

***BEST TRIAL – 2009 AACR Annual Meeting  
Phase II Head and Neck Study – Abstract 3567***

**An open-label, randomized, multicentric study, to assess the safety and efficacy of nimotuzumab (h-R3) monoclonal antibody against EGF-receptor in combination with chemo-radiation therapy or radiation therapy alone in patients with advanced (stage III or IVA) head and neck cancer**

*Krishnamurthy Bayyagari Reddy, Viswanath Lokesh, Vidyasagar M. S Sr., Koteshwar Rao, Ashok Shenoy, Naveen Thimmaiah, Govinda Babu, Nanjundappa Dr, Bindhu Joseph, Ravikiran Bonnathiya, Bapsy P. P. Kidwai Memorial Institute Of Oncology, Bangalore, India, Shirdi Sai Baba Cancer Hospita, Manipal, India, KMC Hospital, Mangalore, India*

**Introduction:** Radiation therapy for inoperable loco-regionally advanced Squamous Head & Neck cancers (SCCHN) has a poor outcome. Extracellular domain of EGF-Receptor (EGF-R) has emerged as a potential oncotherapeutic target. h-R3 mAb (BIOMAb/nimotuzumab/TheraCIM) a humanized monoclonal Antibody (mAb) against the EGF-R retains its murine effectiveness with decreased immunoreactivity and HAMA response.

**Rationale for the Study:** Biological response modifiers (mAb) which enhance radiation and chemotherapy responses might improve the therapeutic outcome.

**Objective of the Study:** to investigate the safety and efficacy of h-R3 mAb against EGF-R in SCCHN along with Chemo-Radiation therapy.

**Material and Methods:** Patients with SCCHN, Stage III or IVA, MRImaging, 18 - 70 yrs, were Group A : Radical Radiation therapy & Group B: Chemo-Radiation therapy. Randomization in the respective arms : Group A: [RT alone arm] v/s [RT + h-R3 mAb] and Group B: [RT + CT] v/s [RT+CT+ h-R3 mAb]. Protocol: Standard Radiotherapy:TD: 6600cGy, 200cGy/Fraction,5 Fr/week,6-6.5wks,2D plan. Radiation sensitizer (chemotherapy): weekly: CDDP:50mgIV/week,For 6 wks. Study Drug (h-R3 mAb):weekly,200mg,60min infusion For 6 weeks.

**Results:** The Study initiated Sept 2004 and subjects followed-up for 2 ½ years (30 months) after end of radiotherapy; 113 subjects screened, 92 patients enrolled and randomized. 76 subjects were evaluable – 36 in Group A and 40 in Group B: (Chemo-Radiation therapy in which 86.96% patients had TNM Stage IV disease). 2 ½ year (30mths) after the End of Radiotherapy the Loco-regional control was: Complete response (CR): Group B: CT+RT+hR3 - 19 (95%) v/s CT+RT- 7(35%), Group A: RT alone - 5 (29.4%) v/s RT+hR3 - 8 (42.1%). Overall Survival : CT+RT+hR3 - NA\* v/s CT+RT- 21.96 mths (Hazard ratio-0.337, P value 0.0018) and RT alone - 25.02 v/s RT+hR3 - NA\* (Hazard ratio-0.678, P value 0.3923). Disease Free Survival : CT+RT+hR3 - NA\* v/s CT+RT- 21.30 mths (Hazard ratio-0.344, P value 0.0052) and RT alone - 25.02 v/s RT+hR3 - NA\* (Hazard ratio-0.599, P value 0.3148). (\*Median is yet to be reached). h-R3 mAb is well tolerated and occasional mild Grade 1 reactions seen, mucositis and skin reaction due to h-R3 were not seen or enhanced.

**Conclusion:** This study demonstrates that hR3 mAb is safe and efficacious for administration along with Radiation therapy or with Chemo-Radiation therapy. The enhanced locoregional control & survival advantage seen with hR3 mAb along with chemoradiation therapy adds to the currently available proof to the principle that adding biological agents to a physically targeted modality improves long term therapeutic outcome in SCCHN.