Background: To examine the efficacy and toxicity of RAD001 when used as a treatment in patients with progressing unresectable adenoid cystic carcinoma.

Methods: Patients with histologically confirmed adenoid cystic carcinoma, with at least one measurable lesion were eligible for the study. Other eligibility criteria included: documented disease progression following RECIST criteria within 12 months prior to the entry, not amenable to curative-intent treatment, ECOG PS 0 or 1, and adequate organ function. RAD001 was given at a dose of 10 mg daily every 4 weeks. Response was assessed according to RECIST (v 1.0) every 8 weeks. Primary endpoint was 4-month progression-free survival rate (PFSR) and 25% increase from baseline SUVmax). Hypothesis was that 4-month PFSR rate would be improved from 50% to 65%.

Results: A total of 34 patients were enrolled. Thirty-one patients were evaluable for response. Partial response was not achieved. Twenty-seven patients (80%) had stable disease and 4 patients (12.9%) showed disease progression. Overall disease control rate was 87.1%. Fifteen patients (87.1%) had stable disease and 4 patients (12.9%) showed early PR metabolic response (>25% increase from baseline SUVmax). Nine patients showed SD metabolic response and one patient showed PD metabolic response (SUVmax). Four patients (12.9%) showed SD on RECIST criteria. Among them, 8 patients post-treatment (after 8 weeks) PET was available in 18 patients. All these patients (48.4%) showed tumour shrinkage within SD. Pre-treatment and post-treatment (after 8 weeks) PET was available in 18 patients. All these 18 patients showed SD on RECIST criteria. Among them, 8 patients showed early PR metabolic response (>25% reduction from baseline SUVmax) and 9 patients showed SD metabolic response and one patient showed PD metabolic response (>25% increase from baseline SUVmax). The PFS was 11.7 months (95% CI, 8.1–15.2 months) and 4-month PFSR was 65%. Mean treatment duration was 6.4 months (range 0.4–23.2 months). The most common AEs (all grades) were: stomatitis (82%), anaemia (67%), asthenia (36%), leucopenia (33%). The major Gr 3/4 toxicities were: asthenia (6%), infection (6%), leucopenia (3%). Dose adjustment was done in 8 patients (24%).

Conclusions: RAD001 showed promising efficacy and good tolerability in unresectable adenoid cystic carcinoma.

Actuarial 5-year univariate analysis showed that the heavy smoking patients had a significant reduced probability of loco-regional control (45% vs 65%, p = 0.002), disease-specific (56% vs 78%, p = 0.002) and overall survival (39% vs 66%, p = 0.0003) compared to non-smoking patients. In a multivariate analyses stratifying by site, the independent prognostic factors were found to be heavy smoking, T and N classification, age and gender, however moderate smoking did not influence the outcome after radiotherapy.

Conclusion: The effect of smoking on radiotherapy outcome in head and neck cancer patients can be explained by a reduced tumour oxygen supply caused by the increased carboxy hemoglobin concentration. The data strongly advocate that smoking should be avoided in order to improve the therapeutic efficacy of radiotherapy.

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