Should combination therapy be used after failure of one or two antiepileptic drugs?

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The case scenario of this debate from my side is an adult patient with new onset focal seizures. Earlier studies of Brodie (2001, 2012) lead us to believe that there is no use of trying the third antiseizure drug (commonly called antiepileptic drug-AED) if the first two fail before going on to polytherapy and that the whole exercise is rather useless. This is not, however, correct because there is still a lot that can be done before going on to polytherapy with all the side effects that can occur with combinations. First an assumption before the argument: The correct AEDs are given to the patient in the first place and that the patient actually takes the drugs and that the patient actually has focal onset epilepsy.

First of all, when 2 drugs fail, then the patient needs to be referred to an epileptologist who understands the full range of AEDs for further dose adjustments or change of medication. Some of the adjustments that can be done are switching to a drug with another mechanism of action, or dose increases up to higher drug concentrations of the drug that the person is currently taking. Time of dosing can also be an important factor in seizure control. Environmental stressors should be analyzed and corrected when possible. According to other studies, a significant minority of patients (about 16%) can be rendered seizure free by changing up to 3-5 AEDs. Recent examples that even refractory patients can become seizure free are the new down-titration to monotherapy drug trials that have shown success for some new AEDs as lacosamide and eslicarbazepine.

Patients should be given more than 2 chances of trying more than 3 AEDs before calling them refractory.