

Esophageal Carcinoma: It is Time to Move on

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Short Communication

Esophageal carcinoma is a rare cancer of the gastro-intestinal tract, but the incidence is increasing annually. This is because of continued smoking (Epidermoid Carcinoma) and the high incidence of acid reflux disorder as in Western Hemisphere (Adenocarcinoma). The later in part may be due to abuse of alcohol, and being overweight. In the seventies the primary treatment of localized disease of the esophagus was surgery alone for mid and lower third operable and resectable early lesion. Post operative radiotherapy (RT) was recommended and given to those with close margin(s) and/or found to have regional lymph node(s) involvement. The patients with cancers of the upper third, regardless of their pathology, and those with locally advanced disease where treated with radiation only [1-6].

In spite of the above, the overall five year survival was very poor and unacceptable. With the introduction of Cisplatin chemotherapy in patients with advanced head and neck cancers, and possible activities in patients with esophageal carcinoma, led to the early combined modality therapy in these patients. Induction Cisplatin followed by RT, concurrent or post total RT where the early of these trials, and results where somewhat encouraging. With our introduction of Platinol and 5FU (PF) as active combination in previously untreated head and neck cancers, this led to the use of PF in locally advanced esophageal carcinoma with or without surgical removal or total RT in these patients. The total RT was reduced to 5,000 cGr when was combined and concurrent with this effective CT because of the overall tolerance and toxicities.

A phase II trial was conducted in the RTOG using two courses of modified PF combined with RT was tolerable, effective and acceptable. This led to the well known intergroup trial, headed by the RTOG of total RT compared to two courses of PF concurrent with RT, followed by additional two courses of the same doses PF post RT. The results of this important trial, was outstanding, and even more than anticipated. This led by a second intergroup randomized trial, comparing total RT to same CT dose and sequence, but the concurrent with increased dose of total RT to 6,000 cGr against the original authors concern. As predicted, the trial ended early with about 10% treatment death in the combined arm. So, the standard

arm reverse back to concurrent two courses of PF with 5,000 cGr, and adjuvant two courses of PF and unfortunately remained the "gold" standard treatment for these patients until today.

The total treatment of locally advanced head and neck cancers, have changed during the last twenty years. Instead, of PF we are given TPF (Taxotere, Platinol, 5FU) which found to be superior in randomized intergroup trial. Unfortunate, TPF was rather toxic, resulted in treatment interruption and even hospitalization to some patients. This led us to modify TPF giving same dose of Taxotere, but instead of Cisplatin, we changed to Carboplatin and instead of 5FU 120 hours infusion, we recommended 5FU 2,600mg/m² 24 hour infusion day 1, 8 and 15. All the three active agents to be repeated on days 22, and 43.

The following is the full modified TPF treatment:

- Taxotere 75mg/m² IV day one and every three weeks
- Carboplatin AUC 5.00 IV day one and every three weeks
- 5FU 2,600mg/m² given as 24 hour IV infusion days 1, 8, and 15 Repeat all agents of days 22 and 43

This resulted in the most active, and the least toxic combination for these patients. Less or eliminated side effects of nausea and vomiting, fluid and electrolytes imbalance, stomatitis/mucositis, renal, hearing, and peripheral neuropathy. Eliminated hospitalization, and increased the overall response rates and the cure rate at five years.

Following the induction CT, concurrent weekly Carboplatin with total RT was administered. Carboplatin AUC 1.5 IV was given on the first day of RT and then weekly during RT and for 2-3 weeks after. This is because the biological effects of RT are still on. Same total and combination where used by us in limited patients with locally advanced esophageal cancers, with the same success rate. It is time to change the course, and the cure rate and survival of these patients with locally advanced esophageal cancers (both of Adenocarcinoma or epidermoid carcinoma) at any third of the esophagus into induction three courses of modified TPF, followed by RT 5,000 cGr concurrent with weekly Carboplatin.

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