A LONGITUDINAL STUDY ON OXALIPLATIN INDUCED PERIPEHRAL NEUROPATHY INCIDENCE AND FACTS ABOUT THE "REAL LIFE" POPULATION AND ACTUAL DOSE

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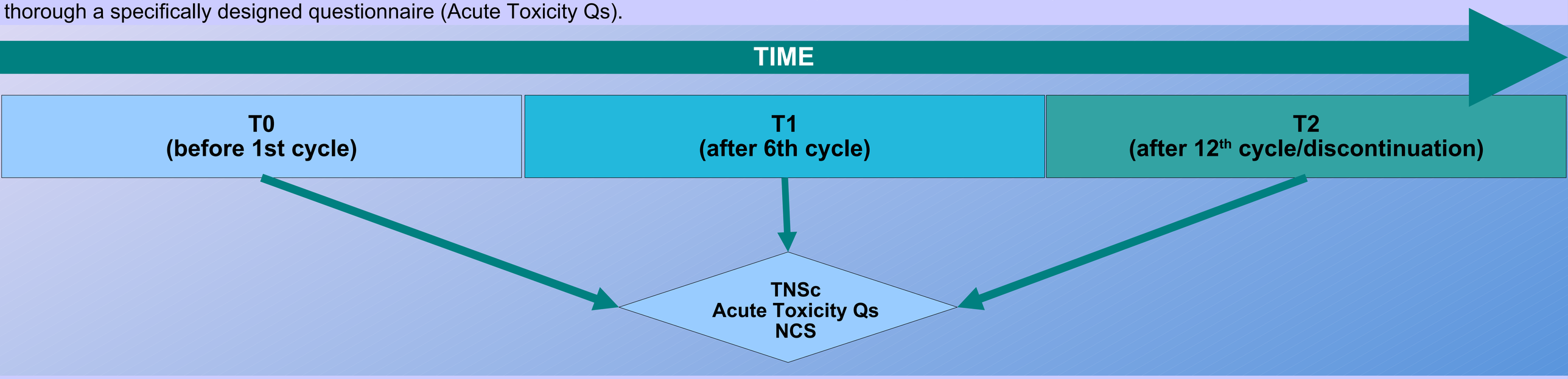
INTRODUCTION: The real incidence of platinum drugs Chemotherapy Induced Peripheral Neuropathy (CIPN) is yet to be defined; the same goes for outcome measure(s) to be selected in this regard. Oxaliplatin (L-OHP) is associated with 2 different pattern of neurotoxicity: 1) acute neurotoxicity, (axonal hyperexicitability symptoms in days following L-OHP iv administration causing transient symptoms, such as cold-induced paraesthesias), without permanent damage on peripheral nervous system; 2) chronic neuropathy, (sensory axonal one) which it is suggested to be developed in 10-20% of patients, with a threshold cumulative dose of 800-1000 mg/m2. Here an ongoing study is reported, aimed to better clarify incidence and issue in assessment, taking into account the actual L-OHP dose received by patients.

METHODS: Patients eligible to undergo L-OHP based chemotherapy (FOLFOX-4) for colorectal cancer, are being enrolled. Subjects undergo a formal neurological examination, using the clinical version of the Total Neuropathy Score (TNSc), before starting CT (T0), after 6 cycles (T1) and at the end of treatment (T2); a neurophysiological assessment of limb distal nerves (Nerve Conduction Study, NCS) is also performed every time and acute toxicity phenomena record is made thorough a specifically designed questionnaire (Acute Toxicity Qs).

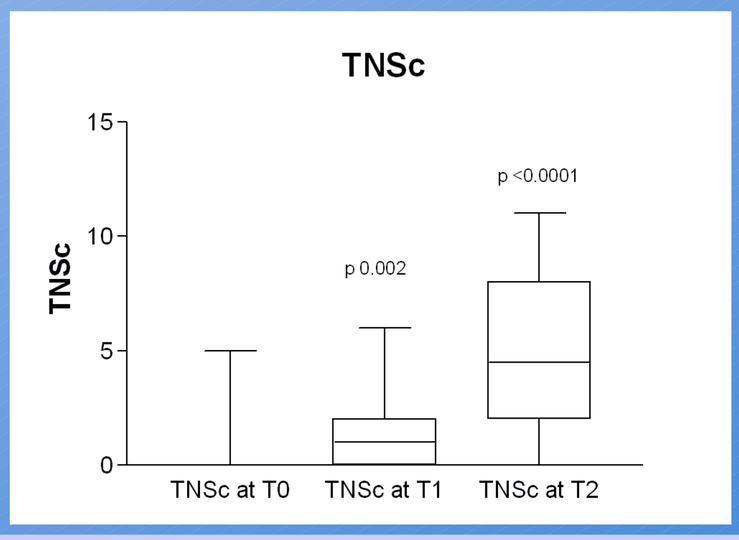


RESULTS: Here data on first 36 consecutive patients are shown. Median age was 62 (42-83); 67% of patients were male. 75% of patients were treated in an adjuvant setting. 6 patients were lost at T1 and 4 at T2, due to L-OHP discontinuation (mainly for haematological toxicities). The actual median cumulative dose was 839,5 (375,7-1021) mg/m2 and actual median dose intensity was 31,02 (14,45-42,50) mg/m2/week, which were, respectively 80% and 70% of the planned ones. At T0: median TNSc score was 0 (0-5); 17% of patients showed neurophysiological alterations. At T1: median TNSc score was 1 (0-6), 20% of patients showed alterations at neurophysiological assessment; 100% of patients showed at least one acute toxicity symptom. At T2: median score for TNSc was 4,5 (0-11), 73 % of patients showed alterations at neurophysiological assessment; 100% of patients showed at least one acute toxicity symptom. There is a statistically significant increase of median TNSc score during the course of the study (p-value < 0.0001).

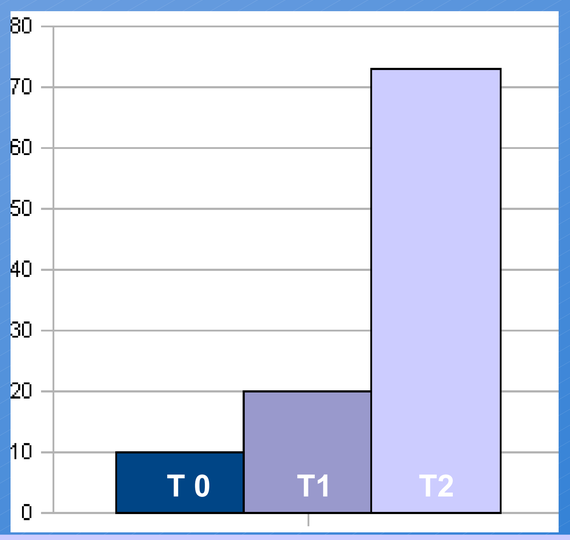
GENERAL DATA ON ENROLLED POPULATION

SEX DISTRIBUTION	67% male, 33% female
MEDIAN AGE	62 (42-83) years
SETTING	-75% adiuvant setting - 25% metastatic setting
MEDIAN CUMULATIVE DOSE	839,5 (375,7-1021) mg/m^2
MEDIAN DOSE INTENSITY	31,02 (14,45-42,50) mg/m^2/week

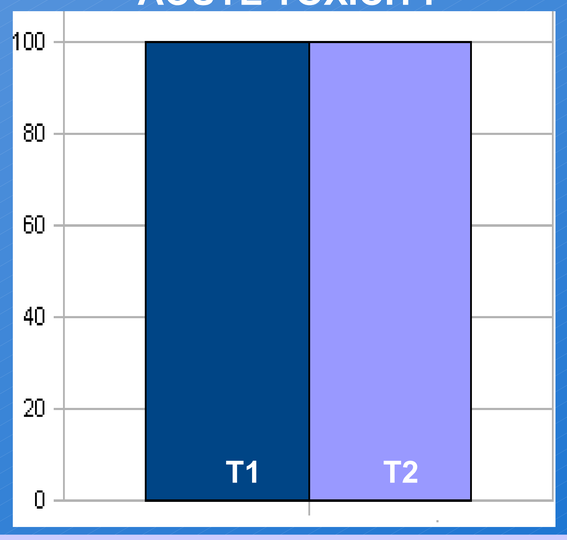
TNSc SCORE



% OF SUBJECTS SHOWING ALTERATIONS ON NCS



% OF SUBJECTS SHOWING AT LEAST ONE SYMPTOM OF ACUTE TOXICITY



DISCUSSION AND CONCLUSIONS: The novelty of this study is the accurate longitudinal neurological assessment (TNSc, neurophysiology, acute symptoms questionnaire), with a concomitant registration of the actual, and not only the planned, doses of L-OHP administred. The real life population received less than the planned dose (here, 80% of planned cumulative dose and 70% of planned dose intensity), a fact that could be expected, even though it is not generally stated in studies reported in literature. This observation strongly supports the fact that L-OHP threshold dose for CIPN might have been underestimated so far and it suggests the need for a revision of the available data in order to analyse them more reliably. It could be then suggested that in future studies a concomitant valid neurological assessment should be coupled with a registration of actual dosages. First data shown here are promising in suggesting the responsiveness for the here selected neurological outcome measures whose validity and reliability has been recently demonstrated (Cavaletti et al. 2012).

REFERENCES
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