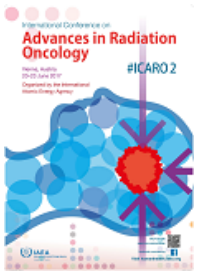

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Skin reaction to cetuksimab (CMb) as a criterion for treatment selection in patients with locally advanced squamous cell carcinoma of the head and neck (LASCCHN): results of prospective study

Friday, 23 June 2017 11:30 (10 minutes)

Introduction of the study: In LASCCHN, a combination of radiotherapy (RT) and CMb: (1) significantly improves overall survival rate compared with RT alone; (2) CMb-treated patients with a prominent CMb-induced rash survived significantly better than patients with no or grade 1 rash, who experience no survival advantage compared to irradiated only patients. Comparing the benefits of concomitant immunoradiotherapy and chemoradiotherapy with RT alone, the outcome in CMb-treated patients with a skin rash of grade 2-4 (hazard ratio [HR] 0.49; Bonner et al, Lancet oncol 2010.) seems more favorable than in cisplatin (CP)-treated patients (HR 0.74; Pignon et al, Radiother Oncol 2009).

The aim of the present single-institution non-randomized prospective phase II study was to test the hypothesis that early assessment of a CMb-induced skin rash can be used for treatment stratification of patients with LASCCHN: in patients who would develop a grade 2-4 skin rash after concomitant CMb administration, the treatment results will be improved compared with RT-CP combination. In patients without a prominent skin rash no beneficial effect of CMb is expected and concomitant chemoradiotherapy with CP should be more effective.

Methodology: Patients with LASCC (stages III-IVB) of the oral cavity, oro- hypopharynx or larynx and WHO PS 0-2 were considered eligible. In the week before RT, all patients received a loading dose of CMb (400 mg/m2). During the first week of RT, a combination of CMb (250 mg/m2) and CP (30 mg/m2) was concurrently administered. At the end of the second week of RT, a multidisciplinary assessment of the skin rash was done: CTCAE v3.0 grade 0-1 –patients proceeded with chemoradiotherapy with CP (arm A); CTCAE v3.0 grade 2-4 –patients proceeded with immunoradiotherapy with CMb (arm B). Concomitant boost IMRT was used in all patients (56-63-70 Gy/35 fractions). The planned number of patients in the study: 120 (recruited over 3 years). The primary objective: the radiological complete response (CR) rate at 12-14 weeks post-therapy. Secondary objectives: locoregional control (LRC), progression-free survival (PFS) and overall survival (OS) at 2 years after therapy, acute and late toxicity.

Results: Between 12/2011 and 7/2013, 39 patients (males 87%; median age 57 years, range 42-75) entered the study which was prematurely terminated due to an unexpectedly high number of CTCAE v3.0 grade 3/4 allergic reactions to CMb. There were 31 active smokers; sites of origin were the oropharynx 30 (p16/HPV positive 8, status unknown 4), hypopharynx 5, oral cavity 2, and larynx 2. The majority (89.7%) of tumors were of TNM stage IV (T4 53.8%, N2b-3 71.8%). The RT dose was 70 Gy in all patients. During administration of the CMb loading dose, an allergic reaction of CTCAE v3.0 grade 3/4 developed in 11 patients (28.2%) who proceeded with chemoradiotherapy with CP (4-8 cycles, median 6); at 12-14 weeks post-therapy, a locoregionally CR was determined in 6 patients (54.5%). A grade 0-1 skin rash was recorded in 10 patients (35.7%) who continued with RT-CP (6-8 cycles, median 7); 8 patients (80%) from this group had a CR. A grade 2-4 skin rash was recorded in 18 patients (64.3%) who proceeded with RT-CMb (3-8 cycles, median 7) and 10 of them (55.6%) were complete responders. The difference in CR rates between the three groups was not significant. No differences in distribution of the primary tumor sites, T- and N-stage, or HPV status were found between the two arms or those with allergic reaction to CMb.

The median follow-up time was 39 months (range, 26-49). Actuarial survival rates at 2 years in patients treated

with chemoradiotherapy (arm A and patients allergic to CMb, N=21) and those treated with immunoradiotherapy (N=18) were as follows: LRC 38% (95% confidence interval [CI], 17-58) vs. 39% (95% CI, 16-61), P>0.05; PFS 35% (95% CI, 14-56) vs. 39% (95% CI, 16-61), p>0.05; and OS 52% (95% CI, 31-74) vs. 44% (95% CI, 21-67), p>0.05. Acute toxicity was assessed separately for patients who received concomitantly with RT either CP or CMb. Evaluation of late toxicity was done only in patients who survived 6+ months post-therapy and had no residual or recurrent disease above the clavicles (Table).
Conclusion: CMb administration resulted in an unexpectedly high rate (28.2%) of grade 3/4 allergic reactions. A prominent CMb-induced skin rash developed in two thirds of the patients. Immunoradiotherapy in these patients did not result in a survival advantage over chemoradiotherapy with CP but increased acute toxicity.

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