Background: Concurrent chemoradiotherapy is the standard treatment for non-surgical care of patients with locally advanced oesophageal cancer. Nimotuzumab (h-R3) is a genetically engineered humanised monoclonal antibody that can recognise an epitope in the extracellular domain of human epidermal growth-factor receptor (EGFR). This phase 1 trial was designed to assess the safety and efficacy of nimotuzumab when given with concurrent chemoradiotherapy.

Methods: Patients age 18–75 years, with ECOG performance status 0–2 and locally advanced squamous oesophageal cancer confirmed by histological assay, were eligible for the study. Patients received radiotherapy to a total dose of 61.2 Gy/32Fx concurrent with two cycles of PF regimen (cisplatin 25 mg/m^2 days 1–3; fluorouracil 600 mg/m^2 continuous IV infusion days 1–3, every 28 days). An escalating weekly fixed dose of nimotuzumab (100, 200, and 400 mg) was administered during radiotherapy in a cohort study. After radiotherapy, patients received consolidation chemotherapy with PF regimen every 28 days for another two cycles. The primary endpoints were safety and early efficacy. The trial was approved by the Chinese State Food and Drug Administration and the protocol has passed ethical committee review and gained institutional review board permission. The trial is registered with clinicaltrials.gov, number NCT00950417. All participants gave written informed consent.

Findings: From July, 2009, to June, 2010, nine patients (seven men and two women) with a median age of 58 years (48–72 years) were enrolled. All patients tolerated the treatment. No adverse events likely to be related to nimotuzumab were noted. The objective remission rate, which can reflect early efficacy, was 66.67–75% based on the evaluable cases.

Interpretation: Nimotuzumab combined with chemoradiotherapy based on the PF regimen was safe and well-tolerated.

Funding: China National Twelfth Five-year Program Fund and Beijing Science Plan.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.050

P50 DOSE–ESCALATION STUDY OF NIMOTUZUMAB PLUS IRINOTECAN AS SECOND-LINE TREATMENT IN METASTATIC COLORECTAL CANCER WITH WILD-TYPE K-RAS

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Background: Nimotuzumab is a humanised monoclonal antibody of epidermal growth-factor receptor (EGFR). We assessed the safety, tolerability, and efficacy of nimotuzumab combined with irinotecan as second-line treatment in Chinese patients with metastatic colorectal cancer (mCRC).

Methods: Patients with mCRC refractory to oxaliplatin, wild-type K-ras, target lesion(s), ECOG performance status $\leqslant$2, and adequate organ function were eligible for this open-label, single-arm trial (NCT00972465). Irinotecan was given as 180 mg/m^2 on day 1 every 2 weeks until progression, or adverse events, for a maximum of six cycles. Nimotuzumab was given as 200, 400, or 600 mg weekly until progression or adverse events. Primary endpoints were objective response rate and toxicity. Secondary endpoints were progression-free and overall survival. Patients gave written informed consent.

Findings A total of 22 patients (male-to-female ratio 14:8; median age 55 years, range 30–78) were enrolled from July, 2009, to July, 2010. Four, seven, and 11 patients received nimotuzumab at a dose of 200, 400, and 600 mg, respectively. The total number of doses of nimotuzumab was 244 (median 6, range 2–30). No grade 3–4 toxic effects relating to nimotuzumab were observed. Two patients developed skin rash (grade 1): one each at the 400 and 600 mg doses. The maximum tolerated dose has not yet been reached. Three patients (two at the 400 mg dose and one at 600 mg) dropped out for personal reasons. In the 600 mg group, partial response was 40% (4/10) and progressive disease (PD) was 60% (6/10). In the 400 mg group, stable disease (SD) was 20% (1/5) and PD was 80% (4/5). In the 200 mg group, SD was 50% (2/4) and PD was 50% (2/4). Follow-up of overall survival is ongoing.

Interpretation: Addition of nimotuzumab 600 mg weekly to irinotecan for second-line treatment of mCRC is safe, and first data suggest promising activity. The maximum tolerated dose of nimotuzumab has not been reached yet.

Funding: Beijing Science Plan.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.051

P51 RANDOMISED, SINGLE-CENTRE, PHASE 2 TRIAL OF NIMOTUZUMAB PLUS CISPLATIN AND S-1 AS FIRST-LINE THERAPY IN PATIENTS WITH ADVANCED GASTRIC CANCER

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Background: Nimotuzumab, a humanised anti-epidermal growth-factor receptor (EGFR) monoclonal antibody, has demonstrated efficacy and an absence of severe skin toxicity in many phase 1 and 2 cancer trials.

Methods: We did a single-centre, randomised, parallel assignment, open-label study of nimotuzumab (N: 200 mg IV on days 1, 8, and 15, every 3 weeks) plus cisplatin (C: 30 mg/m^2 on days 1 and 2, every 3 weeks) plus S-1 (S: 80 mg/m^2 twice daily on days 1–14, followed by 7 days off) versus cisplatin plus S-1, as first-line treatment in patients with advanced or metastatic gastric cancer. If tumour control was achieved, NCS and CS were continued until unacceptable toxicity or disease progression. The primary endpoint was objective response rate (ORR) and the secondary endpoints included time-to-progression (TTP), progression-free survival (PFS), 1-year survival rates, and safety.

Findings: 40 patients, 27 men and 13 women, with a median age of 54 years (range 21–74) and good performance status (ECOG PS 0–2) were treated with NCS (n = 20) or CS (n = 20). Up to January 14, 2011, 36 patients (NCS group 19 cases, CS group 17 cases) have undergone efficacy assessment. ORR was 63.2% (12/19) in the NCS

group and 64.7% (11/17) in the CS group. 18 patients had disease progression (NCS 10, CS 8); median TTP was 5.5 months in the NCS group and 3 months in the CS group, and average TTP was 5.3 months in NCS group and 3.1 months in CS group. The incidence of adverse events was similar for both groups. No adverse events of grade 3 skin rash or grade 3 infusion-related reactions were observed.

Interpretation: This study provides evidence that nimotuzumab combined with cisplatin and S-1 has better outcomes than cisplatin and S-1. Initial results show a benefit in TTP improvement and a potential improvement in OS, and the study is ongoing.

Funding: Beijing Science Plan.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.052

P52 3T MRI DETERMINATION OF CIRCUMFERENTIAL RESECTION MARGIN IN RECTAL CANCER – CORRELATION WITH HISTOPATHOLOGY

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Background: Recent surgical trials show that in patients with rectal carcinoma, evaluating the involvement of the mesorectal fat and mesorectal fascia is more important than T staging for planning treatment. We studied the accuracy of 3T MRI for prediction of mesorectal fascia involvement and circumferential resection margin (CRM; shortest distance between tumour and mesorectal fascia) in patients with rectal cancer.

Methods: 40 consecutive patients with biopsy-proven rectal cancer from the Department of Colorectal Surgery were included in the study. 3T MR imaging was done after patients had a 4-h fast and cleansing water enema. T1-weighted and T2-weighted images were obtained, with high resolution images in 3 planes. The image series were evaluated after verification by an experienced gastrointestinal radiologist, and CRM measurements and mesorectal fascia involvement were documented. These results were compared with the final histopathology report.

Findings: Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 3T MRI for prediction of CRM involvement was 100%, 33.3%, 61.9%, and 100%, respectively.

Interpretation: 3T MRI has high sensitivity and NPV, and low specificity and PPV for prediction of CRM involvement. The low specificity could be due to the high resolution of the images, which picked up areas of tumour reaction, increased flow, and oedema. This low specificity is compounded by the difficulty in assessing CRM in cachectic patients and in low anterior tumours. However, MR imaging has a high sensitivity and NPV for mesorectal fascia assessment, and is therefore indispensable for pre-operative staging of rectal cancer.

Funding: None.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.053

P53 OPEN-LABEL, RANDOMISED, MULTICENTRE, PHASE 2A STUDY OF GAMBOGIC ACID INJECTION (THS) FOR TREATMENT OF ADVANCED CANCER

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Background: Gamboge Acid is a pure active compound isolated from the Camboge (Garcinia morella Desv), a traditional Chinese herb medicine. Based on preliminary results of the completed phase 1 study, this phase 2a study compared the efficacy and safety of different dosage schedules.

Methods: 47 patients were randomly assigned to one of two groups. Group A received a daily intravenous infusion of gamboge acid (THS) of 45 mg/m^2 every day for 5 days, every 2 weeks ($n = 21$). Group B received intravenous THS 45 mg/m^2 every other day five times, every 2 weeks ($n = 26$). All patients had two consecutive courses of treatment prior to safety and efficacy evaluation.

Findings: In group A, the objective remission rate (ORR) was 14.29% and overall disease control rate (DCR) was 76.2%, compared with an ORR of 0% and DCR of 61.5% in group B. Apart from ORR (with a insufficient value of zero) comparison of DCR was statistically significant ($p = 0.0456$), with a positive relative risk and odds ratio and 95% confidence intervals. Adverse events or reactions were mainly grade 1 and 2, and were observed, in most cases, after patients received the trial drugs. The incidence rate of adverse events or reactions did not differ significantly between the two groups.

Interpretation: Preliminary results of this exploratory study showed favourable safety profiles for THS at 45 mg/m^2, and DCR was higher for 5-day consecutive dosing of THS than for an every-other-day schedule.

Funding: Beijing Science Plan.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.054

P54 DOSIMETRIC COMPARISON OF ^{18}FLT AND ^{18}FDG PET-CT IN CONTOURING BIOLOGICAL TUMOUR VOLUME IN THORACIC OESOPHAGEAL CARCINOMA

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