Nadofaragene Firadenovec and Oportuzumab Monatox for BCG-Unresponsive, Non-Muscle Invasive Bladder Cancer: Effectiveness and Value

Public Meeting — November 20, 2020

Meeting materials available at: https://icer-review.org/topic/bladder-cancer/

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Why are we here today?

To this day, when I think about receiving the news, I still have this sinking feeling. When you hear that, it can mean the potential for a very limited lifetime.

And here I was getting ready to slow down and take some time off and be with my grandchild, and now I had a potential death sentence.

Bladder Cancer Patient

Why Are We Here Today?

- What happens the day these treatments are approved by the FDA?
- What happens to patients and others in the health care “system”?

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When There Isn’t Enough Money For Health Insurance

Gustavo Bendeck, Lubbock, Texas

The Whitmans, Bird City, Alaska

Luke Breen, Minneapolis, Minnesota

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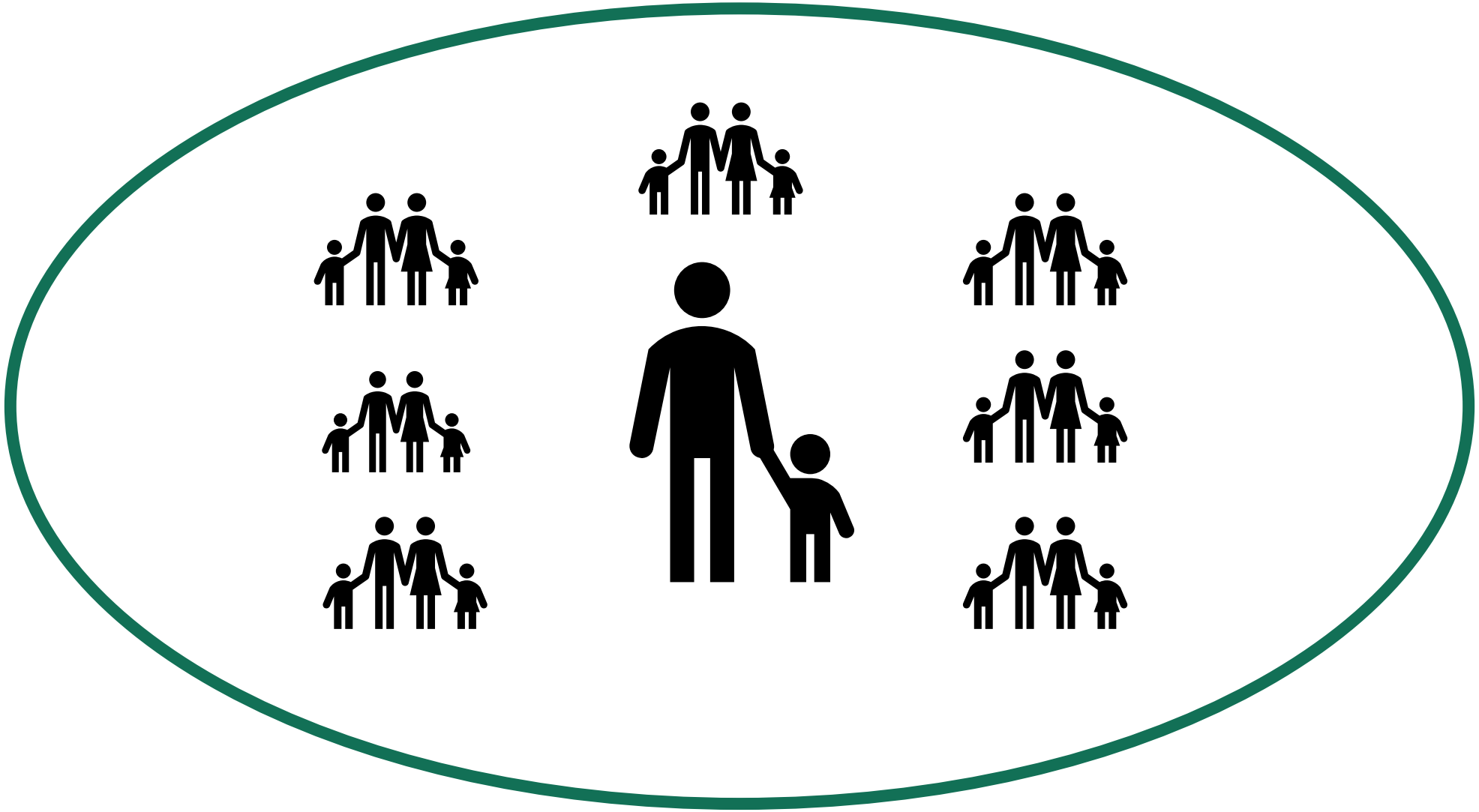

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Organizational Overview

- The Midwest Comparative Effectiveness Public Advisory Council (CEPAC)
- The Institute for Clinical and Economic Review (ICER)

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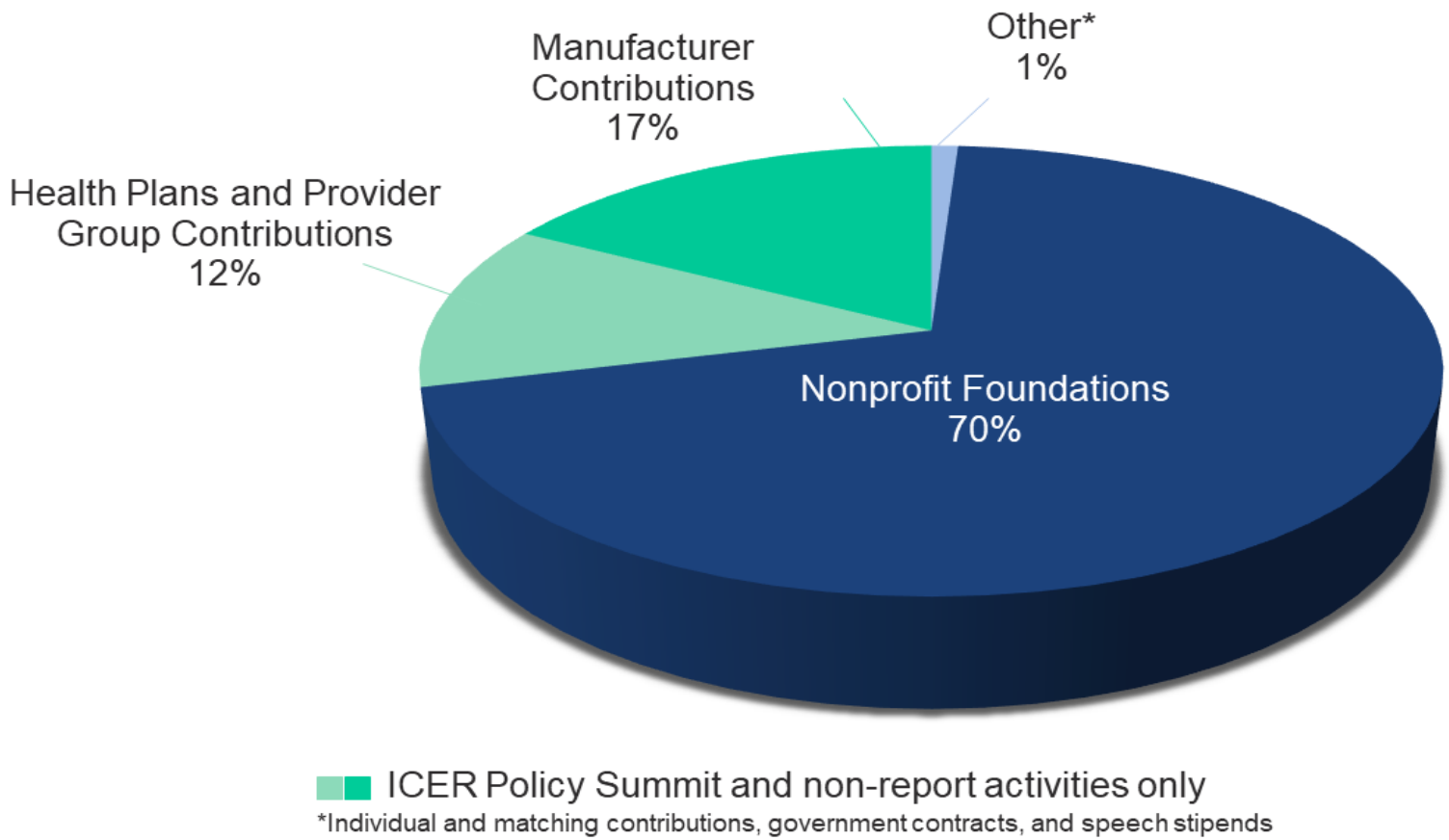
Sources of Funding, 2020

https://icer-review.org/about/support/



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How was the ICER report developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Illinois at Chicago cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - Rick Bangs, MBA, PMP, Bladder cancer patient advocate
  - Aaron Mitchell, MD, MPH, Medical Oncologist, Memorial Sloan Kettering Cancer Center
  - Angela Smith, MD, MS, Director of Urologic Oncology, UNC School of Medicine
- How is the evidence report structured to support CEPAC voting and policy discussion?

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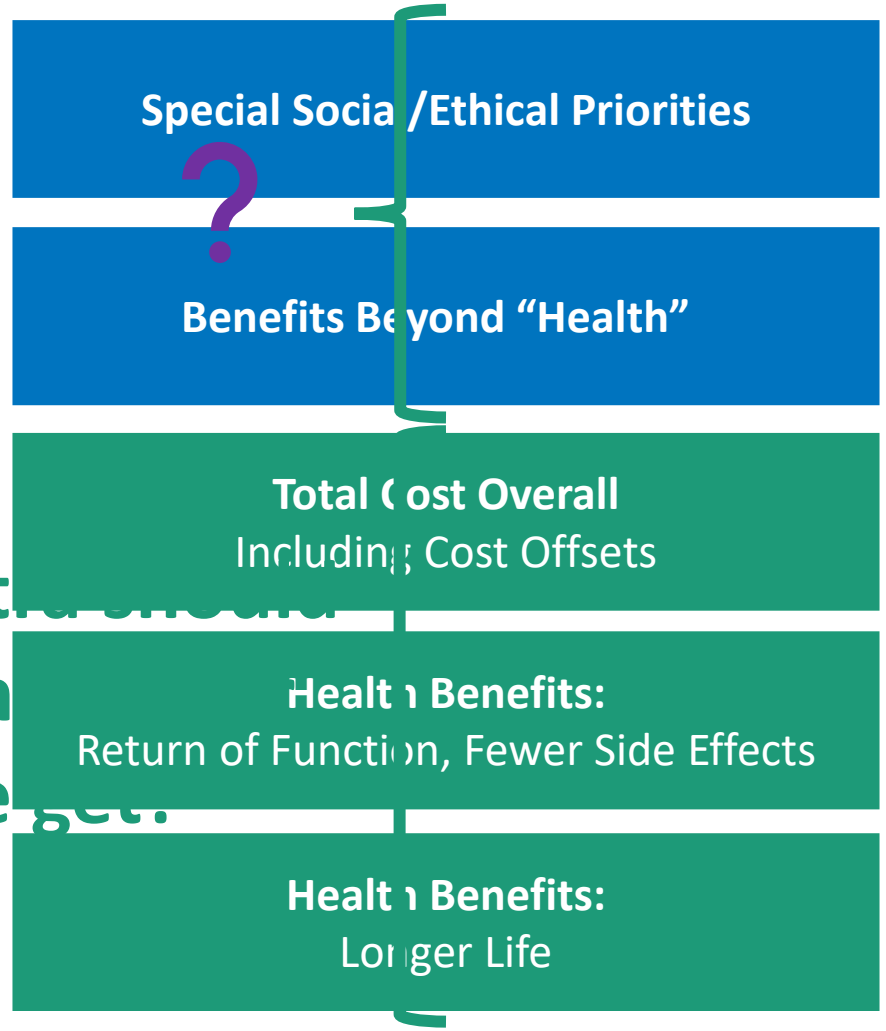
Components of Long-Term Value for Money



How much extra should we pay for th health we get?

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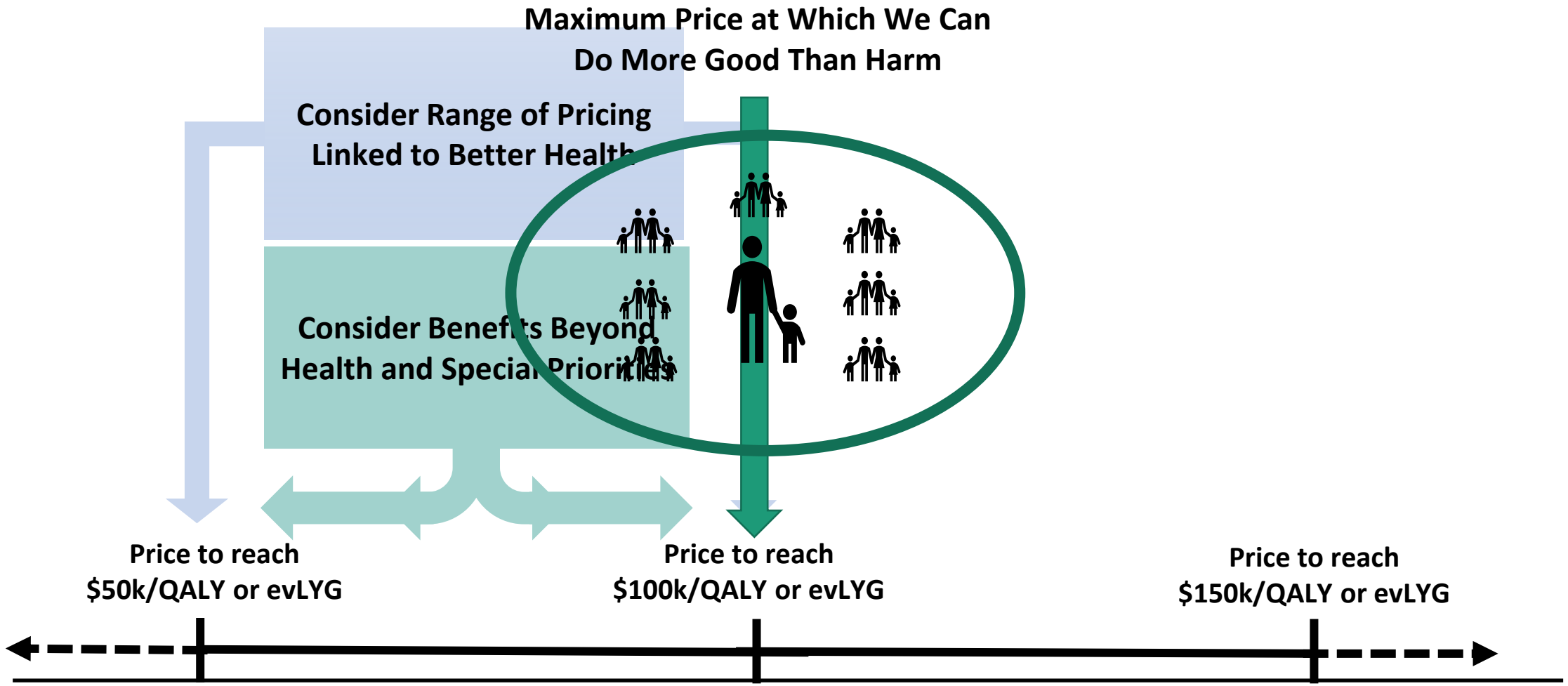
Cost Effectiveness as a Part of Pricing to Value



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Agenda

Time (CT)	Activity
9:00am – 9:20am	**Meeting Convened and Opening Remarks** Steven D. Pearson, MD, MSc, President, ICER
9:20am – 9:40am	**Presentation of the Clinical Evidence** Steven J. Atlas, MD, MPH Director, Primary Care Research & Quality Improvement Network, Massachusetts General Hospital; Associate Professor of Medicine, Harvard Medical School
9:40am – 10:10am	**Presentation of the Economic Model** Daniel R. Touchette, PharmD, MA University of Illinois at Chicago College of Pharmacy
10:10am – 10:30am	**Public Comments and Discussion**
10:30am – 10:45am	**Break**
10:45am – 11:45am	**Midwest CEPAC Vote on Clinical Effectiveness and Value**
11:45am – 12:30pm	**Lunch Break**
12:30pm – 1:30pm	**Policy Roundtable**
1:30pm – 2:00pm	**Reflections from Midwest CEPAC**
2:00pm	**Meeting Adjourned**

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Clinical and Patient Experts

Stephanie Chisolm, PhD, Director of Education and Research, Bladder Cancer Advocacy Network (BCAN)

- *BCAN recieves funding from FerGene and Merck.*

Karen Sachse, RN, MSN, Patient Advocate

- *Karen Sachse has recieved honorium for participating in a patient focus group for FerGene.*

John L. Gore, MD, MS, FACS, Department of Urology, University of Washington

- *Dr. Gore is an investigator for research sponsored by FerGene Pharmaceuticals unrelated to this review.*

Aaron P. Mitchell, MD, MPH, Medical Oncologist, Memorial Sloan Kettering Cancer Center

- *No financial conflicts to disclose.*

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Presentation of the Clinical Evidence

Steven J. Atlas, MD, MPH

Physician / Associate Professor of Medicine

Massachusetts General Hospital / Harvard Medical School

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Key Collaborators

- **Steven J. Atlas, MD, MPH**
  Director, Primary Care Practice Based Research Network, MGH
- **Molly Beinfeld, MPH**
  Research Lead, Evidence Synthesis, ICER
- **Avery McKenna**
  Research Assistant, Evidence Synthesis, ICER
- **Kanya Shah, PharmD**
  Evidence Synthesis Intern, ICER

Disclosures:

We have no conflicts of interest relevant to this report.

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Background: NMIBC

Burden of disease

- Bladder cancer is the 6th most common cancer in the US
- 80,000 new cases each year and 17,700 deaths
- Estimated cost of health care is $4-5 billion annually
- 70% are classified as non-muscle invasive bladder cancers (NMIBC)

Presentation and Symptoms

- Blood in the urine (hematuria), either visible or detected via urinalysis
- Changes in urinary frequency, pain/discomfort during urination

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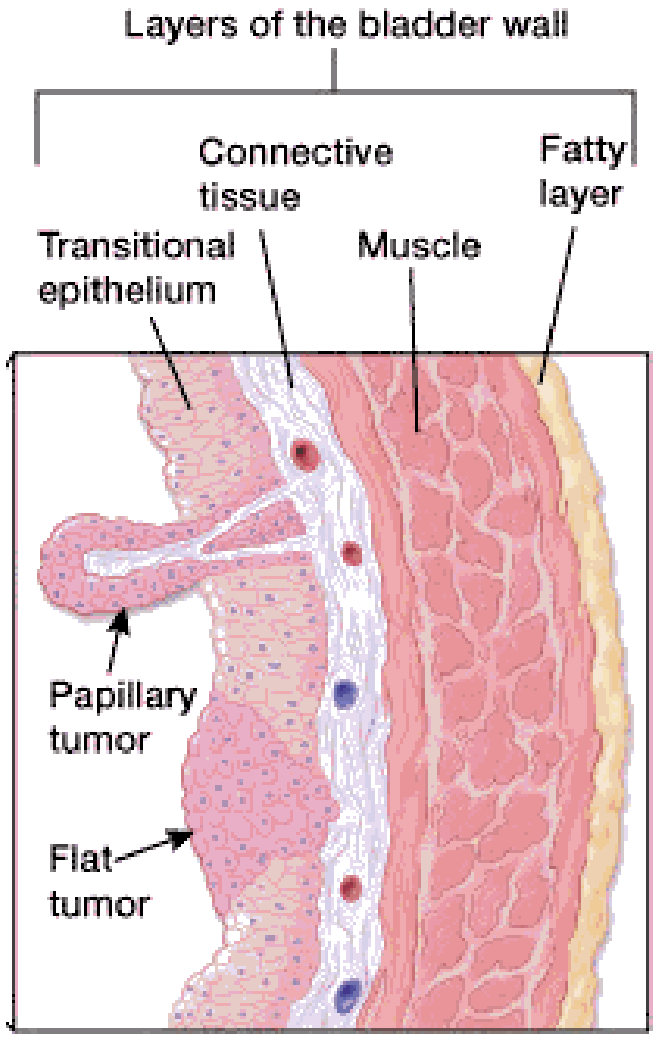
Background: NMIBC

Evaluation

- Fiberoptic scope test of bladder (cystoscopy): biopsy specimen
  - Carcinoma in situ (CIS): 70%
  - Papillary disease (Ta): 20%
  - Superficial invasion (T1): 10%
- Other tests: Urine for cancer cells (cytology) and imaging (CT scan)

Initial Treatment

- Removal of visible tumor (transurethral resection of bladder tumor – TURBT)
- Bladder instillation (intravesical) of chemotherapy



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Treatment of BCG-unresponsive NMIBC

- For those with high risk NMIBC, a course of intravesical Bacillus Calmette Guerin (BCG) or other chemotherapy is recommended
- For patients treated with BCG who have refractory disease or relapse (BCG-unresponsive NMIBC):
  - Cystectomy is often recommended because it is usually curative, but many patients decline and others are not surgical candidates
  - Non-surgical treatments include intravesical chemotherapy (e.g., gemcitabine with or without docetaxel), or systemic pembrolizumab (PD-1 receptor immunotherapy)
- However, current bladder-sparing options all have low response rates and frequent relapse, underscoring the need for new treatments

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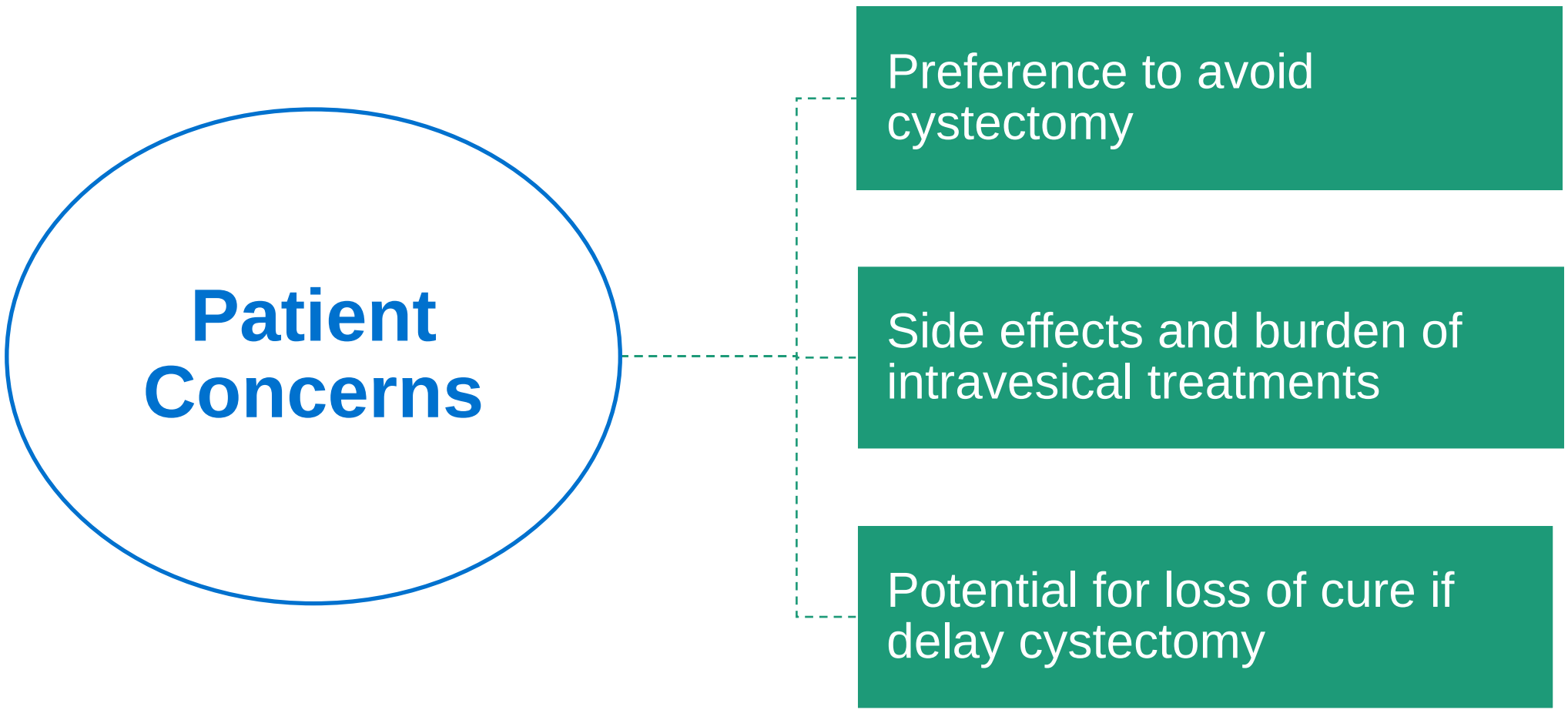
What Patients and Advocates Told Us



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Scope of Review

- To evaluate the clinical effectiveness of nadofaragene firadenovec (Adstiladrin®) and oportuzumab monatox (Vicineum™) for BCG-unresponsive NMIBC in two populations:
  - Population 1: Carcinoma in situ (CIS) ± Ta/T1
  - Population 2: High grade (HG) Ta/T1 disease alone
- Comparators:
  - Systemic pembrolizumab (population 1 only)
  - Gemcitabine with or without docetaxel (populations 1 and 2)

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Interventions

1. Nadofaragene firadenovec (Adstiladrin®):

- Nonreplicating recombinant adenovirus vector encoding human interferon alfa-2b gene with Syn3, a polyamide surfactant, to enhance transfer into cancer cells
- Instilled intravesically every three months
- In May 2020, FDA issued a complete response letter requesting additional information regarding manufacturing

2. Oportuzumab monatox (Vicineum™):

- Recombinant fusion protein with anti-epithelial cell adhesion molecule (EpCAM) antibody linked to *Pseudomonas* exotoxin A that binds and releases toxin into the cell
- Instilled twice weekly for six weeks, weekly for six weeks and then every two weeks
- A rolling Biologics License Application (BLA) was submitted to FDA in December 2019

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Key Clinical Outcomes

- Primary
  - Complete response (CR): for CIS disease
  - High-grade recurrence free survival (HGRFS): for CIS with a CR or completely resected Ta/T1 disease alone
- Secondary
  - Duration of response
  - Progression to muscle invasive bladder cancer (MIBC)
  - Radical cystectomy

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Clinical Evidence

Key Phase III Single-Arm, Open-Label Clinical Trials of Nadofaragene and Oportuzumab

Nadofaragene (n=157):

- 68% CIS ± Ta/T1; 32% high grade (HG) Ta/T1 only
- 82% male; median age 71 years
- 96% had 2+ BCG courses
- 12-month outcome: required all patients to have a biopsy

Oportuzumab (n=133):

- 70% CIS ± Ta/T1; 30% HG Ta/T1 only
- 77% male; median age 73.5 years
- 100% had 2+ BCG courses

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Key Phase II Single-Arm Open-Label Clinical Trial of Pembrolizumab

- Keynote-057 (n=96):
  - 100% CIS ± T1/Ta
  - Patients must have declined or been ineligible for cystectomy
  - 84% male; median age 73

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Selected Trials of Gemcitabine ± Docetaxel (of 15 trials)

Trials	Outcomes	Baseline Characteristics
Dalbagni 2006 **N=30** **Phase II single arm**	• CR • RFS (any type)	• 77% CIS ± HG Ta/T1 • 20% HG Ta/T1 only • 73% Male; median age 70 years
Skinner 2013 **N=47** **Phase II single arm**	• CR • RFS (any type)	• 60% CIS ± HG Ta/T1 • 30% HG Ta/T1 only • 10% Low Grade (LG) Ta/T1 only • 65% Male; mean age 69.3 years
Steinberg 2020 **N=276** **Retrospective chart review**	Primary: • RFS (any type) Secondary: • HGRFS • Progression	• 62.7% CIS ± Ta/T1 • 26% HG Ta/T1 • 11% LG Ta/T1 • 81% Male; median age 73 years

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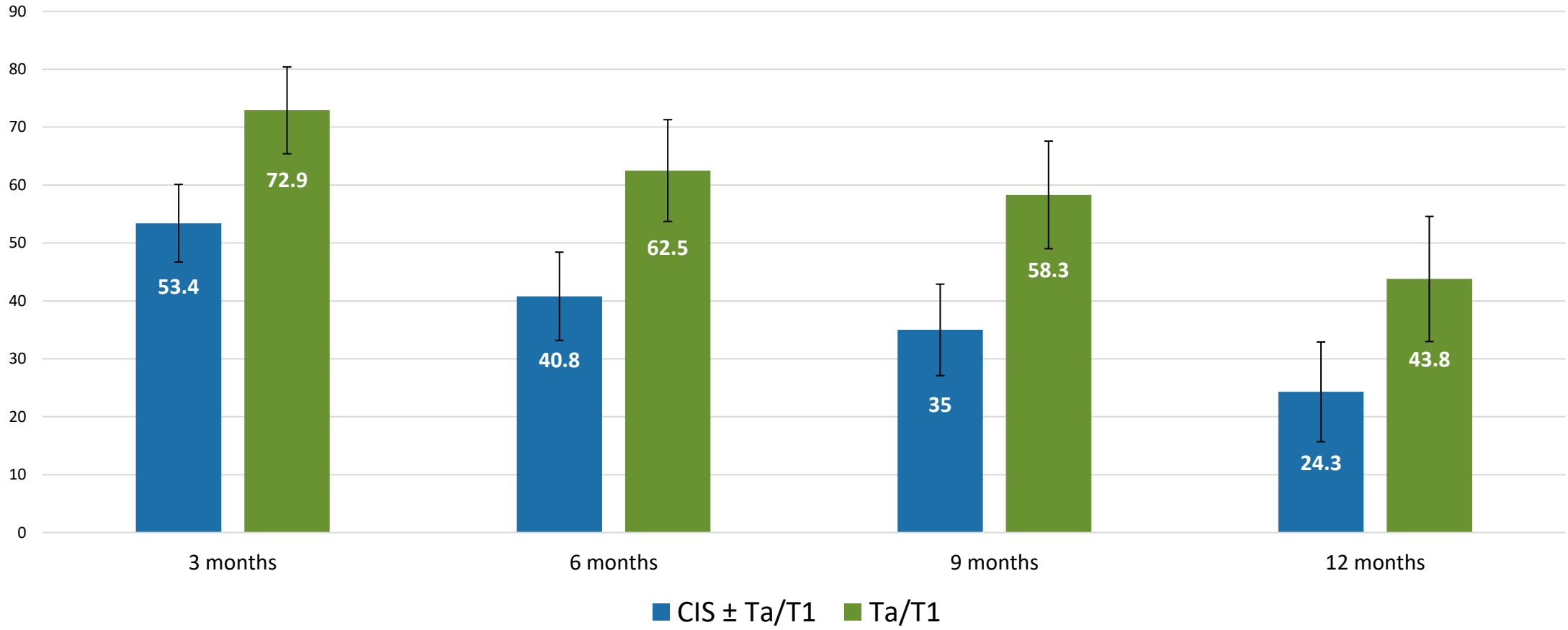
RESULTS: Phase III Trial Nadofaragene (n=151)

Complete Response/High Grade Recurrence Free Survival (%)



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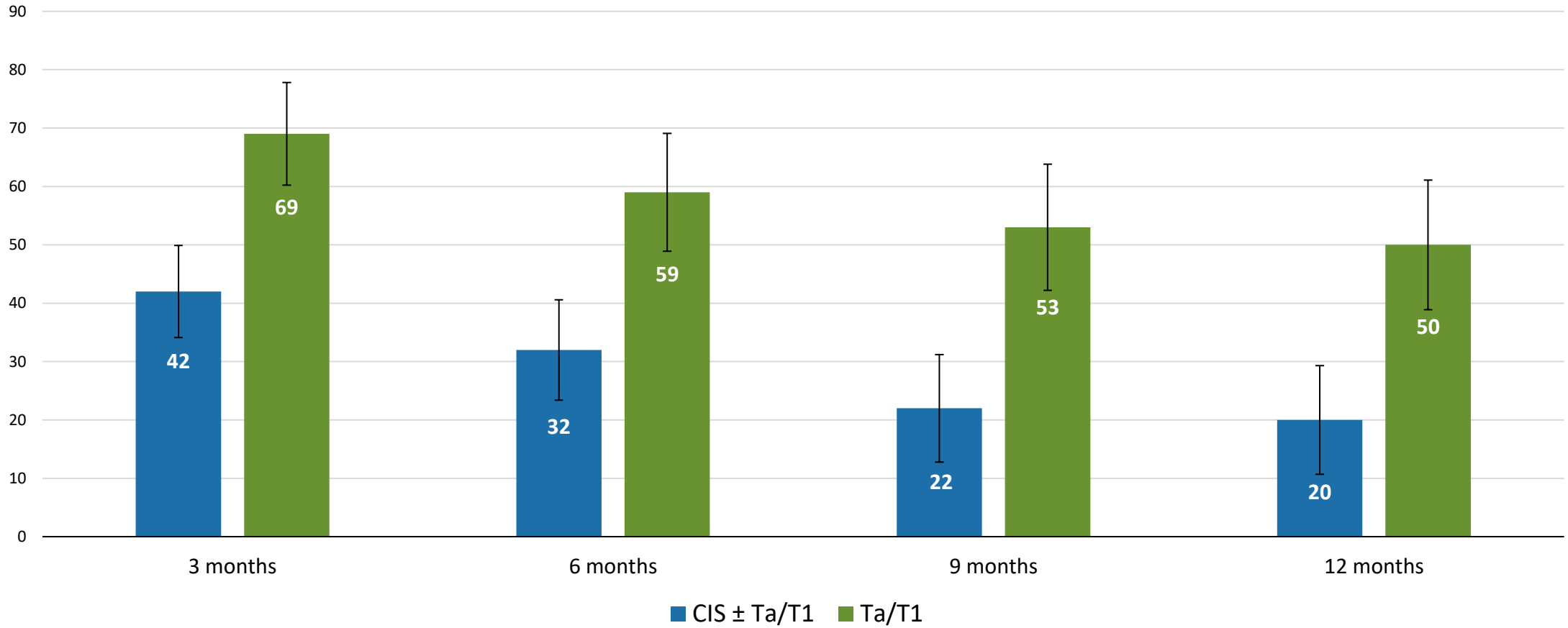
RESULTS: Phase III Trial Oportuzumab (n=133)

Complete Response/High Grade Recurrence Free Survival (%)



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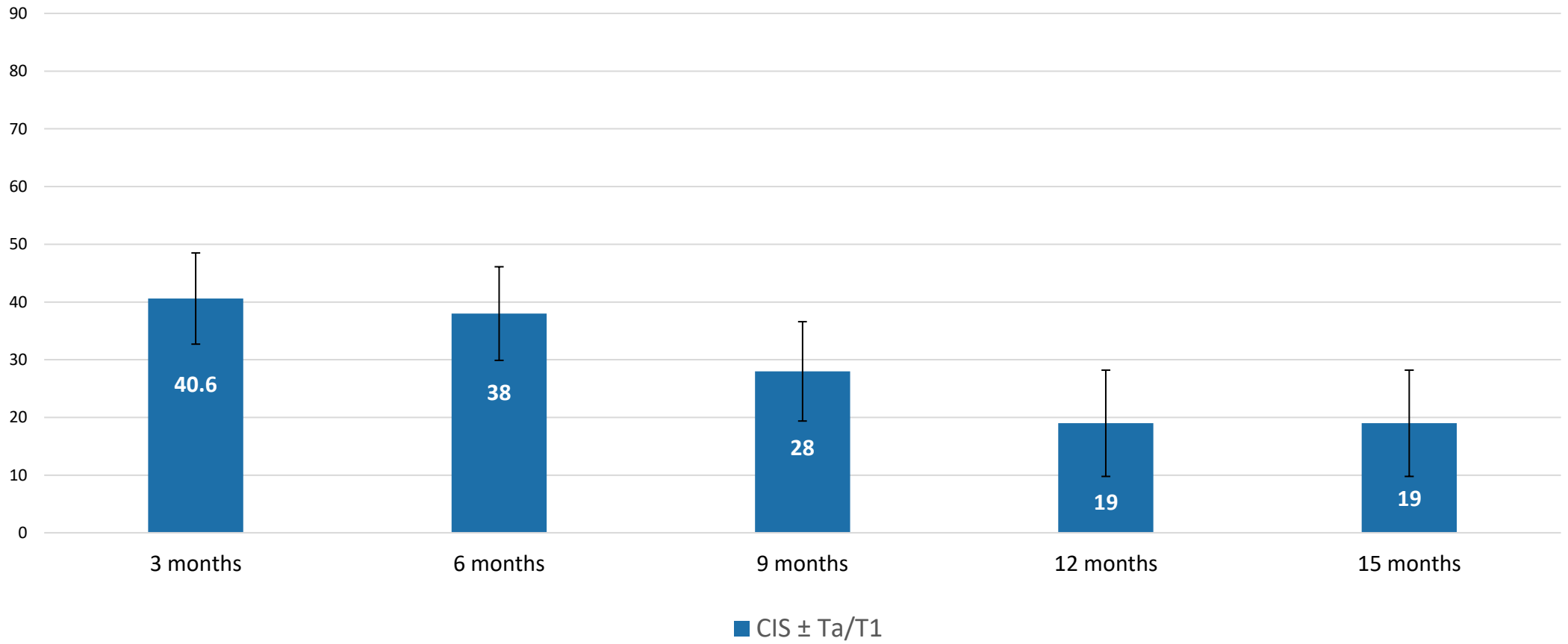
RESULTS: Phase II Trial Pembrolizumab (n=96)

Complete Response (%), CIS ± Ta/T1



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Results: Gemcitabine ± Docetaxel

- **Gemcitabine:** In the mixed CIS and Ta/T1 study populations for two phase II studies of gemcitabine, recurrence free survival (of any type) at 12 months was 21-28%
- **Gemcitabine ± Docetaxel**: In the retrospective study of sequential gemcitabine and docetaxel, HGRFS at 12 months was 60% in the CIS population and 69% in the HG Ta/T1 population

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Patient-Important Outcomes – Progression to Muscle-Invasive Bladder Cancer (MIBC) and Cystectomy

Interventions	Progression to MIBC	Cystectomy
Nadofaragene	5.3%	NR
Oportuzumab	4%	24%
Pembrolizumab	0%	37.5%
Gemcitabine ± Docetaxel	2.6-4%	15-30%

NR: not reported
Note: follow-up time varies between trials

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Harms of Nadofaragene, Oportuzumab, Pembrolizumab and Gemcitabine ± Docetaxel

Trial	Adverse Events	%	Description
Phase III Nadofaragene	Serious AE	2%	Syncope, sepsis, serious hematuria
	Discontinuation due to AE	2%	
Phase III Oportuzumab	Serious AE	14%	Kidney injury, intestinal obstruction
	Discontinuation due to AE	4%	
Phase III Pembrolizumab	Serious AE	25.5%	Hyponatremia, arthralgia
	Discontinuation due to AE	9.8%	
	Immune mediated AE	20.6%	Thyroid issues, pneumonitis, colitis
Gemcitabine ± Docetaxel	Discontinue due to AE	9-12%	Variable/not reported in consistent way

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Uncertainty and Controversies

- Single arm trials and lack of comparative data
- Variation in study populations, outcome definition, and study design
- Preliminary data results and limited long-term follow up

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Potential Other Benefits and Contextual Considerations

- New therapies for NMIBC unresponsive to BCG may reduce patient, caregiver/family burden if outcomes are improved over existing therapies that do not effectively and safely control disease progression
- Nadofaragene and oportuzumab are new therapies that reflect improved understanding of disease mechanisms and cell transfer technologies
- The FDA permitted single-arm trials for new therapies because randomizing patients to placebo or minimally effective therapies was not felt to be ethical, and the recommended alternative is radical cystectomy

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Public Comments Received

- Outcomes seen in single arm trials exceeded a 20% historical response threshold set by the FDA for patients with BCG-unresponsive NMIBC
- For patients with complete response to pembrolizumab at 12 months, none recurred through 24-month follow-up
- ICER should not have included gemcitabine with or without docetaxel as a comparator for patients with BCG-unresponsive NMIBC

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Summary

- **Nadofaragene and oportuzumab:**
  - Single arm studies demonstrate rates of CR and RFS that appear greater than would be expected based on historical data
  - Few serious harms reported with low discontinuation rates
  - Nadofaragene is given much less frequently
- Single arm studies and differences among studies result in uncertainty about the magnitude of benefit of these new agents compared to best supportive care or other comparators
- Since most patients will progress or recur despite treatment over time, will delaying potentially curative cystectomy risk loss of cure and more metastatic disease and disease-related mortality?

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ICER Evidence Ratings for Nadofaragene and Oportuzumab

Intervention	Tumor Grade	ICER Rating
Nadofaragene vs. Best Supportive Care	All	C++
Oportuzumab vs. Best Supportive Care	All	C++
Nadofaragene vs. Oportuzumab	All	I
Nadofaragene vs. Pembrolizumab	CIS ± HG Ta/T1	I
Oportuzumab vs. Pembrolizumab	CIS ± HG Ta/T1	I
Nadofaragene vs. Gemcitabine ± Docetaxel	All	I
Oportuzumab vs. Gemcitabine ± Docetaxel	All	I

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Questions?

Nadofaragene Firadenovec and Oportuzumab Monatox for BCG-Unresponsive, Non-Muscle Invasive Bladder Cancer: Value

Daniel R. Touchette, PharmD, MA

Professor, University of Illinois at Chicago College of Pharmacy

Director, Center for Pharmacoepidemiology and Pharmacoeconomic Research

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Key Review Team Members

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Mrinmayee Joshi, B. Pharm, PhD Student, University of Illinois at Chicago College of Pharmacy

Disclosures:

Financial support was provided to the University of Illinois at Chicago from the Institute for Clinical and Economic Review.

University of Illinois at Chicago researchers have no conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.

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Objective

To evaluate the cost effectiveness of **nadofaragene firadenovec** and **oportuzumab monatox** compared with a **hypothetical comparator** for which effectiveness could be varied in adults with BCG-unresponsive NMIBC graded as:

1. CIS ± high-grade Ta/T1 (CIS)
2. Non-CIS with high grade Ta/T1 only (Ta/T1)

Pembrolizumab (in CIS only) and gemcitabine ± docetaxel (in CIS and Ta/T1) could not be included as comparators due to “I” evidence rating

- Determined the cost effectiveness of all treatments (including pembrolizumab and gemcitabine ± docetaxel relative to a hypothetical comparator
- Hypothetical comparator had a complete response rate of 0% at 3 months, that could be varied in sensitivity analyses, to represent a mix of possible comparators with unknown comparative effectiveness

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Methods in Brief

Methods Overview

- **Model**: *S*emi-Markov model with time-varying proportions of patients with complete response or high-grade recurrence-free survival (HGRFS) and mortality
- **Setting**: United States
- **Perspective**: Health care sector (direct medical costs)
- **Time Horizon**: Patient lifetime
- **Discount Rate**: 3% per year (costs and outcomes)
- **Cycle Length**: 3 months
- **Primary Outcomes**: Time in progression-free state, total costs, total quality-adjusted life years (QALYs), total equal-value life years gained (evLYGs), total life years (LYs), cost-effectiveness ratios for all above outcomes (e.g., cost/QALYs gained and cost/evLYG)

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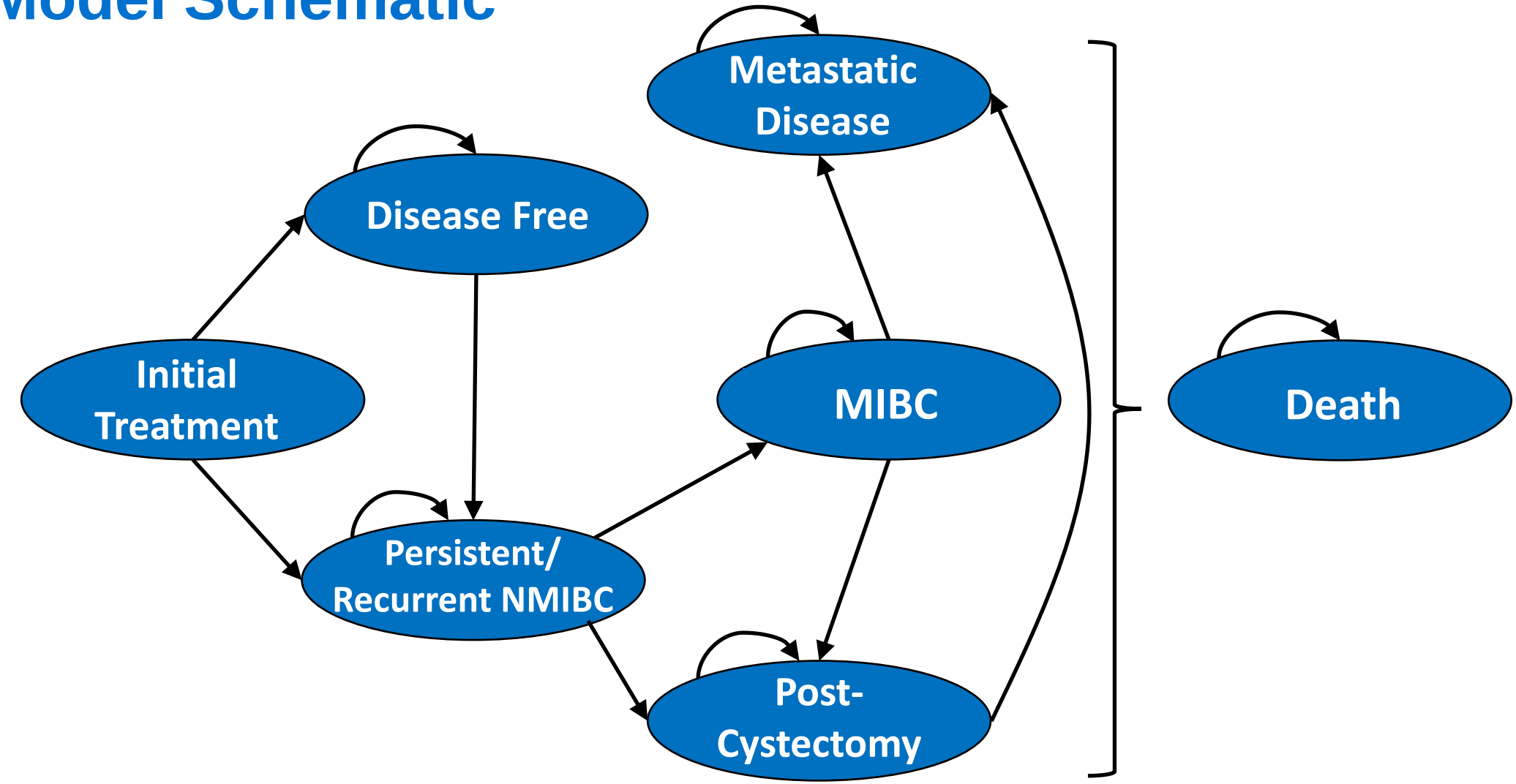
Model Schematic



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Model Characteristics

- **Target Populations:**
  - Adults with BCG-unresponsive NMIBC graded as:
    - CIS ± high-grade Ta/T1
    - High grade Ta/T1 only
  - Starting mean age: 72 years
  - Gender: 80% male

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Key Model Assumptions

- Patients who are disease free or who have metastatic disease will not have a cystectomy.
- Patients with no treatment experience disease progression at the same (average) rate as those from longer-term studies in whom treatment is not effective.

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Key Model Inputs: Treatment-Related Efficacy

Transition Probability	Treatments	Hypothetical Comparator
Complete Response at 3 months	Reported complete response at 3 months from clinical trials	0% for base-case Varied in sensitivity analyses
Complete Response to NMIBC, 6 months	Reported complete response (CIS) or high-grade recurrence-free survival (Ta/T1) reported at time points.	N/A for base-case Varied up to least effective treatment in sensitivity analyses
Complete Response to NMIBC, 9 months		
Complete Response to NMIBC, 12 months		
Complete Response to NMIBC, Each Cycle After 12 months	12-24 month estimates from Kaplan Meier curves, except gemcitabine ± docetaxel	N/A for base-case Varied up to least effective treatment in sensitivity analyses
NMIBC to MIBC, Each Cycle After 12 months	12-24 month estimates from Kaplan Meier curves, except gemcitabine ± docetaxel	Set to least effective treatment

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Key Model Inputs: Adverse Events

Adverse Event	Probability (%)	Cost ($)	Disutility
Urinary Tract Infection, Oportuzumab Monatox	12	167	0
Urinary Tract Infection, Pembrolizumab	12	167	0

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Key Model Inputs: Health State Utilities

Health State	Input Value	Population	Method of Valuation
Initial Treatment	0.86	Patients with NMIBC	EQ-5D
Disease Free	0.87	Patients with NMIBC	EQ-5D
NMIBC	0.76	Patients with NMIBC	EQ-5D
MIBC	0.75	Patients with NMIBC	EQ-5D
Metastatic Disease	0.70	Patients enrolled in KEYNOTE-045 with metastatic urothelial carcinoma	EQ-5D
Post-Cystectomy	0.745	Non-patient urologists	Standard Gamble

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Key Model Inputs: Treatment Costs

Intervention	Administration	Annual Drug Cost ($)
Nadofaragene Firadenovec	$3x10^{11}$ vp/mL (75 mL), administered by intravesical instillation every 3 months **4 doses per year**	164,337*
Oportuzumab Monatox	30 mg administered by intravesical instillation twice weekly for first 6 weeks, then once weekly for 6 weeks, then every other week thereafter **36 doses in first year**	150,000**
Pembrolizumab	200 mg IV over 30 minutes every 3 weeks or 400 mg IV over 30 minutes every 6 weeks for up to 24 months **17.4 doses per year**	164,337
Gemcitabine ± Docetaxel	Gemcitabine 1000 mg and docetaxel 37.5 mg administered weekly for 6 weeks by intravesical instillation **6 doses total**	437
Hypothetical Comparator	**N/A**	0

*Placeholder price equal to annual price of pembrolizumab
**Estimate of price provided by Sesen Bio

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Key Model Inputs: Administration Costs

Input	Description	Cost ($)
Nadofaragene Firadenovec and Oportuzumab Monatox	Bladder instillation of anticarcinogenic agent (HCPCS code 51720)	86
Pembrolizumab	Chemotherapy administration, intravenous infusion technique; up to one hour, single or initial substance/drug (CPT Code 96413)	143
Gemcitabine ± Docetaxel	Bladder instillation of anticarcinogenic agent (HCPCS code 51720)	86

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Key Model Inputs: Health Care Utilization Costs

Health State	Cost per Cycle ($)
Initial Treatment	1,211
Disease Free	1,211
NMIBC	1,458
MIBC	7,027
Cystectomy (One-Time)	30,625
Post-Cystectomy	8,665
Metastatic Disease	24,905
Death	500

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Results

Base-Case Results in CIS ± High-Grade Ta/T1

Treatment	Total Cost ($)	QALYs	evLYGs	Life Years	Time in Progression-Free State (Years)
Results Based on Prospective Studies of Instilled Therapies					
Nadofaragene Firadenovec	313,000	4.87	4.93	6.36	3.50
Oportuzumab Monatox	310,000	4.71	4.75	6.18	3.26
Results Based on Prospective Studies of Systemic Therapy					
Pembrolizumab	265,000	5.04	5.12	6.57	3.81
Results Based on Retrospective Studies of Instilled Therapies					
Gemcitabine ± Docetaxel	172,000	5.88	6.00	7.42	4.82
Results Based on Hypothetical Comparator					
Hypothetical Comparator	189,000	4.38	4.38	5.83	2.80

QALYs: quality-adjusted life years; evLYG: equal value of life years gained

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Base-Case Results in High-Grade Ta/T1 Only

Treatment	Total Cost ($)	QALYs	evLYGs	Life Years	Time in Progression-Free State (Years)
Results Based on Prospective Studies of Instilled Therapies					
Nadofaragene Firadenovec	309,000	5.14	5.24	6.58	3.79
Oportuzumab Monatox	300,000	5.36	5.48	6.84	4.15
Results Based on Retrospective Studies of Instilled Therapies					
Gemcitabine ± Docetaxel	166,000	5.74	5.86	7.20	4.68
Results Based on Hypothetical Comparator					
Hypothetical Comparator	191,000	4.19	4.19	5.58	2.47

QALYs: quality-adjusted life years; evLYG: equal value of life years gained

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Incremental Cost-Effectiveness Ratios Compared with Hypothetical Comparator in CIS ± High-Grade Ta/T1

Treatment	Incremental Cost per QALY Gained ($)	Incremental Cost per evLYG ($)	Incremental Cost per Year in Progression-Free State
Results Based on Prospective Studies of Instilled Therapies			
Nadofaragene Firadenovec	251,000	225,000	178,000
Oportuzumab Monatox	361,000	325,000	265,000
Results Based on Prospective Studies of Systemic Therapy			
Pembrolizumab	114,000	103,000	76,000
Results Based on Retrospective Studies of Instilled Therapies			
Gemcitabine ± Docetaxel	Dominates	Dominates	Dominates

QALYs: quality-adjusted life years; evLYG: equal value of life years gained

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Incremental Cost-Effectiveness Ratios Compared with Hypothetical Comparator in High-Grade Ta/T1 Only

Treatment	Incremental Cost per QALY Gained ($)	Incremental Cost per evLYG ($)	Incremental Cost per Year in Progression-Free State
Results Based on Prospective Studies of Instilled Therapies			
Nadofaragene Firadenovec*	124,000	112,000	90,000
Oportuzumab Monatox	92,000	84,000	65,000
Results Based on Retrospective Studies of Instilled Therapies			
Gemcitabine ± Docetaxel	Dominates	Dominates	Dominates

QALYs: quality-adjusted life years; evLYG: equal value of life years gained

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Scenario Analysis: Accounting for Recurrence Being Assessed via Biopsy Alone

CIS ± High-Grade Ta/T1

Treatment	Base Case ($)	Inclusion of Patients Assessed via Biopsy ($)
Nadofaragene Firadenovec	251,000	251,000
Oportuzumab Monatox	361,000	424,000 ↑

High-Grade Ta/T1 only

Treatment	Base Case ($)	Inclusion of Patients Assessed via Biopsy ($)
Nadofaragene Firadenovec	124,000	124,000
Oportuzumab Monatox	92,000	100,000 ↑

QALYs: quality-adjusted life years; evLYG: equal value of life years gained

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Scenario Analysis: Varying Hypothetical Comparator Effectiveness Patients with CIS ± High-Grade Ta/T1

Effectiveness of Hypothetical Comparator (% with Complete Response at 3 months)	Nadofaragene Firadenovec Cost per QALY Gained ($)	Oportuzumab Monatox Cost per QALY Gained ($)
0 (Base Case)	251,000	361,000
10	256,000	371,000
20	261,000	383,000
30	274,000	413,000

QALYs: quality-adjusted life years

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Scenario Analysis: Varying Hypothetical Comparator Effectiveness Patients with High-Grade Ta/T1 only

Effectiveness of Hypothetical Comparator (% with Complete Response at 3 months)	Nadofaragene Firadenovec* Cost per QALY Gained ($)	Oportuzumab Monatox Cost per QALY Gained ($)
0 (Base Case)	124,000	92,000
10	126,000	94,000
20	133,000	98,000
30	149,000	108,000
40	181,000	125,000
50	245,000	158,000
60	418,000	224,000

QALYs: quality-adjusted life years

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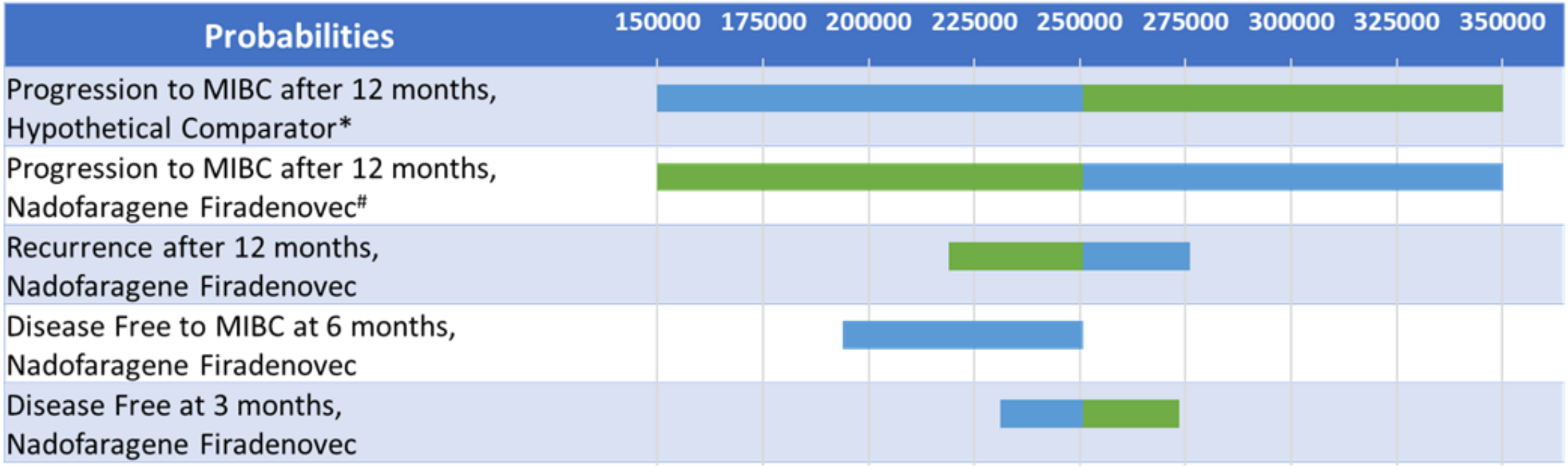
One Way Sensitivity Analysis: Nadofaragene Firadenovec in Patients with CIS ± High-Grade Ta/T1



*Incremental cost-effectiveness ratio range: $(2,787,000) to $147,000 per QALY gained

#Incremental cost-effectiveness ratio range: $123,700 to $428,000 per QALY gained

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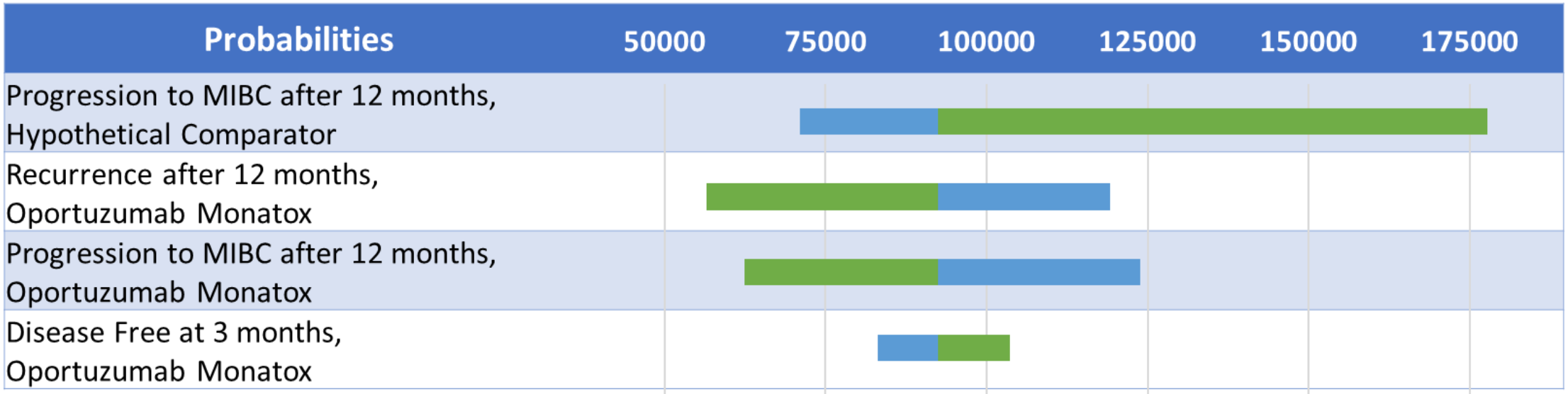
One Way Sensitivity Analysis: Oportuzumab Monatox in Patients with High-Grade Ta/T1 Only



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Limitations

- Lack of randomized, controlled clinical trials evaluating treatment efficacy
- Model assumptions that may not represent reality (e.g., restricting patients with metastatic disease from moving to the post-cystectomy state)
- Poor long-term data on progression of NMIBC from epidemiologic studies, especially in patients whose cancer did not respond to BCG.
- Final prices for nadofaragene firadenovec and oportuzumab monatox are not available yet
- Unable to identify indirect costs to perform an analysis with a societal perspective
- Very limited information in the public domain regarding timing, severity, duration, and management of treatment-related AEs

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Comments Received (and Responses)

- Use Kaplan-Meier (KM) estimates for disease recurrence or treatment duration of response
- Include cost inputs from newer study abstract using SEER Medicaid data (Yang 2020)
- Exclude cost-effectiveness analysis of gemcitabine ± docetaxel

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Conclusions

- Using placeholder and provided prices, base-case incremental cost-effectiveness ratios (ICERs) varied considerably
  - Increasing effectiveness of the comparator markedly increased ICERs for both treatments
  - Threshold prices in the HG Ta/T1 only subgroup are roughly double when compared to those in the CIS ± HG Ta/T1 subgroup for nadofaragene firadenovec and about four times higher for oportuzumab monatox.
- In patients with CIS ± Ta/T1, pembrolizumab resulted in important QALY gains and appeared to be cost effective when compared with the hypothetical comparator.
- Gemcitabine ± docetaxel appears to be a cost effective, if not dominant, option for patients with BCG-unresponsive NMIBC.

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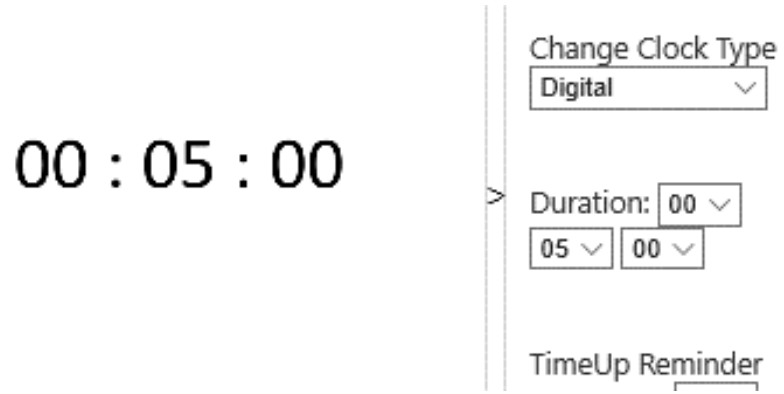
Questions?

Public Comment and Discussion

Tom Cannell, DVM, President & Chief Executive Officer, Sesen Bio

Conflicts of Interest:

- *Dr. Tom Cannell is a full-time employee of Sesen Bio.*



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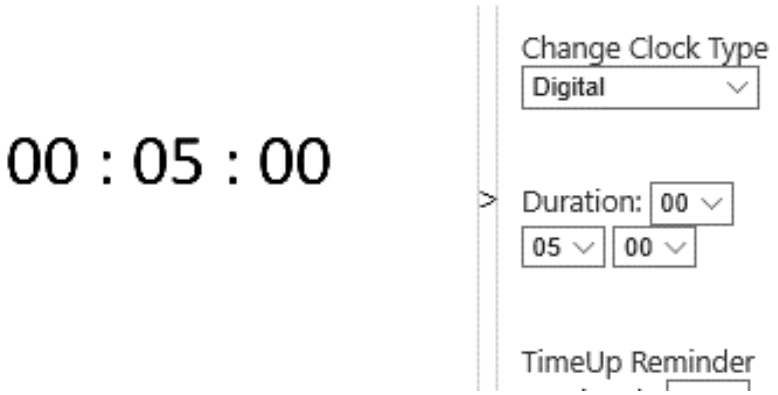
Vijay Kasturi, MD, Vice President, Medical Affairs; Interim Lead – Clinical Development, FerGene, Inc.

Conflicts of Interest:

- *Dr. Vijay Kasturi is a full-time employee of FerGene, Inc.*



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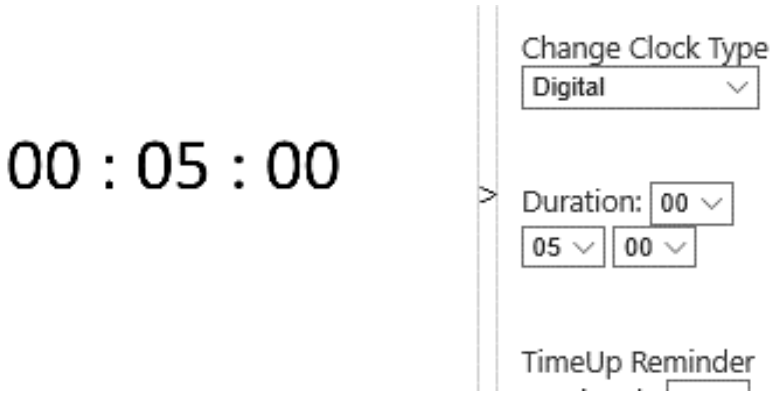
Yair Lotan, MD, Professor, Chief of Urologic Oncology, UT Southwestern Medical Center at Dallas

Conflicts of Interest:

- *Dr. Yair Lotan has received consulting fees from FerGene, Bristol Myers Squibb, Nucleix, Photocure and Ambu.*



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Break

Meeting will resume at 10:45am CT

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Voting Questions

Patient population for questions 1-5: Adults with BCG-unresponsive, high-risk NMIBC (CIS ± Ta/T1 or non-CIS with high grade Ta/T1)

1. Is the evidence adequate to demonstrate that the net health benefit of nadofaragene firadenovec (Adstiladrin®) is superior to that provided by best supportive care?

A. Yes

B. No

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Patient population for questions 1-5: Adults with BCG-unresponsive, high-risk NMIBC (CIS ± Ta/T1 or non-CIS with high grade Ta/T1)

2. Is the evidence adequate to demonstrate that the net health benefit of oportuzumab monatox (Vicineum™) is superior to that provided by best supportive care?

A. Yes

B. No

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Patient population for questions 1-5: Adults with BCG-unresponsive, high-risk NMIBC (CIS ± Ta/T1 or non-CIS with high grade Ta/T1)

3. Is the evidence adequate to distinguish the net health benefit of nadofaragene firadenovec (Adstiladrin®) from oportuzumab monatox (Vicineum™)?

A. Yes

B. No

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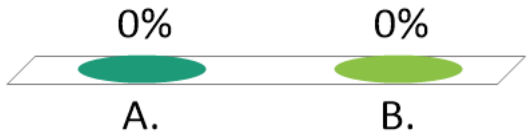
3a. If the answer to question 3 was yes, which therapy has the greater net health benefit?

A. Nadofaragene firadenovec

B. Oportuzumab monatox



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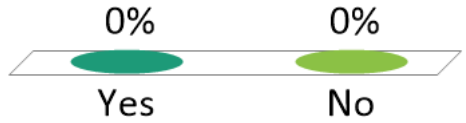
Patient population for questions 1-5: Adults with BCG-unresponsive, high-risk NMIBC (CIS ± Ta/T1 or non-CIS with high grade Ta/T1)

4. Is the evidence adequate to demonstrate that the net health benefit of nadofaragene firadenovec (Adstiladrin®) is superior to that provided by gemcitabine with or without docetaxel?

A. Yes

B. No



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Patient population for questions 1-5: Adults with BCG-unresponsive, high-risk NMIBC (CIS ± Ta/T1 or non-CIS with high grade Ta/T1)

5. Is the evidence adequate to demonstrate that the net health benefit of oportuzumab monatox (Vicineum™) is superior to that provided by gemcitabine with or without docetaxel?

A. Yes

B. No

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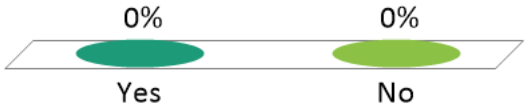
Patient population for questions 6-7: Adults with BCG-unresponsive, high-risk NMIBC with CIS ± Ta/T1

6. Is the evidence adequate to demonstrate that the net health benefit of nadofaragene firadenovec (Adstiladrin®) is superior to that provided by systemic pembrolizumab (Keytruda®)?

A. Yes

B. No



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Patient population for questions 6-7: Adults with BCG-unresponsive, high-risk NMIBC with CIS ± Ta/T1

7. Is the evidence adequate to demonstrate that the net health benefit of oportuzumab monatox (Vicineum™) is superior to that provided by systemic pembrolizumab (Keytruda®)?

A. Yes

B. No

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8. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec and oportuzumab monatox.

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Uncertainty or overly favorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too optimistic.		Uncertainty or overly unfavorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too pessimistic.
Very similar mechanism of action to that of other active treatments.		New mechanism of action compared to that of other active treatments.
Delivery mechanism or relative complexity of regimen likely to lead to much lower real-world adherence and worse outcomes relative to an active comparator than estimated from clinical trials.		Delivery mechanism or relative simplicity of regimen likely to result in much higher real-world adherence and better outcomes relative to an active comparator than estimated from clinical trials.
This intervention could reduce or preclude the potential effectiveness of future treatments.		This intervention offers the potential to increase access to future treatment that may be approved over the course of a patient's lifetime.
The intervention offers no special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.		The intervention offers special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.
This intervention will not differentially benefit a historically disadvantaged or underserved community.		This intervention will differentially benefit a historically disadvantaged or underserved community.
Small health loss without this treatment as measured by absolute QALY shortfall.		Substantial health loss without this treatment as measured by absolute QALY shortfall.
Small health loss without this treatment as measured by proportional QALY shortfall.		Substantial health loss without this treatment as measured by proportional QALY shortfall.
Will not significantly reduce the negative impact of the condition on family and caregivers vs. the comparator.		Will significantly reduce the negative impact of the condition on family and caregivers vs. the comparator.
Will not have a significant impact on improving return to work and/or overall productivity vs. the comparator.		Will have a significant impact on improving return to work and/or overall productivity vs. the comparator.
Other		Other

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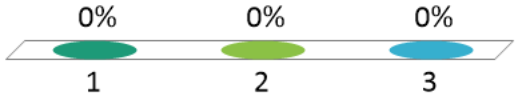
8a. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec and oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
This intervention will not differentially benefit a historically disadvantaged or underserved community		This intervention will differentially benefit a historically disadvantaged or underserved community



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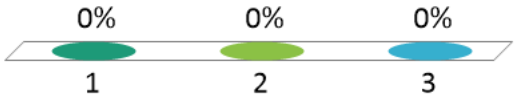
8b. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec and oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Small health loss without this treatment as measured by absolute QALY shortfall.		Substantial health loss without this treatment as measured by absolute QALY shortfall.



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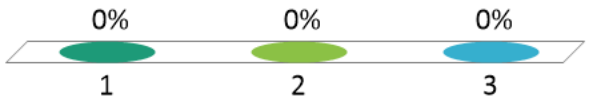
8c. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec and oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Small health loss without this treatment as measured by proportional QALY shortfall.		Substantial health loss without this treatment as measured by proportional QALY shortfall.



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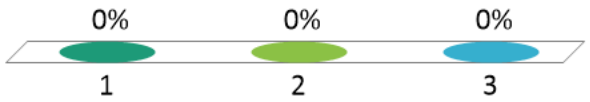
8d. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Uncertainty or overly favorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too optimistic		Uncertainty or overly unfavorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too pessimistic



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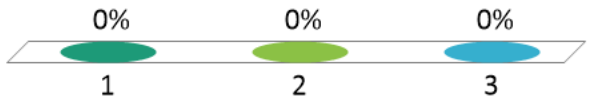
8e. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Uncertainty or overly favorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too optimistic		Uncertainty or overly unfavorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too pessimistic



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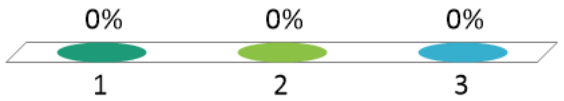
8f. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Very similar mechanism of action to that of other active treatments		New mechanism of action compared to that of other active treatments



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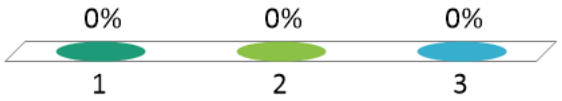
8g. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Very similar mechanism of action to that of other active treatments		New mechanism of action compared to that of other active treatments



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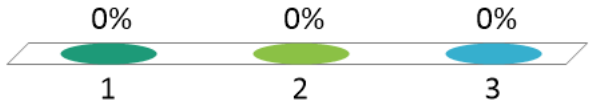
8h. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Delivery mechanism or relative complexity of regimen likely to lead to much lower real-world adherence and worse outcomes relative to an active comparator than estimated from clinical trials		Delivery mechanism or relative simplicity of regimen likely to result in much higher real-world adherence and better outcomes relative to an active comparator than estimated from clinical trials



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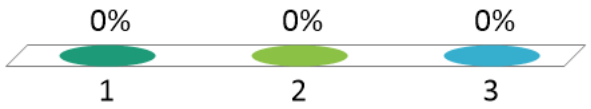
8i. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Delivery mechanism or relative complexity of regimen likely to lead to much lower real-world adherence and worse outcomes relative to an active comparator than estimated from clinical trials		Delivery mechanism or relative simplicity of regimen likely to result in much higher real-world adherence and better outcomes relative to an active comparator than estimated from clinical trials



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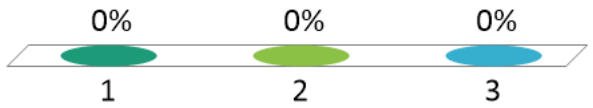
8j. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
This intervention could reduce or preclude the potential effectiveness of future treatments.		This intervention offers the potential to increase access to future treatment that may be approved over the course of a patient's lifetime.



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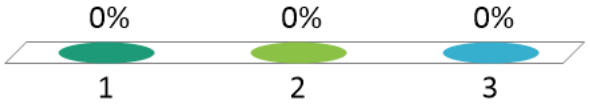
8k. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
This intervention could reduce or preclude the potential effectiveness of future treatments.		This intervention offers the potential to increase access to future treatment that may be approved over the course of a patient's lifetime.



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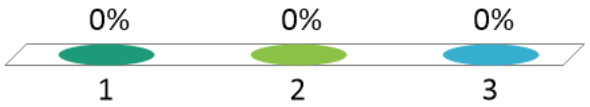
8l. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
The intervention offers no special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.		The intervention offers special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.



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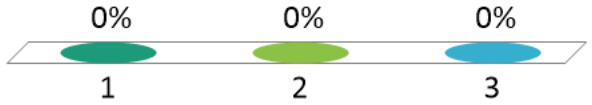
8m. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
The intervention offers no special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.		The intervention offers special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.



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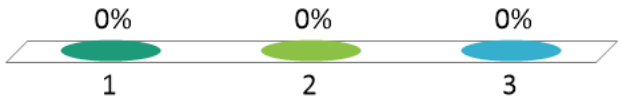
8n. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Will not significantly reduce the negative impact of the condition on family and caregivers vs. the comparator		Will significantly reduce the negative impact of the condition on family and caregivers vs. the comparator



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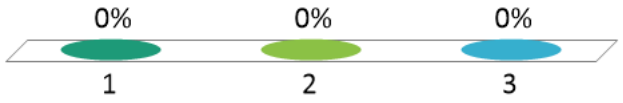
8o. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Will not significantly reduce the negative impact of the condition on family and caregivers vs. the comparator		Will significantly reduce the negative impact of the condition on family and caregivers vs. the comparator



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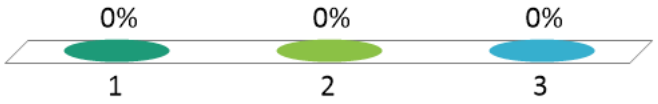
8p. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Will not have a significant impact on improving return to work and/or overall productivity vs. the comparator		Will have a significant impact on improving return to work and/or overall productivity vs. the comparator



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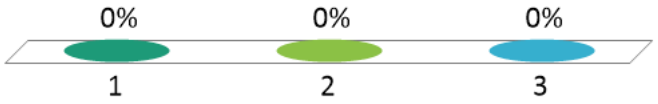
8q. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Will not have a significant impact on improving return to work and/or overall productivity vs. the comparator		Will have a significant impact on improving return to work and/or overall productivity vs. the comparator



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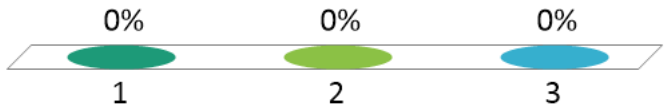
8r. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to nadofaragene firadenovec.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Other		Other



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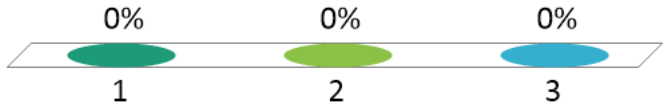
8s. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to oportuzumab monatox.

A. 1

B. 2

C. 3

1 (Suggests Lower Value)	2 (Intermediate)	3 (Suggests Higher Value)
Other		Other



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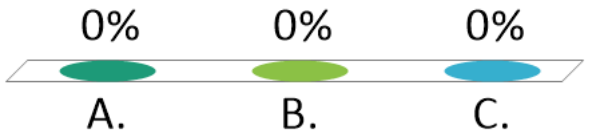
9. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment at current pricing with nadofaragene firadenovec (Adstiladrin®) versus best supportive care?

A. Low long-term value for money

B. Intermediate long-term value for money

C. High long-term value for money



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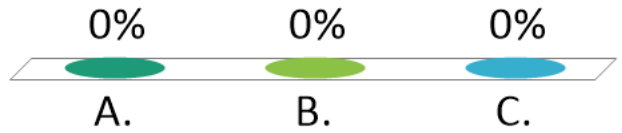
10. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment at current pricing with oportuzumab monatox (Vicineum™) versus best supportive care?

A. Low long-term value for money

B. Intermediate long-term value for money

C. High long-term value for money



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Lunch

Meeting will resume at 12:30pm CT

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Policy Roundtable

Policy Roundtable

Policy Roundtable Participant	Conflict of Interest
Stephanie Chisolm, PhD, Director of Education and Research, Bladder Cancer Advocacy Network	BCAN receives funding from FerGene and Merck.
Rachelle Dillon, PhD, Director, Clinical Operations, Sesen Bio	Dr. Rachelle Dillon is a full-time employee for Sesen Bio.
Leslie Fish, RPh, PharmD, Vice President of Clinical Pharmacy, IPD Analytics	Dr. Leslie Fish is a full-time employee of IPD Analytics.
John Gore, MD, MS, FACS, Associate Professor, Department of Urology; Adjunct Associate Professor, Department of Surgery, University of Washington	Dr. John Gore is an investigator for research sponsored by FerGene Pharmaceuticals unrelated to this review.
John W. McKnight, PharmD, BCPS, Vice President, HPS Clinical and Specialty Strategies, Humana	Dr. McKnight is a full-time employee of Humana.
Aaron Mitchell, MD, MPH, Assistant Attending, Medical Oncologist, Memorial Sloan Kettering Cancer Center	Dr. Aaron Mitchell has no financial conflicts to disclose.
Karen Sachse, RN, MSN, Patient Advocate	Karen Sachse has received honorarium for participating in a patient focus group for FerGene.
Kristen Wachsmuth, DHSc, MBA, Senior Director, Medical Affairs & Clinical Development, FerGene	Dr. Kristen Wachsmuth is a full-time employee of FerGene.

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Midwest CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around December 15, 2020
  - Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer-review.org/topic/bladder-cancer/

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Adjourn

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