

# Prima BioMed

## How will immune-intervention change medicine?

European Business Development Conference  
8 October 2014, Dresden, Germany



ASX:PRR; NASDAQ:PBMD; ISIN:US74154B2034



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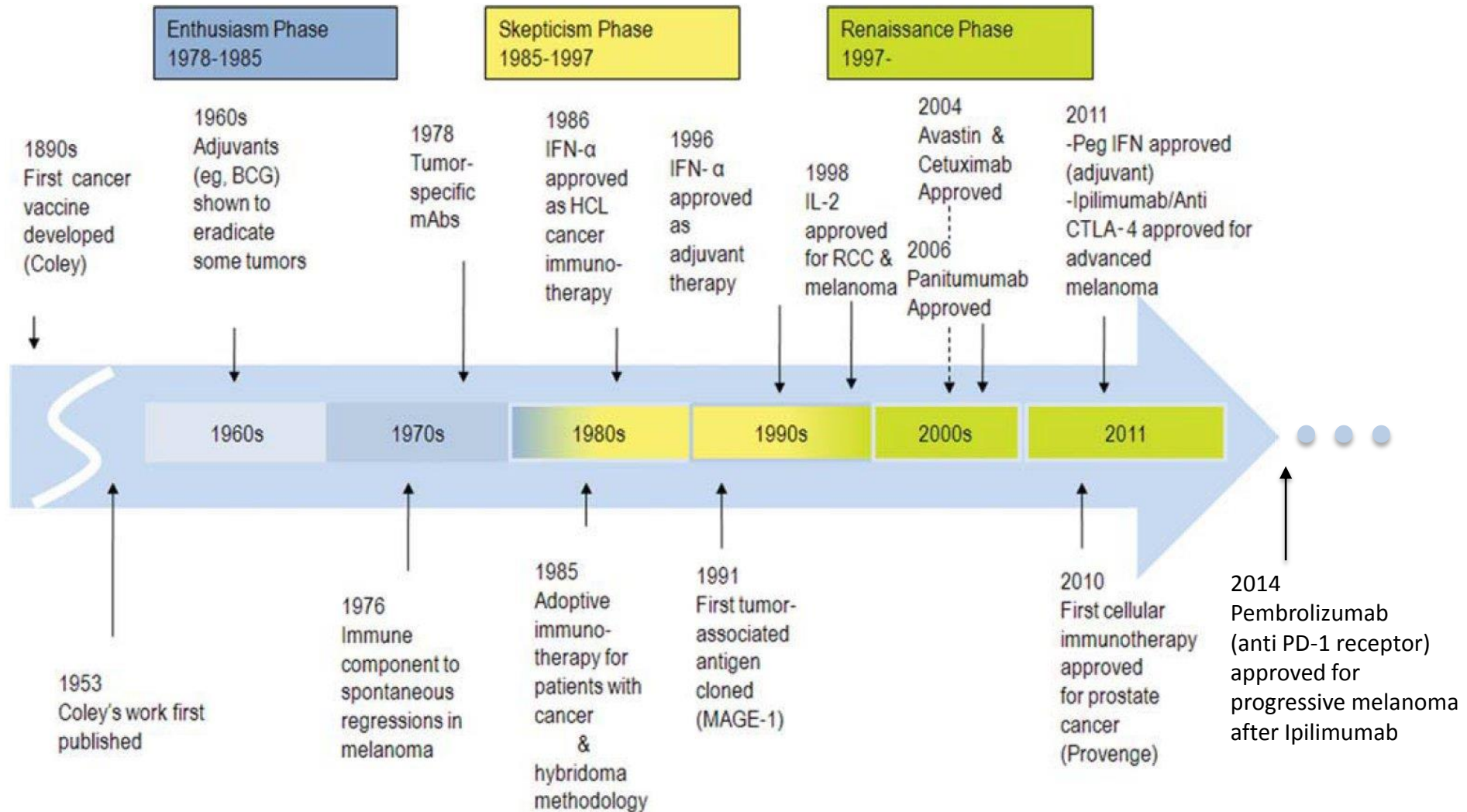
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# Outline

- History of cancer immunotherapy
- Modalities of immunotherapy
- Immunotherapy via dendritic cells (DCs)
  - Priming DCs *in-vivo*
  - Priming DCs *ex-vivo*
  - Clinical development of CVac™
- Combination therapy
- Challenges
- Summary

# History of cancer immunotherapy



# Breakthrough of the year 2013

- 2013 marked a turning point in cancer, as long-sought efforts to unleash the immune system against tumors are paying off.



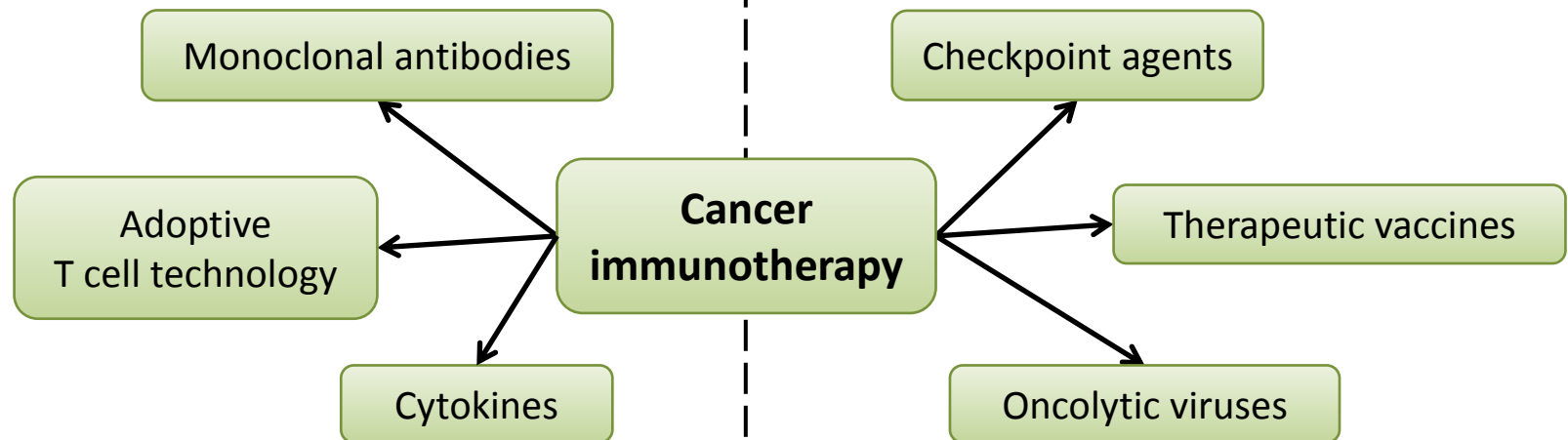
# Modalities of immunotherapy

## Passive immunotherapy

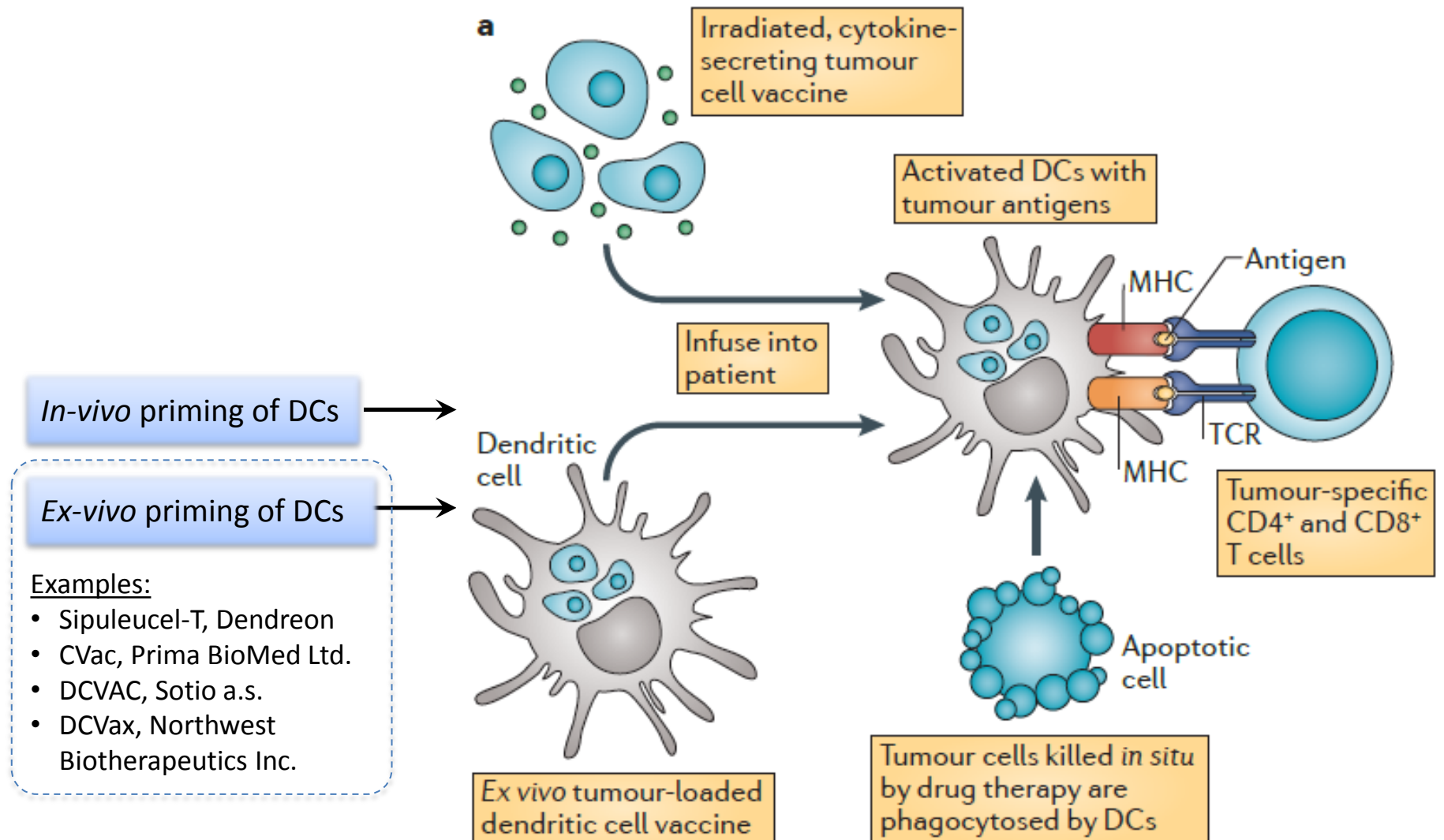
- Enhances pre-existing immune response
- No immunologic memory
- Short-lived effect, requires chronic treatment

## Active immunotherapy

- Stimulates host immune system
- Generates immunologic memory
- Durable effect after treatment is stopped



# Immunotherapy via dendritic cells



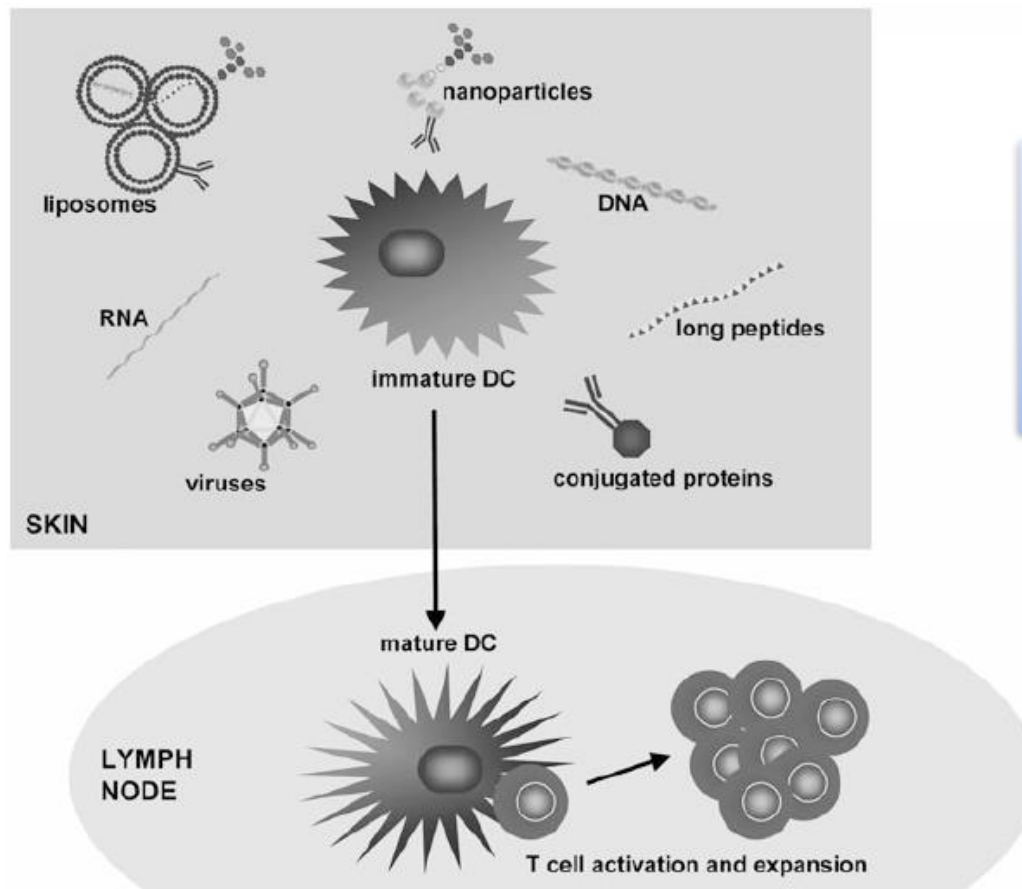
**In-vivo priming of DCs**

**Ex-vivo priming of DCs**

- Examples:
- Sipuleucel-T, Dendreon
  - CVac, Prima BioMed Ltd.
  - DCVAC, Sotio a.s.
  - DCVax, Northwest Biotherapeutics Inc.

# *In-vivo* priming of DCs

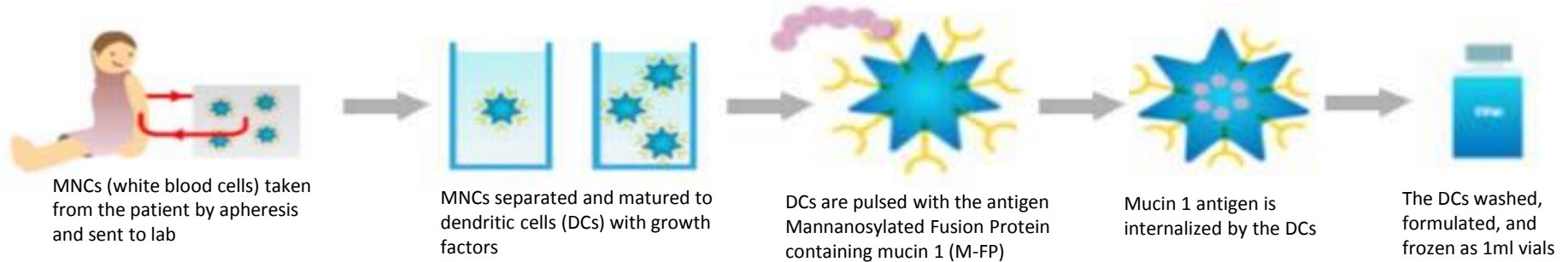
## ➤ Delivery Vehicles



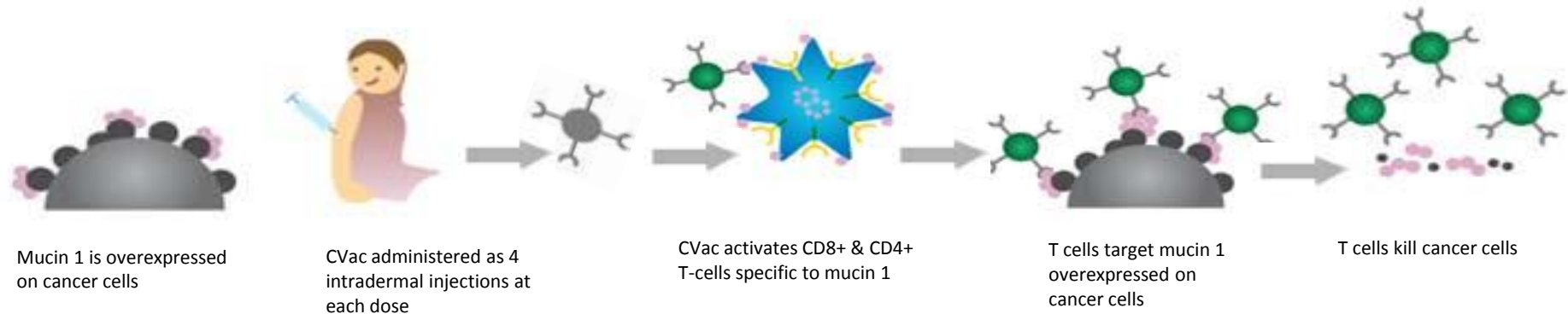
Upon capture, the DCs will start to mature and migrate towards the draining lymph nodes where an antigen specific T cell response can be induced

# Ex-vivo priming of DCs: CVac™

## Manufacturing of CVac

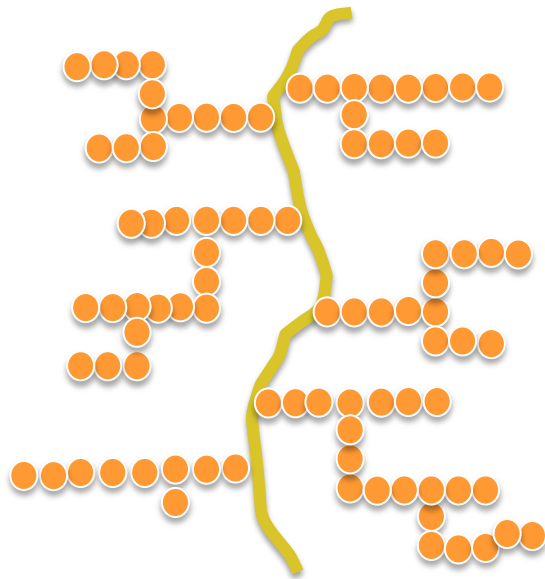


## Mechanism after injection



# Mucin 1: An optimal target for Immunotherapy

**Normal mucin**  
long, branched  
sugar chains



**Tumour mucin**  
fewer, short sugar  
chains; new epitopes  
are exposed



## MUC1 overexpressing cancers

Nasopharyngeal	100%
Lung (NSCLC)	99%
Breast	91%
Renal	84%
Ovarian	83%
Colorectal	81%
Pancreatic	81%
Prostate	79%
Myeloma	73%

# CVac clinical trials

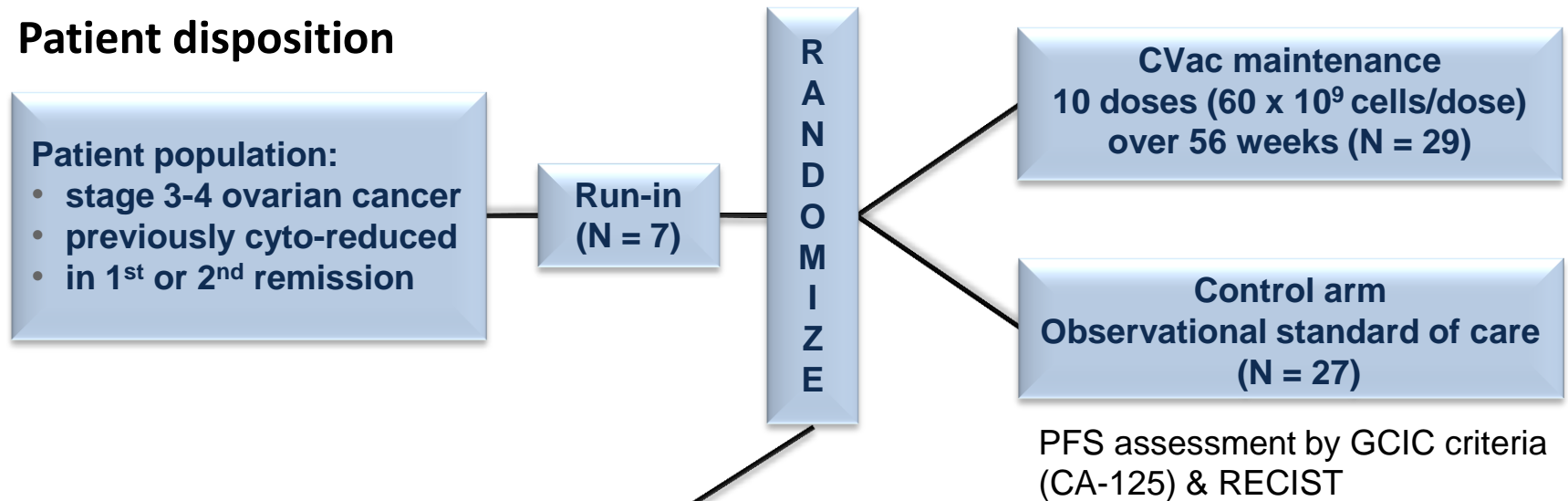
Protocol	N	Patient population	Main Objectives (✓ Accomplished)
Enrollment completed			
CAN-001 Phase 1	10	Incurable adenocarcinoma (single arm)	<ul style="list-style-type: none"> <li>✓ Safety</li> <li>✓ Feasibility</li> <li>✓ Immune response</li> </ul>
CAN-002 Phase 2	28	Ovarian cancer with no other treatment options (single arm)	<ul style="list-style-type: none"> <li>✓ Safety</li> <li>✓ Response by CA-125</li> </ul>
CAN-003 Phase 2	63	Ovarian cancer in 1 <sup>st</sup> or 2 <sup>nd</sup> remission (randomized & observation-only controlled)	<ul style="list-style-type: none"> <li>✓ Safety</li> <li>✓ Immune response</li> <li>✓ Progression-free survival</li> <li>○ Overall survival (est. 2014)</li> <li>✓ Manufacturing comparability</li> </ul>
CAN-003X	9	Extension of CAN-003 for patients who progressed	<ul style="list-style-type: none"> <li>○ Longer-term safety</li> <li>○ Case studies</li> </ul>
CAN-004(A) Phase 2	76	Ovarian cancer patients in 1 <sup>st</sup> remission (randomized & placebo-controlled)	<ul style="list-style-type: none"> <li>✓ Manufacturing comparability</li> <li>○ Safety</li> <li>○ Overall survival (primary)</li> <li>○ Immune monitoring</li> </ul>
Imminent trials			
CAN-004(B) Phase 2	210	Ovarian cancer patients in 2 <sup>nd</sup> remission (randomized & observation-only controlled)	<ul style="list-style-type: none"> <li>○ Overall survival (primary)</li> <li>○ Progression-free survival</li> <li>○ Immune monitoring</li> </ul>
CAN-301 Phase 2A	Up to 40	Resected pancreatic cancer patients (single arm pilot)	<ul style="list-style-type: none"> <li>○ Safety</li> <li>○ Overall survival (primary)</li> <li>○ Inform continued development</li> </ul>

# CAN-003: Study design

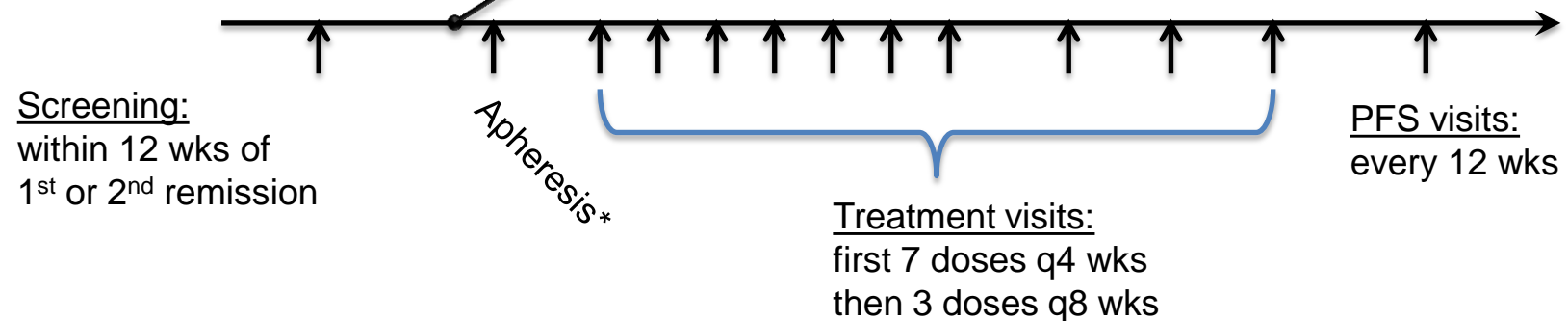
<b>Patients</b>	<ul style="list-style-type: none"><li>• Stage III or IV histologically confirmed epithelial ovarian, primary peritoneal or fallopian tube cancer</li><li>• Complete remission (CR) following surgical cyto-reduction and received first or second line conventional chemotherapy</li><li>• CA-125 <math>\leq</math> ULN with a prior history of an elevated CA-125</li></ul>
<b>Treatment</b>	<ul style="list-style-type: none"><li>• CVac group – 10 doses (60 million cells each) in 56 weeks</li><li>• Control – observation only (standard of care)</li></ul>
<b>Design</b>	<ul style="list-style-type: none"><li>• Randomized, open label, phase 2 trial</li><li>• Enrolled w/in 12 weeks of complete remission after 1<sup>st</sup> or 2<sup>nd</sup> line</li><li>• CVac dosing started within 10 weeks of enrollment</li><li>• Run-in with 7 non-randomized patients to establish manufacturing comparability (AU, US)</li><li>• 2 year observation period</li></ul>
<b>Endpoints</b>	<ul style="list-style-type: none"><li>• Primary: Safety and progression-free survival</li><li>• Secondary: Overall survival and Immune monitoring</li></ul>

# CAN-003: Schematic overview

## Patient disposition



## Visits



\* only performed in the CVac arm, within 3 wks after randomization

# CAN-003: Demographics

Characteristic	CVac (N = 29)	SOC (N = 27)
Remission status		
Achieved after first-line therapy	19 (66%)	17 (63%)
Achieved after second-line therapy	10 (34%)	10 (37%)
Disease stage		
III	24 (83%)	20 (74%)
IV	5 (17%)	7 (26%)
Histology subtype		
Serous	25 (86%)	23 (85%)
Endometrioid	1 (3%)	2 (7%)
Mucinous	1 (3%)	1 (4%)
Other (mixed, not specified)	2 (7%)	1 (4%)
Cytoreduction/debulking surgery		
Optimal	27 (93%)	23 (85%)
Suboptimal	2 (7%)	4 (15%)
Age years		
median (range)	58 (34-75)	49 (43-70)

# CAN-003: Safety

	N	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
1 <sup>st</sup> remission	32	9 (28%)	14 (44%)	7 (22%)	0 (0%)	0(0%)
SOC	14	5 (36%)	7 (50%)	1 (7%)	0 (0%)	0 (0%)
CVac	18	4 (22%)	7 (39%)	6 (33%)	0 (0%)	0 (0%)

2 <sup>nd</sup> remission	18	12 (67%)	3 (17%)	2 (11%)	0 (0%)	0 (0%)
SOC	10	7 (70%)	1 (10%)	1 (10%)	0 (0%)	0 (0%)
CVac	8	5 (63%)	2 (25%)	1 (13%)	0 (0%)	0 (0%)

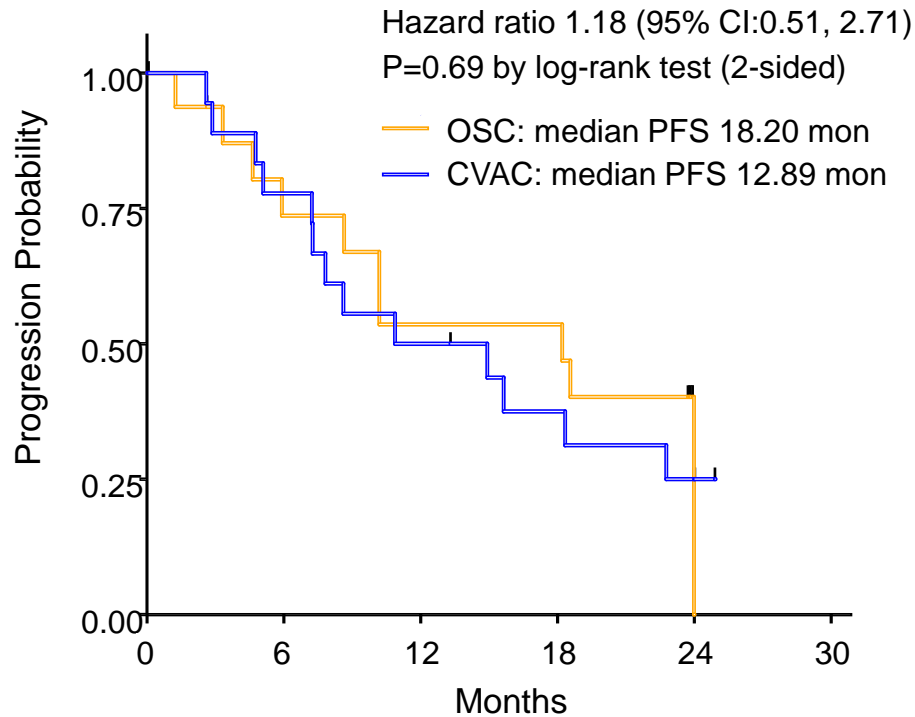
- **Common AEs - symptoms at injection site (localized pain, erythema, redness, swelling, burning), events of fatigue, lethargy, and dizziness were also reported as related to study agent**

# CAN-003: SAEs

Event	Outcome	Causality	Treatment
1. Small bowel obstruction	Recovered with treatment	Unrelated	Cvac
2. Abdominal pain, dehydration, nausea, vomiting	Recovered with treatment	Unrelated	SOC
3. Abdominal pain	Recovered	Unlikely Related	Cvac
4. Respiratory failure	Fatal	Unrelated	SOC
5. Small bowel obstruction	Recovered	Unrelated	Cvac
6. Febrile neutropenia	Recovered	Unrelated	Cvac
7. Surgical removal iliac node (hospitalization for progression)	Recovered with treatment	Unrelated	Cvac
8. Small bowel obstruction	Recovered	Unrelated	Cvac
9. Disease progression / laparoscopy	Recovered with treatment	Unrelated	Cvac

# CAN-003: Efficacy

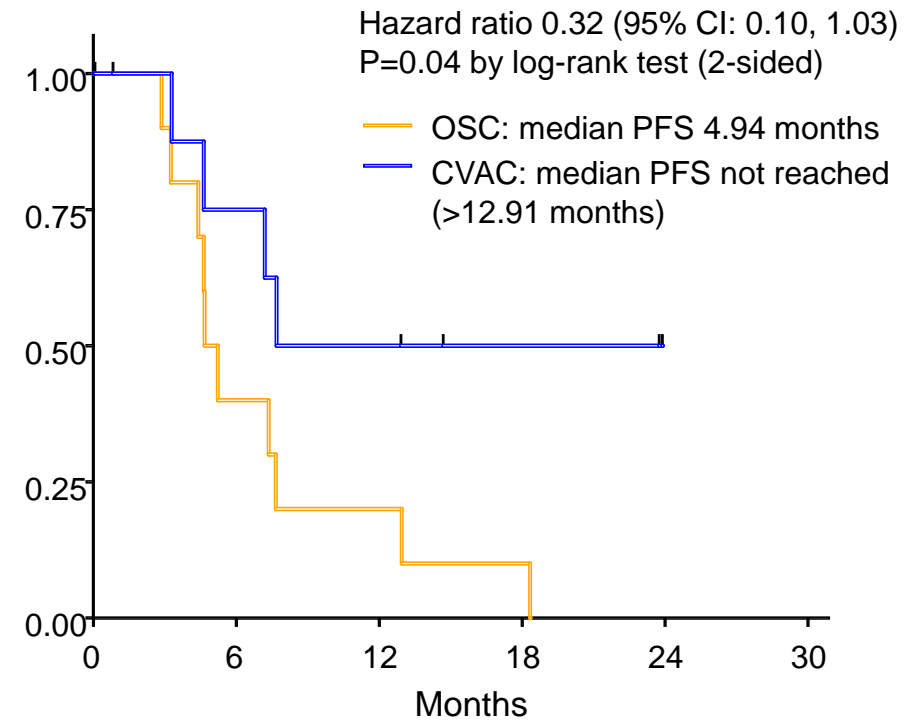
## PFS in 1<sup>st</sup> remission



OSC	4/17	3/11	0/8	3/8	0/0
CVAC	4/19	5/14	2/9	2/6	0/3

(#events/#at risk)

## PFS in 2<sup>nd</sup> remission

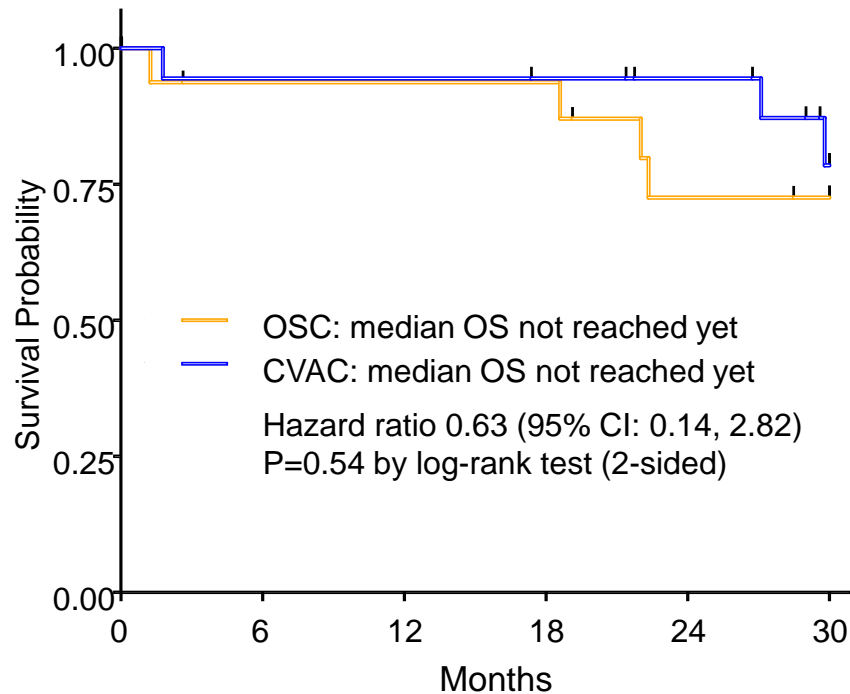


OSC	6/10	2/4	1/2	1/1	0/0
CVAC	2/10	2/6	0/4	0/2	0/0

(#events/#at risk)

# CAN-003: Efficacy (cont.)

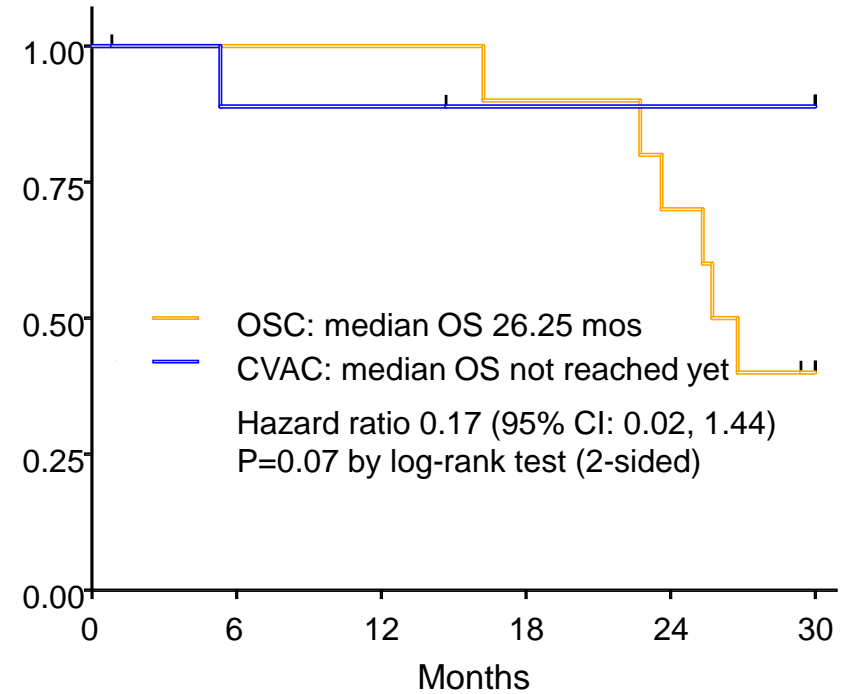
## OS in 1<sup>st</sup> remission



OSC	1/17	0/14	0/14	3/14	0/10
CVAC	1/19	0/17	0/17	0/16	2/14

(#events/#at risk)

## OS in 2<sup>nd</sup> remission



OSC	0/10	0/10	1/10	2/9	3/7
CVAC	1/10	0/8	0/8	0/7	0/7

(#events/#at risk)

# CAN-003: Immune monitoring

- ICS – intracellular cytokine staining
- CVac induces a T cell response that is mucin 1 specific (data not shown)

	CD4 IL-2	CD4 IL-4	CD4 IFNg	CD4 TNFa	CD4 IL-17
<b>1<sup>st</sup> remission</b>	*	*	*		
<b>2<sup>nd</sup> remission</b>	**	**	*		
<b>Overall</b>					
	CD8 IL-2	CD8 IL-4	CD8 IFNg	CD8 TNFa	CD8 IL-17
<b>1<sup>st</sup> remission</b>	*	**		**	
<b>2<sup>nd</sup> remission</b>		*		*	**
<b>Overall</b>		*	*		*

Wilcoxon test: \* P < 0.1, \*\* P < 0.05, blank spaces means non-significant

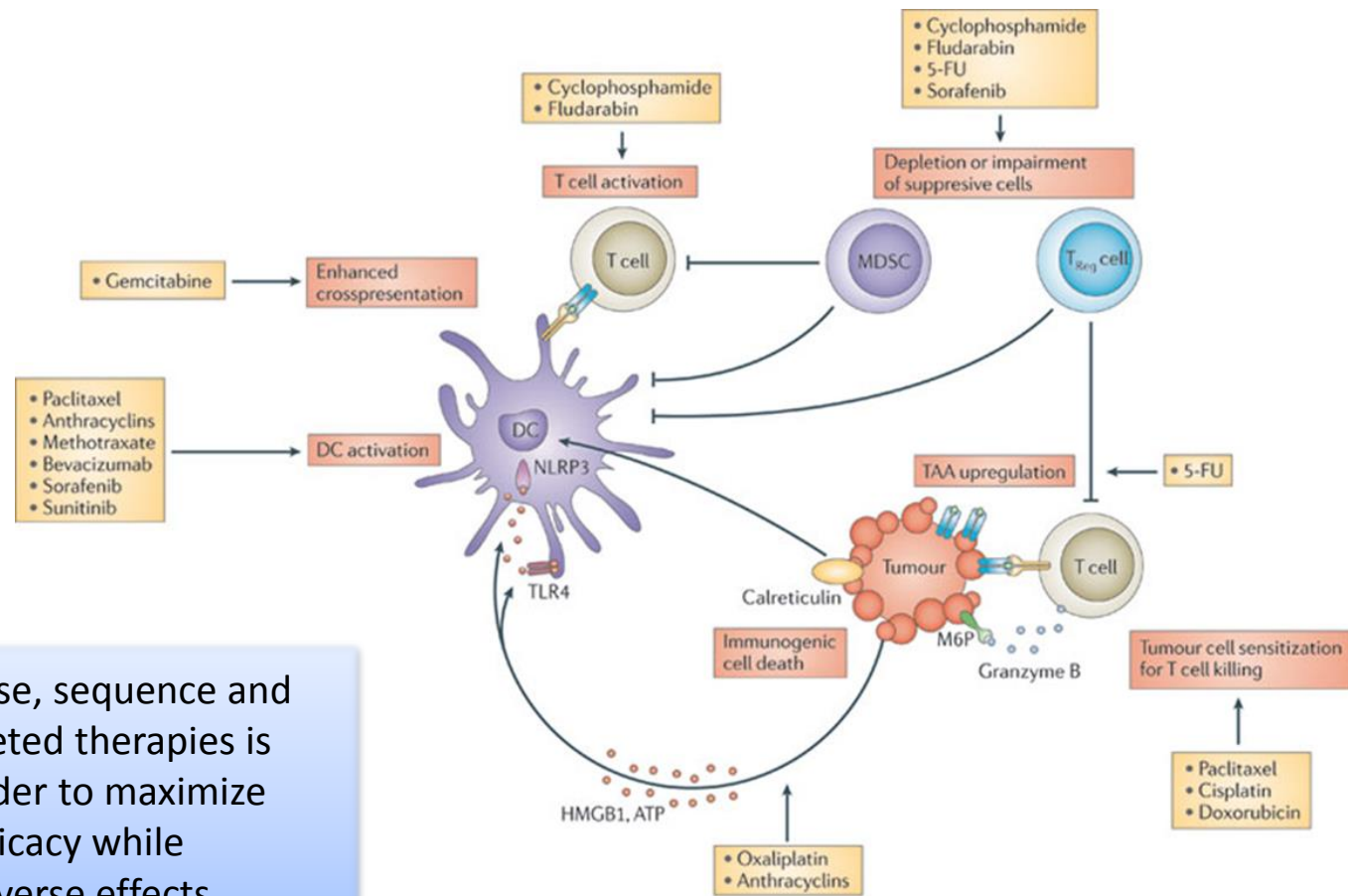
Table shows averaged analysis of baseline vs. values at completion of 3 doses CVac or end of treatment

# CAN-003: Conclusions

- Feasibility - Multinational manufacturing and delivery of CVac was established
- Safe - CVac was well tolerated with minimal toxicity
- Immunogenic - Mucin 1-specific T cell response in CVac treated patients
- PFS signal in second remission
- Interim OS signal in second remission

# Combination therapy

- Positive immunological effects of cytotoxic & targeted therapy



Optimizing dose, sequence and timing of targeted therapies is required in order to maximize anti-tumor efficacy while minimizing adverse effects.

# Challenges in the development of cancer immunotherapy

- Limitations of animal models to predict efficacy in humans
- Lengthy process to obtain approval for clinical trials
- Complexity of cancer, immune response, mechanisms of tumor-induced immunotolerance
- Lack of biomarkers for efficacy
- Current clinical response criteria inappropriate for assessment of immunotherapy (irRC vs. RECIST)
  - Response to immunotherapy is possible in the presence of increased/new lesions

# Summary

- Immunotherapy is a new class of cancer treatment
- Because of the immune system's unique properties, these therapies hold great potential
  - long-term protection against the disease
  - benefit to a variety of cancer types
  - few side effects
- Therapeutic synergy with targeted agents to improve clinical outcomes

Thank you for your attention!