



Editorial – referring to the article published on pp. 1032–1039 of this issue

Surgery is an Essential Part of Salvage Treatment in Refractory Germ Cell Tumors

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Cisplatin-refractory germ cell tumours represent an unfavourable subgroup of testis cancer patients with a less than 10% chance of long-term survival [1]. De Giorgi et al. present a phase 2 trial of 18 patients with a combination chemotherapy regimen that has already proven to be effective in two other phase 2 trials of the German Testicular Cancer Study Group (GTCSG) and the Greek Group (numbers 18 and 19, respectively, in the article's references) [2]. This combination regimen is an effort to avoid high-dose chemotherapy as salvage treatment to reduce toxicity of treatment. The role of high-dose first-line salvage treatment has recently been very well defined by the GTCSG in a matched-pair analysis as well as in a randomized phase 2 trial [2,3]. Results of this trial will be published soon. Another phase 2 trial of Rosti et al. [4] of the same Italian group randomized one course of high-dose chemotherapy to conventional treatment in the salvage setting with no advantage for the high-dose arm.

In all phase 2 trials dealing with this cohort of patients, the results were mainly dependent on entry criteria and on detailed definition of pretreatment schedules. The objective response rates (CR and PR) of the previous phase 2 trials using the same regimens by Kollmannsberger et al. and Pectasides et al. were 8 of 22 (36%) and 9 of 28 (32%), respectively. The difference in the current trial with only 3 of 18 (17%) objective responses is explained only by different patient cohorts and different pretreatment schedules.

As a surgeon, I always have trouble interpreting these results, since the given data do not make clear whether surgery was considered a treatment option during the course of the disease. Two of the cases were late-relapsing patients; surgery usually is a valid option if the disease is localized and resectable [5,6]. In addition, the data are not specific enough to allow for an objective judgement on pretreatment. The initial IGCCCG classification is not given, and many of the patients received six courses of PEB first-line chemotherapy, which is unusual. Thirteen of 18 patients were treated in a third-line situation. There is no information on residual tumour resections after first- or second-line treatment and whether this had been an option at all. Two of the three long-term responders showed this favourable course, because the residual tumor could be resected after gemcitabine–oxaliplatin treatment. In at least six patients, a partial remission with negative markers had been achieved after first-line treatment; no information is given on surgery in this situation.

The long-term cure of advanced testis cancer patients is a goal that can only be achieved by the combination of chemotherapy and surgery. At several points during treatment, the resectability has to be rechecked to avoid cisplatin-refractory situations with a then reduced long-term cure rate. Even patients with positive markers need to be checked for resectability [7,8]. Especially in AFP-positive patients, residual teratoma and yolk sac elements are responsible for the marker status,

and patients may not need further treatment after a complete resection has been achieved [7–10]. In most patients with retroperitoneal disease and in some patients with mediastinal and pulmonary lesions, a complete resection of residual disease is possible. Most problematic are patients with primary extragonadal retroperitoneal and—even worse—mediastinal germ cell tumours. In these patients, experimental data suggest a different tumour biology as compared with germ cell tumours of testicular origin.

In summary, the entry criteria are most important to put a phase 2 trial into the right perspective. Surgery is an essential component of treatment, especially for testicular primaries with retroperitoneal and pulmonary disease. The initial chemotherapy treatment in a first-line recurrent situation is most important, and certain subgroups may benefit from early high-dose regimens to avoid refractory disease. In cisplatin-refractory patients with positive markers, surgery can lead to a long-term cure rate of about 25%. It is evident that, from the beginning of and throughout the treatment, all these patients have to be treated at specialized centers with a minimum number of advanced testis cancer patients a year. Salvage treatment as a rescue treatment after inadequate pretreatment will not lead to satisfying results.

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