



# Treatment of Platinum Resistant Ovarian Cancer?

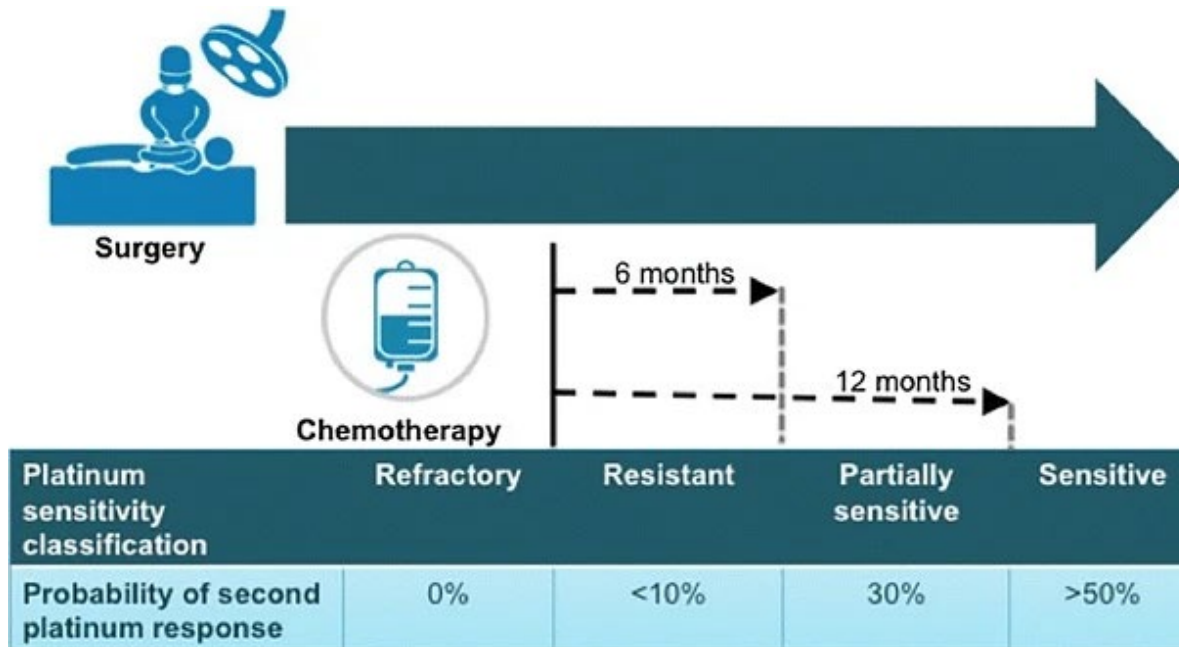
Survive and Thrive  
October 2022

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Gynecology Oncology



# What is Platinum Resistant Disease?

# Platinum Resistant Ovarian Cancer



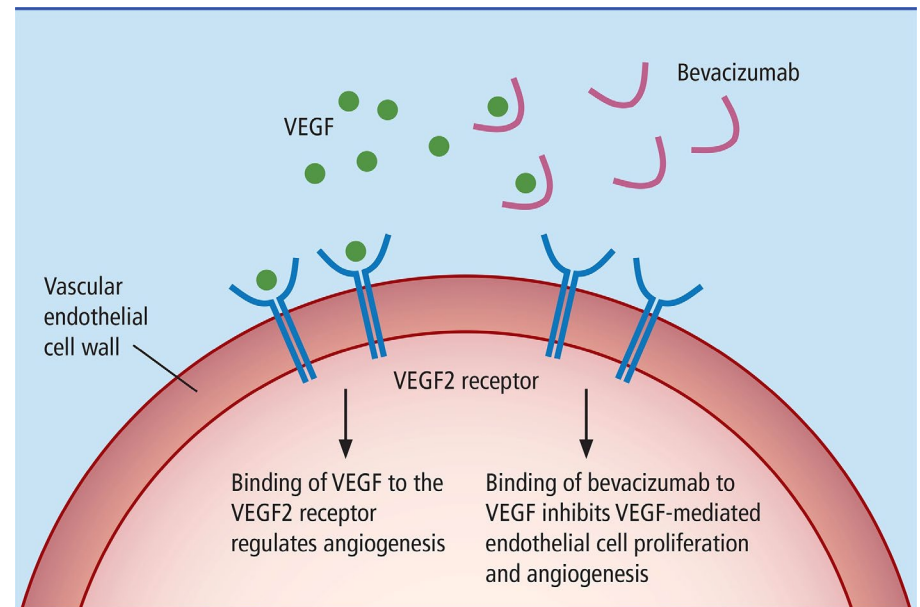
- Single Agent Chemotherapy
- Hormone Therapy
- Anti-Angiogenesis Agents
  - Bevacizumab

## The Benefits of Bevacizumab



# Bevacizumab

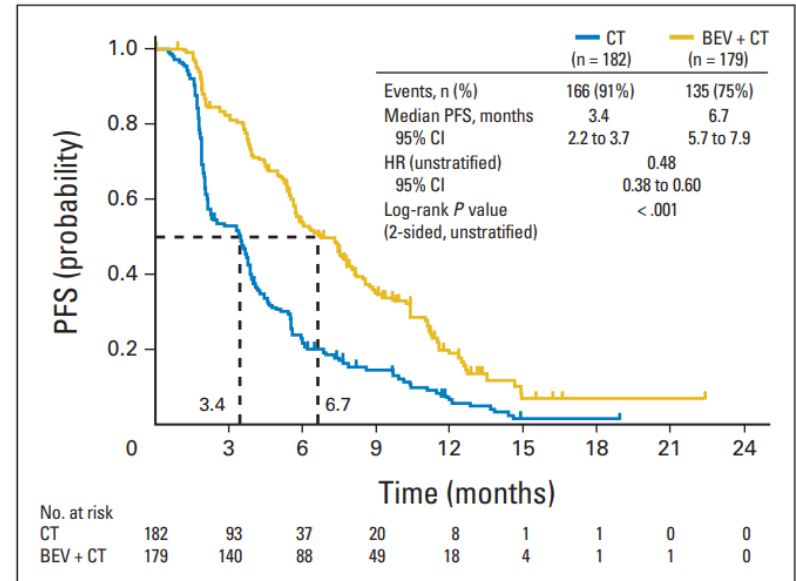
- Recombinant antibody directed against VEGF
- Prevents cancer from recruiting blood vessels
- "Starves" cancer



# AURELIA Trial

Pujade-Lauraine, et al. 2014

- Phase III Randomized Control Trial
- 361 Patients with Platinum Resistant Ovarian Cancer
- Two Arms
  - Chemotherapy
  - Chemotherapy + Bevacizumab



Improved Response Rate

Improved Duration of Response

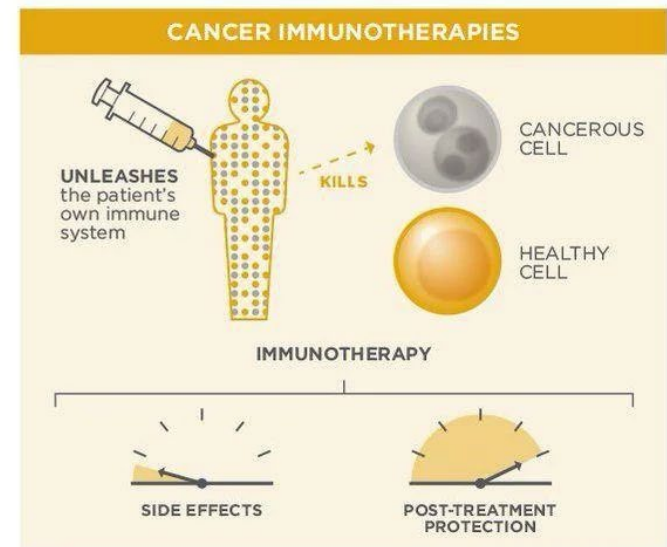
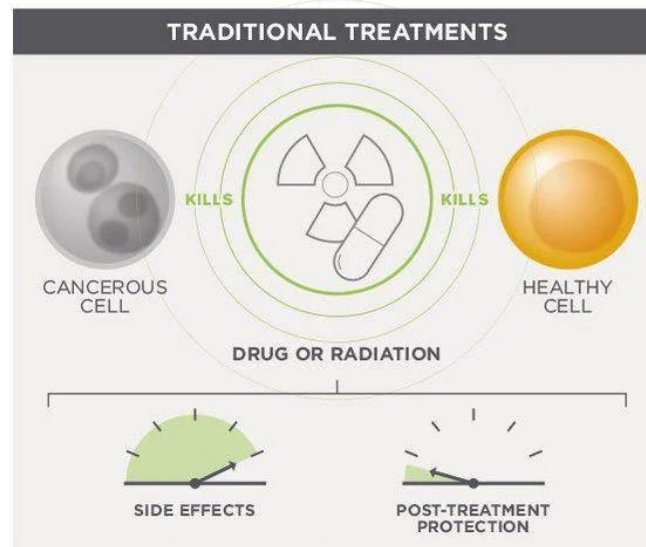


# Immune Therapies

# Immunotherapy

- Checkpoint Inhibitors
- Adoptive Cell Therapy
- Cytokine Therapy
- Vaccine Therapy
- Oncolytic Virus Therapy

## IMMUNOTHERAPY VS. CHEMOTHERAPY



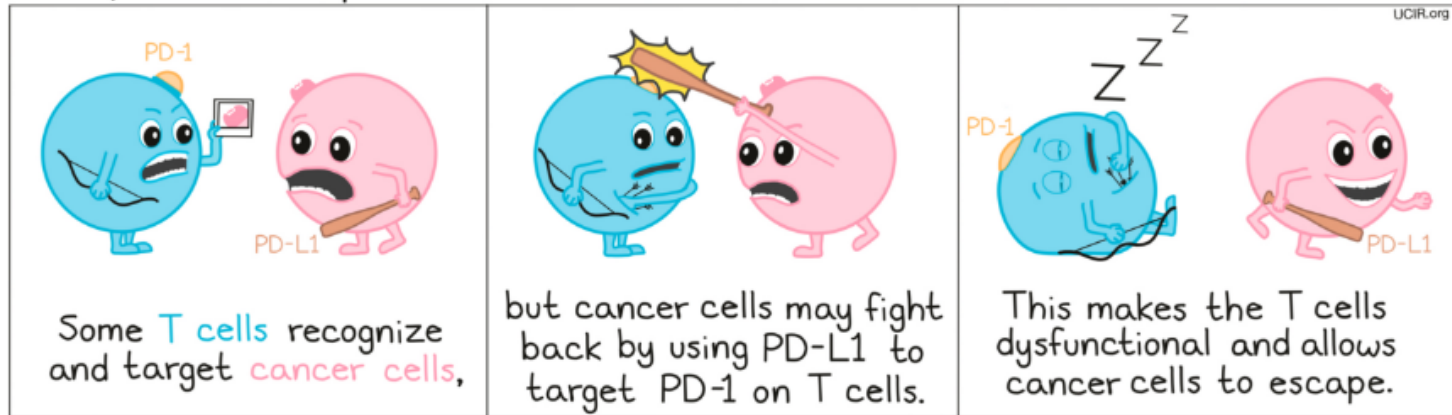
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# Immune Checkpoint Blockade (ICB)

Pembrolizumab, Nivolumab, Durvalumab, Dostarlimab, Atezolizumab, Avelumab

## PD-1/PD-L1 checkpoint



### Not Very Effective

- Single Agent ICB
- Chemotherapy + ICB

### Potentially Effective / Actively Studied

- ICB + PARP inhibitor
- ICB + Bevacizumab ± Chemotherapy
- ICB + other targeted therapy

# TOPACIO/KEYNOTE-162

Konstantinopoulos et al, JAMA Oncology 2019

60 patients

- 30 platinum Resistant
- 17 platinum Refractory

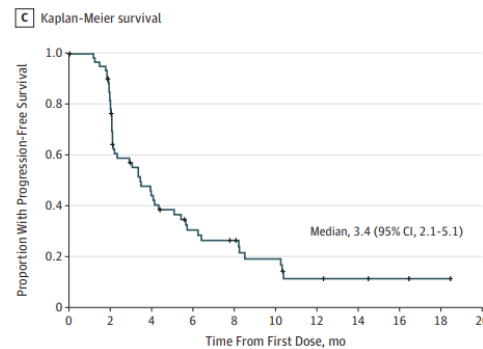
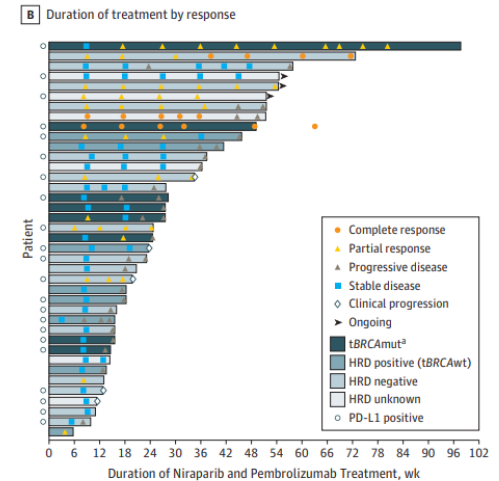
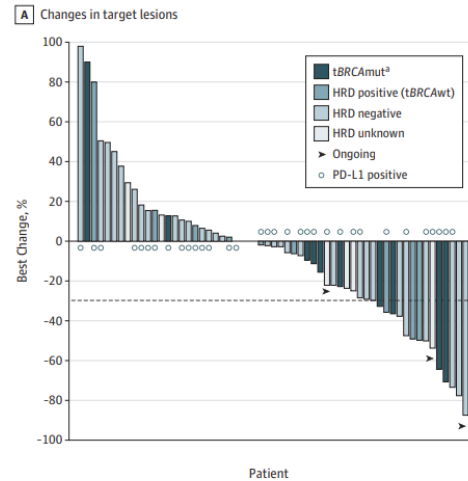
## Pembrolizumab and Niraparib

Response Rate: 18%

Disease Control Rate: 65%

Out of 11 Responders

- 8 had at least 6 months
- 4 had at least 9 months
- median duration of response not yet reached



# Pembrolizumab + Bevacizumab + Cyclophosphamide

Zsiros et al, JAMA Oncology 2021

40 patients

- 30 platinum Resistant

- 10 platinum Sensitive

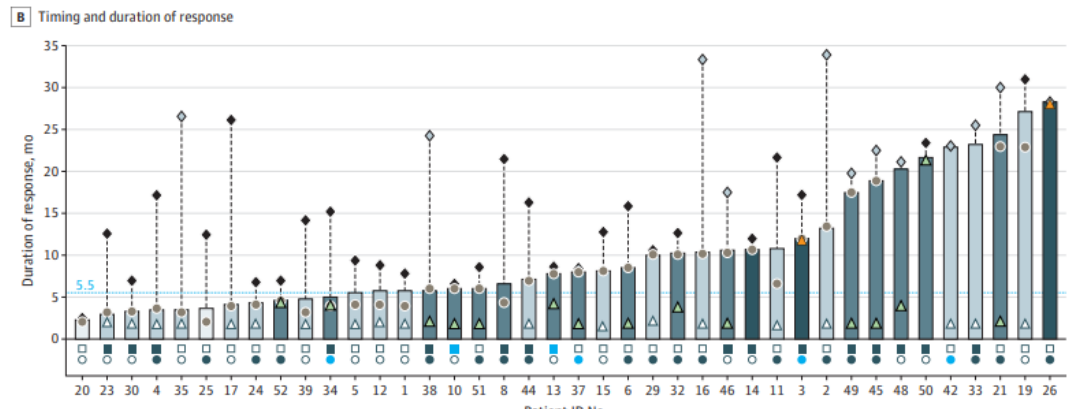
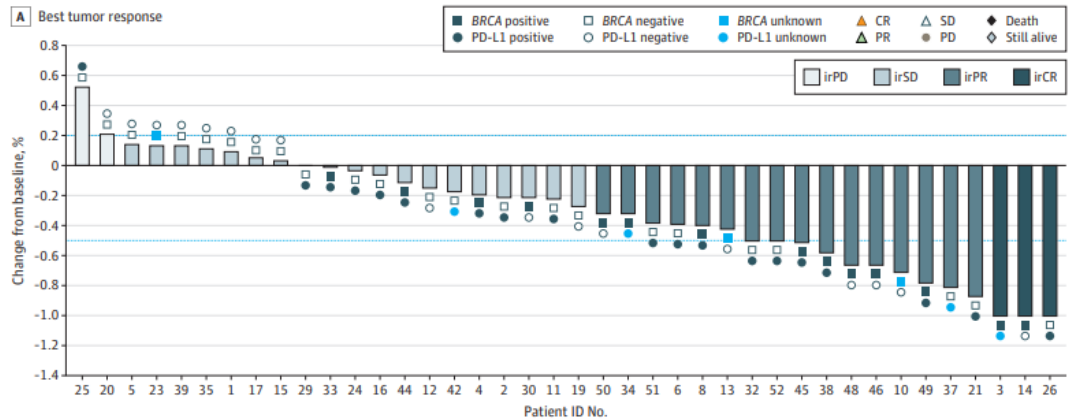
Response Rate: 47.5%

Disease Control Rate: 65%

3/3 Patients with complete Response were PR

13/19 Patients with partial Response were PR

Duration of Benefit > 8 months





# Somatic Tumor Testing

# Next Generation Sequencing (NGS)

## Somatic mutations

- Occur in *nongermline* tissues
- Cannot be inherited










Nonheritable

Mutation in tumor only  
(for example, breast)

- **Type of testing:** Somatic Testing
- **What is tested:** Uses a commercial panel to look for mutations in dozens of genes
- **When is it done:** Analysis is performed at the request of your oncologist. It is ordered from a prior surgical/biopsy specimen (\*usually no need for any more biopsies).
- **Significance:**
  - Unclear at this time
  - May offer new treatment options
    - Certain therapies target specific mutations
  - May provide prognostic information
  - May open eligibility to clinical trials

## GENOMIC VARIANTS

Biologically Relevant	Variant Allele Fraction
<b>CDKN2A</b> p.R58* Stop gain - LOF	74.1% 
<b>TP53</b> p.R273C Missense variant - LOF	42.0% 
<b>KDM6A</b> p.W1310* Stop gain - LOF	35.5% 
<b>TERT</b> c.-124C>T Variant - Promoter mutation	32.9% 
<b>FAT1</b> p.Q1334* Stop gain - LOF	32.3% 
<b>FAT1</b> p.Y1893* Stop gain - LOF	30.5% 
<b>TP53</b> p.R213Q Missense variant - LOF	19.9% 
<b>EGFR</b> Copy number gain	

## Germline - Pathogenic / Likely Pathogenic

No matched normal sample was received, therefore germline sequencing was not performed.

## IMMUNOTHERAPY MARKERS

Tumor Mutational Burden	Microsatellite Instability Status
<b>10.5 m/MB</b> 87th percentile	<b>Stable</b> Equivocal High

## FDA-APPROVED THERAPIES, CURRENT DIAGNOSIS

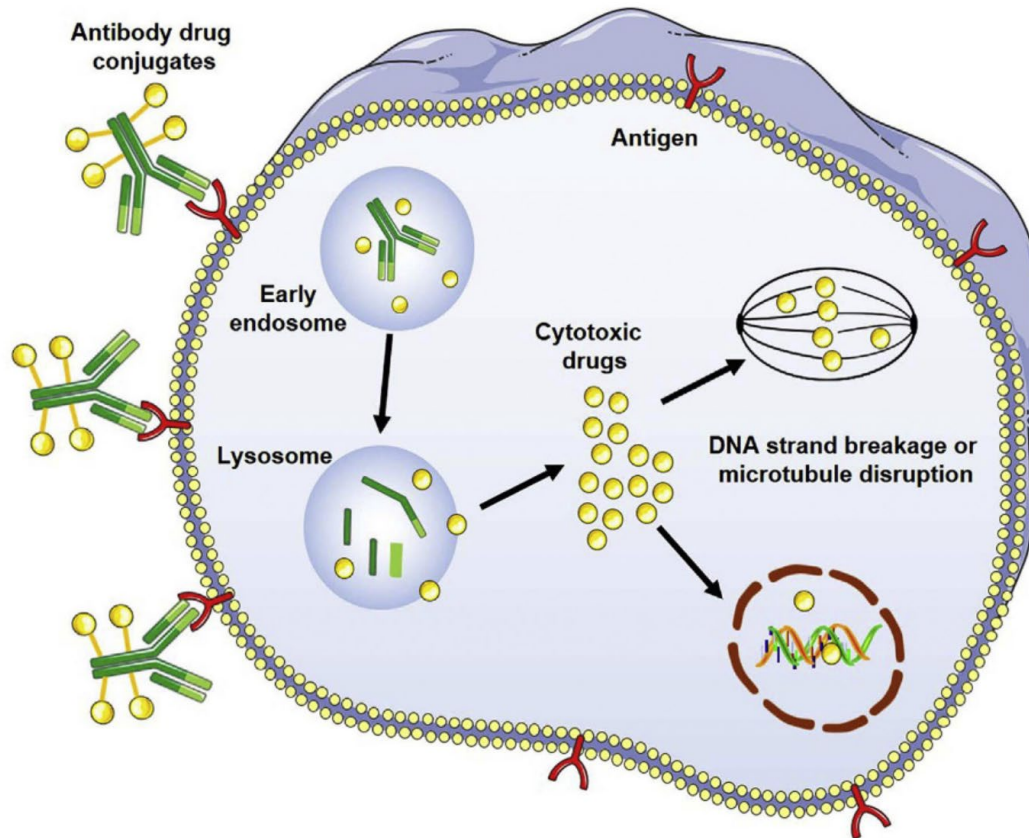
Anti-PD-1 MAb	<b>Pembrolizumab</b>	FDA, Consensus, Solid Tumors
		<b>MSK OncoKB, Level 1</b>
		High TMB

None of the therapies on this report were identified in the clinical notes received and abstracted by Tempus, which may not reflect the complete treatment history.



# Antibody Drug Conjugates

# Antibody Drug Conjugate



# Questions?

Thank You