A PROSPECTIVE COMPARATIVE STUDY ON BIWEEKLY DOCETAXEL, CISPLATIN, 5-FLUOROURACIL, LEUCOVORIN (TPFL) VERSUS TRIWEEKLY TPF AS AN INDUCTION CHEMOTHERAPY IN LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF HEAD AND NECK

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BACKGROUND

- Triweekly TPF (Docetaxel/Cisplatin/5FU) has been an effective induction chemotherapy (ICT) regimen as per TAX 323 and TAX 324 trials in locally advanced squamous cell carcinoma of head and neck (SCCHN).

- However, toxicity was more with neutropenia and febrile neutropenia occurring in 76.9% and 5.2% respectively as per TAX 323 trial and 80% and 12% as per TAX 324 trial.

- Hence, we conducted a phase II randomised prospective study to see if biweekly TPF regimen (dose dense) was associated with equal response rates with lesser adverse events in our setting.

AIMS AND OBJECTIVES

- **AIM**: To assess the efficacy and safety of biweekly TPFL as induction chemotherapy versus triweekly TPF.

- **PRIMARY OBJECTIVE**: To determine the Overall Response Rates (ORR) – Complete Response (CR)/Partial Response (PR) to ICT.

- **SECONDARY OBJECTIVE**: To compare the safety and toxicity profile.

MATERIALS AND METHODS

- **Locally advanced SCCHN**
- Oral cavity/oropharynx/hypopharynx/larynx
- Stage III/IVA/VB (AJCC 8)
- ECOG PS 0-1
- Age >16 years

(March 2020 to September 2021)

- **ARM A: BIWEEKLY TPFL (n=60)**
  - Docetaxel (T) 50mg/m², cisplatin (P) 50mg/m², leucovorin (L) 250 mg/m², 5-fluorouracil (5FU) 2500 mg/m² 24hr QD: D1 Q2weekly 2#

- **ARM B: TRIWEEKLY TPF (n=60)**
  - Docetaxel (T) 75mg/m² D1, cisplatin (P) 575mg/m² D1, 5-fluorouracil(5FU) 750 mg/m² over 6hrs (D1-D4); Q3weekly 2#

In GCSF 300ug s/c was given for 5days in both the arms. The above triweekly regimen used at our institute due to better tolerability has similar CR Rates as TAX 323 / 324. Response assessment: At 6wks by clinical evaluation and imaging as per RECIST 1.1. Toxicity assessment was done as per NCI CTCAE version 5.

It was followed by definitive treatment either surgery or concurrent radiotherapy

RESULTS

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Arm A (Bi)</th>
<th>Arm B (Tri)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>44.2 yrs</td>
<td>42.6 yrs</td>
</tr>
<tr>
<td>Male: Female</td>
<td>5.6:1</td>
<td>6.5:1</td>
</tr>
<tr>
<td>Primary site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>91.7%</td>
<td>90%</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>6.7%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>1.7%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Stage III/IVA/VB</td>
<td>8.3/55/36.7%</td>
<td>5/56/38.3%</td>
</tr>
</tbody>
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- There were two deaths in biweekly and four in triweekly arm.
- Two patients in biweekly and six in triweekly arm defaulted treatment
- Following ICT, 57.1% in biweekly and 56.9% in triweekly arm underwent surgery and 42.9% in biweekly and 43.1% in triweekly arm underwent chemoradiation (p = 1.00).
- There was trend towards better PFS and OS in biweekly arm but survival data is yet to mature

DISCUSSION

- Dose dense chemotherapy arms achieve maximum tumor kill by shortening interval of chemo delivery. It is associated with better response rates and is well tolerated. Such studies are scarce in head and neck.
- Biweekly arm showed statistically significant better response rates with acceptable grade 3/4 toxicities when compared to triweekly arm in locally advanced SCCHN with a trend towards better PFS and OS.
- Thus, biweekly TPF could be a feasible regimen in our setting. However, further phase 3 studies are required to substantiate.

KEY MESSAGE

Induction chemotherapy in SCCHN is not well established. Biweekly TPF could be a feasible regimen in developing country like India. Phase III data is warranted to establish recommendations considering a delicate balance between efficacy, toxicity, and quality of life.

REFERENCES


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