Visceral and retroperitoneal sarcoma working group

Date: December 6, 2016

Chairman: T. Hølmebakk.

Summary from the meeting

The visceral and retroperitoneal sarcoma session on Tuesday, December 6, was well attended by surgeons and oncologists, mainly from Sweden and Norway.

Tumour rupture of GIST. T. Hølmebakk, Oslo Sarcoma Group, presented their study on tumour rupture of GISTs of the small intestine, published in the *British Journal of Surgery* this year. 71 patients undergoing complete surgery for non-metastatic disease from 2000 to 2012 were included. Tumour rupture was classified as absent (31 patients); minor (21 patients); or major (19 patients). Minor rupture was defined as peritoneal tumour penetration, iatrogenic peritoneal laceration, and microscopically involved margins. Major rupture was defined as tumour spillage, tumour fracture or piecemeal resection, bowel perforation at the tumour site, blood-tinged ascites, infiltration into adjacent organ, and surgical biopsy. The 5-year recurrence rate was 64, 29 and 31 per cent in patients with major, minor and no rupture respectively (P =0·001). The hazard ratio (HR) for major rupture versus no rupture was 3·55 (95 per cent c.i. 1·51 to 8·35). Peritoneal recurrence rates for major, minor and no rupture were 52, 25 and 19 per cent respectively (P =0·002), and the HR for major rupture versus no rupture was 4·98 (1·69 to 14·68). On multivariable analysis, mitotic index, major rupture, tumour size and age were independently associated with risk of recurrence. To conclude, major but not minor rupture should be considered rupture with prognostic significance.

Long term survival in metastatic GIST. K. Boye, Oslo Sarcoma Group, on behalf of I. Hompland, presented their study on 133 patients with metastatic GIST identified in the Oslo Sarcoma Database from 1993 to 2013. Patients were classified as (i) tumour free following primary or secondary surgery; (ii) oligometastatic with ≤ 3metastases; (iii) polymetastatic with > 3 metastases. Median survival for the whole group was 6.9 years with a median follow-up of 9 years. Five year survival for patients with polymetastatic disease was 48 per cent vs. 89 per cent for patients with oligometastatic disease; HR 6.62(P<0.001). There was no statistically significant difference in survival between tumour free and oligometastatic patients. Apart from the number of metastases, ECOG status and the size of the largest metastasis significantly influenced prognosis. Based on these data, it seems that oligometastatic GIST may be considered a separate entity comparable in outcome to high risk primary GIST.

K. Boye went on to present the Stop-GIST trial, sponsored by Oslo University Hospital and opening early next year. Patients with an initial number of metastases ≤ 3 rendered surgically tumour free and having been treated with imatinib for at least 5 years, will discontinue imatinib. The primary endpoint is three years progression free survival after discontinuation of imatinib. Thirty-one patients will be recruited.

Neoadjuvant imatinib for GIST. K. Boye, Oslo, presented studies and international guidelines on the neoadjuvant use of imatinib in GIST. Based on the ESMO Guidelines, the following indications were suggested: (i) patients with large gastric tumours requiring multi-visceral resections for complete removal; (ii) patients with tumours of the oesophagus, duodenum or rectum; (iii) patients with tumours at any site that are considered marginally resectable or might rupture on surgical manipulation. Neoadjuvant treatment is recommended for 6 to 12 months, and patients should be followed with CT every 3 months. Biopsy, mutational analysis and MDT discussion are required before starting. Following complete surgery, adjuvant treatment should be given according to standard criteria; mitotic count, however, is unfeasible after neoadjuvant treatment, and when tumour site, size or rupture do not indicate a high risk tumour, individual decisions must be taken based on multidisciplinary discussions.

T. Hølmebakk, Oslo, presented cases for discussion.

Crenolanib in advanced GIST with D842V mutation. K. Sundby Hall, Oslo Sarcoma Group, presented this trial which will open for accrual early 2017. Patients will be randomised to crenolanib or placebo in a non-cross over design. Few patients are expected to be eligible.

Other GIST studies and trials. An up-date by M. Eriksson, Lund.

SSGXXII: THREE VERSUS FIVE YEARS OF ADJUVANT IMATINIB AS TREATMENT OF PATIENTS WITH OPERABLE GIST WITH A HIGH RISK FOR RECURRENCE: A randomised phase III multicentre study.

ALT-GIST: A randomised phase II trial of imatinib alternating with regorafenib compared to imatinib alone for the first line treatment of advanced gastrointestinal stromal tumour (GIST).

Neoadjuvant radiotherapy for retroperitoneal sarcoma. There is no common practice regarding radiotherapy for retroperitoneal sarcoma within the SSG. Our radiotherapy guidelines merely states that RT could be considered after incomplete or R1 resection. Oslo, Stockholm and Copenhagen participate in the STRASS-trial, in which patients are randomised to up-front surgery or neoadjuvant RT. This trial will be closed early next year having included some 260 patients. Preliminary results are due in 2020. It is uncertain whether this trial will give a clear-cut answer to the question. T. Hølmebakk, Oslo, presented data from the US National Cancer Data base, published by Nussbaum et al. in *Lancet Oncology* this year. Overall survival in 9 068 patients undergoing curatively intended surgery for retroperitoneal sarcoma was assessed; 563 had received preoperative RT; 2 215 had received postoperative RT; and 6 290 had received no RT. Matched case-control analyses were performed. Hazard ratio (HR) for death was 0.70 when preoperative RT was compared to surgery alone ($P<0.0001$); 0.78 when postoperative RT was compared to surgery alone ($P<0.0001$). SSG recommendations will be discussed further in Aarhus next September.

Off agenda: B. Nilsson, Gothenburg, presented some experimental data on GIST.