SUPPLEMENTARY MATERIAL

RESULTS

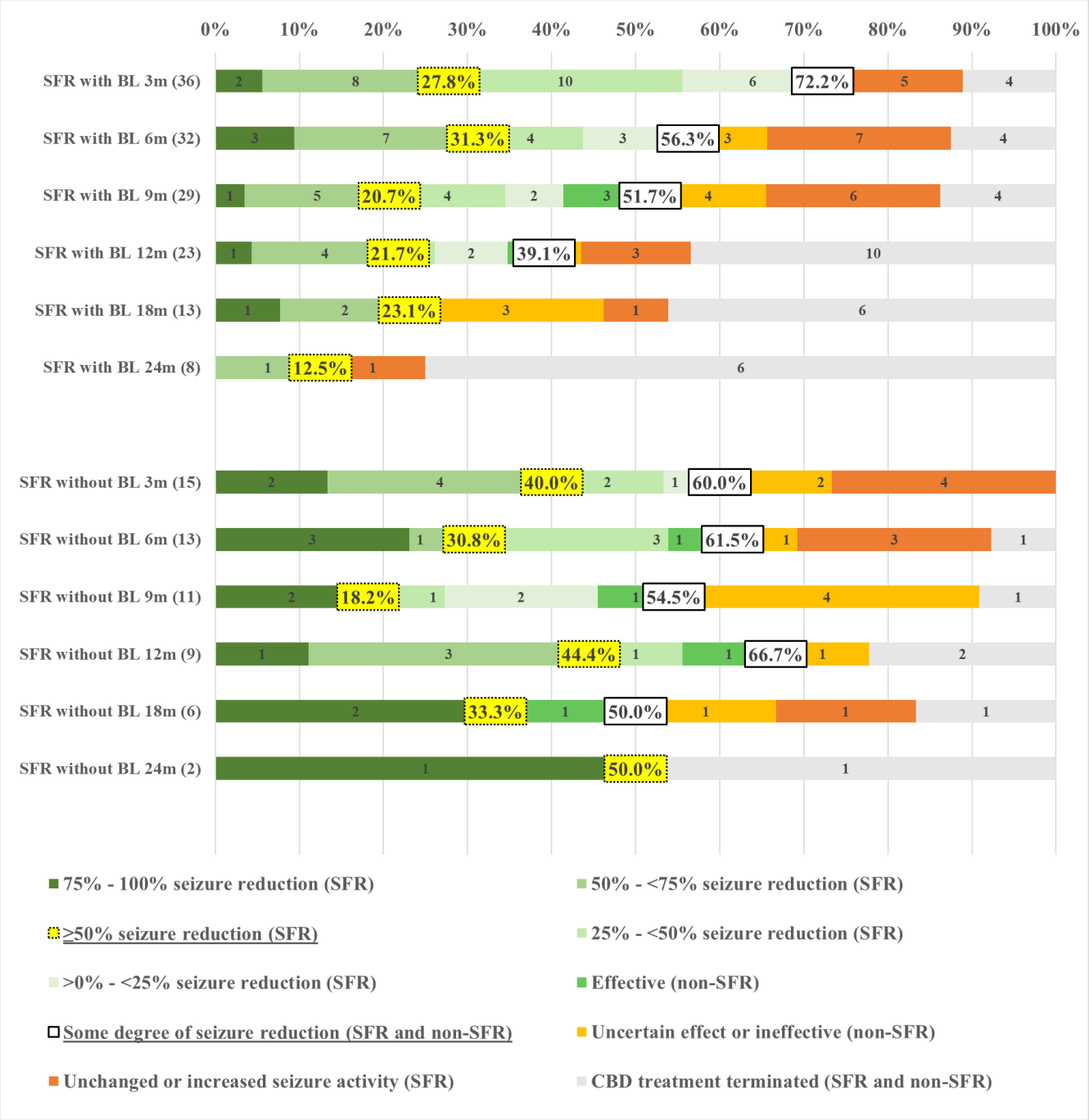

Figure 0 / Seizure reduction results in patients with seizure frequency registration (SFR) with and without baseline registration (BL). ( ) are showing number of patients followed-up. Yellow boxes: percentage of patients having ≥50% seizure reduction. White boxes: percentage of patients with some degree of seizure reduction (>0% seizure reduction + 'effective').

Paraclinical changes

No paraclinical changes or only expected changes in plasma CLB (increment or unchanged) were seen in 69.2% of patients (n=54). In 17.9% of patients (n=14), more than 10% increase in TDM of a concomitant AED (other than CLB) was seen after CBD start without dosage increment (median increase 35.0%, range 13.0–64.2%). TDM increase was seen in valproate, perampanel, clonazepam, eslicarbazepine, ethosuximide, lacosamide, rufinamide and topiramate.

Increase in alanine transaminase (ALT) above the reference interval (RI) was seen in 12.8% of patients (n=10) (median increase 1.9xRI, range 1.2x–4.2xRI). ALT increase beyond RI was more frequent in patients on concomitant valproate compared to patients without valproate medication (34.6% vs. 1.9%, p=0.0001). In 6.4% of patients (n=5) reduction in either leucocytes, thrombocytes, haemoglobin, or alkaline phosphates was seen to a degree, where CBD had to be reduced.

EEG changes

Ten patients had readable start and control EEGs. In seven patients with effect of CBD on seizure activity, two patients had a less abnormal control EEG and five patients had unchanged control EEG. Out of three patients with increased seizure activity on CBD, two patients had control EEG with worsened epileptic activity, and in one patient, the control EEG was unchanged. In the patient with CSWS, 24 hours EEGs at four and 10 months after CBD start were unchanged compared to the 24 hours EEG prior to treatment, with EEGs showing epileptiform activity with spike-wave index between 91–93%.

Effect on mental state and sleep

CBD treatment effect on patient mental state and sleep was evaluated by patient records and ELDQOL if present. In 71.8% of patients (n=56) in the total patient group, the guardian described some sort of positive effect on the patient's mental state such as the patient being more alert, more awake and present in activities, having more energy, better contact, improvement of mood, less autistic behaviour, improved social behaviour, more at ease, improvement in concentration, improvement in language, general positive effect on well-being. In 25.6% of patients (n=20), better sleep was reported. No significant differences between groups (CLB vs. non-CLB and DS/LGS vs. non-DS/LGS) were found.

DISCUSSION

In previous studies of CBD treatment, quality of life questionnaires have shown significant improvement not correlated to reduction in seizure frequency [1]. One randomised controlled trial found a significant improvement in Caregiver Global Impression of Change in the CBD treated group [2]. Positive effect on patient mental state was also found in this present study. The positive effect of CBD on the mental state in this patient group can be important for the quality of life for both patients and families in this seriously ill and much challenged patient group with a high prevalence of serious mental comorbidity (**Table 1**).

LITERATURE

1. Rosenberg EC, Louik J, Conwasy E, et al. Quality of Life of Childhood Epilepsy (QOLCE) in pediatric patients enrolled in a prospective, open-label clinical study with cannabidiol (CBD). Epilepsia 2017;58(8):e96–e100.
2. Devinsky O, Cross JH, Laux L, et al. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. N Engl J Med 2017;376(21):2011–20.