RESPONSE TO NEoadjuvant CHEMORADIATION IN RECTAL CANCER: TIME TO CONSIDER RISK-ADAPTED ADJUVANT CHEMOTHERAPY

Ahmad Al Zahrani1, Mahfoudh Mohammed2, Alaa Abdul Jabbar3, Samar Al Homoud4, Ali Al Jubran4, Hadeel Al Manae3, Shouki Bazbarashi3, Mohammed Mohuiddin2, Nasser Al Sanea2
1King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, 2King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, 3King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, 4King Faisal Specialist Hospital and Research Center-King Faisal Cancer Center, Riyadh, Saudi Arabia

Background: Randomization of clinical trial in locally advanced rectal cancer has long been based according to pre-chemotherapy clinical stage including recently published CAO/ARO/AIO-04 German trial. Pathological stage post chemoradiation seemed to better risk-stratify patients than initial clinical stage. Few studies have been published so far pertaining the relationship of pathological stage grouping post neoadjuvant therapy and long term outcomes. To further explore on this issue, we report our experience at a single institution.

Methods: 196 patients between July 2001 and December 2010 with clinical T3-4 or node positive rectal cancer who received neoadjuvant radiation only (51 pts, 26%) or 5-FU based chemoradiation (145 pts, 74%) followed by curative tumor specific mesorectal excision and had adjuvant single agent fluoropyrimidine-based chemotherapy (5-FU/LV: 115 pts, 58.7%; and capecitabine: 81 pts, 41.3%) were retrospectively reviewed. Median radiation dose: 5040 cGY. Postoperatively, the 7th edition of AJCC TNM colorectal cancer staging system was used. End points include three-year disease free survival (DFS) and five-year overall survival (OS) according to clinical and pathological stages. Differences between curves were evaluated using the log-rank test.

Results: Median follow up was 46 months (2.4 -130). Median age: 55 years (range 26-89). Male: 102 (52%). Similar three year DFS has been observed for clinical stage II and III at 66.2% and 68.3%, respectively (p= 0.909). Likewise, five-year OS was equal at 84.3% and 79.8%, respectively (p = 0.466). Three year DFS according to pathologic stages were as follows: 93% in pathologic complete remission (ypCR, n = 15), 86% in stage I (ypT1-2N0, n = 38), 78% in stage II (ypT3-4N0, n = 58), 65% in stage III (ypT1-4N + , n =85), p = 0.006. The 5-year OS rates of these respective stages were: 100%, 92%, 86%, and 72%, p = 0.005. In ypN negative patients, multivariate analysis showed that perineural invasion was the only independent prognostic factor for DFS. None of the proposed variables emerged as an independent factor for survival.

Conclusion: Pathological stage grouping post neoadjuvant therapy as opposed to clinical stage correlates well with long term outcomes in locally advanced rectal cancer. Our findings justify risk-adapted adjuvant therapy in which adjuvant chemotherapy may be omitted in ypCR and adapted in ypT3-4N0 and ypN positive patients in the context of randomized clinical trials.

© The Author 2013. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com.