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Abstract CT004: KEYLYNK-007: Tumor agnostic trial of olaparib plus pembrolizumab in homologous recombination repair mutation- and homologous recombination deficiency- positive advanced cancers FREE

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Cancer Res (2025) 85 (8_Supplement_2): CT004.

https://doi.org/10.1158/1538-7445.AM2025-CT004

Abstract

Background:

Early data suggest poly (ADP-ribose) polymerase inhibitor (PARPi)/anti-PD-[L]1 synergy in homologous recombination repair-mutated (HRRm) or homologous recombination deficient (HRD) cancers. KEYLYNK-007 (NCT04123366) is a tumor-agnostic trial that evaluated the PARPi olaparib plus pembrolizumab in HRRm/HRD advanced tumors.

Methods:

This phase 2 trial enrolled participants (pts) with HRRm or HRD+ advanced solid tumors to 3 cohorts: BRCAm (except breast and ovarian), non-BRCA HRRm, and non-HRRm HRD. HRRm/HRD was centrally confirmed using the Lynparza HRR-HRD Assay before treatment with 300 mg olaparib BID + 200 mg pembrolizumab Q3W (≤35 cycles). Primary endpoint was ORR per RECIST 1.1 by central review. Secondary endpoints were duration of response and PFS per RECIST 1.1 by central review, OS, and safety.

Results:

At data cutoff (May 16, 2024), 332 pts were enrolled (n = 132 [BRCAm], n = 104 [non-BRCA HRRm], n = 96 [non-HRRm HRD]) (Table). Median follow-up was 13.4 (BRCAm), 10.4 (non-BRCA HRRm), and 10.8 months (non-HRRm HRD). ORR was 27% (BRCAm), 12% (non-BRCA HRRm), and 12% (non-HRRm HRD). Confirmed RECIST 1.1 responders beyond PARPi-approved indications included pts with advanced breast, ovarian, pancreatic, urothelial, renal,

biliary, cervical, esophageal SCC, CRC, gastroesophageal adenocarcinoma, duodenal, small intestine, thyroid, salivary gland, HNSCC, NSCLC, SCLC, leiomyosarcoma, and other sarcomas. There were also multiple responses in HRRm prostate cancer. Grade ≥3 drug-related adverse events occurred in 30% pts; 1/332 (0.3%) pt died from septic shock.

Table

	***BRCA 1/2*m**	**non-BRCA HRRm**	**non-HRRm HRD**
	N = 132	**N = 104**	**N = 96**
ORR, n (%) [95% CI]	36 (27.3) [19.9 - 35.7]	12 (11.5) [6.1-19.3]	12 (12.5) [6.6-20.8]
CR, n (%)	11 (8.3)	2 (1.9)	5 (5.2)
PR, n (%)	25 (18.9)	10 (9.6)	7 (7.3)
Median DOR mo (95% CI)	19.1 (10.7-NR)	8.3 (4.2-NR)	11.5 (6.2-26.7)
15-mo DOR rate, %	53.7	47.6	41.7
Median PFS mo (95% CI)	4.4 (4.1-8.2)	3.7 (2.3-4.1)	4.1 (2.2-5.7)
12-mo PFS rate, %	31.6	9.3	12.0
Median OS mo (95% CI)	14.0 (11.5, 17.4)	10.4 (7.9, 14.6)	10.8 (8.3, 15.5)
12-mo OS rate, %	57.2	47.1	47.9

CR, complete response; DOR, duration of response; HRRm, homologous recombination repair-mutated; HRD, homologous recombination deficient; mo, months; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response

Conclusions:

In this tumor-agnostic trial, olaparib plus pembrolizumab showed promising durable antitumor activity and manageable safety in HRRm and HRD+ (particularly BRCAm) advanced cancers beyond currently approved indications. Biomarker analysis is ongoing for other predictive biomarkers of response.

Citation Format:

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Abstracts); 2025 Apr 25-30; Chicago, IL. Philadelphia (PA): AACR; Cancer Res 2025;85(8_Suppl_2):Abstract nr CT004.

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Online ISSN 1538-7445 **Print ISSN** 0008-5472