

## Efficacy of Cisplatin with Nimotuzumab for Locally Advanced Head and Neck Cancer, A Single Institution Study

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### ABSTRACT:

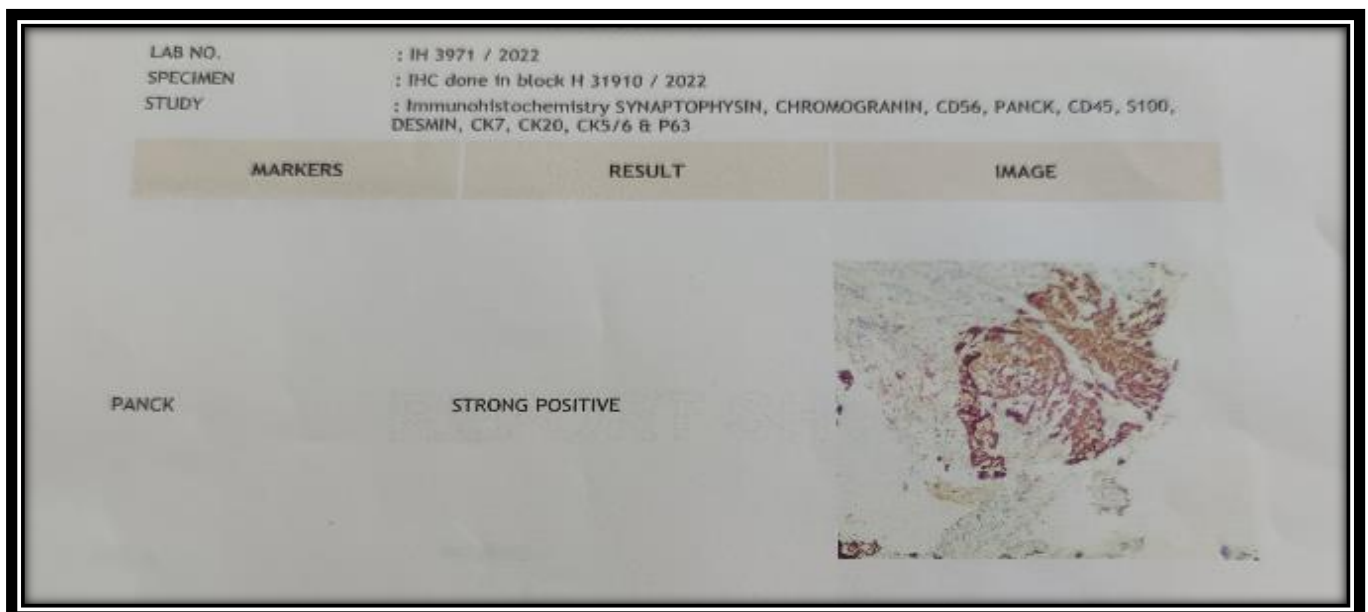
Locally advanced head and neck squamous cell carcinoma (LAHNSCC) is approached with a multimodality therapy. Radical chemoradiation is the nonsurgical approach of choice and is associated with improved survival and better organ-preservation rates compared with radical radiation. Most head and neck cancers, express epidermal growth factor and are associated with an inadequate response to radiotherapy and chemotherapy. Anti-epidermal growth factor receptor (EGFR) monoclonal antibodies (mAb) increases response rates and survival when combined with radiotherapy or chemoradiotherapy. This case report presents a study of the combined effect of Nimotuzumab with chemoradiation on a locally advanced cancer of tonsil.

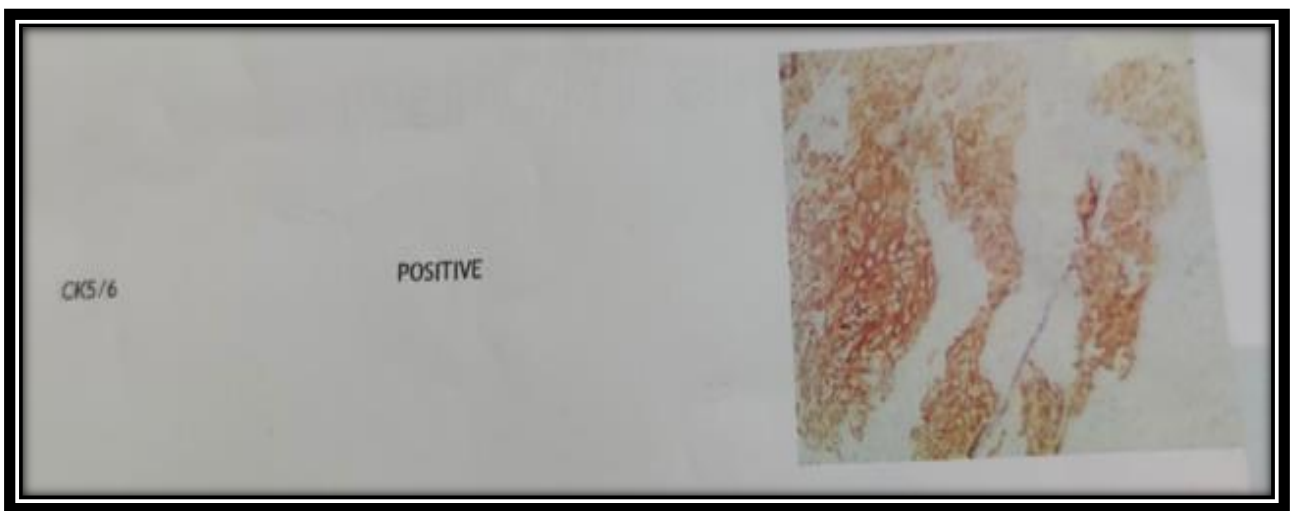
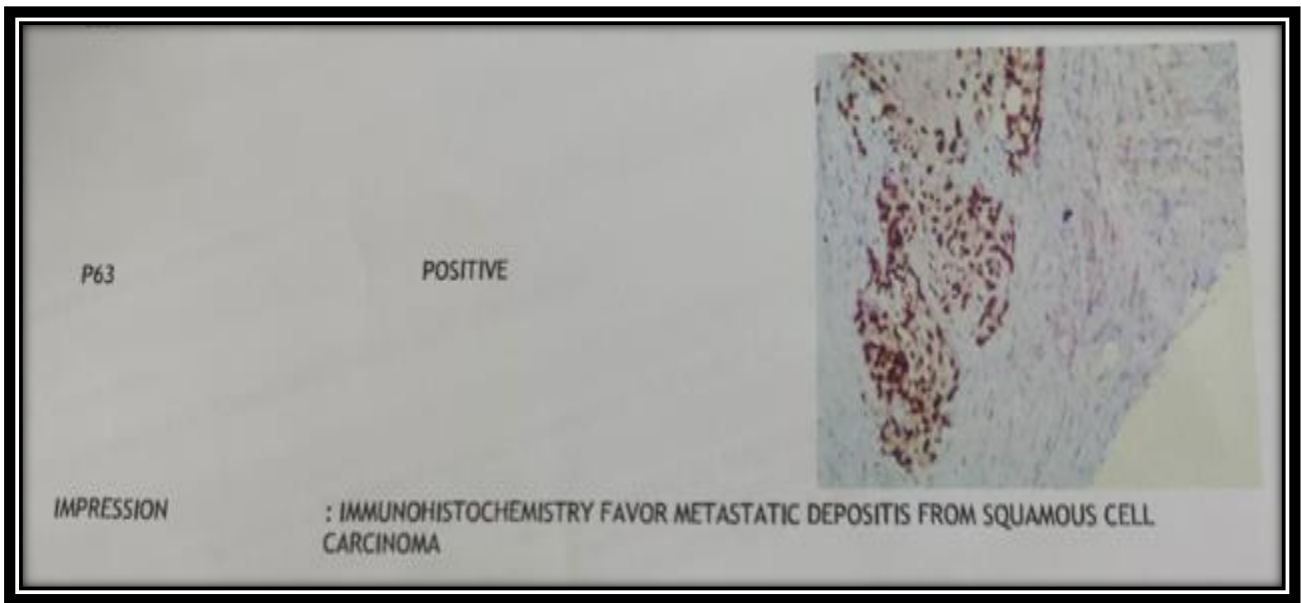
**Keywords:** Cisplatin, Nimotuzumab, Head and Neck Cancer

### CASE PRESENTATION:

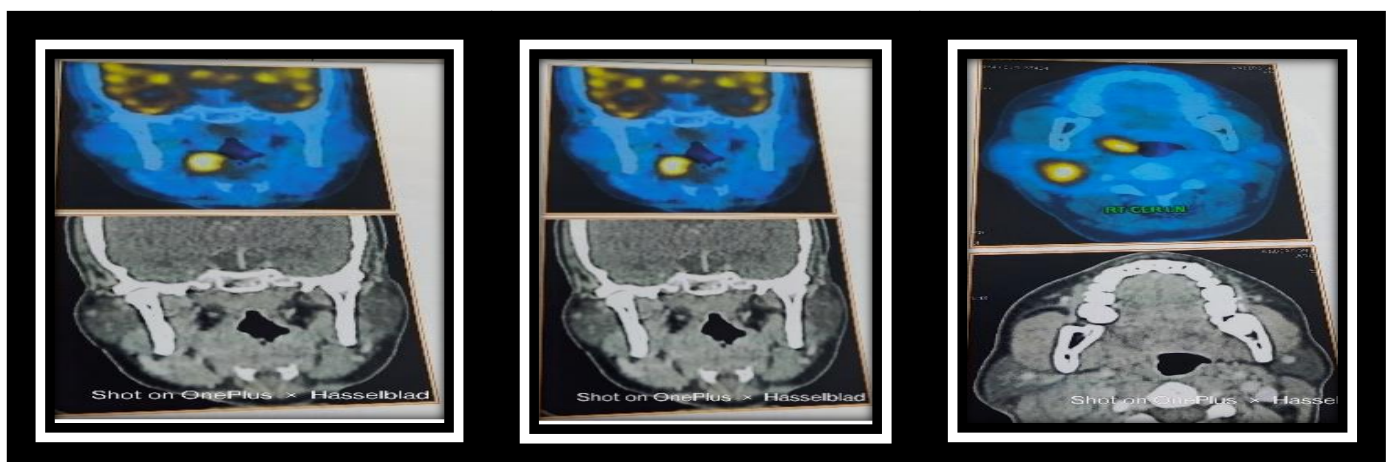
A 56 yr old female patient was evaluated for complaints of odynophagia and radiating pain to the right ear since 4 months. She does not give any history of voice change, difficulty in mouth opening, tinnitus, giddiness. Symptoms like fever, weightloss were ruled out in view of lymphoma. On examination, there was a growth in the right tonsil, approximately 2x2 cms in size, involving anterior and posterior tonsillar pillars

and extending to base of tongue. There was also a Right Level II neck node, mobile, firm in consistency, measuring 4cm. Ultrasound guided biopsy from the lymphnode reported as poorly differentiated tumor. It was followed up with Immunohistochemistry which reported it as metastatic deposits from scc, P63-positive, CK5/6-positive, PANCK-positive, whereas it was negative for synaptophysin, CHROMOGRANIN, CD56, S100, desmin, CK7, CK20, CK5/6 & P63.





PET CT fusion showed an FDG avid ill defined heterogenosly enhancing soft tissue lesion measuring 2.5x2.5x2.3cm in right tonsillar fossa ( SUV-10.6).Anteriorly the lesion was abutting base of tongue with indistinct fat plane, Inferiorly- extending upto lingual tonsils with no evidence of midline extension. FDG avid prominent and enlarged right level II,III,IV cervical nodes , largest right level II measuring 2.4x2cm ( SUV 10.5), node is seen compressing right IJV.



Following investigations, she was diagnosed as Carcinoma right tonsil- TNM stage: T2N2bMo.

After discussion with the tumor board, she was taken up for definitive chemoradiation with radical radiation

and weekly Cisplatin with Nimotuzumab. She was planned for 50.4Gy in 28fractions along with 30mg/m<sup>2</sup>

Cisplatin and 200mg/m<sup>2</sup> Nimotuzumab. Patient was Immobilized with a thermoplastic mask on headrest - B on an indexed carbon fibre flat table top and simulated with Siemens Somatom . Go. Now which is a 16 slice CT machine with a 70 cm bore. Slice thickness of 3 mm was acquired from vertex to T6 without contrast in view of serum creatinine being 1.2. MRI was done maintaining the same chin to notch distance as in CT simulation and T1weighted, T2 weighted, FLAIR sequences were acquired.

**TARGET VOLUME DELINEATION:**

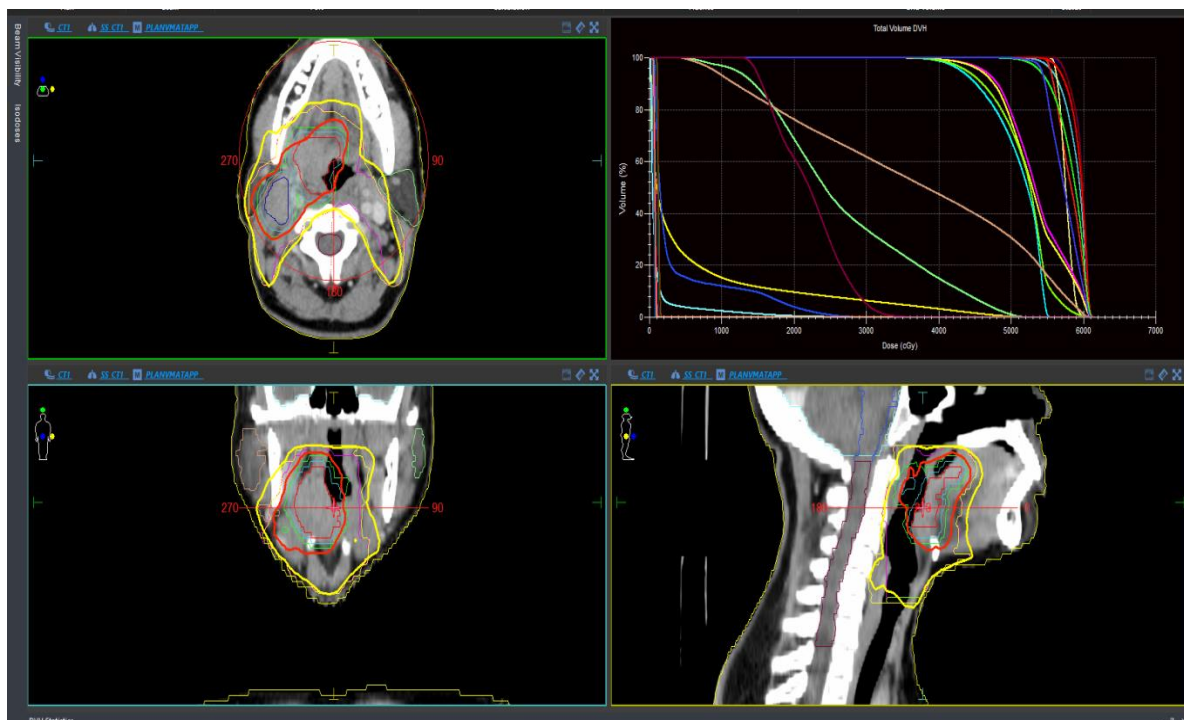
The gross tumor volume was delineated based on clinical and imaging findings. Keeping in mind the subclinical disease, a margin of 0.5 cm for clinical target volume was decided upon which also included the Bilateral level I to Level V neck nodes. With the help of image guidance, to account for set up error, a margin of 0.5cm was created to the planning target volume.

**Planning:**

Planning was done in Monaco treatment planning system version 5.51.1 using VMAT technique in a sequential manner. In Phase 1 of the treatment plan, we treated upto 28 fractions using 360° full arc, 6MV photons. Gross tumor volume received 56Gy at the rate of 2 Gy per fraction And Planning target volume received 50.4Gy at 1.8 GY per fraction. Patient was assessed After 28 # RT and 4 cycles of Cisplatin with nimotuzumab, with a CT scan and was observed to have shrinkage of tumor with good response. She was decided to be boosted with 10Gy in 5 # to GTV. Phase 2: partial arc of 190° from gantry angle 40 to 210 in a counterclockwise direction. Plans were evaluated such that the 95% of target volumes were covered with 95% of prescribed isodose values. Brain, brainstem, eye apparatus, spinal cord were taken as organ at risks and their constraints were achieved.

**DOSE CONSTRAINTS TO ORGANS AT RISK:**

OAD	MAX DOSE ( cGY)	MEAN DOSE ( cGY)	
LEFT EYE	134	77.0	
RIGHT EYE	114.8	66.6	
RIGHT LENS	86.1	71.1	
LEFT LENS	90.2	79.6	
RIGHT OPTIC NERVE	126.8	87.2	
LEFT OPTIC NERVE	134.1	94.2	
OPTIC CHIASMA	58.8	131.5	
PITUITARY	185.5	145.3	
SPINAL CORD	4304.0	2561.4	
RIGHT PAROTID	7113.8	4374.1	
LEFT PAROTID	5603.0	2856.5	
BRAINSTEM	3535.9	424.8	



Patient had grade 3 dysphagia after 5 cycles nimotuzumab and 20 fractions of RT. She received symptomatic treatment and radiation was interrupted for 5 days. After seeing the improvement in general condition, treatment was resumed. The entire treatment was completed in 45 days.

### **Outcome:**

MRI head and neck was done after 1 month which reported mild thickening with enhancement in the right tonsillar fossa, right lateral pharyngeal wall extending upto right aryepiglottic fold with no evidence of residual disease

### **DISCUSSION:**

In locally advanced oropharyngeal cancers, concurrent chemoradiation is used primarily for management as The anatomical location along with multiple physiological functions associated with this structure makes open surgical resection a difficult and moribund procedure.<sup>1</sup> The prognosis of these tumors is heavily dependent on the Human Papilloma Virus (HPV) status. Patients with HPV positive disease have a favorable prognosis as opposed to HPV negative disease. The incidence of HPV positive disease is variable across the globe with the incidence in North America in the range of 48–81.4% and 15–22.8% in the Indian subcontinent.<sup>2</sup> Several large clinical trials have shown the effectiveness of anti-EGFR mAb in combination with radiotherapy or standard CRT. According to Bonner et al., cetuximab in combination with radiotherapy increased median OS from 29.3 to 49 months, decreased mortality rate by 27% ( $p = 0.018$ ), total five-year survival from 36.4% to 45.6%, median PFS from 12.4 months to 17.1 months ( $p = 0.006$ ); PFS at two years increased from 37% to 46%.<sup>3</sup>

Rodriguez et al., when incorporating mAb nimotuzumab into radiotherapy, also found similar results with OS (mean and median) in the antibody nimotuzumab plus CRT group at 21.71 and 12.5 months versus placebo at 17.71 and 9.47 months. Ramakrishnan et al. conducted a study among 40 patients treated with CRT with or without nimotuzumab, and they reported 34 cases had partial or complete response accounting for 85%, with complete response in 32 cases accounting for 80% of the cohort.<sup>4</sup> In a study conducted by Huo et al, tumor response rate in nimotuzumab plus CRT group and CRT alone arm was 90.6% and 70.4%, respectively; the difference was statistically significant ( $p = 0.029$ ). The lymph node response rate and general response rate were higher in the nimotuzumab plus CRT group compared with the CRT group, but the difference was not statistically significant. The improvement in PFS with the addition of nimotuzumab is largely contributed by an improvement in locoregional control

**IN Our study:** patient received 66Gy in 33 fractions radiation along with 6 cycles of nimotuzumab (200mg/m<sup>2</sup> with cisplatin 30mg/m<sup>2</sup>. Post 28#RT, and 4 cycle of chemotherapy, a reassessment CT scan was taken and was noted that the gross tumor now measured 1.85x 1.56cm ( in contrast to the initial tumor size on CT measuring 2.77x2.05cm), the gross node had near complete shrinkage insize in comparison to the upfront 2.33x 1.66 cm size on CT scan. we decided to boost primary to another 10 Gy, and she completed the total treatment with within 45days. There have been studies and observations made that The cumulative cisplatin dose correlates with the overall survival outcome. Cisplatin at 100 mg/m<sup>2</sup> every 3 weeks for two to three doses comes out

to 200 to 300 mg/m<sup>2</sup>, and cisplatin at 40 mg/m<sup>2</sup> weekly for 6 to 7 weeks equals a total dose of 240 to 280 mg/m<sup>2</sup>. And in this study, at 30 mg/m<sup>2</sup>, we're dosing below that at 180 to 210 mg/m<sup>2</sup>. However, 200 mg/m<sup>2</sup> is considered an adequate dose of cisplatin

**Limitations:**

**Single institution study, Short duration of follow up, HPV as a prognostic factor was not tested**

**CONCLUSION:**

Addition of Nimotuzumab to the standard practice of chemoradiation can be considered for local good response in case of advanced cancer of tonsil.

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