

# EVALUATION OF OXALIPLATIN-SPECIFIC NEUROTOXICITY BASED ON TOTAL CUMULATIVE DOSE

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## Background

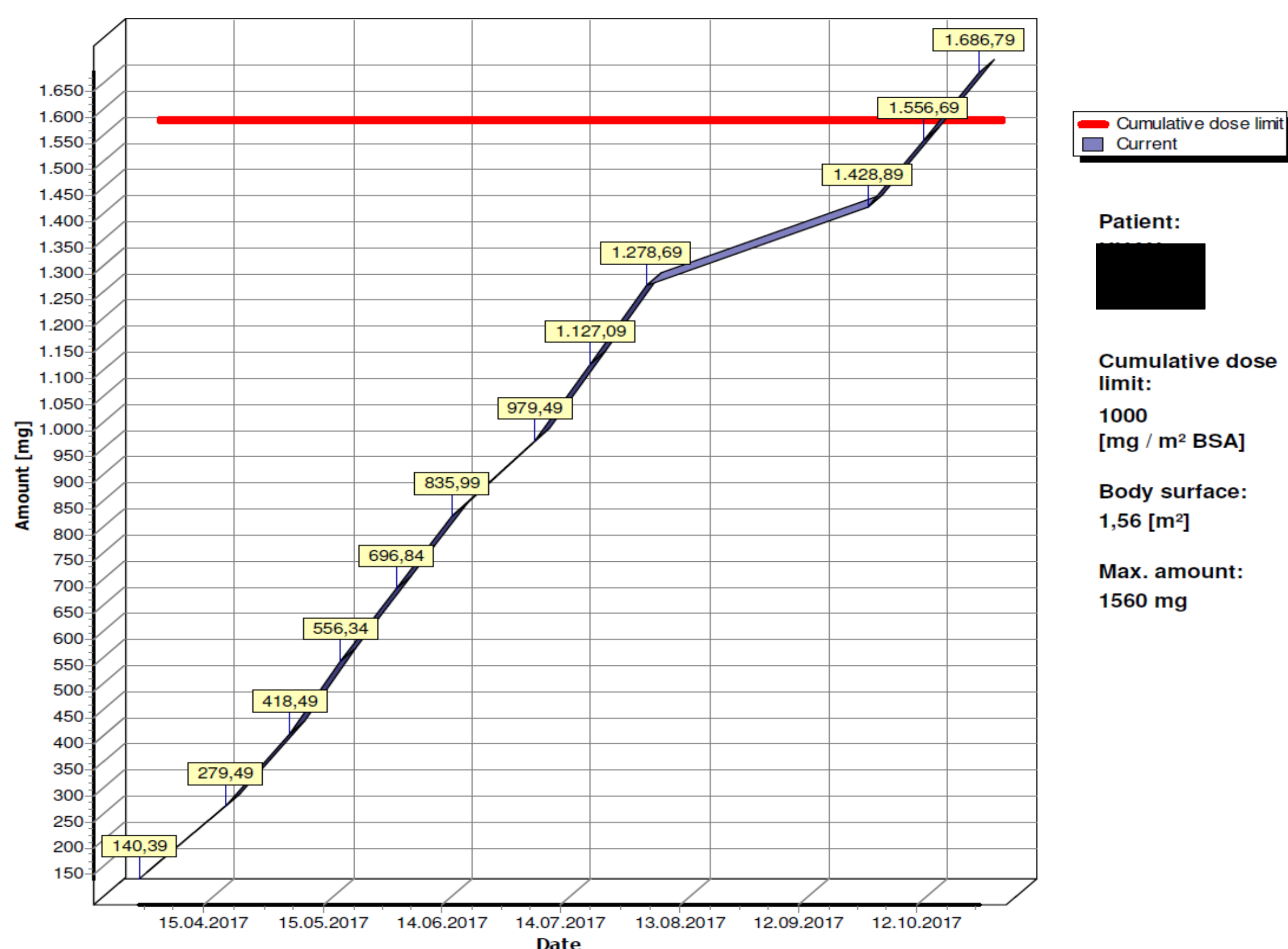
Oxaliplatin is an effective drug for adjuvant or metastatic treatment of patients with colorectal cancer (CRC). Common side effects include acute cold-induced as well as chronic neurotoxicity resulting in dose reduction or even complete oxaliplatin discontinuation and treatment modification. For patients receiving high cumulative doses of oxaliplatin (780-850 mg/m<sup>2</sup>), the incidence of grade 2 or 3 neurotoxicity has been shown to be 12-18% (1).

## Purpose

The aim of our study was to investigate both the incidence and significance of neurotoxicity in patients receiving cumulative oxaliplatin doses of 1000 mg/m<sup>2</sup> or higher. We could then determine whether a pre-emptive intervention of a clinical pharmacist is justified.

## Materials and methods

In the period from January 2016 to July 2017 484 patients diagnosed with CRC received oxaliplatin as part of their treatment regimen. Among them, 40 patients who had received cumulative doses 1000 mg/m<sup>2</sup> or higher were selected based on automatic alerts generated by the software used for prescribing and preparation of cytotoxic drugs. For patients which the predetermined cumulative dose limit has been exceeded, therapy is validated for preparation by the pharmacist only after additional confirmation by the prescribing physician.



### The cumulative maximum dose is exceeded.

The past dose for Oksaliplatin amounts to: 1686,7941 mg  
The cumulative maximum dose amounts to: 1560 mg  
By administering this prescription a value of 1842,7941 mg would arise.

### Would you like to save the prescription anyway?

Physician's confirmation:

Pharmacist's confirmation:

The past dose for Oksaliplatin amounts to:  
1686,7941 mg  
The cumulative maximum dose amounts to:  
1560 mg  
By administering this prescription a value of  
1842,7941 mg would arise.

Physicians confirmation:  
OK

Inserted at: 19.01.2018 07:42

from:

The physician confirmation was based on other amounts as the pharmacy warning

OK

Do not save

Figure 1. Example of cumulative oxaliplatin dose chart for an individual patient (above) and automatic software-generated alert for exceeded cumulative dose limit (below).

## Materials and methods

An oxaliplatin specific scale (NCI-CTC 2.0) was used to assess the level of neurotoxicity (2).

Table 1. Classification systems for Oxaliplatin-induced neurotoxicity.

Grade	NCI-CTC 2.0	Oxaliplatin-Specific Scale
0	Normal	Normal
1	Loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function	Sensory symptoms of <b>short duration</b>
2	Objective sensory loss or paresthesia (including tingling), interfering with function, but not with activities of daily living	Sensory symptoms <b>persisting between cycles</b>
3	Sensory loss or paresthesia interfering with activities of daily living	Sensory symptoms causing <b>functional impairment</b>
4	Permanent sensory loss that interferes with function	—

Abbreviation: NCI-CTC, National Cancer Institute common toxicity criteria.

## Results

Symptoms presented as moderate paraesthesia (grade 1) occurred in 11 patients (28%), while 6 patients (15%) reported of mild or moderate objective sensory loss (grade 2). Dose-limiting neurotoxicity (grade 2 and 3) was observed in 9 patients (22.5%) with a complete oxaliplatin discontinuation being required in 3 patients (7.5%) due to sensory loss, polyneuropathy and pain (grade 3). 11 patients (27.5%) remained asymptomatic according to the NCI-CTC scale.

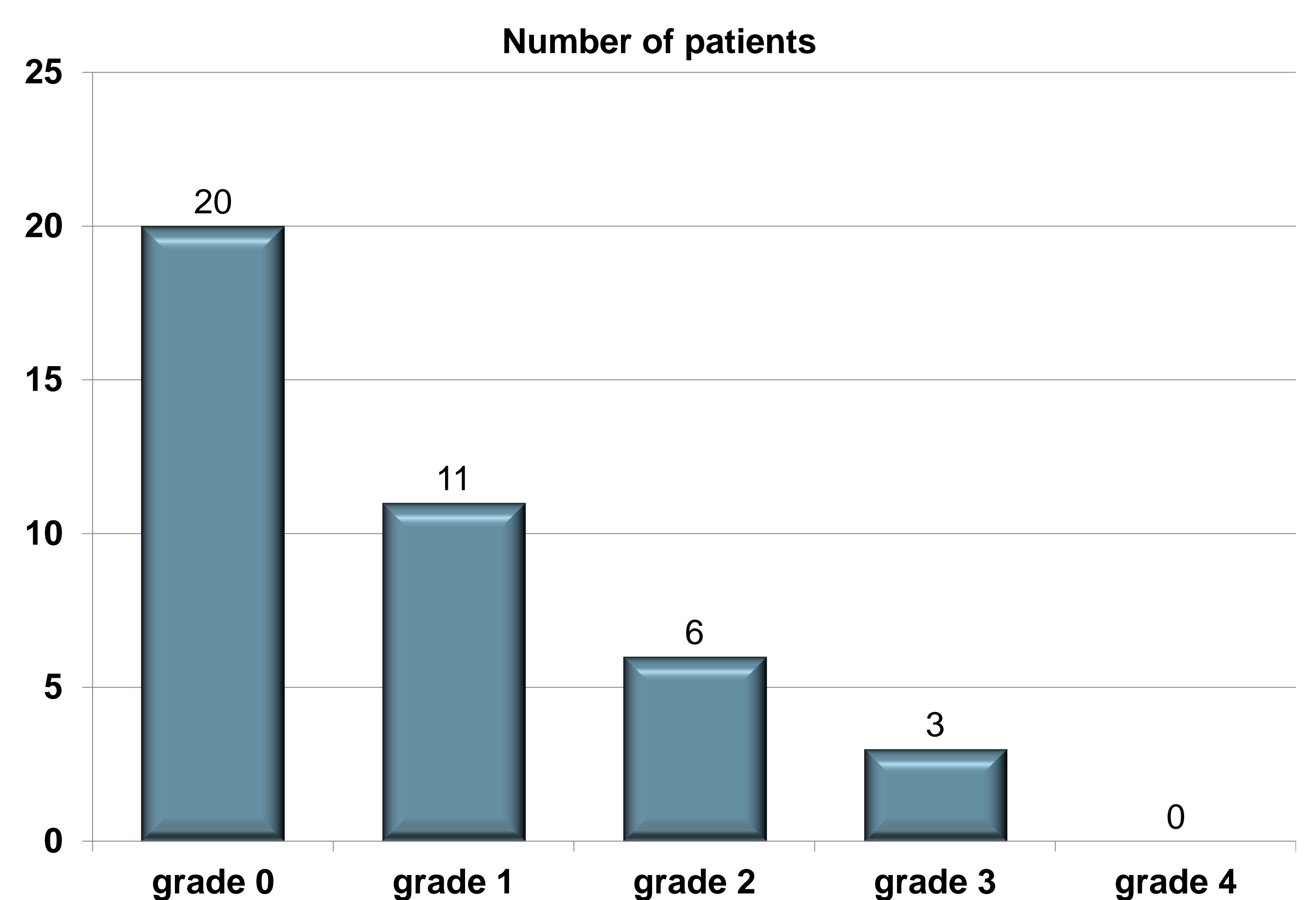


Figure 2. Number of patients with oxaliplatin-specific symptoms of neurotoxicity.

## Conclusion

The results of our study are in agreement with published data. Based on the findings that over one-fifth of patients receiving high cumulative doses of oxaliplatin experience significant neurotoxicity (grade 2 and 3), a clinical pharmacist's intervention in the form of a consultation with the physician is thereby warranted in order to re-evaluate the benefit of chemotherapy treatment versus the impact on a patient's quality of life.

## References

- de Gramont A, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. *J Clin Oncol.* 2000;18:2938–2947.
- Grothey A. Oxaliplatin-Safety Profile: Neurotoxicity. *Seminars in Oncology*, Vol 30, No 4 Suppl 15 (August), 2003: pp 5-13.