MADRID 2026 ESMO congress

**LBA85**

# HRS-4642 plus chemotherapy ± adebrelimab as perioperative therapy in KRAS G12D-mutant pancreatic cancer: Preliminary results of a phase 2 study

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## Background

Despite progress with KRAS G12D-directed therapies in advanced PDAC, perioperative treatment still relies on chemotherapy like gemcitabine and nab-paclitaxel(GnP). Here we report the data of HRS-4642 (KRAS G12D inhibitor) in combination with GnP ± adebrelimab as perioperative therapy in resectable or borderline resectable KRAS G12D-mutant pancreatic cancer.

## Methods

This open-label, prospective phase II trial enrolled patients (pts) with treatment-naive, resectable disease, KRAS G12D-mutant pancreatic cancer. Pts received 8 three-week perioperative cycles of HRS-4642 (500 mg d1, 1200 mg d8) plus GnP (nab-paclitaxel 125 mg/m$^2$ d1, d8; gemcitabine 1000 mg/m$^2$ d1, d8), without (Cohort 1) or with (Cohort 2) adebrelimab (1200 mg d1). The study employed a BOP2 design. Primary endpoints were objective response rate (ORR) per RECIST v1.1 and safety. Secondary endpoints included R0 resection rate, major pathological response (MPR; CAP Score 0-1) rate, event-free survival (EFS), overall survival, and exploratory biomarkers.

## Results

As of Sep 3, 2026, 30 pts were enrolled per cohort. Baseline: median age 64 years (range 47-73 vs 39-75); all had ECOG 1; male 70% vs 60%; stage I/II/III 3%/67%/30% vs 0%/60%/40%. All received neoadjuvant therapy and ≥1 post-treatment assessment. All pts experienced treatment-related adverse events (TRAEs). Grade ≥3 events occurred in 47% (Cohort 1) and 53% (Cohort 2), most commonly neutropenia and leukopenia. No TRAEs were fatal or precluded surgery. Tumor shrinkage was observed in all pts. ORRs were 63% (Cohort 1, 19 PR) and 87% (Cohort 2, 26 PR). Surgery was performed in 23 (Cohort 1) and 29 (Cohort 2) pts; one pt per cohort declined surgery, and four pts in Cohort 1 are still in neoadjuvant cycles. Among resected pts, R0 resection rate was 100% and MPR rate was 17% in both cohorts. Six-month EFS rates were 87% (Cohort 1) and 96% (Cohort 2); survival data remain immature. All pts with baseline CA19-9 > ULN had a reduction of ≥50%.

## Conclusions

HRS-4642 plus GnP shows promising neoadjuvant activity in KRAS G12D-mutant pancreatic cancer, with high ORR, R0 resection, favorable MPR and manageable safety; adding adebrelimab shows potential for enhanced efficacy. Updated data will be presented.

## Clinical trial identification

NCT06587061, NCT07131514.

## Legal entity responsible for the study

The authors.

## Funding

Has not received any funding.

## Disclosure

All authors have declared no conflicts of interest.

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