A Phase-1b Dose Escalation Study to Assess the Effect of NG11-2 on Radiation Induced Oral Mucositis in Patients with Head and Neck Cancer

This study involved hospitals in 5 UK locations (2 England, 2 Scotland, 1 Northern Ireland). A total of 15 patients being treated for Head and Neck cancer were enrolled into the study.

The purpose of this study was to investigate whether a novel investigational pharmaceutical product (codenamed NG11-2) was well tolerated at certain dose-levels and whether certain dose-level(s) could be used to prevent the development of severe oral mucositis (mouth ulceration) in patients with head and neck cancers undergoing treatments involving high-dose radiation to the mouth cavity. Severe oral mucositis (SOM) is a debilitating side effect of radiotherapy for which there is currently no preventative treatment available.

The study included a dose-escalation phase and a dose-expansion phase. Each enrolled patient received the study drug NG11-2 as a mouthwash a few minutes before each of their daily fractional radiotherapy, until completion of the whole radiotherapy treatment, typically for up to 7 weeks.

Four dose-levels of NG11-2 mouthwash were tested in the dose-escalation phase with two patients treated at each dose-level. After a Safety Committee assessment, the highest dose-level was chosen for the dose-expansion phase and was given to an additional 7 patients before the study completed.

The study's primary endpoints were safety based and were assessed across both the dose-escalation phase and dose-expansion phase. The preliminary efficacy endpoints, including the duration, incidence and time-to-onset of severe oral mucositis (SOM), as the secondary endpoints of this study, were analysed on a total of 9 patients treated at the highest dose-level and were analysed using the Kaplan-Meier approach based on the oral mucositis readouts across the World Health Organisation (WHO), Radiation Therapy Oncology Group (RTOG) and National Cancer Institute Common Toxicity Criteria Adverse Event (NCI-CTCAE) scales.

For the primary endpoint, no Dose-Limiting-Toxicity (DLT) was identified among the four dose-levels tested, and all dose-levels were considered well tolerated. There were no Serious Adverse Events reported relating to the NG11-2 product. The main local safety signal identified relating to NG11-2 was a "stinging" sensation in the mouth or some oral pain especially when there was co-occurrence of oral thrush. There was no correlation or pattern between the local signal identified and the dose-levels tested.

As the secondary endpoints results, the preliminary efficacy readouts based on WHO, RTOG and CTCAEv5 scales were:

- **WHO scale**:
  1) Median duration of SOM was 15.5 days, compared to 18 to 19 days seen in published studies, presenting a notable reduction in SOM for participants with prophylactic NG11-

2 treatment, including 2 participants who only received approximately half of the planned NG11-2 treatments.
2) Incidence of SOM was 44.4%, comparing to 64-74% in the control groups reported in the literature.
3) Median time-to-onset of SOM was 54.0 days;

- **RTOG scale**:
  1) Median duration of SOM was 14.0 days.
  2) Incidence of SOM 33.3%.
  3) Median time-to-onset of SOM could not be calculated because the probability of not reaching SOM was above 50% at the end of the reporting period.

- **CTCAEv5 scale**:
  1) Median duration of SOM was 17.0 days.
  2) Incidence of SOM 33.3%.
  3) Median time-to-onset of SOM was 54.0 days.

In conclusion, the results from this study support the continued development of NG11-2 and a further large scale study is being planned to confirm whether NG11-2 can significantly reduce the incidence and duration of severe oral mucositis.

More information about the study can be found on the ISCRTN registry website (ISCRTN #87831050) or at ClinicalTrials.Gov (NCT06669390).