2022 ASCO® ANNUAL MEETING

QUILT 3032: Final clinical results of pivotal trial of IL-15RαFc superagonist N-803 with BCG in BCG-unresponsive CIS and papillary nonmuscle-invasive bladder cancer (NMIBC)

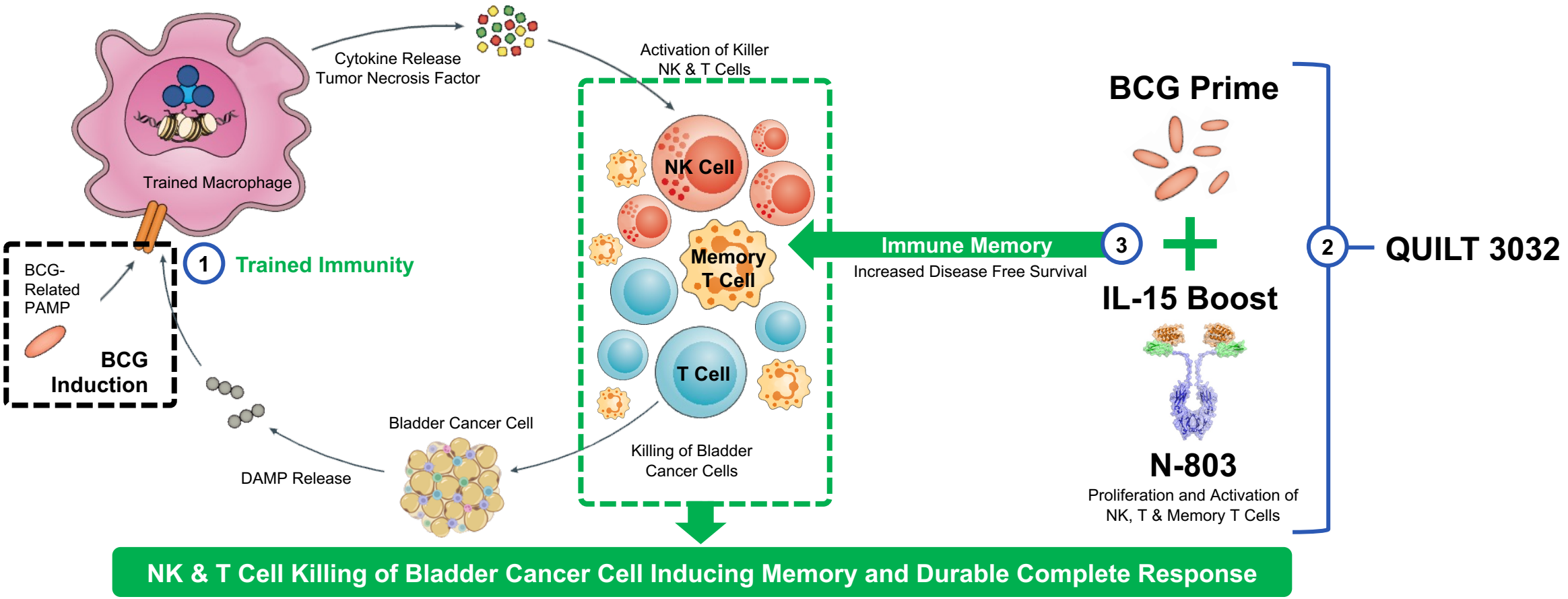
QUILT 3032

Dr. Karim Chamie, UCLA

Disclosures

- Urogen Pharma: Consultant and Scientific Advisory Board
- BMS: Speaker and Advisory Board
- Merck: Scientific Advisory Board
- ImmunityBio: Scientific Advisory Board

QUILT 3032: BCG Induces Trained Immunity
BCG (Prime) + N-803 (Boost) in NMIBC for Immune Memory



Mechanism of Action References

① **BCG**
- NK Cells Are Essential for Effective BCG Immunotherapy. Sven Brandau, 2001 April. Wiley, Intl Journal of Cancer
- Trained Immunity as a Molecular Mechanism for BCG Immunotherapy in Bladder Cancer. Jelmer H van Puffelen, 2020 Jul Nature Rev Urology
- BCG therapy downregulates HLA-I on malignant cells to subvert antitumor immune responses in bladder cancer. Mathieu Rouanne et al., 2022 May, Journal of Clinical Investigation

② **N-803**
- The IL-15-based superagonist N-803 promotes the antigen-independent conversion of memory CD8+ T cells into innate-like effector cells with antitumor activity. Hing Wong., 2013 Nov, OncoImmunology
- IL-15 superagonist/IL-15RαSushi-Fc fusion complex markedly enhances specific subpopulations of NK & memory CD8+ T cells, & mediates potent anti-tumor activity. Peter S. Kim, 2016. Oncotarget
- Phase I Trial Characterizing the Pharmacokinetic Profile of N-803, a Chimeric IL-15 Superagonist, in Healthy Volunteers. Mark P. Rubinstein et al., 2022 Feb. Journal of Immunology

③ **N-803 + BCG**
- Intravesical N-803 and BCG treatment reduces tumor burden in a carcinogen induced bladder cancer rat model; a role for cytokine production and NK cell expansion. Evan Gomes-Giacoia, June 2014 PLos One
- Innate Immune Memory is Associated with Increased Disease-Free Survival in Bladder Cancer Patients Treated with BCG. Charles H. Graham, 2021 Aug Can Urol Assoc J.
- Intravesical BCG in Patients with Non-Muscle Invasive Bladder Cancer Induces Trained Immunity and Decreases Respiratory Infections. Jelmer H van Puffelen, 2021 Feb. BioRxiv

QUILT 3032

Phase 2 / 3: IL-15RαFc Superagonist N-803 with BCG in BCG-Unresponsive Non-Muscle Invasive Bladder Cancer CIS & Papillary

BCG Unresponsive Disease

- Histologically Confirmed
- Persistent or recurrent CIS (+/- recurrent Ta/T1 disease) within 12 months of receiving adequate BCG
- CIS (Cohort A), Papillary (Cohort B)

QUILT 3032 - Treatment

50 mg BCG **plus** 400 µg N-803 intravesically
weekly x 6 induction or re-induction x 6
+ maintenance for up to two years with option to extend

Safety Endpoints

- Serious Adverse Events
- Immune Adverse Events

Efficacy Endpoints

Primary Endpoint:
- CR at any time, with lower bound 95% CI of ≥ 20%

Secondary Endpoints:
- Duration of CR,
- Cystectomy Avoidance
- Time to Cystectomy

Data extract: Nov 2021

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Demographics: Heavily Pre-treated NMIBC Subjects

Demographics	Cohort A - CIS	Cohort B - Papillary
N	83	77
AGE (yrs)	73	72
>65 yrs (%)	84	74
M:F (%)	87 / 13	74 / 26
ECOG 0 (%)	82	77
ECOG 1 (%)	18	17
ECOG 2 (%)	0	6

Number of Prior TURBT

Mean	4	4

Disease Type	Cohort A - CIS	Cohort B - Papillary
CIS	70%	1%
CIS / Ta	19%	1%
CIS / T1	11%	5%
HG Ta	0	43%
T1	0	44%
Ta / T1	0	4%

Number Prior BCG Doses

Mean	16.6	12.3

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Adverse Events: Cohorts A (CIS)

Treatment-Related AE's

GRADE 1-2 (CIS & Papillary)

Adverse Event (AE)	%
Dysuria	22%
Pollakiuria	19%
Haematuria	18%
Fatigue	16%
Micturition urgency	12%
Chills	7%
Bladder spasm	6%
Pyrexia	5%
Urinary tract infection	5%
Cystitis noninfective	4%
Nocturia	3%
Diarrhoea	3%
Nausea	2%
Bacterial test positive	2%
Cystitis	2%
Influenza like illness	2%
Urinary tract pain	2%

GRADE 3 (CIS & Papillary)

Adverse Event (AE)	%
Arthralgia	<1%
Bacteraemia	<1%
Dysuria	<1%
Encephalopathy	<1%
Escherichia bacteraemia	<1%
Haematuria	<1%
Myalgia	<1%
Pain in extremity	<1%
Pollakiuria	<1%
Sepsis	<1%
Urinary tract infection	<1%
Urine flow decreased	<1%

Treatment-Related SAE's (CIS)

1%

Immune-Related SAE (CIS)

0%

Treatment-Related Discontinuation (CIS)

2%

No Treatment Related Grade 4 & 5 Events

N-803 Activity is **Local to the Bladder** with **Zero Systemic** IL-15 Levels per PK

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Efficacy
COHORT A (CIS)

(Data Cutoff: January 15, 2022)

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Clinically Meaningful Efficacy Results Cohort A (CIS)

	Overall Intent to Treat Population Efficacy	QUILT 3032
Complete Response	Complete Response (n)	58 / 82
	CR Rate	71% (95% CI: 59.6, 80.3)
Median DoR	Median Duration of Response in Months	26.6 Months (95% CI: 9.9, Not Reached)
Duration of Response	Duration of Response ≥12 Months per KM	61.6% (95% CI: 47.3, 73.1)
	Duration of Response ≥18 Months per KM	56.4% (95% CI: 41.5, 68.8)
	Duration of Response ≥24 Months per KM	53.2% (95% CI: 38.0, 66.2)

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Clinically Meaningful Efficacy Results Cohort A (CIS)

	Overall Intent to Treat Population	QUILT-3.032
Duration of Follow Up	Median Duration of Follow Up	23.9 Months
	Cystectomy Rate	
Cystectomy Rate	Responders	9%
	Overall	16%
	Bladder Cancer Specific Progression Free Survival	
Bladder Cancer Specific Progression Free Survival	12 Months per KM	96.4% (95% CI: 86.2, 99.1)
	18 Months per KM	96.4% (95% CI: 86.2, 99.1)
	24 Months per KM	96.4% (95% CI: 86.2, 99.1)
Disease Specific Overall Survival	Bladder Cancer Specific Overall Survival	100%

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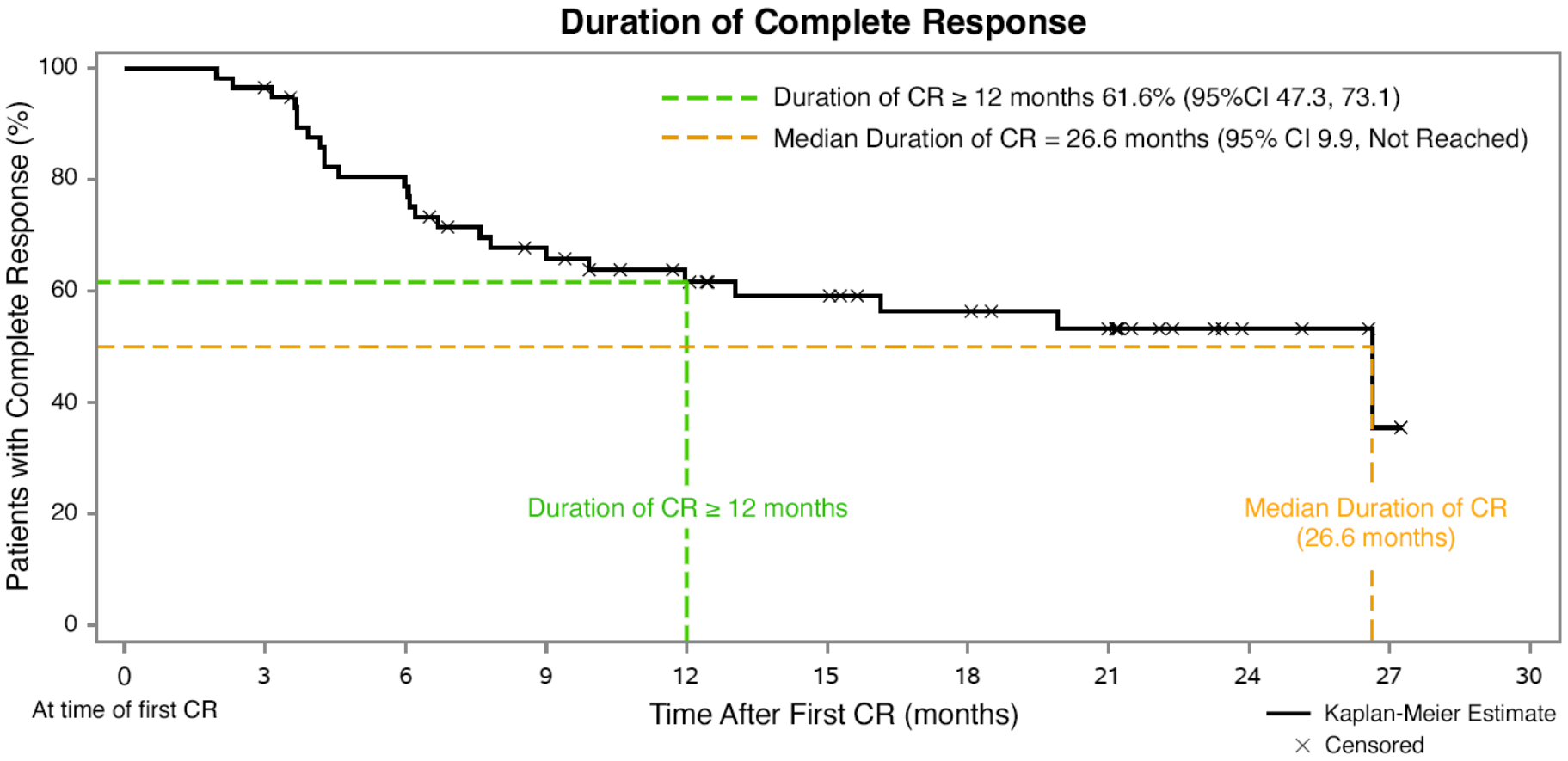
QUILT 3032
26.6 Month Durable Complete Remission in CIS (Cohort A)



Median Duration of CR
26.6 Months

Ongoing Response, Still on Study
21 / 58 (36%)

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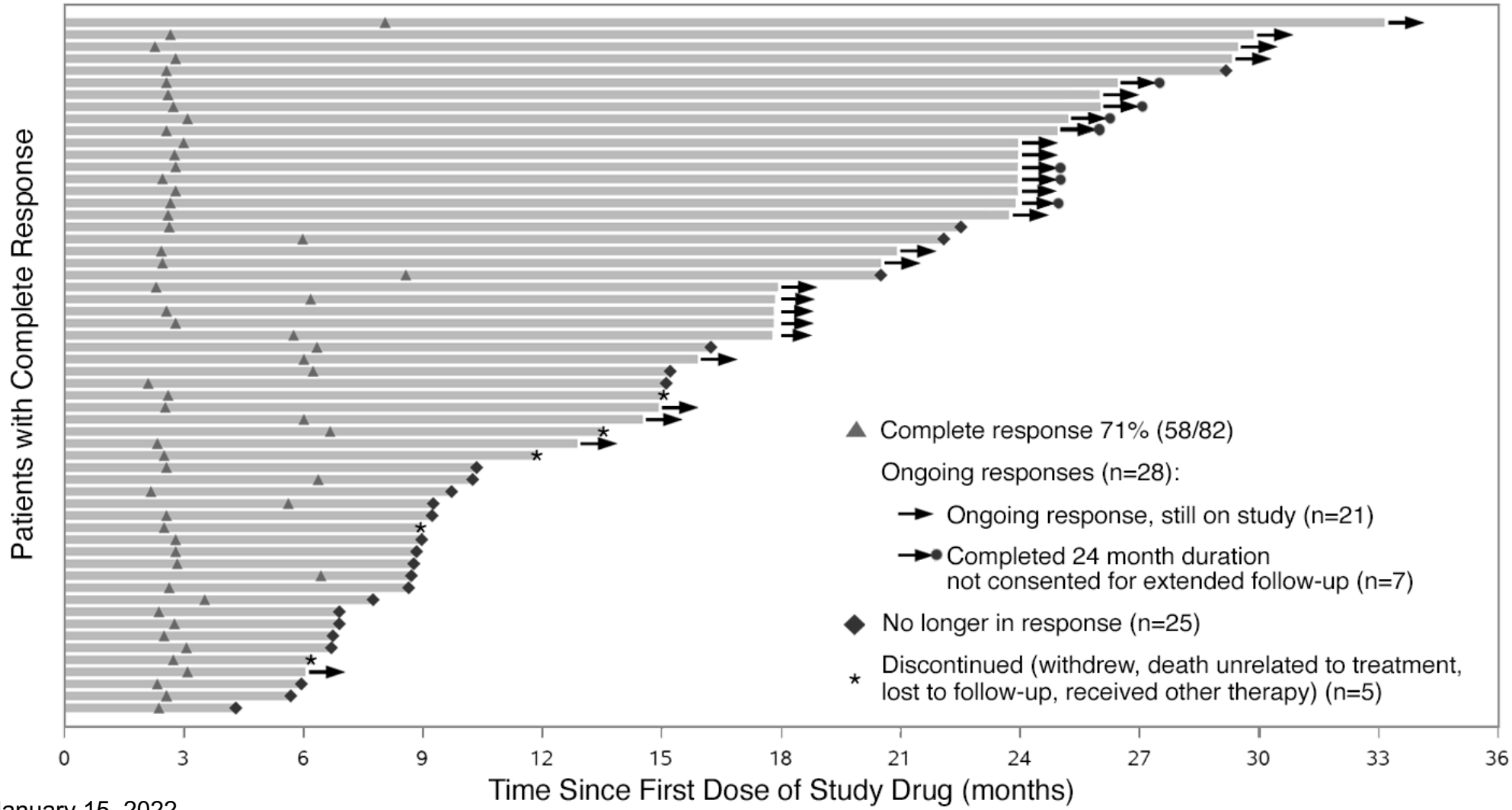
Overall Complete Response & Duration of Response

Time to Complete Response and Duration of Complete Response (Overall Responder Population)



Data Cutoff: January 15, 2022

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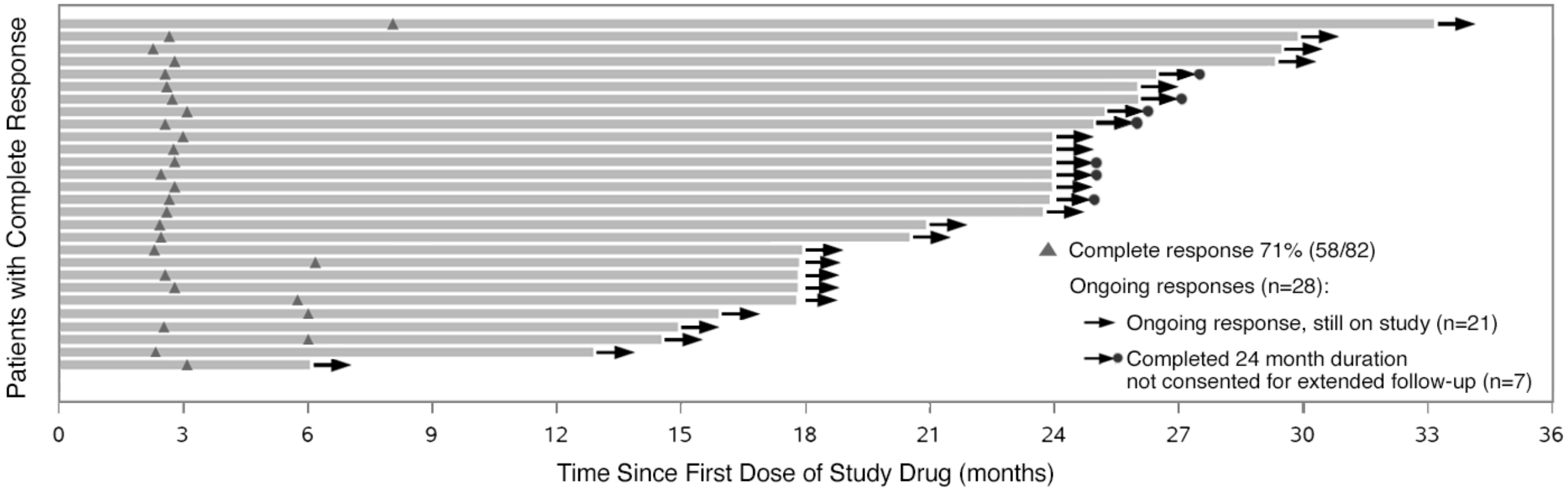
Durable Response: Responders Still Ongoing

Data Cutoff: January 15, 2022

Time to Complete Response and Duration of Complete Response (Ongoing Responder Population)



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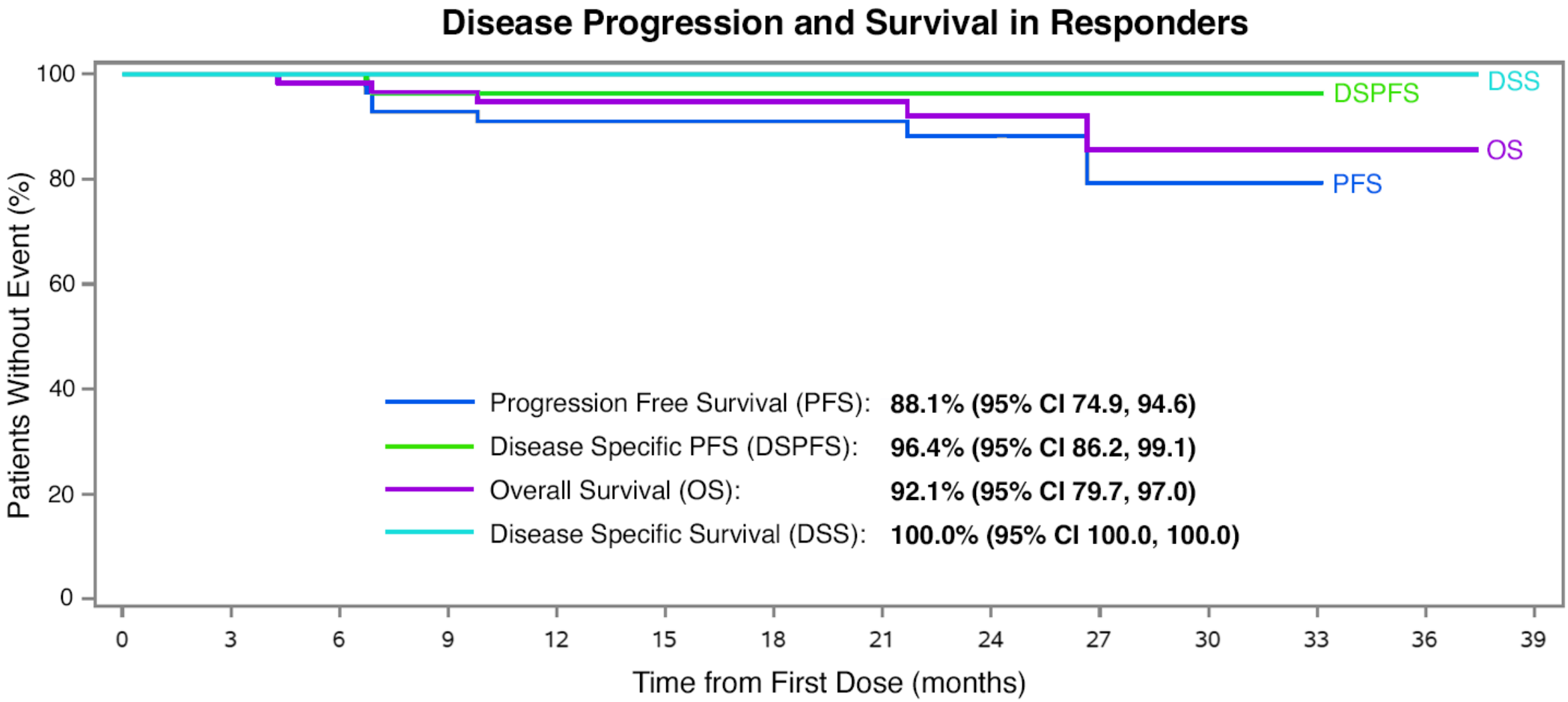
Progression Free Survival and Overall Survival (Cohort A: CIS)



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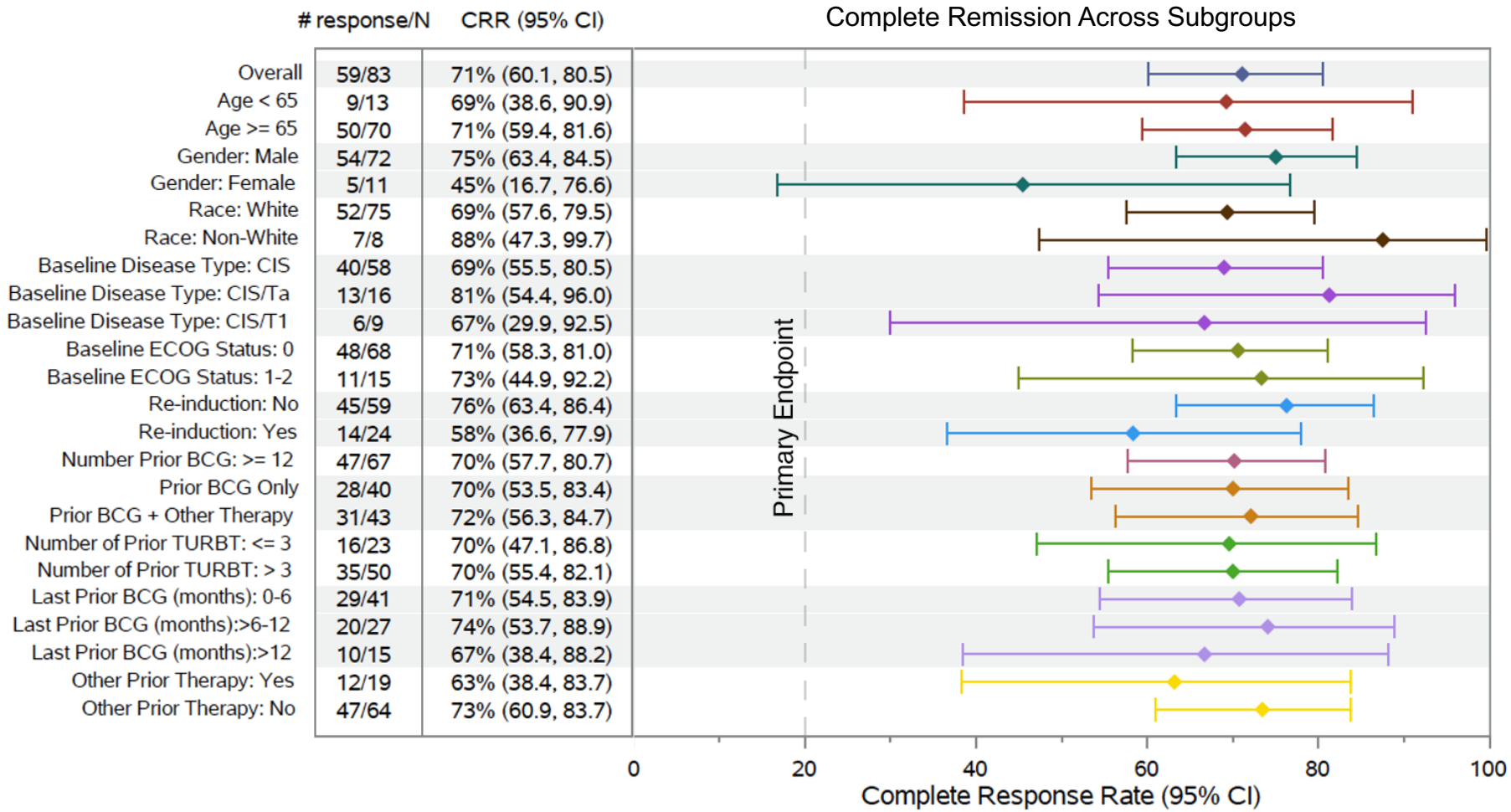
Efficacy Retained Across All Subgroups

COHORT A (CIS +/- Ta T1)



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Efficacy
COHORT B (PAPILLARY)

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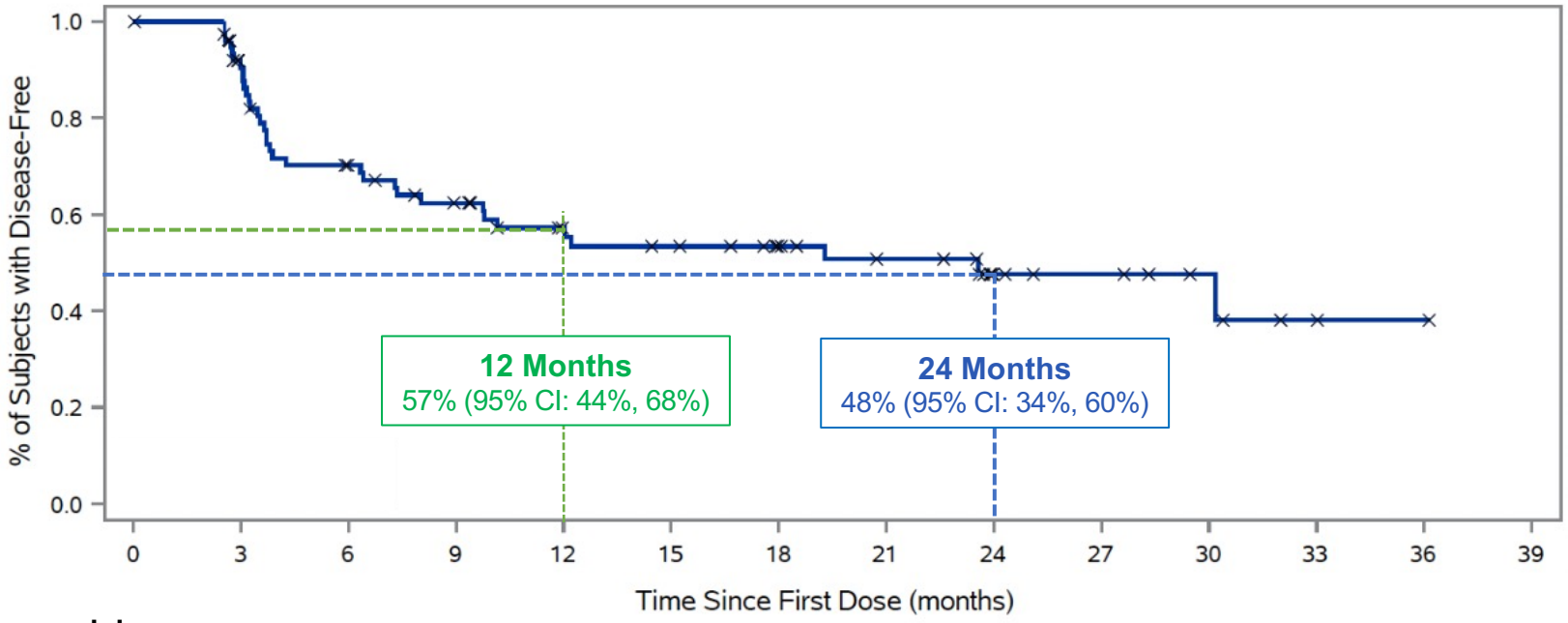
Durable 24 Month Disease Free Survival in Papillary

- 77 patients have been accrued
- Median DFS: 23.6 months
- 57% DFS rate at 12 months
- 53% DFS rate at 18 months
- 48% DFS rate at 24 months
- Primary endpoint met
- Median F/U is 20.7 months
- 73 of 77 (95%) radical cystectomy avoidance

Disease-Free Survival

Efficacy Population – Cohort B (HG Papillary)



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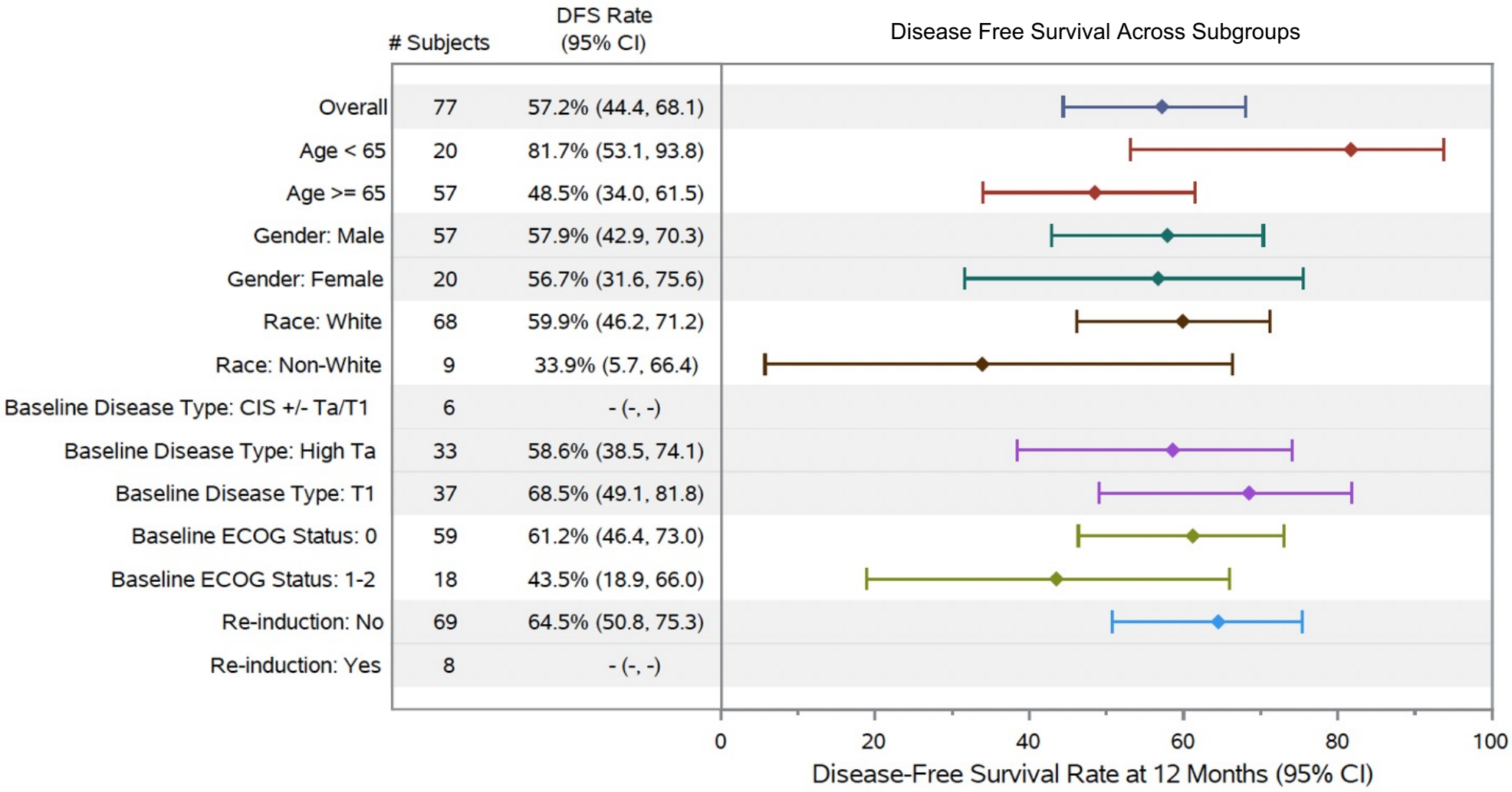
Efficacy Retained Across All Subgroups

COHORT B Papillary (Ta /T1)



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QUILT 3032: Clinically Meaningful Benefit: N-803 + BCG in CIS

High Efficacy Rate and Durable Response

- **71%** Complete remission (CR) rate at anytime
- **26.6** Months median durable complete remission
- **96%** Avoidance of bladder cancer progression at 24 months in responders
- **91%** Avoidance of cystectomy at 24 months in responders
- **100%** Bladder cancer specific overall survival at 24 months

Excellent Safety and Tolerability Profile Comparable to BCG Alone

- **1%** treatment related SAEs
- **0%** immune related SAEs
- **2%** treatment related discontinuation
- **0%** grade 4 and 5 AE

Favorable & Familiar Dosing Schedule with Activity Localized to the Bladder

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QUILT 3032: Clinically Meaningful Benefit: N-803 + BCG in Papillary

High Efficacy Rate and Durable Response

- **56%** Disease free survival rate at 12 months
- **23.6 months** median disease free survival
- **99%** Overall bladder cancer specific survival
- **96%** Cystectomy avoidance rate

Excellent Safety and Tolerability Profile

- **0%** treatment related SAEs
- **0%** immune related SAEs
- **4%** treatment related discontinuation
- **0%** grade 4 and 5 AE

Favorable & Familiar Dosing Schedule with Activity Localized to the Bladder

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Thomas Jefferson University, PA	Philadelphia, PA	Edouard Trabulsi, MD
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Thank You to all the patients, caregivers, and investigators