2024 ASCO® ANNUAL MEETING

Long term results of a randomized phase III study of nimotuzumab in combination with concurrent radiotherapy and cisplatin versus radiotherapy and cisplatin alone, in locally advanced squamous cell carcinoma of the head and neck.

Professor Vijay Maruti Patil
On behalf of Department of Medical Oncology
Head and Neck DMG
Tata Memorial Centre, Mumbai

Background

- Addition of nimotuzumab to weekly cisplatin as radiosensitizer (CTRT) had improved progression free survival(PFS) in a phase 3 study in locally advanced head and neck squamous cell carcinoma (LAHNSCC). [1]
- Whether it leads to an improvement in long term OS is unknown.

- This analysis was performed to evaluate the 10-year OS and late term adverse events of the addition of nimotuzumab to CTRT in LAHNSCC.

1. Patil VM, Noronha V, Joshi A, et al. A randomized phase 3 trial comparing nimotuzumab plus cisplatin chemoradiotherapy versus cisplatin chemoradiotherapy alone in locally advanced head and neck cancer. *Cancer*. 2019;125(18):3184-3197. doi:10.1002/cncr.32179

Trial Design

ELIGIBILITY CRITERIA

- Age ≥ 18 years
- SCC of oral cavity/ oropharynx/ hypopharynx/ larynx
- Stage III / IV, no distant metastasis
- Definitive CRT
- Adequate organ function

Stratify

- T-group (T0,1,2 vs T3,4)
- N-group (N0,1 vs N2,3)
- Site (Oropharynx versus non oropharynx)
- Technique of radiation (conventional versus others)

Randomized 1:1 Open Label

n=268

Nimotuzumab (200mg) -weekly cisplatin 30mg/m² with of RT (NCRT)

RT: 70 Gy/35# /-7 weeks

n=268

Weekly cisplatin 30mg/m² with RT (CRT)

Primary endpoint: 10-year overall survival
Key secondary endpoint: Late adverse events

PRESENTED BY: Professor Vijay M Patil

Consort Diagram

Enrollment

Assessed for eligibility (n=754)

Excluded (n= 218)
- ¨ Not meeting inclusion criteria (n= 143)
- ¨ Participating in another trial (n= 57)
- ¨ Declined to participate (n= 18)
- ¨ Other reasons (n= 0)

Randomized (n= 536)

Allocation

Allocated to chemoradiation arm (n=268)
- ¨ Received cisplatin based chemoradiation (n= 266)
- ¨ Did not receive cisplatin based chemoradiation (n=2)
- •Patient defaulted (n=1)
- •Received carboplatin instead of cisplatin (n=1)

Allocated to nimotuzumab-chemoradiation arm (n=268)
- ¨ Received nimotuzumab- chemoradiation (n=266)
- ¨ Did not receive nimotuzumab chemoradiation (n=2)
- •Patient defaulted (n=1)
- •Patient received NACT followed by cisplatin –radiation alone (n=1)

Therapy

- Completed chemoradiation: (n=252)
  - Did not complete chemoradiation (n=16)
  - Did not start chemoradiation (n=1)
  - Defaulted during chemoradiation (n=9)
  - Disease progression during chemoradiation (n=2)
  - Therapy stopped because of toxicity (n=2)
  - Others (n=2)

- Completed nimotuzumab- chemoradiation: (n=250)
  - Did not complete nimotuzumab-chemoradiation (n=18)
  - Did not start nimotuzumab-chemoradiation (n=1)
  - Defaulted during nimotuzumab-chemoradiation (n=7)
  - Disease progression during chemoradiation (n=2)
  - Therapy stopped because of toxicity (n=6)
  - Others (n=1)
  - Neurosis-Mania (n=1)

Analysis

Analysed for outcome measures (n=268)
Analysed for safety measures (n=267)

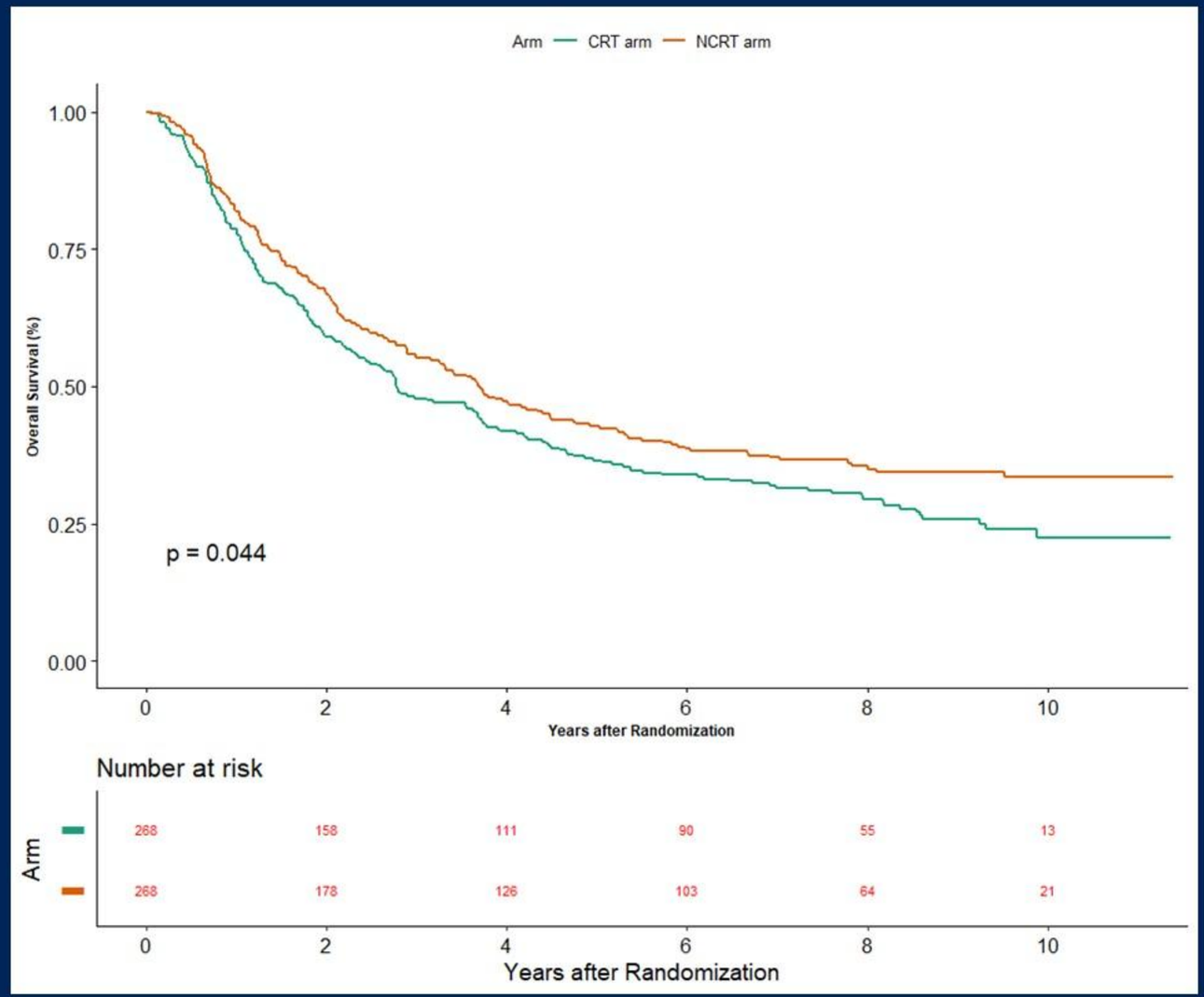
Analysed for outcome measures (n=268)
Analysed for safety measures (n=267)

Baseline characteristics

Variable	Cisplatin - Radiotherapy arm	Nimotuzumab-cisplatin - Radiotherapy arm	P value
Median age	54.00 (26-77 years)	55.00 (20-73 years)	0.636
ECOG PS 0-1 ECOG PS 2	267 (99.6%) 1 (0.4%)	267 (99.6%) 1 (0.4%)	1
Oropharynx Hypopharynx Larynx Oral cavity	135 (50.4) 47 (17.5) 83 (31) 3 (1.1)	134 (50) 62 (23.1) 72 (26.9) 0 (0)	0.119
T0-T2 T3-T4	56 (20.9%) 212 (79.1%)	41 (15.3%) 227 (84.7%)	0.113
N0-N1 N2-N3	131 (48.9%) 137 (51.1%)	122 (45.5%) 146 (54.5%)	0.488
Stage III Stage IVA Stage IV B	87 (32.5%) 172 (64.2%) 9 (3.4%)	80 (29.9%) 177 (66.0%) 11 (4.1%)	0.753
HPV positive **HPV negative** **HPV equivocal**	14 (10.4) 91 (67.4) --	10 (7.5) 96 (71.6) 1 (0.7)	.517

OS (overall)

- The median OS was 2.78 years (95% CI 2.31-3.69) versus 3.69 years (95% CI 2.90-4.49) in the CRT and NCRT arm respectively (P value by log rank test=0.04).
- The 10 year OS was 22.5% (95% CI 16.7-28.8) versus 33.5% (95% CI 27.6-39.4) in the CRT and NCRT arm respectively (Hazard ratio=0.811; 95%CI 0.664-0.995, P=0.044).



Adverse events

Variable	Cisplatin - Radiotherapy arm		Nimotuzumab-cisplatin - Radiotherapy arm		P value
	All Grades	Grade 2 and above	All Grades	Grade 2 and above	Grade 2 and above
Shoulder	191 (100%)	184 (96.3%)	191 (100%)	184 (97.4%)	0.771
Xerostomia	185 (96.9%)	137 (71.7%)	178 (94.2%)	122 (64.6%)	0.152
Pigmentation	176 (92.1%)	29 (15.2%)	170 (89.9%)	32 (16.9%)	0.677
Skin thickening	180 (94.2%)	102 (53.4%)	174 (92.1%)	101 (53.4%)	1.000
Dysphagia	78 (40.8%)	18 (9.4%)	76 (40.2%)	25 (13.2%)	0.260
Dysgeusia	150 (78.5%)	53 (27.7%)	139 (73.5%)	47(24.9%)	0.561
Hypothyroidism	78 (40.8%)	38 (19.9%)	84 (44.4%)	47 (24.9%)	0.269
Hypercholesterolemia	47 (24.6%)	0 (0%)	40 (21.2%)	1 (0.5%)	0.497
Hearing loss	28 (14.7%)	17 (8.9%)	23 (12.2%)	12 (6.3%)	0.440
Increased creatinine	11 (5.8%)	3 (1.6%)	6 (3.2%)	1 (0.5%)	0.623

Conclusion

- Addition of nimotuzumab to weekly cisplatin leads to improvement in long term overall survival in locally advanced HNSCC without any additional increase in late-term adverse events.
- These results are largely applicable in HPV negative patients.

Acknowledgements

Patients and their families

Statistics & Randomization
Sadhana Kannan
Kumar Prabhash
Atanu Bhattacharjee

Funding: Biocon ltd & TRAC

Head and Neck DMG

Thank you