# Phase III, international, multicentre, double-blind, dose increment, parallel-arm, randomised controlled trial of duloxetine versus pregabalin over 14 days for opioid-unresponsive Neuropathic cancer pain

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## INTRODUCTION

ancer pain （NCP） is experienced by approximately 33% of people ncer pain [1]. Neuropathic pain is less responsive to opioid drugs. The gabapentinoids (gabatentin and pregabalin) for this population has already RCTs compared with placebo making this a standard of care [2, 3]. Duloxetine tonin noradrenalin reuptake inhibitor (SNRI) and offers the potential of oid unresponsive neuropathic cancer pain. However, there are no randomised of oral duloxetine for the management of opioid unresponsive cancer n as a 1st line treatment. Both classes of drug have the potential to reduce cer pain, but there has been no head-to-head comparison for the net effect differing side-effect profiles.

## AIMS

ence base for the pharmacological treatment of opioid refractory neuropathic

nalgesic efficacy of duloxetine versus pregabalin in patients with opioid pathic cancer pain.

## METHODS

:

ulticentre, prospective, randomised, double-blinded, two-parallel arm, dose- hich would evaluate the effectiveness and safety of duloxetine and pregabalin cancer pain. This study will comprise:

andomised controlled parallel-arm of duloxetine versus pregabalin over 14 athic cancer pain.

-study: patient experience of the intervention will be explored.

**n criteria:**

outpatients with cancer and opioid refractory neuropathic pain

r older

rmance Scale (KPS) or Australian Karnofsy Performance Scale (AKPS) ≧50

cancer with a worst pain score of 4 or greater in the past 24 hours on an 11- Rating Scale (NRS) (BPI-SF Item 3)

ain on the Leeds Assessment of Neuropathic Symptoms and Signs Pain score 12 or greater

pioid dose which is defined as titration to the maximum tolerated dose or st a dose of 60mg/day oral morphine equivalent dose for 24 hours.

our primary outcome, which is worst pain intensity (BPI items 3) at Day 14, we participants per group would detect a mean difference of 1.0 (SD 2.0) (80% o-sided significance level of 0.05 for comparison). Considering withdrawal, , we plan to recruit 160 participants into the study, from 6 sites in Japan tes in Australia (n=60).

**ctive:**

difference of the net clinical effect (benefits and harms) of duloxetine regabalin for people with a neuropathic cancer pain at day 14. Primary comparison of the worst pain intensity (BPI items 3) at day 14.

**number and research period:**

lomisations: 80 in each group, totaling 160 randomisations.

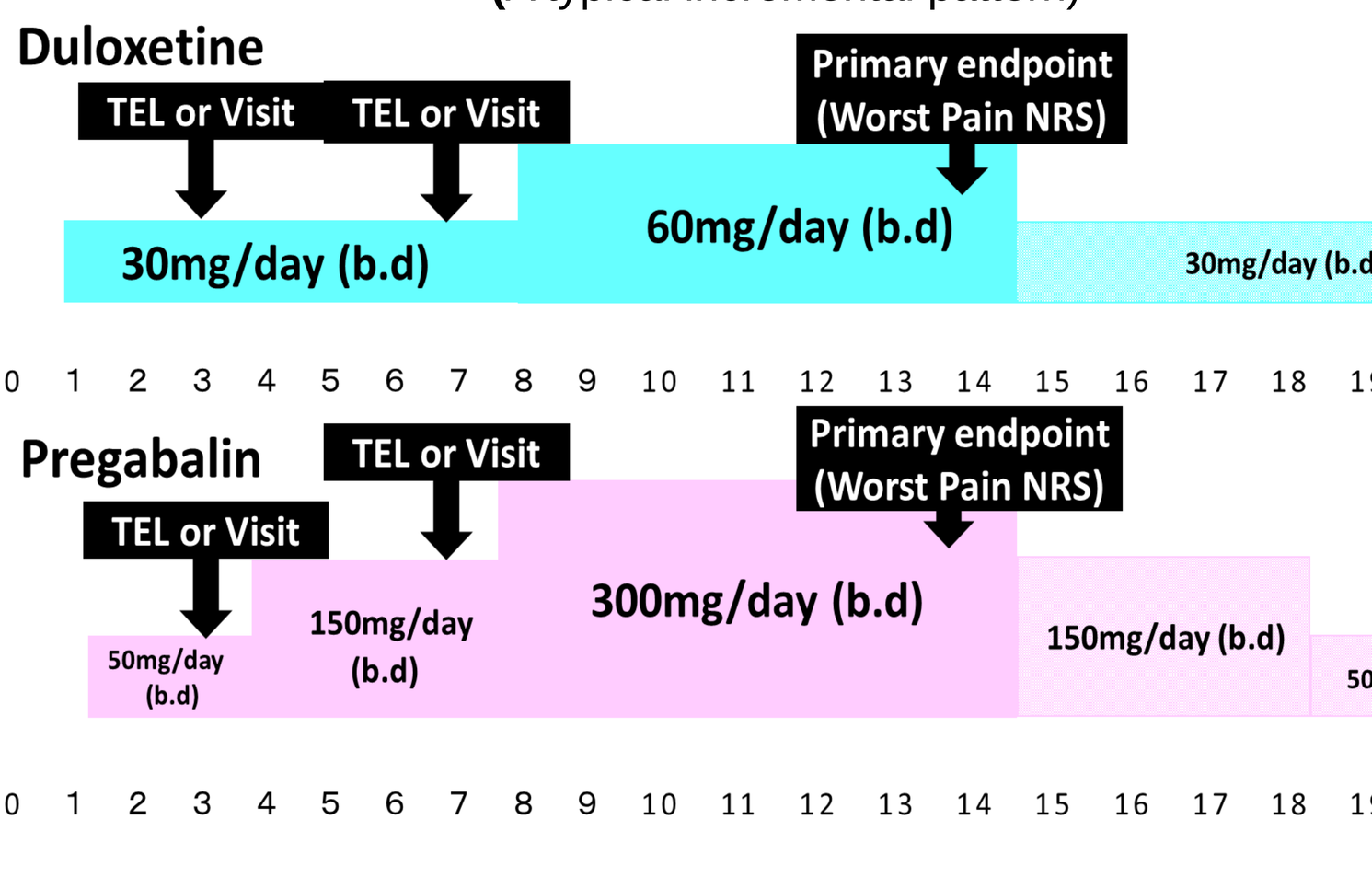
l: From February 2020 to December 2024.

iod: 4.5 years

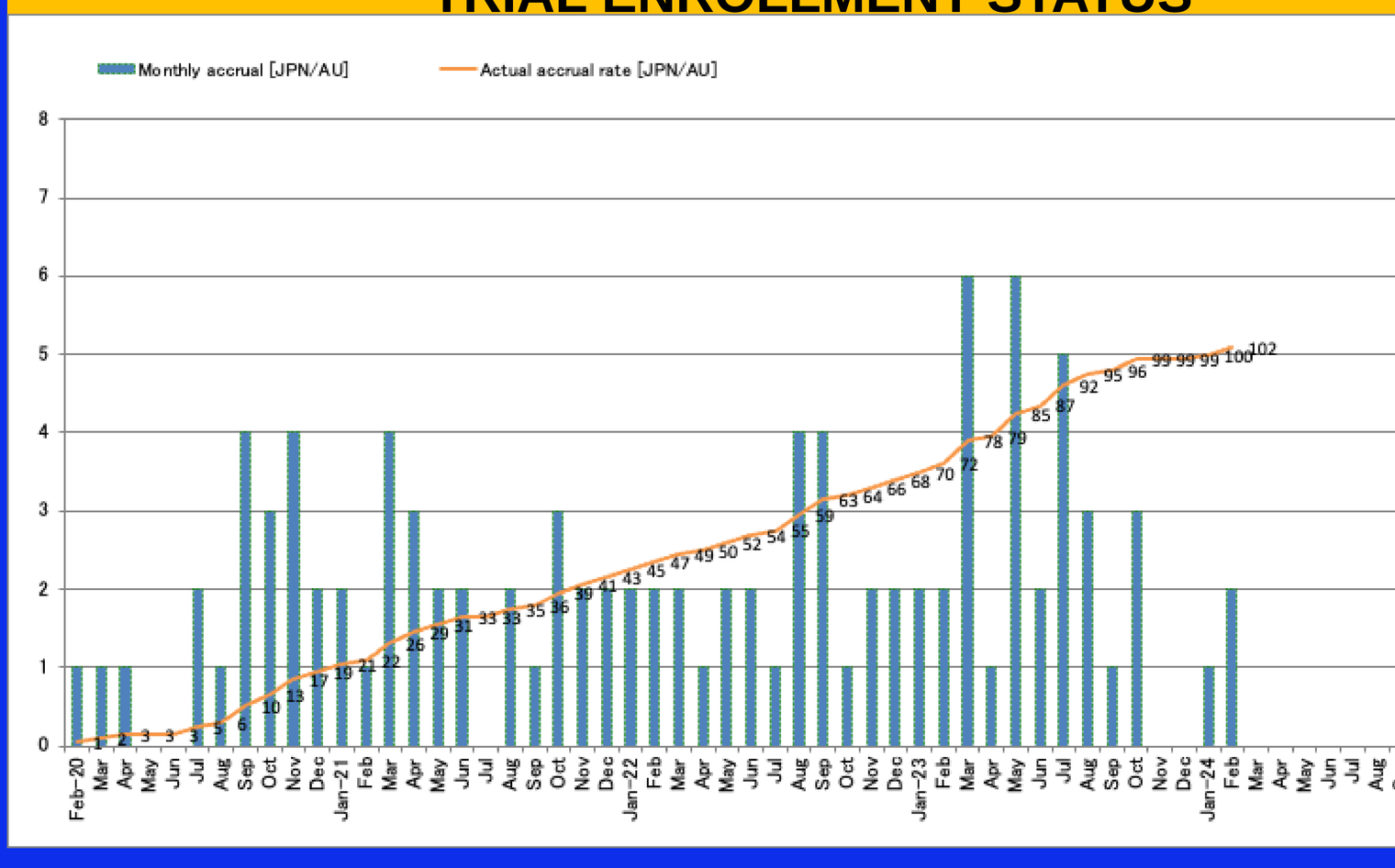
## INTERVENTIONS

**Dose schedule diagram**

(A typical incremental pattern)




## TRIAL ENROLLMENT STATUS




## DISCUSSION

using this approach may also allow international recommendations to be updated.

sidered a crossover design, but a parallel design was finally chosen, given that the crossover design has several limitations [4]. The crossover design is suitable for patients in a stable condition, but this is patients with cancer with NP refractory to opioids. We also believe that the treatment might have carryover effects and alter the response to subsequent treatments and that patients may not be in a com he start of each treatment period in a crossover trial.

es related to the content of the trial require discussion. There will be three major concerns: (i) the heterogeneity of causes of NP, (ii) the choice of the primary endpoint and (iii) the dose of each drug.

e heterogeneous causes of NP, we excluded patients with CIPN, and targeted patients with NCP nonresponsive or intolerant to opioid therapy.

endpoint is the difference in worst pain intensity score at day 14 between two groups. Although we acknowledge that the average pain intensity is adopted by many clinical trials about NP [5], including tw ncer with NP, some authors recommend worst pain intensity in the last 24 hours as primary endpoints because it satisfies most key recommendations in the draft guidance by the Food and Drug Adminis

g dose titration schedule has been devised to maximize the likelihood of benefit while minimizing the risk of adverse events. The participant will commence duloxetine or pregabalin at 30mg and 50mg re a maximum of 60mg (Duloxetine) and 300mg (Pregabalin). Dworkin et al. conducted a systematic review of pharmacologic management of NP and made the recommendations for maximum dosing [9] a mprehensive Cancer Network (NCCN) guideline of adult cancer pain [10;] we have defined initiation dose and maximum dose of both drugs.

## AUTHOR AFFILIATIONS

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