STATISTICAL ANALYSIS PLAN

A phase IV, post-marketing, single arm, observational study for safety evaluation of Alvopem® use in Iranian patients with non-small cell lung cancer and malignant pleural mesothelioma.

Name of Test Drug:	Alvopem®
Phase:	IV
Methodology:	Phase IV, post-marketing, single arm, observational study for safety evaluation of Alvopem® use in Iranian patients with non-small cell lung cancer and malignant pleural mesothelioma.
Sponsor:	NanoAlvand 7th West St, Simin dasht industrial Area, Karaj, Alborz, Iran.
NCT Number:	NCT04843007
Sponsor Representatives:	Dr. Araz Sabzevari Orchid Pharmed company CEO
Statistical Analysis Plan Date:	20 June 2020
Statistical Analysis Plan Version:	Version 1.0

1. Section 1: Administrative information

1.1. Title and Trial registration

1.1.1. Descriptive title that matches the protocol, with 'Statistical analysis plan' either as a fore runner or sub title, and trial acronym

Statistical analysis plan for Alvopem® study (Phase IV): A phase IV, post-marketing, single arm, observational study for safety evaluation of Alvopem® use in Iranian patients with non-small cell lung cancer and malignant pleural mesothelioma.

1.1.2. Trial registration number

NCT04843007

1.2. SAP Version (SAP version number with dates)

Version: 1.0, Date: 20 June 2020

2. Section 2: Introduction

2.1. Objectives

The objective of this PMS study is to monitor and assess the safety of Alvopem® in patients with non-small cell lung cancer and malignant pleural mesothelioma over a period of 4.5 to 9 months.

Primary objective(s):

The objective of this study is the safety assessment of Alvopem®.

3. Section 3: Trial Methods

3.1. Trial design – description of trial design

This is a, phase IV, single-center, open-label, single-arm, and post-authorization study.

3.2. Randomization

The subjects will not be randomized because the study is single arm and all subjects will receive Alvopem®.

3.3. Sample size

In a cohort study with no background incidence of a particular adverse reaction (interstitial pneumonitis), the probability that 1 or more adverse reactions will not occur in a sample of 190 patients with an anticipated incidence rate of 0.0085 is 0.19889. The power of this study is 80%. Based on the PASS® output, the sample size required is 190. Considering a drop-out rate of about 5% total sample size required is 200.

4. Section 4: Statistical Principles

4.1. Protocol Deviations

4.1.1. Description of which protocol deviations will be summarized

The number (and percentage) of patients with major and minor protocol deviations will be summarized with details of type of deviation provided. No formal statistical testing will be undertaken.

4.2. Analysis populations

Safety population:

Includes all subjects who receive study intervention.

5. Section 5: Trial Population

5.1. Details of how baseline characteristics will be descriptively summarized

Categorical data will be summarized by numbers and percentages. Continuous data will be summarized by mean and SD. Tests of statistical significance will not be reported for the baseline characteristics.

6. Section 6: Analysis

6.1. Analysis methods

All Patients who will be included in the study will be analyzed. Safety evaluation will be reported using summary statistics. For each AE, data will be summarized using incidence according to system organ class and preferred term of AEs and SAEs. Moreover, causality assessment will be done and its results will be reported by frequency and percentage.

6.1.1. List and describe each primary and secondary outcome including details of: methods used for assumptions to be checked for statistical methods

There is no assumption to check based on the reporting the incidences.

6.2. Statistical Software

The analysis will be carried out using Stata version 14.