

Phase II study of durvalumab plus olaparib in patients with metastatic pancreatic cancer and DNA damage repair genes alterations

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Key Takeaway Message

Durvalumab plus olaparib demonstrated promising and durable antitumor activity, with a manageable safety profile, in patients with DDR-mutated mPC following platinum-based chemotherapy.

Background and study design

Metastatic pancreatic cancer (mPC) with DNA damage repair (DDR) alterations such as *BRCA1*, *BRCA2* and *PALB2* is associated with sensitivity to platinum-based chemotherapy (CT) and PARP inhibition.

Evidence suggests PARP inhibition with immune checkpoint blockade may enhance antitumor activity.

This study evaluates the combination of durvalumab and olaparib in DDR-mutated mPC patients with no progression to platinum-based CT.

- Open label
- Single arm
- Multicenter



Olaparib:
300 mg PO BID
Durvalumab:
1500 mg IV q4w



Endpoint:

- Primary: ORR
- Secondary: DCR, PFS, OS, Safety

Results (baseline characteristics)

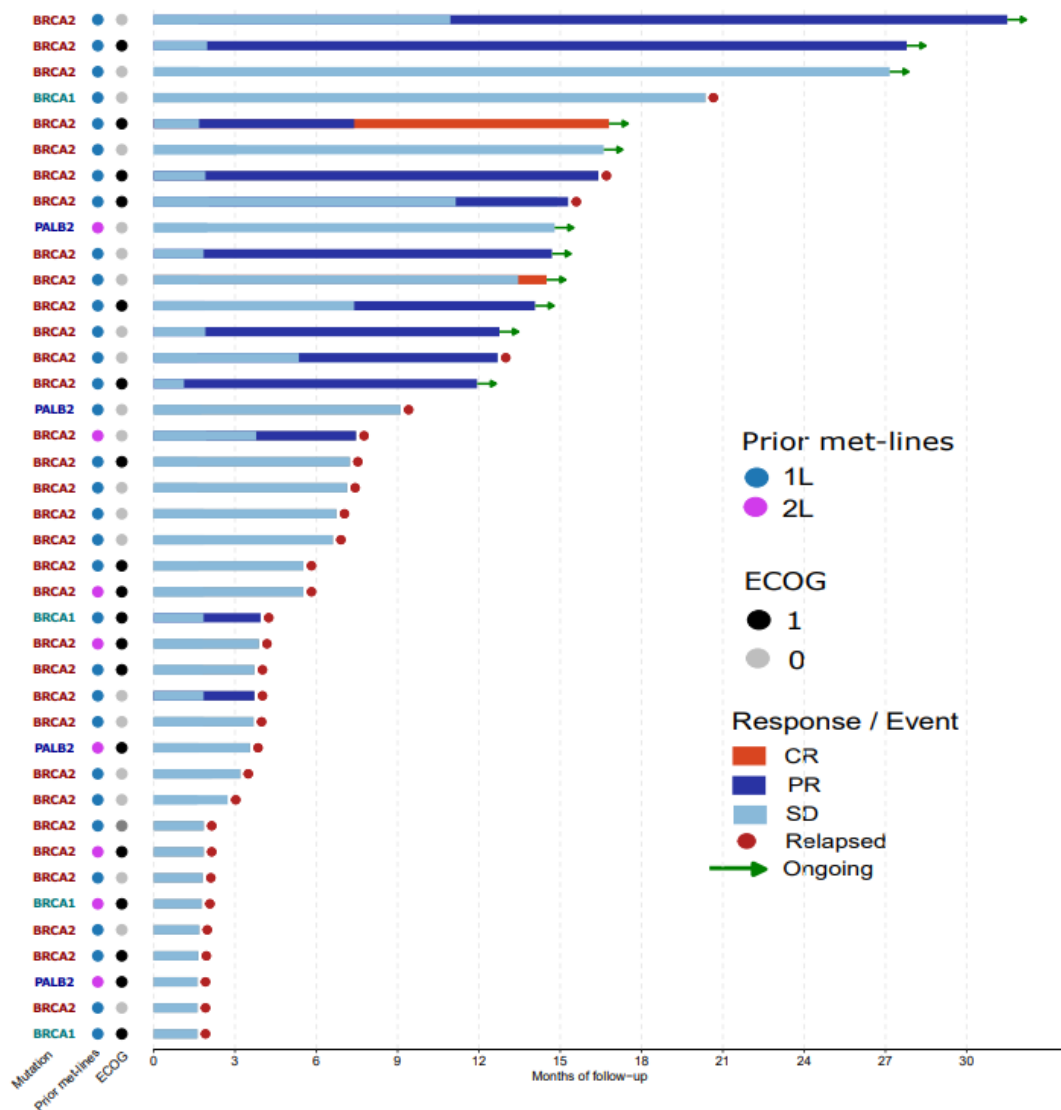
40 patients from 14 centers were enrolled between Dec 2022 and Oct 2024.

Characteristic	N = 40 (%)
Gender (female)	21 (52.5)
Median age (IQR)	57 (50-65)
Diagnosis location	
Head of pancreas	14 (35.9)
Body of pancreas	11 (28.2)
Tail of pancreas	11 (28.2)
Body and tail	3 (7.7)
Missing	1
Diagnosis initial Stage	
II	1 (2.6)
III	4 (10.3)
IV	34 (87.2)
Missing	1
ECOG C1D1	
0	21 (53.8)
1	18 (46.2)
Missing	1

Characteristic	N = 40 (%)
Prior neoadjuvant CT	5 (12.5)
Prior adjuvant CT	8 (20.0)
Prior surgery	16 (40.0)
Prior RT	5 (12.5)
Metastasis locations	
Liver	34 (85.0)
Lung	9 (22.5)
Distant nodes	5 (12.5)
Peritoneum	6 (15.0)
DDR alterations	
BRCA1 mutation	4 (10.0)
BRCA2 mutation	32 (80.0)
PALB2 mutation	4 (10.0)
N prior metastatic lines	
1L	32 (80.0)
2L	8 (20.0)
Prior 1L platinum-based CT	
Oxaliplatin	28 (70.0)
Cisplatin	8 (20.0)
Prior 2L platinum-based CT	
Oxaliplatin	3 (7.5)
Cisplatin	2 (5.0)

Results (ORR, DCR, DoR)

Swimmer plot



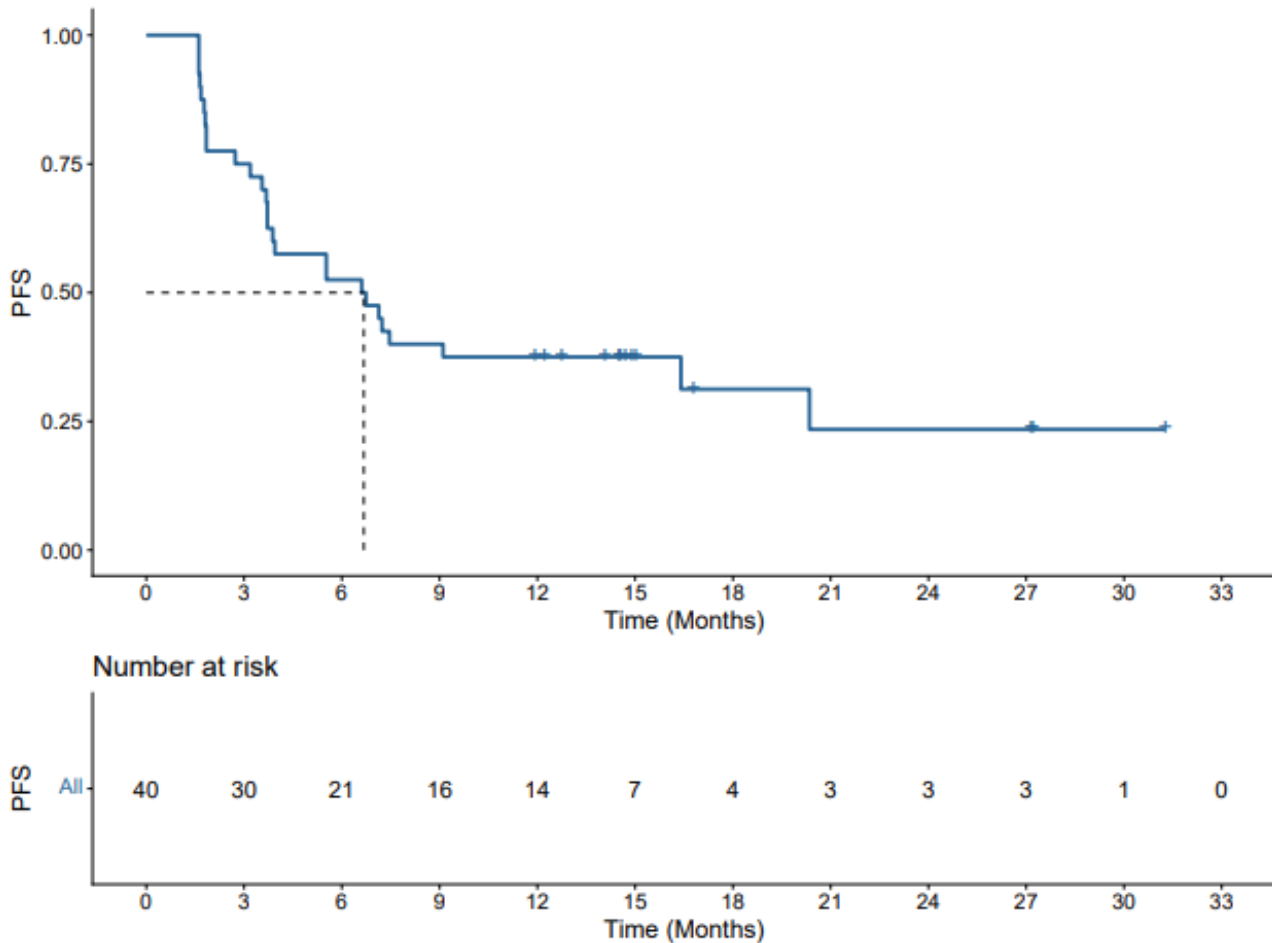
Objective response rate (ORR) and disease control rate (DCR)

Characteristic	N = 40 (%)
Median follow up months (95% CI)	15.0 (14.5, 24.9)
Objective response	
Complete Response (CR)	2 (5.0%)
Partial Response (PR)	12 (30.0%)
Stable Disease (SD)	17 (42.5%)
Progressive Disease (PD)	9 (22.5%)
ORR (CR + PR)	14 (35.0%)
DCR (CR + PR + SD)	31 (77.5%)
DCR 6 months	23 (57.5%)
Median DoR months (95% CI)	14.5 (14.5, -)
Ongoing response	13 (32.5%)

Results (PFS)

PFS (all patients)

Characteristic	6 months	12 months	24 months	Median (95% CI)
PFS rates (95% CI)	53% (39, 70)	38% (25, 56)	23% (11, 51)	6.7m (3.7, -)



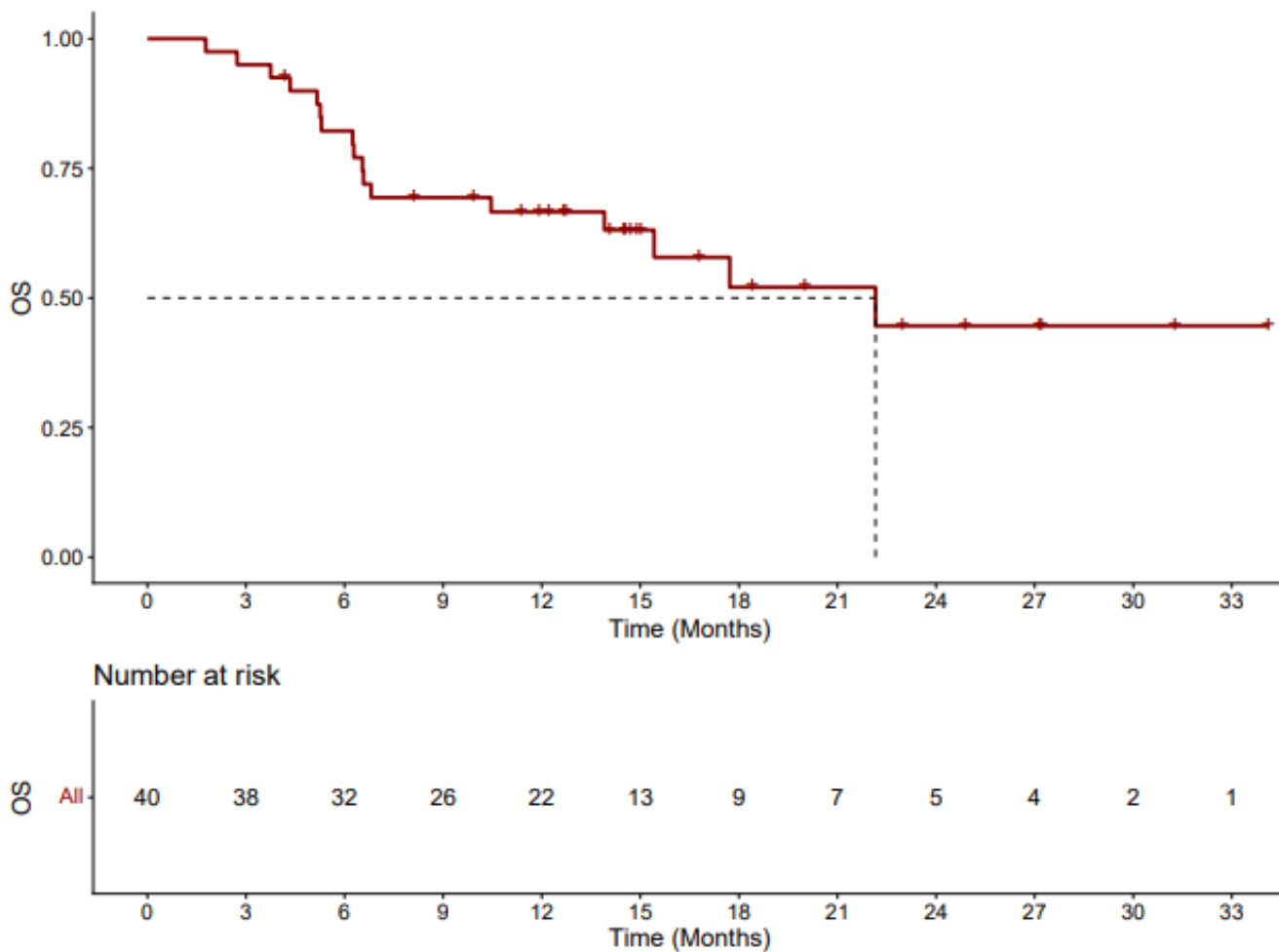
Subgroup analysis for PFS

Variable	N	Hazard ratio	HR [95% CI]	p-value
Gender				
Male	19		Reference	
Female	21		1.12 (0.52, 2.39)	0.778
Age at C1				
<65 yr	30		Reference	
65+ yr	10		0.84 (0.34, 2.09)	0.708
ECOG				
0	21		Reference	
1	18		1.44 (0.66, 3.12)	0.357
Metastasis prior lines				
1L	32		Reference	
2L	8		2.22 (0.92, 5.35)	0.077
Diagnosis location				
Head of pancreas	14		Reference	
Body of pancreas	11		0.71 (0.25, 2.05)	0.528
Tail of pancreas	11		1.31 (0.52, 3.32)	0.566
Body of pancreas, Tail of pancreas	3		1.02 (0.22, 4.72)	0.984
Liver metastasis				
No	6		Reference	
Yes	34		1.94 (0.58, 6.47)	0.282
Lung metastasis				
No	31		Reference	
Yes	9		1.55 (0.66, 3.69)	0.317
Distant nodes				
No	35		Reference	
Yes	5		2.05 (0.75, 5.62)	0.163
Peritoneum				
No	34		Reference	
Yes	6		0.91 (0.31, 2.64)	0.864
Type				
Germinal	25		Reference	
Somatic	13		1.05 (0.47, 2.37)	0.900
Mutation				
BRCA1	4		Reference	
BRCA2	32		0.47 (0.16, 1.38)	0.169
PALB2	4		0.67 (0.15, 3.09)	0.611

Results (OS)

OS (all patients)

Characteristic	6 months	12 months	24 months	Median (95% CI)
OS rates (95% CI)	82% (71, 95)	67% (53, 83)	45% (28, 72)	22.2m (13.9, -)



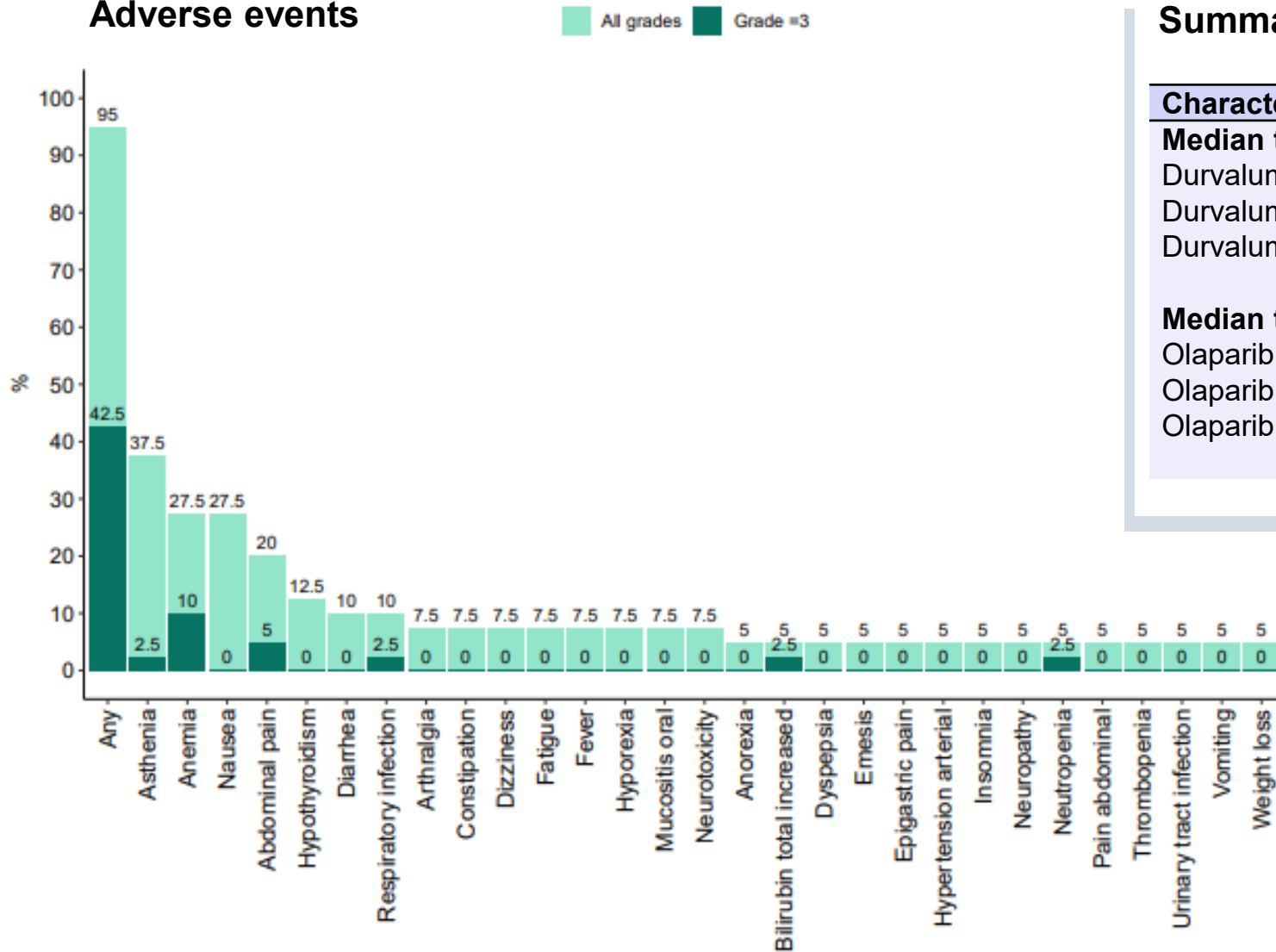
Subgroup analysis for OS

Univariate OS

Variable	N	Hazard ratio	HR [95% CI]	p-value
Gender				
Male	19		Reference	
Female	21		1.24 (0.47, 3.27)	0.659
Age at C1				
<65 yr	30		Reference	
65+ yr	10		1.43 (0.49, 4.14)	0.514
ECOG				
0	21		Reference	
1	18		1.80 (0.67, 4.85)	0.245
Prior metastasis lines				
1L	32		Reference	
2L	8		1.564 (0.502, 4.867)	0.440
Diagnosis location				
Head of pancreas	14		Reference	
Body of pancreas	11		1.20 (0.29, 4.90)	0.798
Tail of pancreas	11		1.98 (0.58, 6.80)	0.278
Body of pancreas, Tail of pancreas	3		1.26 (0.14, 11.40)	0.838
Liver metastasis				
No	6		Reference	
Yes	34		2.62 (0.34, 19.92)	0.353
Lung metastasis				
No	31		Reference	
Yes	9		1.59 (0.51, 4.91)	0.424
Distant nodes				
No	35		Reference	
Yes	5		2.51 (0.68, 9.30)	0.169
Peritoneum				
No	34		Reference	
Yes	6		1.86 (0.60, 5.72)	0.279
Type				
Germinal	25		Reference	
Somatic	13		1.15 (0.42, 3.14)	0.782
Results				
BRCA1	4		Reference	
BRCA2	32		0.39 (0.11, 1.39)	0.146
PALB2	4		0.21 (0.02, 2.01)	0.174

Results (safety)

Adverse events



Summary of safety characteristics

Characteristic	N = 40 (%)
Median time of Durvalumab treatment duration (months)	6.9
Durvalumab dose changes	0 (0.0%)
Durvalumab dose delays	12 (30.0%)
Durvalumab dose interruptions	3 (7.5%)
Median time of Olaparib treatment duration (months)	6.0
Olaparib dose changes	10 (25.0%)
Olaparib dose delays	5 (12.5%)
Olaparib dose interruptions	10 (25.0%)

Conclusions

- DDR-mutated mPC patients treated with durvalumab plus olaparib, following a first or second line of platinum-based chemotherapy, presented an ORR of 35.0% with 12 PR and 2 CR.
- Median DoR in these patients was 14.5 months (95% CI 14.5-NA) and 13 patients had ongoing treatment at the time of the analysis.
- The most common grade ≥ 3 adverse events were anemia (10%) and abdominal pain (5%).
- This treatment suggests a maintained disease control benefit and manageable safety in DDR-mutated mPC.

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