EFFICACY OF PEMBROLIZUMAB IN COMBINATION WITH BEVACIZUMAB AND ORAL METRONOMIC CYCLOPHOSPHAMIDE IN THE TREATMENT OF PLATINUM-RESISTANT RECURRENT OVARIAN CANCER: *A RETROSPECTIVE OBSERVATIONAL STUDY*

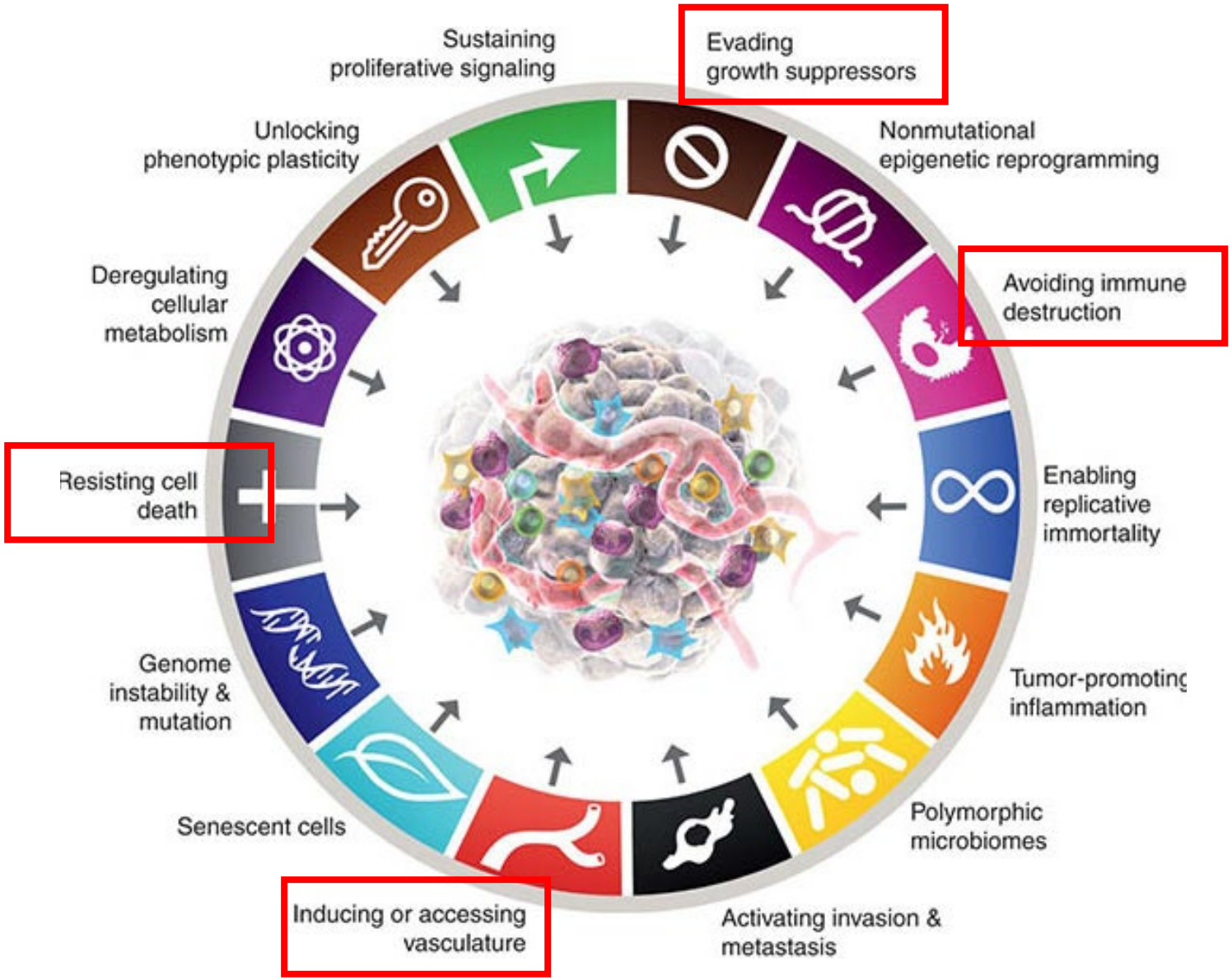
Alexandra R. Steck, Jovana Y. Martin, Timothy J. McElrath, Anne Wilkinson, Lisa Armao, Siobhan Muscanelli-Hecox, Patrick F. Timmins III, Joyce N. Barlin.

PLATINUM-RESISTANT RECURRENT OVARIAN CANCER

- 2022 Cancer Statistics (CA Cancer J Clin.)
  - 19,880 new cases of ovarian cancer
  - 12,810 deaths
- 68% of all epithelial ovarian cancers are classified as high-grade serous cancer
  - 20% of these patients are at risk of developing chemoresistance after up-front chemotherapy
- There is an acute need for non-platinum-based therapies to improve patient QOL

BACKGROUND: THE PRECEDENT FOR IMMUNOTHERAPY IN OVARIAN CANCER TREATMENT

- Targeting the various hallmarks of cancer
- PD-L1 expression and high-grade serous ovarian cancer prognosis
- Possible approach for patients that are no longer responding to chemotherapy standards of care



Licculi, S. "New Dimensions in Cancer Biology: Updated Hallmarks of Cancer Published." AACR, 28 Jan. 2022.

A NOVEL COMBINATION: PEMBROLIZUMAB, BEVACIZUMAB, AND ORAL METRONOMIC CYCLOPHOSPHAMIDE

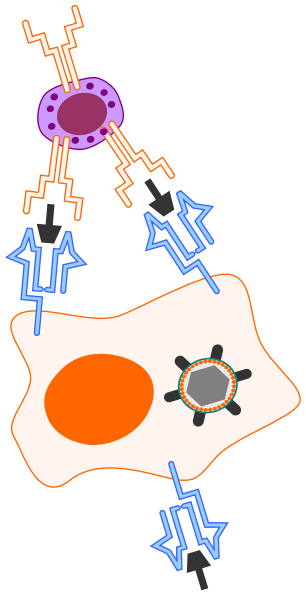
A multi-targeted approach

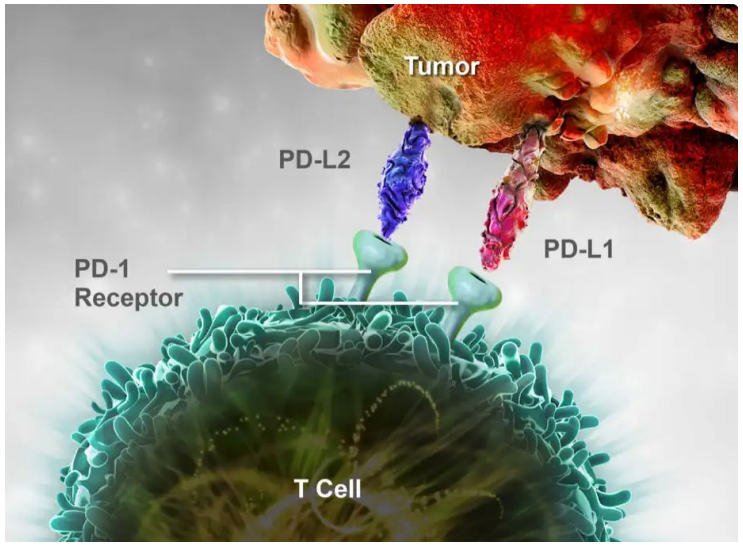
Immunomodulation
- Increased cytotoxic activity
- T_{reg} cell depletion

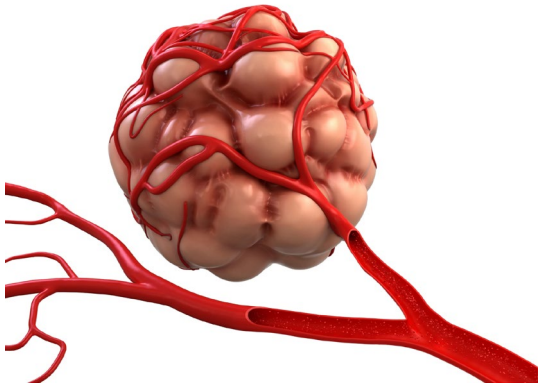
Restoration of immune response via binding of PD-1 receptors

Decreased angiogenesis

VEG-F







National Cancer Institute, "Angiogenesis Inhibitors"
KEYTRUDA® (*Pembrolizumab*), "Mechanism of Action of Keytruda ® (Pembrolizumab): Health Care Professionals"
Andre, N et al. Metronomics: towards personalized chemotherapy? *Nature Reviews Clinical Oncology*. 2014.

From: **Efficacy and Safety of Pembrolizumab in Combination With Bevacizumab and Oral Metronomic Cyclophosphamide in the Treatment of Recurrent Ovarian Cancer: A Phase 2 Nonrandomized Clinical Trial**

JAMA Oncol. 2021;7(1):78-85. doi:10.1001/jamaoncol.2020.5945

Table. Best Responses to Efficacy Measures

Best response	Patient group[a]		
	Platinum-sensitive disease (n = 10)	Platinum-resistant disease (n = 30)	All (n = 40)
Unevaluable	0	0	0
Complete response	0	3 (10.0)	3 (7.5)
Partial response	6 (60.0)	10 (33.3)	16 (40.0)
Stable disease only, wk			
≥24	3 (30.0)	8 (26.7)	11 (27.5)
<24	1 (10.0)	7 (23.3)	8 (20.0)
Progressive disease	0	2 (6.7)	2 (5.0)
Objective response rate (complete plus partial responses)	6 (60.0)	13 (43.3)	19 (47.5)
Total clinical benefit rate (complete plus partial responses plus stable disease)	10 (100)	28 (93.3)	38 (95.0)
DOR, median (IQR) [range], mo[b]	11.5 (4.1-16.3) [1.6-21.3]	5.5 (2.4-8.7) [0-26.4]	5.8 (3.1-10.7) [0-26.4]

Abbreviations: DOR, duration of response; IQR, interquartile range.

[a] Unless otherwise indicated, data are expressed as number (percentage) of patients. Responses are based on immune-related Response Evaluation Criteria In Solid Tumors.

[b] Differences were not statistically significant (*P* = .14) with a minimum of 6 weeks for confirmation of stable disease.

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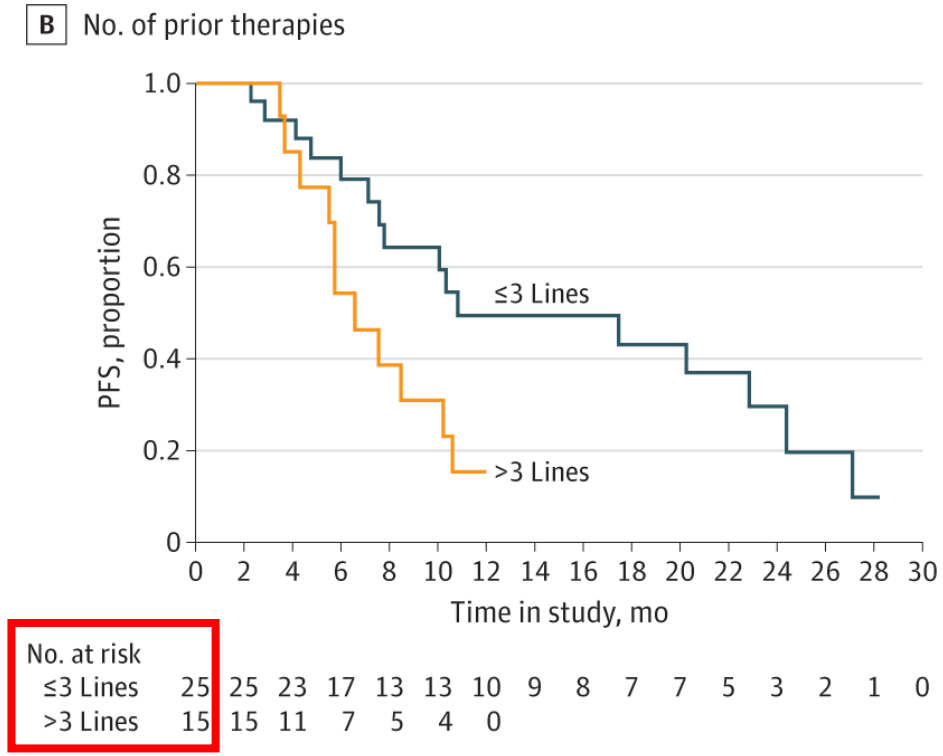
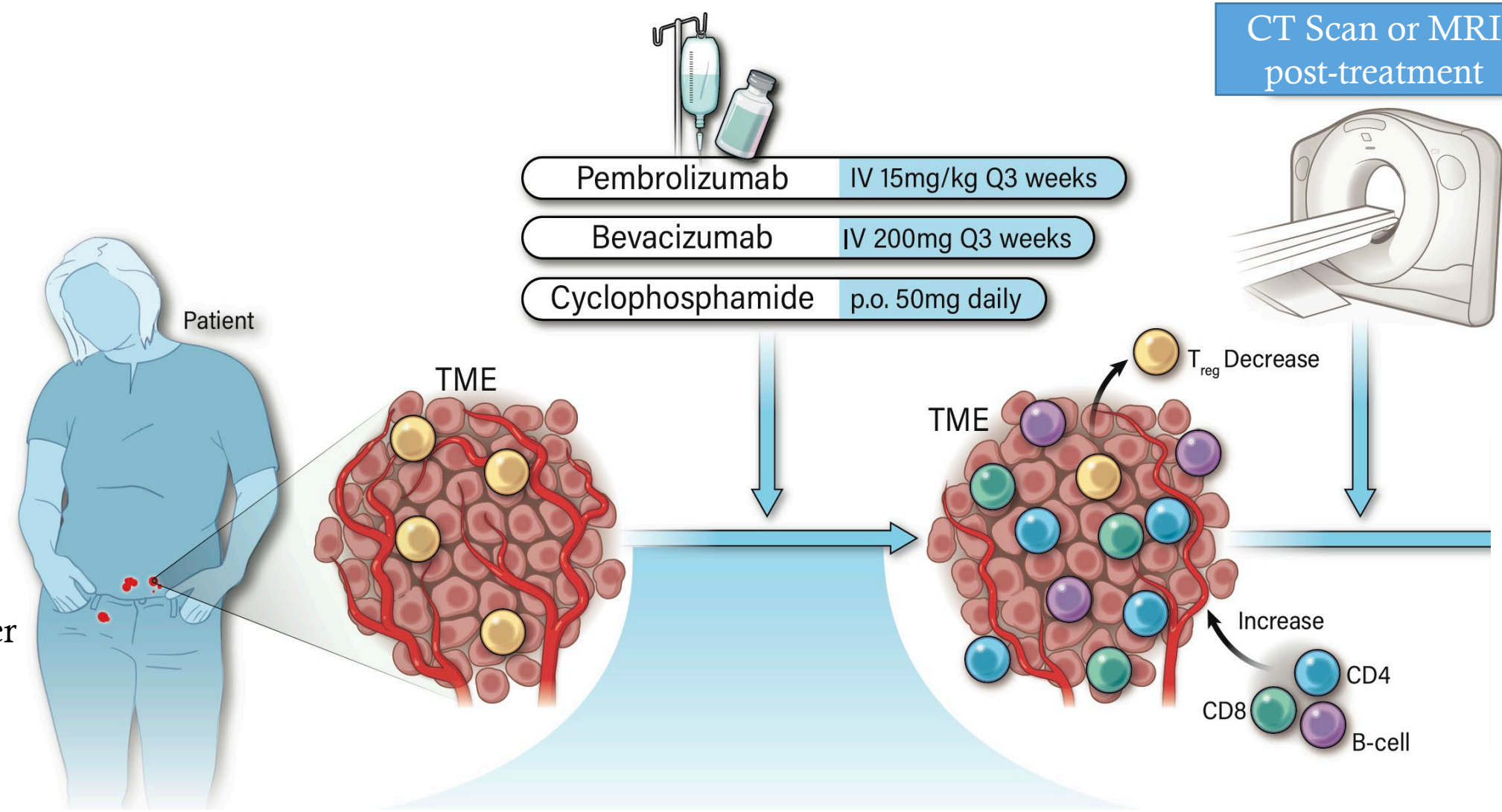


Figure Legend:
Progression-Free Survival (PFS) Among Evaluable Patients Receiving Combination Pembrolizumab With Bevacizumab and Oral Cyclophosphamide. B, Among patients with 3 or fewer prior lines of chemotherapy, median 6-month PFS rate was 0.79 (90% CI, 0.57-0.91); median PFS, 10.8 (90% CI, 7.6-24.4) months. Among patients with more than 3 prior lines of chemotherapy, median 6-month PFS was 0.54 (90% CI, 0.25-0.76); median PFS, 6.5 (90% CI, 4.3-10.2) months (P = .03).

STUDY DESIGN

Platinum-resistant recurrent ovarian cancer



Gaulin, N. B. et al. Lecture presented at: SGO Conference; March 18-21, 2022; Phoenix, AZ.

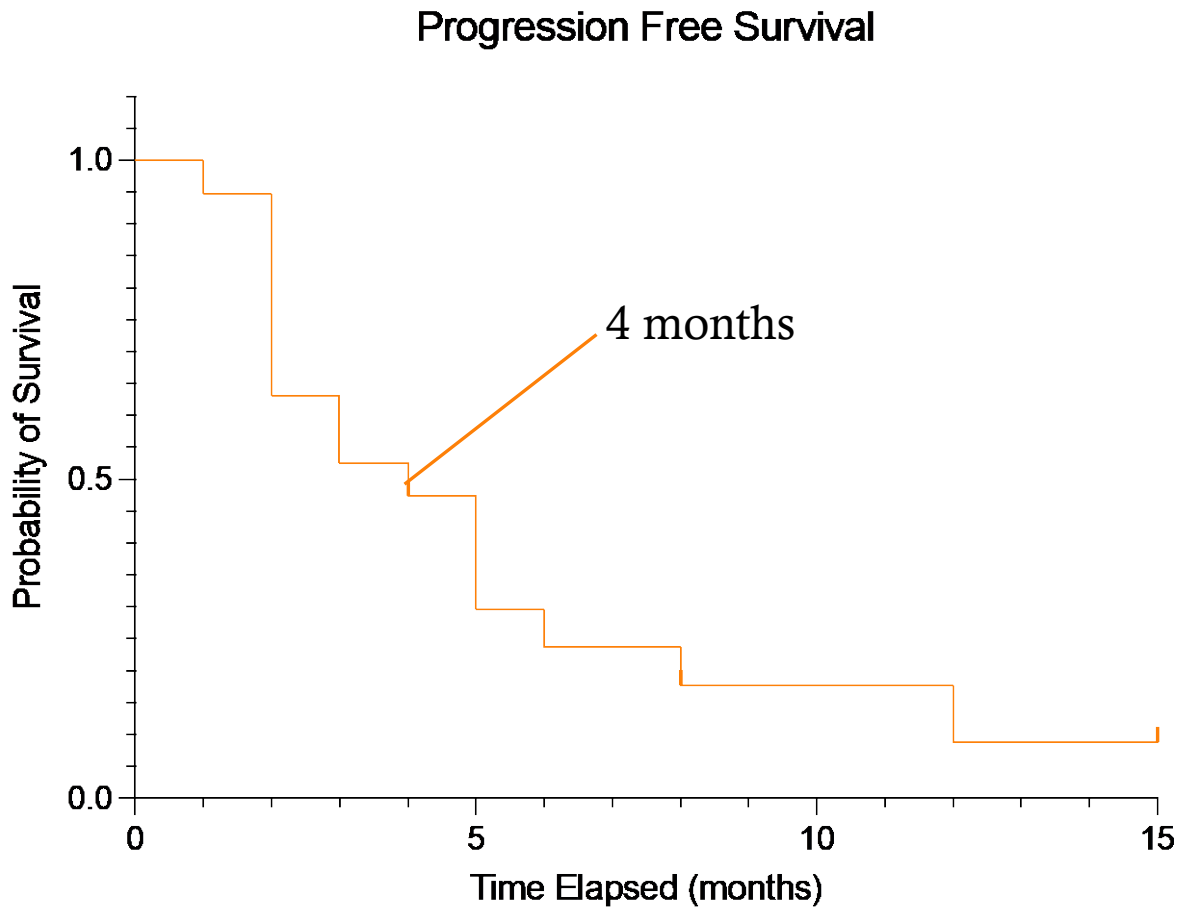
STUDY COHORT DEMOGRAPHICS

Platinum-resistant patients	n=19
Cancer Type	
Ovarian Fallopian Peritoneal	12 6 1
Histological Subtype	
High-grade serous Clear cell	17 2
Stage at Diagnosis	
IC IIB IIIB IIIC IV IVA	2 1 2 10 2 2
PD-L1 Status	
Positive Negative Unknown	3 9 7
Number of Previous Chemotherapy Lines	
Median, Range	4 (2-9)

CLINICAL OUTCOME

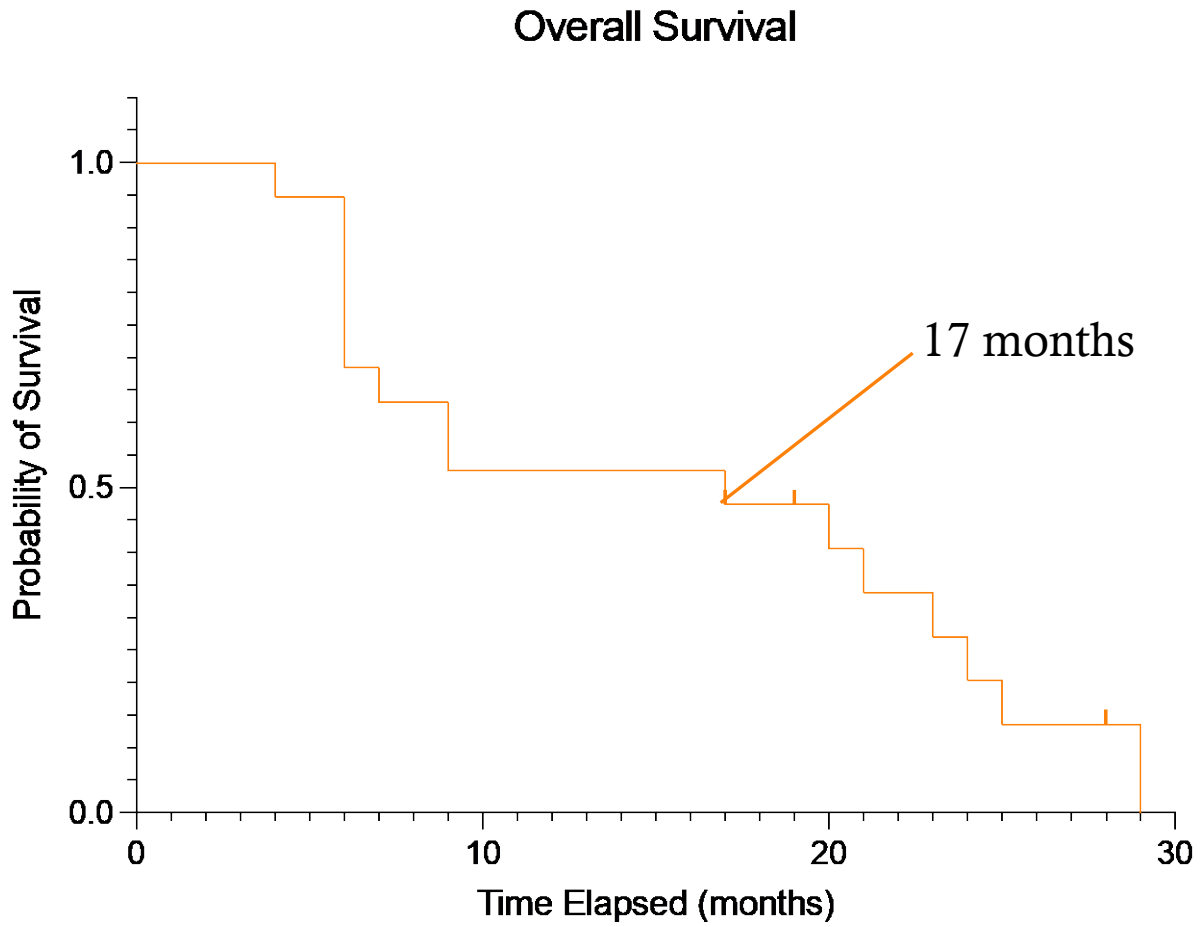
Best response	Platinum-resistant disease (n=19)
Complete response	0
Partial response	4
Stable disease only, wk	4
≥ 24	2
< 24	2
Progressive disease	11
Objective response rate (complete plus partial responses)	4 (21.1)
Total clinical benefit rate (complete and partial responses plus stable disease)	5 (26.3)

CLINICAL OUTCOME: MEDIAN PFS



	0.000	1.000	2.000	3.000	4.000	5.000	6.000	8.000	12.000	15.000
No. at risk	19	19	18	12	10	8	5	4	2	1

CLINICAL OUTCOME: MEDIAN OS



	0.000	4.000	6.000	7.000	9.000	17.000	19.000	20.000	21.000	23.000
No. at risk	19	19	18	13	12	10	8	7	6	5

COMBINATION THERAPY TOXICITY

Adverse Event	# of patients	% of population
Fatigue	9	47.4
Nausea	6	31.6
Abdominal pain	5	26.3
Diarrhea	3	15.8
Constipation	3	
Peripheral neuropathy	3	
Vomiting	2	10.5
Taste alteration	2	
Pruritus	2	
Abdominal distension	1	5.3
Hypertension	1	
Cough	1	
Muscle spasms	1	
Hypothyroidism	1	

CONCLUSION

- Combination bevacizumab and pembrolizumab with oral metronomic cyclophosphamide was well tolerated
- 21.1% response rate in heavily pre-treated population
- 26.3% total clinical benefit rate
- Combination therapy modulation of the tumor microenvironment provides an opportunity to increase response rate for platinum-resistant patients and warrants further study

CITATIONS

- Gaulin, N B et al. Turning Cold into Hot: combination of pembrolizumab with bevacizumab and oral metronomic cyclophosphamide increases immune cell migration into the tumor microenvironment in responding patients with recurrent ovarian cancer. Lecture presented at: SGO Conference; March 18-21, 2022; Phoenix, AZ.
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THANK YOU!




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  - Siobhan Muscanelli-Hecox



WCCA
Women's Cancer Care Associates

QUESTIONS?