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# Installationstherapy beyond BCG in NMIBC

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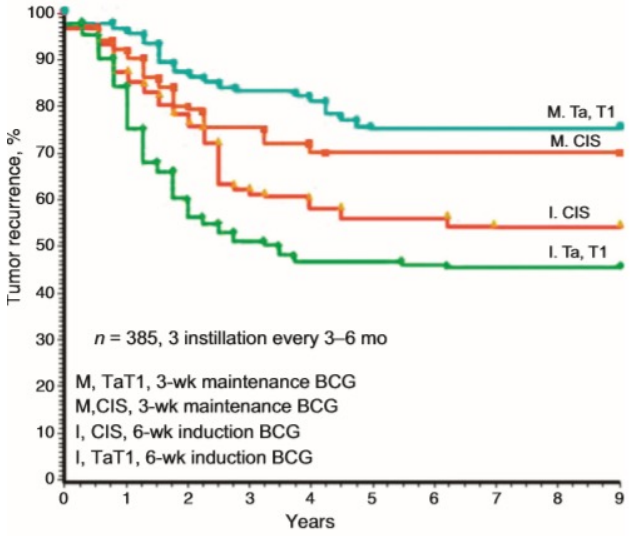
# What is important to know regarding BCG

## BCG Naïve

BCG reduce **progression** and **recurrence risks**: LEVEL OF EVIDENCES 1a

Sylvester et al. European Urology 2003

## Intermediate (induction + 1 yrs maineinence) vs. high risk (induction + 3 yrs mainteinence)




60% OF PATIENTS WHO HAVE AN INITIAL RESPONSE REMAIN TUMOR FREE FOR >5 YEARS

ONLY INDUCTION? ONLY 40% ARE FREE OF TUMOR AT 5 YEARS

Sylvester et al. European Urology 2003

Lamm et al. J Urol 2000

# What is important to know regarding BCG

**OPTIMAL SCHEDULE:**

Induction consist of 6 weekly insillation

Morales et al. J urol 1976

The EORTC metanalyses was unable to assess which BCG maintenance scheme was more effective, however at least one year of maintainence is necessary to achieve superiority vs MMC only

Böhle et al. Urology 2004
Sylvester et al. J Urology 2002

Monthly maintainance or one instillation every 3 months seem suboptimal

Oddens et al. Eur Urol 2013

The three year maintainence scheme with 3 weekly instillation at 3,6,12,18,24,30 and 36 months reduces recurrence rate compared to one year but not in intermediate risk patients/ SUGGESTED BY IBCG

Oddens et al. Eur Urol 2013

# What is important to know regarding BCG

Time of Recurrence

Type of recurrence

Re-induction, When?

When do we need to continue BCG?: all the low grade recurrence

**Table 5.** Classification of BCG Failures

| Classification | Description |
|---|---|
| Refractory | Persistent high-grade disease at 6 months despite adequate BCG* treatment. This category also includes any stage or grade progression by 3 months after the first BCG cycle (ie, high-grade T1 at 3 months after initial Ta, T1, high-grade disease, or CIS). |
| Relapsing | Recurrence of high-grade disease after achieving a disease-free state at 6 months after adequate BCG.* Although this category has previously been subdivided based on time to recurrence after stopping BCG (ie, early [< 12 months], intermediate [1-2 years], or late [> 24 months]), for the purpose of being included in the BCG-unresponsive category, patients should be within 6 months of the last BCG exposure (eg, patient receiving maintenance therapy). |
| Intolerant | Disease persistence as a result of inability to receive adequate BCG* because of toxicity. With current attention to abrogation of BCG adverse effects, we expect this category to represent a small portion of the BCG-treated population. |
| Unresponsive[23] | BCG refractory and BCG relapsing disease. The term BCG unresponsive, which essentially includes BCG refractory and BCG relapsing (within 6 months of last BCG exposure), is meant to denote a subgroup of patients at highest risk of recurrence and progression for whom additional BCG therapy is not a feasible option. These patients can be considered for single-arm studies.† |

Abbreviations: BCG, bacillus Calmette-Guérin; CIS, carcinoma in situ.

*For clinical trials, adequate BCG therapy is when a patient has received at least five of six induction instillations and at least one maintenance (two of three instillations) in a 6-month period.

†Because there are often delays in referral to and enrollment in trials, we recommend that study designs account for a window from tumor recurrence, and patients can be within 6 to 9 months of the last BCG exposure, thereby allowing a 3-month lead time for referral.

# When BCG fails: the BCG-unresponsive disease

- Persistent or new **T1 HG** disease
  - at first evaluation (3 mos) following induction BCG
- Persistent or recurrent **CIS**
  - within 12 months of completion of adequate BCG therapy
- Recurrent **HG Ta/T1** disease
  - within 6 months of completion of adequate BCG therapy

*Adequate BCG therapy defined as:*
*at least 5 of 6 doses of iBCG + at least 2 additional doses of mBCG*

Courtesy of Prof Kamat

# EAU guidelines definition of BCG failures

| | |
|---|---|
| | **BCG-refractory tumour** |
| REFRACTORY | 1. If T1G3/HG tumour is present at 3 months [196, 291, 294] (LE: 3).<br>2. If TaG3/HG tumour is present after 3 months and/or at 6 months, after either re-induction or first course of maintenance [43] (LE: 4).<br>3. If CIS (without concomitant papillary tumour) is present at 3 months and persists at 6 months after either re-induction or first course of maintenance. If patients with CIS present at 3 months, an additional BCG course can achieve a complete response in > 50% of cases [43, 44, 284] (LE: 1b).<br>4. If HG tumour appears during BCG maintenance therapy*. |
| | **BCG-relapsing tumour** |
| RELAPSING | Recurrence of G3/HG (WHO 1973/2004) tumour after completion of BCG maintenance, despite an initial response [288] (LE: 3). |
| | **BCG unresponsive tumour** |
| UNRESPONSIVE | BCG unresponsive tumours include all BCG refractory tumours and those who develop T1Ta/HG recurrence within 6 months of completion of adequate BCG exposure** or develop CIS within 12 months of completion of adequate BCG exposure [292] (LE: 4). |
| | **BCG intolerance** |
| | Severe side effects that prevent further BCG instillation before completing treatment [266]. |

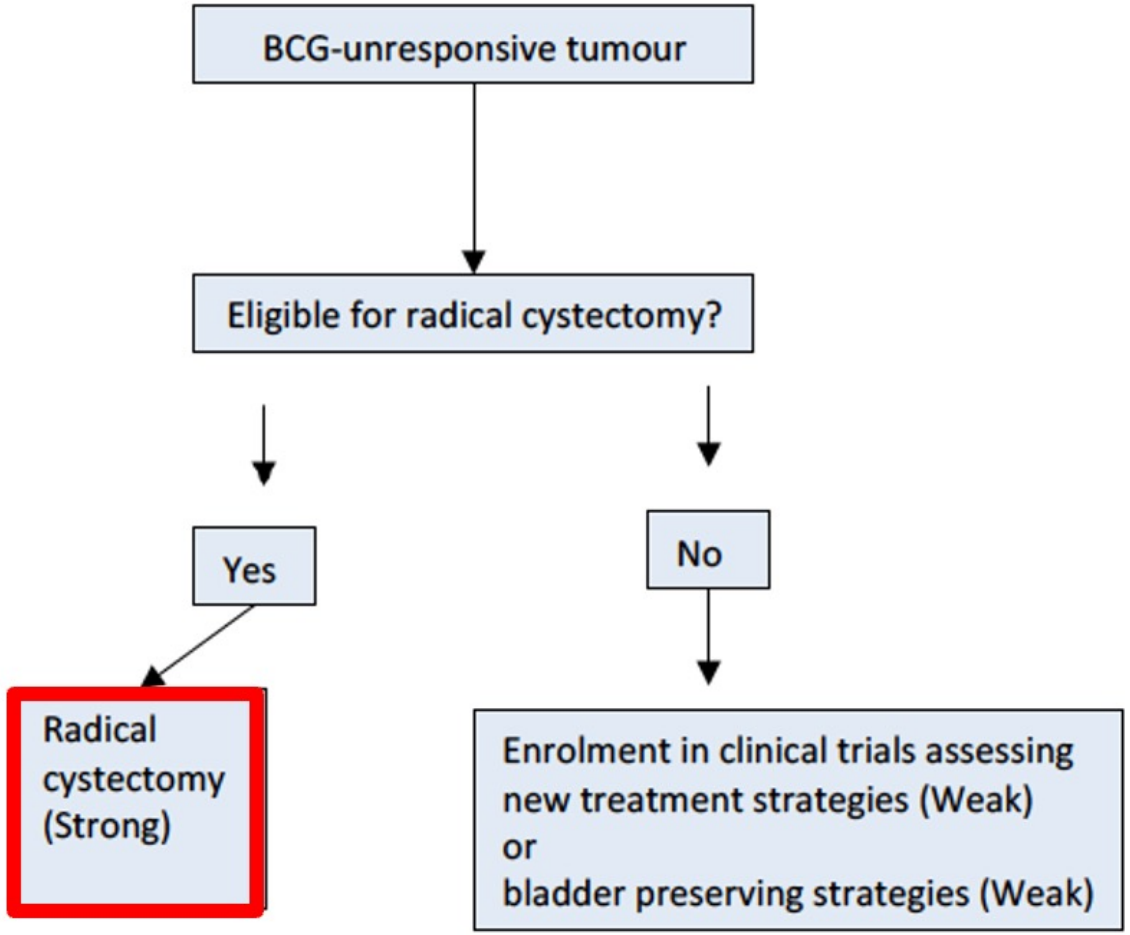
** Patients with LG recurrence during or after BCG treatment are not considered to be a BCG failure.*
*** Adequate BCG is defined as the completion of at least 5 of 6 doses of an initial induction course plus at least 2 out of 6 doses of a second induction course or 2 out of 3 doses of maintenance therapy.*

# The rationale behind the definition of "BCG unresponsive" disease

- To identify patients that have been sufficiently exposed to BCG and thus unlikely to respond to further instillations
- It comprises the BCG refractory category and some early high risk BCG relapses
- Developed in conjunction with FDA to identify patients' categories for single arm trials in the setting
- A formal validation of the definition is lacking
- Adopted by EAU guidelines

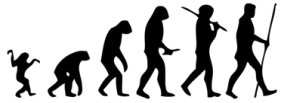
# Definitions in NMIBC

European Association of Urology




**This paradigm is changing**

# NMIBC treatment: a rapidly evolving landscape



**1960s**
Thiotepa

**1970s**
Doxorubicin
Mitomycin C

**1976**
BCG - Morales

**1998**
Valrubicin

**2002**
Gemcitabine

**2020**
Pembrolizumab

**2022**
Nadofaragene Firadenovec

# BCG-unresponsive: the past

BCG + IFN alfa

(increaseT1 helper response)

Seminar article

## Final results from a national multicenter phase II trial of combination bacillus Calmette-Guérin plus interferon α-2B for reducing recurrence of superficial bladder cancer☆

Fadi N. Joudi, M.D.[a], Brian J. Smith, Ph.D.[b], Michael A. O'Donnell, M.D.[a,*], and the National BCG-Interferon Phase 2 Investigator Group

**Table 1.** Cancer-free survival rates for BCG-N patients and those with different failure patterns

| Treatment Group | 2-yr Cancer-Free Survival Rate (%) | *P* Value* |
|---|---|---|
| BCG-N (n = 536) | 59 | |
| BCG refractory (n = 57) | 34 | <0.001 |
| Recurrence (mo) | | |
| ≤6 (n = 167) | 41 | 0.0011 |
| 6–12 (n = 129) | 43 | 0.0006 |
| 12–24 (n = 68) | 53 | 0.97 |
| >24 (n = 46) | 66 | 0.335 |

BCG = bacille Calmette-Guérin; BCG-N = BCG naïve.
* Reference: BCG-N.

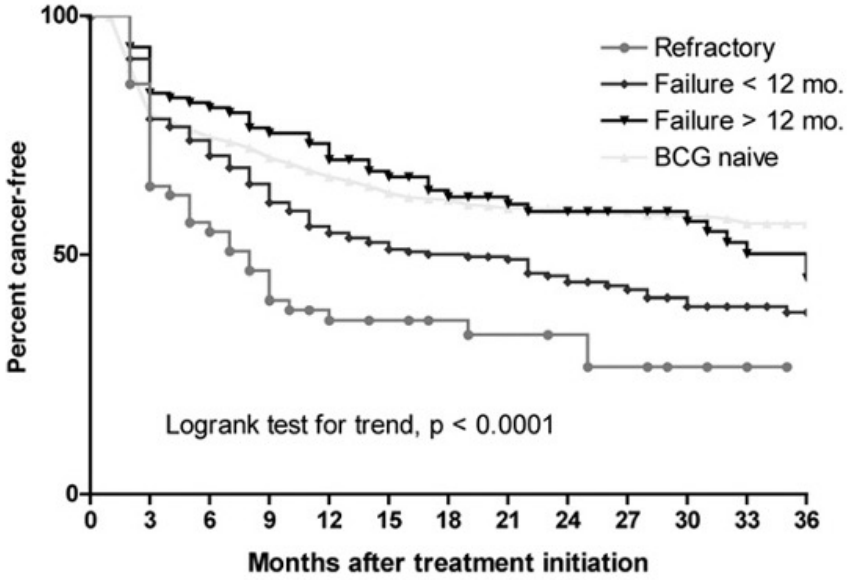
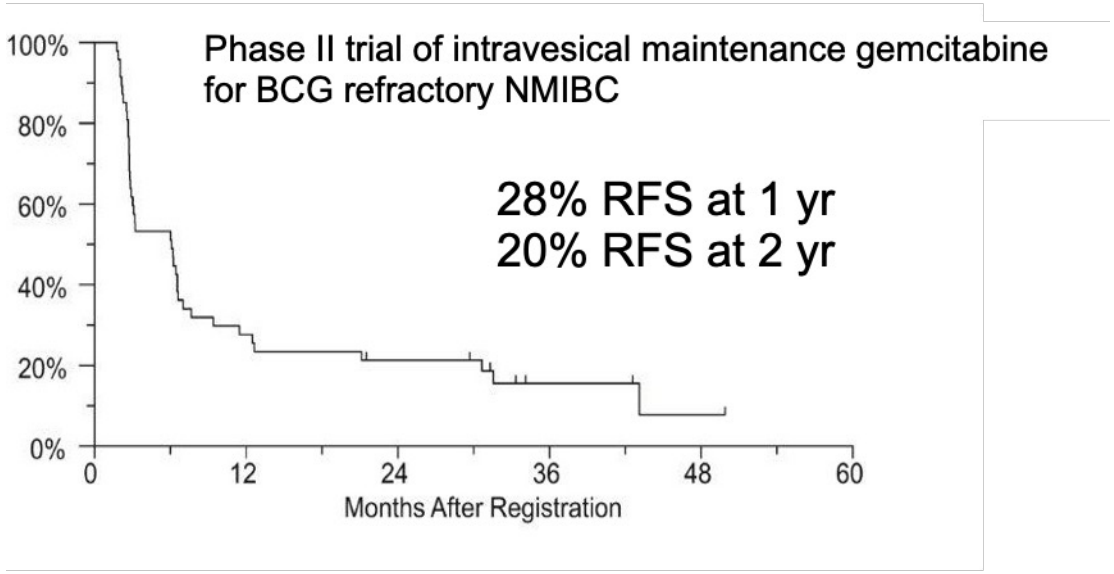


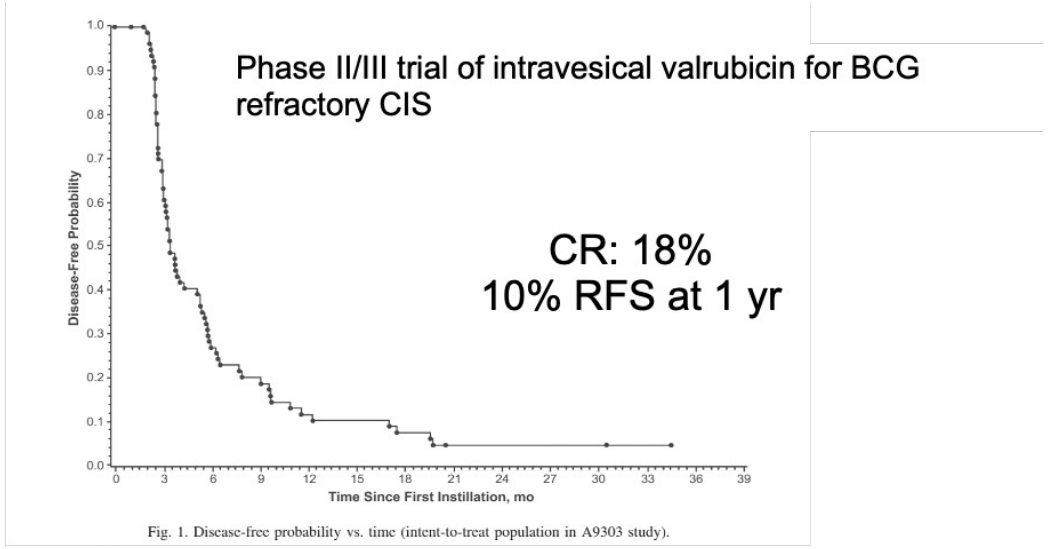

**Figure 1.** Cancer-free survival rates for BCG-N and BCG-F patients with different failure patterns.

*Gallagher, Urology 2008*

# Intravesical chemotherapy

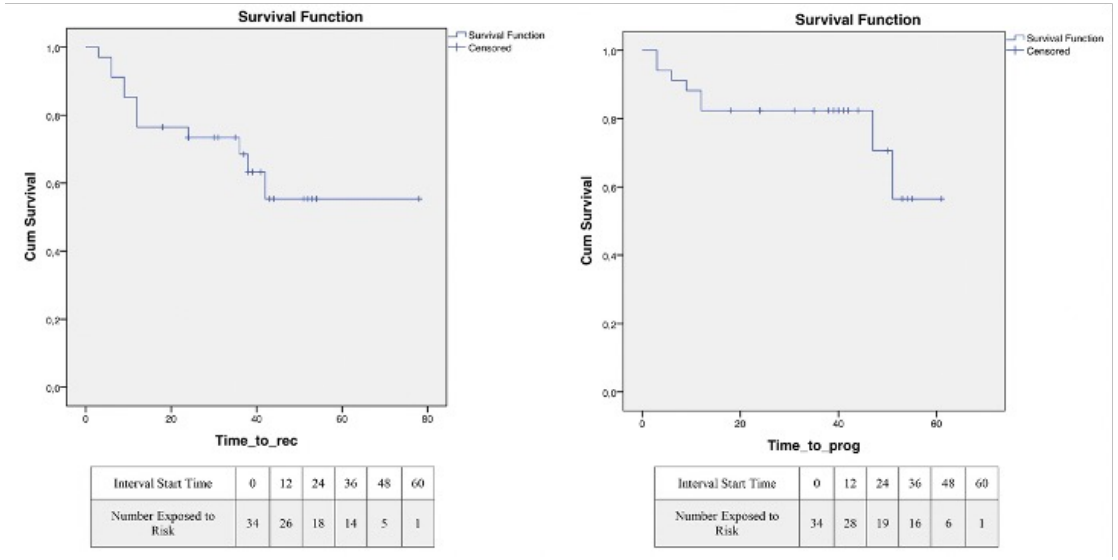



Skinner et al, J Urol, 2013



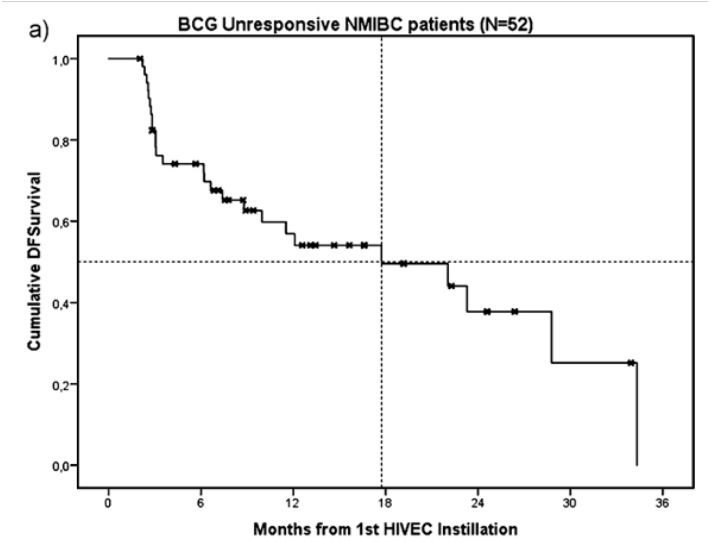

Dinney et al, Urol Oncol, 2012

# Device-assisted therapy




| Interval Start Time | 0 | 12 | 24 | 36 | 48 | 60 |
|---|---|---|---|---|---|---|
| Number Exposed to Risk | 34 | 26 | 18 | 14 | 5 | 1 |

| Interval Start Time | 0 | 12 | 24 | 36 | 48 | 60 |
|---|---|---|---|---|---|---|
| Number Exposed to Risk | 34 | 28 | 19 | 16 | 6 | 1 |




Unithermia
34 non G3 BCG failure
59% RR
1 yr PFS 82%
1 yr RFS 75%

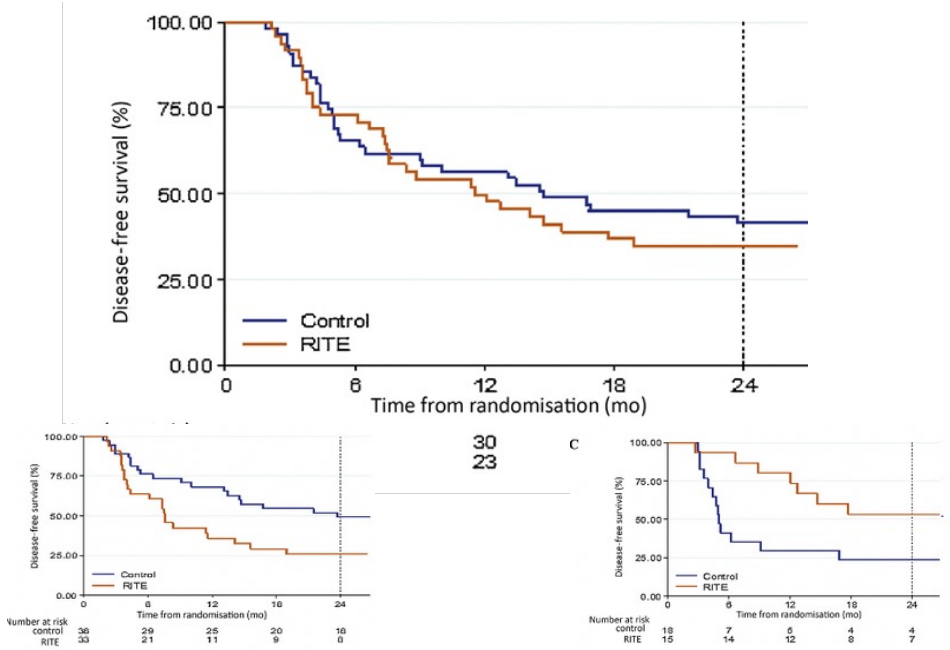
Soria et al, WJU 2016

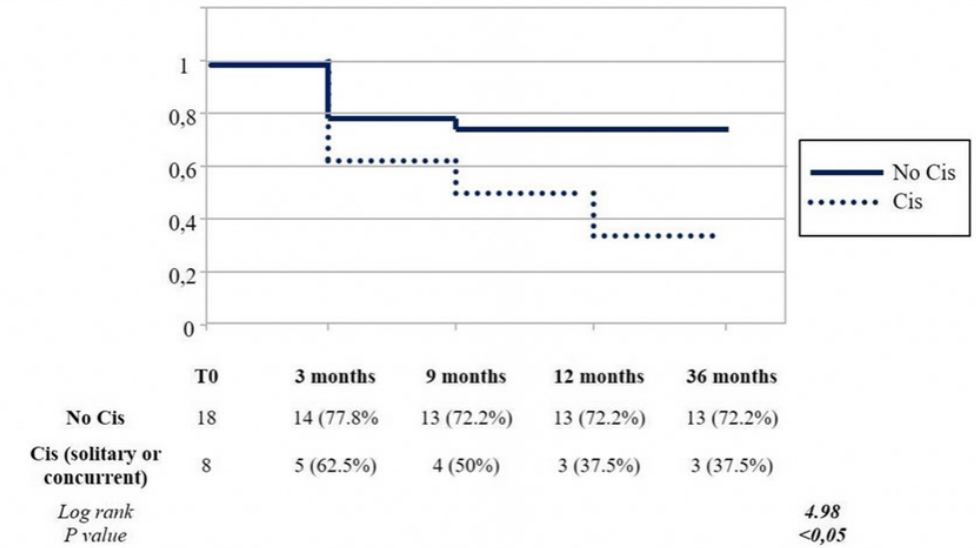
Hivec
54 BCG unresponsive
1 yr DFS 47%

De Jong et al, Bladder Cancer 2018

# BCG-unresponsive: the past

## Device-assisted therapy




RITE (Synergo)

2-yrs DFS 35%

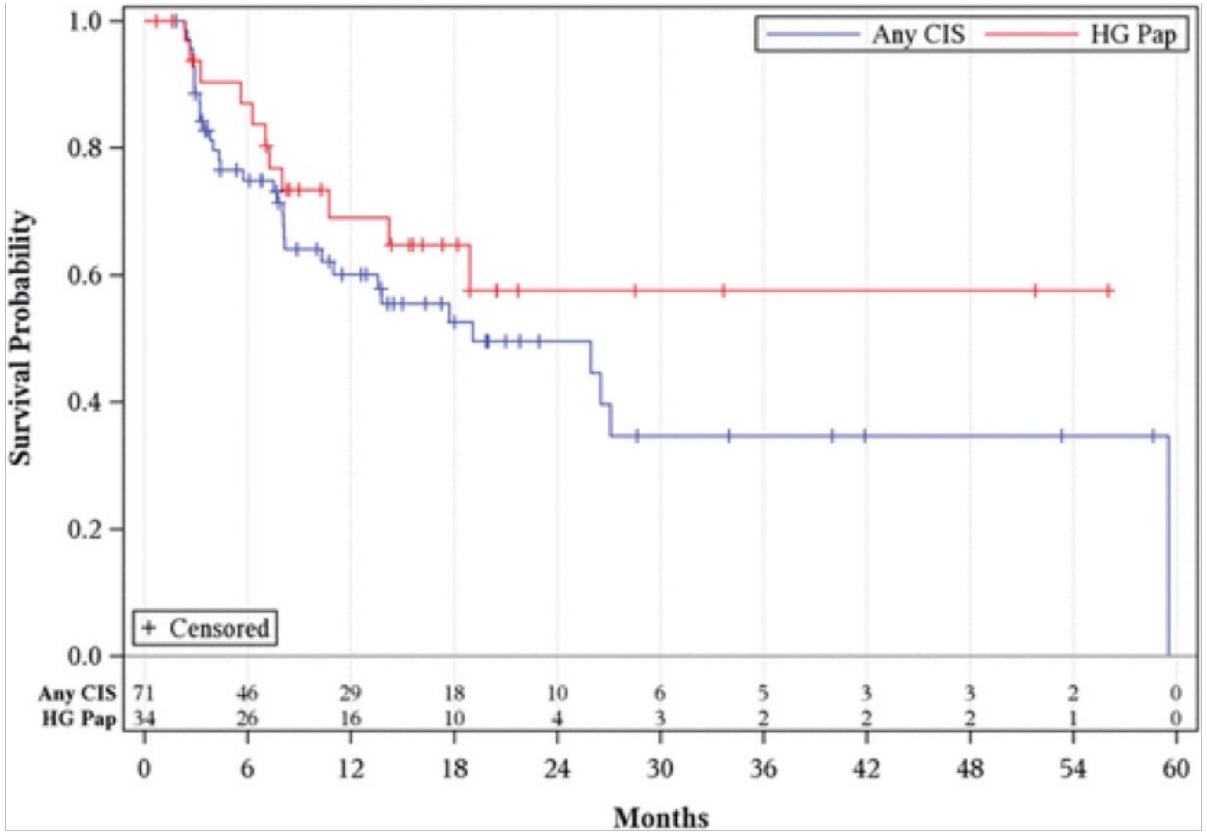
Tan et al, Eur Urol 2019

EMDA (single center, 26 pts)

PFS 85%

Racioppi et al, BMC 2018

# Gemcitabine + Docetaxel




276 pts
Safe (only 9 pts did not complete the course)
65% RFS at 1 yr
52% RFS at 2 yrs

Retrospective
NCT04386746 in BCG naïve under way
No prospective trials launched in BCG unresponsive setting

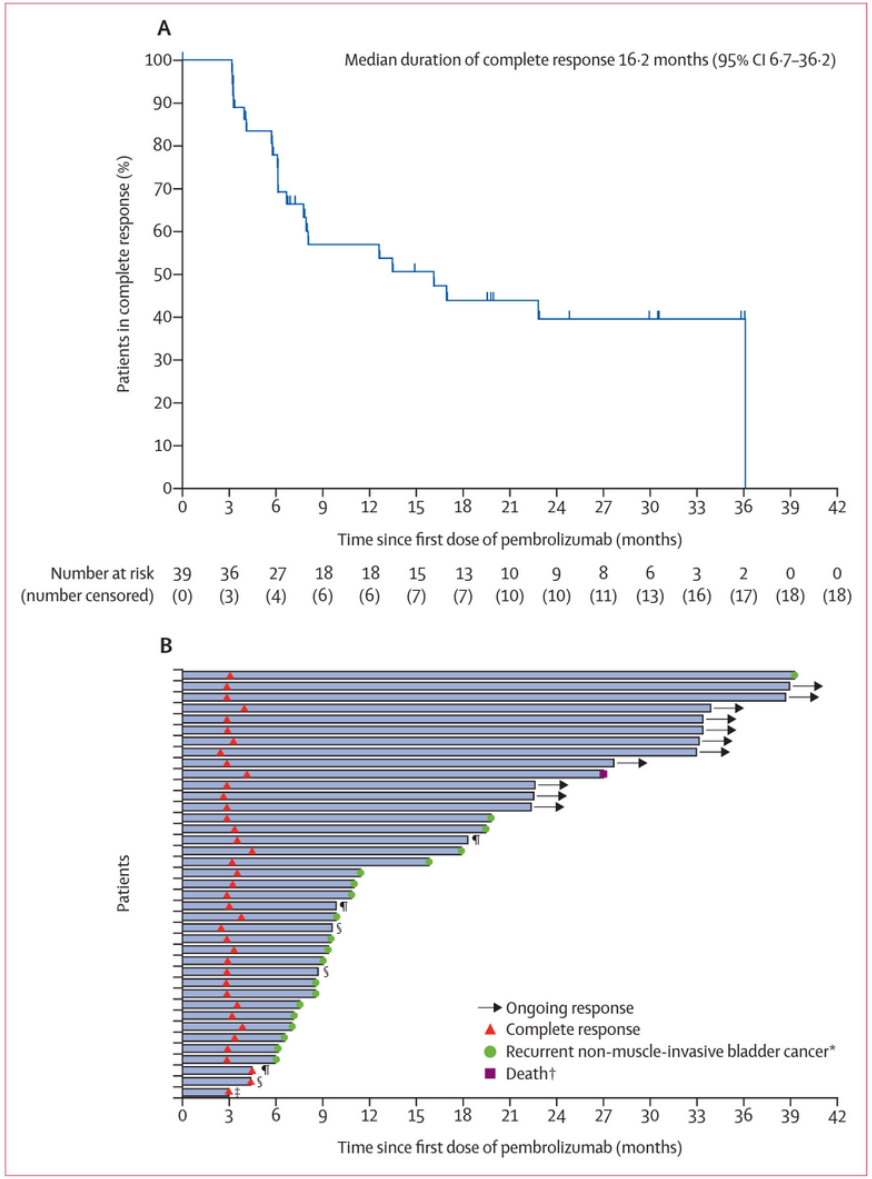
Steinberg et al, Urol Oncol, 2020

# Trials in BCG unresponsive disease

| | | |
|---|---|---|
| KEYNOTE-057 | Phase II | Pembrolizumab |
| SWOG S1605 | Phase II | Atezolizumab |
| NCT02773849 | Phase III | Nadofaragene Firadenovec |
| QUILT-3.032 | Phase II | NAI ± BCG |
| CORE-001 | Phase II | CG0070 + pembro |
| ADAPT | Phase II | Durvalumab |
| BOND2 | Phase II | GC0070 |
| VISTA | Phase III | Opportumab Monatox |

CIS cohort -----> papillary cohort

# Keynote-057 (Pembrolizumab)



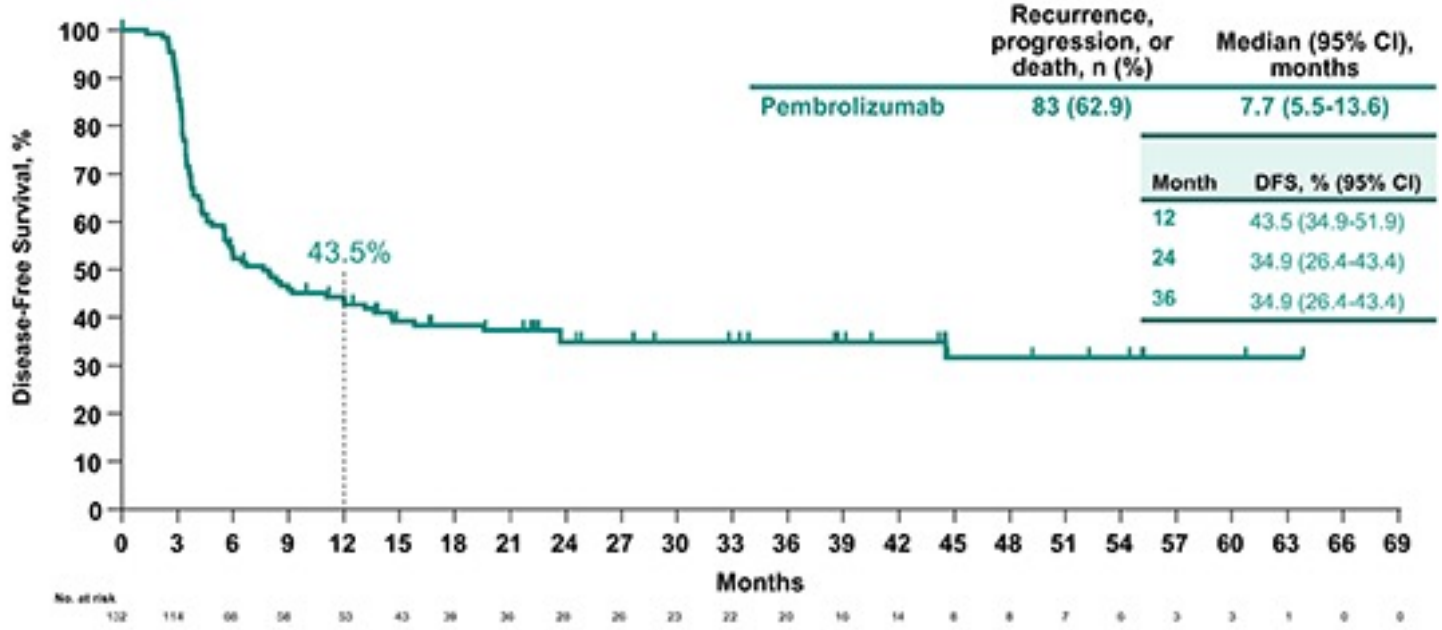

| | Cohort A efficacy population (n=96)* |
|---|---|
| Complete response | 39 (41%, 30·7–51·1) |
| Non-complete response | 56 (58%, 47·8–68·3) |
| Persistent disease†‡ | 40 (42%, 31·7–52·2) |
| Recurrent disease | 6 (6%, 2·3–13·1) |
| Non-muscle-invasive bladder cancer stage progression§ | 9 (9%, 4·4–17·1) |
| Non-bladder malignancy¶ | 1 (1%, 0·0–5·7) |
| Progression to muscle-invasive disease (T2) | 0 (NA–NA) |
| Non-evaluable‖ | 1 (1%, 0·0–5·7) |

Balar et al, Lancet Oncol 2021

# Keynote-057 (Pembrolizumab)

## Patients without CIS

**Figure 1.** Disease-Free Survival for HR NMIBC[a]

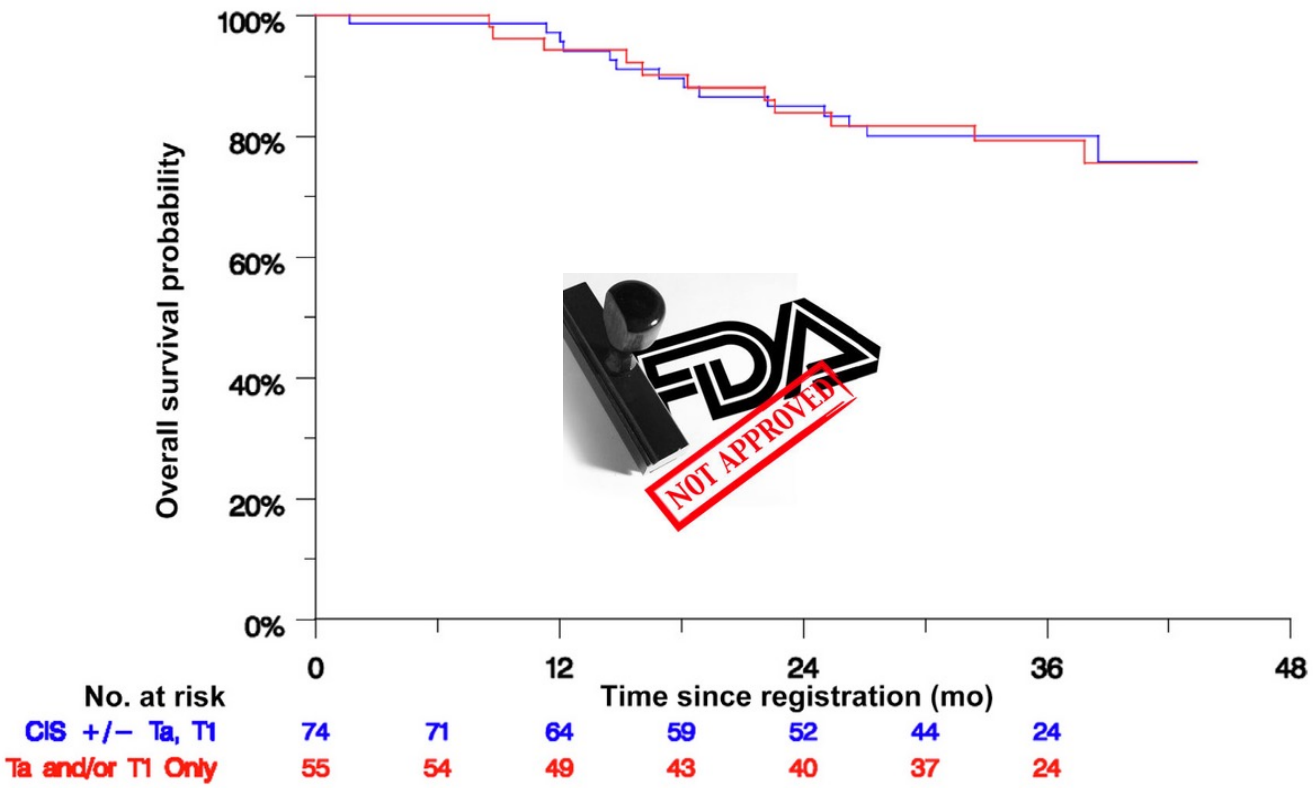



| | Recurrence, progression, or death, n (%) | Median (95% CI), months |
|---|---|---|
| Pembrolizumab | 83 (62.9) | 7.7 (5.5-13.6) |

| Month | DFS, % (95% CI) |
|---|---|
| 12 | 43.5 (34.9-51.9) |
| 24 | 34.9 (26.4-43.4) |
| 36 | 34.9 (26.4-43.4) |

[a]For central pathology/radiology review.
Data cutoff: October 20, 2022.

# SWOG S1605 (Atezolizumab)




129 eligible pts

CIS cohort

74 pts, median fu 41m

6m CR 27% -----> 3m CR 43%

56% of responders maintained response up to 12m

Median duration of response 17m

Ta-T1 cohort

55 pts

18m EFS 49%

Black PC et al, Eur Urol 2023

# ICI safety in NMIBC

| | Grade 1 or 2 | Grade 3* | Grade 4† |
|---|---|---|---|
| Any | 54 (53%) | 11 (11%) | 2 (2%) |
| Diarrhoea | 11 (11%) | 0 | 0 |
| Fatigue | 11 (11%) | 0 | 0 |
| Pruritus | 10 (10%) | 1 (1%) | 0 |
| Hypothyroidism | 7 (7%) | 0 | 0 |
| Rash maculo-papular | 6 (6%) | 0 | 0 |
| Hyperthyroidism | 5 (5%) | 0 | 0 |
| Rash | 5 (5%) | 0 | 0 |
| Nausea | 5 (5%) | 0 | 0 |
| Arthralgia | 4 (4%) | 2 (2%) | 0 |
| Dry mouth | 3 (3%) | 0 | 0 |
| Pneumonitis | 3 (3%) | 0 | 0 |
| Rash pruritic | 3 (3%) | 0 | 0 |
| Abdominal pain | 2 (2%) | 0 | 0 |
| Alanine aminotransferase increased | 2 (2%) | 0 | 0 |
| Asthaenia | 2 (2%) | 0 | 0 |

Pembrolizumab

Any AE

66% vs 86%

Grade 3-4

13% vs 14%

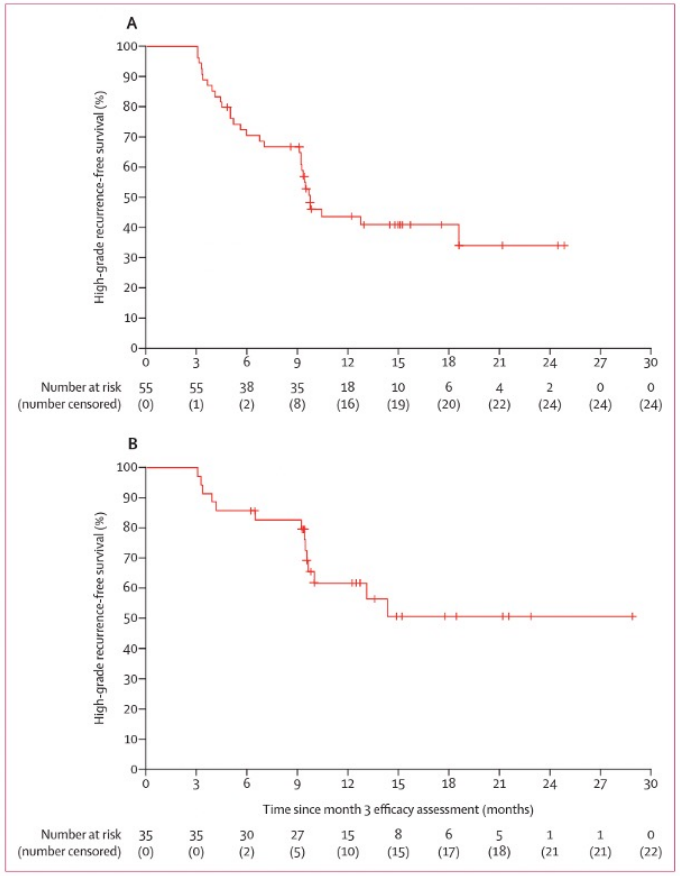
3 pts died due to AEs

| Adverse event | Patients with at least one AE, *n* (%) | | |
|---|---|---|---|
| | CIS cohort (*n* = 96) | Non-CIS cohort (*n* = 70) | All patients (*n* = 166) |
| Any adverse event | | | |
| Any cause | 93 (97%) | 69 (99%) | 162 (98%) |
| Treatment-related | 81 (84%) | 61 (87%) | 142 (86%) |
| Grade 3–4 AEs | | | |
| Any cause | 36 (38%) | 26 (37%) | 57 (34.3%) |
| Treatment-related | 13 (14%) | 10 (14.3%) | 23 (14%) |
| Grade 5 AEs | | | |
| Any cause | 2 (2%) | 1 (1%) | 3 (2%) |
| Treatment-related | 2 (2%) | 1 (1%) | 3 (2%) |
| Serious AEs | | | |
| Any cause | 18 (19%) | 15 (21%) | 33 (20%) |
| Treatment-related | 9 (9%) | 8 (11%) | 17 (10%) |
| AE leading to ATZ discontinuation | 9 (9%) | 6 (9%) | 15 (9%) |
| AE leading to ATZ dose interruption/delay | 19 (20%) | 18 (26%) | 37 (22%) |

AE = adverse event; ATZ = atezolizumab; CIS = carcinoma in situ.
[a] Includes AEs occurring on or after the start of treatment and up to 90 d after the date on which the last ATZ dose was administered.

Atezolizumab

# Nadofaragene Firadenovec (Adstiladrin)




**Intravesical nadofaragene firadenovec gene therapy for BCG-unresponsive non-muscle-invasive bladder cancer: a single-arm, open-label, repeat-dose clinical trial**

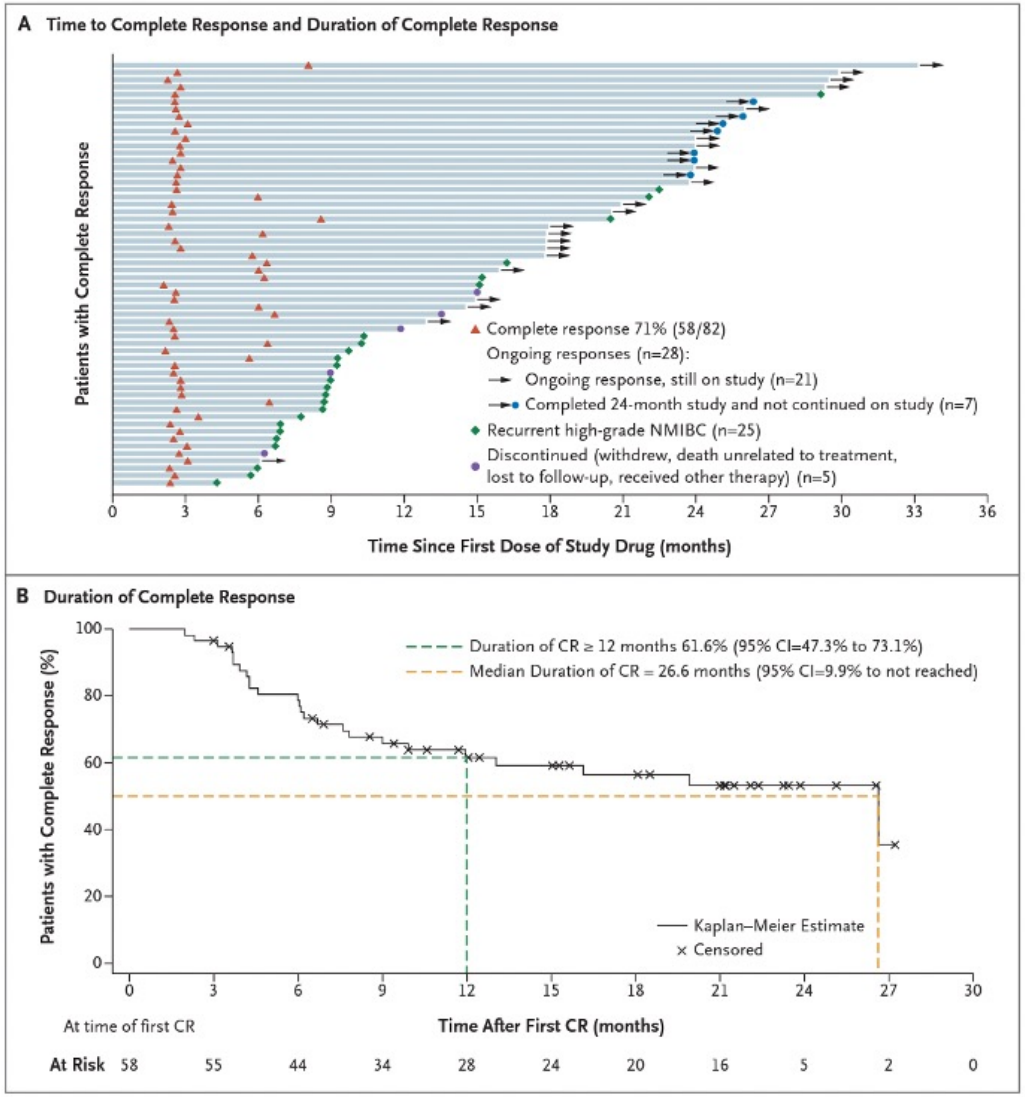
Stephen A Boorjian, Mehrdad Alemozaffar, Badrinath R Konety, Neal D Shore, Leonard G Gomella, Ashish M Kamat, Trinity J Bivalacqua, Jeffrey S Montgomery, Seth P Lerner, Joseph E Busby, Michael Poch, Paul L Crispen, Gary D Steinberg, Anne K Schuckman, Tracy M Downs, Robert S Svatek, Joseph Mashni Jr, Brian R Lane, Thomas J Guzzo, Gennady Bratslavsky, Lawrence I Karsh, Michael E Woods, Gordon Brown, Daniel Canter, Adam Luchey, Yair Lotan, Tracey Krupski, Brant A Inman, Michael B Williams, Michael S Cookson, Kirk A Keegan, Gerald L Andriole Jr, Alexander I Sankin, Alan Boyd, Michael A O'Donnell, David Sawutz, Richard Philipson, Ruth Coll, Vikram M Narayan, F Peter Treasure, Seppo Yla-Herttuala, Nigel R Parker, Colin P N Dinney

Phase III
151 pts (103 CIS)
3m CR (CIS): 53%
Duration of response (45% at 12 months)

No grade IV-V toxicity

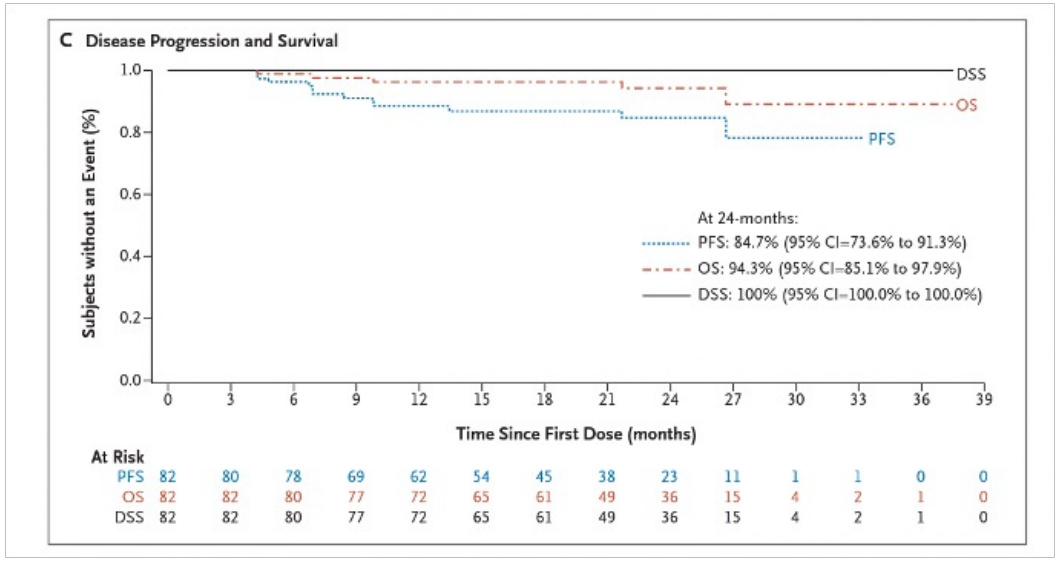
Boorjian et al, Lancet Oncol 2021

# IL 15 superagonist + BCG (Quilt 3.302)



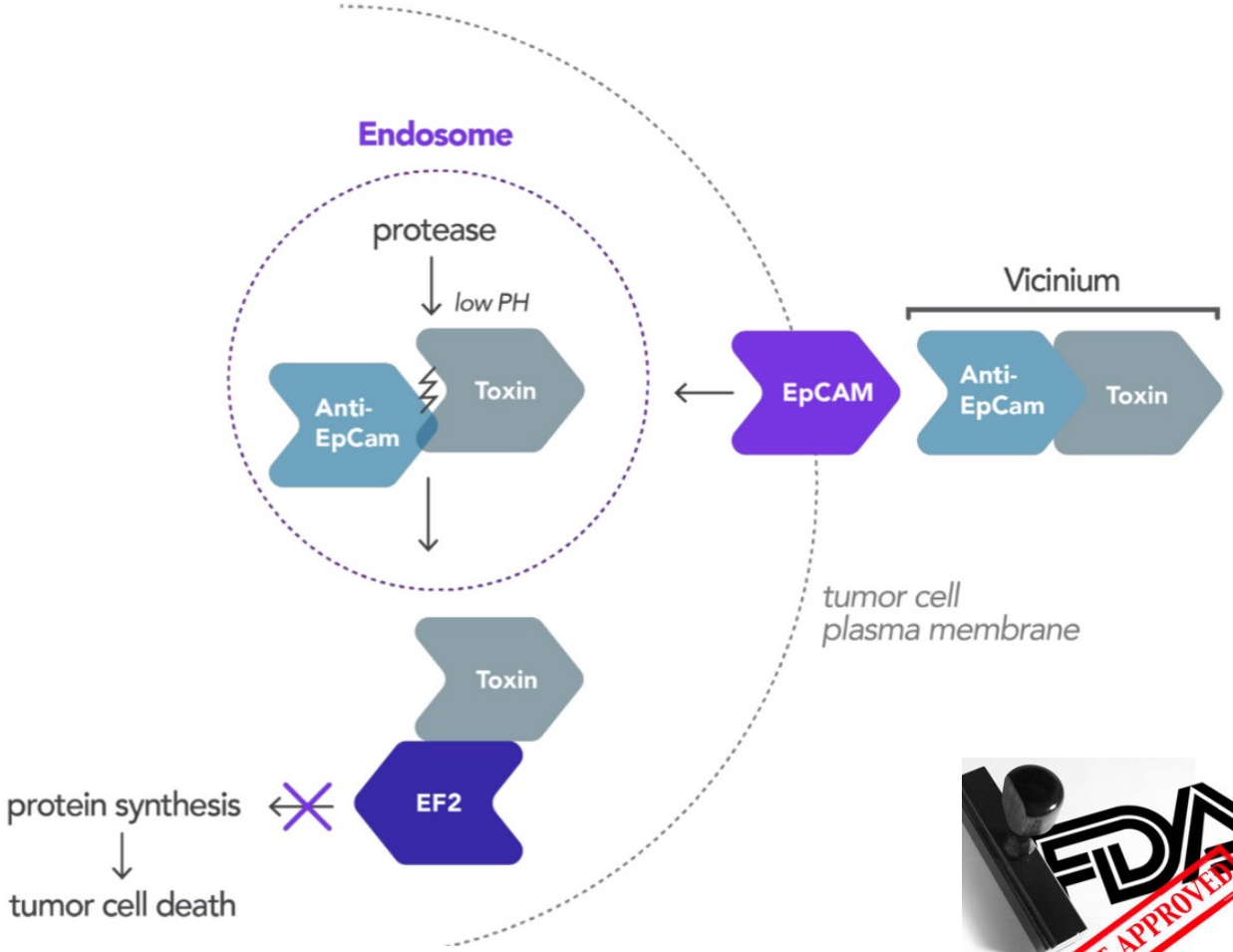

84 CIS pts enrolled in cohort A (NAI + BCG)

3m CR 71%
12m CR 45%
Median duration of response 27 months




Chamie et al, NEJM Ev 2022

# VISTA (opportuzumab monatox) "Vicinium"



PHASE III trial

128 BCG unresponsive pts

Data on 89 CIS pts

3m CR: 40%

52% retained the response up to 12m

Well tolerated

Shore et al, AUA 2020

# Summary of current options for BCG unresponsive disease

| CIS cohort | 3m CR | 12m CR |
|---|---|---|
| Pembrolizumab | 41% | 19% |
| Atezolizumab | 43% | 20% |
| Nadofaragene | 53% | 24% |
| N-803 | 55% | 40% |
| Oportuzumab | 40% | 17% |

| Ta-T1 cohort | 12m EFS | 24m EFS |
|---|---|---|
| Pembrolizumab | 42% | 33% |
| Atezolizumab | 18m EFS 48% | |
| Nadofaragene | 44% | / |
| N-803 | 57% | 48% |
| Oportuzumab | / | / |

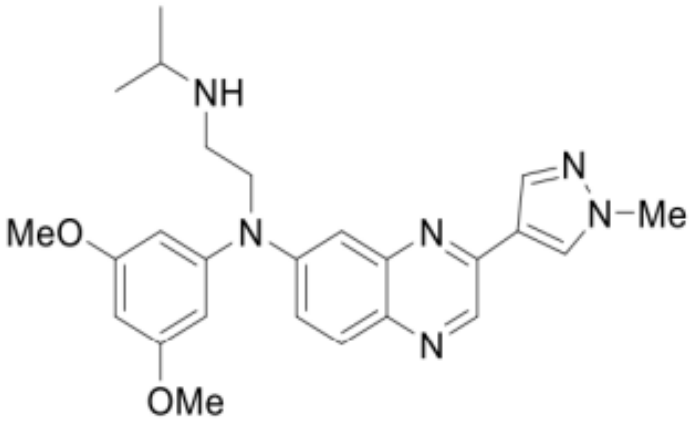
# Precision medicine in NMIBC

- ***FGFR* alterations** are commonly detected in NMIBC and may function as oncogenic drivers[1-4]

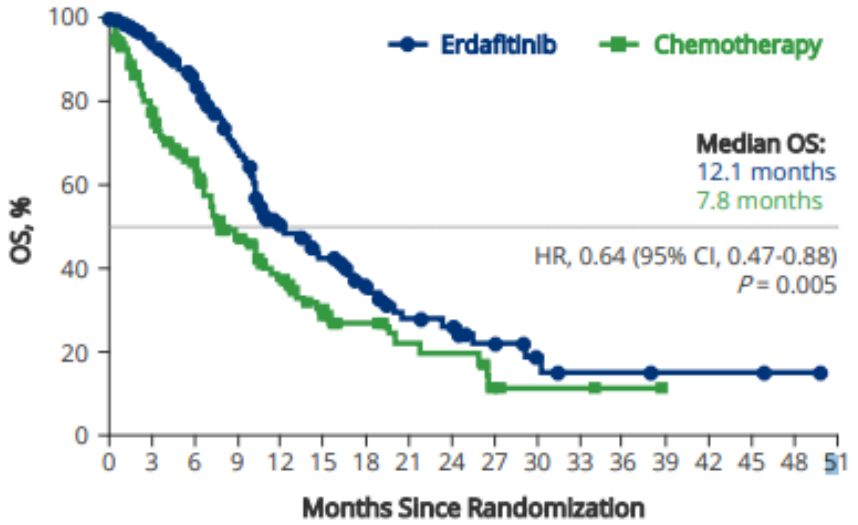
  - 60%-70% of patients with low-risk NMIBC have *FGFR* alterations[1]
  - **≥30% of patients** with HR papillary NMIBC have *FGFR* alterations[2-4]

# Precision medicine in NMIBC

**Erdafitinib is an oral selective pan-FGFR tyrosine kinase inhibitor approved in the United States and 18 other countries to treat *FGFR*-altered advanced or mUC after progression on platinum-containing chemotherapy[1-4]**



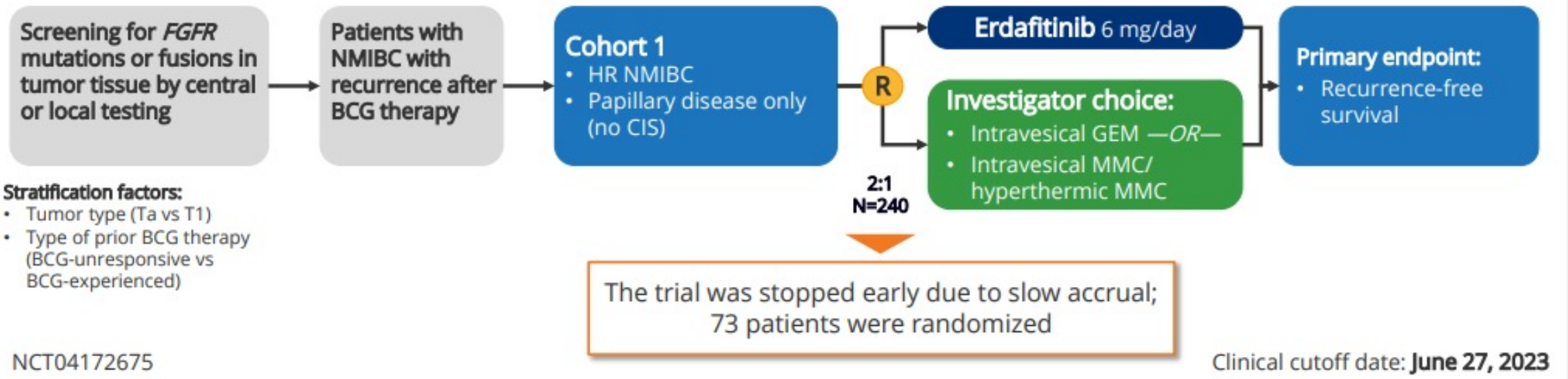

**In Cohort 1 of the phase 3, randomized THOR study, erdafitinib improved survival versus chemotherapy in patients with *FGFR*-altered mUC[5]**



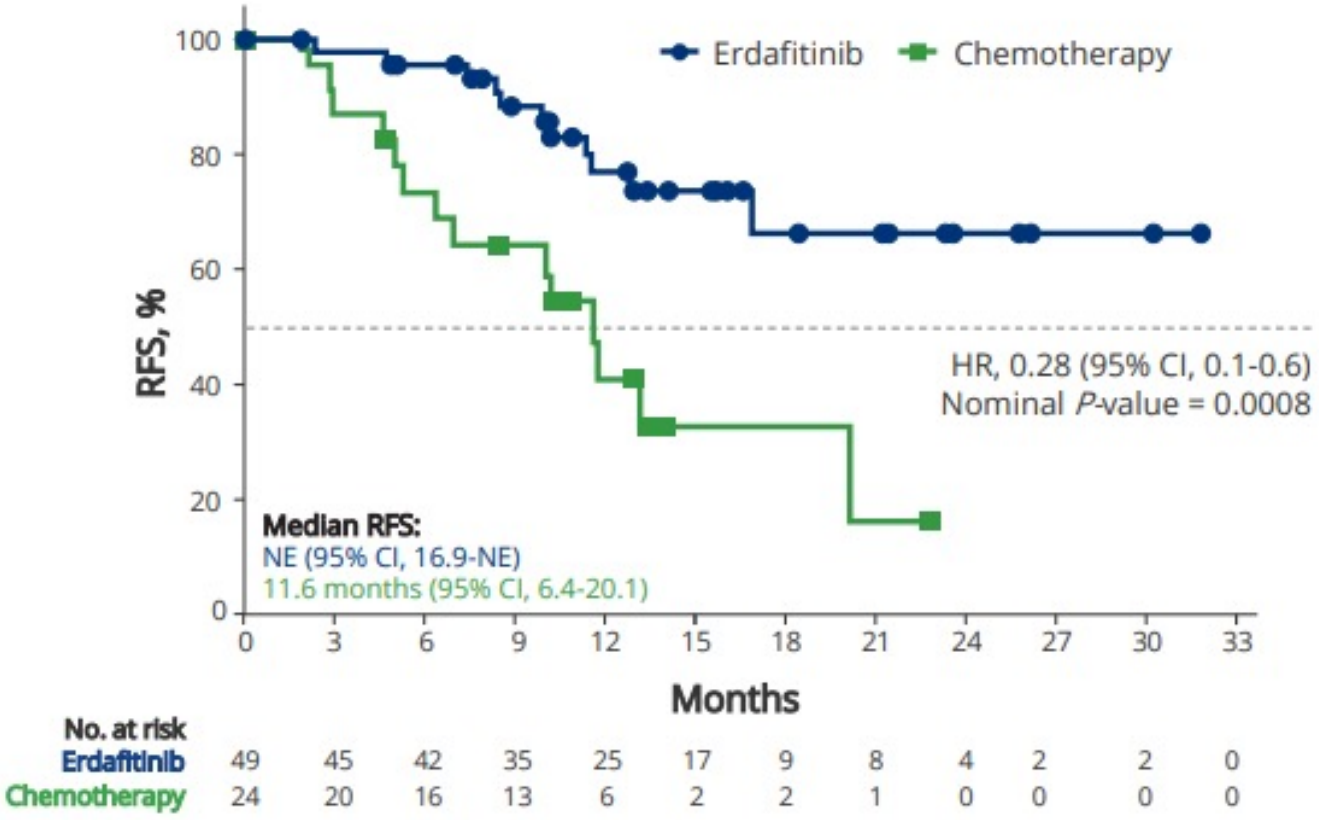

| No. at risk | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Erdafitinib | 136 | 117 | 97 | 74 | 46 | 35 | 25 | 17 | 15 | 9 | 5 | 3 | 3 | 2 | 2 | 2 | 1 | 0 |
| Chemotherapy | 130 | 87 | 66 | 43 | 30 | 18 | 13 | 9 | 8 | 3 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |

Patients received erdafitinib 8 mg/day with pharmacodynamically guided uptitration to 9 mg/day

# Precision medicine in NMIBC



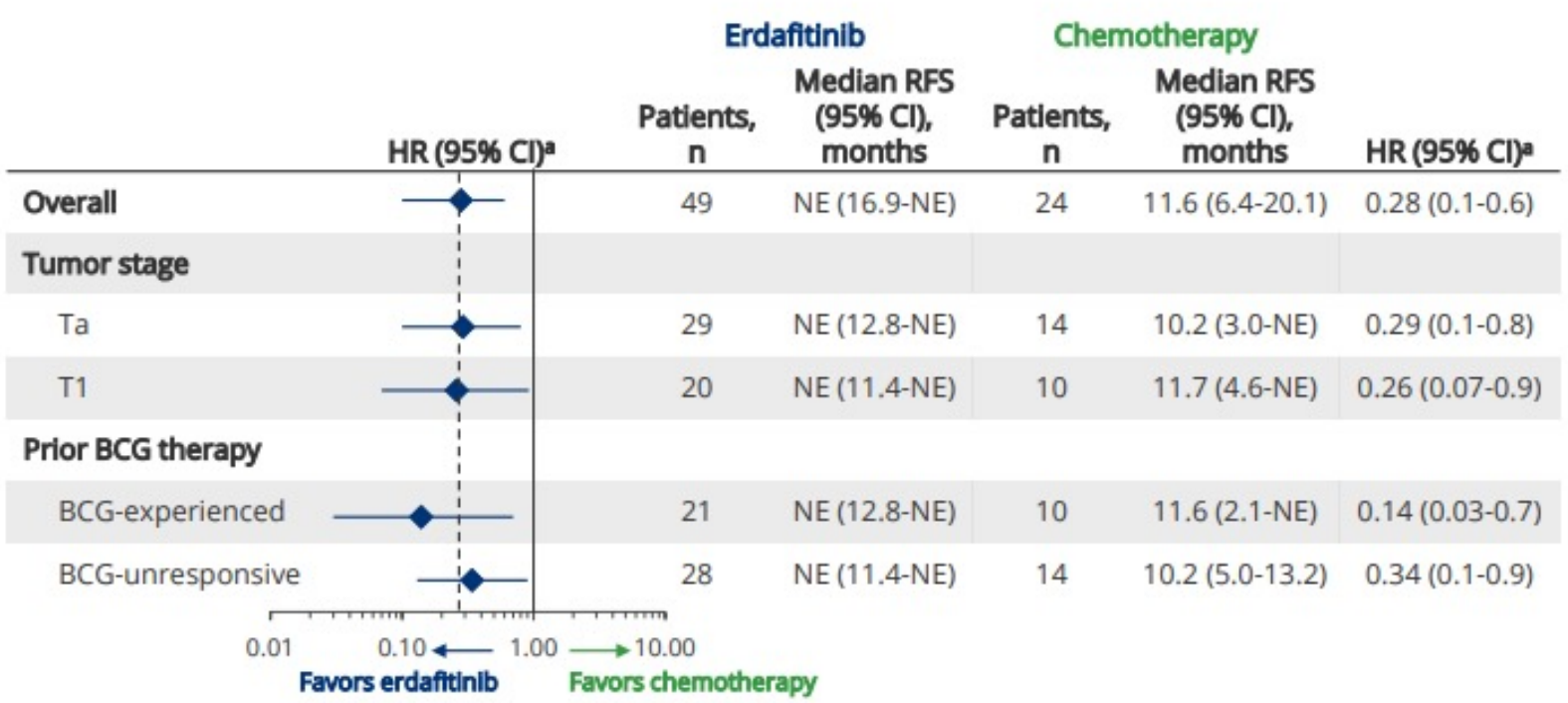
# THOR 2 - FGFR mutation




- At median follow-up of 13.4 months, **median RFS was not reached for erdafitinib** and was 11.6 months for chemotherapy
- At clinical cutoff, 25 total RFS events had occurred (11, erdafitinib; 14, chemotherapy)

| RFS rate (95% CI), % | Erdafitinib (n=49) | Chemotherapy (n=24) |
|---|---|---|
| At 6 months | **96 (84-99)** | **73 (50-87)** |
| At 12 months | **77 (60-87)** | **41 (19-62)** |

# THOR 2 - FGFR mutation




| | HR (95% CI)[a] | Erdafitinib Patients, n | Erdafitinib Median RFS (95% CI), months | Chemotherapy Patients, n | Chemotherapy Median RFS (95% CI), months | HR (95% CI)[a] |
|---|---|---|---|---|---|---|
| **Overall** | | 49 | NE (16.9-NE) | 24 | 11.6 (6.4-20.1) | 0.28 (0.1-0.6) |
| **Tumor stage** | | | | | | |
| Ta | | 29 | NE (12.8-NE) | 14 | 10.2 (3.0-NE) | 0.29 (0.1-0.8) |
| T1 | | 20 | NE (11.4-NE) | 10 | 11.7 (4.6-NE) | 0.26 (0.07-0.9) |
| **Prior BCG therapy** | | | | | | |
| BCG-experienced | | 21 | NE (12.8-NE) | 10 | 11.6 (2.1-NE) | 0.14 (0.03-0.7) |
| BCG-unresponsive | | 28 | NE (11.4-NE) | 14 | 10.2 (5.0-13.2) | 0.34 (0.1-0.9) |

- The observed RFS benefit for erdafitinib was generally consistent across:
  - Tumor stage (Ta vs T1)
  - Prior BCG therapy (BCG-experienced vs BCG-unresponsive)

# THOR 2 - FGFR mutation

| Patients with ≥1 event, n (%)[a] | Erdafitinib (n=49) | |
|---|---|---|
| | Any grade | Grade ≥3 |
| Any adverse events of interest | 49 (100) | — |
| Nail toxicity[b] | 38 (77.6) | 3 (6.1) |
| Hyperphosphatemia | 36 (73.5) | 0 |
| Eye toxicities (excluding central serous retinopathy)[c] | 29 (59.2) | 2 (4.1) |
| Skin toxicity[d] | 25 (51.0) | 0 |
| Dry mouth | 23 (46.9) | 0 |
| Stomatitis | 20 (40.8) | 5 (10.2) |
| Central serous retinopathy[e,f] | 19 (38.8) | 2 (4.1) |

ANNALS OF ONCOLOGY
driving innovation in oncology

ORIGINAL ARTICLE

# Erdafitinib in BCG-treated high-risk non-muscle-invasive bladder cancer

**J. W. F. Catto[1,2*], B. Tran[3], M. Rouprêt[4], J. E. Gschwend[5], Y. Loriot[6], H. Nishiyama[7], J. P. Redorta[8], S. Daneshmand[9], S. A. Hussain[1,2], H. J. Cutuli[10], G. Procopio[11], V. Guadalupi[11], N. Vasdev[12,13], V. Naini[14], L. Crow[15], S. Triantos[15], M. Baig[15] & G. Steinberg[16], for the THOR-2 Cohort 1 Investigators[†]**

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# THOR 2 - FGFR mutation

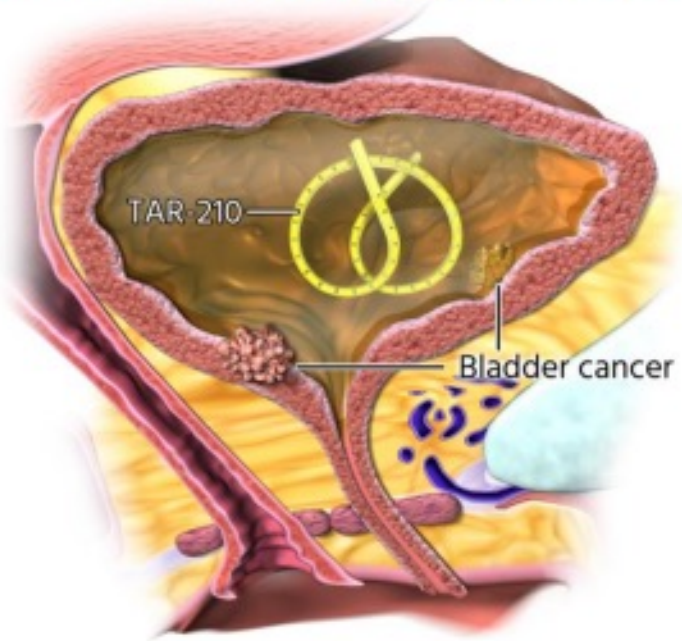
- **Oral erdafitinib reduced the risk of recurrence of disease or death by 72%** compared with intravesical chemotherapy in patients with high-risk resected papillary Ta/T1 NMIBC harboring *FGFR* mutations or fusions with recurrence after BCG treatment and who refused or were ineligible for radical cystectomy
  - Median follow-up for RFS was 13.4 months for both groups
  - **Median RFS** was **not reached for erdafitinib** (95% CI, 16.9-NE) and was **11.6 months** (95% CI, 6.4-20.1) for intravesical chemotherapy
  - Estimated **HR of 0.28** (95% CI, 0.1-0.6)
- Despite lower dose, oral erdafitinib tolerability was challenging in this patient population

# THOR 2 - FGFR mutation

- Targeted therapy is a valid approach in the NMIBC population
- This study makes the case for wider biomarker testing in NMIBC and also shows it is possible to randomize to two arms in this setting
- To limit systemic toxicity, there is a need for new locally delivered targeted therapies in NMIBC
  - TAR-210 is an **intravesical drug delivery system** designed to provide local, sustained release of erdafitinib within the bladder and is being evaluated in patients with *FGFR*-altered HR and IR NMIBC

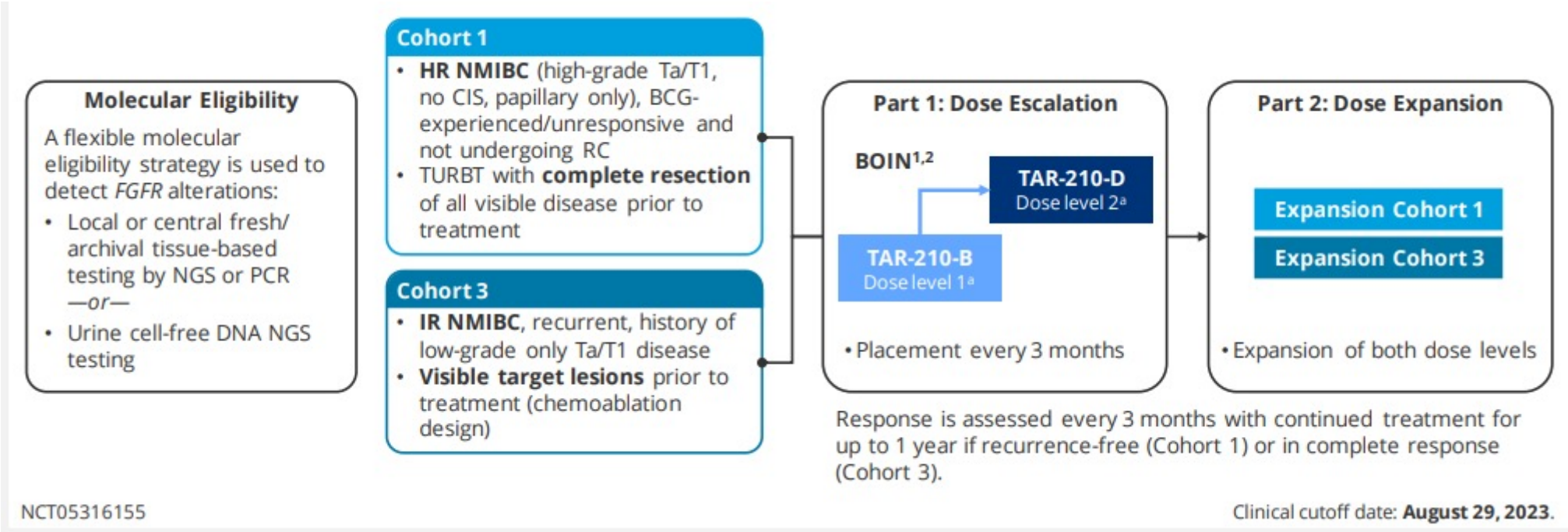
# BCG unresponsive: the future

**TAR-210 is designed to provide local, sustained release of erdafitinib within the bladder for 3 months while limiting systemic toxicities**

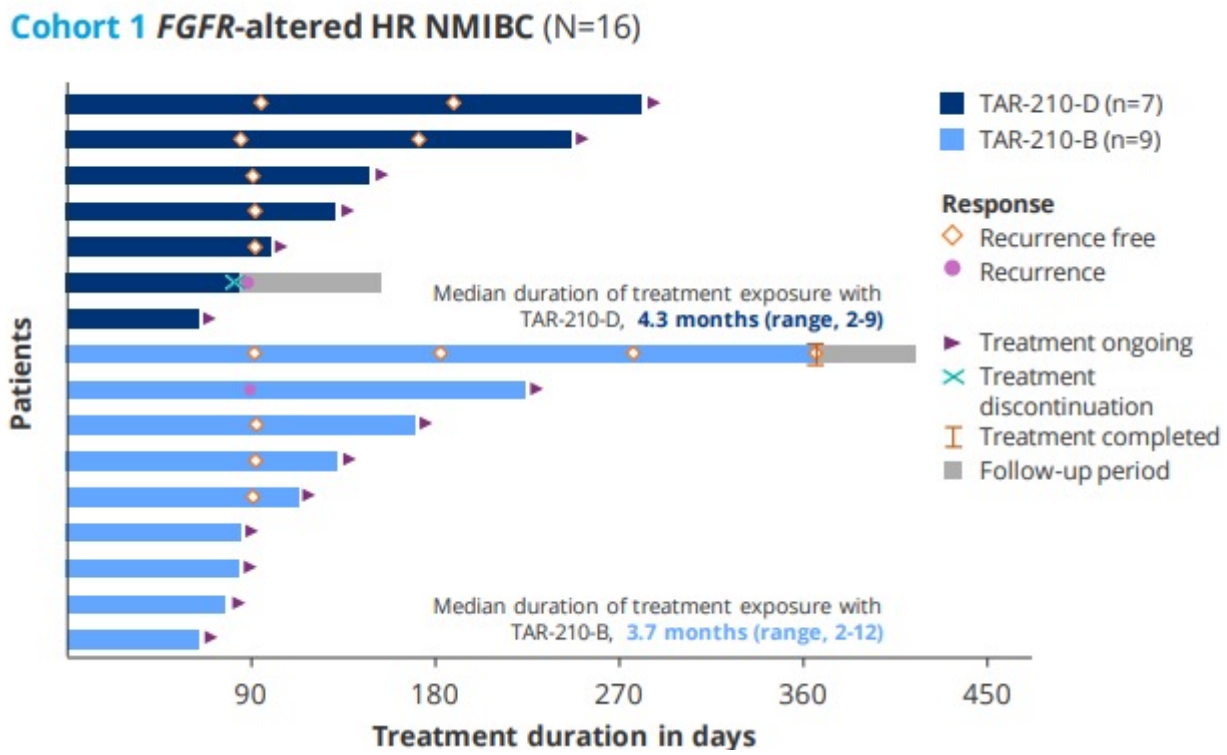



TAR-210 is inserted into the bladder through a dedicated urinary placement catheter and removed via cystoscopy.

# BCG unresponsive: the future

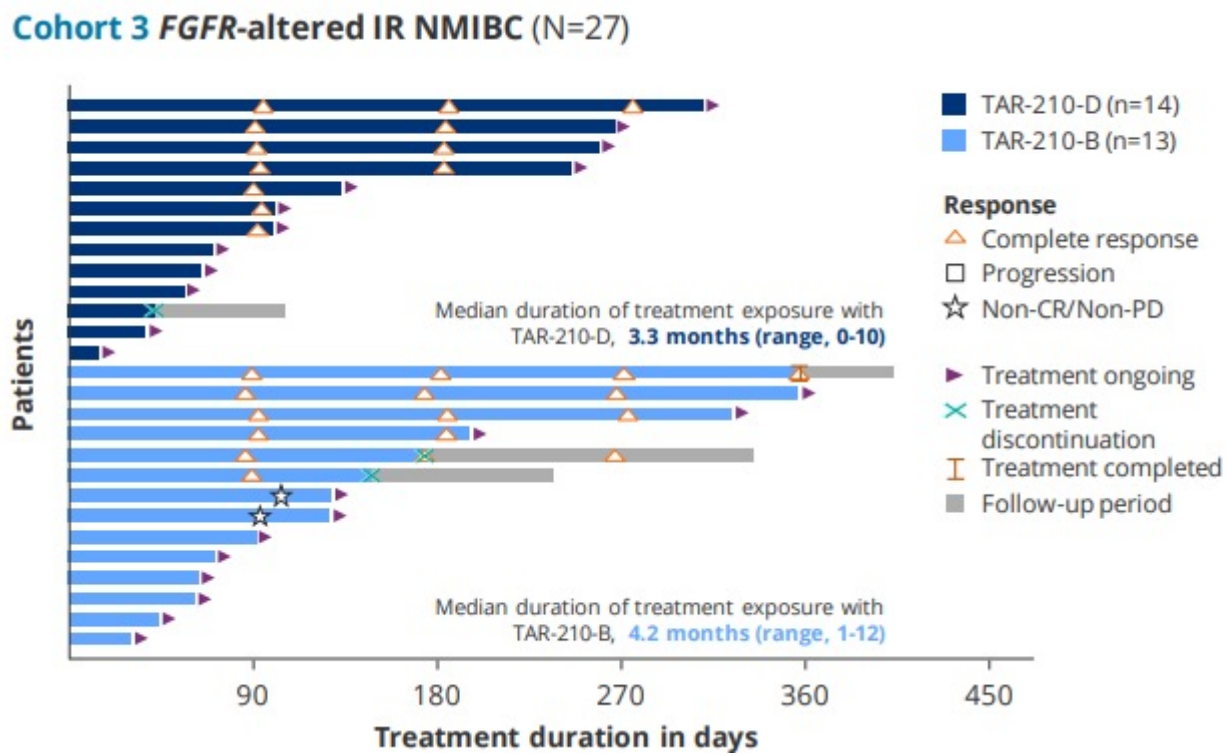


# BCG unresponsive: the future




- Patient characteristics (N=16):
  - Median age was 73.5 years (range, 62-90)
  - 75% were male
  - 75% and 25% had tumor stage Ta and T1, respectively
  - 44% had multiple tumors
  - 100% had prior BCG
- In 11 patients with a response assessment, 9 were recurrence free (**recurrence-free rate, 82%**)
  - First response assessment was at 3 months
- Median recurrence-free survival was NE (95% CI, 2.96 months-NE)

# BCG unresponsive: the future



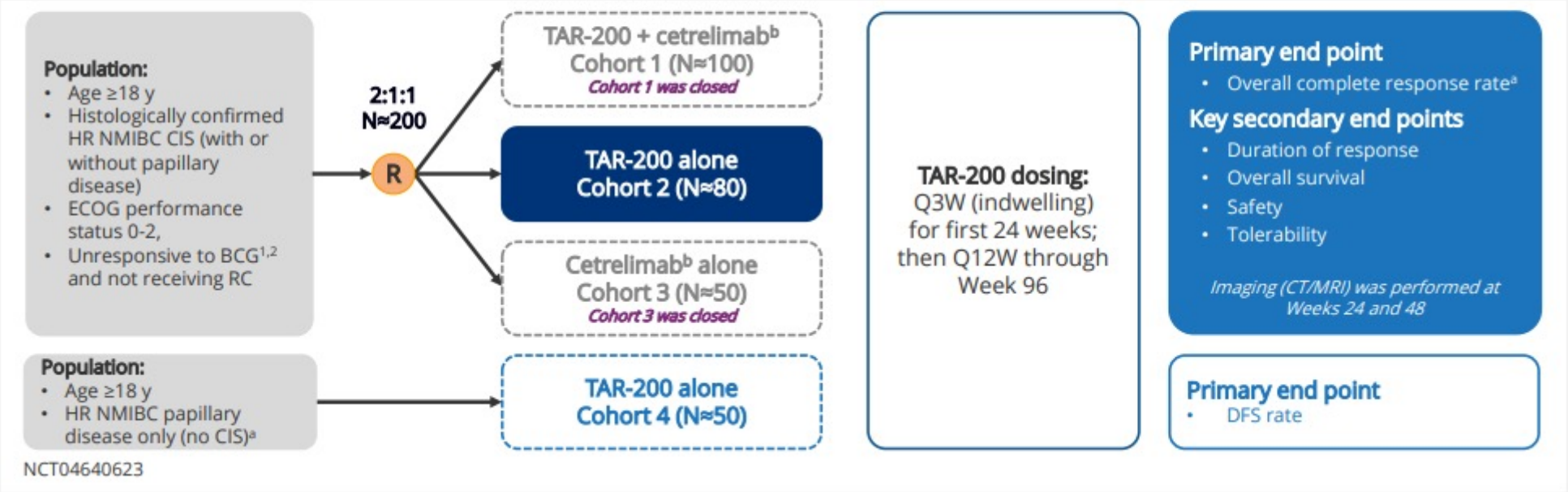

- Patient characteristics (N=27):
  - Median age was 67 years (range, 41-87)
  - 85% were male
  - 100% had tumor stage Ta
  - 41% had multiple tumors
  - 59% had prior intravesical chemotherapy
  - 22% had prior BCG
- In 15 patients with a response assessment, 13 achieved a CR (**complete response rate, 87%**)
  - First response assessment was at 3 months
- All CR are ongoing as of the clinical cutoff
  - Median duration of response was NE (95% CI, NE-NE)

# BCG unresponsive: the future

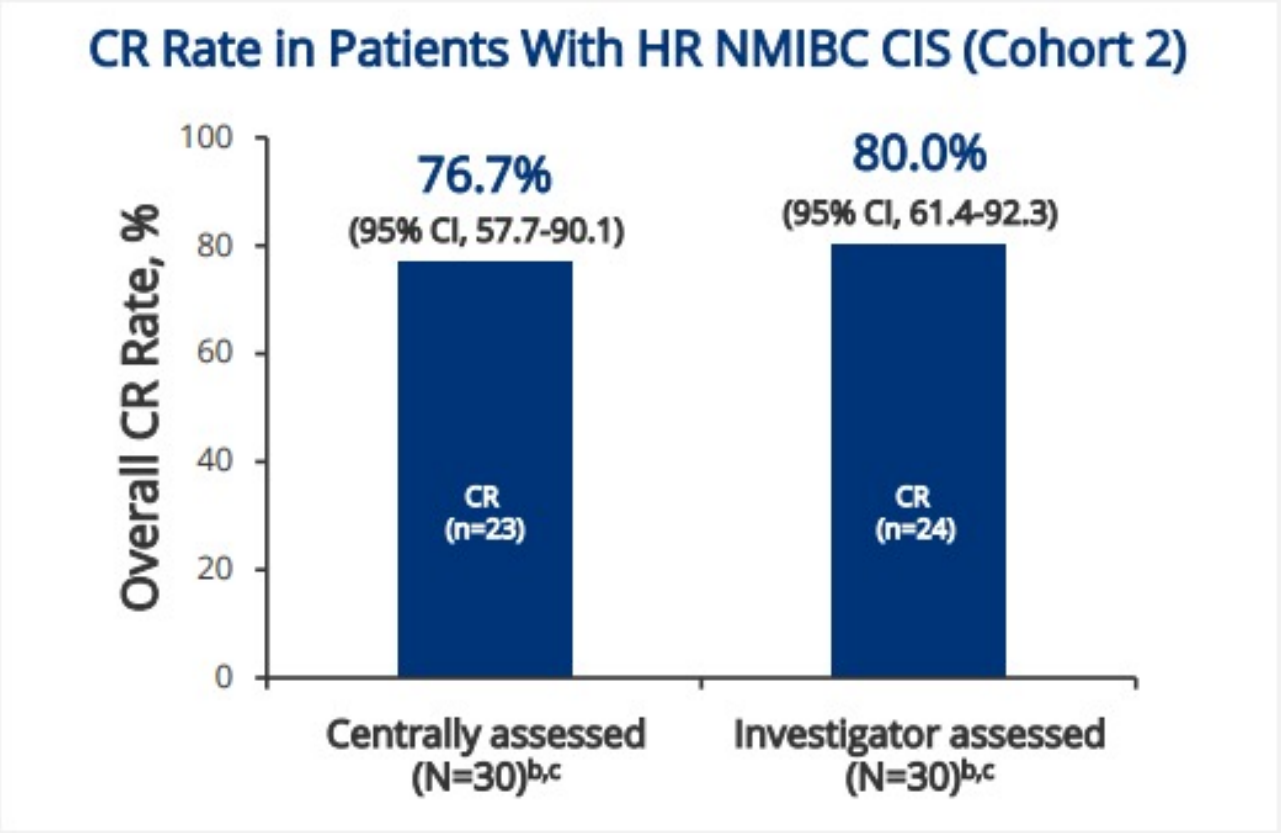
- There were no dose-limiting toxicities
- Overall, common treatment-related AEs were grade 1/2 lower urinary tract AEs
- 2 patients discontinued due to AEs of low-grade urinary symptoms
- 1 patient had SAEs of pyelonephritis and sepsis unrelated to TAR-210
- No deaths were reported

| Patients with events, n (%) | Cohort 1 HR NMIBC | | Cohort 3 IR NMIBC | | All Patients (N=43) |
|---|---|---|---|---|---|
| | TAR-210-B (n=9) | TAR-210-D (n=7) | TAR-210-B (n=14) | TAR-210-D (n=13) | |
| ≥1 AE | 9 (100) | 6 (86) | 13 (93) | 7 (54) | 35 (81) |
| ≥1 treatment-related AE[a] | 6 (67) | 2 (29) | 6 (43) | 3 (23) | 17 (40) |
| Haematuria | 3 (33) | 1 (14) | 5 (36) | 1 (8) | 10 (23) |
| Dysuria | 3 (33) | 1 (14) | 3 (21) | 1 (8) | 8 (19) |
| Micturition urgency | 1 (11) | 0 | 3 (21) | 0 | 4 (9) |
| Urinary tract infection | 0 | 0 | 2 (14) | 1 (8) | 3 (7) |
| ≥1 treatment-related AE of Grade ≥2 | 2 (22) | 0 | 4 (29) | 1 (8) | 7 (16) |

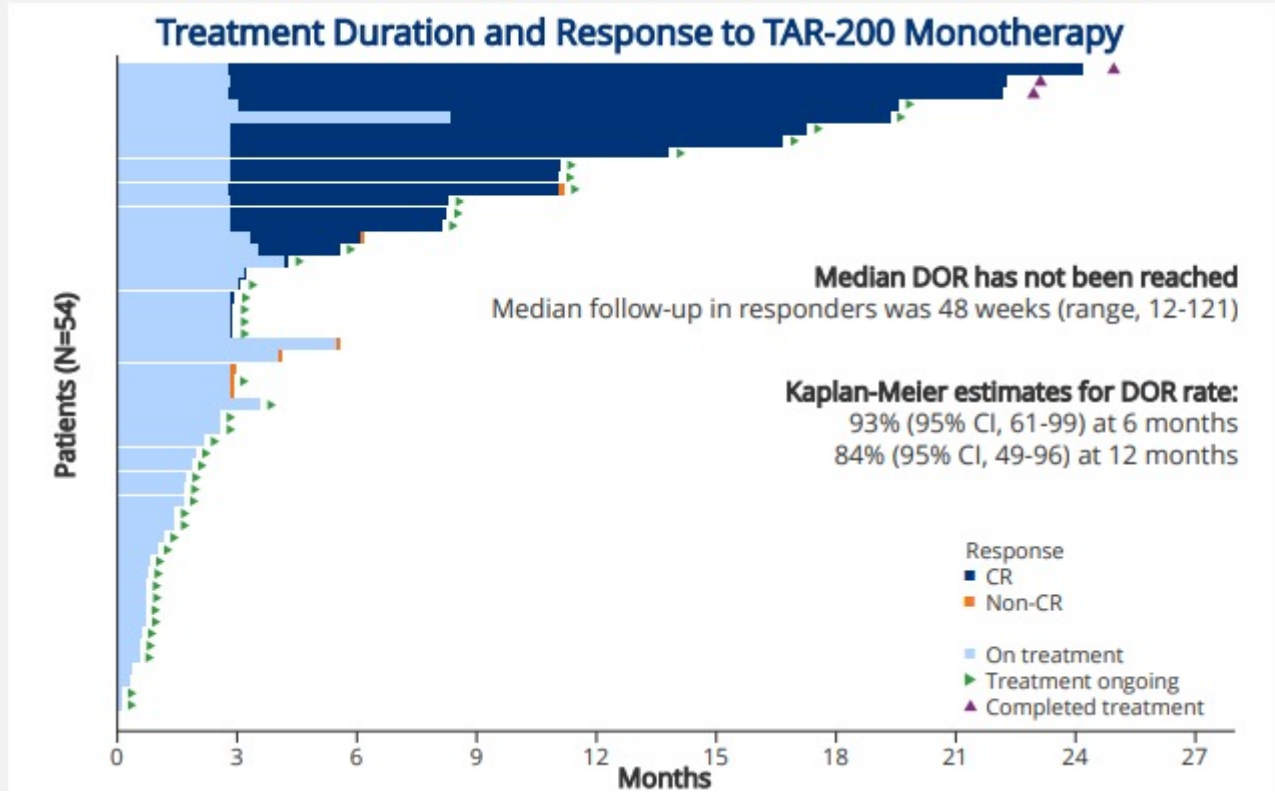
# SunRISe-1 is an Ongoing Phase 2b Randomized, Open-label Study



# BCG unresponsive: the future



# BCG unresponsive: the future




- **21 of 23 responses are ongoing**
  - 11 patients had DOR ≥6 months (10 of 11 ongoing)
  - 6 patients had DOR ≥12 months (all ongoing)
- **None of the patients with CR have undergone radical cystectomy**

# BCG unresponsive: the future

- Overall, most AEs in the TAR-200 cohort were Grade 1 or 2
- 29 patients (53.7%) had ≥1 treatment-related AE[a]
- 1 patient (1.9%) had ≥1 serious treatment-related AE
- 4 patients (7.4%) had grade ≥3 treatment-related AEs
- Low rate of treatment discontinuation due to adverse events; 2 patients (3.7%)[b]
- No deaths were reported

| Patients with events, n (%) | TAR-200 (N=54) | |
|---|---|---|
| | Any grade | Grade ≥3 |
| ≥1 AE | 37 (68.5) | 9 (16.7) |
| ≥1 treatment-related AE[c,d] | 29 (53.7) | 4 (7.4) |
| Pollakiuria | 12 (22.2) | 1 (1.9) |
| Dysuria | 11 (20.4) | 0 |
| Micturition urgency | 10 (18.5) | 0 |
| Hematuria | 6 (11.1) | 0 |
| Noninfective cystitis | 4 (7.4) | 0 |
| Urinary tract pain | 3 (5.6) | 1 (1.9) |
| Urinary retention | 2 (3.7) | 1 (1.9) |
| Renal impairment | 1 (1.9) | 1 (1.9) |
| Urosepsis | 1 (1.9) | 1 (1.9) |

# What I do

These patients need options

Trials:

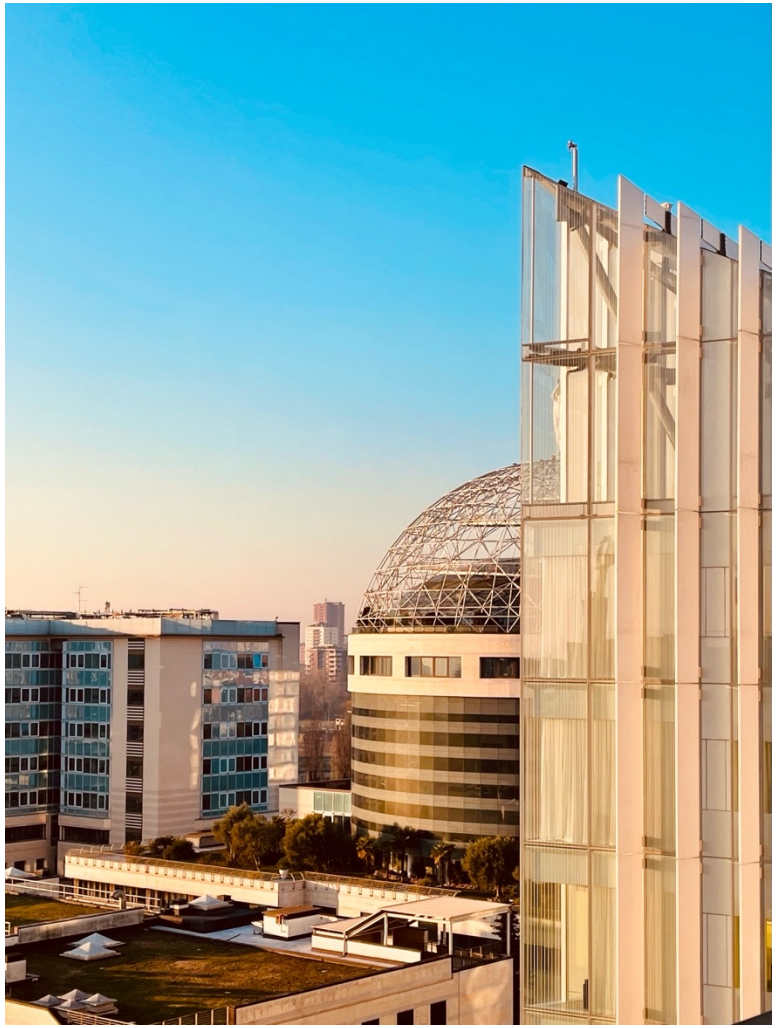
1 Phase 1- Intravescical Zenfrelimab

2

3

4

5



# NCT05375903

A Phase 1, Open-label, Dose-escalation Study to Investigate the Safety, Tolerability, and Pharmacokinetics of UGN-301 (**Zalifrelimab**) in the treatment of **recurrent NMIBC** with HG Ta and/or T1 disease and/or CIS.

Treatment arms will include:

- UGN-301 monotherapy
- UGN-301 + UGN-201 (imiquimod)
- UGN-301 + gemcitabine

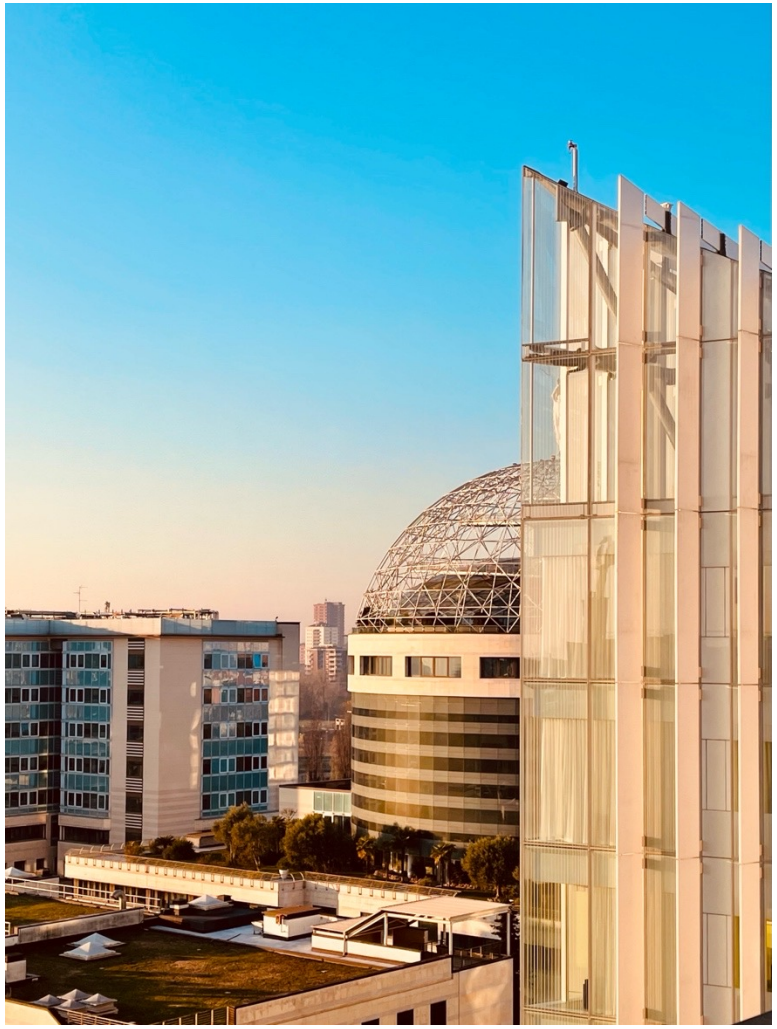
**Primary endpoint:**
To determine the biologically effective dose (BED) and maximum tolerated dose (MTD) of UGN-301 either as monotherapy or in combination with other agents.

UroGen® Pharma

# What I do

1 Phase 1- Intravescical Zenfrelimab

2 Phase 3- Paclitaxel- Hyaluronic acid



# ONCOFID-P-B

A phase III, single-arm study to evaluate the efficacy and safety of **ONCOFID-P-B (paclitaxel-hyaluronic acid conjugate)** administered intravesically to patients with BCG-unresponsive Carcinoma *in Situ* of the bladder with or without Ta-T1 papillary disease

## Primary efficacy objective:

To evaluate the antitumor activity of ONCOFID-P-B using centrally assessed complete response rate (CRR) following 12 weekly intravesical instillations (induction phase).

## Primary safety objective:

To evaluate the safety of ONCOFID-P-B over the entire course of the study.
To evaluate the tolerability of ONCOFID-P-B over the entire course of the study

fidia

# What I do

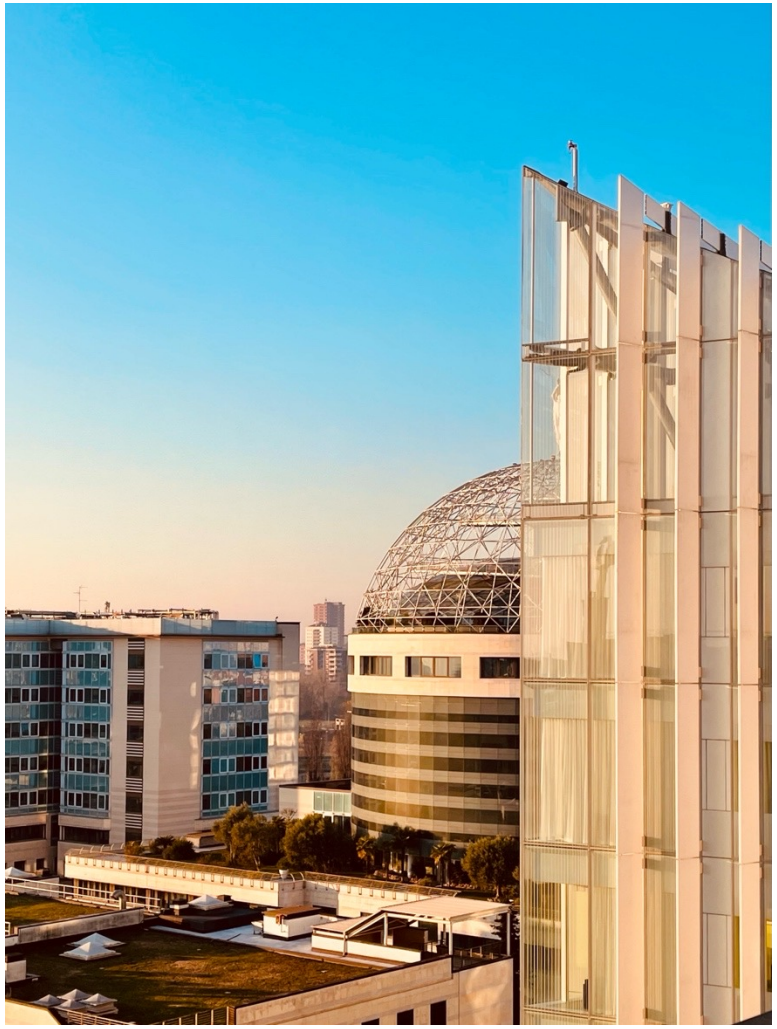
1 Phase 1- Intravescical Zenfrelimab

2 Phase 3- Paclitaxel- Hyaluronic acid

3 Off label use intravesical docetaxel/gemcitabine

4 EMDA

5 Radical cystectomy



# What we need...

- Efficacy but safety first (RC is an effective treatment!)
- RCTs both in CIS and in papillary cohorts
- Head to head comparisons
- Treatment deintensification (intravesical administration? )
- Biomarkers - patients' selection

The right treatment for the right patient

# Thanks for your attention!

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