden of epilepsy and its treatment on the lives of PWE. PWE were found to have a lower QoL compared to those without epilepsy, with both their physical and mental health being severely affected by epilepsy. PWE struggled in particular with their daily activities, accomplishing their goals, enjoying leisure and social activities, and completing their work tasks.[8] Most PWE had negative feelings about living with epilepsy and complained about how this condition affects their concentration and anxiousness; they were also more likely to suffer from depressive symptoms than controls.[8] When asked what matters the most, PWE noted that epilepsy impacts their ability to drive, their mood, their level of self-esteem, and their ability to achieve good sleeping habits.[8] Dr Strzelczyk highlighted that all PWE included in the survey were taking more than one ASM, with some PWE taking >3 ASMs, suggesting that polytherapy may represent an additional burden for PWE.

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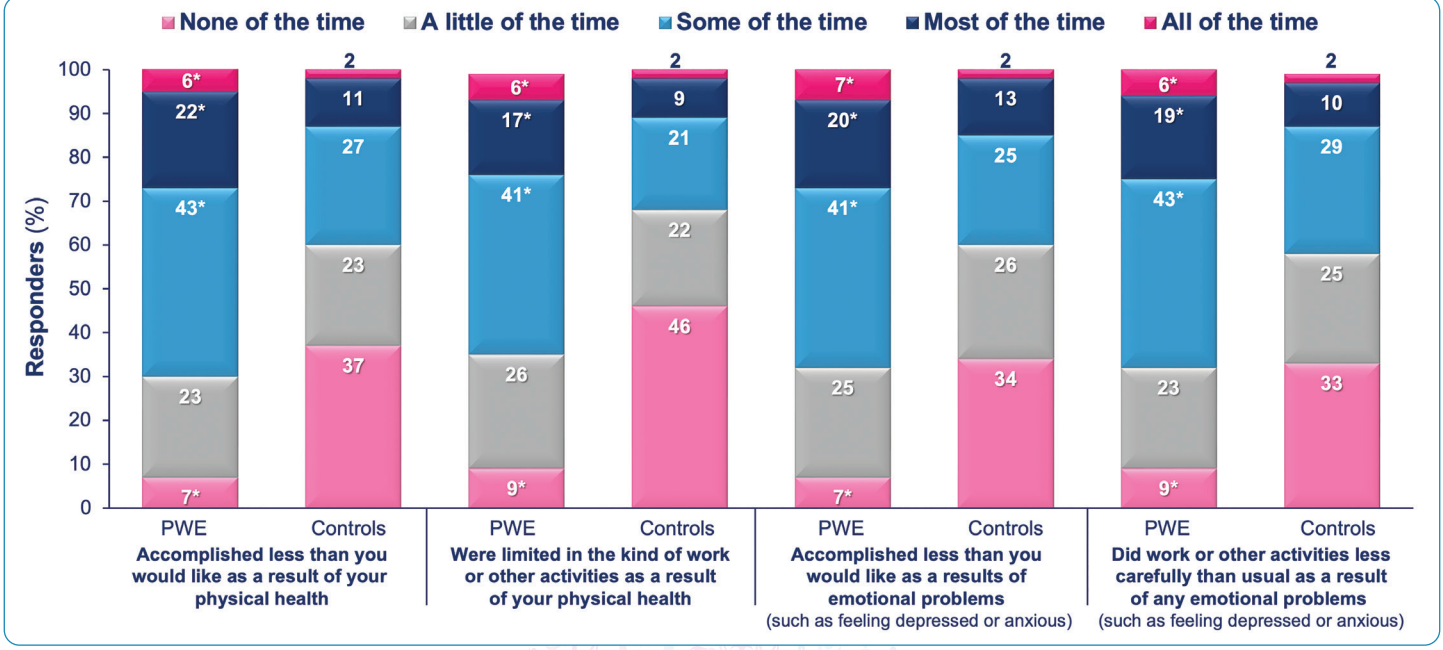
PWE included in the European survey struggled with their work and leisure activities[8]



"I think that tells [us] that polytherapy is associated with an additional burden on depression and quality of life"

Dr Strzelczyk recommended considering the safety profile of ASMs when making treatment decisions, especially psychiatric and behavioural adverse events. However, he acknowledged that selecting the right therapy might be challenging as each ASM can have different effects on cognition, sedation, sleep, behaviour, and mood. Clinicians therefore need to tailor treatment to the individual patient.[9,10] Dr Strzelczyk went on to discuss data on prices and prescription patterns of ASMs collected in Germany between 2000 and 2017, showing that the introduction of third-generation ASMs did not increase the cost of epilepsy therapy. He therefore concluded that the best treatment option for each patient can be selected without concerns over affordability.[11]

Take-home messages:

- Epilepsy has a significant impact on the physical and mental health of PWE, affecting their everyday lives
- When making treatment decisions, it is essential to consider the patient's needs and how these change over time, the patient's QoL, comorbidities, and the different tolerability profiles of ASMs
  - If PWE depend on caregivers (e.g., elderly, children or those with refractory epilepsy), the impact on their QoL also needs to be taken into account
  - Third-generation ASMs may be suitable and affordable treatment candidates

When to consider adjunctive antiseizure medications and importance of individualising treatment decisions

The next presentation was jointly given by Dr Michael Kinney from the Belfast Health and Social Care Trust in Belfast, Northern Ireland and Dr Seán Slaght from the Wessex Neurological Centre, University Hospital Southampton in Southampton, England and the Queen Alexandra Hospital in Portsmouth, England.

Dr Kinney started the presentation by noting that monotherapy should be considered the first-line approach in the management of epilepsy, and that adjunctive therapy should be initiated when monotherapy fails. If seizures persist with adjunctive therapy, referral to a tertiary epilepsy centre and re-assessment of diagnosis are required.[12] He added that a wide range of ASMs is now available allowing for numerous combinations of treatment options. However, matching the right ASM to the right patient can be challenging as many factors need to be taken into account, including the drug's properties and the patient's characteristics, some of which (e.g., biological features) might be unknown.[13–14]

Drug-related factors

- Spectrum of efficacy
- Tolerability (compliance/formulation
- Pharmacokinetics/pharmacodynamics
- Speed of titration
- Cost (especially in some countries)

PWE-related factors

- Type of seizures/epilepsy/(focal or generalised)/syndrome/aetiology
- Comorbidities (cognitive, psychiatric, vascular etc.) and QoL
- Gender/ethnic considerations
- Risk of adverse effects, blood monitoring

Despite the introduction of numerous ASMs and consequential changes in prescribing patterns over the past few decades, the proportion of PWE becoming seizure free has not increased. However, the introduction of third-generation ASMs has notably improved PWE's experience with polytherapy. In addition, studies have shown that patients with refractory epilepsy can benefit from multiple ASMs.[15] Dr Kinney noted that, due to the high number of ASMs available, it would not be feasible to try all the possible combinations. Clinicians should therefore communicate with each other, share their clinical experience, and collaborate on large studies investigating polytherapy in order to explore treatment combinations and understand how to combine ASMs.

Several factors might lead to the use of polytherapy in PWE: 1) early epilepsy onset which may result in long treatment duration and large drug burden as there is a tendency to add drugs to therapy regimens, 2) wide choice of ASMs, 3) poor drug evaluation due to inconsistent patient follow-up, 4) lack of specific guidelines for adjunctive treatment, 5) poor prognosis of some epilepsy syndromes and 6) recurrence of drug withdrawals leading to relapse seizures.[16]

Using polytherapy in the management of epilepsy has the following key advantages:[17-19]

- The possibility to achieve better efficacy through a synergistic action of different ASMs
- The use of lower doses of each ASM in a treatment regimen might result in less toxicity
- Protection against a broader range of seizures

However, there are also disadvantages associated with multiple concomitant ASMs:[17,19–21]

- Increased number and intensity of side effects
- Potentiation of dose-related or idiosyncratic side effects (including seizures)
- Drug-drug interactions
- Difficulty in attributing the reponse to a given individual drug
- Possible change in the therapeutic range of plasma levels
- Costs and complexity of a treatment regimen
- Poor compliance

Studies have shown the existence of synergism between different ASMs, with the combination of lamotrigine and valproate being particularly efficacious. However, substitution is also a suitable option and there are occasions where clinicians should consider to remove drugs.[22] Dr Kinney provided some examples showing that adding or substituting an ASM can have the same effect on seizure outcomes, confirming the importance of considering all treatment options and individualising therapies.[23,24] He also advised careful consideration when selecting adjunctive therapies in special populations, such as those with intellectual disabilities, the elderly and pregnant patients due to teratogenicity, adverse events and drug interactions.[17,19]

During his part of the presentation, Dr Slaght reiterated that factors, such as patient characteristics (e.g., comorbidities and fertility), seizure burden, QoL, and risks of sudden unexpected death in epilepsy (SUDEP) and side effects should all be considered when selecting adjunctive ASMs. He explained that the aim of combining different ASMs in the treatment of epilepsy is to achieve a synergistic (or supra-additive) effect, with two drugs being more effective when administered concurrently than separately. Rational polytherapy aims to maximise the efficacy of concomitant ASMs while minimising side effects.[17,25] It is based on the concept that combining ASMs with different mechanisms of action may have synergistic effects and may therefore be more effective than combining drugs with similar mechanisms of action.

"What we're effectively trying to do is maximise efficiency and minimise adverse events so that the patient has the best quality of life"

There are currently limited clinical studies on different combinations of ASMs, and definitive evidence supporting the existence of additive or supra-additive pharmacodynamic interactions in the clinical setting is scarce. Thus, the selection of ASM combinations in clinical practice is based on animal studies, anecdotal evidence and empirical considerations.[26,27]

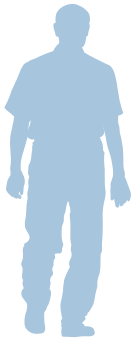
Dr Slaght recommended that, when selecting ASMs, all evidence on efficacy (clinical trials, meta-analyses, guidelines, and clinical experience), safety, drug-drug interactions (based on the Summary of Product Characteristics) and mechanisms of action should be evaluated. However, he pointed out that these theoretical considerations might not always be applicable to everyday clinical practice, because firstly, patients do not behave according to textbooks and secondly, data on a specific combination of ASMs may not be available. He went on to summarise key aspects to consider when selecting adjunctive therapy:

How to select adjunctive ASMs:

- Drugs with different mechanisms of action
- Drugs with few or no pharmacokinetic interactions
- Drugs with different side effect profiles
- Drugs with evidence of synergistic efficacy
- Drugs that do not exacerbate comorbidities

At the end of his presentation, Dr Slaght described a case from his own practice to provide an example of rational polytherapy, explaining that the patient had been given several different ASMs, without achieving seizure control, and was therefore on the waiting list for neurosurgery. Perampanel was added (in conjunction with the removal of valproate) to the treatment regimen because its mechanism of action is different from all the previously administered ASMs. The addition of parampanel was effective for focal to bilateral tonic-clonic seizures and hospital admissions and was well tolerated. The patient therefore decided to forego surgery.

Case study



- Epilepsy – Focal onset
- Aetiology – malformation of cortical development
- Onset – age 44
- MRI (3T) - cortical malformation at junction of the left insular and superior temporal gyrus
- fMRI – left sided language dominance
- VT – No seizures. significant left sided interictal abnormalities including left temporal slowing and left anterior mid temporal sharp waves and spikes
- 2020 on valproate and lacosamide with rescue midazolam
  - Clusters of focal to bilateral convulsions every 4-5 weeks
  - X2 admissions with status epilepticus
- Previously had tried:
  - Phenytoin during status epilepticus
  - Levetiracetam which caused side effects at low doses
  - Topiramate which caused side effects at low doses
  - Lamotrigine (500 mg/day) no effect
  - Clonazepam (4 mg/day) sedation and only minimal benefit

2020

- Lacosamide 200 mg BD, Valproate 800 mg BD
- Clusters of focal to bilateral convulsions every 4–5 weeks
- Monthly admissions with x2 admissions with status epilepticus

Rational Polytherapy

- Valproate withdrawn
- Perampanel added late 2021 and titrated gradually to 10 mg nocte

2022 and 2023

- Ongoing clusters of focal seizures every 4–5 weeks
- Improved focal to bilateral convulsions
- Improved status and no admissions to hospital
- No midazolam used
- Patient opts to not progress to epilepsy surgery
- Therapy was well tolerated

Take-home messages:

- Polytherapy is an acceptable treatment strategy, but requires continuous monitoring and evaluation
- The introduction of third-generation ASMs makes polytherapy a more viable option due to their better pharmacokinetic and tolerability profiles
- Taking medicines out as an alternative option should also be considered by clinicians
- There is still a lack of guidance on when and how to combine ASMs
- Selecting adjunctive ASMs should be based on the patient's and the drug's profile
- Rational polytherapy aims to maximise efficacy and minimise side effects, but there is little evidence on synergistic combinations in humans so far
- Drug candidates for adjunctive therapy should have different mechanisms of action, few pharmacokinetic interactions, and different side effect profiles

Perampanel as an early adjunctive treatment: data from the PERMIT study

Professor Vicente Villanueva from the Refractory Epilepsy Unit at the Hospital Universitario y Politécnico La Fe in Valencia, Spain, gave an overview of the clinical relevance of real-world studies. While clinical trials provide critical evidence on the efficacy and safety of a drug necessary for its approval, real-world studies can offer advantages over traditional trials, such as the possibility to study a drug's safety and tolerability in larger populations over a long period, to evaluate different drug combinations at different stages of treatment, and to include patient cohorts that would have been excluded from clinical trials.[28] However, real-world studies also have some disadvantages, such as lower level of evidence, lack of control group, presence of confounding factors associated with comorbidities, and heterogeneity of data. Dr Villanueva emphasised that both types of studies are needed to provide a full assessment of a drug's effectiveness and safety.[28] He added that regulatory agencies are now acknowledging the importance of real-world evidence as shown by the fact that the European Medicines Agency are integrating real-world studies into their regulatory process.[29]

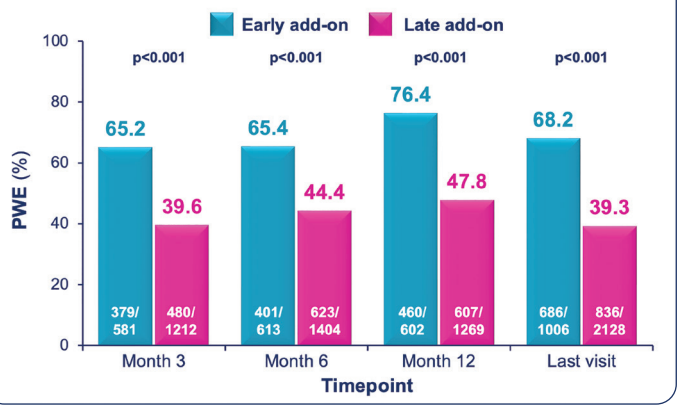
When conducting real-world studies, it is essential to use a good methodology to produce robust data and to report these in a comprehensive and accurate way; the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were created to ensure high-quality presentation of the conducted observational study methodology.[30] Professor Villanueva noted that pooled analyses, which have been conducted for clinical trials for a long time, can also be carried out for real-world studies. The main disadvantage of this methodology is the heterogeneity of data collected. However, combining multiple datasets from different clinical studies allows for analyses of variables that could not be analysed in smaller datasets.[31]

> *"This drug [perampanel] is working particularly well [as adjunctive] in generalised tonic-clonic seizure, either primary or secondary in the old-fashioned terminology"*

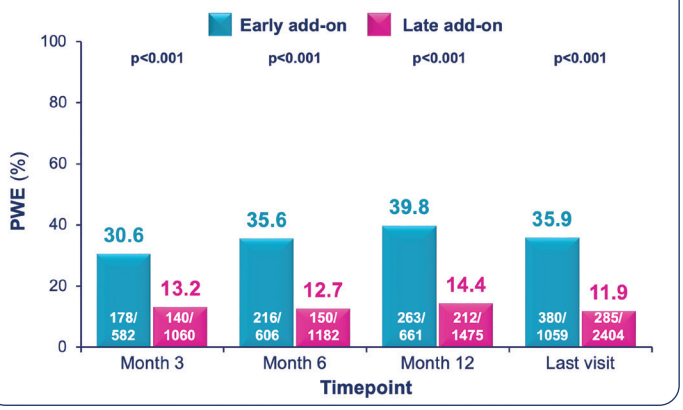
Professor Villanueva described the PERMIT Study as an example of such analysis: The PERaMpanel pooled analysIs of effecTiveness and tolerability (PERMIT) study was a pooled analysis of real-world data from 44 prospective, retrospective and cross-sectional studies and work groups from all over the world in which PWE with focal and generalised epilepsy and other related seizure conditions

Responder rate (≥50% seizure frequency reduction from baseline) and seizure freedom rate with perampanel[34]

Responder rates at Month 3, Month 6, Month 12 and the last visit in the early and late add-on subgroups for total seizures



Seizure freedom rates at Month 3, Month 6, Month 12 and the last visit in the early and late add-on subgroups for total seizures



were treated with perampanel. The study aimed to investigate the effectiveness, safety and tolerability of perampanel when used in everyday clinical practice over a period of 12 months.[32]

In Europe, perampanel is indicated for the adjunctive treatment of:[33*]

- Partial-onset seizures with or without secondarily generalised seizures in patients from 4 years of age and older
- Primary generalised tonic-clonic seizures in patients from 7 years of age and older with idiopathic generalised epilepsy

Importantly, all studies included in the analyses applied broad inclusion criteria to ensure a sample representative of patients encountered in everyday clinical practice. With a population of >5000 PWE, PERMIT allowed meaningful subgroup analyses to be conducted, and one of these subanalyses assessed the efficacy and safety of perampanel when used as early adjunctive therapy or late-adjunctive therapy.[34]

At 12 months of perampanel treatment, retention rates were significantly higher in the early versus the late adjunctive therapy group (67.7% vs 62.4%; p=0.004), which might be partially due to the lower dosage used in the early adjunctive group compared with the late adjunctive group, resulting in better tolerability of perampanel in the early adjunctive therapy group.[34] Responder and seizure freedom rates for total seizures were significantly higher in the early versus late adjunctive subgroup at all timepoints throughout the year. Similar results were also observed for focal seizures. However, the difference in the proportion of patients with generalised tonic-clonic seizure achieving seizure controls with perampanel between the two groups was not significant at all timepoints. Dr Villuanueva suggested that this was due to perampanel being very effective at reducing generalised tonic-clonic seizures, regardless of the stage of treatment.[34]

The incidence of adverse events was significantly lower in the early versus late adjunctive subgroup (42.1% vs 54.7%; p<0.001), as was the rate of discontinuation due to adverse events over 12 months (15.0% vs 18.1%; p=0.031), which, according to Dr Villanueva, is perhaps unsurprising due to the higher drug load in the late adjunctive therapy group.[34] This study demonstrated that perampanel was effective and generally well tolerated when initiated as early or late adjunctive therapy, but it was significantly more effective and better tolerated when initiated early.

Very common and common adverse events as per Summaries of Product Characteristics[33]

System organ class	Very common (≥1/10)	Common (≥1/100)
Metabolism and nutrition disorders		Decreased appetite, increased appetite
Psychiatric disorders		Aggression, anger, anxiety, confusional state
Nervous system disorders	Dizziness, somnolence	Ataxia, dysarthria, balance disorder, irritability
Eye disorders		Diplopia, vision blurred
Ear and labyrinth disorders		Vertigo
Gastrointestinal disorders		Nausea
Skin and subcutaneous tissue disorders		
Musculoskeletal and connective tissue disorders		Back pain
General disorders		Gait disturbance, fatigue
Investigations		Weight increased
Injury, poisoning and procedural complications		Fall

Summary of perampanel safety in the PERMIT study[32]

Total patients	N=4617
Patients with any adverse event, n/N[a] (%)	2303/4617 (49.9)
Most frequently reported adverse events (≥5% of patients), N[a]	4617
Dizziness/vertigo, n (%)	701 (15.2)
Somnolence, n (%)	491 (10.6)
Irritability, n (%)	386 (8.4)
Behavioural disorders, n (%)	249 (5.4)
Patients with adverse events leading to discontinuation	
12 months, n/N[a] (%)	739/4201 (17.6)
Longer term (>12 months), n/N[a] (%)	856/4164 (20.6)
Patients with any psychiatric AE, n/N[a] (%)	965/4590 (21.0)

[a]N refers to number of patients for whom datum in question was available.

Please refer to the Summaries of Product Characteristics for the full list of adverse events

Take-home messages:

- Real-world studies are considered lower-level evidence than clinical trials, but allow the inclusion of a population that is more representative of the patients seen in routine clinical practice, allow the investigation of combinations, and can provide long-term information regarding side effects
- Pooled analyses from real-world studies allow us to generate data from larger populations and different subpopulations of these
- In PERMIT, a pooled analysis of real-world studies, perampanel was effective when used to treat PWE in routine clinical practice, and appeared to be more effective and better tolerated when initiated as an early versus late adjunctive therapy
  - It was generally well tolerated and no unexpected safety signals emerged over the long term
- Perampanel was effective for both focal and generalised seizures, supporting its use as a broad-spectrum, early adjunctive therapy for use in PWE with focal and generalised seizures

Other highlights from the IEC 2023 congress

Neurosurgery

The introduction of new technologies in neurosurgery over the past few years was discussed across various sessions. It was highlighted that, despite the increased number of surgical procedures available to patients and studies showing that the earlier surgery is associated with better outcomes, there are still barriers to the referral of epilepsy patients to neurosurgery.[35–41] It was suggested that, in children, neurosurgery should be offered as a treatment option even in patients who are not pharmacoresistant[42] and should also be considered as a palliative therapy, conducted with the aim of improving certain aspects associated with epilepsy such as cognition, learning, and QoL, rather than achieving seizure freedom.[43–46] These measures should therefore be established as standard assessments in order to define the outcomes of surgery (e.g., the use of scales pre- and post-surgery could be useful).[47,48]

Neuromodulation is gaining importance as a therapy option for epilepsy.[49–53] A deeper understanding of the pathophysiology of thalamic nuclei and the cortical regions affected by epilepsy is required in order to combine neuromodulation tools and achieve 'rational neuromodulation' in the same way rational polytherapy is achieved when combining ASMs.[54]

As patients prefer less invasive procedures which are associated with fewer or no complications, procedures such as thermal ablation, and radiofrequency ablation should be considered, even if less effective than more invasive techniques.[55–57]

Paediatric epilepsy and epilepsy syndromes

During the paediatric sessions, several aspects on the management of patients with developmental and epileptic encephalopathies (DEEs) were discussed. It was highlighted that the identification of the aetiology of epilepsy is critical in order to apply precision medicine[58,59]; however, the identification of the gene responsible for the condition might not be sufficient, as the development of epilepsy also depends on the function of the gene.[60,61] For example, loss-of-function of the brain voltage-gated sodium channel gene *SCN1A* causes Dravet syndrome and milder epilepsy phenotypes, whereas gain-of-function of *SCN1A* results in neonatal developmental and epileptic encephalopathies with movement disorder and arthrogryposis (NDEEMA).[62,63] Various tools to predict gene function in order to make treatment decisions are available to clinicians.[61,63]

The transition from paediatric to adult epilepsy services was also discussed. It was noted that the process needs to be improved, as it is particularly challenging in this population.[64,65] Another topic explored during the meeting was the limited understanding of comorbidities in children with DEEs.[66–69] Autism was discussed as a key example because of its high prevalence in patients with DEEs.[70] Autism is still underdiagnosed in children with DEEs because its diagnosis is particularly challenging in this population[71]: its phenotype is different from that of children without DEEs and its diagnosis is complicated by the presence of profound and multiple intellectual disabilities and severe seizures.[72]

Clinical epileptology

One of the key topics discussed during the clinical epileptology session was the development of new technologies and tools that can help with the management of epilepsy.[73–76] For example, wearables and apps that use algorithms in order to forecast the occurrence of seizures, and tools and models that help clinicians to decide when to withdraw ASMs in patients who have undergone surgery.[74,77–79]

The withdrawal of ASMs following surgery was further explored during this session, as it represents a complex issue for clinicians due to the lack of guidelines and trials to guide clinicians during this process. It was advised that ASMs should be withdrawn because their use is associated with side effects, effects on cognition, teratogenicity and healthcare costs.[79,80]

Neurobiology

The findings of new studies were presented across different neurobiology sessions, providing insights into the pathophysiology of epilepsy and identifying new targets for the treatment of

epilepsy. In particular, a few studies focussed on the role of extracellular spaces in the development of acquired and genetic epilepsy, highlighting how its composition and mechanical properties affect the behaviour and activity of neural circuits.[81–83]

The following new targets were explored in more detail:

- Chloride regulation: intraneuronal chloride dysregulation interferes with the gamma-aminobutyric acid (GABA) neuroinhibitor effect inducing seizures[81,84]
- Blood brain barrier: loss of proteins in brain endothelial tight junction cause damages in the blood brain barrier causing seizure in mice[85–87]
- mTOR signalling pathway: mutations in mTOR has been linked to the development of epilepsy[83,88,89]

The viability of chronotherapy, involving the delivery of a greater dose of ASMs at the time of greatest seizure susceptibility usually associated with predictable seizure peaks, was also discussed. Our increasing understanding of the association between the circadian rhythm and seizures, the discovery of genes associated with the circadian cycle in the brain and the development of algorithms that can predict the occurrence of seizures make chronotherapy a possible treatment option.[74,90–92]

Neuropsychology

Sessions across the IEC congress placed strong emphasis on the importance of considering the psychological and cognitive effects of epilepsy, on the impact of this condition on PWE and their carer's QoL, mental health and everyday life, and on the importance of discussing these issues with the patients and their families.[93–95] In particular, the cognitive impact of epilepsy needs to be explored as it affects all ages and there seems to be a bidierectional relationship between seizures and cognition.[67,96,97] However, despite increasing awareness of the psychological impact of epilepsy, it was acknowledged that more needs to be done in order to recognise and address these aspects in clinical practice. The lack of resources represents a barrier to addressing these issues, but several programmes providing support to PWE and families are now available, and clinicians need to familiarise themselves with these tools in order to signpost their patients to these programmes.[98–100]

*Fycompa is indicated for:

adjunctive treatment of focal seizures with or without secondary generalisation in patients with epilepsy aged 4 years and older.

adjunctive treatment of primary generalised tonic-clonic seizures in patients with epilepsy aged 7 years and older.

For approved indications and prescribing instructions in Switzerland see Fycompa Product Information (www.swissmedicinfo.ch).

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