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Durvalumab plus definitive chemoradiotherapy versus definitive chemoradiotherapy in patients with locally advanced esophagus carcinoma: ARION PRODIGE 67 randomized phase 2 trial

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Background

In locally advanced or unresectable esophageal cancer, definitive chemoradiotherapy (CRT) is the standard of care (SoC) combining radiotherapy with platinum-based chemotherapy, resulting in a 2-year disease-free survival of 25%, which remains an unmet medical need. As immune checkpoint inhibitors increase survival in the metastatic setting, a multicentric, this open-label, comparative phase II ARION trial was designed to assess efficacy and safety of PD1/PDL1 blockade by durvalumab (D) added to SoC.

Methods

Patients (pts) ≥18 years old, WHO performance status ≤1, non-metastatic, locally advanced squamous cell carcinoma (SCC) or unresectable adenocarcinoma (ADK), (stratified by tumor stage, histology, centers) were randomized between arm A with 12 monthly 1500 mg (D) infusions added to SoC (IMRT 50 Gy/25 daily fractions over 5 weeks) and 6 cycles of FOLFOX regimen: oxaliplatin 85 mg/m<sup>2</sup>, Leucovorin 200 mg/m<sup>2</sup>, 5-FU 400 mg/m<sup>2</sup> bolus then continuous 2400 mg/m<sup>2</sup> over 46 h) or arm B (SoC). Primary endpoint was centrally reviewed progression-free survival (cPFS). Overall survival (OS), PFS and safety were secondary endpoints. 74 cPFS events were required to detect a hazard ratio (HR) of 0.55 with 90% power (10% one-sided alpha).

Results

Between May 2019 and May 2024, 112 pts were randomized (Arm A: SoC + D, n=58 / Arm B: SoC, n=54) in 13 French sites. Analysis was performed after a 24-month follow-up. Median age was 67 years, 68% were male, 77% were SCC, 70% had nodal extension. There was no significant difference between arms for cPFS, PFS and OS (table). Treatment-related adverse events (AE) were higher in arm A. Grade ≥ 3 AE rates were similar in both arms.Table: 2879R0

|      | Arm A (exp) 12-month rate [95%CI] | Arm B (SoC) 12-month rate [95%CI] | Adjusted HR* [95%CI] | [80%CI]      | 1-sided p-value    |
|------|-----------------------------------|-----------------------------------|----------------------|--------------|--------------------|
| cPFS | 48.6% [34.6; 61.3]                | 48.9% [34.7; 61.7]                | 0.91                 | [0.55; 1.49] | [0.66; 1.25] 0.351 |
| PFS  | 50.1% [36.2; 62.5]                | 48.1% [33.7; 61.2]                | 0.92                 | [0.56; 1.50] | [0.67; 1.27] 0.369 |
| OS   | 75.1% [61.6; 84.4]                | 67.9% [53.6; 78.7]                | 0.99                 | [0.59; 1.68] | [0.70; 1.40] 0.489 |

\*for Histological subtype, Stage

Conclusions

In this indication, Durvalumab with CRT compared to SoC did not improve PFS. There was no new safety signal. Longer survival, follow-up and predictive factors for treatment efficacy will be presented.

**Clinical trial identification**

NCT03777813.

**Legal entity responsible for the study**

Unicancer.

**Funding**

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**Disclosure**

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