RETROSPECTIVE ANALYSIS OF NIMOTUZUMAB VS CHEMOTHERAPY IN LOCALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS RECEIVING CONCURRENT RADIOTHERAPY

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Abstract:

Background: In advanced malignancies, it is important to ensure that the quality of life is not comprised, when treating the disease. Therefore there is immense need for the data on the QOL parameters for the newer agents/indications. In view of the paucity of data for the Nimotuzumab, we thought of conducting a retrospective data analysis in patients with head and neck squamous cell carcinoma

Methods: This is a multi institutional, two arm retrospective data collection exercise done in subjects with head and neck cancer stage III or less receiving radical radiotherapy(IMRT) with either nimotuzumab or chemotherapy (weekly cisplatin) between 2015-2018 with three years follow up. Standard format for the QOL (a part of dissertation thesis by PG) was used for analysis along with demographics and outcome in terms of clinical data and survival.

Results: During the study period a total of 84 subjects were meeting the criteria for the study and the case records were retrieved with 1:1 case/control (matched population) for stage, age and other variables. Response rate was higher in the Nimotuzumab arm (86% versus 81%; P=NS).. No differences were observed in median progression-free survival and overall survival. Nimotuzimab had better TWIST score of 653+238vs 508+173 (Mean+ SD) days and better overall QOL score improvement 4.6+1.5 vs 3.1+1.3 points(Mean+ SD)compared to the cisplatin arm

Conclusions: The results indicate that, though more expensive, the Nimotuzumab scores over the conventional cisplatin (weekly) in terms of better response rates, Quality of life TWIST score and ease of administration. However retrospective nature of the data and the subject selection bias remain a major challenge for this study, which can be addressed in future prospective trials.

Keywords: concurrent, nimotuzumab, chemotherapy , head and neck cancers

Introduction:

Head and neck cancers are a significant problem in our country constituting approximately one-third of all cancer cases in contrast to 4–5% in the developed world. Surprisingly we still follow western guidelines in the management of these

cancers.[1,2] However the recent efforts of researchers like Tuljapurkar et al., who compiled Indian studies made an impact and paved path for Indian guidelines changing the practice and challenged dogma in the management of head and

neck cancers in the last decade, though none of them could reach level I/II evidence.[3]

The unique difference of Indian data vs global is that

1. Majority of cancers present as locally advanced Stage III/IV disease
2. The field of Radiation is larger
3. Response rates are inferior
4. More cases of tobacco induced malignancy.

These things warrant exploration of the newer adjunct modalities or improvising the existing ones [4] Though NCCN and other bodies still recommend the cisplatin as the first choice in recent time we started seeing few of the EGFR inhibitors coming and occupying the list, in various indication in view of the better Overall and cancer specific survival as well as better Quality of life. [5,6,7] The same may not be applicable directly in developing nations in view of the economic constraints. However as there are few economic options like “Indian version of EGF- Mab- Nimotuzumab”, we thought of analyzing the data on the same in retrospective manner to see the response and quality of life parameter (done as a part of validation of QOL questionnaire. The choice of Nimotuzumab is due to its Bivalent binding to EGFR, (a more tumour specific action) and proven safety. There is some data on the Efficacy is proven when added to chemoradiotherapy / radiotherapy. [8] The results of this study were shared in the ESMO meeting Singapore (poster) and were published in short format [9].

Methods

This is a multi institutional, two arm retrospective data collection exercise done in subjects with head and neck cancer stage III or less receiving radical radiotherapy(IMRT) with either nimotuzumab or chemotherapy (weekly cisplatin) between 2015-2018 with three years follow up. Standard format for the QOL (a part of dissertation thesis by PG) was used for analysis along with demographics and outcome in terms of clinical data and survival.

Patients received nimotuzumab 200 mg or chemotherapy (weekly cisplatin 40 mg /m²) along with Radiotherapy (IMRT).

Mean with Standard deviation was used to compare the both arms with P value represented for significance. We used Medcal version 7.0 for the statistical analysis.

The records were selected if they meet the following eligibility criteria

Key Eligibility criteria- for record selection

1. Histological proven squamous cell carcinoma of the head and neck regions
2. PS 2 or below
3. Stage III B or less at the time of initial diagnosis
4. Patients must have at least one measurable lesion as per the (RECIST) criteria and have follow-up scans done
5. Adequate Marrow, hepatic and renal functions
6. Must have completed a minimum 80% of planned therapy
7. Patients should not have had any contraindications for the therapy
8. Availability of all clinical, pathological, and QOL- related details

Results

During the study period a total of 84 subjects were meeting the criteria for the study and the case records were retrieved with 1:1 case/control (matched population) for stage, age and other variables. Response rate was higher in the Nimotuzumab arm (86% versus 81%; P=NS). No differences were observed in median progression-free survival and overall survival. Nimotuzumab had better TWIST score of 653+238 vs 508+173 (Mean+ SD) days and better overall QOL score improvement 4.6+1.5 vs 3.1+1.3 points (Mean+ SD) compared to the cisplatin arm

The details of the same were described in table-1. The selection of case records was depicted in the figure 1

Table 1: Demographics, response rates and QOL of the two arms

Character	Nimotuzumab+RT	Csiplatin+RT	P value
Number of subjects	42	42	NS
Age (Median+SD)	34.6+12.6	38.2+11.8	NS
Male:Female	29:13	28:14	NS
Major adverse events			
Neutropenia	26(62%)	31(73%)	NS
Nausea/Vomiting	31(73%)	38(90%)	NS
Rash	12(29%)	1(2%)	0.01
Mucositis	27(64%)	29(69%)	NS
Response to therapy			
Stable disease	6 (14%)	8 (19%)	NS
Complete response	18 (43%)	12 (29%)	0.05
Partial response	12 (29%)	14 (33%)	NS
Progressive disease	6 (14%)	8 (19%)	NS
Survival			
Survival	32.4+6.9	26.6+5.6	0.04
Quality of life parameters			
QOL change	4.6+1.5	3.1+1.3	0.03
TWISTT (in days)	653+238	508+173	0.03

Figure 1: Distribution of cases among the arms and method of selection

Discussion

A clear and significant observation made in this study is the significant betterment of Quality of life and lesser side effects with higher response rates (though statistically non significant) in the nimotuzumab arm in association with chemoradiation. The response rates are much higher in bulky disease compared to the cisplatin arm, which makes this more attractive option.

We also observed lesser frequency and intensity of the adverse reactions in the nimotuzumab arm compared to the cisplatin arm. The results indicate that, though more expensive, the Nimotuzumab scores over the conventional cisplatin (weekly) in terms of better response rates, Quality of life TWIST score and ease of administration for patients with HNSCC receiving definitive Radiotherapy and had better QOL and TWIST.

While Small sample size, Single institution study, Non randomized design and Retrospective analysis are major limitations of this study, the significant p value is a point to be noted in terms of response rates and quality of life.

A prospective study was planned and submitted to the local ethics committee based on above results to validate these results. If the trends are proven, this could be a choice with patients having borderline renal function and poor performance status.

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