Abstract 5581

Phase II Study of Pembrolizumab and Lenvatinib in Platinum Sensitive Recurrent Ovarian Cancer NCT 04519151

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BACKGROUND

- ✓ Ovarian cancer is the deadliest form of gynecologic cancers with over 12,700 deaths expected in the US in 2024 [1]
- ✓ Despite high response rate to primary chemotherapy and benefit of maintenance bevacizumab and PARP inhibitors, majority of the patients will experience relapse [2,3,4,5]
- ✓ Patients with recurrent disease are candidates for multiple chemotherapy lines with accumulating toxicity and decreasing efficacy. The backbone of chemotherapy regimen will be platinum salt chemotherapy either as monotherapy or with non platinum agents as long as disease is defined sensitive or eligible for repeating platinum and safety profile is acceptable
- ✓ There is no proven survival benefit for early onset chemotherapy at non-symptomatic recurrence [6]
- ✓ Currently non-chemotherapy alternative has emerged as standard option
- ✓ While checkpoint blockade (with anti-PD-1) has altered treatment landscape in multiple cancers, affecting response probability, duration of response, progression free survival and overall survival, their role in ovarian cancer (alone/combined with chemotherapy or with PARPi) is yet to be defined [7,8]
- ✓ Combined pembrolizumab and lenvatinib has proven efficacy in checkpoint blockade resistant tumors such as advanced MMR-P endometrial cancer, melanoma and kidney cancer suggesting synergistic effect of angiogenesis targeting tyrosine kinase inhibitors and checkpoint blockade immunotherapy [9,10,11,12]
- ✓ LEAP 005 study explored the combination of pembrolizumab and lenvatinib in a small cohort of heavily pre-treated platinum resistant recurrent ovarian cancer with 30% RR [13]
- ✓ NCT 04519151 aim was to explore the role of combined pembrolizumab and lenvatinib in patient with platinum sensitive recurrent ovarian cancer

Study Design (a) (b)

Phase 2, Single Arm, Single Site Study

Key Eligibility Criteria

- Platinum-sensitive recurrent ovarian cancer (c) (d)
- High grade serous or endometrioid histology
- ECOG PS 0-1
- Received up to 2 prior chemotherapy lines (e)
- Adequate organ function (f)
- Measurable disease per RECIST 1.1

Treatment

- Pembrolizumab 200mg IV Q3W up to 35 cycles
  and
- Lenvatinib 20mg PO QD (g) (h)

Study End Points

- Primary - ORR (investigator assessed)
- Secondary Endpoints
  - PFS
  - OS (i)
  - Safety and Tolerability (j)
  - QoL (k)
- Exploratory endpoints: Candidate biomarkers that correlate with likelihood of clinical benefit (l)

(a) A single site, phase 2, single arm study
(b) This is an investigator-initiated study supported by research grant from MSD
(c) Includes primary ovarian, fallopian tube or primary peritoneal cancer
(d) Platinum sensitive disease is defined by imaging (CT/MRI) evidence for disease relapse over 6 months from prior platinum containing regimen
(e) Prior maintenance therapy with bevacizumab or PARP inhibitors is allowed as well as prior hormonal treatment- either as maintenance or active disease
(f) Defined by blood count and chemistry
(g) Lenvatinib treatment can be maintained beyond 35 cycles in non progressing patients and upon investigator discretion.
(h) Pembrolizumab dose can be delayed but not reduced, Lenvatinib dose could be withheld and reduced upon grade 2 non tolerable toxicity or G3-4 toxicity
(i) Abbreviations: ORR= overall response rate by RECIST 1.1, PFS=progression free survival, OS=overall survival
(j) By CTCAE v5.0
(k) Assessed by EORTC QLQ 30 and EORTC OV28 at screening, C4D1,every 3 cycles thereafter and at end of treatment
(l) Includes archival/fresh baseline tumor tissue and blood PBMCs, baseline fecal and vaginal microbiome samples, recurrent blood samples and vaginal microbiome and optional tumor biopsy upon progression

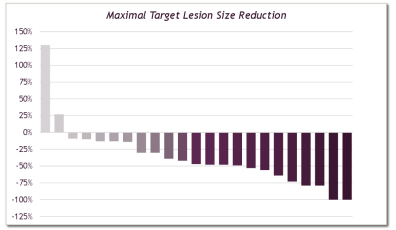
Patient Characteristics (n=24)

Enrolled between May-2021 and July-2023

Age, median (range)		*60 (45-78)*
< 65 years, n (%)		*12 (50)*
Stage at enrollment, n (%)	*IIIc*	*11 (46)*
	IV	*13 (54)*
Histology, n (%)	*HGS*	*19 (79.2)*
	Adenocarcinoma	*5 (20.8)*
Received neoadjuvant chemotherapy as first line, n (%)		*11 (46)*
Interval from last Platinum, n (%)	*6-12 months*	*10 (42)*
	> 12 months	*14 (58)*
BRCA mutation carrier, n (%)		*5 (21)*
HRD (non BRCA), n (%)	*Positive*	*1 (4)*
	Negative	*11 (46)*
	Unknown	*7 (29)*
ECOG PS, n (%)	*0*	*18 (75)*
	1	*6 (25)*
Prior treatment lines, n (%)	*1*	*9 (37.5)*
	2	*15 (62.5)*
CA-125 level	*Up to 10*ULN*	*17 (71)*
	*> 10*ULN*	*7 (29)*
Prior Bevacizumab, n (%)		*12 (50)*
Prior PARP-I, n (%)		*11 (46)*

Results Data Cutoff May 20, 2024

Maximal Target Lesion Size Reduction

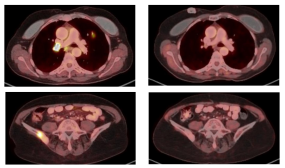


	n	%
Overall Response	13	54
Complete Response	3	13
Partial Response	10	42
Stable Disease	7	29
Progressive Disease	3	13

* One patient was not assessed for response due to toxicity related early study withdrawal

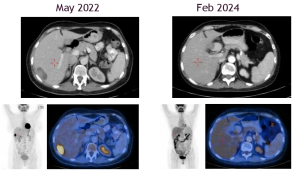
61 YO, Complete Resolution of Bone and Lymph Node Metastases

Mar 2022 Aug 2022

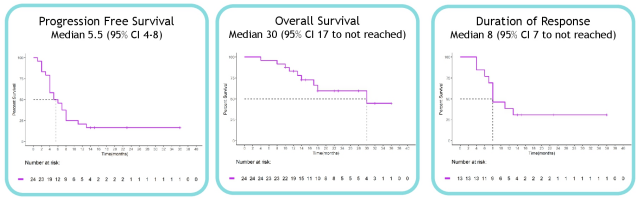


47 YO, Complete Resolution of Liver and Peritoneal disease

May 2022 Feb 2024

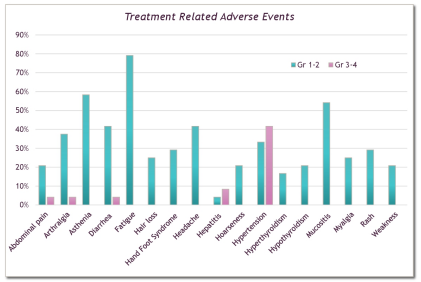


Efficacy



Safety and Tolerability n = 24

Treatment Related Adverse Events



Adverse events	*n*	*%*
Gr 1-2	23	96
Gr 3-4	16	67
AE leading to discontinuation	*n*	*%*
Nephrotic range proteinuria	1	4
Hepatitis	1	4
Diabetic ketoacidosis	1	4
AE leading to dose reduction	*n*	*%*
Any	19	79

CONCLUSIONS

- *The combination of pembrolizumab and lenvatinib yielded meaningful response in patients with platinum sensitive recurrent ovarian cancer with 54% response rate, 8 months median response duration, 31% persisting over 18 months*
- *Adverse events were manageable with hypertension being the most prevalent G3-4 toxicity; adverse events, except from endocrinopathies, were reversible upon treatment withdrawal*
- *Overall survival is comparable with standard of care practice for platinum sensitive recurrence*
- *Biomarker analysis, including tumor RNA sequencing, immune phenotyping, fecal and vaginal microbiome composition is currently in progress to define patients with likelihood of benefit*
- *Quality of life at baseline and during treatment change is being analyzed for future presentation*

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References: **1.** http://seer.cancer.gov **2.** Tewari K.S et al., J Clinical Oncology 2019; 37(26):2317-2328 **3.** Moore K et al., NEJM 2018; 379:2495-2505 **4.** Gonzales-Martin A et al., NEJM 2019; 381(25):2391-2402 **5.** Monk B.J et al., J Clinical Oncology 2022; 40(34):3952-3981 **6.** Rustin G et al., The Lancet 2010; 376(9747):1155-1163 **7.** Pignata S et al., Gynecol Oncol 2023; 177:20-31 **8.** Matulonis U.A et al., Ann Oncol 2019; 30(7):1080-1087 **9.** Makker V et al., NEJM 2022; 386:437-448 **10.** Arance A. et al., J Clinical Oncology 2022; 41(1):75-91 **11.** Motzer R.J et al., J Clinical Oncology 2024; 42(11):1222-1235 **12.** Boudin L et al., Current Oncol 2022; 29(10):7718-7731 **13.** Gonzales-Martin et al., Gynecol Oncol 2024; 186:182-190