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Postoperative adjuvant radiochemotherapy with cisplatin (aRCH) vs. aRCH plus pembrolizumab in locally advanced head and neck squamous cell carcinoma (HNSCC): First data of the ADRISK trial

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Background

Primary curative resection of locally advanced HNSCC often reveals pathologically intermediate or high risk features for relapse requiring adjuvant cisplatin-based radiochemotherapy (aRCH). Adding pembrolizumab (aPD-1) to aRCH may improve event-free survival (EFS).

Methods

The 1:1 randomized phase IIB trial ADRISK (NCT03480672) aimed to improve EFS (primary endpoint) by adding pembrolizumab to standard aRCH (stratified for p16+ oropharynx and localizations, q1w/q3w cisplatin regimen). 240 patients with 100 events were expected to show significantly improved EFS with 80% power in a Cox regression model. Patients and treatment: From 2018 until 2023, 211 patients with resected stage III or IV HNSCC of oral cavity, oropharynx, hypopharynx or larynx with pathologic high (R1, extracapsular nodal extension) or intermediate risk (R0 < 5 mm; pN ≥ 2) needing aRCH were randomized, of which 204 were treated. Patients received standard aRCH (64 Gy with 202 mg/m^2 cisplatin [total dose, median]; *n* = 102, arm A) or aRCH + pembrolizumab (64 Gy, 202 mg/m^2 + 2600 mg; 200 mg iv q3w, max. 12 months; *n* = 102; arm B). To avoid transition to CTIS, enrollment did not reach the planned case number.

Results

We present results after 30 months median follow up. Pembrolizumab improved EFS numerically (28/34 events in B/A). Due to fewer events than expected, neither EFS (HR 0.81 [95% confidence interval 0.52; 1.46]; *p* = .423) nor OS (HR 0.85 [0.46; 1.57]; *p* = .591) were significantly different. Only 11 EFS events (5/6 in B/A, HR 0.91 [0.28; 2.98]) were observed in p16+ oropharynx patients (44%). All other patients (56%) had similar benefit (HR 0.89 [0.51; 1.54]) favoring arm B (51 events, 23/28 in B/A). The highest difference in EFS events (18/23 in B/A) was among the 80 HPV-unrelated cases with CPS ≥ 10 (38/42 in B/A; HR 0.80 [0.43; 1.48]; *p* = .470). No new safety signals were detected.

Conclusions

Due to 44% p16+ cases with fewer events ADRISK could not demonstrate significantly improved EFS through added pembrolizumab. Especially patients with HPV-unrelated, CPS ≥ 10 HNSCC (39%) could benefit from added pembrolizumab.

Clinical trial identification

NCT03480672.

Legal entity responsible for the study

University of Leipzig.

Funding

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Disclosure

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