BERLIN 2025 ESMO congress

1317O

Results from CompARE phase III RCT: Neoadjuvant durvalumab plus chemoradiotherapy (CRT) followed by adjuvant durvalumab immunotherapy (IO) vs CRT alone in intermediate and high-risk oropharyngeal cancer (OPC)

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Background

Trials of IO in the radical CRT setting for locally advanced head neck cancer have been negative to date, postulated to be due to concomitant delivery of IO with CRT (Javelin-100, KeyNote412) or starting adjuvant IO late (ImVOKE-10). CompARE is a phase III RCT [ISRCTN41478539] using an adaptive, multi-arm multi-stage design that evaluates neoadjuvant and adjuvant IO immediately after end of CRT.

Methods

Patients with intermediate risk OPC (HPV-positive TNM7 N2b+ and >10 pack year history of smoking, N3 or T4), or high-risk OPC (HPV-negative), aged 18-70 years with ECOG PS 0-1 were randomised to standard therapy (70Gy in 35 fractions with concurrent cisplatin, Arm1) or neoadjuvant 1500mg durvalumab, followed by standard therapy, then within 2-6 weeks, durvalumab 1500mg, repeated every 4 weeks for 6 months (Arm5). Primary outcome was overall survival (OS) with interim outcome of event-free survival (EFS). Secondary outcomes included toxicity, QoL, swallowing and gastrostomy dependence.

Results

594 patients (306 Arm1; 288 Arm5) were recruited in 34 centres. 85% patients had intermediate risk OPC; 15% high risk. In Arm5, 98% received induction durvalumab; 81% received adjuvant durvalumab. Overall median follow up was 37 months (95% CI. 28, 37). 3y-OS was 84% (95%CI 79, 88%) and 82% (95%CI 76, 86%) in Arm1 and Arm5 respectively (stratified logrank p=0.99); Cox regression Hazard Ratio (HR) Arm5:Arm1 =0.97 (95% CI 0.65, 1.46). 3y-OS rates for the intermediate group, Arm1, were 90% (95%CI 84, 93) and Arm5 84% (95%CI 78, 89), HR=1.24 (95%CI 0.75, 2.03, p=0.40). For the high-risk group, 3y-OS rates for Arm1 were 52% (95%CI 35, 67) and Arm5, 65% (95%CI 45, 80); HR= 0.60 (95%CI 0.30, 1.24, p=0.17). PD-L1 sample analysis is underway and will be presented as well as secondary outcomes and updated follow up data.

Conclusions

Addition of neoadjuvant and adjuvant durvalumab to standard of care did not demonstrate benefit in OPC patients, but high-risk patients may potentially derive some benefit, warranting further exploration of PD-1/PD-L1 inhibition in HPV-negative disease. This work was supported by Cancer Research UK [C19677/A17226] and AstraZeneca.

Clinical trial identification

EudraCT 2014-003389-26.

Legal entity responsible for the study

University of Birmingham.

Funding

Cancer Research UK and AstraZeneca.

Disclosure

H.M. Mehanna: Financial Interests, Institutional, Research Grant: AstraZeneca, MSD; Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca, Johnson and Johnson, Pfizer, MSD, Sanofi Pasteur, Merck, Johnson and Johnson; Financial Interests, Personal, Advisory Board: Eisai Inc, Nanobiotix, Seagen, Merck, Pfizer; Non-Financial Interests, Personal, Member: Macro; Non-Financial Interests, Institutional, Other: Chair Head Neck Cancer international Group. R. Moleron: Financial Interests, Institutional, Advisory Board: MSD, Vasodynamics, Bicara, Novocure. All other authors have declared no conflicts of interest.