926P Real-world data in the era of immune checkpoint inhibitors (ICIs): Cetuximab-containing first-line therapy in patients with recurrent and/or metastatic head and neck squamous cell carcinoma

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Background: Immune checkpoint inhibitors (ICIs) have been shown to improve treatment efficacy in patients with recurrent and/or metastatic head and neck squamous cell carcinoma (RM HNSCC). We assessed the clinical outcomes, treatment patterns, and prognostic factors in real-word practice after ICI therapies for RM HNSCC patients receiving first-line cetuximab plus chemotherapy.

Methods: This retrospective observational study was conducted at two tertiary medical centres in Taiwan. Patients with RM HNSCC who received cetuximab plus chemotherapy as first-line therapy were included between January 2017 and July 2019. The study endpoints were response rates, progression-free survival (PFS), and overall survival (OS). Univariable and multivariable analyses of prognostic factors were estimated using the Cox proportional hazards model.

Results: We identified 290 patients treated with first-line cetuximab and chemotherapy. Median OS was 9.1 months (95% confidence interval [CI] 8.2 to 10.4), whereas the median PFS was 5.0 months (95% CI 4.3 to 5.7). In patients with platinum resistance, the median OS was 10.4 months (95% CI 8.1-13.3) with ICIs versus 6.3 months (95% CI 5.1-7.6) without ICIs ($P<0.01$). In patients with platinum-sensitivity, the median OS was 20.6 months (95% CI 11.3-22.6) with ICIs versus 9.1 months without ICs (95% CI, 7.9-10.9)($P<0.01$); OS benefit with ICIs was similar in patients who received ICIs after progression on cetuximab and patients who received cetuximab in combination with ICIs. On multivariable analysis, independent favourable prognostic factors for OS were platinum-sensitivity, better objective response to cetuximab and ICIs.

Conclusions: ICIs appeared to improve OS, even in platinum-resistant populations, which supports the use of these agents in patients with RM HNSCC who were treated with cetuximab plus chemotherapy as first-line therapy. The reduction in risk of death with ICIs was similar for the combination or sequencing of cetuximab.

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927P Initial results from a phase II study (TACTI-002) of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab as 2nd line treatment for PD-L1 unselected metastatic head and neck cancer patients

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Background: Eftilagimod alpha (efti) is a soluble LAG-3 protein that binds to a subset of MHC class II molecules to mediate antigen presenting cell (APC) activation and CD8 T-cell activation. The stimulation of the dendritic cell network and subsequent T cell recruitment with efti may lead to stronger anti-tumor responses in combination than observed with pembrolizumab alone. We hereby report initial results of the 2nd line head and neck squamous cell carcinoma (HNSCC) part of the phase II trial (NCT03625323).

Methods: The study has a Simon's 2-stage design, with objective response rate (ORR) as primary endpoint. Secondary endpoints included tolerability, disease control rate, progression free and overall survival, PK, PD and immunogenicity. Second line, PD-X naïve PD-L1 unselected HNSCC patients (pts) are eligible for the trial. Initially 18 pts were recruited in stage 1, an additional 18 pts (total N=36) recruited into stage 2 if the pre-specified threshold of >2 responses was reached. Efti was administered as 30 mg subcutaneous injection every 2 wks for 8 cycles and then every 3 wks for 9 cycles with pembrolizumab (200 mg intravenous infusion every 3 wks for up to 2 yrs).

Results: Between Mar 2019 and Dec 2019, 18 pts were enrolled into stage 1. The median age was 66 yr (range 48-84) and 94 % were male. The ECOG PS 0:1 was 56 % and 44 % respectively. Pts from all PD-L1 subgroups (CPS < 1 %, 1-20%, ≥20 %) were recruited. Pts received a median of 5 pembrolizumab and 7 efti administrations. All pts in stage 1 (n=18) were evaluable. Six pts (33 %) had a partial response (iPR), 1 patient (6 %) had a complete response and 2 (11 %) had stable disease according to iRECIST representing an ORR (DCR) of 39 % (50 %). Threshold for opening stage 2 (> 2 responses) was met. The most common (> 10 %) adverse events (AEs) were cough (29 %), asthenia (24 %), decreased appetite (18 %), dyspnea (18 %), fatigue (17 %), diarrhea (15 %) and nausea (12 %). Seven (7; 41 %) pts are still on therapy and median PFS is not yet reached.

Conclusions: Efti in combination with pembrolizumab is safe and shows encouraging antitumor activity in 2nd line HNSCC patients.

Clinical trial identification: EudraCT Number: 2018-001994-25; NCT03625323.

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928P Phase I dose-expansion (part II) study of ISU104 (a novel anti-ErbB3 monoclonal antibody) alone and combination with cetuximab (CET), in patients (pts) with recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC)

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Background: ISU104 demonstrated anti-tumor efficacy in cetuximab-sensitive and -resistant preclinical models as monotherapy or combination therapy with CET. Dose-escalation study to evaluate the safety, tolerability and pharmacokinetics (PK) of ISU104 was conducted in various advanced solid tumor pts (Ann Oncol, abst #454 PD, 2019). Here we report a dose-expansion study (PART II).

Methods: R/M HNSCC pts, excluding nasopharyngeal cancer, were enrolled and allocated to ISU104 alone (20 mg/kg/day, Q3W; Mono, N=6) or in combination with CET (400 mg/m2 followed by 250 mg/m2, Q1W; Comb, N=12). The study evaluated safety, PK, anti-tumor efficacy and occurrence of anti-drug antibodies. Paired pre-and post-treatment biopsies were conducted to analyze biomarkers including EGFR, ERBB2, ERBB3, pERBB3, NRG1, HPV and other genetic alterations.

Results: Median age of the 18 pts was 62 (range; 30-76, M/F 15/3). As of 17th Jul. 2020, response assessments were available in 17 of 18 pts (4 ongoing, 2 withdrawn, 6 in Mono and 12 in Comb). Most common treatment emergent adverse events (TEAEs) included anorexia (66.7%), mucositis oral (50%) and diarrhea (33.3%) in Mono and diarrhea (75%) and acneiform rash (50%) in Comb. Serious AEs were reported 16.7% in Mono and 58.3% in Comb, but no AEs led to treatment discontinuation. Six pts had dose modification of ISU104 or/and CET in Comb and no case in Mono. Overall response rate and disease control rate were 0% and 50% (3 SD) in Mono (6 pts) and 36.4% (1 CR and 3 PR) and 81.8% (1 CR, 3 PR and 5 SD) in Comb (11 pts), respectively. Duration of response were 62, 46, 162+ and 170+ days (4 pts in Comb), and median progression-free survival was 45 days in Mono and 99 days in Comb group, respectively, with median follow-up of 156 days. Results from mature clinical efficacy data, biomarker analysis and PK will be presented.