Health-related quality of life (QoL) in PROFIT study: a phase 3 trial of HR20013 for prevention of highly emetogenic chemo induced nausea and vomiting

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Introduction

- Several studies showed that the fixed-dose combination of an NK-1 receptor antagonist and palonosetron (PALO, a 5-HT3 receptor antagonist) was a convenient highly effective prophylactic antiemetic regimen preventing chemo-induced nausea and vomiting (CINV) associated with highly emetogenic chemo (HEC).[1,2]
- **HR20013** is a mixed formulation of HRS5580 and PALO for intravenous infusion, which could simultaneously antagonize NK-1 and 5-HT3 receptors.
- PROFIT study (NCT05509634) is a multicenter, randomized, double-blind, double-dummy, positive-controlled phase 3 trial, which has demonstrated that HR20013 + dexamethasone (DEX) was non-inferior to standard triple therapy of fosaprepitant (FAPR) + PALO+DEX in complete response (no emesis/no rescue) rate during overall phase (0–120 hours) in cycle 1 in patients receiving HEC.
- Herein we present QoL analysis result of PROFIT study.

Methods

- Chemo-naive patients were randomized to receive HR20013 or FAPR+PALO prior to each cycle of cisplatin-based HEC (2 cycles in total), along with oral DEX (D1–D4).
- Endpoints related to QoL were changes of functional living index-emesis (FLIE) score and proportions of patients reporting no impact on daily life (NIDL) in cycle 1 and cycle 2.
- FLIE questionnaire was completed at baseline, 24, 120, and 168 hours after initiation of HEC.
- NIDL was defined as overall FLIE score >108; or nausea/vomiting score >54.

Key eligibility criteria

- Histologically or cytologically confirmed malignant solid tumors;
- Naive to chemo;
- Scheduled to receive the single-day cisplatin-based chemo (dose of cisplatin ≥ 60 mg/m^2);
- ECOG PS of 0-1.

R 1:1

N=373

D1: HR20013+DEX
HR20013: HRS5580 218 mg/PALO 0.25 mg, IV
DEX: 12 mg, PO, QD
D2–D4: DEX
DEX: 3.75 mg, PO, BID

N=377

D1: FAPR+PALO+DEX
FAPR: 150 mg, IV
PALO: 0.25 mg, IV
DEX: 6 mg, PO, QD
D2–D4: DEX
DEX in D2: 3.75 mg, PO, QD
DEX in D3–D4: 3.75 mg, PO, BID

Figure 1. Trial design

Results

Participants

- Baseline characteristics were comparable between two groups.
- 373 patients in HR20013+DEX group and 377 patients in FAPR+PALO+DEX group received the cycle 1 study treatment, while 314 and 336 patients received the cycle 2 study treatment.

Results

Changes in FLIE scores from baseline

- In cycle 1, changes in overall/nausea/vomiting FLIE score from baseline didn't differ between two groups (all P>0.05; Figure 2).
- In cycle 2, HR20013+DEX showed lower decreases from baseline in overall score during delayed phase (24–120 hours; LS mean, -3.5 vs -6.0; P=0.03), vomiting score during delayed phase (-1.2 vs -2.4; P=0.03), and nausea score during beyond delayed phase (120–168 hours; -1.1 vs -2.1; P=0.04) compared with FAPR+PALO+DEX (Figure 3).

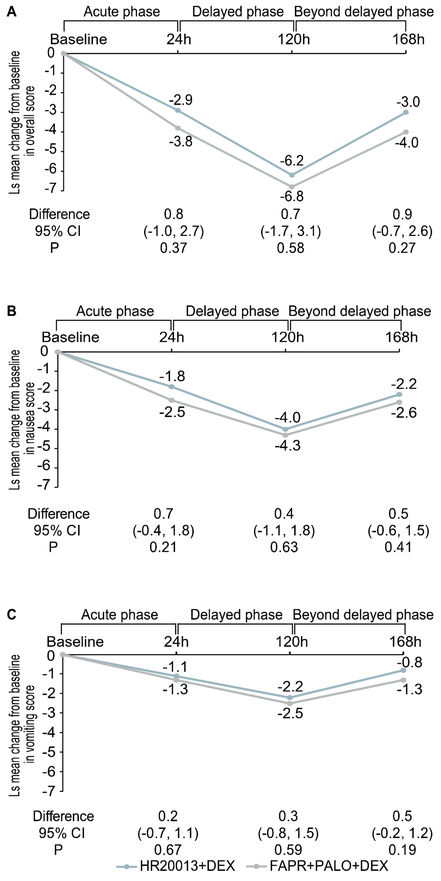

Figure 2. Changes in FLIE score in cycle 1: overall score (A), nausea score (B), and vomiting score (C)

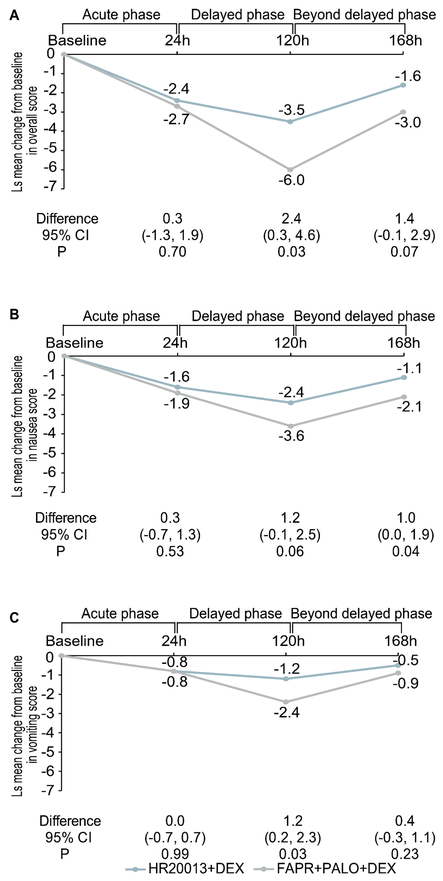

Figure 3. Changes in FLIE score in cycle 2: overall score (A), nausea score (B), and vomiting score (C)

Results

Proportions of patients reporting NIDL due to FLIE scores

- In cycle 1, proportions of patients reporting NIDL for overall domain, nausea domain, and vomiting domain at all three phases (acute phase [0–24 hours], delayed phase, and beyond delayed phase) didn't differ between two groups (all P>0.05; Figure 4).
- In cycle 2, HR20013+DEX showed greater proportions of patients reporting NIDL for overall domain at delayed phase (93.6% vs 87.8%; P=0.01), vomiting domain at delayed phase (95.2% vs 90.8%; P=0.03), overall domain at beyond delayed phase (96.8% vs 92.9%; P=0.03), and nausea domain at beyond delayed phase (95.9% vs 91.1%; P=0.02) compared with FAPR+PALO+DEX (Figure 5).

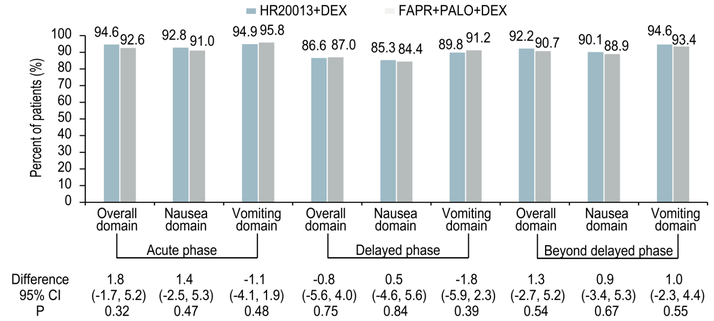

Figure 4. Proportions of patients reporting NIDL due to FLIE scores in cycle 1

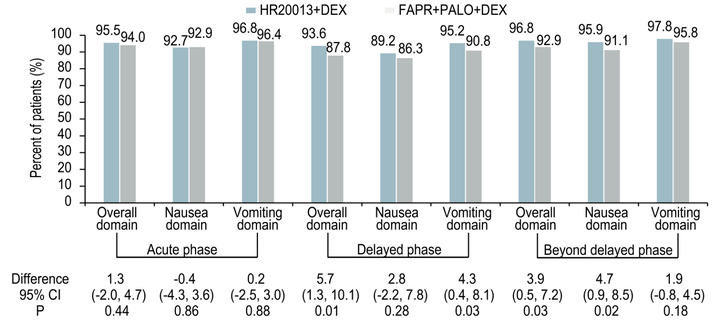

Figure 5. Proportions of patients reporting NIDL due to FLIE scores in cycle 2

Conclusions:

Compared with FAPR+PALO+DEX, HR20013+DEX showed potential to improve QoL in patients receiving HEC, especially during delayed phase and beyond delayed phase.

Reference: 1. Chang J, Chen G, Wang D, et al: Efficacy of NEPA, a fixed antiemetic combination of netupitant and palonosetron, vs a 3-day aprepitant regimen for prevention of chemotherapy-induced nausea and vomiting (CINV) in Chinese patients receiving highly emetogenic chemotherapy (HEC) in a randomized Phase 3 study. Cancer Med 9:5134-5142, 2020.
2. Zhang L, Lu S, Feng J, et al: A randomized phase III study evaluating the efficacy of single-dose NEPA, a fixed antiemetic combination of netupitant and palonosetron, versus an aprepitant regimen for prevention of chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy (HEC). Ann Oncol 29:452-458, 2018.

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