Kanglaite Reduce the Toxicity of Radiotherapy of Head and Neck Cancer Phase II Study

NCT03101514

January 6, 2017

Study Protocol and Statistical Analysis Plan

Patients

Patients aged 18–80 years with pathologically confirmed head and neck cancer receiving radical or postoperative radiotherapy and Karnofsky score greater than 80 points were eligible for recruitment. Patients who received radiotherapy only, radiotherapy concurrent with single-drug platinum chemotherapy, or induction chemotherapy with fewer than three cycles were eligible. Patients with a history of head and neck radiotherapy, distant metastases, and targeted drug or non-platinum drug chemotherapy during radiotherapy were excluded.

Treatments

All patients received 20 g Kanglaite (200 mL) daily, administered as an intravenous injection for 5 days a week, concurrently with radiotherapy. Kanglaite injection was used before or after radiotherapy, no time interval requirement between Kanglaite and radiotherapy. The dosage of radiotherapy was adjusted as follows: 70 Gy for gross tumors and positive lymph nodes, 66 Gy for tumor bed (operation bed), 60 Gy for high-risk lymph node drainage area, and 50 Gy for low-risk lymph node drainage area. Single fraction dose was 1.82–2.12 Gy for 5 days a week, once a day. Intensity-modulated radiation therapy was used and the radiotherapy planning system used was Eclipse 7.0. Recombinant human granulocyte colony-stimulating factor and antibiotics were not allowed as prophylactic treatments. After the final patient completed radiotherapy and observation data was recorded, the trial stopped.

Study end-points

Primary end-point was the incidence of radiation-induced mucositis. Secondary end-points were as follows: (i) blood toxicity, liver and kidney functions, and other toxic events; (ii) nutritional status, overall QOL, and QOL specifically related to head and neck.

All the end-points could be observed in the course of radiotherapy; therefore, long-term follow-up data may be reported in the future. After radiotherapy, patients

were evaluated for recurrence, metastases, and death every 3 months in the first 3 years, and every 6 months thereafter until death.

Evaluation of data

Acute toxicity indicators

Mucositis and the associated symptoms (manifested as pain, dysphagia, or dry mouth), blood cell count, liver and kidney functions, and other toxic events were assessed at baseline (before radiotherapy), every week during radiotherapy, and post radiotherapy. All adverse events were graded according to NCI Common Terminology Criteria for Adverse Events v4.0 (NCI-CTCAE4.0).

Mucositis in patients with head and neck cancer receiving radiotherapy usually occurs in the oral cavity, oropharynx, hypopharynx, and larynx. In NCI CTCAE4.0, grade 1 oral mucositis, pharyngeal mucositis, and laryngeal mucositis are defined as those causing mild discomfort in normal oral intake, requiring no intervention. Grade 2 mucositis is defined as that causing moderate pain, not interfering with oral intake, but altering oral intake. Grade 3 mucositis is defined as that causing severe pain, with severely altered eating/swallowing, requiring medical intervention. Grade 4 mucositis is defined as that with life-threatening consequences, requiring urgent intervention. Grade 5 mucositis is defined as that causing death.

Blood cell count, liver and kidney functions were assessed at baseline (before radiotherapy)—via blood test—every week during radiotherapy, and post radiotherapy. The lowest scores during radiotherapy were recorded and considered as data.

Nutritional status

Nutritional status was scored using the Patient-Generated Subjective Global Assessment (PG-SGA). The scores 0–1 is well-nourished or anabolic, scores 2–8 is suspected or moderate under-nutrition, score ≥9 is severely undernourished. The PG-SGA scores were recorded at baseline (before radiotherapy), every week during radiotherapy, and post radiotherapy. The highest PG-SGA scores recorded every week during the course of radiotherapy were used as the data obtained during

radiotherapy.

Therapeutic nutritional supports were provided based on the grade of dysphagia. Nutritional supports were divided into oro–enteral nutrition preparation, tube feeding, total parenteral nutrition, and separated nutrition infusion. Total parenteral nutrition was defined as a combination of amino acids, carbohydrates, and fats administered intravenously. Separate nutrition infusion was defined as intravenous administration of any one amino acid, carbohydrate, and fat. Nutritional treatment was not considered for those receiving nutritional treatment for less than 3 days or <10 kcal/kg per day.

Quality of life score

European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire was used to evaluate the overall QOL. European Organization for Research and Treatment of Cancer QLQ-Head and Neck 35 (EORTC QLQ-H&N35) questionnaire was used to evaluate QOL specific for head and neck. Quality of life for each patient was assessed at baseline (before radiotherapy), every week during radiotherapy, and post radiotherapy using the EORTC QLQ-C30 and EORTC QLQ-H&N35 questionnaires. The QLQ-C30 and QLQ-H&N35 questionnaires were distributed to patients weekly during radiotherapy, and the lowest scores were recorded as data during radiotherapy. Using the EORTC Group scoring guidelines, each item of the QLQ-C30 and QLQ-H&N35 questionnaires was scored from 0 to 100. Higher scores for functions in QLQ-C30 implied a better quality of life; higher scores for the symptoms in QLQ-C30 and all items in QLQ-H&N35 indicated worsening quality of life.

Statistical analysis

Descriptive statistics were used to summarize patient baseline characteristics. Normally distributed data are reported as mean and standard deviation. Qualitative data are presented as number of observations and percentages. All statistical analyses were conducted using SPSS Statistics v. 18 (IBM Corporation, NY, USA). A two-tailed $p < 0.05$ was considered statistically significant.