



#### **WCN**

# Symptom management in Neuro-Oncology: anticonvulsants, steroids and anticoagulants Santiago, 4 November 2015



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#### Learning objectives

- Treating symptomatic epilepsy in brain tumor patients with high efficacy and good tolerability
- Avoiding, recognizing and treating side effects of corticosteroids in brain tumor patients
- Understanding risk benefit ratios of anticoagulation in brain tumor patients





### Symptomatic epilepsy in brain tumor patients

- High incidence
- High risk of cognitive side effects of pharmacotherapy
- High risk of relevant interactions of pharmacotherapy
- Controversies regarding duration of treatment and choice of agent





### Incidence of symptomatic seizures

Low-grade gliomas 70% (manifestation)

Glioblastomas
 35% (manifestation)
 30% (disease course)

Oligodendrogliomas 70-90% (manifestation)

Metastases 15-25%

Meningiomas 20-70%

• ZNS lymphomas 15%





- Primary prophylaxis: treat all brain tumor patients?
- Primary prophylaxis: prior to surgery in all patients?
- Secondary prophylaxis: treat after the first seizure?
- Secondary prophylaxis: which agent?
- Secondary prophylaxis: what if no success?
- Secondary prophylaxis: how long if successful?





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# Anticonvulsive therapy in brain tumor patients Old school drugs & Side effects

Phenobarbitone Sedation, allergy

**Enzyme induction (cytochrome P450)** 

Phenytoin Dizziness, allergy, liver enzymes↑, gingival

hyperplasia, cerebellar atrophy

**Enzyme induction (cytochrome P450)** 

**Increased dexamethasone requirement** 

(50%)

Carbamazepine Dizziness, nausea, ataxia, hyponatremia,

gaze-evoked nystagmus, saccadic eye

movements, allergy, liver enzymes 1

**Enzyme induction (cytochrome P450)** 

Valproic acid Tremor, weight gain, coagulation

disorders, thrombopenia, teratogenicity

**Enzyme inhibition: increased toxicity of** 

cytotoxic agents







Lamotrigine Allergy, tremor, sedation (rare)

Gabapentin Sedation

Levetiracetam Sedation (rare), psychiatric side

effects

Topiramate Sedation, fatigue, inappentence,

psychosis

Lacosamide Dizziness, fatigue





#### Anticonvulsive therapy in brain tumor patients Interactions with chemotherapy

- Enzyme-inducing anticonvulsants (phenobarbitone, phenytoin, carbamazepine) may reduce the efficacy of cytotoxic agents (vincristin, epipodophyllotoxins, taxanes, alkylators, methotrexate) and steroids
- Cytotoxic agents (cisplatin) may reduce the activity of anticonvulsants (phenytoin, valproic acid, carbamazepine)
- Enzyme-inhibitory anticonvulsants (valproic acid) may increase the toxicity of cytotoxic agents
- Probably no interactions for lamotrigine, gabapentin, levetiracetam, topiramate or lacosamide





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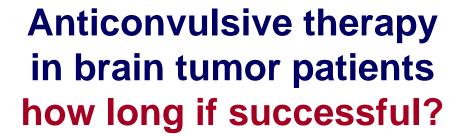
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- Secondary prophylaxis: how long if successful?
   Depending on histology, prognosis, tolerability...







- Only preoperative seizures: try to taper within three months of surgery
- Postoperative (> 48-72 h) seizures: commonly treatment for life
- Surgery-independent freedom from seizures for one year and favorable tumor prognosis: try to taper (again)
- Surgery-independent freedom from seizures for one year and unfavorable tumor prognosis: individual decision, consider tolerability versus consequences of seizures, e.g., fractures with bone metastases or osteoporosis





Agent	Trade name	Dose (mg)	Serum level (µg/ml)	Cost/day (CHF)
Phenobarbitone	zB Luminal®	50-300	10-40	0.1-0.5
Phenytoin	zB Phenhydan®	200-350	10-20	0.15-0.5
Carbamazepine	zB <b>Tegretol</b> ®	600-2000	4-8	0.7-2.5
Valproic acid	zB Orfiril®	1200-2400	50-100	1-2
Lamotrigine	zB Lamictal®	100-300	2-15	3-7
Gabapentin	zB Neurontin®	900-2400	2 - 20	2-5
Topiramate	zB Topamax®	50-200	2 - 25	2-5
Levetiracetam	<b>Keppra</b> ®	1000-3000	5 - 30	4-13
Lacosamide	<b>Vimpat</b> ®	100-400	5 – 10	4-13
Zonisamide	Zonegran®	300-500	10 - 40	5-12





#### Key message I Anticonvulsants

- Efficient control of symptomatic epilepsy is often possible in brain tumor patients
- It greatly impacts quality of life of patients and carers
- Increasing complexity of cancer pharmacotherapy and repertoire of anticonvulsants requires expertise and specialization





#### **Steroids in Neuro-Oncology**

- Tumor-associated vasogenic edema responds well to corticosteroids
- Edema is a major cause of neurological morbidity
- Prolonged corticosteroid use has a major negative impact on quality of life





#### Adverse events and side effects of corticosteroids

- Cushing syndrome
- Immunosuppression
- Myopathy
- Osteoporosis
- Vascular complications
- Depression, psychosis, cognitive decline





## **Key message II Steroids**

- Golden rule for steroid use in Neuro-Oncology: as much as necessary, as little as possible
- No use of corticosteroids in patients with suspected primary CNS lymphoma
- Regular monitoring of corticosteroidassociated side effects and adverse effects





# Vascular complications in Neuro-Oncology

- Deep vein thrombosis
- Pulmonary embolism
- Arterio-arterial embolism: surgery-associated, radiogenic, tumorigenic
- Increased risk with cytotoxic and antiangogenic therapies





# **Key message III Anticoagulants**

- Deep vein thrombosis and pulmonary embolism are probably underdiagnosed and undertreated in brain tumor patients
- Experience with novel anticoagulants is limited
- Drug drug interactions gain increasing importance





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