CONVERSION CHEMOTHERAPY FOR TECHNICALLY UNRESECTABLE COLORECTAL LIVER METASTASES: A RETROSPECTIVE, SINGLE-CENTER STUDY COMPARING CHEMOTHERAPY ALONE OR IN COMBINATION WITH CETUXIMAB OR BEVACIZUMAB

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Introduction: Surgery for easily resectable colorectal liver metastases can offer a chance of cure. For this reason many efforts have been made to improve response rate in initially unresectable patients in order to convert their disease to surgery. The benefits of conversion chemotherapy are still debatable since the outcome of easily resectable patients can not be automatically considered well-founded also for unresectable patients. We collected data of initially unresectable patients with liver limited disease to evaluate resection rate, DFS and OS according to surgery or not and according to different chemotherapy regimens.

Methods: We retrospectively collected patients with liver only disease (between June 2006 and June 2013) considered technically unresectable at a multidisciplinary evaluation. Patients were divided into three groups: group 1 (G1), patients treated with neoadjuvant chemotherapy without biologics (FOLFOX or FOLFIRI); group 2 (G2), chemotherapy plus bevacizumab; group 3 (G3), chemotherapy plus cetuximab.

Primary endpoint was resection rate. Secondary endpoints were disease free survival (DFS) and overall survival (OS).

Results: A total of 92 patients were analyzed, n.29 in G1, n.34 in G2, n.29 in G3. All G3 patients were KRAS wild-type. Among G1 and G2 patients, 10/29 and 17/34 carried a KRAS mutation, respectively. Resection rate was 44.8% (13/29), 32.3% (11/34) and 58.6% (17/29), respectively in G1, G2 and G3 groups, with a trend toward statistical significance in favour of G3 (p .06), when compared to G1 or G2. Median DFS was 14.5 months in G1, 12.1 months in G2 and 15.6 months in G3 (progression was observed in 26/29, 28/34 and 25/29, respectively), without significant statistical differences between groups. OS was significantly higher in resected patients, when compared with non-resected ones. Median OS of non-resected patients was 28.9, 23.9 and 19.4 months in G1, G2 and G3, respectively. With a mean follow-up time of 35.7, 27.1, and 29.4 months respectively, median OS in resected patients has not been reached yet.

Conclusion: The strength of our study lies in the mono-institutional nature of the trial, although two bias were identified: 1. surgeon “aggressiveness” increased over the study period; 2. the time of diagnosis affected the choice of chemotherapy (older diagnosed patients were most likely to receive chemotherapy alone). Our data confirm a benefit on survival in converting to surgery patients initially judged as unresectable. In our study the addition of cetuximab to chemotherapy seems to improve resection rate (although criteria for resectability could affect this data), but it does not translate in significant differences on DFS. Data on OS are still immature for resected patients. Our data seem to suggest that technically unresectable patients receiving chemotherapy plus cetuximab are more likely to become resectable compared to patients treated with bevacizumab or chemotherapy alone, whether these findings are still immature to demonstrate a trend toward an OS improvement. Interestingly enough, if only non-resected patients are considered, G3 patients show a short median OS (19.4 months), thus suggesting that only patients with a very advanced disease are not considered for surgery.